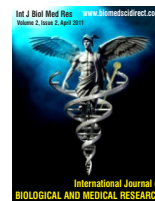


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Review Article

The Effect of Smoking on Cancer-A review

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ABSTRACT

Smoking is a major cause for several types of cancer. Smoking increases the risk of cancers of the lungs, bladder, cervix, kidney, larynx (voice box), pharynx (upper throat), nose, mouth, oesophagus (foodpipe), pancreas, stomach, liver and some types of leukaemia. And smokers are 7 times more likely to die of these cancer than non-smokers. Scientists have identified about 4,000 different chemicals in tobacco smoke. Chemicals such as nitrosamines, benzo(a)pyrene, benzene, acrolein, cadmium, and polonium-210 can damage DNA. Within this review article we will focus on the correlation between smoking and oxidative stress and the role of smoking in increasing the risk of gastric cancer.

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1. Introduction

Cancer is defined as disturbance of growth characterized by excessive proliferation of cells without apparent relation to the physiological demands of the organs involved. Cancer is the uncontrolled growth and spread of cells that may affect almost any tissue of the body. Cancer causes 6 million deaths every year or 12% of deaths worldwide. Smoking is the single biggest cause of cancer in the world. Smoking causes over a quarter of cancer deaths in developed countries. The effects of smoking on human health are serious and in many cases, deadly. There are approximately 4000 chemicals in cigarettes, hundreds of which are toxic. The ingredients in cigarettes affect everything from the internal functioning of organs to the efficiency of the body's immune system. The effects of cigarette smoking are destructive and widespread. A large number of studies have shown that stopping smoking can greatly reduce the risk of smoking-related cancers (Table 1) [1].

Several studies have shown that breathing in other people's smoke causes cancer in non-smokers. Second-hand smoke contains several cancer causing chemicals. Many of these chemicals are present in higher concentrations than in the smoke inhaled by the smoker themselves. Smoking may reduce the life expectancy of an individual (Figure.1) [2]. One study estimates that passive smoking may kill over 11,000 people every year in the UK from cancer, heart disease, strokes and other diseases. Second-hand smoking also causes other health problems in non-smokers including asthma and heart disease. One study showed that even 30 minutes of exposure to second-hand smoke can reduce blood flow in a non-smoker's heart.

The cocktail of chemicals in tobacco smoke is even more dangerous as a mix. Chemicals such as nitrosamines, benzo(a)pyrene, benzene, acrolein, cadmium and polonium-210 can damage DNA. Studies have shown that benzo(a)pyrene damages a gene called p53 that normally protects our cells from cancer. Many tobacco poisons disable the cleaning systems that our bodies use to remove toxins. Cadmium overwhelms cleaner enzymes that mop up toxins and convert them into more harmless forms. And many gases such as hydrogen cyanide and ammonia kill cilia, tiny hairs in our airways that help to clear away toxins (Table 2) [3].

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Table 1 . The table summarize the impact of smoking as a cause of death from cancer. For each of these cancer types, the tables provide several statistics. These estimates are based on results of the American Cancer Society's Cancer Prevention Study II (CPS II). The difference in the numbers for men and women is caused by several factors, including the average number of cigarettes smoked, how deeply each sex inhales, the age at which they started smoking, and, for former smokers, the age at which they quit. [1]

Cancer Type	RR for current smokers	RR for former smokers	Annual deaths*	SAM*	PAR (%)	YPLL*
Lip, oral cavity, pharynx	10.9	3.4	5,100	3,700	73	65,300
Esophagus	6.8	4.5	9,700	7,000	72	108,800
Stomach	2.0	1.5	7,100	1,900	27	27,600
Pancreas	2.3	1.2	14,800	3,100	21	50,200
Larynx (voice box)	14.6	6.3	3,000	2,400	82	38,000
Lung	23.3	8.7	90,000	78,700	87	1,118,400
Urinary Bladder	3.3	2.1	8,500	3,900	46	44,200
Kidney, other urinary	2.7	1.7	7,500	2,800	38	43,900
Acute myeloid leukemia	1.9	1.3	3,900	900	22	12,500
TOTAL	-	-	149,600	104,500	-	1,508,900

*Rounded to the nearest hundred

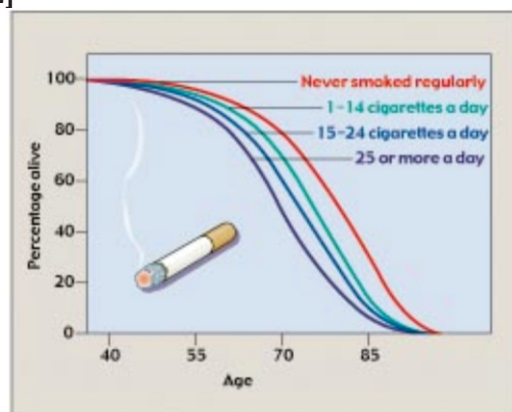
*Smoking attributable mortality (SAM)

*Population attributable risk (PAR)

*Years of potential life lost (YPLL)

Cancer Type	RR for current smokers	RR for former smokers	Annual deaths*	SAM*	PAR (%)	YPLL*
Lip, oral cavity, pharynx	5.1	2.3	2,500	1,100	46	19,000
Esophagus	7.8	2.8	2,900	1,600	56	25,400
Stomach	1.4	1.3	5,000	600	12	9,000
Pancreas	2.3	1.6	15,500	3,500	23	53,300
Larynx (voice box)	13.0	5.2	800	600	72	9,900
Lung	12.7	4.5	66,900	46,800	70	770,700
Cervix uteri	1.6	1.1	3,800	400	12	11,900
Urinary Bladder	2.2	1.9	4,000	1,100	27	13,200
Kidney, other urinary	1.3	1.1	4,500	200	5	3,700
Acute myeloid leukemia	1.1	1.4	3,200	300	11	5,500
TOTAL	-	-	109,000	56,400	-	921,700

Fig 1:Tobacco reduces life expectancy. The world's longest-running survey of smoking, begun in 1951 in Britain, revealed that by 1994 the death rate for smokers had climbed to three times the rate for nonsmokers among men 35 to 69 years of age. [2]



One study found that chromium makes PAHs stick more strongly to DNA increasing the chances of serious DNA damage. Others have found that chemicals like arsenic, cadmium and nickel stop our cells from repairing DNA damage. This worsens the effects of chemicals like benzo(a)pyrene and makes it even more likely that damaged cells will eventually turn cancerous.

The many toxins in tobacco smoke can harm many different parts of your body. Many tobacco poisons can damage your heart and its blood vessels. By comparing the amounts and strengths of different chemicals, one study found that hydrogen cyanide and arsenic alone can cause major damage to our bodies' blood network [4].

Acrolein, acetaldehyde and formaldehyde are most likely to cause diseases in our lungs and airways. Gases like hydrogen sulphide and pyridine can also irritate our airways, radioactive polonium-210 deposits damage surrounding cells, and nitrogen oxide constricts the airways, making breathing more difficult.

A protein called haemoglobin carries oxygen round our bloodstream. But carbon monoxide and nitrogen oxide stick more strongly to haemoglobin than oxygen, and reduces the levels of oxygen in our blood. This starves our organs of this vital gas.

Toluene can interfere with the development of brain cells. It also disrupts the insulating sheath that surround nerve cells, making them less efficient at carrying signals. Nicotine reaches the brain within 10 seconds after smoke is inhaled. It has been found in every part of the body and in breast milk. Carbon monoxide binds to hemoglobin in red blood cells, preventing affected cells from carrying a full load of oxygen. Cancer-causing agents (carcinogens) in tobacco smoke damage important genes that control the growth of cells, causing them to grow abnormally or to reproduce too rapidly. The carcinogen benzo (a) pyrene binds to cells in the airways and major organs of smokers. Smoking affects the function of the immune system and may increase the risk for respiratory and other infections

Table 2: Selected cigarette smoke composition [3]

Substance	Effect(s)
"Tar"*	Carcinogen
Polynuclear aromatic hydrocarbons	Carcinogens
Nicotine	Neuroendocrine
Phenol	Stimulant and depressant; addicting drug
Cresol	Cocarcinogen and irritant
β-Naphthylamine	Cocarcinogen and irritant
N-Nitrosornicotine	Carcinogen
Benzo[a]pyrene	Carcinogen
Trace metals (e.g, nickel, arsenic, polonium 210)	Carcinogen
Indole	Tumor accelerator
Carbazole	Tumor accelerator
Catechol	Carcinogen

Gas Phase	
Carbon monoxide	Impairs oxygen transport and utilization
Hydrocyanic acid	Ciliotoxin and irritant
Acetaldehyde	Ciliotoxin and irritant
Acrolein	Ciliotoxin and irritant
Ammonia	Ciliotoxin and irritant
Formaldehyde	Ciliotoxin and irritant
Oxides of nitrogen	Ciliotoxin and irritant
Nitrosamines	Carcinogen
Hydrazine	Carcinogen
Vinyl chloride	Carcinogen
Catechol	Carcinogen

There are several likely ways that cigarette smoke does its damage. One is oxidative stress that mutates DNA, promotes atherosclerosis, and leads to chronic lung injury. Oxidative stress is thought to be the general mechanism behind the aging process, contributing to the development of cancer, cardiovascular disease, and COPD.

Table 3: Carcinogens in tobacco smoke [5]

Group 1: Carcinogenic to Humans

Tobacco Smoke
Tobacco Products, Smokeless
4-Aminobiphenyl
Benzene
Cadmium
Chromium
2-Naphthylamine
Nickel
Polonium-210(Radon)
Vinyl Chloride

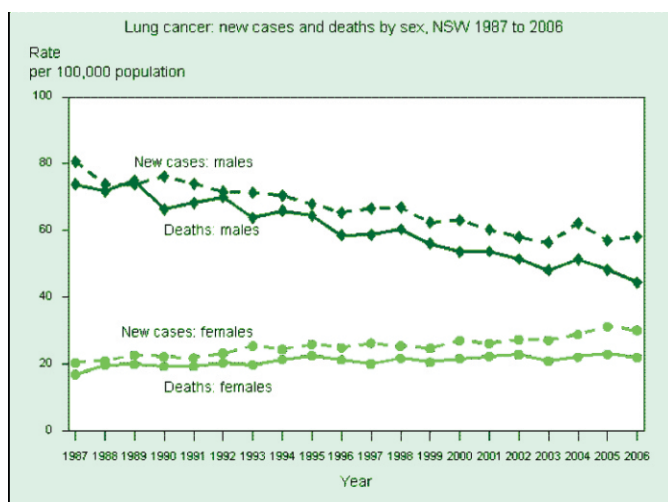
Group 2A: Probably Carcinogenic to Humans

Tobacco Smoke
Acrylonitrile
Benzo[a] anthracene
Benzo[a]pyrene
1,3-Butadiene
Dibenz(a,h)anthracene Formaldehyde
N-Nitrosodiethylamine
N-Nitrosodimethylamine
Polonium-210(Radon)
Vinyl Chloride

Tobacco Smoke
Acetaldehyde
Benzo[b]fluoranthene
Benzo[j]fluoranthene
Dibenz[a,h]acridine
Dibenz[a,j]acridine
7H-Dibenz[c,g]carbazole
Dibenzo(a,i)pyrene
Dibenzo(a,l)pyrene
Hydrazine
Indeno[1,2,3-cd]pyrene
Lead
5-Methylchrysene
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone
N-Nitrosodiethanolamine
N-Nitrosomorpholine
N-Nitrosophyrrolidine
Quinoline
Ortho-Toluidine
Ortho-Toluidine

Group 3: Unclassifiable as to Carcinogenicity to Humans**Table 2: Selected cigarette smoke composition [3]**

Substance	Effect(s)
Chrysene	Carcinogen
Crotonaldehyde	Carcinogens
N'-Nitrosoanatabine(NAT)	Neuroendocrine

Fig 3: Cancers were classified by ICD-9 up to 1998 and by ICD-10 from 1999 onwards. Rates were age-adjusted using the Australian population as at 30 June 2001. Numbers for 2006 include an estimate of the small numbers of deaths that were registered in 2007, data for which were unavailable at the time of production. [6]

Any atom or molecule capable of independent existence that contains one or more unpaired electrons in its outermost orbital is called a free radical. Reactive oxygen species (ROS) are the side-products generated endogenously by all aerobic cells as a result of the metabolism of oxygen. They are oxygen-containing molecules that have higher chemical reactivity than ground-state molecular oxygen. ROS include not only oxygen-centered radicals such as superoxide oxygen anion (O_2^-) and hydroxyl radical (OH^\cdot), but also molecules such as singlet oxygen (1O_2) and hydrogen peroxide (H_2O_2).

2. Lung cancer

Lung cancer is a disease of uncontrolled cell growth in tissues of the lung. This growth may lead to metastasis which is the invasion of adjacent tissue and infiltration beyond the lungs. The vast majority of primary lung cancers are carcinomas of the lung, derived from epithelial cells. Lung cancer, the most common cause of cancer-related death in men and women, is responsible for 1.3 million deaths worldwide annually, as of 2004 Lung cancer is the most common cause of cancer death in both men and women. The main types of lung cancer are small cell lung carcinoma and non-small cell lung carcinoma. This distinction is important, because the treatment varies; non-small cell lung carcinoma (NSCLC) is sometimes treated with surgery, while small cell lung carcinoma (SCLC) usually responds better to chemotherapy and radiation. Non-small lung cancer is staged based on the characteristics of the tumor (T), lymph nodes (N), and distal spread (M). Survival is directly related to tumor stage. Symptoms develop in late stages (Figure.3) [6].

The most common cause of lung cancer is long-term exposure to tobacco smoke. The occurrence of lung cancer in nonsmokers, who account for as many as 15% of cases, is often attributed to a combination of genetic factors, radon gas, asbestos and air

pollution including secondhand smoke. Smoking may also lead to increased oxidative stress caused by increased free radical concentration and increased antioxidant levels (Table 4) [7].

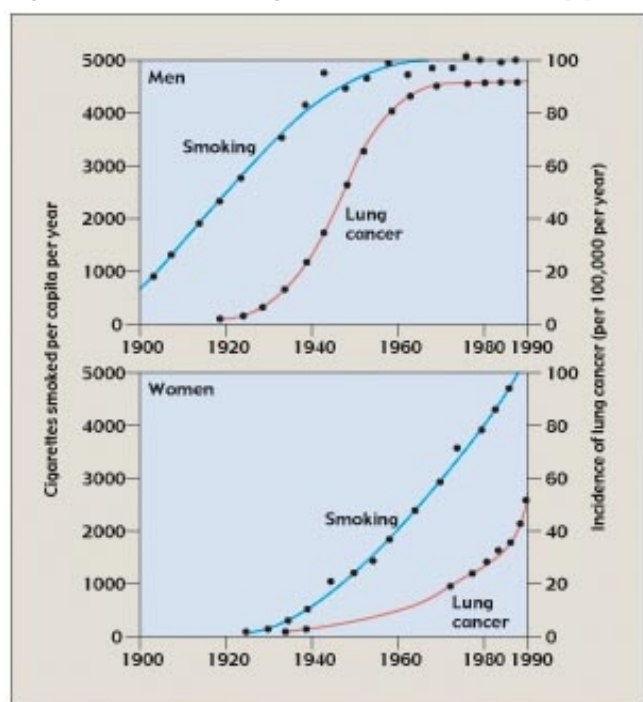
Table 4: Selected cigarette smoke composition [3]

The Radicals	Effect(s)
Superoxide O_2^-	Oxygen- centered radical with selective reactivity. This species is produced by a number of enzyme systems, by autoxidation reactions and by nonenzymatic electron transfers that univalently reduce molecular oxygen. SOD accelerates the dismutation of O_2^- , converting it to hydrogen peroxide (H_2O_2) and oxygen (O_2).
Hydroxyl OH^\cdot	Oxygen- centered radical with selective reactivity. This species is produced by a number of enzyme systems, by autoxidation reactions and by nonenzymatic electron transfers that univalently reduce molecular oxygen. SOD accelerates the dismutation of O_2^- , converting it to hydrogen peroxide (H_2O_2) and oxygen (O_2).
Peroxy, alkoxyl RO_2^\cdot , RO^\cdot	Oxygen- centered radical with selective reactivity. This species is produced by a number of enzyme systems, by autoxidation reactions and by nonenzymatic electron transfers that univalently reduce molecular oxygen. SOD accelerates the dismutation of O_2^- , converting it to hydrogen peroxide (H_2O_2) and oxygen (O_2).
Oxides of nitrogen NO , NO_2	nitric oxide is formed in vivo from the amino acid L-arginine. Nitrogen dioxide is formed when NO reacts with O_2^- and is found in polluted air and smoke.
The Non Radicals	
Hydrogen peroxide H_2O_2	Formed in vivo when O_2^- dismutates and also by many oxidase enzymes. Higher levels of H_2O_2 can attack several cellular energy-producing systems. H_2O_2 also forms OH^\cdot in the presence of transition metal ions (Fe^{2+}). O_2^- can facilitate this reaction
Hydrogen peroxide H_2O_2	A powerful oxidant formed in the human neutrophils at sites of inflammation by action of the enzyme myeloperoxidase. May also react with O_2^- to generate OH^\cdot in neutrophils.
Ozone 1O_2	This noxious gas has been shown to deplete plasma antioxidants vitamin D, Vitamin E, and uric acid.

Oxygen- centered radical with selective reactivity. This species is produced by a number of enzyme systems, by autoxidation reactions and by nonenzymatic electron transfers that univalently reduce molecular oxygen. SOD accelerates the dismutation of O_2^- , converting it to hydrogen peroxide (H_2O_2) and oxygen (O_2).

The rise in lung cancer over the last half century is directly related to cigarette smoking. Lung cancer is directly related to smoking. Over 40 carcinogens have been identified in cigarette smoke. The risk of developing lung cancer is directly related to the number of cigarettes smoked. The change in consumption from unfiltered high tar cigarettes to filtered low tar cigarettes parallels the change in incidence from squamous cell carcinoma to adenocarcinoma. There is a long interval between quitting smoking and elimination of lung cancer risk. Up to 40% of newly diagnosed lung cancer occurs in former smokers. (median abstinence duration 9 years) 40% of newly diagnosed lung cancer occurs in former smokers. (median abstinence duration 9 years) (Figure.2) [8].

Fig 2: The incidence of lung cancer in men and women [8]



Treatment for lung cancer depends on the cancer's specific cell type, how far it has spread and the patient's performance status. Common treatments include surgery, chemotherapy and radiation therapy. Small cell lung carcinoma is treated primarily with chemotherapy and radiation, as surgery has no demonstrable influence on survival. Primary chemotherapy is also given in metastatic non-small cell lung carcinoma.

The combination regimen depends on the tumor type. Non-small cell lung carcinoma is often treated with cisplatin or carboplatin in combination with gemcitabine, paclitaxel, docetaxel, etoposide or vinorelbine. In small cell lung carcinoma, cisplatin and etoposide are most commonly used. Combinations with carboplatin, gemcitabine, paclitaxel, vinorelbine, topotecan, and irinotecan are also used. In extensive-stage small-cell lung cancer celecoxib may safely be combined with etoposide, this combination showed improved outcomes.

Radiotherapy is often given together with chemotherapy, and may be used with curative intent in patients with non-small cell lung carcinoma who are not eligible for surgery. This form of high intensity radiotherapy is called radical radiotherapy. A refinement of this technique is continuous hyperfractionated accelerated

radiotherapy (CHART), in which a high dose of radiotherapy is given in a short time period. For small cell lung carcinoma cases that are potentially curable, chest radiation is often recommended in addition to chemotherapy. The use of adjuvant thoracic radiotherapy following curative intent surgery for non-small cell lung carcinoma is not well established and is controversial. Benefits, if any, may only be limited to those in whom the tumor has spread to the mediastinal lymph nodes [9,10,11,12].

For both non-small cell lung carcinoma and small cell lung carcinoma patients, smaller doses of radiation to the chest may be used for symptom control (palliative radiotherapy). Unlike other treatments, it is possible to deliver palliative radiotherapy without confirming the histological diagnosis of lung cancer [13,14,15,16,17].

In recent years, various molecular targeted therapies have been developed for the treatment of advanced lung cancer. Gefitinib (Iressa) is one such drug, which targets the tyrosine kinase domain of the epidermal growth factor receptor (EGFR), expressed in many cases of non-small cell lung carcinoma. It was not shown to increase survival, although females, Asians, nonsmokers, and those with bronchioloalveolar carcinoma appear to derive the most benefit from gefitinib.

Recent researches have discovered that the expression of genes belonging to one specific cancer-related pathway P13K, are activated in the cells that line the airway of smokers with Lung Cancer. This gene expression activity in normal cells of the proximal airway, precedes the development of Lung Cancer and may be reversed with a specific chemopreventive agent Myo-Inositol. Myo-Inositol targets this pathway.

3. Bladder cancer

Cancer occurs when normal cells undergo a transformation whereby they grow and multiply without normal controls. Bladder cancer is most common in industrialized countries. It is the fifth most common type of cancer in the United States—the fourth most common in men and the ninth in women. Bladder cancer can occur at any age, but it is most common in people older than 50 years of age. The average age at the time of diagnosis is in the 60s. However, it clearly appears to be a disease of aging with people in their 80s and 90s developing bladder cancer as well [18].

The greatest risk factor for bladder cancer is smoking. Smokers are more than twice as likely to get bladder cancer as nonsmokers. Caucasians are two times more likely than non-Caucasians to develop bladder cancer, and men are four times more likely than women to develop the disease. Risks also increase with age. The carcinogens in bladder are absorbed from the lungs and enter the blood. The blood is then filtered by the kidneys and concentrated in the urine. The bladder, which stores and discharges urine, has a lining that consists of a mucous layer of surface cells (urothelial cells), smooth muscle, and a fibrous layer. The carcinogens in the urine damage the urothelial cells that line the bladder walls. It is this damage that increases a smoker's chance of developing tumors. Tumors may be superficial (categorized as low-stage) or muscle invasive (categorized as high stage).

The primary symptom of bladder cancer is blood in the urine, a condition known as hematuria. Other symptoms may include frequent and painful urination. Hematuria may not necessarily be visible to the naked eye; microscopic examination may be necessary for detection.

Urological and imaging tests are used to diagnose bladder cancer. Some laboratory tests used are Bladder Chek, urinalysis, urine cytology, and urine culture. Imaging tests, such as an intravenous pyelogram (IVP) can also be used for detecting bladder cancer. An IVP may be a more effective approach for detection in that it provides information about the structure and function of the kidneys, ureters, and bladder. This imaging test uses an intravenously administered, radiopaque dye to produce a contrasting image visible in x-rays. As the dye moves through the urinary tract, x-rays are taken.

If bladder cancer is suspected, the urologist will use a local anesthesia to perform a cystoscopy of the bladder and a biopsy of the tumor. A cystoscope, which is a tiny, telescopic camera, is inserted through the urethra into the bladder. Tissue samples are taken from the lesion(s) and examined for cancerous cells.

There are many methods of treatment for bladder cancer. The best treatment method depends on the stage of the disease, the type of cancer, and the patient's age and overall health. Surgery, chemotherapy, radiation, and immunotherapy are some options to be considered [19].

4. Cervical cancer

Cancer of the cervix is a cancer that begins in the lining of the cervix. Cancer of the cervix can take many years to develop and before it does, early pre-cancerous changes will take place on the cervix. There is a very gradual change from a normal cervix to pre-cancer to cancer. This is why cervical cancer is one of the few cancers that can be prevented. Smoking is considered a risk factor, possibly because smoking causes some abnormal changes in the cells and these cells have a higher likelihood of becoming cancerous. The Hopkins researchers examined the personal cigarette smoking and household passive smoking exposures of two cohort groups in 1963 and 1975. The researchers found a stronger association between passive smoking and an increased risk for developing cervical neoplasia in the earlier cohort study. It is found that both active and passive smoking increases a woman risk for developing cervical neoplasia [20].

Treatment for cervical cancer depends on the stage of the disease and the extent of its spread. Three standard modes of treatment are surgery, radiation therapy and chemotherapy.

A radical hysterectomy removes the entire uterus, the ovaries and the upper of the vagina that is next to the cervix and the lymph nodes from the pelvic region.

5. Kidney cancer

The researchers found that among men, those with a history of smoking were more than 50 percent more likely to develop kidney cancer than those who had never smoked. Among women, smokers had a 22 percent greater risk of developing the disease. Even light smokers — those who averaged fewer than 10 cigarettes a day — were 60 percent more likely than non-smokers to develop the disease. The odds were still higher with moderate smoking, defined as 10 to 20 cigarettes per day [21].

Smoking is one of the factors that raise a person's risk of developing kidney cancer. A person can reduce his chance of developing kidney cancer by avoiding tobacco products and limiting exposure to secondhand smoke. Renal cell carcinoma (RCC) is the most common form of kidney cancer. Studies show that smokers are twice as likely as nonsmokers to develop this type

of kidney cancer. In addition to RCC, smokers are more likely to develop renal failure, renal cell sarcoma or Transitional cell carcinoma.

In addition to avoiding tobacco products, people can take the following steps to reduce their risk of ever developing kidney cancer—Avoid second hand smoke, eat right, exercise, maintain an ideal weight and schedule regular physical exams [22].

6. Larynx cancer

Laryngeal cancer occurs when cells in the lining of the throat grow uncontrollably and form tumors that can invade normal tissues and spread to other parts of the body. Many risk factors have been implicated in the development of laryngeal cancer. These include chronic irritation from laryngitis or voice abuse, chronic gastric reflux, and exposure to certain chemicals, such as wood dust, nitrogen mustard, and asbestos. However, far and away the largest risk factor for the development of laryngeal cancer is smoking [23].

Pipe smoking, cigar smoking, and cigarette smoking have all been strongly associated with the development of larynx cancer. There is also an association between heavy alcohol intake and laryngeal cancer. Although it has classically been thought of as a co-risk factor that only increases the risk of smoking, some more recent studies have shown that heavy alcohol use can increase the risk of laryngeal cancer by itself. It is estimated that heavy drinking increases the risk of laryngeal cancer by 2-6 times, while smoking increases the risk between 5-25 times, depending on how much one smokes. In a person who both smokes and drinks, the risk is increased to up to 40 times the risk of someone who neither smokes nor drinks [24].

For small, early stage cancers of the larynx, we can have radiotherapy or surgery. Radiotherapy is the most common treatment. This will cure most people with small tumours of the larynx. For larger tumours it is more usual to have surgery than radiotherapy. Then larynx has to be partially or completely removed. If the whole larynx removed, the patient will not be able to speak normally afterwards. Depending on the size of the tumour, the patient undergoes chemotherapy and radiotherapy at the same time. This is called chemoradiation. Chemotherapy may be used to shrink an advanced cancer before surgery or radiotherapy - this is called induction therapy.

7. Pharynx cancer

Pharynx cancer or squamous cell carcinoma of the pharynx is a cancer of the head and neck. In oncology squamous cell cancers of the head and neck are often considered together because they share many similarities - in incidence, cancer type, predisposing factors, pathological features, treatment and prognosis. Up to 30% of patients with one primary head and neck tumour will have a second primary malignancy.

All cancers of the head and neck show a strong association with alcohol consumption and tobacco smoking, particularly of cigarettes - in fact, tobacco is thought to be implicated in well over 80% of cases of pharynx cancer. Chronic exposure of the epithelial surfaces of the head and neck to these irritants are thought to result in a "field cancerisation" sequence of hyperplasia, dysplasia and carcinoma. That is, the development of premalignant lesions may then undergo malignant change to become a pharynx cancer [25].

Smoking and alcohol act synergistically in the development of pharynx cancer - the risk when both of these factors is present is more than double the risk of exposure to one factor alone. There is a dose-response relationship between exposure to tobacco smoke and the development pharynx cancer - the more you smoke the greater the risk. Smokers are up to 25 times more likely to develop pharynx cancer than their non-smoking counterparts. Passive smoking, tobacco chewing and cigar smoking are also risk factors for the development of pharynx cancer. Up to the point of development of overt carcinoma, many of the changes associated with cigarette smoking will reverse if the cancer patient quits smoking.

The most popular treatment of pharynx cancer is radiotherapy. Surgery is not generally indicated in the treatment of pharyngeal cancer due to the inaccessibility of the site of the cancerous tumour and the high likelihood of macro and micro metastases at the time of diagnosis of the cancer. In addition, pharyngeal carcinomas and their metastatic deposits show a good response to radiotherapy, but high doses are commonly required. Radiotherapy fields should be quite extensive to minimise the likelihood of pharynx cancer recurrence. Cancer surgery can play a role in the management of very small lesions. Chemotherapy has not been found to be of much benefit in the clinical trials conducted to date, but adjuvant cisplatin and 5-FU can be given. Improvement in symptoms of cancer is an important measurement [26].

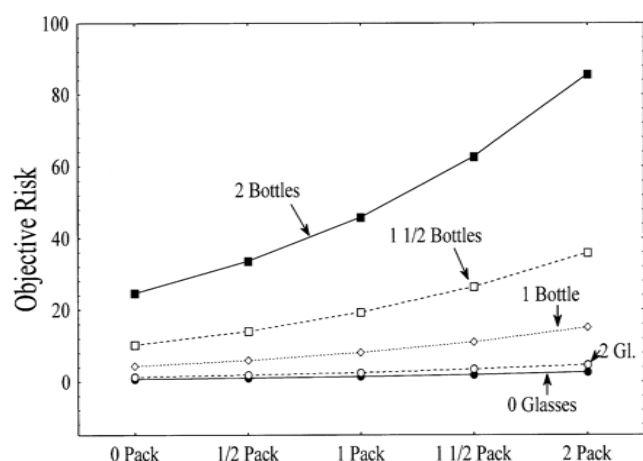
8. Oral cancer

Oral cancer most commonly involves the tissue of the lips or the tongue. Smoking and other tobacco use are linked to 70 - 80% of oral cancer case.

Workplace chemicals can increase the risk of nasal cavity and paranasal sinus cancers. Substances that have been linked to these types of cancers include, wood dust, formaldehyde, nickel, and dust from chromium or leather. Surgery alone will cure some tumours, but others will respond better to radiotherapy. Some specialist may advise that surgery is the best treatment because of the stage or position of the cancer. In other circumstances, it may be better to have radiotherapy (with or without chemotherapy) because of the have fewer problems after treatment with eating or speaking, for example [27].

10. Esophageal cancer

Fig 4: Ecological model of the relationship between the combined daily intakes of cigarettes (the horizontal axis) and wine (the curves), and the risk of esophageal cancer (expressed on a 0–100 scale on the vertical axis). [28]



Esophageal cancer starts at the inside lining of the esophagus and spreads outward through the other layers as it grows. Cigarette smoking is a major cause of esophageal cancer in the United States. Reductions in smoking and smokeless tobacco use could prevent many of the approximately 12,300 new cases and 12,100 deaths from esophageal cancer that occur annually. Cigarette smoking is a major cause in the United States (Figure.4)[28].

Reductions in smoking and smokeless tobacco use could prevent many of the approximately 12,300 new cases and 12,100 deaths from esophageal cancer that occur annually.

Smoking is a significant risk factor for esophageal cancer. When smoke is inhaled, damage is caused to the esophagus cells' DNA. According to the American Cancer Society, smoking a pack a day doubles your risk factor for esophageal cancer. The link between smoking and esophageal cancer is found to be very strong that it is associated along with two-esophageal cancer forms just the way alcohol consumption is strongly linked with stomach cancer. Persons who are prone to esophageal cancer as those who have the habit of smoking for a longer time or who begin to smoke at a very young age or smoke the most number of cigarettes daily.

Esophageal cancer is treated with chemotherapy, radiation therapy and surgery. Surgical options include the removal of part of the esophagus. This intricate surgery is not simple and comes with many risks. Chemotherapy alone will not usually cure esophageal cancer. It is often used in conjunction with radiation therapy and surgery. It is also used to relieve painful symptoms and prior to surgery in hopes of reducing the size of a tumor. [29]

11. Pancreatic cancer

Pancreatic cancer is the fourth leading cause of cancer-related deaths in the United States. Pancreatic cancer is the fifth leading cause of cancer-related mortality in the United States, with an estimated 33,370 deaths attributable to this disease in 2007. In fact, the annual mortality rate almost approximates the annual incidence rate, which reflects the generally short survival time associated with pancreatic cancer, most often less than one year. On a stage for stage basis, cancer of the pancreas is met with the shortest median survival time out of all cancer types.

Advancing age is the strongest risk factor for pancreatic cancer, with the vast majority of cases occurring after the age of 60 years. There is also a clear association between cigarette smoking and pancreatic cancer; however, the roles of diet, alcohol, and coffee have not been substantiated and should not be considered proven risk factors. Cigarette smoke contains a large number of carcinogens (cancer causing chemicals). Therefore, it is not surprising that cigarette smoking is one of the biggest risk factors for developing pancreatic cancer [30].

There are several treatment options available for pancreatic cancer such as chest X-ray, physical exam, CT scan, MRI, PET scan, Endoscopic Ultrasound, and Laparoscopy etc.

12. Stomach cancer

Stomach cancer, also called gastric cancer, is a malignant tumor arising from the lining of the stomach. There has been a significant decrease in the number of people diagnosed with stomach cancer in the past 60 years. Stomach cancers are classified according to the type of tissue where they originate. The most common type of stomach cancer is adenocarcinoma, which starts in the glandular tissue of the stomach and accounts for 90% to 95% of all stomach cancers. Other forms of stomach cancer include

lymphomas, which involve the lymphatic system and sarcomas, which involve the connective tissue (such as muscle, fat, or blood vessels).

People who use tobacco or drink alcoholic beverages regularly have a risk of developing stomach cancer. Smoking has recently been recognised as causally associated with the development of gastric cancer (GC). However, evidence on the effect by sex, duration and intensity of smoking, anatomic subsite and cessation of smoking is limited [31].

The treatment of stomach cancer depends upon a number of factors such as the location of cancer, the level of the growth of the cancer, the patient's overall health and lastly the patient's own preference. The surgeons mainly aims at removing the cancer completely however, in other cases the tumor is removed as much as is possible in order to decrease the growth or the cause of harming in the stomach.

A surgery to remove the major part of the cancer is the most common treatment of this ailment. In order to cure the cancer the surgeon may remove partial or total gastrectomy of the stomach as well as some of the surrounding tissue.

Chemotherapy is yet another treatment which includes usage of drugs in order to kill cancerous cells. This medication is either injected or is taken orally and travels through the blood stream to kill the cancer cells post surgery or to treat the cancer, which has spread to other organs of the body. This treatment is also used to control the growth of cancerous cells and to relieve the symptoms of the cancer [3].

Radiation therapy is yet another treatment for killing cancer cells with the usage of high-energy X- rays. The radiation therapy affects only those parts of the body through which the radiation beam passes.

13. Liver cancer

The most common risk factor for liver cancer is infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). These infections lead to cirrhosis and are common in many parts of the world. In the US, hepatitis C is the most common cause of liver cancer, while in other countries, hepatitis B is more common. These viruses are spread from person to person through sharing dirty needles (such as in drug use), unprotected sex, or childbirth. They can also be passed on through blood transfusions.

Smoking, alcohol abuse, being infected with hepatitis, or having other liver diseases are all factors that increase the chance of developing liver cancer. Studies have shown a consistent association of cancer of the stomach with cigarette smoking in both men and women in many cohort and case-control studies conducted in various parts of the world. Risk increases with duration of smoking and number of cigarettes smoked, and decreases with increasing duration of successful quitting. In studies that had adequate numbers, the relative risks for men and women were similar (Figure 5)[32].

The treatment for hepatocellular carcinoma mainly includes Partial hepatectomy , Liver transplantation, Cyroablation Chemoembolization, Radiotherapy, Sorafenib Radiofrequency ablation, Radiofrequency ablation combined with local chemotherapy [33].

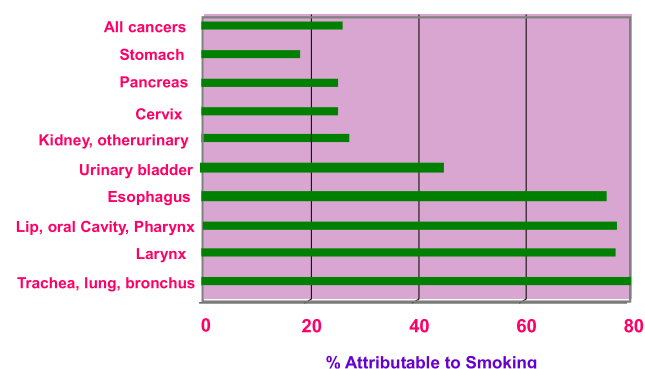
Esophageal cancer starts at the inside lining of the esophagus and spreads outward through the other layers as it grows. Cigarette smoking is a major cause of esophageal cancer in the United States. Reductions in smoking and smokeless tobacco use could prevent many of the approximately 12,300 new cases and 12,100 deaths from esophageal cancer that occur annually. Cigarette smoking is a major cause in the United States (Figure.4)[28].

Reductions in smoking and smokeless tobacco use could prevent many of the approximately 12,300 new cases and 12,100 deaths from esophageal cancer that occur annually.

Smoking is a significant risk factor for esophageal cancer. When smoke is inhaled, damage is caused to the esophagus cells' DNA. According to the American Cancer Society, smoking a pack a day doubles your risk factor for esophageal cancer. The link between smoking and esophageal cancer is found to be very strong that it is associated along with two-esophageal cancer forms just the way alcohol consumption is strongly linked with stomach cancer. Persons who are prone to esophageal cancer as those who have the habit of smoking for a longer time or who begin to smoke at a very young age or smoke the most number of cigarettes daily.

Esophageal cancer is treated with chemotherapy, radiation therapy and surgery. Surgical options include the removal of part of the esophagus. This intricate surgery is not simple and comes with many risks. Chemotherapy alone will not usually cure esophageal cancer. It is often used in conjunction with radiation therapy and surgery. It is also used to relieve painful symptoms and prior to surgery in hopes of reducing the size of a tumor. [29]

Fig 5: Tobacco and cancer incidence [32]



16. Conclusion

Several major reviews have determined that exposure to environmental tobacco smoke increases the relative risk of coronary heart disease. The American Heart Association, the California Environmental Protection Agency, and the US surgeon general have concluded that the increase in coronary heart disease risk due to environmental tobacco smoke is 30% (relative risk 1.30). Smoking harms nearly every organ of the body, causing many diseases and reducing the health of smokers in general.

In short, Smoking harms nearly every organ of the body, causing many diseases and reducing the health of smokers in general. Quitting smoking has immediate as well as long-term benefits, reducing risks for diseases caused by smoking and

improving health in general. Smoking cigarettes with lower machine-measured yields of tar and nicotine provides no clear benefit to health. The list of diseases caused by smoking has been expanded to include abdominal aortic aneurysm, acute myeloid leukemia, cataract, cervical cancer, kidney cancer, pancreatic cancer, pneumonia, periodontitis, and stomach cancer. These are in addition to diseases previously known to be caused by smoking, including bladder, esophageal, laryngeal, lung, oral, and throat cancers, chronic lung diseases, coronary heart and cardiovascular diseases, as well as reproductive effects and sudden infant death syndrome.

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