DOI: 10.56511/JIPBS.2016.v3.i02.pp45-53

Journal of Innovations in Pharmaceuticals and Biological Sciences
www.jipbs.com

JIPBS

ISSN: 2349-2759

Review article

Role of environment in development of cancer

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Abstract

Many people wonder if the environment they live in "causes cancer" to answer such difficult questions, it is necessary first to make them understand what cancer is, how it develops and what environmental factors contribute to cancer. Cancer is the formidable disease of 21st century. It is frightening because it is unpredictable and indiscriminate action. The statistical analysis of epidemiological studies all over the world suggests that 80-90 % of cancers have an environmental etiology and therefore can be controlled. The objective of the paper is to educate ourselves on: what cancers is? What are the causes of cancer and how can we keep ourselves away from it.

Cancer is an uncontrolled growth of cells that disrupts body tissues and organs. Cancer cells are not normal in their structure and functions. They grow and multiply to form tumors that invade local tissues and sometimes scatter throughout the body either by direct growth into the adjacent tissue or by implantation into distant sites by metastasis. The study of cancer is called Oncology. Cancer is caused by changes in a cell's DNA– its genetic "Blueprint". Some of these changes may be inherited from our parents while others may be caused by outside exposures, which are often referred to as environmental factor. Environmental factors can include a wide range of exposures such as: Lifestyle factors (nutrition, tobacco use, physical activity etc.), Naturally Occurring Exposures (ultraviolet light, radon gas, infectious agents etc.), Medical treatments (chemotherapy, radiations, immune system suppressing drugs, etc.), Workplace exposures, Household exposures, Pollution.

Key words: DNA-Deoxy ribonucleic Acid, Carcenogens-Cancer promoter, Epidemiology-Scientific study of spread and control of diseases, Endometrium-Uterine tissue lining, Etiology-the scientific study of the causes of disease.

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1. Introduction

The study of cancer is called oncology. The statistical analysis of epidemiological studies all over the world suggest that 80-90% of cancers have an environmental etiology and therefore can be controlled The science of epidemiology enables researchers to determine causes of diseases such as specific type of cancer, and also to estimate or project number of deaths that can be attributed to the cause on an annual basis.

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Originally, the term "environmental causes of cancer" was used to refer all cancers that were not caused by inherited factors. This definition included all cancers caused due to life style practices such as diet and tobacco use, carcinogens present in the environment etc. For the sake of convenience, the term "environment" has been further divided into two categories "personal environment" and "external environment".

Causes of cancer related to an individual personal environment includes life style choices and other factors, which can keep a person at high risk of cancer development. Up to 85% of cancers is due to life style choices made by individuals. For example tobacco is directly related to more than 30% of cancer deaths. 500,000 deaths per year are caused by tobacco alone.

The external environmental factors causing cancer include environmental pollutants, exposure to carcinogens in the work place, household exposure etc.

What is cancer? How is it defined? No oncologist so far has been able to give a satisfactory definition of cancer. This is because still there is lack of full knowledge of cancer and also because there are variety of cancers. However, J. Ewing a pathologist defined it; cancer is a heritably altered, relatively autonomous growth of cells.

The word "tumor" is now commonly used, not just any localized swelling but specifically a true neoplasm (new growth synonymous with cancer). A tumor may contain normal tissue but the major mass consists of cancerous tissue.

Generally, cancer starts as growing lump, which spreads in body through blood or by other body fluids such as lymph. The important feature of cancer is that the cancer cell reproduces exactly its own kind, which retains the capacity to multiply defying the controls operating in the living body.

Cancer is a cellular disease arising from normal cells of any organ or tissue at any age. A cell or cells not known how get initiated and acquire capacity to multiply unrestrictedly. The cells grow into a mass called tumor and tend to become nutritionally less dependent on the host. The tumor cells may acquire mobility so that they can move out of the tumor and spread out in the body. The spreading of the tumor is called metastasis meta means change and stasis means position. When the cancer cells are lodged in another organ or tissue, they start growing there. These tumors are called secondary. These secondary growths develop into tumors causing structural and functional damage to the host organs. Metastasizing tumors are therefore fatal. A metastasizing cancer may be controlled but is difficult to cure.

For more than a century, researches are working on finding ways and means to eradicate or control cancer. Although there is so far no discovery of target hitting drug or any other method to cure cancer, considerable advances have been made during last several decades. The cure rate in western countries is now 1 out of 3 which was 1 out of 5 a few decades ago. It is therefore thought that people must know how the problem of malignancy is being tackled by oncologist, scientists, the break-through in the knowledge about the disease the anticancer drugs and various experimental systems being used to understand cancer. The purpose of this paper is to induce people to control smoking, tobacco chewing, and alcohol consumption and keep themselves hygienically clean and away from life style choices causing the disease.

Self-examination after guidance from a well trained physician is the cheapest and easiest

mode of screening for abnormal deviations in the in the normal health in developing countries [1].

2. Review of Literature

How many Cancers are caused by the Environment? [1]

Some experts say a decade - old estimate that six percent of cancers are due to environmental and occupational exposures is out dated and far too low.

More than 60% of U.S. cancer deaths are caused by smoking and diet. But what about the rest?

From womb to tomb, people around the world are exposed to countless carcinogens in their food, water, air and consumers goods. The National Institute of cancer has classified 54 compounds as known human carcinogens. For example Benzene, a known cause of human leukemia, is a common pollutant in vehicle exhaust. Radon a natural radioactive gas found in many homes raises the risk of cancer. Arsenic, linked to skin, liver, bladder and lung cancer contaminates some drinking water supplies. Other known human carcinogens include asbestos, hexavalent chromium, aflatoxins and vinyl chloride.

Since 1981, agencies and institutes have cited the same estimate when regulating carcinogens in the workplace, air, water, and consumers products. Roughly 4% of cancer deaths or 20,000 deaths per year- may be attributed to occupational exposures and 2% or 10,000 deaths per year- to environmental exposures.

In its new report, the panel appointed by former president Bush, called that estimate “woefully out of date” reporting that the true burden of environmentally induced cancers has been grossly underestimated.

The role of environment in human health is generally a subject only briefly touched in medical school training. It wasn’t until I attended the world Breast Cancer Conference in 1997 that I first heard discussion amongst a number of prominent scientists, physicians and other health professional about the growing body of evidence linking environmental contamination and cancer. [2] I became very interested in this subject since I developed breast cancer at the age of 37 with no risk factors and having breast fed three children.

An obvious place to start looking for the root causes of cancer is with substances that are known to cause cancer in animal models, that is carcinogens. One such class of carcinogenic substances, the organochlorines (OCs) are found all around us. They are in our drinking water, in much of our pesticide treated food in many laundry detergents and cleaning products as well. DDT a well known OC, is persistent that its use has been banned in North America for more than 25 years, it is still found in detectable levels in the tissues and blood of people living from Florida to high Arctic. This ban notwithstanding, OCs are still produced in North America and exported abroad, particularly to developing countries. As a consequence imported fruits and vegetables which end up back on our dinning tables often have detectable levels of substances known as human carcinogens.

Aside from being potentially carcinogenic some of these chemicals behave like much weaker version of our own body’s estrogen (hormone). Because these estrogen like chemicals are outside the body, they are classified as xenoestrogens, “xeno” meaning foreign in Greek.

The proposed link between chemical xenoestrogen and breast cancer came about by accident in 1991 when Tufts University researchers noticed that breast cancer cells, which need estrogen to reproduce, were growing rapidly in plastic dishes. They discovered that Nonlyphenol, a chemical added to plastic to prevent cracking was leaching out of the plastic and triggering the growth of breast cancer cells. In other words it was acting like estrogen. The researchers then exposed the other cancer cells to common pesticides, detergents and plastics and observed the same results. The implications are disturbing, considering how common these products are in our lives.

Thus, I have discussed mainly the link between pesticides and breast cancer because that is my special interest but also consider the following:

Farmers exposed to herbicides for more than 20 days per year have been found to have a six fold increase in non Hodgkin's lymphoma.

There is significant association between yard treatment with pesticides and pediatric soft tissue sarcomas, leukemia and brain cancer.

The provincial and federal health department reports that there are instances where maximum allowable DDT intake may be exceeded in breast fed infants.

In the last 30 years the global average human sperm count has decreased by 50%. Some argue that this is a result of high exposure to xenoestrogens.

3. Experiences and Case Studies

Author's Experience of Breast Cancer His Wife Had:

I was on employment in a Gulf country called Oman from 1992 to 2006. I was working as Director of Education and my wife (Naheed Jamal Siddiqui aged 52 at the time of malignancy) had been a homemaker with a daughter of teen age in Oman and three grown up children in India. We had very interesting days of life full of joy, enthusiasm and a strong will to live a long happy life.

In the month of March 2005, my wife told me little pain in her left arm pit, later she felt some hard swellings in her neck region just above the collar bone. Consequently, we visited a lady general physician Dr. Fatima to get relief from the pain in the knees and left arm pit of my wife. During clinical check up Dr. Fatima advised us to visit Oman Govt. hospital for investigation about the hard parts in the neck region.

Within a week, the result came out after fine needle aspiration test and the hard parts were found malignant. The Sur Hospital Oman provided the following investigation report:

Impression: Suggestive of Carcinomatous deposits in left axillary and supraclavicular lymph node.

-FNAC breast- No significant pathology seen.

-Primary in the breast could be a possibility.

-Advised further work up.

Slides sent to Royal Hospital for opinion.

After a few days Royal hospital Oman confirmed carcinomous tissues in the lymph nodes. We were extremely shocked (Paron Tale Zamin Khisak Gai), immediately we decided to leave Oman and come back to India for treatment.

We contacted the oncologists at Lucknow as we are the residents of Lucknow, and took the appointment of an oncologist Dr. I.D. Sharma for 2nd April 2005. Dr. Sharma (Professor of Oncology, K.G.M.C. Lucknow,

retired now) advised for immediate surgery of the patient. We agreed and after so many tests such as mammography, fine needle aspiration and blood test doctor decided to operate my wife, the victim of cancer on 5th April 2005. She entered the Operation Theater with a smiling face. After two hours duration surgical operation Dr. Sharma called me inside the O.T., I with a frightened heart entered the O.T., Dr. showed me the left breast tissue mass and 32 malignant lymph nodes he had removed from the body of the patient. He said you are too late; rest is in the hands of Almighty God.

Table 1. List of Cigarette Smoke Carcinogens [3]

Chemical (carcinogens)	Amount(Per Cigarette)
Acetaldehyde	980 micrograms to 1.37 milligrams
Acrylonitrile	1-2 milligrams used as fumigant
4-Aminobiphenyl	0.2-23 nanograms per cigarette
0-Anicidine hydrochloride	Unknown
Arsenic	Unknown
Benzene	5.9-75 micrograms
Beryllium	0.5 nanograms
1,3 Butadine	152-400 micrograms
Cadmium	1.7 micrograms
1,1 Dimethylhydrazine	Unknown
Ethylene oxide	Unknown
Formaldehyde	Unknown
Furan	Unknown
Hetrocyclic amines	Unknown
Hydrazene	32 micrograms
Isoprene	3.1milligrams
Lead	Unknown
2-Napthylamine	1.5-35nanograms
Nitromethane	Unknown
N-Nitrosodiethanolamine	24-36 nanograms
N-Nitrosodimethylamine	5.7-43 nanograms
N-Nitrosodimethylamine	Up to 8.3nanograms
N-Nitrosodi-n-propylamine	1 nanogram
4-(Nitrosomethylamino)-1-(3-peridyl)-1butanone	Upto 4.2 micrograms
N-Nitrsonornicotine	14 micrograms
N-Nitrosopiperidine	Unknown
N-Nitrosonitrosopyrrolidine	113 nanograms
N-Nitrososarcosine	22-460 nanograms
Polonium-210	Variable depending on soil & fertilizer used to grow tobacco
Polycyclic aromatic hydrocarbons	28-100 milligrams
O-Toluidine	32 nanograms
Vinyl chloride	5.6-27 nanograms

During the operation I had prayer time of Asr, (third prayer of the day) at about 4:30 p.m., I went to a nearby mosque and prayed for the life of my beloved wife and requested all the people of the mosque for the same.

With the grace of Allah she recovered from the post operational heal up and was advised to undergo 6 cycles and 5 cycles of chemotherapy and radiotherapy respectively. She had miserable days after chemotherapy and radiotherapy due to temporary side effects of the treatment. But she could withstand all the side effects bravely as a result of moral support given by our children and myself. Further she was advised for monthly clinical check up and six monthly investigations. Thanks to Almighty Allah, she is still surviving with normal health and carries normal routine work. She performs all the house hold activities efficiently. I shall always remain grateful first to Almighty Allah and then to Dr. I.D. Sharma.

4. Techniques

The author has been highly interested in finding out the real cause of cancers specifically that of breast, since my wife had breast cancer in the year 2005-6. The review paper has been developed as a result of reading and writing articles on "Cancer an Enigma". The paper could not be materialized without the help of Google, internet and books on cancer. Specifically thorough reading of the book on cancer [4]. Google has been a source of knowledge on various aspects of cancer. The author has searched out a number of papers regarding role of environment in development of cancer.

Diagnosis and staging

Breast cancer is usually first detected as a palpable mass or as a mammographic abnormality, but it can also be manifested initially by nipple discharge, breast skin change, or breast pain. Suspicious palpable and mammographic breast lesions are investigated by biopsy. Most breast masses, especially those that are found in young premenopausal women are benign. Most (75 to 85 percent) of the masses found to be cancerous are invasive with the remaining 15 to 25 percent in situ. Carcinoma in situ is characterized by the proliferation of malignant cells within the ducts or lobules of the breast without invasion of stromal tissue. The two major subtypes are ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS)[5].

LCIS, unlike DCIS, is microscopic and lacks both clinical and mammographic signs. LCIS is also more likely to have bilateral involvement. The cells are grouped in a small, solid mass and have small, uniform, round to ovalnuclei [6].

All breast cancers are classified using a scheme that encompasses all attributes of the tumor that define its life history. The American Joint Committee on Cancer (AJCC) TNM classification is based on the premise that cancers of the same anatomic site and histology share similar patterns of growth and extension. The system is based on the size of the primary tumor (T), regional lymph node involvement (N), and distant metastasis (M) (Table 2). The combination of the T, N, and M classification indicates the extent of the disease at the time of clinical evaluation [7].

The stage grouping system is often used for the purposes of tabulation and analysis (Table 3). This grouping system was

adopted to ensure, as far as possible, that each group is more or less homogeneous in respect of survival, and that the rates of these groups for each are distinctive [8].

Notes:

1. T1 includes 1mic;
2. The prognosis of patients with pN1a is similar to that of patients with pN0.

Treatment options

Effective means of treating breast cancer are widely available and may be used alone or in combination, depending on individual circumstances. Surgery is the most commonly used treatment for localized breast cancer. The surgical procedures most often used are lumpectomy with axillary node dissection and modified radical mastectomy. Lumpectomy with axillary node dissection entails excision of the tumor mass, including a clear margin of normal breast around the tumor, along with lymph nodes under the arm. Modified radical mastectomy entails complete removal of the breast, the underlying pectoral fascia, and some of the axillary nodes [9].

Table 2. The TNM system of staging of breast cancer [7].

Tumor Size T (LargestDiameter)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraductal carcinoma, lobular carcinoma in situ, or Paget's disease of the nipple with no tumor.
T1	Tumor <2 cm in greatest dimension
T2	Tumor >2 cm but not > 5 cm in greatest dimension
T3	Tumor > 5 cm in greatest dimension
T4	Tumor of any size with direct extension to chest wall* or skin (includes inflammatory carcinoma)
Nodal Involvement - N (Nodal Status)	
NX	Regional lymph nodes cannot be assessed (e.g., previously removed, not removed)
N0	No regional lymph node metastases
N1	Metastasis to movable ipsilateral axillary nodes
N2	Metastasis to ipsilateral axillary nodes fixed to one another or to other structures
N3	Metastasis to ipsilateral axillary nodes fixed to one another or to other structures
Metastases - M	
M0	No evidence of distant metastasis
M1	Distant metastases (including metastases to ipsilateral supraclavicular lymph nodes

The use of radiation therapy in the management of breast cancer has been increasing in recent years. For many early-stage cancers, radiation of the breast is used in combination with lumpectomy and surgical examination of the axillary lymph glands. In larger but still localized cancers, the breast, axilla, and chest wall may be irradiated following surgical treatment. A number of complications due to the spread of cancer to a distant site (e.g., pain) may be successfully treated with radiation. In these situations, hormone or drug treatment may be given as well.

Surgery and radiotherapy are very effective in removing or destroying cancerous tissue if it is known exactly where the cancer is and if adjacent normal

organs and tissues can be preserved without injury. Chemotherapy, on the other hand, is distributed through the body and is capable of destroying cancer cells wherever they exist.

Table 3: Stage grouping system of staging of breast cancer: Conversion from TNM [5].

Stage	T	N	M
Stage 0	Tis	N0	M0
Stage I	T11	N0	M0
Stage IIA	T0	N1	M0
	T11	N12	M0
	T2	N0	M0
Stage IIB	T2T0	N1	M0
	T3 1	N0	M0
Stage IIIA	T0 T4	N2	M0
	T11	N2	M0
	T2	N2	M0
	T3	N1,N2	M0
Stage IIIB	T4	Any N	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

Chemotherapy is often used, as adjuvant therapy where the primary tumor has been controlled by surgery or radiotherapy but a secondary tumor is known to exist. It is also used in some situations where the cancer is localized to one site. In a great many cases the growth of breast cancers has been shown to be dependent on the hormonal environment provided by the individual's body. Hormonal therapy provides another approach to suppress the growth of hormone-sensitive tumors. Sometimes suppression of tumor growth is achieved by reducing the level of appropriate hormones in the body through surgical removal or x-ray destruction of the organ that normally produces those hormones (such as the ovary or adrenal gland). Drugs are now also available that counteract the action of certain hormones. Tumor suppression is sometimes achieved by elevating the level of certain other hormones by providing them in the form of drugs [10].

5. Results and Discussions

The author has focused his study on breast cancer since his wife had been a victim of this fatal disease. After studying a number of articles on breast cancer and based on the self experience how his wife was saved from the breast cancer, following evaluating diagnostic tools have been found effective:

Mammography: there was evidence that mammography is more sensitive than clinical examination diagnosing breast cancer in women of all ages. There was evidence that population based mammography screening improves survival in women aged 50 to 65.

Fine needle aspiration: the sensitivity is generally high (over 90%) but the specificity varies 78 to 95%. Both sensitivity and specificity vary depending on the placement of needle. In lesions more than 1cm. core biopsy may be an alternative to fine needle aspiration.

Triple test: triple testing with mammography, fine needle aspiration, and clinical examination is more accurate than any of the test alone.

Treatment and elimination of cancer is possible through surgical operation, chemotherapy and radiation. One has to be optimistic of survival, adaptive to medical advancement and technologies and strong faith in almighty Allah**.**

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