UNIVERSITY OF JAFFNA
SRI LANKA

Professor

Sivapathasuntharam Mageswaran Memorial Lecture – 2008

"Chemical Carcinogenesis & its Possible Impact in Jaffna Peninsula"

By:

Dr. N. Jeyakumaran

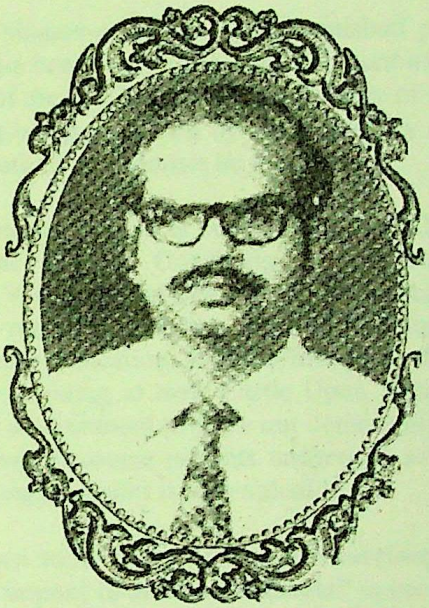
MBBS (SL), MD (SL)
Consultant Clinical Oncologist
Teaching Hospital, Jaffna.

December 15, 2008

Professor

Sivapathasuntharam Mageswaran

Memorial Lecture – 2008



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Professor Sivapathasuntharam Mageswaran Memorial Lecture – 2008

Vice Chancellor's Message

It is my privilege to extend warm welcome to esteemed guests to this memorial event to pay tribute to our Late Professor. S. Mageswaran.

Prof. S. Mageswaran was a distinguished personality who contributed immensely to the development of our University and one of the key builders of the Faculty of Science and his memories being cherished by the University community and the generations of chemists he trained.

This memorial address is being given by Dr.N.Jeyakumaran, Consultant Clinical Oncologist of our Jaffna Teaching Hospital. We are proud that one of our medical graduates has achieved recognition in the field of Oncology. He had his postgraduate education at the University of Colombo and Post MD Training at New Castle Upon Tyne, The UK. His empathic commitment to serve our community especially at a time on which cancer patients underwent severe difficulties in obtaining treatment is very valuable.

His chosen topic today **"Chemical carcinogenesis and its possible impact in Jaffna Peninsula"** is very relevant to the present day medical education especially in the field of preventive medicine.

Prof. N. Shanmugalingam
Vice-Chancellor
University of Jaffna
23.10.2008.

"CHEMICAL CARCINOGENESIS & ITS POSSIBLE IMPACT IN JAFFNA PENINSULA"

The Vice Chancellor, the Dean Faculty of Science, Head, Department of Chemistry, members of the family of Professor S.Mageswaran, my dear teachers, colleagues, friends and students,

It is indeed an honour and great pleasure to be invited to deliver the Professor Sivapathasuntharam Mageswaran Memorial Lecture - 2008. First of all I thank Head, Department of Chemistry for inviting me to undertake this task of delivering the Professor Sivapathasuntharam Mageswaran Memorial Lecture.

Though I am in the Department of Health, I had association with Late Professor S.Mageswaran when I was involved in undergraduate research in the Chemistry laboratory of Dept. of Chemistry as well as when I was the Captain of the University Chess Team.

Today I wish to present a topic related to both Cancer and Chemistry: ***"CHEMICAL CARCINOGENESIS & ITS POSSIBLE IMPACT IN JAFFNA PENINSULA"***

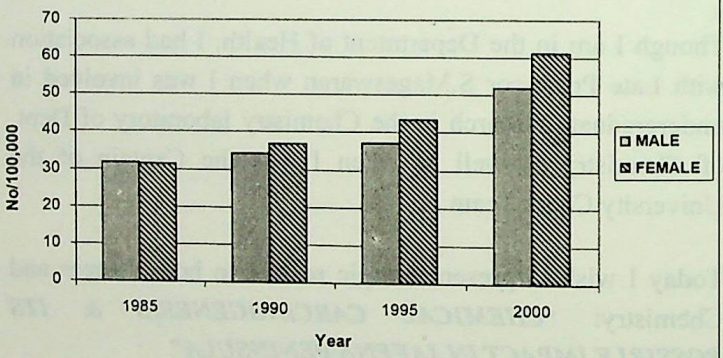
I feel that it is a very suitable topic to honour the memory of a man who devoted his entire life for the upgrading of Chemistry in particular and Science in general to the whole world.

INTRODUCTION:

Cancer is a major source of disease burden in Sri Lanka, and the cost from morbidity and mortality is enormous in human and economic terms. Cancer is the fifth leading cause of death and the leading cause of premature mortality.[1]

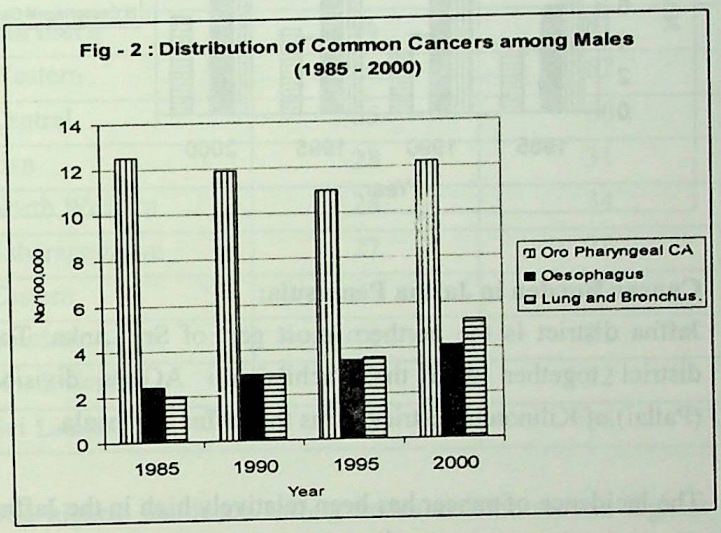
In Sri Lanka, among males and females, the cancer incidence is in the increasing trend from 1985 to 2000. Overall cancer incidence among males has increased from 31.7 per 100,000 to 52.0 per 100,000 and that among females, it has increased from 31.5 per 100,000 to 61.1 per 100,000 during the period of 1985-2000.[2-5] (Fig - 1).

Fig - 1: Pattern of Cancer Incidence (1985 - 2000)

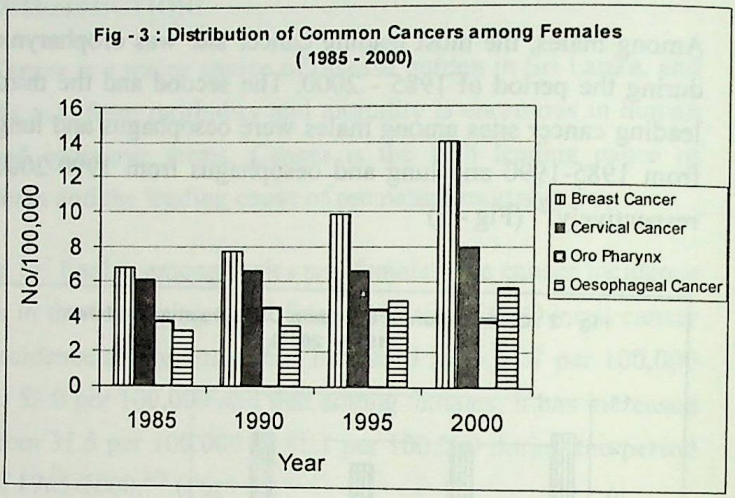


The number of cancer cases can be expected to increase further because of the growth of ageing population in coming decades.

Among males, the most leading cancer site was oropharynx during the period of 1985 - 2000. The second and the third leading cancer sites among males were oesophagus and lung from 1985-1990 and lung and oesophagus from 1990-2000 respectively.[2-5](Fig - 2)



Among females, most leading cancer site and the second were breast and cervix respectively during the period of 1985 - 2000. The third leading cancer site among females was oropharynx from 1985 - 1990 and oesophagus from 1990 - 2000 respectively.[2-5] (Fig-3)



Cancer Burden in Jaffna Peninsula:

Jaffna district is the northern most part of Sri Lanka. The district together with the Pachilaipalli AGA's division (Pallai) of Kilinotchi district forms the Jaffna peninsula.

The incidence of cancer has been relatively high in the Jaffna district. A five year study [6] on the geographical pathology of malignant tumours in Sri Lanka, from 1973-1977, confirmed this.

The study involved the examination of 24,029 biopsy specimens examined at the 9 provincial hospitals in Sri Lanka. The incidence of malignant tumours in the 9 provinces is given in Table-1.

Table-1: Incidence of Malignant Tumours in each of the 9 Provinces of Sri Lanka 1973 - 77 (per 100,000 population)[6]

Province	Malignant Tumours	
	Males	Females
Northern	**96**	**81**
Western	80	87
Central	55	60
Uva	28	31
North Western	28	34
Sabaragamuwa	27	28
Eastern	21	39
Southern	16	21
North Central	12	12
Sri Lanka	**48**	**56**

The highest incidence among males and the second highest incidence among females are among the people in Jaffna district.

The same study also reveals that the Tamils have the highest incidence of cancer in Sri Lanka as seen in Table-2.

Table-2: Cancer Incidence (1973 - 77) of Malignant Tumours in different Ethnic groups in Sri Lanka.[6]

Ethnic Group	Incidence (per 100,000 population)
Tamils	**108**
Sinhalese	91
Muslims	57
Sri Lanka	**92**

The increased incidence among Tamils may be due to the fact that Jaffna peninsula is populated by Tamils as the incidence in Eastern province did not show much high incidence.[7]

This geographical variation may have correlations with something connected to the soil, water, environment or any special habits or activities that is unique in the Jaffna peninsula.

The same paper also reveals that the common cancers in Jaffna peninsula are that of Oro pharynx, Oesophagus, stomach, breast and liver.[6]

Since 1985, the National Cancer Registry[2-5] has been publishing that the incidence of cancer has been reported low in Jaffna peninsula. This may be due to the commencement

of war in the Jaffna Peninsula in 1983 and consequent deterioration of health care services with minimal investigatory facilities and under reporting as the source of data were obtained from the Cancer Units in Sri Lanka.

Since the establishment of first inward cancer care services in the Teaching Hospital, Jaffna, on the 14th of December 2004, efforts have been taken to regularize the cancer registration with better reporting from the Jaffna peninsula. This will improve the reliability of our statistics in the forthcoming Cancer Registry.

Cancer Control:

Prevention and screening of common cancers are important scientific and public health challenges to reduce the burden of cancer. Scientific researches have demonstrated that cancers occur not as sudden catastrophic events, but rather as the result of a complex and long evolving process called ***Carcinogenesis***. The process of carcinogenesis can take decades to complete, providing time and opportunity for us to intervene, to stop or to reverse its progress either before the clinical appearance of cancer or at its earliest stages.

Due to the continuing burden, public health interventions have to be focused on prevention and early detection to reduce cancer incidence and mortality. Logically, reducing

cancer incidence through primary prevention is the most desirable goal, and major reductions in cancer incidence are possible through improved nutrition, physical activity and avoidance of carcinogens as well as other cancer risks.

In this talk, I will be mainly concentrating on Chemical Carcinogenesis and its possible impact in Jaffna Peninsula quoting few studies.

Carcinogenesis:

Many different types of human cancers are caused by occupational exposure, while others have been attributed to environmental exposure to chemical and/or viral agents. A genetic basis for human carcinogenesis has been established through biochemical and molecular analyses of the disease. The molecular mechanisms of human carcinogenesis are emerging through an increasing appreciation of the genetic and epigenetic changes that result from chemical - DNA interactions.[8,9]

It is now recognized that carcinogenesis requires the malignant conversion of hyperplastic cells from a preneoplastic state and that invasion and metastasis are manifestations of further genetic and epigenetic changes.

Activation of proto oncogenes and loss of tumour-suppressor genes are genetic changes that have been found in association with carcinogenesis.

Multistage Carcinogenesis:

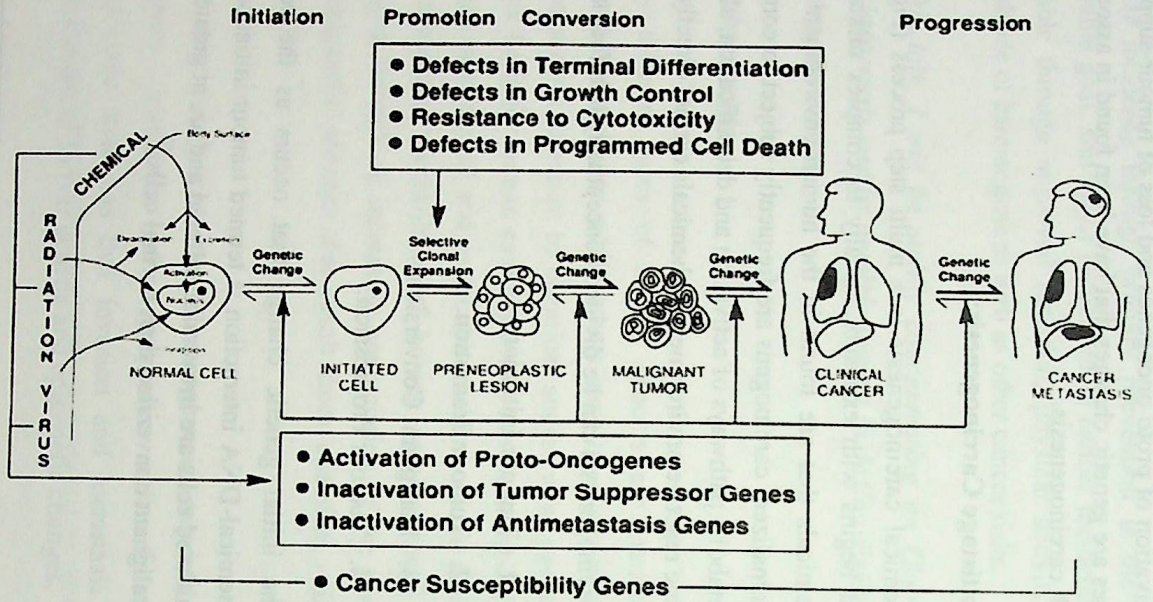
Chemical carcinogenesis is a multi step process (Fig-4, 5) that begins with exposure, usually to complex mixtures of chemicals that are found in the human environment. Once internalized, carcinogens are frequently subject to competing metabolic pathways of activation and detoxification, although some reactive environmental chemicals can act directly.

Carcinogenesis can be divided conceptually into four steps....

1. Tumour Initiation.
2. Tumour Promotion.
3. Malignant Conversion.
4. Tumour Progression.

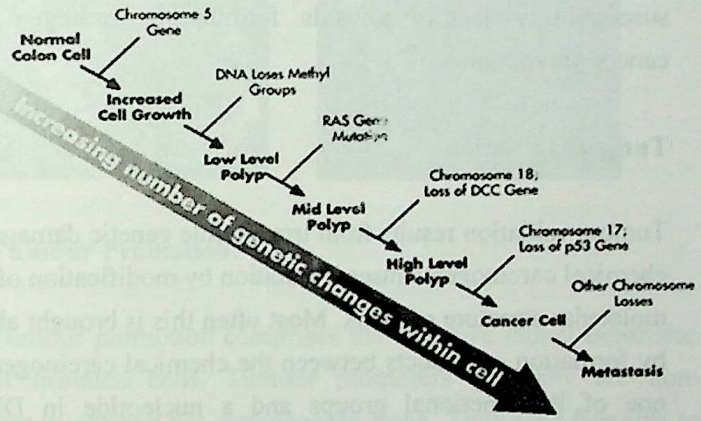
The initial genetic change that occurs as the result of chemical-DNA interaction is termed tumour initiation. Thus, initiated cells are irreversibly altered and are at greater risk of malignant conversion than normal cells.[10]

Fig-4: Multi Step Carcinogenesis[9]



In colorectal tumorigenesis, a model has been developed in which accumulated alterations include at least one dominantly acting oncogene and several tumor-suppressor genes. These same studies provided evidence for the progressive nature of genetic changes in carcinogenesis.

Fig-5: Multiple Stages of Human Colon Cancer[11]



The epigenetic effects of tumour promoters facilitate the clonal expansion of the initiated cell. This selective, clonal growth advantage results in the formation of a focus of preneoplastic cells. These cells are more vulnerable to progression towards tumourigenesis, because they present a larger, more rapidly proliferating target population for the further action of chemical carcinogens and other cofactors. Additional genetic changes occur, and consequently, the

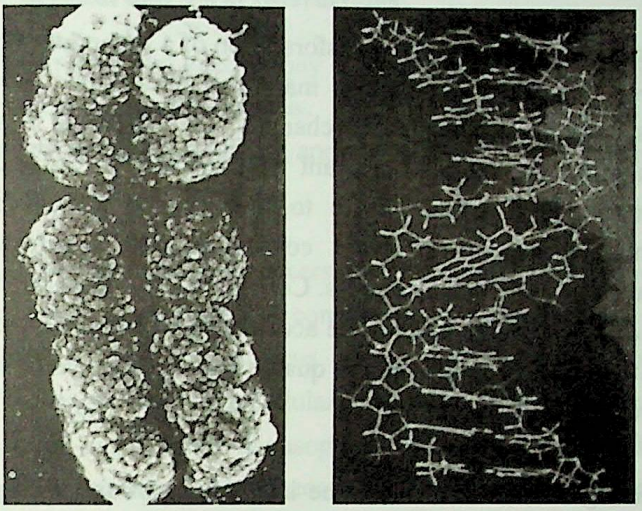
accumulation of mutations, which may activate protooncogenes and inactivate tumour-suppressor genes, lead to malignant conversion, tumour progression, and metastasis.

The underlying genetic mechanisms that regulate chemical carcinogenesis are becoming increasingly well understood, and the insights generated have assisted in the development of methodologies designed to assess human cancer risk and susceptibility factors towards formulating strategies for cancer prevention.

Tumour Initiation:

Tumour initiation results from irreversible genetic damage. A chemical carcinogen causes a mutation by modification of the molecular structure of DNA. Most often this is brought about by formation of adducts between the chemical carcinogen or one of its functional groups and a nucleotide in DNA. Carcinogen-DNA adduct (Fig-6) formation is central to theories of chemical carcinogenesis, and it can be considered to be a necessary, but not a sufficient, prerequisite for initiation.

Fig-6: Carcinogen-DNA Adduct.[9]



Tumour Promotion:

Tumour promotion comprises the selective clonal expansion of initiated cells. Tumour promoters generally are non-mutagenic and not carcinogenic alone. They are often able to mediate their biologic effects without metabolic activation. These agents are characterized by their ability to reduce the latency period for tumour formation after exposure of a tissue to a tumour initiator. In addition, they induce tumour formation in conjunction with a dose of an initiator that is too low to be carcinogenic alone.

Malignant Conversion:

Malignant conversion is the transformation of a preneoplastic cell into one that expresses the malignant phenotype. This process requires further genetic changes. The total dose of a tumour promoter is less important than frequently repeated exposure, and if the exposure to a tumour promoter is discontinued before malignant conversion has occurred, premalignant lesions may regress. Conversion of a fraction of these cells to malignancy will be accelerated in proportion to the rate of cell division and the quantity of dividing cells in the preneoplastic lesion.

The malignant conversion can be increased substantially by the exposure of preneoplastic cells to DNA-damaging agents, and it appears that this process may be mediated through the activation of protooncogenes and inactivation of tumour-suppressor genes.

Tumour Progression:

Tumour progression comprises the expression of the malignant phenotype and the tendency of already malignant cells to acquire more aggressive characteristics with propensity for genomic instability and uncontrolled growth over a period of time. Metastasis also may involve the ability of tumour cells to secrete proteases that allow invasion beyond the immediate location of the primary tumour.

Chemical and Viral Interactions:

Chemicals and viruses may have interactive effects in certain forms of carcinogenesis. There is good evidence from experiments that viruses and chemicals also can interact in a synergistic manner.

A number of human cancers now are considered to have both a viral and a chemical component to their etiology. These include hepatitis B virus and aflatoxin B1 or alcoholic beverages in hepatocellular carcinoma, Epstein-Barr virus and N-nitrosamines in nasopharyngeal carcinoma, and human papilloma virus and tobacco smoke components in cancers of the uterine cervix, oral cavity, and larynx.

In essence chemicals can act as tumor promoters following tumor initiation by viral agents, and viruses can act as promoters following chemical initiation

DNA Damage and Repair:

There are several ways in which the chemical structure of DNA can be altered by a carcinogen, including the formation of bulky aromatic-type adducts, alkylation, oxidation, dimerization and deamination. Chemical carcinogens also can cause epigenetic changes, such as alteration in DNA methylation status. Carcinogen-DNA adducts vary in their promutagenic potential. Although DNA adduct appears to be

the most common form by far of DNA damage induced by chemicals, other possible mechanisms include covalent binding of metabolites to deoxyadenosine.

DNA repair enzymes act at sites of DNA damage caused by chemical carcinogens. There are five major mechanisms in repair.

1. Direct DNA repair.
2. Nucleotide excision repair.
3. Base excision repair.
4. Post-replication repair.
5. Mismatch repair.

Inter Individual Variation:

Variations among individuals in the metabolism of carcinogens together with differences in DNA-repair capacity and response to tumour promoters govern the relative risk of an individual.

Polymorphisms arise in genes through nonlethal mutations that occur during evolution. The spectrum of functional polymorphisms among humans for proteins that have, or may have, a role in chemical carcinogenesis include enzymes that metabolize (activate and detoxify) xenobiotic substances, enzymes that repair DNA damage, oncogenes, tumor-

suppressor genes, and the cell surface receptors that activate the phosphorylation cascade.

The cytochrome P-450 (CYP) multigene family is largely responsible for the metabolic activation and detoxication of many different chemical carcinogens in the human environment. Cytochrome P-450s act by adding an atom of oxygen onto the substrate; they also are inducible by polycyclic aromatic hydrocarbons and chlorinated hydrocarbons. Cytochrome P-450s are known as phase-I enzymes.

Phase-II enzymes act on oxidized substrates and also contribute to xenobiotic metabolism. Some phase-II enzymes are methyltransferases, acetyltransferases, glutathione transferases, uridine diphosphoglucuronosyl transferases, sulfotransferases, Nicotinamide Adenine Dinucleotide (NAD) and Nicotinamide Adenine Dinucleotide Phosphate (NADP)-dependent alcohol, aldehyde and steroid dehydrogenases, quinone reductases, NADPH diaphorase, azo reductases, aldoketoreductases, transaminases, esterases and hydrolases.

The pathways of activation and detoxication frequently are in competition, so the propensity of an individual to convert a procarcinogen to an ultimate metabolite that can bind covalently with DNA may vary strikingly. Moreover, differences in DNA-repair rates potentially influence the

extent of carcinogen–adduct formation which is the biologically effective dose and, consequently, the total amount of genetic damage that accumulates.

Historical Perspective:

Historical observations made by John Hill on nasal cancer occurrence among snuff users in 1761 and by Sir Percival Pott on scrotal cancer occurrence among chimney sweeps in 1775, revealed that human exposures to certain chemicals can be associated with the occurrence of cancer.[9]

In 1933, the first chemically pure carcinogens were isolated from coal tar pitch. These chemicals were identified as polycyclic aromatic hydrocarbons, which are composed of variable numbers of fused benzene rings. Polycyclic aromatic hydrocarbons are formed in the incomplete combustion of fossil fuels and vegetable matter and they are common environmental contaminants. The polycyclic aromatic hydrocarbons are chemically unreactive, and it was shown that enzymic metabolites of these compounds could bind covalently to cellular macromolecules.[9]

Polycyclic aromatic hydrocarbons are activated in a multi-step process involving initial epoxidation, hydration of the epoxide, and subsequent epoxidation across the remaining

olefinic bond to form the ultimate carcinogenic metabolite; a diol-epoxide that led to scrotal cancer.

Another class of chemical carcinogens, aromatic amines, was linked with increased bladder cancer among dye workers. A principal aromatic amine thought to be responsible for bladder cancer among workers in the rubber industry is 4-aminobiphenyl. This and many related compounds are components of cigarette smoke, diesel exhaust, and the pyrolysis of certain foods. In addition, nitrated polycyclic aromatic hydrocarbons are also environmental contaminants resulting from the incomplete combustion of vegetable matter and diesel fuel, and they are related to aromatic amines by nitroreduction.

Impact of Possible Chemical Carcinogens in Jaffna Peninsula:

I would like to discuss few chemical carcinogens that can play a role for the increasing burden of cancer in the Jaffna peninsula.

Nitrosamines and Nitrates:

Carcinogenic N-nitrosamines are ubiquitous environmental contaminants and can be found in food, alcoholic beverages, cosmetics, oils, rubber, and tobacco. Endogenous nitrosation

also can occur because of the reaction of an amine with nitrate alone or nitrite in the presence of acid. The N-nitrosamines are activated primarily by CYP2E1. This isozyme is inducible by alcohol.

Nitrate is potentially hazardous when present at sufficiently high concentrations in drinking water. Nitrates which could be converted into carcinogenic substances such as nitrosamines within the body are of importance in the carcinogenesis of oesophageal and stomach cancers.[8,9,12]

In the Jaffna peninsula, ground water is the main source of water for human consumption, hence any pollution of ground water resource is a matter of serious concern. Many studies have shown that water nitrate-nitrogen levels in Jaffna peninsula are above the safe level specified in the WHO International standard for drinking water (ie. above 10mgs/l)[13,14,15-17] (Fig-7 -13 and Table-3). This may be due to the mixing up of abundant nitrogenous waste matter and heavy use of nitrogenous fertilizers in agriculture with shallow ground water. It is also possible for nitrates to enter the ground water from human waste matter in the septic tanks.

Increased nitrogen in the soil also may cause serious health problems because some plants such as carrots could store this excess nitrate and then reduce it partly to nitrite within

itself.[15] These nitrous compounds can be converted to nitrosamine in the body leading to carcinogenesis.

Contamination of shallow ground water aquifer or soil in Jaffna Peninsula is a silent threat to the health of the people who consume it. Hence promoting the recommended use of fertilizers, efficient use of irrigation, continuous monitoring and quality assessment of well water are necessary to avoid health hazards to the people in this area.

The Dept. of Agriculture, Health and Water Board should jointly take responsibility in the preservation of ground water resource in Jaffna Peninsula.

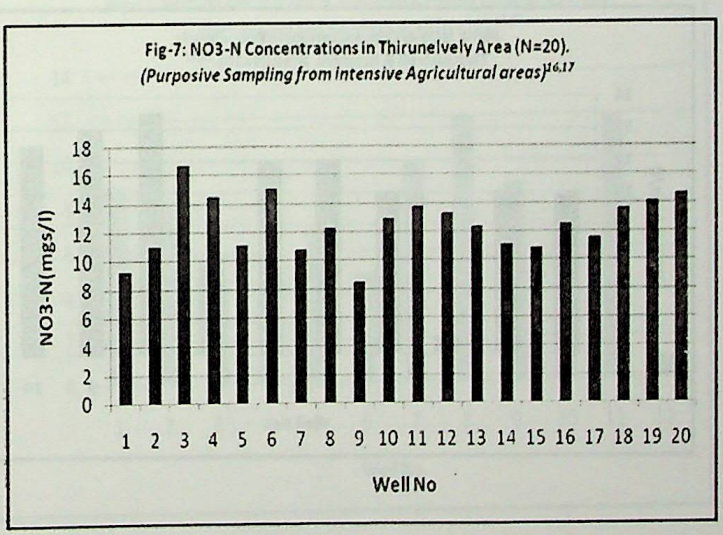


Fig-7: NO3-N Concentrations in Thirunelvely Area (N=20).
(Purposive Sampling from intensive Agricultural areas)[16,17]

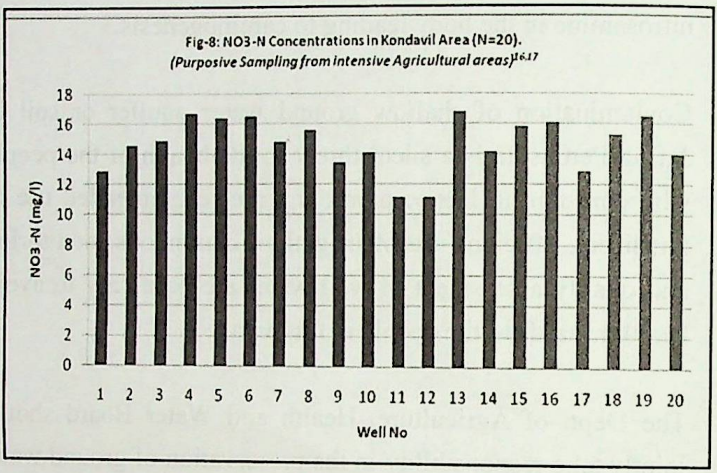


Fig-8: NO3-N Concentrations in Kondavil Area (N=20).
(Purposive Sampling from intensive Agricultural areas)[16,17]
NO3 -N (mg/l)
0
2
4
6
8
10
12
14
16
18
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Well No

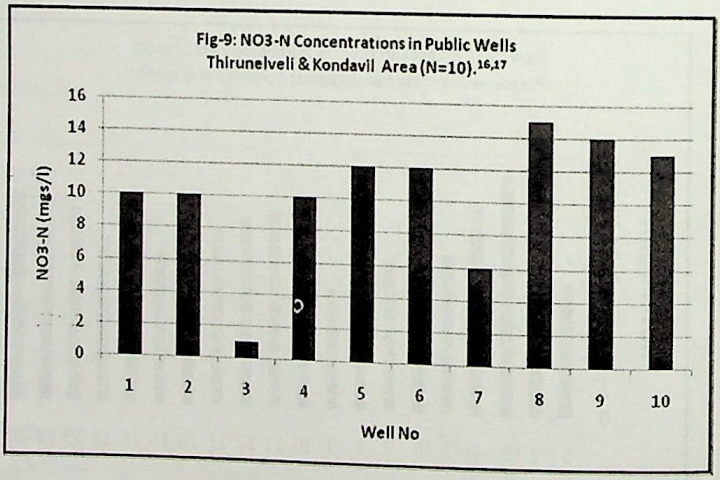


Fig-9: NO3-N Concentrations in Public Wells
Thirunelveli & Kondavil Area (N=10).[16,17]
NO3-N (mg/l)
0
2
4
6
8
10
12
14
16
1 2 3 4 5 6 7 8 9 10
Well No

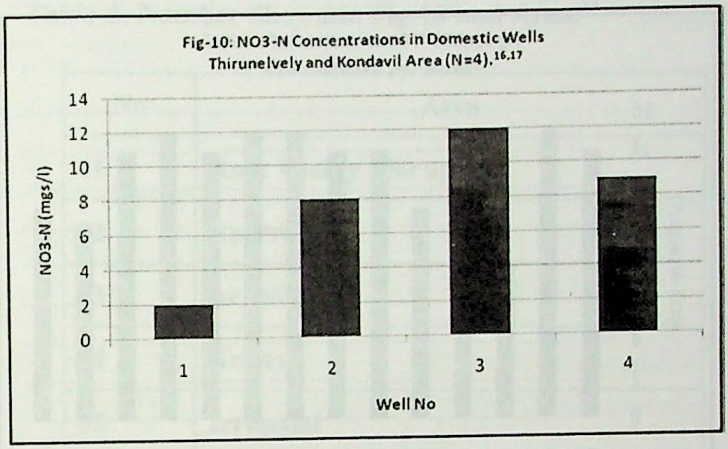


Fig-10: NO3-N Concentrations in Domestic Wells
Thirunelvely and Kondavil Area (N=4).[16,17]
NO3-N (mgs/l)
14
12
10
8
6
4
2
0
1
2
3
4
Well No

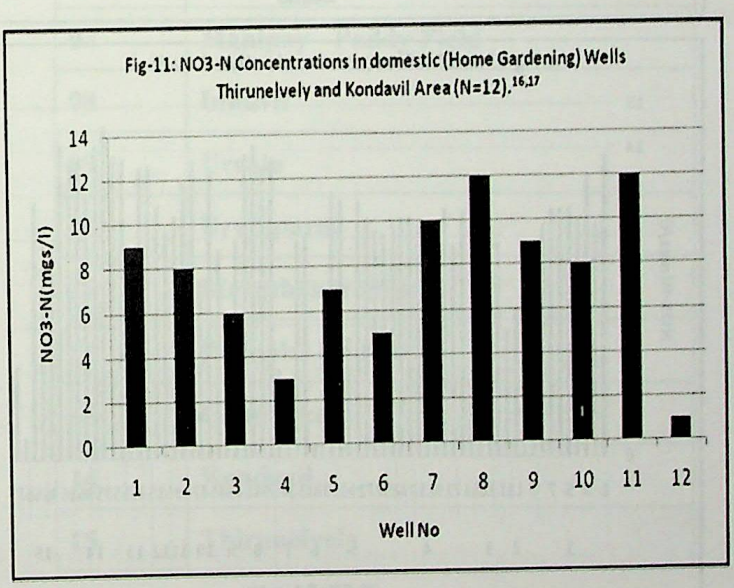


Fig-11: NO3-N Concentrations in domestic (Home Gardening) Wells
Thirunelvely and Kondavil Area (N=12).[16,17]
NO3-N(mgs/l)
14
12
10
8
6
4
2
0
1
2
3
4
5
6
7
8
9
10
11
12
Well No

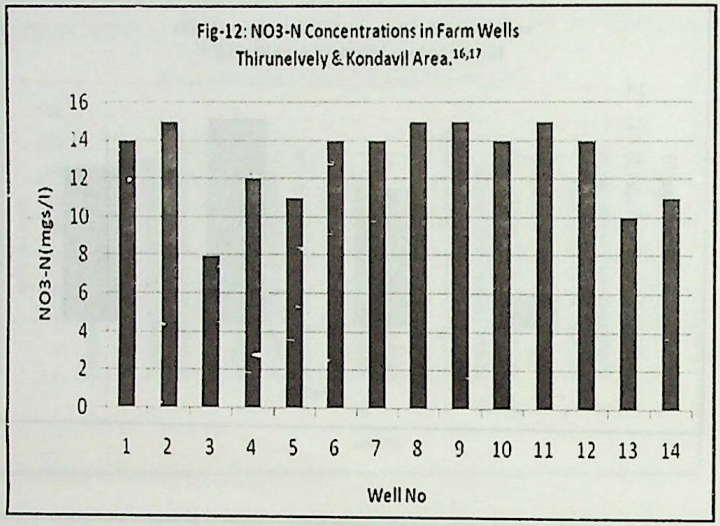


Fig-12: NO3-N Concentrations in Farm Wells
Thirunelvely & Kondavil Area.[16,17]
NO3-N(mgs/l)
16
14
12
10
8
6
4
2
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Well No

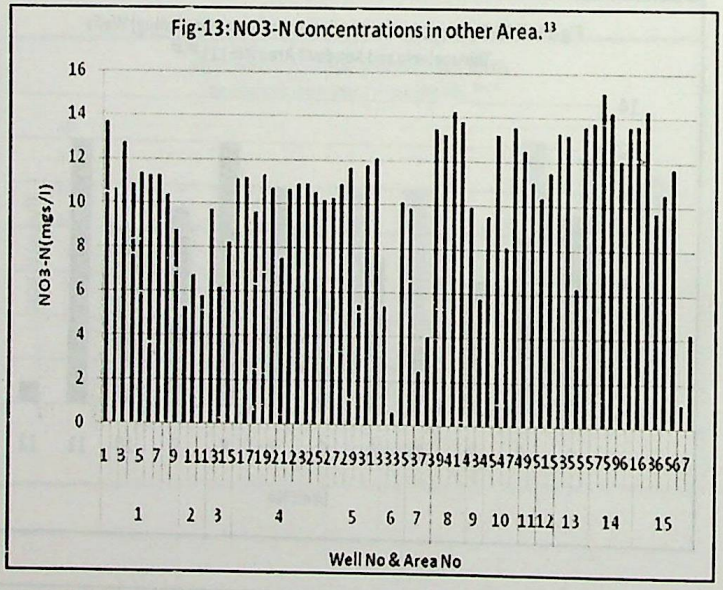


Fig-13: NO3-N Concentrations in other Area.[13]
NO3-N(mgs/l)
16
14
12
10
8
6
4
2
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Well No & Area No

Table-3: Number Shown in Fig-13 and Area.[13]

No	Area
01	Raja Veethy - Sirupiddi
02	Neervely
03	Achchelu
04	Kopay
05	Irrupalai
06	Sirupiddi - Paddy Field
07	Manipay - Paddy Field
08	Innuvil
09	Urealu
10	Urumparai
11	Maruthanarmadam
12	Punnalai Kadduvan
13	Chunnakam
14	Kondavil
15	Thirunelvely

Pesticide residues:

Possible cancer hazards from pesticide residues in food have been much discussed and hotly debated in the scientific literature. Farmers are not adhering to the regulations with regard to the use of pesticides and fertilizers. The farm products which we consume would be having pesticide residues, above permissible levels.

To assess the Knowledge, Attitude, Practice and Toxicity Symptoms with regard to the use of pesticides and fertilizers, a questionnaire based study was performed among farmers (N=212) in Jaffna district jointly by Faculty of Agriculture, University of Jaffna and Cancer Treatment Centre, Teaching Hospital, Jaffna recently.[19]

This unpublished preliminary study[19] reveals many malpractices by the farmers and also reveals that they were not well instructed about safe use of pesticides and fertilizes by the appropriate persons like those from Agricultural sectors and Health sectors.

Majority (72.6%) of farmers are doing open farm and most of them (97.6%) are using pesticides for pest control. Most of the farmers (80.7%) get the pesticides from pesticide sellers than from Dept. of Agriculture. More than half of the farmers (56.5%) use more than one pesticide at a time. Nearly a

quarter of farmers (23.1%) use the pesticides in greater concentrations than recommended.[19]

Majority of farmers (86.0%) spray on their own and spray most of the time in early mornings or in evenings. Most of the farmers (74.4%) use separate vessels for dissolving the pesticides and the rest even use the vessels used for cooking or buckets that is being used to fetch water from well.

Though no one is using the empty bottles or cans for storing food or drink, majority of the farmers (65.2%) throw the used ones. After that what happens to those empty bottles is not known.

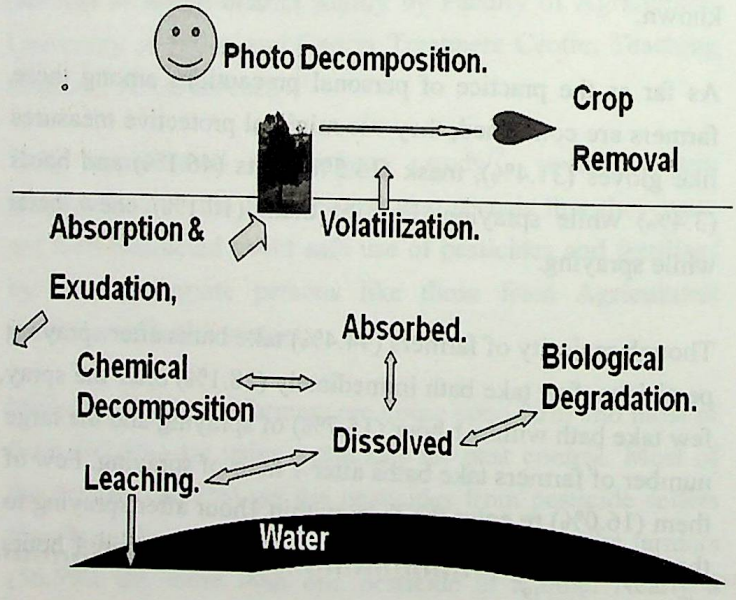
As far as the practice of personal precautions among these farmers are concerned, they use minimal protective measures like gloves (31.4%), mask (13.5%), hats (46.1%) and boots (3.4%) while spraying. Few of them (10.1%) chew betel while spraying.

Though majority of farmers (94.4%) take baths after spraying pesticides, few take bath immediately (28.1%) after the spray, few take bath within 1 hour (15.7%) of spraying and the large number of farmers take baths after 1 hour of spraying. Few of them (16.0%) re enter the farm within 1hour after spraying to the field. Just above a halve (56.6%) re enter within 4 hours after spraying.[19]

Concept of Pre Harvest Interval:

When the pesticides are sprayed to crops it acts against the pest and undergo various chemical changes within the crop and by the environmental factors (Fig- 15). After the last spray of a particular pesticide, farmers have to wait for the recommended period before harvesting so that the consumers will not get poisoned. That period is known as Pre Harvest Interval. This period usually varies from 1- 2 weeks.

Fig-15: Various processes that Pesticide undergoes after spray.



Control of Pesticide Act[20] of the Democratic Republic of Sri Lanka has a sub section about harvesting of crops. This section says: ***"No person shall harvest or offer for sale any food crops, in which pesticides have been used unless a time limit as may be prescribed by regulations has elapsed between such use and harvest, or if the food crops shall contain pesticide residues in excess of levels as may be prescribed."***

In our study[19], when the time of marketing after the last spray was analyzed, that revealed about 10% of the farmers do market on the next day of spraying. A one fifth (19.8%) of farmers, market the harvest within 2 to 3 days. About 54% of farmers do market after 4 to 7 days and only a few farmers (17%) do harvest 2weeks after the last spray. This clearly shows that the vegetables in the market will have more pesticide residues and that may have some influence in carcinogenesis.

The National Research Council (NRC) classifies chemicals that cause cancer into two groups. One is that directly affects DNA to form DNA adducts are called *Genotoxic Chemicals.* Other group is that not directly affects the DNA but through other mechanisms like hormonal effects on receptors or through toxic cell death are called *Non Genotoxic Chemicals.*[21,22]

Some agrochemicals are linked with carcinogenesis. Phenoxy acid herbicides or contaminents are linked with soft tissue sarcoma and malignant lymphoma. Organochlorine insecticides are linked with soft tissue sarcoma, Non

Hodgkin's Lymphomas, leukaemias, cancers of lung and breast. Organo phosphorous compounds are linked with Non Hodgkin's Lymphomas and leukaemias. Triazine herbicides are linked with ovarian cancers. Increased incidence of stomach cancer and Multiple myeloma are noted among farmers.

To analyze the possibility of changing the practice among the farmers in this study, we had to explore the educational levels, involvement of the Dept. of Agriculture and Health and about the participation of seminars.

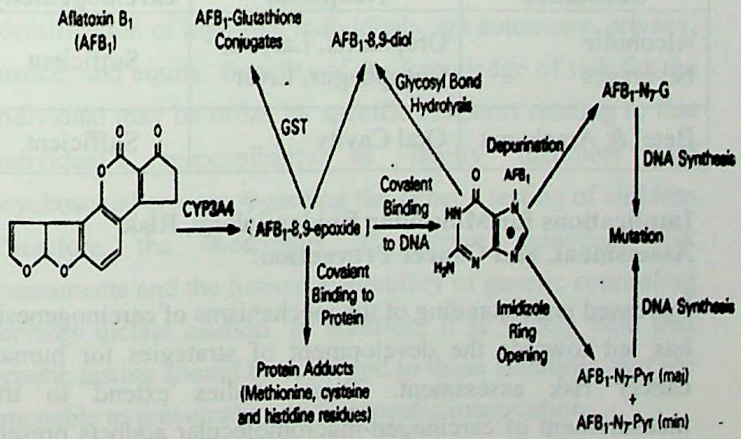
Most of the farmers (80.7%) have studied upto Ordinary Levels (O/L) or below that level. Agriculture instructors have visited only 50% of the farmers. There is not much health education especially for farmers related to pesticide and its health hazards. The participation of farmers (35.8%) in seminars arranged by the Dept. of Agriculture, Agriculture Association or by NGOs is less. About two thirds of the farmers (63.7%), have expressed willingness for organic farming while 80.6% of farmers emphasized that pesticide use in farming is a must.[19]

I believe that with the joint action of the Dept. of Agriculture, Faculty of Agriculture, Dept. of Health, NGOs and Legal bodies, these farmers can be educated to have good practices which would contribute towards a healthy life. At the same time steps are to be taken to promote organic farming, Integrated Pest Management (IPM) and pesticide free home gardening.

Aflatoxins:

Aflatoxins are metabolites of Aspergillus flavus. They are fungal mutagens that contaminate cereals, grain, nuts and palmyrah legume. In Jaffna, consumption of ground nuts and palmyrah legumes is very high. A positive correlation exists between dietary aflatoxin exposure and incidence of liver cancer in developing countries, where grain spoilage is high. More recently, urinary levels of certain aflatoxin adduct and metabolites have been correlated with incidence of liver cancer in China[9]. It also should be noted that hepatitis B virus infection independently increases the risk of liver cancer, but the effects of hepatitis B infection together with ingestion of aflatoxin are multiplicative. (Fig-14)

Fig-14: Carcinogenic effects of Aflatoxin. [9]



Other Chemicals:

We may be consuming or exposing ourselves to other chemicals that may cause cancers. With our busy life style, we may be consuming foods that have additives, colouring agents, preservatives, flavouring agents and solvents. These chemicals may enter the food during production, processing, packaging and storage.

We also use chemicals such as repellents of mosquitoes and other nuisance flies or insects. These chemicals itself or partially burnt materials of those chemicals may be carcinogenic to human.

Table-4: Chemical carcinogenic factors associated with life style.[22]

Chemical Substance	Associated Neoplasm	Evidence for carcinogenicity
Alcoholic beverages	Oropharnx, Larynx, Oesophagus, Liver	Sufficient
Betel & Arackanut	Oral Cavity	Sufficient

Implications for Molecular Epidemiology, Risk Assessment, and Cancer Prevention:

Increased understanding of the mechanisms of carcinogenesis has led towards the development of strategies for human cancer risk assessment. These studies extend to the measurement of carcinogen-macromolecular adducts present

in a target organ or surrogate and of phenotypic determinants of disease disposition.

The two facets of molecular epidemiology of human cancer risk are the assessment of carcinogen exposure and inherited or acquired host cancer susceptibility factors. The interaction between these two facets determines cancer risk.

When combined with carcinogen bioassays in laboratory animals and classical epidemiology, molecular epidemiology can contribute to the four traditional aspects of cancer risk assessment:

1. Hazard identification.
2. Dose-response assessment.
3. Exposure assessment.
4. Risk characterization.

Important bioethical considerations accompany the identification of high-risk individuals, are autonomy, privacy, justice, and equity. Benefits of the knowledge of risk for the individual may be offset by specific concerns relating to that individual's responsibility to family members and psychosocial anxiety regarding the genetic testing of children. Therefore, the uncertainty of current individual risk assessments and the limited availability of genetic counseling services dictate caution. In addition, it is widely held that genetic testing should be restricted to those situations that are amenable to preventative or therapeutic intervention.

In Conclusion, Ladies and Gentlemen.....

The increased incidence of cancer in the Jaffna peninsula may be related to the altered environment, the peculiar habits of the people in this area and any chemical adulterations of food or water. The threshold of carcinogenesis may be lowered with the presently prevailing war situation and accumulated stress among the people and consequent reduction of immunity levels. These causal agents can be minimized to a lower level by cooperative efforts with dedication on the part of many with a strong leadership and good intention towards building up a Healthy Nation!

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