

Larynx, Oesophagus and Urinary Bladder. Together cancers of the sites where tobacco is known to play a major role account for about 60% of all male and 35% of all female tumours in Karachi. If somehow the people can be persuaded to give up the use of all forms

of Tobacco a significant number of the cancer cases presently being seen in Karachi would be prevented. The medical profession has to take the lead in this direction otherwise the number of cancer cases will keep rising as the sales of tobacco products is on the increase.

Table I — PMRC Multicentre Study
The ten commonest tumours in Males and Females (1977 — 1980)

Site	Male		Site	Female	
	No.	%		No.	%
1. Bronchus	1085	9.7	Breast	2250	25.1
2. Oral Cavity	956	8.6	Oral Cavity	907	10.1
3. Hypopharynx	705	6.3	Cervix	762	8.5
4. Skin	632	5.7	Ovary	426	4.7
5. Larynx	623	5.6	Oesophagus	408	4.5
6. Lymph nodes	620	5.4	Skin	306	3.4
7. G. I. Tract	567	5.1	Hyopharynx	290	3.2
8. Oesophagus	531	4.8	Haematopoietic	241	2.7
9. Hematopoietic	520	4.7	Ill defined sites	240	2.7
10. Bones & Joints	467	4.2	G. I. Tract	236	2.6
Total No. of Cases	11,563	100		9073	100

Table II — J. P. M. C. records
The ten commonest tumours in Males and females (1977 — 1980)

Site	Male		Site	Female	
	%	%		%	%
1. Bronchus	14.2		Breast	20.8	
2. Hypopharynx	12.9		Oral Cavity	14.2	
3. Oral Cavity	12.4		Cervix	10.6	
4. Oesophagus	7.9		Oesophagus	8.0	
5. Hematopoietic	6.5		Hypopharynx	5.3	
6. Larynx	6.0		Hematopoietic	4.7	
7. Liver	3.7		Ovary	4.3	
8. Skin	3.5		Liver	3.9	
9. Oropharynx	3.5		Oropharynx	3.1	
10. Urinary Bladder	3.3		Uterus	2.8	
Total No. of cases	4193			3089	

tic cells. On the other hand these cells may remain as such or even revert to their original state.

This model of carcinogenesis has important implications for planning a rational strategy for the control of cancer. First and foremost is the realization that about 80% of all human cancers are determined by environmental factors. If the factors can be identified then efforts may be made either to completely remove them or at least reduce the level of human exposure to them. Removing or reducing the exposure to carcinogens or initiators one could block the process before it started. This is PRIMARY PREVENTION.

Primary prevention is still possible even though the first stage has taken place and transformed cells are present in the body. It can be achieved by reducing the exposure to the promoters. Simply one could prolong the period of time required for promoters to produce neoplastic cells. By reducing the dose of promoters the second stage can be lengthened from 30 to 60 years which would altogether make the age of clinical presentation the eighties or nineties. If one could totally eliminate promoters from the environment, the process of carcinogenesis could be aborted. In either case cancer would be prevented.

The idea that cancer is preventable has only recently found general acceptance but has been in practice for more than fifty years. The greatest success story of primary prevention of tumour is that of malignancies in workers handling radio-active material. As is well known the carcinogenic nature of Xrays was not known until many of the early pioneers had died of tumour. Once the carcinogenic nature of Xrays was realized stringent and effective protection measures were taken. The two factors which have made this a success story are first establishing the fact that Xrays are causally related to some forms of cancer and secondly that everyone was willing to accept stringent regulations and procedures to keep exposure below threshold level.

Before Primary Prevention can be started the initiators and the promoters have to be identified. As these agents are different for the various types of cancer the first step is to record and catalogue all the tumours seen in any given area. Thus, setting up of cancer registries is a must. Unless we are aware of the tumours occurring in our area we can not go looking for initiators and promoters. Cancer registries also help in establishing the priorities of any cancer prevention programme.

Once the priorities have been established the next step is to identify causal factors (initiators and promoters).

This is done by epidemiological studies, which again are difficult without cancer registries. After the causal factors for the common tumours of a given population have been identified ways and means of either removing these factors or at least reducing the exposure to them are devised. This is very difficult, as has been proven by recent events. The continued use of Tobacco, of various suspect manufacturing process, and certain chemicals only go to show that education of the public, government and the industrialists is not an easy task.

One of the more hopeful aspects of the carcinogenic model presented above is that TIME IS IN OUR FAVOUR. As stated above the time lag between the initial exposure to an initiator and clinical presentation is upwards of 25 years. The period available for intervention is very long. As the British doctors' and other studies have shown, the risk of Lung cancer in smokers who discontinue comes down to that of non smokers in about five years. Removal of promoters contained in cigarettes (also contain many initiators) will abort the process of carcinogenesis.

The other hopeful aspect of the prolonged time lag is that it provides an opportunity for early detection. Cancer is not something that comes up overnight. The period available for early detection is also long. If we can find ways and means of detecting transformed cells we can intervene before the process goes out of hand. Early detection of an established neoplasia also is a positive advantage in the management of a cancer case as early detection means better and more definitive treatment. This is referred to as SECONDARY PREVENTION.

In Pakistan figures on the frequency of various tumours have been made available through the multicentre study funded by Pakistan Medical Research Council. This study has provided figures from seven centres around the country for the years 1973 - 74 and then for five centres from 1977 to date. These five centres are JPMC Karachi, LMC Jamshoro, KEMC Lahore, IRNUM Peshawar and AFIP Rawalpindi. In Karachi the Departments of Radiotherapy and Pathology of JPMC has data available from 1959 onwards. Tables 1 & 2 show the ten commonest tumours in males and females in Pakistan and Karachi. Carcinoma Lung is the commonest tumour amongst the males while Breast is the commonest among females. The causative factors for Breast cancer are not well understood but that for Lung cancer are well established. Cancer Lung is causally related with cigarette smoking. In JPMC 95% of the lung cancer cases are smokers. In addition to lung cancer, tobacco is also related to cancers of the Oral Cavity, Pharynx,

SPECIAL ARTICLE

CANCER CONTROL: The Rationale

N. A. JAFAREY

Jinnah Postgraduate Medical Centre, Karachi.

The conversion of a normal cell to a neoplastic cell (CARINOGENESIS) is a multi-stage process. In the first stage various carcinogens (radiation, chemicals, viruses etc.) alter the DNA of a susceptible cell and convert it into a TRANSFORMED or altered cell. This alteration is referred to as mutation and the process as INITIATION (Fig. 1)

Figure 1

FIRST STAGE

Susceptible Host cells + Initiators = Transformed

SECOND STAGE

Transformed cell + Promoters for sufficient time and in sufficient dose = Preneoplasia

THIRD STAGE

Preneoplasia + Promoters = Neoplasia

Most of the carcinogens or initiators are in the environment around us and their action is episodic and of a short duration. The future of these transformed cells

depends on whether they remain capable of reproducing or die out. If they are able to reproduce then a group or a colony of such transformed cells is formed. The important thing to remember is that all cells are not susceptible to all the carcinogens and even if susceptible the degree of this susceptibility varies from species to species and from one cell type to another cell type. Secondly the number of cells which are transformed will depend upon the dose.

In the second stage various substances called as PROMOTERS help the transformed cells to continue to proliferate and eventually become neoplastic. Here again most of the promoters are in the external environment although some, like a few hormones, are within the body. Unlike the initiators the action of promoters has to continue for a long period of time and is dose dependant, i.e. the higher the dose the shorter the time and vice versa. Secondly the promoters are incapable of producing neoplasia on their own. They can only do so by acting on cells transformed by carcinogens. Experimental and epidemiological evidence suggests that in most human cancers the period between initiation and clinical appearance of a tumour is between 20 and 30 years. In other words the cancer that is seen by the clinician at the age of 50 years was in all probability initiated in the late teens or early twenties. This is the major reason why it has been so hard establishing the connection between the exposure which caused the initial change and the disease which occurred so many years later.

There is considerable evidence that before the transformed cells become neoplastic they show changes of what has been called PRENEOPLASIA. Continued action by promoters converts the preneoplastic cells to neoplas-

Received for publication on 5.2.85

Requests for reprints to Professor N.A. Jafarey, Professor of Pathology, Jinnah Postgraduate Medical Centre, Karachi.