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CONTENTS

CANCER IN DEVELOPING COUNTRIES ITS PREVENTION AND CONTROL

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Summary

According to WHO statistics, 5.9 million new cases of cancer are reported annually, more than 3 million of these are in developing countries. Cancer is responsible for 4.3 million deaths yearly, 2 million of which occur in developing countries. We should add that, considering the lack of cancer registery this data is probably under estimated. Cancer of the breast, lungs, liver, buccal cavity and cervix are the most common. In cases of cancer, prevention is the best cure. Prevention has three levels, the first called "Primary Prevention", is prevention of cancer itself, and this involves life-style change i.e. avoidance of smoking etc. The second and equally important level of cancer, prevention termed "Secondary Prevention", consists of ways of preventing the consequences of the diseases once it has started. This means early detection through screening for cancer. "Tertiary" level of cancer prevention has also assumed a large role in the management of cancer problem. Treatment of cancer whether by surgery, or radiotherapy produces physical as well as emotional problems for the patient. Anticipating and handling these problems adequately in time prevents many of the complications.

Introduction

Cancer is becoming an increasingly serious problem all over the world. In the developed countries, communicable diseases have been already controlled and populations are showing a marked demographic aging so that more people live longer and develop cancers in middle and old age. The developing countries, have other health priorities-communicable diseases, malnutrition, rapid populations growth-and a relatively young age structure of their populations. Nevertheless, in absolute numbers there are now more cases and more deaths from cancer in the developing than in the developed world.

Recent studies by the Pakistan Medical Research Council in collaboration with WHO have identified the pattern of cancer in the country as ranging through the whole scale, from lung cancer and lymphoma to breast, skin and throat cancer. Several environmental factors have been implicated, such as pollution and industrial carcinogens, personal habits like smoking and chewing betel nut. Alarmingly, 100,000 new cases are estimated to occur each year in Pakistan, and even more alarmingly, diagnostic and therapeutic facilities for cancer patients are surely deficient, and where available, extremely expensive.

In this country, public awareness about any disease precesses is minimal; cancer is invariably diagnosed at a late stage, rendering treatment both difficult and costly. Whereas some cancers respond better to therapeutic measures, in others management can be pragmatical. According to many studies, as many as 80% of cancers are actually avoidable. Cigarette smoking, for example. with its corollary lung cancer, accounts for 30% of all cancer deaths. With available knowledge it is estimated that one third of all cancers can be prevented. Another one third of cases can be cured if existing methods of early diagnosis are used.

In the mid 1970s the commonest form of cancer world-wide (excluding skin cancer) was cancer of the stomach (about 0.7 million new cases per year), followed by lung cancer (0.6 million cases).

But since stomach cancer incidence is generally decreasing and lung cancer is generally increasing, by now lung cancer may well account for far more deaths than any other neoplastic disease. At present, of course, the lung cancer deaths chiefly occur

in the developed countries, where prolonged cigarette smoking is common. Although smoking has been spreading very rapidly in the developing countries, this has happened only recently. So the developing countries can expect vast numbers of lung cancers in the next century, unless drastic measures are taken to curb smoking.

BACK GROUND STATISTICS OF PAKISTAN

Main Indicators

Total population	115.00 millions
per capita G.N.P.	$300 approx.
Access to Health Services (% of population)	85%
Life expectancy at birth (Years)	61
Urban population	28%
Literacy rate	26.2%

CURRENT HEALTH SCENE IN PAKISTAN

The disease pattern indicates an increase in hypertension, heart diseases, metabolic disorders, accidents, mental diseases, gastrointestinal diseases and cancer, the most deadly disease.

The morbidity due to cancer is estimated at 6 - 65 per 100,000 or high.

Available evidence indicates that incidence and mortality from cancer have been increasing and will continue to increase in the future.

In Pakistan knowledge about cancer is lacking. Ignorance has very harmful effects on human civilization. It is the root cause of all the evils and ills. The latest figures show that 72% of our population is illiterate and ignorant. They are not well-informed about the modern concept of health and about what is available in their community for prevention, diagnosis and treatment.

The Government has provided health facilities upto 85% of population. But unfortunately due to ignorance these services are grossly under-utilized. Due to illiteracy, ignorance, lack of information and education, the over-whelming majority of our population is victim of mythical and magical thinking.

Table 1: **Statistics of Health Facilities in Pakistan**

Facility	No's
Basic Health Units	3496
Rural Health Centres	492
MCH Centres/Dispensaries	6050
Hospital Beds	63619
Doctors	360000
Nurses	10000
Paramedicals	65000
T.B.A.	45000

Source : Planning Commission of Pakistan

Fatalistic Attitude

The fatalistic beliefs and attitude is another reason for the delay in seeking help or ignoring it. In our society and among other Muslims societies of the world, the elements of fatalism has a strong hold and we have a very fatalistic view of the future. Some of our people are fully aware of that although there is a risk associated with certain types of behaviour but they refuse to change their behaviours because they believe fatalistically and consider that the risk cannot be reduced because all happenings are due to the out come of good or adverse fate, our public is anesthetized by fate and traditions.

People use fatalistic arguments, for example urging that if you are going to die from cancer you will die from it even if you do not smoke, so smoking cannot be harmful. Fatalistic tendency prevent people to, go to the doctors clinic and to take early action. If one sees himself in control of his life situations, he can be motivated to improve his existence, to conquer disease but if he resigns himself at the hand of fate, he cannot be induced to seek a higher standard of living.

It is therefore very necessary that the public should be informed that:

(a) Cancer is a preventable diseases.
(b) Cancer is a curable disease when detected early.
(c) It is the responsibility of the Community to fight against it.

Table 2: **Ten Commonest Cancer in Male (Pakistan)**

	Men	%
1.	Lung	12.7
2.	Lymphoma	8.5
3.	Mouth	7.9
4.	Urinary Bladder	5.5
5.	Intestine	5.3
6.	Larynx	5.2
7.	Skin	5.1
8.	Throat	4.6
9.	Leukemia	4.4
10.	Bones	3.8

Table 3: **Ten Commonest Cancer in Female (Pakistan)**

	Women	%
1.	Breast	26.1
2.	Mouth	8.3
3.	Cervix	6.8
4.	Ovary	6.0
5.	Lymphoma	4.3
6.	Skin	4.0
7.	Oesophagus	3.7
6.	Urinary Bladder	3.4
7.	Intestine	3.4
8.	Throat	2.8

The above figures are based upon 4277 male and 3462 female cases registered at four centres in the country - Jinnah Postgraduate Medical Centre, Karachi, Liaquat Medical College, Jamshoro, King Edward Medical College, Lahore and the Armed Forces Institute of Pathology, Rawalpindi. These 7739 cases represent an approximate 7.7.% sample of the estimated 100,000 new cases that occur in Pakistan each year.

Table 4: **Estimate of Preventable Cancers (1980)**

Association	Site	Incidence	Preventable
Cigarette smoking Alcohol Industrial Exposure	Lung & Larynx	90,000	80,0000
	Head Neck & esophagus	13,500	8,500
	Bladder	9,000	5,000
Site	Breast	30,000	10,000
	Colon	30,000	10,000
Sex	Cervix	7,500	7,500
Sunlight	Melanoma and other skin tumor	5,000	1,500
Total :		185,000	122,500

USA National Cancer Institute Data Source (Schneiderman).

Prevention of Cancer

Cancer research now reveals that possibly 80% of all cancers may be prevented by adopting a cancer-resistant life-style.

Primary Prevention

The external influences or risk factors are more varied and complex as shown by the following paragraphs, these should be avoided. The following are some of the factor which influence the incidence of cancer.

1. The geographic areas of the world in which a person lives is a determining factor due to physical and cultural practices. In some parts of the world, the soil may be high or low in selenium. If the selenium level in the soil and diet is low, an increased or decreased amount of selenium in food may affect the occurrence of cancer.

   The diet of a country may include little or no meat and lot of vegetables and grain and this might reduce colon cancer. In some countries a specific cultural pattern, such as betel nut chewing in India and Pakistan can increase the cancer rate.

2. *Specific Cultural and Religious Practices* relate to cancer, prevention and incidence. Early or late marriages, age at first pregnancy, monogamy, the number of sexual partners, sexual hygienic and the dietary patterns can all play a part in cancer and cancer prevention.

3. *Occupational Risks* relate to specific groups of people, who are exposed to agents such as asbestos, silver, nickle, cadmium and uranium. Although specific exposures do seem to promote cancers, industrialization as a whole is not correlated to the patterns of cancer incidence. An example is Japan where incidence of cancer did not change with its industrialization.

4. *Viruses Play* a part in the risk of cancer. We now know of many viruses that are associated with tumor production both benign and malignant. Methods for combating the action of the virus may be aimed at stimulating the immune response.

5. *Diet A Definite Relationship has been established* between cancer and a high-fat diet. A diet high in fat (especially beef or pork) has been associated with an increased risk of breast, colonrectal, ovarian, endometrial, prostate, pancreatic and renal cancer. A diet high in fiber, conversely, seems to have a preventive influence on colon cancer. Vitamins may play a protective role including Vitamin A. A betacarotene which may reduce or partially control cell growth, Vitamin C, which can neutralize nitros aminse and Vitamin E and selenium which act an anti-oxidant agents. All of these may help to protect cells from becoming malignant. Epidemiological studies have shown some interesting cases in terms of nutrition and the development of human cancer. In Japan a study was carried out about the protective role of diet. This study was done by Hira Yamaha of Japan. The study was carried out from 1966 to 1981. The following points were deduced from this study; positive nutritional advise i.e. asking the people to add some beneficial food in the diet is more effective in preventing the stomach cancer rather than negative Nutritional advise i.e. asking the people not to eat a particular things. In this study it was found that incidence of cancer of stomach decreased by the use of green vegetable and certain other vegetable which contain beta-carotene.

6. *Hormones* such as estrogen, as well as other chemicals and medications have been associated with cancer.

7. *Smoking Tobacco* is clearly identified as one of the most important factor causing cancer (Lungs, bladder, oral pharyngeal esophageal, Laryngeal, Pancreatic and possible renal). The evidence is clear at least 30% of all cancers are due to smoking and to tobacco related, including chewing and snuffing.

8. *Alcohol* is a factor in approximately 2% to 4% of cancer, Usually those of the head and beck area and of the liver. The risk factor of alcohol is markedly increased by smoking.

9. *Psychologic States* can have a biochemical effect on our body, releasing certain hormones, increasing heart rate, respiratory rate and tightening of muscles. It has not been shown that cancer is a stress related disorder, but stress can result in an impaired immune response, as measured by laboratory tests which could effect a cancer growth rate. Behavioural factors or life style can influence cancer risk directly by affecting immune competence and also in part, by determining whether one smokes or not, which will alter a person's cancer risk. The evidence is week that stress can cause cancer or that there is a cancer prone personality. It is our choice as how we live and or abuse our body that results in the life style/behavioural cause of cancer.

10. *Sunlight and Other Ultraviolet Exposure* the skin cancer both squamous cell and more dangerous melanomas are likely to occur due to ultraviolet rays of sun. Those with fair skin are at higher risk. The risk can be reduced by appropriate use of a sun cream. The essential treatment of skin cancer is prevention. The causes are known and can be avoided and protective measures adopted but to be completely effective these must be taken before any exposure of objective skin changes are present.

11. *Radiation Exposure* can also be a factor; cancer is a health risk from low dose ionizing radiation. Over a lifetime the total dose from background exposure (0.1 rad per year) is added to medical radiation (0.08 rad per year)

to add up to about 14 red average life dose. The increased risk is when the lifetime cumulative dose exceeds 40 to 50 rad thus we need not fear normal low level radiation exposure. The exceptions are fatal injury during X-Ray filming and occupational hazards. Radiologist, X-Ray technicians when possible try to limit the amount of radiation exposure when taking X-Ray films by using lead apron shields. Early diagnosis will not only improve the progress but also reduce risk of complication. It is like stamping out the "Spark" rather than calling the fire brigade to put out fire. The early diagnosis of cancer is developing countries is a big problem and it is due to sociological and cultural back ground of the population. The most important thing in our country seems to be ignorant of the concept of cancer. Every mean and media including T.V., radio etc., should be used for communication and information for the people.

Book let on self examination of breast and others should be distributed in the communities will be one of the spot measures but this is a timed approach when may be and improve upon. This may be the goal of our cancer control society.

Seven Warning Signals

1. Change in bowel or bladder habits.
2. A sore that does not heal.
3. Unusual bleeding or discharge.
4. Thickening or lump in breast or elsewhere.
5. Indigestion or difficulty in swallowing.
6. Obvious change in wart or mole.
7. Nagging cough or hoarseness.

If you have a warning signal, see your Doctor immediately.

Secondary Prevention

In recent years another area of development which has reduced the mortality of cancer is early detection. Whenever and where-ever preneoplastic change occur and early cancer can be detected steps taken to prevent its further progress through early treatment. This is secondary level of cancer prevention.

It is estimated that up to one-third of cancers are curable if they are detected early enough, though this is of little immediate relevance of many developing countries, where screening costs m... prohibitively high.

Cancer of the uterine cervix has been sh... several developed countries to be largely am... to secondary prevention, through screeni... grammes. It is the commonest form of c... the developing countries and is a major ... death in Latin America & the Caribbean ... Screening programmes can be beneficial in ... tries which have the resources to run them ... provide follow-up treatment of cases wh... detected. But they are difficult to implement ... developing countries, which lack the necessary organization, technical skills and resources.

Oral cancer can to some extent be controlled by screening, owing to the slow progression of the precursor lesion, leukoplakia. Up to 15 years may elapse before a lesion turns malignant, and thus there is plenty of time to detect and treat cases. This is not generally done, however, and oral cancer is one of the commonest types of Cancer in many developing countries.

Breast cancer is the commonest type of cancer among women in the developed countries, and the second most common type in the developing countries. It can be detected early by self examination (which must be taught) or by mammography. But there is still some uncertainty as to what such programmes could offer in developed countries, and in view of the costs of support services they are unlikely to be of much immediate relevance in the developing countries.

Screening procedures are technically difficult, inconvenient for the patient and expensive. Screening programmes are not generally advocated even in most advanced countries and would be even less appropriate in the developing countries. An exception is Japan, which has developed sophisticated screening methods and where the very high prevalence of the condition appears to make screening worthwhile.

GENERAL GUIDELINES

For Reducing Cancer Risks

Diet :

1. Reduce consumption of red meat and animal fats.
2. Avoid obesity; Keep trim and fit.

3. Increase consumption of foods with vitamins A (BETA-CAROTENE), C, E, minerals Zinc and Selenium.
4. Increase proportion of basic whole foods in your diet, such as grains fresh fruits, and vegetables, increase intake of fibers.

Life-Style :

1. Do not smoke.
2. Stop alcohol; in take.
3. Do not drink and smoke together.
4. Reduce stress or practice stress management.
5. Protect yourself from sexually transmitted viruses.
6. Use care in taking medications and hormones.

Environment

1. Avoid excessive exposure to sunlight or use a sunscreen.
2. Reduce or control exposure to know chemical careiogens and industrial asbestos with protective techniques.
3. Avoid using dangerous or carciongenic chemicals whenever possible.
4. Help enact legislation to establish clean air and water standards.

Tertiary Prevention

Disability limitation is halting the disease process by instituting adequate treatment and therapy to limit the disability. Rehabilitation is combined and coordinated use of medical, social, educational and vocational measures for training and retraining the individual to the highest possible level of functional ability (WHO), i.e. to live and work with in the limit of his disability to the hilt of his capacity.

Tertiary level of cancer prevention has also assumed a larger role in the management of cancer problem. Treatment of cancer whether by surgery, or radiotherapy produces physical as well as emotional problems for the patient. Anticipating and handling these problems adequately in time prevents many of the complications. Thus a mastectomy patient needs exercise to bring back the functions of the arm as well as psychological support. Failure to do will result in a physically handicapped person even the cancer has been cured. Other examples of this type to prevention are the aftercare of colostomy opening, speech retraining after laryngectomy and rehabilitation of the amputee.

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CONSANGUINITY AND OFFSPRING MORTALITY IN SIALKOT (PUNJAB, PAKISTAN) POPULATION

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Consanguinity data were collected in 1037 marriages from Sialkot City, Punjab (Pakistan). Of these 51.76% marriages were inbred parallel and cross-first cousin marriages were represented in this population. The coefficient of inbreeding (F) calculated for the present generation was 0.0264. Postnatal offspring mortality shows significant trends with increasing consanguinity.

Introduction

Inbreeding leads to increase in homozygous recessive lethal genes in offsprings and likewise there will be an increase in genetic load. This results in higher mortality and morbidity among the offsprings of consanguineous unions. Pronounced effects of inbreeding on mortality among offsprings of consanguineous unions than non-consanguineous unions were reported in the populations of Pakistan (1 - 7). India (8,9), and Japan (10). Effects of consanguinity on the continuously variable characteristics in a study by Morton (12) demonstrated significant increase in weight height and chest girth with inbreeding. Magnus et al (13) reported significant decrease in birth weight in Norwegian population, among offsprings from consanguineous marriages than controls.

This paper presents parental consanguinity effects on offspring mortality in a population from Sialkot city, Punjab, Pakistan.

Materials and Methods

The present study is based on 1037 marriages from the population of Sialkot. A door to door survey was carried out to collect information by interviewing the subjects. The information collected includes age at marriage of husband and wife, time taken to first pregnancy, total pregnancies, abortions, stillbirths, livebirths and postnatal offspring mortality.

Results

Sialkot population is constituted mainly of first cousin and bradari unions. The lowest representation is that of second cousin unions. (Table 1).

Wives in first cousin unions are slightly younger than in unrelated unions, but are not significantly different from the latter. The husbands in first cousin marriages are significantly younger than unrelated ones ($P < 0.40$). Mean age differences among unrelated spouses is significantly large compared to first cousin spouses ($P < 0.02$). The first cousin unions take long time in first conception compared to unrelated parents, but the difference between the two is not significant ($P > 0.40$) (Table 1).

Table 2 gives consanguinity effects on offspring mortality in parental relationships. Higher abortion rates in first cousin parents are not significantly different from those in unrelated unions. Stillbirths are fairly equally distributed in all the parental relationships. High mean postnatal deaths are observed in offspring from double first co- and first cousin unions. Deaths of offspring from first cousin parents ($P < 0.01$). Total deaths of offspring from first cousin unions are significantly higher compared to those of unrelated parents ($P < 0.01$).

Live births, total surviving and total pregnancies are highest in first cousin couples and baradari distant marriages. These are not statistically significant compared to those in unrelated unions.

Table 1. **Proportions of parental relationships(p), mean maternal age (MA), paternal age (PA), differences in maternal and paternal ages (M-P), mean time taken in first conception (FP).**

Parental Relationships

Item	D1C	1C	1-1/2C	D2C	2C	BDR	B	U
p	0.0057	0.3008	0.0202	0.1890	0.0019	0.0771	0.2681	0.1369
n	6	312	21	196	2	80	278	142
MA	20.33	19.61	19.09	19.49	-	19.50	19.76	19.93
	±	±	±	±		±	±	±
	2.11	0.20	0.84	0.25	-	0.35	0.22	0.35
PA	23.66	24.39	25.57	23.84	-	25.05	24.89	25.60
	±	±	±	±		±	±	±
	2.11	0.29	1.86	0.38	-	0.54	0.35	0.45
M - P	3.33	4.91	6.42	4.76		5.70	5.35	6.02
	±	±	±	±		±	±	±
	0.92	0.23	2.09	0.32		0.46	0.29	0.39
FP	0.83	1.62	1.52	1.71	-	1.41	1.63	1.51
	±	±	±	±		±	±	±
	0.16	0.07	0.25	0.09		0.09	0.09	0.09

D1C - double first cousin; 1C - first cousin; 1-1/2 C - first cousin; once removed ;
D2C - double second cousin; 2C - second cousin; BDR - bradari distant relation;
B - bradari relation; U - unrelated

Table 2 gives consanguinity effects on offspring mortality in parental relationships. Higher abortion rates in first cousin parents are not significantly different from those in unrelated unions. Stillbirths are fairly equally distributed in all the parental relationships. High mean postnatal deaths are observed in offspring from double first cousin and first cousin unions. Total deaths of offspring from first cousin unions are significantly higher compared to those of unrelated parents ($P < 0.01$).

Live births, total surviving and total pregnancies are highest in first cousin couples and baradari distant marriages. These are not statistically significant compared to those in unrelated unions.

There is an equal representation of parallel and cross-first cousin marriages in this population. Out of four first cousin marriages brother-brother and sister-sister unions are popular (54.80%).

Table 3 shows deaths of children during different periods of life. During first month after birth, first year after birth deaths among the offsprings of first cousin and unrelated parents are not statistically significant, but reaching 10+ years of age children show highly significant deaths in double first cousin marriages compared to unrelated ($P < 0.001$) and first cousin unions compared to unrelated parents ($P < 0.01$).

Discussion

The present population is constituted of 51.76% of consanguineous marriages and 30.08% of first cousin marriages. In other populations of Punjab

Table 2. **Mean abortions (A), stillbirths (SB), prenatal deaths (PD), postnatal deaths (Pt.D), total deaths (TD), livebirths (LB), total surviving (TS) and total pregnancies (TP) in parental relationships.**

Item	Parental Relationships							
	D1C	1C	1-1/2C	D2C	2C	BDR		U
A	-	0.15 ±	-	0.13 ±	-	0.20 ±		0.119 ±
	n 1	47	2	25		16		17
SB	-	0.035 ± 0.01	-	0.035 ± 0.016	-	0.05 0.02	0.02	- ± -
	n 1	11	1	7	-	4	10	1
PD	-	0.18 ± 0.14	-	0.16 ± 0.04	-	0.25 ± 0.11	0.13 ± 0.04	0.13 ± 0.04
	n 1	58	3	32	-	20	37	18
Pt.D	1.33 ± 0.67	0.625 ± 0.064	0.47 ± 0.15	0.46 ± 0.06	-	0.42 ± 0.12	0.42 ± 0.05	0.41 ± 0.06
	n 8	195	10	90	1	34	117	58
TD	1.50 ± 0.83	0.81 ± 0.20	0.62 ± 0.29	0.62 ± 0.11	-	0.67 ± 0.23	0.55 ± 0.09	0.53 ± 0.11
	n 9	253	13	122	1	54	154	76
LB	3.38 ± 1.22	4.34 ± 0.15	3.85 ± 0.48	4.16 ± 0.18	4.00 ± 1.00	4.41 ± 0.30	4.06 ± 0.15	4.00 ± 0.24
	n 23	1355	81	816	8	353	1130	568
TS	2.50 ± 0.72	3.72 ± 0.13	3.38 ± 0.43	3.70 ± 0.16	3.50 ± 0.50	3.98 ± 0.26	3.64 ± 0.13	3.59 ± 0.21
	n 15	1160	71	726	7	319	1013	510
TP	4.00 ± 1.26	4.53 ± 0.16	4.00 ± 0.47	4.32 ± 0.18	4.00 ± 1.00	4.66 ± 0.32	4.19 ± 0.15	4.12 ± 0.23
	n 24	1413	84	848	8	373	1167	586

"KUSHTA" OF MERCURY AND DAMAGE TO KIDNEY - AN EXPERIMENTAL STUDY

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Summary

An experimental toxic nephropathy has been induced in Wistar rats using an indigenous preparation of mercury known as "Mercury Kushta". Proteinuria and associated renal lesions glomerular and tubular, of variable severity were observed in the animals on kushta feed those injected with sodium salt of mersalyl acid.
This experimental model shows that an immune complex disease can be produced in animals after repeated prolonged use of "Mercury Kushta". These lesions are identical to those seen after a prolonged use of mercurial diuretics in rats. The harmful effects of "Mercury Kushta" on human kidneys ultimately leading to significant damage and clinical disease is quite evident from this experiment. The practice of prescribing these "wonder drugs" for the remedy of most of the times irrelevant problems, particularly as "sex or muscle tonic" needs to be discouraged by proper health education and better awareness of the people.

Introduction

Mercury compounds, like other heavy metals, such as gold, arsenic, iron, bismuth etc. have been used as therapeutic agents, most frequently in the form of mercurial diuretics, mercury containing skin ointments and bleaching creams which are known to manifest both nephrotoxic (1) and neurotoxic effects (2). Amongst the nephrotoxic effects the most commonly observed changes were acute tubular necrosis (1,3) and progressive renal lesions (4,5,6,7) which can result in the clinical picture of nephrotic syndrome. These authors also observed that the most remarkable change in the kidney of mercury toxicity was the renal tubular epithelial cell degeneration in the form of granular or vacuolar changes. All, these renal changes are associated with variable albuminuria.

Although mercury compounds are no longer in use as diuretics or as mercury ointments, in Into Pakistan subcontinent it is still being dispensed as oxide in powder form, which is used as an oral therapeutic agent popularly known as "Mercury Kushta". It is mainly prescribed for acute chest infection, asthma, pain in chest, chronic upper respiratory infection and backache.

This form of mercury is prescribed either in daily doses or on alternate days for a period of 4 to 12 weeks. The exact amount of each dose is not standardised, however, a roughly estimated dose equivalent to the size of rice grain is prescribed containing about 5 mg of mercury) (8,9). Although this form of mercury is fairly expensive, it is considered as an effective oriental (Auyervedic) medicine in this part of the world.

The idea of designing the present experiment came to us, when we studied the renal functions, and a renal biopsy from a patient who came with the clinical features of nephrotic syndrome following prolonged (12 weeks) intake of mercury kushta. The purpose of this experiment therefore is to describe the renotoxic effects of "Mercury Kushta" and compare them with the lesions produced after repeated injections of Mersalyl (a mercurial diuretic containing 5 mg mersalyl acid and theophyllin in water) which once was used as a popular diuretic.

Animals

A total of 48 wistar rats were used as experimental animals. The average weight of the animals

at the commencement of the experiment was 150 grams.

Khushta Feed Preparation

Mercury Kushta (an oxide of mercury) was purchased as a patent preparation from a reputed oriental drug manufacturer in Pakistan. It was chemically analysed at the Pakistan Council of Scientific and Industrial Research Laboratories and reported to contain 75 percent of mercury. The kushta was mixed and homogenised with rat diet which was reconstituted into palettes. They were prepared in such a way that each palette contained 0.25 mg of mercury.

Schedule of Kushta Feed and Injections

Group A: Twelve male rats were included in this group. During the course of feeding each rat was isolated in small wire cage for nearly 3-4 hours. As the feed container was projecting out, the waste could be collected into a plastic container, from where it was weighed for exclusion from the initial of the palettes. Each animal was fed on two palettes containing 0.50 mg of mercury. On the average a total of 0.25 to 0.30 mg of mercury was ingested by each rat (this dose was calculated according to Kg, of body weight from the dose prescribed for human patients). This procedure was repeated twice a week for a period of six weeks.

Group B: Each of the twelve animals received a single dose of 250 mg of bovine serum albumin (BSA) per Kg of body weight using the intravenous route. On the 11th day each animal received 0.30 mg of mercury in Kushta palette by the oral route as in group A. This dose was repeated twice a week for a period of six weeks.

Group C: Each of the 12 rats received 0.2 ml of sodium salt of mersalyl acid (Injection Mersalyl was diluted to 1 : 10 ml) using the intramuscular route at weekly intervals for a period of six weeks.

Group D: Twelve animals received only sterile normal saline by intramuscular route alongwith normal rat diet.

Group E: Each of the 12 rats received 1.0 ml of sodium salt of mersallyl acid (Injection Mersalyl was diluted to 1 : 10 ml) using the intramuscular route daily for three days.

Urinary Protein Estimations

Urinary excretion of proteins was estimated at weekly intervals for a period of sixteen weeks. The urine samples were collected by keeping the rats in metabolic cages for 24 hours. During this collection of urine the animals were allowed only water to drink. Proteinuria was estimated using biuret method.

Processing of Tissue

The renal tissues removed at the time of termination of the experiments were fixed in 10 percent formal saline. They were dehydrated in ascending grades of ethanol and cleared in xylene. Paraffin blocks were made. Sections 3-4 micron thick were cut and stained with hematoxylin - eosin, periodic acid Schiff reaction and methenamine silver stains.

Results

Urinary Proteins

Proteinuria was observed in all the test groups of animal i.e. group A, B, C and E. It was maximum in all group B animals; whereas group A and C showed slightly lesser amount of urinary protein excretion in 11 and 10 animals respectively. The remaining one animal in group A and two in group C did not show any proteinuria. all the animals in group E developed proteinuria of moderate severity followed by their death by the end of fifth day. The control group D rats remained free of any significant proteinuria.

Morphological Appearances

Microscopic features observed in various groups of animals revealed that all the three groups i.e. A, B, and C showed almost identical changes both at the glomerular and tubular levels. However, animals in group B showed relatively more marked damage than in the other two groups. In group A and C animals the glomeruli showed a mild to moderate irregularity of the basement membrane with the presence of a few methanamine silver positive epithelial projections. A mild cellular proliferation was observed in about 10 percent glomeruli involving mainly the mesangial cells. The proximal convoluted as well as the distal tubules showed cytoplasmic granular degeneration of their lining epithelial cells. Some tubules at both these levels contained hyaline casts in their lumens. In group B all those changes were observed in a more severe form. The glomeruli after methenamine sil-

ver stain showed numerous silver positive epithelial projections. A more severe granular degeneration was observed in the cells of the distal portion of proximal convoluted tubules. In group E all the animals showed a marked degree of necrosis of the proximal as well as distal convoluted tubules; whereas the glomeruli were normal in structure. The interstitial tissue and the blood vessels were free of any remarkable change.

Discussion

Toxic effects of mercury and its compounds are known and are well documented. They are both neurotoxic (10, 11) ; and renotoxic (11, 6, 12, 13) in nature. Amongst the nephrotoxic effects the most commonly observed changes are acute tubular necrosis (14) and progressive renal failure (6).

In the present experiments both oral and injectable preparations of mercury have resulted in renal tubular as well as glomerular lesions. These changes were more marked in group B of the animals which underwent BSA - induced acute serum sickness phase prior to the administration of mercury preparations. The renal lesions observed in group A and C animals as the results of oral and injectable preparations of mercury respectively i.e. Mercury Kushta and Mersaly1 acid were less marked compared with group B animals. These results indicate that the oral preparation of Mercury Kushta like Mersaly1 acid (a patent preparation) can definitely produce a progressive renal lesion recognised by glomerular mesangial cellular proliferation, the presence of immune complexes, and renal tubular necrosis. These lesions are morphologically identical to those described in animals (15, 10), as well as in human cases (16, 17, 18).

The mechanism by which mercury salts induce renal lesions is not clear. However, it has been observed that mercury has a special affinity for kidney. Based upon this observation, it has been suggested that in acute poisoning, mercury has a direct action on the renal tubular epothelium (19, 20, 21). With the observation that the severity of tubular lesion is dose dependant. The biochemical mechanism whereby mercury produces renal cellular damage appears to be that well known sequence in which it combines with the sulfhydryl groups of proteins in the mitochondrial membrane and inhibits various enzyme systems including mitochodrial enzymes which are particularly sensitive to mercury with inhibition of oxidative pathways (10, 11, 22).

Regarding the mechanism that produced the renal disease in our experimental groups of animals, we believe that an immune mechanism may be responsible for the resulting lesions. All animals manifested a progressive proteinuria which continued to increase even after the administration of mercury preparation was stopped. Morphologically the lesion were recognised by glomerular basement member thickening associated with immune complex deposits, and degenerative changes with breakdown of subcellular components mainly of proximal convoluted tubular epithelial cells.

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EVALUATION OF LETHAL EXPOSURE TIME AND PHOTOREACTIVATION PROCESS AFTER ULTRAVIOLET LIGHT EXPOSURE TO ASPERGILLUS NIGER AND ASPERGILLUS FLAVUS

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Summary

Aspergillus is not uncommon contaminant of air, tissue and food products. Study was thus carried out to reduce its population by exposure to ultraviolet light. Aspergillus niger and Aspergillus flavus were exposed to ultraviolet lamp for different exposure time extending from zero second to 35 minutes. Lethal exposure time was 25 minutes for Aspergillus niger and 30 minutes for Aspergillus flavus. No photoreactivation process was observed. It was concluded that ultraviolet light exposure can prevent the opportunist infection in immunodeficients (Aspergillus niger) and can reduce the risk of cirrhosis and cancer of liver (Aspergillus flavus).

Introduction

Aspergillus niger causes opportunist infection in immunodeficient patients and are found in air and tissue. Aspergillus flavus which liberates aflatoxins is now blamed to cause cirrhosis and liver cell cancer in Africa and this subcontinent (1, 2). The later organism causes contamination of food and its pathological effects are substantiated mainly by epidemiological data.

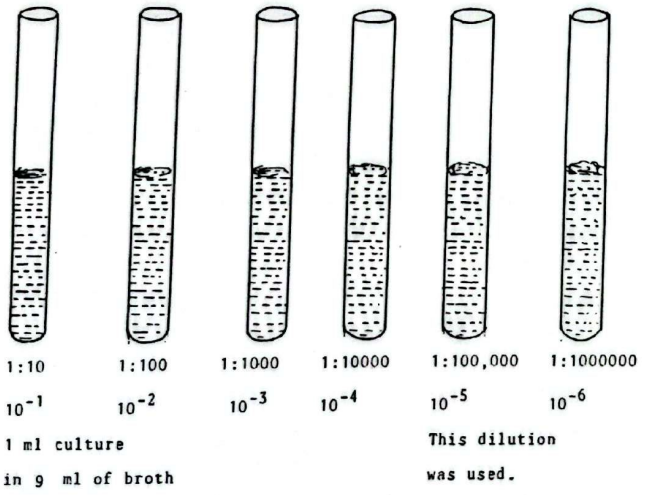

Fig. 1 Serial Ten Fold Dilutions

The present study was aimed at preventing prevalence of above mentioned diseases by the use of ultraviolet light. Such exposure leads to chemical modification of the mucleoproteins mainly DNA,. This creates cross linkages between pairs of thymine molecules i.e. thymine dimmers (3).

Material and Methods

The present work was conducted in a ultraviolet room at room temperature at Department of Microbiology University of Agriculture, Faisalabad. The cultures of fungi, Aspergillus niger and Aspergillus flavus were taken from a known source of these. The reason of selecting known source was that these are the common fungal contaminants of air and food. These were incubated into nutrient broth for 24 hours at room temperature and then serial 10 fold dilutions were prepared (fig. 1). For this one ml of the fungal culture was transferred to 9 ml of nutrient broth in the test tube No. 1. Then from tube No. 1, i ml of culture was transferred to tube no. 2, and so on. By using pour plate method, growth of the both fungi was noted in sabouraud agar. In each petri dish, 0.1 ml of each dilution was taken with dilution of 10^{-5} spreaded growth of grey green colonies of them were noted. Ten petri dishes were so prepared and each of them was exposed to ultraviolet light at a standard distance of 2 meters for time extending from zero seconds to 35 minutes and the observations noted.

Then fresh cultures were obtained and exposed to ultraviolet light for same calculated lethal period as noted in the study. A dark period of variable duration of zero second to 15 minutes was provided to each of them and petri dishes were then taken to ordinary light and the observations recorded.

Table 1: **Lethal Exposure time for Aspergillus Niger and Aspergillus Flavus after Ultraviolet Light Exposure**

Dilution = 10-5
Wavelength = 2650ao
Incubation = upto 72 hours time

Exposure Time	GROWTH	
	Aspergillus Niger	Aspergillus Flavus
Zero	+	+
30 seconds	+	+
1 inutes	+	+
3 minutes	+	+
8 minutes	+	+
15 minutes	+	+
20 minutes	+	+
25 minutes	-	+
30 minuts	-	-
35 minutes	-	-

Table 2: **Photoreactivation in Aspergillus niger and Aspergillus flavus**

dilution used 10 -5
media used = sabouraud agar time

	GROWTH	
	Lethal exposure time (minutes)	Photo-reactivation
Aspergillus Niger	25	-
Aspergillus flavus	30	-

Results

The growth of Aspergillus niger and Aspergillus flavus on sabouraud agar was exposed to ultraviolet light and again noted after about 72 hours of incubation (Table 1). The lethal exposure time was 25 minutes for Aspergillus niger and 30 minutes for Aspergillus flavus. All the petri dishes were also studied for process of photoreactivation. No photoreactivation was observed in both the types perhaps due to irreparable damage to DNA. (Table 2).

Discussion

It is alarming that Aspergillus flavus have now been accused to cause cirrhosis and hepatocellular carcinoma in humans in different studies. This is due to the aflatoxins which are found in the contaminated food especially in Africa and Sub-continent. It is also observed that Aspergillus niger causes opportunist infection, pulmonary aspergillosis, especially in immunodeficient patients (1). It has become now a common and serious problem in many countries and its diagnosis has become difficult as it is not easily demonstrated in sputum or blood (4).

Due to all these reason it is now time to avoid such big hazards just by the use of germicidal ultraviolet lamp. These lamps should be used for sterilization of operation theatres and food industry. Regarding the later it should be noted that improperly stored grains and nuts are often contaminated with Aspergillus flavus. The metabolites of its aflatoxin act as chemical initiator of carcinoma (2). They are also blamed to suppress cell mediated immune response which in turn leads to persistence of Hepatitis B Virus (5). To prevent these hazards, the food should be treated with the ultraviolet light for specific lethal exposure time. The similar treatment should be done with hospital environment. The lethal effect of ultraviolet light on working persons is easily avoidable by its proper use (6).

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HYPOMAGNESAEMIA IN HUMAN DIABETES MELLITUS ITS RELATION TO GLUCOSE HOMEOSTASIS

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Summary

The serum magnesium concentrations of 116 diabetic patients and 58 control subjects were measured by atomic absorption spectorophotometry. Mean serum magnesium (±S.D) was significantly lower in diabetic patients (0.74 ±0.07 mmol/L) than in the control subjects (0.8 ±0.06 mmol/L), and 31 (36%) diabetics had values below those of all control subjects except one. Serum magnesium correlated best with serum glucose concentrations (= - 0.28, p < 0.001) and other significant associations were also observed with glycosuria, insulin treatment and oral hypoglycemic therapy.

Introduction

The magnesium ion has a fundamental role in carbohydrate metabolism in general[1] and the action of insulin in particular[2], yet its status in diabetes mellitus is not very clear. In diabetic acidosis, gross urinary loss of magnesium occurs[3] and marked hypomagnesaemia may develop during therapy[4]. Both low and high mean values have been reported[5] in relatively small studies using dye techniques to measure magnesium. However, there are conflicting reports on serum magnesium concentrations in diabetic patient, In the present study an attempt is made to investigate this factor in detail and to correlate serum magnesium with glucose homeostasis in diabetes mellitus.

Materials and Methods

The study was conducted on 116 diabetic patients, age ranged 15-76 years. Most of them were male but few number of female cases were also included. They were selected from Medical Indoor and Outdoor Units of B.V. Hospital and Private Clinics of Bahawalpur City. 38 patients were receiving insulin, 65 patients oral hypoglycemic agents and 13 patients were being treated by diet alone. All cases had normal renal and liver function values. Those who were having malabsorption and diarrheal conditions, were excluded from the study. The control group of 58 non-diabetic normal subjects, was chosen from the general population matching for age, sex, weight and socio-economic status.

The age, weight and blood pressures of patients and controls were recorded. The urine samples of diabetics were tested for glucose using Clinistix. Blood samples were obtained after an overnight fast. Serum was extracted and analysed for magnesium by Pye Unicam sp-9 Atomic Absorption Spectophotometer and glucose by Glucose Oxidase Method. Statistical significance of the results was evaluated by Students't test.

Results

Table 1 indicates the general characteristics and biochemical parameters of overall diabetic patients and controls. The mean values of age, weight and blood pressures were almost indentical. The mean (± S.D) duration of diabetic disease was 3.2 ± 0.6 years. Serum glucose levels were significantly higher in diabetic patients (8.3 ± 1.2 mmol/L) than the normal limits of controls (4.8 ± 0.9 mmol/L) whereas average glycosuria in diabetics was found to be 1 %. The fall in mean values of magnesium concentrations of diabetics was highly significant ($P < 0.001$). Out of 116, thirty one (36%) diabetic patients had values below 0.69 mmol/L, whereas only one control subject did so. Serum magnesium inversely correlated with glucose concentrations ($r = - 0.28$, $P < 0.001$).

The relation with the degree of glycosuria (as assessed by testing urine samples with Clinistix) is shown in Table 2. The mean serum magnesium of patients with 2% glycosuria was significantly lower than those with 0.25 to 1% glycosuria who in turn had a lower mean serum magnesium than those patients with no glycosuria.

The relation with type of treatment is represented in Table 3. The mean serum magnesium of patients receiving insulin therapy was significantly lower than those of patients treated by either oral hypoglycemic therapy or dietary restriction alone; the difference between the later two groups was not significant. There was also no significant correlation between insulin dosage and serum magnesium concentrations.

Discussion

We found that hypomagnesaemia occured commonly in diabetic patients; 36% had values below those of all control subjects except one. Our results confirm the over all findings of some previous studies[6] in which less accurate techniques were used to measure magnesium. In one study[7] of 181 male diabetics and 17 controls, significant hypomagnesaemia was observed in patients receiving over 20 units of insulin daily, but not in patients on smaller doses of insulin or treated by diet alone. In contrast other workers[8] found an elevation of the mean serum magnesium in 100 diabetic patients compared with 35 controls, although the young diabetics had low values. An other study[9] reported mean serum values in diabetics and control subjects which were similar to our results.

Hypomagnesaemia occured most frequently in young poorly controlled diabetic patients. The strongest correlation was the negative one observed with blood glucose, and the association with the presence and degree of glycosuria was also significant. Thus, poor diabetic control appears to be the most important factor associated with hypomagnaesemia. This may be related to the increase in urine magnesium exerction which occurs both in diabetics with glycosuria and in normal subjects following an oral glucose load[10].

The disturbance in magnesium concentration is an important factor in glucose metabolism and might at least partially explain its postulated role in diabetic retinopathy and large vessels disease. Cardiovascular disease is a major cause of illness and death in diabetics and it is intriguing to speculate whether the elemental disturbance described here, reflects any link with ischaemic heart disease (I.H.D). We feel that it is at least conceivable that the hypomagnesaemia occurring in diabetic patients may predispose to their markedly increased incidence and mortality of I.H.D. Other authors have also referred to this possibility[11]. However, studies are needed to assess soft tissue magnesium content in diabetics and to see wheather the incidence of I.H.D. correlates with hypomagnesaemia in diabetic patients. These studies are currently in progress.

Acknowledgement

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Table 1. **General Clinical data of overall diabetic patients and control subject. The values are represented as mean ± S.D.**

Parameters	Controls	Diabetics	Signficance
Number	58	116	
Age (Years)	42.6 % 7.3	43.8 % 8.1	N.S
Weight (Kg)	65.4 % 8.5	67.5 % 8.9	N.S
Blood pressure : Systolic	120.5 % 13.4	124.7 % 14.7	N.S
Duration of Diabetes (Years)	-	3.2 % 0.6	-
Insulin dose (IU/Kg/day)	-	5.1 % 0.8	-
Oral hypoglycemics (Tablets/day)	-	1.5 % 0.1	
Serum Magnesium (mmol/L)	0.83 % 06	0.74 % 07	P <.001
Serum glucose (mmol/L)	4.8 % 0.9	8.3 % 1.2	P < 0.001
Glycosuria percent	-	1%	-
Relation between Mg. and Glucose r-0.05	r-0.28 N.S	P < 0.001	

Table 2. **Correlation of serum magnesium with the degree of Glycosuria in diabetic patients**

Glycosuria %	No. of Patients	Serum magnesium (mean ± S.D mmol/L)	Significance
0%	25	0.75 ± 0.07	
0.2 % to 1%	62	0.73 ± 0.06	P < 0.01
2%	29	0.71 ± 0.06	P < 0.05

Table 3. **The relation between type of treatment and serum magnesium in diabetic patients**

Type of treatment	No. of Patients	Serum magnesium (mean ± S.D mmol/L	Significance
Insulin	38	0.72 ± 0.06	
Oral hypoglycemic	65	0.74 ± 0.07	P < 0.001
Dietary restriction alone	13	0.76 ± 0.07	P < 0.10

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THE COMMUNITY - BASED PREVENTION OF CARDIOVASCULAR DISEASES

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Summary

Cardiovascular diseases (CVD) are a major cause of morbidity and mortality. In Pakistan, although infectious diseases account for a high morbidity and mortality, there is evidence to show that with the decline in these diseases, the cardiovascular diseases are increase. This is due to the rise in the expectation of life in the country compled with other risk factors.
In the next century, community-based approaches will be an essential part of preventive programme due to the simple reason that mortality will be very high by the time symptoms are noticed in cardiovascular diseases.

Introduction

Today's physician interacts with patients only when the disease symptoms bring him to the health facility whether public or private. Physician of the next decade will interact not only with patients but also with healthy people for the simple reason that he will guide individuals and families for a healthy life style and therefore he will be a 'friend, a philosopher and a guide to the family and to the community. A physician's involvement in preventive technology, therefore, is the order of the day to meet the health manpower requirement of the Global strategy of Health for all.

Cardiovascular diseases form a very important component of the preventive strategy in the primary health care system because they are the major cause of mortality. A great variability exists in the death rate in different countries. In the technologically advanced countries, a large portion of the health budget is utilized due to these disease. In the developing countries, there is a rise in the average expectation of life at birth from a figure of 26 for males and 28 for females in 40s, to 57 for males and 56 years for females in the current decade. With this rise there is a threat of increase in CVD. It is also evident from the epidemiological findings that high mortality and morbidity from CVD is not only as a result of aging population but also due to high risk factors as in the case of advanced countries.

Preventive Approaches

Since the problem relates to life style situation, the work of prevention has to be closely related within the behavioural framework. This would naturally relate this task to the social science. Therefore a collaborative effort of community health worker (physician) and the social scientist would be a suitable approach for the preventive program of CVD. Although continuous progress is taking place in medical and technological advances in research, a good deal of knowledge is available for prevention if effectively applied. This relates to the identification of the risk factors in the population, like smoking habits, dietary pattern, diabetes and hypertension. Other risk factors that may also be included are the lack of physical activity and alcohol consumption. In order to apply intervention it is imperative to identify the magnitude of these factors in the community.

Although individual risks of CVD in general and coronary heart disease (CHD) in particular, increase with increasing risk factor levels, it is realized that high risk individuals alone cannot produce a large proportion of cases in the community. Many cases arise among persons with only moderate elevation, but when multiple risk factors are acting in combination therefore the whole community with these factors has to be subjected to preventive approaches so that the potential number of cases of CVD may be reduced.

Form the epidemiological point of view, major reduction in the disease rates in the community can be achieved by widespread reduction in the levels of the multiple risk factors. This implies community-wide efforts to promote lifestyles that are likely to reduce the risk of CVD. Such lifestyle changes are also likely to be beneficial for prevention of other diseases.

The different approaches that my be useful in community-based programs are as under:

1. The Behavioral Change Approach
2. The Communication - behaviour change Approach.
3. The Innovation-diffusion approach.
4. The Community organization approach.

The Behavioral Change Approach:

Following steps are helpful to modify the behaviour of individuals:

1. Information to educate people about the relationship between behaviour and health.
2. Persuasion to motivate people and to promote the intentions to adopt the healthy action.
3. Training of health manpower in basic approaches of behavioural sciences.
4. Social support to help people to maintain the initial action.
5. Community organization to mobilize the community for broad-ranged changes to support the adoption of the new lifestyles in the community.

The Communication-Behaviour Change Approach:

The task of introducing new behaviours in the community is basically achieved by mass communication and interpersonal communication. A mass communication includes messages to people through the TV, radio and local dailies. It should however be remembered that the influencing behaviour changes through mass communication is far from easy. However several continuous TV programs might influence behavioral effects and people may change their dietary habits, smoking habits and possibly resort to exercise.

The Innovation-Diffusion Approach:

New lifestyles are innovations that diffuse with time through the natural network of the comm unity to the members of the given social system. This diffusion, causing social change, takes a considerably long period. The innovation-diffusion theory argues that mass media are more effective in creating knowledge of innovation while interpersonal channels are more effective in actually changing attitudes and behaviours.

The innovation process occurs in four stages: (a) Knowledge (b) Persuasion, (c) Decision and (d) Confirmation.

The innovation-diffusion theory classifies people on the basis of their innovativeness, early adopters, early majority, late majority or laggards. The social structure has several norms that have a strong influence on the rate of diffusion. Early adopters usually have the greatest social influence in the community and are thus in key position to influence a wider adoption of the innovation.

The Community Organization Approach:

Broad-ranged changes in the community can be achieved only through the existing community structures. The community organization approach emphasizes efforts to influence individuals through changing organizations to meet the desired ends.

The secondary level prevention is principally concerned with early detection through screening program and undertaking treatment. Earlier detection is far from easy because of sudden deaths that may occur without the knowledge of the person being at a high risk and also due to silent cases which come without warning.

The community therefore should develop mechanism to quicker approach to reach the health facility on the appearance of the slightest symptoms. This action involves some knowledge of the problem of CVD. The best way to handle this is to train community health workers to keep a vigilance on the high risk individuals. Regardless of the efforts and secondary level prevention, and control of CVDs.

In conclusion it is stated that CVD and particularly CHD have shown evidence of increasing in this part of the world and therefore great justification exists in designing preventive approaches for their control and without this it may be too late for any action to save high risk individuals or those with multiple risk factors.

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