RISK FOR LUNG CANCER AMONG SUGAR CANE FARMERS AND PROCESSING WORKERS

by

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ABSTRACT

There has been recent interest in the possible carcinogenic potential of vegetable fibers (plant fibers) containing amorphous silica. These fibers referred to as Biogenic Amorphous Silica Fibers (BAS) are the normal constituents of number of plant species such as sugar cane, wheat, barley, oats, rice etc. Exposure to fibers within the respirable range has been documented during sugar cane and rice farming and processing operations. Some studies have suggested that such exposure could increase the risk for lung cancer while others have suggested the contrary. In countries like India, sugar cane farming is the major occupation in a number of provinces. A large workforce is involved in its farming and processing. In order to investigate the risk for lung cancer among one such population in Western Maharashtra, we carried out a hospital-based case-control study in the region. As part of this study we measured the exposures to BAS fibers during the harvesting of the sugar cane and the processing of the cane in the mills.

Cases of lung cancer were ascertained from 6 cancer treatment centers and matched to controls who had other types of cancers on age, sex, area of residence and timing of diagnosis. After controlling for potential confounding variables such as smoking, asbestos exposure, family history of lung cancer, income, education and farming of other crops, the risk for lung cancer was elevated in workers involved in the farming of the sugar cane, Odds ratio (OR) 1.92; 95% Confidence Interval (CI) 1.08 - 3.40. Specifically, the risks were elevated for those involved in the preparation of the farm (OR: 1.81; 95% CI: 0.99 - 3.27) and in the burning of the

farms after harvesting (OR: 1.82; 95% CI: 0.99 - 3.34). Risks were moderately elevated for those involved in the harvesting of the crop (OR: 1.41; 95% CI: 0.70 - 2.90) and in the processing of the crop in the sugar mills (OR: 1.70; 95% CI: 0.20 - 12.60). Smoking modified the relationship between sugar cane farming and lung cancer. Sugar cane farmers who smoked had a 6-fold higher risk compared to those who never farmed and did not smoke.

Environmental measures both during harvesting and processing of the crop in the mills showed exposure to vegetable fibers. Some of these fibers contained silica and resembled BAS fibers in morphology. However a majority of the fibers lacked mineral content and were unlikely to be those of BAS.

The epidemiological study showed increased risk for lung cancer among sugar cane farmers but the limited exposure data did not show high concentration of BAS fibers. The role of polynuclear aromatic hydrocarbons and crystalline silica in particular needs to explored in future studies.

RÉSUMÉ

Le potentiel carcinogénique des fibres végétalés (fibres des plantes) suscite depuis peu de l'intérêt. Ces fibres qu'on appelera fibres de silice biogénique amorphe (SBA) des constituants normaux d'un grand nombre d'espèces de plantes tels la canne à sucre, le blé, l'orge, l'avoire, le riz etc. Des études ont documente l'exposition à des fibres de type respirable dans l'exploitation de la canne à sucre et du riz et durant les opérations de traitement de ces plantes après la cueillette. Ces etudes ont suggéré qu'une telle exposition pouvait augmentes le risque de cancer du poumon alors que d'autres n'ont pas rapporté aucune augmentation du risque.

Dans un pays comme l'Inde, ou retrouve plusieurs travailleurs impliqués dans de la canne à sucre dans les diverses provincees. Une grande population de travailleurs est impliquée dans l'agriculture et le traitement de la canne 'a sucre. A fin d'etudier le risque de cancer du poumon dans la population de Maharashtra Quest, nous avons fait une étude cas-témoin de type hospitales dans cette région. Nous avons de plus dans cette étude mesuré l'exposition aux fibres de silice biogénique amorphe durant la cueillette de la canne à sucre et son traitement dans les moulins.

Les cas de cancer du poumon ont été choisis dans six centres de cancer et appariés à des témoins ayant un autre type de cancer, pour l' âge, le sexe, la région de résidence et la date du diagnostic. Aprés avoir ajusté pour le tabagisme, l'exposition à l'amiante, une histoire familiale de cancer pulmonaire, le revenu, la

scolarité et le travail d`agriculture pour d`autres types de culture, le risque de cancer du poumon était élevé parmis les travailleurs impliqués dans l`agriculture de la canne à sucre, ratio des cotes ou odds ratio (OR): 1.92; intervalle de confiance 95% (IC): 1.08 - 3.40. Plus spécifiquement le risque était augmenté pour les travailleurs impliqués dans la préparation de la terre (OR: 1.81; 95% IC: 0.99 - 3.27) et la mise à feu de la terre aprés la cueillette (OR: 1.82; 95% IC: 0.99 - 3.34). Le risque était modérément élevé parmis ceux qui était impliqués dans la cueillette de la culture (OR: 1.41; 95% IC: 0.70 - 2.90) et le traitement de la culture dans les moulins. Le tabagisme modifiait la relation entre le travail l`agriculture de la canne à sucre et le cancer du poumon. Les fourniers de la canne à sucre qui fumaient avaient un risque 6 fois plus élevé comparé à ceux qui n`avaient pas en ce type d`emploi et ne fumaient pas.

Des mesures environmentales durant la cueillette et le traitement de la culture dans les moulins ont monté une exposition à des fibres végétales. Certaines de ces fibres contenaient de la silice et resemblaient morphologiquement à des fibres de SBA. Cependant, une majorité de fibres n`avaient pas un contenu minéral et danc il peu plausible que ce soient des fibres de SBA.

L`étude épidémiologique a monté une augmentation du risque de cancer du poumon parmis les farmers de la canne à sucre mais les données limitées sur l`exposition n`ont pas indiqué une concentration élevée de fibres de SBA. Le rôle des hydrocarbures polycicliques aromatiques et de la silice cristalline en particulier devra être étudié dans des études futures.

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I have been guided well by my co-supervisors, Dr's Dufresne Andre and Ernst Pierre. Dr. Andre was kind enough to provide me with the required instruments for the dust sampling and assisted in their analysis. In addition he critically reviewed the written text. Dr Ernst provided valuable financial assistance and critically reviewed the drafts of the manuscript. I sincerely acknowledge their help.

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PREFACE

Having obtained training in Medicine at a rural-based hospital within a sugar cane farming population, I was in some ways aware of their health problems. Exposure to dusts was by and large the commonest environmental health hazard recognized. However, the possibility that there could be a high risk for cancer had never crossed my mind. It was during the discussions with my supervisor and after scanning the literature that the possibility of increased cancer risks within this population seemed possible.

Having a hypothesis is only the beginning. To design an appropriate study and implement it are the biggest challenges. It took nearly six months of field work to study the facilities and resources available for conducting the study. During these six months I had to perform the difficult task of convincing different people at different hierarchies (hospitals and sugar mills, farmers etc.) of the validity of the hypothesis. Nevertheless at the end of it, there were enough resources available to design and implement a case-control study and carry out the sampling of the environmental exposures.

The findings from the case-control study have been accepted for publication in "Occupational and Environmental Medicine".

STATEMENT OF ORIGINALITY

I acquired my medical training in a rural hospital located in the sugar cane farming region of the province of Maharashtra, India. It was during this training that I became aware of the potential respiratory hazards posed by exposures to dusts during the farming and processing of sugar cane. It was however after discussions with my supervisor and after scanning the literature on the subject that the possibility of increased risk for lung cancer among this population originated.

I undertook the pilot study to develop the design for investigating the proposed hypothesis. Based on the findings of the pilot study, and in consultation with my supervisory committee I designed both the epidemiological and environmental studies. I designed the questionnaire and supervised the interview process. In addition I conducted the air sampling survey.

After the data were collected I analyzed the data from the case-control study. The dust samples were analyzed by Dr. Andre Dufresne (he was part of my supervisory committee) at the Dust Research Unit of McGill University. Finally I combined the results from the case-control and hygiene studies and wrote the thesis.

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1. INTRODUCTION

Exposure to plant dusts, or vegetable dusts and their products, represent the most prevalent form of occupational and environmental exposure to respiratory hazards. These exposures vary in their nature, their concentration, and their health effects. The population at greatest risk for exposure to these dusts are those involved in agriculture. In the developing countries, where 50% to 70% of the population are engaged in agriculture, the number of exposed persons is likely to be very large.

A wide range of respiratory health effects have been attributed to exposures to such dusts. Both acute and chronic respiratory diseases have been reported in workers involved in either the harvesting, the processing, the transportation and the storage of a number of agricultural crops. Table 1 (page 2) provides a summary of the respiratory conditions associated with exposures to different plant dusts.

1.1 Exposure settings

There is a common pattern to occupational and environmental exposure to vegetable dusts. Exposures typically begin with harvesting and may result in significant respiratory exposures, especially to those harvesting and transporting the plant products for storage or to terminals for further transport or processing. Harvesting is typically a family affair involving wives, children, and the aged, often retired farmer. Seasonal migrant workers and other seasonal subgroups are also exposed.

The storage of plant products on the farm may result in significant exposures to spoiled grain when grain bins are cleaned out, or to moldy silage when a silo is uncapped. Vegetable dust exposure also occurs from grinding

Table 1. Respiratory conditions among workers exposed to plant dusts.

Dust types	Occupations	Respiratory Conditions
Vegetable fibers		
Cotton	Ginners, textile workers,	bysinnosis, acute febrile syndromes,
Flax	upholstery workers, and	nonspecific airway obstruction,
Soft hemp	rope and twine makers	chronic bronchitis, bagassosis
Sisal		
Jute		
Sugar cane		
Grain dusts		
Corn	farm workers, grain	Occupational asthma,
Rye	handlers, millers, food	hypersensitivity pneumonitis,
Barley	processors	acute febrile syndromes,
Oats		nonspecific airway obstruction,
Rice		chronic bronchitis, rhinitis
Wood dusts		
Western red	Sawmill workers, carpentry,	Occupational asthma,
cedar		hyper-sensitivity pneumonitis,
California red	cabinet making, furniture	nonspecific airway obstruction,
wood	making, wood processing	chronic bronchitis, rhinitis
Oak		
Mahogany		
Other plants		
Coffee	cutters, packers, blenders,	Occupational asthma,
		Non-specific airway
		obstruction, chronic bronchitis,
Black tea	processors, printers and	
Tobacco	gum manufacturers	
Gum Acacia		

Adapted from World Health Organization Study Group. *Recommended Health-Based Occupational Exposure Limits for Selected Vegetable dusts.* Technical Report Series, No. 684, Geneva, World Health Organization, 1983.

the grain for feeding livestock and in handling processed grain in the form of animal feed.

Besides those workers involved in the farming of the crop, the workers involved in the processing of the crop represents another major group exposed to these dusts, especially those involved in the processing of plants yielding vegetable fibers. The ginning of cotton seed results in the initial occupational exposure to cotton dust. Similarly, the retting of flax, especially traditional water retting, may result in very substantial exposures to flax dust. These agricultural operations remove substantial vegetable material arising from the leaf and stem of these plants, but they also result in entrainment of vegetable dust in the vegetable fiber or grain.

1.2 Health effects

A range of acute and chronic health effects have been associated with exposure to vegetable dusts (Table 1, page 2). Acute effects range from acute febrile syndromes, rhinitis, non-specific airway obstruction, hypersensitivity pneumonitis to asthma. Most of these are not specific to any particular dust exposure.

With prolonged exposure to vegetable dust, as commonly occurs in the cotton textile industry and among grain handlers, many workers develop chronic irreversible airway obstruction. Exposures to even low doses of cotton dust (below the standard of 0.2 mg/m^3) may result in chronic bronchitis if the worker also smokes. It has also been found that workers who develop acute symptoms are likely to develop chronic airway obstruction (Merchant, 1994).

During the farming and processing of crops such as cotton, sugar cane and rice, workers are exposed to fibrous dust particles. As mentioned above, inhalation of these fibers has been associated with non-malignant respiratory diseases such as byssinosis (during the processing of cotton, hemp, and sisal), bagassosis (a type of hypersensitivity pneumonitis) the result of exposure to bagasse, the crushed form of sugar cane, and chronic bronchitis (from exposure to rice dust). As of now, exposure to these plant fibers has not been related to carcinogenic health effects. However, in recent years interest has been drawn to the possible carcinogenic potential of these fibers. Although vegetable (organic) in origin, these fibers are composed of amorphous silica (inorganic) and are hence referred to as "biogenic amorphous silica fibers" (Rabovsky, 1995).

1.3 Biogenic amorphous silica

1.3.1. Plant silica

A number of different plant species have been shown normally to contain substantial amounts of silicon in the form of silica (SiO_2) and complex silicates. In dry plant matter, SiO_2 concentrations have been measured up to 12% by weight in rice (Nayyar et al, 1977), 3.4 – 5.6% in wheat (Kowalski and Davies, 1982), up to 16.6% in corn (Lanning et al, 1958) and 11% in oats (Handreck and Jones, 1968). Prairie grass has been found to average about 3% silica by dry weight with a range of 1% to 7.7% (Klein and Geis 1978). Wood plant species that have been found to contain biogenic silica include oak, sugar maple and red pine (Sangster and Hodson, 1986). In sugar cane, silica was shown to represent about 5-7% of the dry weight of the mature leaf (Newman, 1983).

The mechanism of deposition of silica in sugar cane tissue that is believed most plausible is that soluble monosilic acid (H_4SiO_4) is taken up from the soil by the plant and is primarily deposited in the plant epidermal cells (Fox et al, 1969). In some species the deposition is believed to be passive since the highest silica concentrations are typically found where the greatest rate of transpiration occurs, such as the leaves (Kowalski and Davies, 1982). This uptake and deposition is a function of the amount of silica available in the soil.

The morphological characteristics of biogenic silica vary among different plant species. Studies have reported the presence of cubic and fiber-like opal silica in conifer needles and a wide variety of ribbed and smooth sided elongated bodies in grasses (Klien and Geis, 1978; Beavers and Stephen, 1958). Others have shown the existence of a variety of opal phytoliths in oat chaff, grass, corn, wheat and sorghum (Baker, 1960; Baker, 1961; Lanning et al, 1958). Recently, opaline silica fibers were detected in the mature leaves of the cane (Newman, 1983) and in the husks of the rice crop (Lawson, 1995)). Of interest was the fact that these fibers were long and had very small diameters, falling in the category of "long, thin fibers". Besides, they shared a morphological resemblance with asbestos fibers. These observations gave rise to the possibility that they could have similar carcinogenic properties.

1.3.2. Diatomaceous earth

Another source of particulate biogenic amorphous silica is diatomaceous earth. This is the geologic product of decayed unicellular organisms called diatoms (Iler, 1979; Sullivan, 1986). As part of the normal life cycle, diatoms take up soluble silica, probably as silicic acid ($Si(OH)_4$) from the surrounding water and transport it across the plasma membrane in saturable, energy-dependent steps (Sullivan, 1980; Sullivan, 1986). The transported ($Si(OH)_4$) then undergoes a series of reactions that ends in biomineralization producing biogenic amorphous silica and deposition in the diatom valve (frustule). The BAS levels in diatoms vary with species and range from less than 1 to almost 50% by weight

(Iler, 1979). Over geologic time, the siliceous frustules of the diatoms accumulate and become diatomaceous earth.

Possible risks for cancer from exposure to BAS fibers was suggested more than 30 years ago. Actual evidence of exposure to these fibers and their cancer causing potential is however limited. In recent years some epidemiological studies have suggested that exposure to these fibers may be associated with increased risks for lung cancer. The purpose of the present study was to investigate whether sugar cane farming could be associated with elevated risks for lung cancer.

In the following section a brief description of the sugar cane and rice farming activities is first given in order to introduce a review of studies investigating exposure to BAS fibers during these and other activities and a review of studies evaluating the association between BAS fibers and cancer.

2. REVIEW OF THE LITERATURE

2.1. Overview of rice and sugar cane farming

Sugar cane is a multi-seasonal crop. The farming and processing of the crop is done concurrently. The workforces involved in these operations are distinct. Sugar cane farmers are involved in the sowing (includes preparation of the crop), cutting (harvesting) and post-harvest treatment of the farms (includes burning of the farm). The cut crop is transported to mills where it is processed to form sugar. The workers in the mill are involved in the loading/unloading of the crop, the crushing of the crop and the handling of the crushed remnants of the crop (bagasse handling).

Unlike sugar cane, rice is a seasonal crop. It is usually sown just prior to the monsoons (rains) and harvested just prior to the subsequent one. Also unlike sugar cane, it is not further processed. The activities typically involved in its farming are: preparation of the soil (ploughing, tilling and irrigating), sowing of the crop, harvesting and post-harvest burning of the fields. Field preparation activities are carried out by either one or many workers depending on the size and number of the fields. These are typically done using bulldozers (to level the field) and tractors (to plough the field). When fully mature, harvesting of the crop is done either manually (in most developing countries) or by combine harvesters and bank wagons (in most developed countries). After the harvest, the field is burnt (to destroy the straw and stubble) by means of a torch either manually or with the aid of tractors.

2.2. Occupational exposure to BAS fibers

Exposures to BAS fibers have been measured during the farming and processing of rice and sugar cane. Boeniger et al (1988, 1991), in two independent studies measured exposures to BAS fibers in workers employed in the sugar cane industry. In the first study, exposures of workers involved in the harvesting of the cane in Florida were characterized. Besides BAS fibers, the authors measured exposure to polynuclear aromatic hydrocarbons (PAHs), suspecting their release during the burning of sugar cane prior to its harvesting. Personal and area samples were collected on nucleopore filters that were analyzed by transmission electron microscopy. Airborne fiber counts ranged from non-detectable to about 300,000 fibers/l. The highest exposure was found during the cutting operations (300,000 fibers/l). During the burning of the sugar cane, exposures as high as 58,000 fibers/l were measured. The mean length of the fibers was 12 µm and the mean diameter, 0.6 µm. All the fibers detected contained amorphous silica. No PAHs were detected in any of the personal or area samples.

In a subsequent study, the authors measured the exposures of sugar cane farmers and sugar mill workers in Hawaii, USA. Of particular interest were exposures to BAS fibers and to smoke resulting from the burning of the cane. The highest air concentration of fibers among the harvesting workers was 56,000 fibers/l. The majority of these fibers were between 0.5 µm and 2 µm in diameter and 10 to 40 µm in length. The highest concentration among the mill workers was 8350 fibers/l. Similar fibers were identified in the bulk samples of the leaves.

Lawson et al (1995), measured exposures to respirable BAS fibers, respirable crystalline silica and total dust in workers involved in rice farming operations. Personal and area measurements were made during the harvesting of the rice, during preparation of the field and during the burning operations. BAS fibers were detected during all the activities. The highest personal exposure was 1.9 fibers/cc for fibers greater than 5 µm. This was detected during the field preparation activities. The highest level seen during area sampling was 9.9 fibers/cc (for fibers greater than 5 µm in length) on tractors performing field preparation. The median fiber length was 2.8 µm. Ninety percent of the fibers were less than 9 µm in length. The median fiber width was 0.9 µm. Quartz exposures ranged from 0.02 – 0.09 mg/m3. The highest quartz exposure was noted during the field preparation activities (0.08 mg/m3). Cristobalite and tridymite were not detected in any of the samples.

2.3. BAS fiber exposure and risk for cancer

2.3.1. Toxicological studies

Bhatt et al (1984) conducted experiments to investigate the potential toxicity of BAS fibers in animals. They observed that addition of fibers from the grass species Phalaris canariensis (mean diameter 15 µm, modal length 200 µm) to the diet of the mice previously initiated by a polynuclear hydrocarbon, induced tumors in the skin around the mouth and the nose. This was the region most in contact when the mice were fed. Tumors were similarly induced when these fibers were applied to the skin on the dorsum of the mice. The majority of the tumors were benign neoplasms but some squamous cell carcinomas were also present.

In a subsequent study (Bhatt et al, 1991), the authors investigated the respiratory effects of BAS fibers on intra-pleural injection in rats. Groups of rats were injected singly or in combination with:

1. crocidolite
2. 11-methyl-17-ketone
3. BAS
4. BAS and 11-methyl-17-ketone

No tumors of the lung and pleura were observed in rats injected only with BAS or 11-methyl-17-ketone (a known cancer-inducing agent). When both these substances were injected, there was an increased incidence of mesothelioma. The tumors produced by the combination of BAS fibers and 11-methyl-17-ketone were histologically similar to the ones produced by crocidolite. Silica fibers were found on examination of the tumor tissue.

In order to study the possible mechanisms involved in the production of these tumors, the authors carried out further experiments (Bhatt et al, 1992) that indicated that tumor production was associated with the induction of ornithine decarboxylase activity, an activity similarly induced in tumors produced by other carcinogenic agents.

2.3.2. Epidemiological studies

2.3.2.1. Non-occupational exposure to BAS and risk for cancer

In the 1960's there were reports of a high incidence of esophageal cancer in Transkei region of Africa. Upon investigation, it was found that there was a geographical variation in the distribution of the cases. More cases were seen in areas where the soil contained a higher percentage of silica. As the plants grown on this soil were commonly consumed by the inhabitants, Rose et al (1968) studied the silica content of some of the common plants cultivated on this soil and consumed by the inhabitants. Minute intracellular particles of silica, 5 μm – 20 μm in size were identified. The authors then referring to these particles as "phytoliths", put forward the hypothesis that continuous irritation of the esophageal mucosa by a diet constituted by such plants, in combination with tobacco smoking and alcohol consumption could increase the risk for esophageal cancer. The ecologic nature of the study did not allow for information to be obtained at the individual level. At best it served in generating a possible hypothesis, which could be evaluated in further well designed epidemiological studies.

In the early 1980's, a similar high incidence of esophageal cancer was noted in the North East of Iran. Suspecting a role for dietary factors, O'Neill et al (1980) studied the constituents of the wheat flour used by the inhabitants to prepare bread. On microscopy, amorphous silica fibers with smooth tapering ends, between 50 – 150 μm in length and diameters between 1 and 10 μm were seen. They were found to have originated from the grass "phaleris minor" that contaminated the wheat. On incubation with cells of the 3T3 mouse fibroblasts, the fibers stimulated the growth of these cells. Based on these observations the authors hypothesized that the high incidence of esophageal cancer could be the result of constant irritation of the mucosa by these plant fibers. The findings of this study suffered from the same problems of interpretation as the ones observed by Rose et al (1968) above.

2.3.2.2. BAS fibers exposure during farming and processing of crops and risk for cancer

Five cases of mesothelioma were diagnosed at one particular hospital during 1974 and 1976 in a non-industrial rural area in the province of Maharashtra, India. In order to investigate this unusually high number of cases, Das et al (1976) explored their occupational histories. Four of these cases were sugar cane farmers and one had worked as a chemist in a local sugar mill. None of the cases reported exposure to asbestos. The authors suggested that exposure to dust or fumes of burnt sugar cane could be responsible for the disease. It is difficult to reach any specific conclusions based on this case study.

The observed cluster of cases of mesothelioma involved in sugar cane farming could be solely due to chance. The interpretation of these findings is further hampered by the lack of comparison with an appropriate control population.

When studying the familial aggregation of lung cancer in Louisiana, USA, Rothschild et al (1982) observed that a large number of cases had been employed in sugar cane farming. In order to investigate the association, they carried out a case-control study in this geographical region. A total of 815 cases of lung cancer occurred during the study period (1971-77) in the defined geographical region. Of these, 400 were randomly selected. From among these 400 cases, the investigators were able to contact the family of 284 cases for an interview, a response rate of 71%. Controls were subjects who had died of any other cause besides lung cancer, matched for sex, race, age at death within 10 years, year of death and parish of usual residence. When the occupational histories were explored, an increased risk was found for workers who had worked for more than 6 months on the sugar cane farm (OR = 2.4; 95% CI = 2.0-2.9). The increased risks persisted after controlling for the effects of smoking and asbestos exposure. The observations from this study point to a possible association of sugar cane farming with lung cancer. However a number of factors could have influenced the results: the low response rates could possibly have introduced selection bias; as all the study subjects were dead, information on occupational exposures and confounding variables was obtained from relatives. In over 20% of the subjects, this information was provided by a first-degree relative. Whether this information was valid is questionable. Employment in shipbuilding and construction were taken as indicators of asbestos exposure. As many other occupations could lead to asbestos exposure, the indicator used by the investigators could have lead to inadequate control of the confounding effects of asbestos exposure.

Malker et al (1983) studied the incidence of mesothelioma among workers employed in different occupations in Sweden. 3051 males were identified from the 1960 National census and followed up for cancer onset through the Swedish Cancer Environment Registry. After a 19 year follow-up, the SIR (Standardized Incidence Ratio) for employment in sugar refineries or sugar factories was estimated to be 6.3. This was in comparison with the age-sex- and region-adjusted rates in the Swedish population. The elevated risk was however based only on 7 cases. Because of the design of the study (register linkage) the relation of risk with specific work exposures in the sugar refineries/factories could not be studied. Although possible asbestos exposure during the dismantling of the machinery was suggested as a cause for the elevated risks, quantitative exposure measurements were not available.

In a case-control study conducted in Florida, USA, Brooks et al (1992) compared occupational histories of 136 cases (98 of lung cancer and 44 of mesothelioma) selected from the Florida Cancer Registry and an equal number of age- and race-matched community controls. After controlling for asbestos exposure, smoking and exposure to pesticides or herbicides, an increased risk for lung cancer from employment in the sugar cane industry was observed (OR 1.8, 95% CI: 0.5-7.5). Only 1 case of mesothelioma had reported working in the sugar cane industry and no control did. In this study, the risk for lung cancer was not associated with living near sugar cane farming areas. In addition, the cases and controls had on average worked for similar durations in the sugar cane industry. Except for the burning activities where more controls than cases were involved, no details were available on risks within other work activities. Both the low response rates, especially for the mesothelioma cases (62%), and the use of surrogate information provided by the offspring of the subjects (35% for the mesothelioma cases and 28% for the lung cancer cases) could have affected the results.

Sinks et al (1994) conducted a case-control study in Hawaii, USA to determine whether mesothelioma was associated with employment in the sugar cane industry. Ninety-three cases of mesothelioma occurring between 1960-1987 were selected from the Hawaii tumor registry. Cancer controls matched for age at diagnosis, decade of diagnosis and gender were selected from the same source. After controlling for asbestos exposure, workers employed in sugar cane industry were not found to have an elevated risk: OR = 1.13; 95% CI = 0.46-2.80. The exclusion of controls with cancers of the trachea, bronchus, lung and stomach showed moderately elevated risks (OR = 1.37; 95% CI = 0.52-3.65). In this study, employment in the sugar cane industry was established by using 3 sources of information: union records, death certificates and the 1942 population census. The risks for mesothelioma from sugar cane farming differed according to the source of information, ranging from 1.1 to 2.3, the highest risks were seen when data were obtained from union records. These differences question the reliability and validity of the sources of information used in the study and make interpretation of findings difficult.

In order to investigate mortality and morbidity from a number of disease end points among sugar cane workers in Hawaii, Miller et al (1993) followed up the cohort established for the Honolulu Heart Program in 1965. The cohort comprised men of Japanese ancestry born between 1900-1919. It was classified into two groups: those who had ever worked for at least one or more years on a sugar cane plantation and those who had not. This cohort was followed up for 18 years. A moderately elevated risk for lung cancer was observed: RR = 1.26; 95% CI = 0.89-1.78. A statistically non-significant increasing trend in risk with increasing duration of employment in the sugar cane industry was seen. None of the cohort members developed mesothelioma. The only slight increase in risk observed could have resulted from two major limitations of the study. Firstly, most of the sugar cane workers had quit working very early in the follow-up. Hence very few workers were involved in this occupation for more than 10 years. It is possible that the duration of exposure was insufficient for lung cancer to develop. Secondly, little or no information was available on confounding variables such as smoking and no information was available on the possible exposures to lung cancer causing agents in the comparison population (non-sugar cane workers).

Maltoni and Pinto (1997) studied the occupational histories of a large series of mesothelioma cases diagnosed at one particular cancer center in Italy during a 10-year period (1986-1996). Of the 335 cases identified, 12 cases reported having worked in a sugar refinery. From their occupational histories, it was found that all of them were involved in activities likely to lead to exposure to asbestos. Three of these were also exposed to man-made mineral fibers (MMMF). The authors attributed these cases to asbestos exposure. Although a large number of cases were studied, no details were available on the procedures used for estimating exposure to asbestos and MMMF. Exposures to other dusts (vegetable) were not evaluated. The absence of a comparison group also limits the interpretation of the findings.

2.4. Summary of the evidence for the association between BAS fiber exposure and risk for cancer

Exposure monitoring studies conducted among workers in sugar cane farming and the rice farming-industry, have provided evidence that these workers are exposed to BAS fibers within the respirable range. During activities such as harvesting the sugar cane crop, exposures as high as 300,000 fibers/l were found. These levels are above the limits set for exposures to asbestos fibers (100,000 fibers/l)(ACGIH, 1998). Exposures to fibers within the respirable range were also found during the processing of the cane in the sugar mills. In the rice farming industry, exposures were detected during most activities. Besides exposure to BAS fibers, during the preparation of the field, exposures to quartz were detected. Exposures to PAHs were not detected during any of the above operations.

Toxicological and epidemiological studies have mainly investigated the association between BAS fibers and two cancer endpoints: lung cancer and mesothelioma. Evidence for these endpoints is presently limited and controversial. Animal studies carried out by Bhatt et al (1984, 1991, and 1992), point towards the possibility of risk for mesothelioma from inhalation exposure to BAS fibers in the presence of other promoters of cancer. However, no lung cancer was detected in their studies. Among the epidemiological studies investigating lung cancer, one reported a more than two-fold increase in risk (Rothschild et al, 1982) and three reported moderately elevated risks (Brooks et al, 1991; Sinks et al, 1993; Miller et al, 1993). For mesothelioma, one study reported a more than six-fold increase in risk (Malker et al, 1983), whereas others did not find any elevated risks (Brooks et al, 1991; Sinks et al, 1994).

Based on these studies, the evidence for the presence or absence of an increased risk for either mesothelioma or lung cancer is presently unclear.

Sugar cane farming and its processing is a large industry contributing to the economy of a number of countries such as Brazil, China, Argentina, The Caribbean Islands, Mauritius and India among others. India is one of the leading producers of sugar chiefly from sugar cane. In the province of Maharashtra, a large workforce is employed in the farming and processing of the cane. In the present study the risk for lung cancer within this population was investigated.

3. RATIONALE FOR THE STUDY

Sugar cane farming and its processing are occupations with potential exposure to BAS fibers. Hygiene studies have documented exposures to fibers within the respirable range. However whether such exposures could pose cancer risks is presently uncertain. If the carcinogenic potential of fibers in general is attributed chiefly to their morphological characteristics, it could be hypothesized that, like asbestos fibers, exposure to fibers released during these occupations could have cancer causing potential.

During the processing of diatomaceous earth, workers are exposed to particulate BAS. During the heating (calcining) step at temperatures of 982-1100°C, which includes addition of a flux agent such as sodium carbonate, some amorphous silica in diatomaceous earth is transformed into a polymorph of crystalline silica, cristobalite (Cooper and Cralley, 1958). Such exposures have been associated with increased risk for lung cancer (Checkoway, 1993). During the burning of the sugar cane field (post-harvest), there is a possibility that some of the BAS fibers get converted to crystalline silica (cristobalite) when subjected to the high temperatures. In parallel with the observations made for exposure to cristobalite during the processing of diatomaceous earth, it could be hypothesized that such exposures during sugar cane farming could increase the risk for lung cancer.

In order to further investigate the association between sugar cane farming/processing and lung cancer we carried out a case-control study in the province of Maharashtra in India.

4. OBJECTIVES

- To investigate the risk for lung cancer among workers employed in the sugar cane industry

- To characterize exposures to BAS fibers during the farming and processing of sugar cane

Before setting up a study in the province of Maharashtra in India to meet the above objectives, it was felt necessary to carry out a pilot study.

5. PILOT STUDY

5.1. Justification

Maharashtra is the leading sugar cane producing province situated in the Western part of India. It accounts for nearly 30 percent of the total sugar produced in the country. Farming of sugar cane is the major occupation in many parts of the province. In addition, there are over 100 sugar cane processing mills. In order to define the study population and to assess the availability of facilities and information for the conduct of an epidemiological and environmental monitoring study within such a population, a pilot study was undertaken.

5.2. Objectives

The objectives of the pilot study were:

- The identification and definition of the target population
- The assessment and evaluation of facilities and information available for the conduct of an epidemiological investigation
- The assessment of facilities available and necessary for the conduct of a pilot environmental monitoring survey and
- The determination of the amount of funding required and sources from where such funding could be obtained

To achieve these objectives, the principal investigator visited the province in October 1995. He undertook the following tasks:

5.3. Tasks

5.3.1. Visit to the "Sugar cane farmers co-operative society"

The sugar farming industry in Maharashtra (and in the rest of the country) is a co-operative industry. Farmers contribute (financially) to the co-operative society.

These contributions depend upon the amount of sugar cane farmed that in turn determine their share in the profits. Meeting with personnel of the society (Administrative Department, at the office located in Mumbai), information was sought on:

1. the sugar cane farming districts in the province;
2. the number and location of sugar cane mills;
3. the approximate number of people involved in the farming of sugar cane;
4. the approximate number of workers employed in the sugar mills and
5. the nature and description of the farming and processing activities.

5.3.2. Survey of the sugar cane farming districts.

Sugar cane is mainly farmed in the districts of Western Maharashtra (as determined from Step 1). The investigator visited this region to:

- Study details of the sugar cane farming operations (from meetings with the sugar cane farmers)
- Study the sugar cane processing operations (from meeting with the President of the Sugar Workers Federation and survey of the major sugar mills in the region)
- Survey the delivery of health care in the region (number of hospitals and their locations, the number of cancer management centers and their locations)
- Investigate sources of information, their completeness and adequacy for the conduct of an epidemiological study (population registry, cancer registry, union records, electoral lists, hospital records, telephone services etc.)
- Assess procedures to obtain requisite permission in the event of the conduct of an epidemiological study (hospitals, population registries, cancer registries, electoral offices, sugar cane mill owners, union's etc.)

5.4. Findings from the pilot study:

The region of Western Maharashtra (Appendix 1) is comprised of the districts of Kolhapur, Satara, Sangli, Ahmednagar, Colaba, Ratnagiri and Pune. Sugar cane farming is mainly farmed in the districts of Kolhapur, Satara, Sangli, Ahmednagar, and Pune. Approximately 30% of the population in this region farms sugar cane. Approximately 70% of the 104 sugar mills in the province are located in these districts, employing on average 700 workers each.

5.4.1. Sugar cane farming

Sugar cane farming is a rotating multi-seasonal crop. The main activities are: preparation of the field, sowing of the crop, harvesting (cutting of the crop) and burning of the fields. The preparation of the farm is done either manually or by tractors. Preparation operations include activities such as, ploughing/tilling, irrigating, de-weeding and watering. The duration of these activities depend on the area of land farmed and the number of personnel employed. Annually from 30 – 120 days are spent in these activities. After preparing the soil, the crop is sown. Once sown, depending on the variety of the crop, it takes from 9 months to 14 months for the crop to grow. It is then harvested, an activity that lasts for approximately 6 months. Harvesting begins in October and lasts till the end of April. During harvesting, a stem of about one foot is left in the soil. A subsequent crop grows on this stem. After two harvests, the whole field is burnt and a new stem is planted. The harvested cane is then transported to the local mills for processing. Most farmers usually, prepare the farm, sow the crop and burn the field. To harvest the crop, laborers are employed (contract) by the local sugar mill, where the crop will be processed. These laborers are migrant workers residing mainly in the Marathwada region of the province.

5.4.2. Processing of the cane (Appendix 2)

The processing of the cane is done in the engineering departments of the sugar mills. The activities include the following:

- The cut cane from the fields is transported to the mills and unloaded by large cranes onto feeding tables.
- From the feeding tables it is transported on conveyor belts, first to the cutting machines where it is cut into small pieces and further on to the crushers where the cut pieces of cane are crushed and the juice is extracted.
- The crushed cane residue termed as bagasse is transported to the bagasse section. In this section, the collected bagasse is re-circulated to large boilers to be used as fuel for the boiling of the sugar cane juice. The excess bagasse is piled up into bales for transportation to the paper and pulp mills.
- The cane juice is boiled in large boilers. It is then filtered, purified and crystallized to form sugar.

The processing of the cane lasts for about 6 months in a year, corresponding with the harvesting of the cane. Once the crushing is over, the machinery in the mill is dismantled and cleaned. Appropriate modifications/repairs are made before it is pieced back for reuse. This maintenance operation lasts for about 6 months.

5.4.3. Health care delivery

The health care delivery in the province is based on a three-tier system. Primary health centers located in the villages provide primary health care to the rural population. One primary health center drains a population of 30,000. Secondary health care is provided by government hospitals, private nursing homes and hospitals. Tertiary health care is provided by hospitals situated mainly in the towns or cities of the region. Comprehensive management of cancer patients is done at the secondary or tertiary level hospitals. In the proposed study region, such care was provided by four major treatment centers situated in the cities of Miraj, Sangli, Karad and Pune in the districts of Sangli, Satara and Pune respectively. These hospitals were the only hospitals in the region that had facilities for providing radiotherapy treatment to cancer patients.

5.4.4. Facilities and sources available for the conduct of an epidemiological study

Population registries were located in the major cities of each of the districts of the region. These registries maintained information on the permanently resident population in the region. For each person in the registry, information on his/her birth date, age, sex, address, income and occupation was available.

Electoral lists were maintained at the electoral offices located in the main cities of the districts. These lists comprised the name, age, sex and address of the eligible voting population in the region (males 18 years and above and females 21 years and above).

There was no cancer registry in the region. The individual cancer treatment centers maintained records on the cancer cases managed at their hospitals.

At the four major cancer treatment centers (cf. section on health care delivery), information on patients admitted to the hospitals was maintained both centrally and at the respective departments where the case was admitted (medicine, surgery, obstetrics & gynecology, radiotherapy etc.). The central registers collected information on the name, age, sex, address, date and time of admission, presumptive diagnosis and specific department to be admitted in. A unique identification number was also provided to each patient. Similar registers were maintained at each individual department. In addition to the information collected at the central admission offices, information on the treatment given, the investigations performed and their reports and the final diagnosis of the patient was entered (once this was reached).

The departments of labor at each individual mill maintained information on present and past employees of the mill. These records provided information on the name, age, sex, address, date of commencement, department, job title, wages earned and in the case of retired workers, the date of retirement.

Based on the findings of the pilot study, an evaluation on the available sources of information was made in order to select the design for the study. The possibility of a prospective cohort study was not considered as it would necessitate follow-up into the future, for at least 5 years (even if a population with at least 30 years of exposure were selected). Limited time and financial constraints would make this design difficult to implement. A historical cohort study was considered. The major task was to define a population of workers employed in the sugar cane industry in the past (25-30 years). As the populations involved in the farming and processing of the cane are distinct, different sources would be needed to identify these populations. The population registries in the region and the union records in the sugar mill (largest mill in the region) were reviewed for this purpose. The major limitation of the population registries was the nature of the occupational information provided. All farmers were recorded as being "farmers" without information on the type of crop farmed. This precluded their use in the identification of a cohort of sugar cane farmers. On reviewing the union records in the largest sugar mill, it was found that records prior to 1980 were unavailable. Considering the above difficulties in defining a study population, a historical cohort study was not deemed feasible.

There were four major cancer treatment centers in the proposed study region. Any case of lung cancer developing within this population was likely to be referred to and managed at one of these hospitals and at the provincial cancer referral center located in Mumbai. These hospitals were a good source for the identification of cases. The hospital authorities agreed to provide access to the medical records and other information necessary for the conduct of a case-control study. A hospital-based case-control study was thus considered an adequate design to investigate the proposed hypothesis.

6. METHODS

6.1. Case-control study

A multi-hospital-based case-control study was carried out between May 1996 and April 1998.

6.1.1. Source of cases

As mentioned above, there were four major hospitals draining the defined population. These four hospitals were the source for the cases. Harvesting workers are migrant workers residing mainly in the Marathwada region of the province. In order to cover this migrant population, one major hospital from the district of Solapur (covering this migrant population) was selected as another source for the cases. Although most if not all the cases of lung cancer developing in the study population would have been expected to be managed at any of the above hospitals, some could be directly referred to the major cancer treatment center for the province, located in Mumbai. In order to achieve as complete an ascertainment of cases as possible, this hospital was also recruited.

The central admission registers and those at the departments of medicine, surgery and radiotherapy were used to identify the cases. Only those cases, whose medical files had an attached histopathological confirmation report were finally selected between May 1996 and April 1998.

6.1.2. Source of controls

Controls were recruited from the hospitals from where the cases were identified. Controls were other cases of cancer selected from the lists maintained at the radiotherapy departments of the respective hospitals. These departments were a readily available source for controls as they kept lists of all patients in the hospital that required radiotherapy. In addition as the duration of this treatment lasts for an average of about 45 days, it would enable the re-interviewing of subjects if necessary. Three controls each, matched to the case for age (± 10 years), sex, district of residence and timing of diagnosis (within 2 months of that of the case) were selected on a consecutive basis.

6.1.3. Instrument

Cases and controls were interviewed face-to-face by questionnaire. The questionnaire was developed by the investigators based on the information obtained on surveying the sugar cane farming and processing activities in the region (Appendix 3). The following information on socio-demographic variables was collected: age, sex, address of permanent residence, address stayed longest at, number of years stayed at the longest residence, gross annual income and education. Measured confounding variables were: smoking (whether current, past or never, number smoked per day, and number of years smoked), asbestos exposure (defined as involvement in any one of the following jobs: insulating furnaces, repairing ships, construction work, maintaining boilers, manufacturing cement sheets, manufacturing refractory bricks and fitting pipes), history of lung cancer in the family and farming of other crops besides sugar cane. In the section on occupational history, detailed information was collected on lifelong work experiences (including jobs held, duration of each job, departments, job titles and exposures within each job). A separate section on farming elicited information on the type of crop farmed as well as the nature and duration of each farming activity. For sugar cane farming, subjects were asked about specific tasks such as ploughing/tilling and cleaning the farm, sowing and cutting the crop and burning the field after cutting. Finally, information was collected on specific jobs (crane operation, boiler operation, bagasse handling, etc.,) and activities within such jobs during cane processing in the sugar mills.

The questionnaire-based interviews were conducted by interviewers appointed at the respective hospitals. In most cases they were employees of the hospitals. They were first explained the details of the questionnaire. A separate handout was presented with the set of questionnaires (see Appendix 3) providing further details on the questionnaire and the methods to be employed to select the cases and controls.

6.1.4. Statistical analysis

Data were coded and entered in the Paradox (Windows) spreadsheet. Analysis was carried out using procedures available in the SAS software. Conditional logistic regression analysis, accounting for the matching in the design was used. Odds ratios (OR) (as estimates of risk ratios) and their approximate 95% confidence intervals (95% CI) were determined.

The data was first examined by looking at the relationship between lung cancer and sugar cane farming (yes, no) and sugar cane processing (yes, no). The association between sugar cane farming and lung cancer was further explored for each individual activity (preparation and sowing of the crop, harvesting the crop and burning the farm).

In the multiple logistic regression analysis, sugar cane farming was examined as a dichotomous (yes, no) exposure variable. Each specific activity such as: preparation of the farm (including activities such as ploughing/tilling, cleaning and sowing); cutting the crop (harvesting) and burning the field after cutting the crop, was also individually analyzed. Employment in the processing of cane in the sugar mill was analyzed separately. As the number of subjects involved in the latter jobs was small, it was not possible to explore individual activities within these jobs.

A cumulative duration of employment index for each sugar cane farming activity and all the activities combined was calculated as follows:

- cumulative employment in each individual activity = number of days per year worked in the particular activity times the number of years employed on a sugar cane farm;
- cumulative employment in all the activities combined = sum of the number of days per year worked in each individual activity times the number of years employed on a sugar cane farm.

The cumulative indices were analyzed both as continuous and categorical variables. When using them as categorical variables, those who had never farmed sugar cane belonged to the reference category and the other categories were constructed such that there was an approximately equal proportion of subjects within them.

When using variables such as years of employment and cumulative duration of employment as continuous variables, a check of the linearity assumption was made. To do this, variables were first categorized into quartiles and a plot of the logits (log odds of the outcome variable) with the midpoint of the quartiles was examined. The linearity assumption was satisfied when the plots showed a linear relationship (Hosmer, 1989).

Smoking was put in the model either as categorical (never, ever) or as pack-years (continuous or categorical) of smoking. In order to control for any residual confounding, the final models included pack-years of smoking. The potentially modifying effect of smoking on sugar cane farming was assessed. Smoking, asbestos exposure and other confounding variables such as family history of lung cancer, income, education and farming of other crops (rice, wheat, jowar, bajra etc.) were accounted for in the analysis.

6.2. The environmental monitoring study

The main objective of this study was to characterize the exposures of workers employed in the farming and processing of sugar cane, chiefly exposures to BAS fibers. These findings would provide the necessary information for a more detailed analysis of the environment of these workers.

6.2.1. Strategy

In order to develop a strategy for the measurement of exposures, the farming and processing activities were personally surveyed by the investigator. In addition, information on these activities was collected by personally interviewing farmers, harvesting workers and mill workers.

As the purpose of the study was to determine the presence of BAS fiber exposure, only those activities during which high exposures had been previously reported were monitored. During the farming of cane, highest exposures were reported during the harvesting of cane (Boeniger et al, 1988, 1991). For workers in the sugar mill, the highest reported exposures were for the bagasse handlers. However, during the survey of the mills in the study region, it was observed that many other activities could present high levels of exposure. Hence an attempt was made to collect at least one representative sample from each work-station. Exposures during maintenance operations although also likely to present potentially high exposures could not be measured due to time and feasibility constraints.

In order to get a comprehensive picture on exposures, an ideal "exposure monitoring strategy" would consider among other things: the number of workers to be sampled per activity (sample size); activities to be sampled; peak exposures periods; sampling of shift workers; inter and intra-worker variability in exposures; seasonal variations etc. However given the limited resources available for the study, a feasible strategy had to be adopted. Efforts were however made to sample activities likely to involve high exposures, to sample at least one worker within each activity and to sample during at least two work shifts. Thus by-and-large a "worst case" sampling strategy was adopted. The measurements so collected were not expected to represent actual average exposures that would enable the construction of a job-exposure matrix. As a result, it was not possible to utilize these measures to construct the life-time exposures of the subjects (cases and controls) in the epidemiologic study. At best these measures would provide a picture of the possible gamut of exposures, enabling the development of a more detailed "exposure monitoring strategy" for future studies.

6.2.2. Sampling during harvesting

The cutting of the cane begins in the early dawn and lasts till noon. These activities involve cutting the foliage, followed by cutting the leaves and the stem of the cane. They are by-and-large done manually (with a sickle). The number of workers involved in this operation depends on the area of the farms and the number of farms to be harvested during a fixed period of time. Anywhere from 10-20 workers could be employed on any particular day. The activities are uniform with each worker performing the same task.

6.2.2.1. Sampling Instrument

Personal samples were collected on mixed-esters cellulose filters (diameter 25 mm and pore size 0.8 μm) with air drawn by Gilian pumps attached to the waist of the worker. The flow rate used was 1.7 litres/minute. Calibration of the pumps was done prior to and after the collection of the samples by a primary calibrator (soap bubble method).

6.2.3. Sampling of Mill workers

The processing of the cane is done in the engineering department of the mill. During the pilot study it was observed that although the operations in most mills were uniform, there were some differences which were mostly in the capacity of the mill to crush sugar cane (amount of sugar cane that can be crushed) and in the number of workers employed therein. Such differences could result in different levels of exposure, with the larger mills (having more crushing capacity) likely having higher exposures. Thus for the characterization of exposures, the largest mill in the area was selected. Appendix 2 shows the schematic layout of the different operations involved in the processing of the cane. The major operations were: cable operation; feeding table operation; clutch operation; bagasse handling and boiler operation. Following is a brief description of these operations:

6.2.3.1. Cable operation:

During this operation, the sugar cane is unloaded from the trucks onto the feeding tables. This is done by first tying the sugar cane by cables and lifting the cables with the help of cranes. The cane is then transported onto large feeding tables. The cranes are operated by cable operators.

6.2.3.2. Feeding table operation:

During this operation, the sugar cane loaded onto the tables is unloaded onto conveyor belts. This operation is manned by feeding table operators.

6.2.3.3. Clutch operation:

During this operation, the sugar cane is transported via conveyer belts to enclosed cutters that cut the sugar cane into small pieces. The cut cane is further transported to large crushers where the cut pieces get crushed and the juice extracted. These two operations are managed by clutchmen who regulate the amount of cane transported to the cutters and the crushers.

6.2.3.4. Boiling of the cane juice:

The extracted juice is collected in large boilers. Herein it is heated to high temperatures (more than 1000°C). It is then filtered and sent to the extraction section of the mill, where it is processed to form sugar. The different tasks performed during this operation are:

Operating the boilers:

Boiler operators regulate the temperatures of the boilers and clean the fuel tanks (below the boilers) at regular intervals. During cleaning, the burnt remnants of the fuel (bagasse is used as fuel, refer to the section on bagasse handling) are removed from the boilers.

Extinguishing flames:

During the removal of the burnt remnants of the cane, flames emanating from the boiler are extinguished by a constant flow of water. This water is supplied via hoses operated by firemen. This also reduces the amount of smoke released during the operation.

6.2.3.5. Collection and handling of bagasse:

The crushed remnants of sugar cane are collected as bagasse in the bagasse section of the mill. Herein workers perform tasks such as:

- bagasse feeding: The bagasse is re-transported through large ducts to the boilers that heat the sugar cane juice.
- bagasse tractor operation: The bagasse collected is transported to the bagasse feeding section by open tractors operated by tractor operators.
- bagasse bulldozer operation: The bagasse collected is leveled with bulldozers is order to assist the tractor operators to transport it to the feeding section.
- bagasse carrier operation: Bagasse that has to be transported to the paper mills is organized into bales. These bales are carried on conveyers which transport them to a nearby bale storeroom.

Of the above operations, cable operation, feeding table operation and the clutching operations are stationary jobs. All the other jobs are ambulatory. For the stationary operations, area samples were collected, whereas personal samples were collected for the ambulatory jobs. Some area samples were also collected near the region of the boilers.

6.2.3.6. Sampling Instrument

Personal and area samples were collected with hi-flow sampling pumps (Gilian, USA) at a flow rate of 1.7 L/min. The sampling medium was a 0.8 μm pore size, 25-mm diameter, mixed esters cellulose membrane filter placed in front of a 5 μm pore size cellulose diffuser loaded in a PCM cassette with a 50-mm extended cowl.

6.2.4. Bulk samples

Field samples (soil samples) were collected to detect the presence of biogenic silica fibers deposited on the soil during the harvesting of the crop and post-harvest burning of the field. Samples of the ash and from the soil beneath the ash were collected from four different areas of the field.

6.2.5. Sample analysis

6.2.5.1. Optical Microscopy (Phase Contrast Microscopy)

All the analyses were carried out by Dr. Dufresne Andre at the Dust Research Unit at McGill University, Montreal, Canada. Counting of the fibers was done by Phase Contrast Microscopy. Analysis was done using standard techniques recommended for asbestos fibers (NIOSH, 1984). To prepare the samples, a section of the cellulose-ester filter was cut (about $1/4^{th}$) with a scalpel and placed on a pre-cleaned glass slide. This was then clarified and permanently mounted by exposing it to acetone vapors. On evaporation of the acetone, a drop of triacetin was put on the filter, which was then covered with a glass slip. To further clarify the filter, the glass slide was then heated on a slide warmer and cooled.

The fibers were visualized under a magnification of 500X. 100 random fields were observed. A fiber was defined as any particle with a length greater than 5 μm, a diameter less than 3 μm and a length to diameter ratio of 3:1 or greater. Only particles meeting these criteria were counted. The concentration of the fibers was determined by the following equation:

Concentration = (number of fibers/number of fields) X (1/volume of air sampled) X 48.4

= fibers/ml

where: volume of air sampled = flow rate X amount of time sampled

6.2.5.2. Transmission Electron Microscopy

Some of the samples analyzed by PCM were later analyzed by TEM (JOEL 100CX II) to study the morphology and mineral characteristics of the fibers. For this purpose, a section of the filter was cut ($1/4^{th}$) with a scalpel and placed on a pre-cleaned glass slide. The glass slide was then subjected to acetone vapors to clarify the filter. On evaporation of the acetone, the filter was carbon coated in a vacuum evaporator. A small section of the carbon-coated filter was then cut, peeled of the slide and placed on a copper mesh grid. This grid was then placed on a filter paper pre-soaked in acetone and left overnight for further clearing. The grid was then observed under TEM at a magnification of 14,000X.

7. RESULTS

7.1. Case-control study

7.1.1. Number of cases and controls

A total of 128 cases of lung cancer were identified at the 6 hospitals during the study period (May 1996 to April 1998). Of these, 118 cases were successfully interviewed (92.2%). Histological confirmation of the diagnosis could not be obtained for 4 cases and the remaining 6 cases, had left the hospital or refused to be interviewed (2 and 4, respectively). Of the 310 controls which were eligible, 298 (96.1%) were interviewed. A histological confirmation could not be obtained for the 12 controls not interviewed.

Three controls each could be obtained for 81 (68.6%) cases, 2 each for 18 (15.3%) cases and 1 each for 19 (16.1%) cases. All controls were not from the same area of residence in five risk sets. The remaining controls were selected from the district geographically closest to the residence of the case. For 7 (5.9%) cases and 10 (3.4%) controls, the next of kin provided information. In most instances it was the spouse. Patients with cancers of the oral cavity (14.9%) and of the female reproductive system (11.3%) formed the largest proportion of control diseases. Cancer of the pharynx (8.7%) and esophageal cancer (7.7%) were the other major diagnoses among controls.

7.1.2. Distribution of demographic variables

Table 2 (page 42) shows the demographic characteristics of the subjects. The mean age of the cases was 57.3 years (SE ± 11.3) and that of the controls was 57.7 (SE ± 9.7). Except for the 35-44 year age group, where there were 11.0% of cases in comparison with 6.1% of controls, the age distribution was similar. The unequal distribution of subjects (after matching) was the result of the unequal case-control ratio. Subjects were predominantly male (81%). There were more cases in the lower levels of education categories and likewise in the lower income groups.

7.1.3. Type of occupations

About 70 percent of the study subjects reported farming as their major occupation. Besides sugar cane, rice, wheat, jowar and bajra were the other crops farmed. Approximately 30% of the total subjects were involved in sugar cane farming. Only 5 subjects reported ever working in a sugar cane mill. The major non-farming occupations were business, service (public or private sector) and contract labor. About 5% (20/416) of the subjects were unemployed.

7.1.4. Distribution of confounding variables

Smoking, asbestos exposure, education, income, family history of lung cancer and farming other crops were considered as confounding variables. Table 2 (page 42) shows the distribution of these variables in the cases and controls. More cases (56%) than controls (43%) reported ever smoking, which was reflected in the distribution of pack-years of smoking. Only 12 (2.9%) subjects reported work involving exposure to asbestos, 6 of these were cases. Most of these reported having worked as construction workers. A history of lung cancer in the family was reported less frequently among cases. An equal proportion of cases and controls had farmed other crops (rice, wheat, jowar, bajra etc.) besides sugar cane.

7.1.5. Association between sugar cane farming/processing and lung cancer

Table 3 (page 44) shows the crude risks for lung cancer from sugar cane farming. Sugar cane farming was shown to be associated with an increased risk for lung cancer. Sugar processing in the mill was associated with an increased risk; the confidence interval was large.

Lung cancer cases were more likely to be involved in the preparation of the crop and the burning of the field than their counterparts. The mean duration of employment on a sugar cane farm was also slightly higher in cases (26.5 years, SE ± 16.8) than the controls (25.3 years, SE ± 14.7).

Using conditional logistic regression analysis (Table 4, page 45) the elevated risk for sugar cane farming persisted after adjusting for potential confounding variables. In comparison to those who never farmed sugar cane, the risk for lung cancer was increased for workers ever employed on a sugar cane farm (OR: 1.92; 95% CI: 1.08 – 3.40). On excluding the 7 cases for whom surrogate information was provided by the relatives, slightly higher risks were obtained (OR = 2.2; 95% CI = 1.21 – 4.00). However as these results were consistent with those obtained with their inclusion, they were retained in subsequent analysis. Further exploration of the risks within individual farming activities, showed that risk was increased for workers involved in the preparation of the crop (OR: 1.81; 95% CI: 0.99 – 3.27) and for those involved in the burning of the crop after harvesting (OR: 1.82; 95% CI (0.99 – 3.34). The risk observed for workers who harvested the crop was also increased (OR: 1.41; 95% CI: 0.70 – 2.90).

For workers involved in the processing of the sugar cane in the mills, risk was increased but the confidence interval was wide as only 2 cases and 3 controls reported ever working in a sugar cane mill (OR: 1.70; 95% CI: 0.20 – 12.60)(Table 4, page 45). The small numbers of workers in the mills precluded further analysis of risks within individual activities.

The association between duration of employment (years) and the risk for lung cancer was compatible with a linear trend on the logistic scale in which the ORs increased by a factor of 1.21 (1.02 – 1.40) for each 10 year duration of employment on the sugar cane farm. Workers involved in the burning of the sugar cane farms for more than 210 days of their lifetime, had more than two and a half times greater risk than those never involved in this activity (OR: 2.60; 95% CI: 1.20 – 5.70)(Table 5, page 46). Slightly lower, but increased risk was also observed for workers involved in preparing the farm for more than 1160 days of their lifetime (OR: 2.30; 95% CI: 1.10 – 4.70). Only modest increases in risk were seen with increasing duration of harvesting. For the combined duration of work in all the activities, the risk was seen to increase with levels of duration: for workers with more than 1470 days of work in their lifetime the OR was 2.30 (95% CI: 1.20 – 4.40) in comparison with never working on the sugar cane farm.

Smoking (Table 6, page 48) modified the relationship between sugar cane farming and lung cancer. More than 225 pack-years of smoking and farming sugar cane resulted in a six fold greater risk for lung cancer in comparison with neither smoking nor farming sugar cane. The risk for lung cancer for the combined effects of smoking and farming sugar cane was greater than the product of their individual effects.

Table 2: Distribution of socio-demographic variables in the study population.

Variable	Cases Nb (%)	Controls Nb (%)
Age (years)		
25 – 34	3 (2.5)	5 (1.7)
35 – 44	13 (11.0)	18 (6.1)
45 – 54	26 (22)	67 (22.6)
55 – 64	39 (33.1)	120 (40.4)
> 64	37 (31.4)	88 (29.5)
Sex		
Males	96 (81.4)	241 (80.9)
Females	22 (18.6)	57 (19.1)
Education		
None	49 (41.5)	100 (33.6)
Primary	39 (33.1)	131 (44.0)
Secondary	26 (22.0)	57 (19.1)
Post secondary	4 (3.4)	10 (3.3)
Income per year (rupees)*		
< 5000	15 (12.7)	47 (15.8)
5001 – 10,000	55 (46.6)	142 (47.8)
10,001 – 15,000	29 (24.6)	79 (26.6)
15,001 – 20,000	18 (15.3)	20 (6.7)
> 20,000	1 (0.9)	10 (3.4)
Smoking		
Never	52 (44.1)	170 (57.1)
Ever	66 (55.9)	128 (42.9)

Pack years		
None	52 (44.1)	170 (57.1)
1 - 225	29 (24.6)	61 (20.5)
more than 225	37 (31.3)	67 (22.4)
Asbestos exposure		
No	112 (94.9)	292 (98.0)
Yes	6 (5.1)	6 (2.0)
Farming crops besides sugar cane		
No	51 (43.2)	135 (45.3)
Yes	67 (56.8)	163 (54.7)
Family history of lung cancer		
No	117 (99.2)	289 (97.0)
Yes	1 (0.8)	9 (3.0)

* One rupee is equivalent to 0.03 American dollar

Table 3: Crude risks for lung cancer from sugar cane farming and processing.

Exposure	Odds ratio	95% Confidence Interval
Ever worked on sugar cane farm	1.72	1.03 - 2.87
Ever employed in sugar mill	1.59	0.25 - 9.95

Table 4: Lung cancer risks for ever working in a sugar cane farm and for specific cane farming activities.

Occupation/Job	Cases Nb (%)	Controls Nb (%)	Odds Ratio (95% CI)
Ever worked on cane farm			
Yes	39(33.1)	64(21.5)	1.92 (1.08 – 3.40)
No	79(66.9)	234(78.5)	1.00
Ever prepared cane farm			
Yes	36(30.5)	60(20.1)	1.81 (0.99 – 3.27)
No	82(69.5)	238(79.9)	1.00
Ever harvested cane			
Yes	15(12.7)	27(9.1)	1.41 (0.70 – 2.90)
No	103(87.3)	271(90.9)	1.00
Ever burnt cane field			
Yes	30(25.4)	48(16.1)	1.82 (0.99 – 3.34)
No	88(74.6)	250(83.9)	1.00
Ever worked in a sugar cane mill			
Yes	2 (1.7)	3(1.0)	1.7 (0.20 – 12.60)
No	16(98.3)	295(99.0)	1.00

† Adjusted for smoking (pack-years), asbestos exposure, income, education, family history of lung cancer and farming of other crops.

Table 5. Cumulative duration of employment in individual and combined sugar cane farming activities and risk† for lung cancer.

Cumulative duration¶ of employment (days)	Cases Nb (%)	Controls Nb (%)	Odds Ratio (95%Confidence Interval)
Preparation of the farm¶			
None	82 (69.5)	238 (79.9)	1.0
1 - 1160	15 (12.7)	32 (10.7)	1.3 (0.6 - 2.6)
more than 1160	21 (17.8)	28 (9.4)	2.3 (1.1 - 4.7)
Burning of the farm¶			
None	88 (74.6)	250 (83.9)	1.0
1 - 210	13 (11.0)	28 (9.4)	1.3 (0.6 - 2.8)
more than 210	17 (14.4)	20 (6.7)	2.6 (1.2 - 5.7)
Cutting of the crop¶			
None	103 (87.3)	271 (90.9)	1.0
1 - 750	8 (6.8)	14 (4.7)	1.4 (0.5 - 3.7)
more than 750	7 (5.9)	13 (4.4)	1.5 (0.5 - 3.9)
All activities combined‡			
None	79 (66.9)	234 (78.5)	1.0
1 - 1470	16 (13.6)	33 (11.1)	1.4 (0.7 - 2.8)
more than 1470	23 (19.5)	31 (10.4)	2.3 (1.2 - 4.4)

¶ Cumulative Duration of employment = Number of days worked in either preparation or cutting or burning of the farm per year, times the number of years cane farmed.

‡ Cumulative Duration of employment for all activities combined = Number of days worked in preparation, cutting and burning of the farm per year, times the number of years cane farmed.

† Adjusted for smoking (pack-years), asbestos exposure, income, education, family history of lung cancer and farming of other crops.

Table 6. Interaction between smoking and employment on sugar† cane farm

Pack-years of smoking	Never farmed sugar cane Odds ratio (95% CI)	Farmed sugar cane Odds ratio (95% CI)
None	1.00‡	1.10 (0.5 – 2.2)
1 – 225	1.45 (0.7 – 3.0)	2.7 (0.9 – 8.0)
More than 225	1.41 (0.7 – 3.0)	5.9 (2.3 – 14.7)

‡ Reference category

† Adjusted for asbestos exposure, family history of lung cancer, farming of other crops, income and education

7.2. Results of the environmental monitoring study

7.2.1. Sugar cane farming

A total of 13 personal samples were collected during the harvesting of the cane. Five of these samples were initially analyzed by Optical Microscopy (PCM). Fibers were detected on all the samples (Table 7, page 50). Most of the fibers were long and thick. Two samples were further analyzed by TEM. The fiber count was found to be substantially reduced. Few fibers matching the description of BAS fibers (wavy borders and containing only silicon) were detected. The reduced fiber count suggested that most of the fibers detected on PCM were probably of vegetable origin lacking mineral content (and not of BAS). On processing for TEM, these fibers get digested and hence are not visualized. Two other samples collected during the boiler operation were analyzed for the presence of PAHs. These samples were analyzed as they were likely to contain PAHs released during the removal of the burnt fuel from the boilers. No PAHs were detected in these samples.

Bulk samples

Four samples from the soil of a burnt field were analyzed by TEM. Few fibers consistent with the morphology and mineral characteristics of BAS were detected.

7.2.2. Sugar cane mill

A total of 48 samples were collected during the processing operations in the mill. Of these 20 samples could be analyzed by Optical Microscopy. The other samples were overloaded. Table 7 (page 50) shows the concentration of the fibers/ml during the different operations.

Table 7: Exposures to fibers during harvesting and processing the crop.

Activity/Job title	Concentration (fibers/cc)
Harvesting	
Harvestor1	0.026
Harvestor3	0.057
Harvestor4	0.057
Harvestor11	0.026
Harvestor13	0.042
Processing in the mill	
Cable operator1	None detected
Cable operator2	None detected
Feeding table operator	0.010
Clutchman1	0.029
Clutchman2	0.022
Boiler operator1	0.178
Boiler operator2	0.105
Boiler 3 (Area)	0.088
Boiler 4 (Area)	0.058
Boiler 5 (Area)	0.007
Boiler 6 (Area)	none detected
Boiler 7 (Area)	none detected
Bagasse laborer1	0.034
Bagasse laborer2	none detected
Bagasse tractor operator	none detected
Bagasse bulldozer operator	0.038
Bagasse carrier operator	0.003
Sweeper1	0.023
Sweeper2	0.022
Fireman	None detected

The concentration of fibers detected during the processing operations in the mills ranged from non-detectable to 0.178 f/ml. The highest exposure was found for the boiler operators. Except for the cable operators and the fireman, exposures were found during all other operations.

Five of these samples were later analyzed by TEM to determine their mineral content and morphological characteristics. Some fibers with mineralogy and morphology consistent with that of BAS fibers were found. Few fibers resembling erionite were also detected. No asbestos was found in any of the samples. Similar to the findings for the harvesting samples, it was noted that the number of fibers was less than that observed on PCM suggesting exposure mainly to vegetable fibers lacking mineral content.

8. DISCUSSION

We observed an increased risk for lung cancer in sugar cane farmers. Workers involved in the preparation of the farm and in the burning of the farm after harvesting the crop showed the highest risks. The risk was also seen to increase with increasing years of employment on the sugar cane farm and with increasing number of days worked over the lifetime in preparing and burning the fields and for all the individual activities combined. Increases in risk compatible with the null hypothesis were observed for sugar cane farmers involved in harvesting of the crop and for workers employed in the sugar cane mills.

8.1. A comparison with previous epidemiological studies

Few epidemiological studies have assessed the risk of lung cancer among sugar cane farmers. Rothschild and Mulvey (1982) reported a more than twofold increase in risk for lung cancer (OR: 2.40; 95% CI: 1.70 – 3.60) in Louisiana sugar cane farmers after controlling for the effects of smoking and asbestos exposure. However risks within specific activities were not determined. Brooks et al (1992) observed an increase in risk for lung cancer within sugar cane farmers in Florida (OR: 1.80; 95% CI: 0.50 – 7.50). No details were provided however on the risks during individual farming activities. Miller et al (1993) observed a modest increase in lung cancer mortality in a cohort of sugar cane farmers in Hawaii (RR: 1.26; 95% CI: 0.89 – 1.78). In this study, data on specific job activities were not available. As most of the cohort members had short work durations on the sugar cane plantations, it is possible that the exposure duration was insufficient for the development of lung cancer.

8.2. Exposures likely to be associated with the observed elevated risks

Sugar cane farmers are exposed to BAS fibers (Boeniger et al, 1988, 1991). Exposure to such fibers with aspect ratios greater than 3:1, has been reported during the burning of the crop prior to harvesting, during harvesting and during the processing of the cane in the sugar mills. Although not documented for sugar cane farmers, during activities such as burning of the farms after harvesting and preparation of the burnt farm (ploughing, tilling, sowing), workers are likely to be exposed also to airborne crystalline silica formed as a result of conversion of the BAS during the burning of the field. Such temperature-dependent conversion and subsequent exposure to crystalline silica (cristobalite) has been reported during the processing of diatomaceous earth (Cooper and Cralley, 1958). Besides exposures to silica, during the burning of the fields there is a possibility that carcinogenic elements are formed and airborne-released. Some authors, have considered the likelihood of exposure to polynuclear aromatic hydrocarbons during the actual burning operations and the subsequent preparation of the burnt farm (Boeniger, 1988, 1991). An increase in risk observed during these activities in the present study could possibly be explained by exposures to these substances either singly or in combination. In the present study, BAS fibers were detected in all the samples collected during the harvesting activities. Their concentration was however lower than those reported by previous studies. Whether such low exposures could contribute to the observed moderately elevated risks is uncertain. It is however possible that other exposures such as crystalline silica could be involved. The exposures during activities such as preparation of the farm and its post-harvest burning were not characterized and hence it is presently only possible to speculate on their nature. A comprehensive exposure monitoring study needs to be done in order to fully characterize these exposures.

We found a increased risk for lung cancer in workers employed in the sugar cane mill. Although the small numbers precluded further analysis of risk within specific activities, a study of activities within the sugar cane mill (walk-through surveys and personal communication with sugar mill workers) brought forward the following. Besides possible exposure to BAS fibers, during certain activities, workers are also likely to be exposed to crystalline silica. This is especially true during the use of crushed sugar cane as fuel for evaporating the juice; during this process (which is carried out in large boilers), the high temperature in the boilers (1000 - 1200ºC) is likely to convert the BAS to crystalline silica. Workers involved in activities within the boiler area (such as feeders, sweepers, supervisors, etc.,) are thus at risk of exposure to both forms of silica. We monitored exposures to fibers during different activities of the processing of the cane. High exposure to fibers was detected during boiler operations and bagasse handling. Most of the fibers were in the respirable range. A number of fibers resembled BAS fibers, however, the majority were likely to be vegetable fibers lacking mineral content. The limited exposure data and the walk through surveys, however suggest that these workers are likely to be exposed to a range of substances, including asbestos. This is possible especially, during the maintenance operations, where the workers are involved in activities such as cleaning the boilers (lined by refractory bricks), dismantling the machinery, and other operations that are likely to present exposure to asbestos-containing dust.

8.3. Interaction between smoking and sugar cane farming

We observed that smoking modified the lung cancer risk associated with sugar cane farming. This risk increased with increasing number of packs of cigarettes smoked. It is too early to draw definite conclusions on the observed interaction, and it is almost impossible to give a specific biological interpretation to statistical interaction. Nevertheless, it is possible to hypothesize that cigarette smoke enhances the delivery of BAS fibers and crystalline silica to the bronchial epithelium and delays their clearance. It has been shown that cigarette smoking retards ciliary action and clearance of fibers and other particulates (McFadden et al, 1986). Cigarette smoke generates reactive oxygen species: these could enhance the uptake of BAS fibers and/or crystalline silica by the tracheal epithelial cells (Hobson et al, 1990). A combination of these mechanisms could increase the risk for lung cancer associated with exposures to BAS fibers and/or crystalline silica. Such interaction has been well documented for exposure to asbestos fibers (Vainio and Boffeta, 1994).

8.4. Study strengths and limitations

In the present study, some of the limitations of the previous ones were overcome. Efforts were made to reduce selection bias. Cases were ascertained at all the major hospitals draining the geographically defined sugar cane farming population and that draining the migrant-harvesting workers. In addition, to cover any cases not referred to the designated hospitals, the main cancer referral center of the province was included in the study. Response rates achieved for both cases and controls were high.

Histologically confirmed cases and controls were included. Few if any of the subjects changed their jobs and information on exposure was obtained directly from 94% cases and 96.6% controls. Use of other cancer cases as controls likely enhanced comparability of recall. As a result of the above, it is likely that misclassification of either exposure or disease was minimized.

Cancer controls were selected as opposed to other hospital controls. The choice of these controls was motivated by the following reasons:

1. Firstly, they were a readily available source of controls. The radiotherapy departments at the 6 hospitals in the study kept records (lists) on all cancer patients (from all departments) that require radiotherapy. Controls answering the matching criteria could be selected and interviewed as they came for their scheduled treatment following diagnosis. Such treatment schedules usually last for a period of 45-60 days that would enable the interviewer to contact and interview the patient. In addition, it would also permit the re-interviewing of the controls if necessary.

2. Secondly it was felt that choosing cancer controls would ensure comparability of recall of past exposures. Differential recall bias can lead to invalid results. Using cancer controls would give some assurance that even if mis-classification of exposure would occur, it would likely be non-differential. Such assurance would be less by using controls suffering from diseases not as severe as cancer. Such cases may not be motivated as their cancer counterparts to find a cause for their illness. Differential recall could ensue if comparable information was not obtained (Wacholder et al, 1992).

There were however, some limitations to the study. Selecting population controls would have been ideal with regards to the study base principle. However, firstly, information required to identify the base population was not available. Secondly, even if such a list had been available, accessing the population for information would have been difficult (limited access to telephones and in the case of farmers contact during day-time would be difficult as the farms are usually long distances away from the actual place of residence), possibly resulting in reduced response rates. Furthermore the limited access to telephones would have necessitated acquiring information by personal interviews in the house or the use of a mail survey. Resources for the latter were not deemed adequate.

The use of other cancer controls could have led to selection bias (Linet and Brookmeyer, 1987; Smith et al, 1988). Although sugar cane farming has not been found to be associated positively or negatively with any cancer with certainty, it is possible that the exposure distribution within such controls is different (and likely greater if some of the cancers happen to be associated with the exposure) than that in the source population of the cases and could result in bias towards the null. Some studies have suggested the possible association between exposure to BAS fibers and esophageal cancer (Rose, 1968; O'Neill et al, 1982). In the context of the present study, this would mean that the actual risks are greater than those observed if a large proportion of the controls had esophageal cancer. About eight percent of the controls in our study had esophageal cancer (see section on results, page 39). An analysis after exclusion of these controls however did not change the results indicating that the effect of such a bias if present was minimal.

The interviewers were not blinded to the case/control status. This could have resulted in overestimation of risk if cases were probed with more insistence.

The quantitative exposure measurements obtained could not be used to construct a job-exposure matrix as they did not represent all the different activities and all possible exposures. The surrogate measures used to determine exposure duration and intensity (years of employment and the cumulative duration indices), may not represent accurately the actual exposures. More detailed exposure information will be necessary to study the putative association and any dose-response relationships.

Although efforts were made to gather accurate information on the major confounding variables, it is possible that other exposures not accounted for may be responsible for the elevated risks. Some reports suggest that exposure to pesticides such as DDT (banned but still widely used in India) may be associated with an increased risk for lung cancer (Barthel, 1981; Axelson, 1987). Although the frequency of use of any pesticide within the study population was reported to be negligible (oral communication with the Sugar Cane Workers Federation, personal interviews with sugar cane farmers), confounding by such exposure cannot be ruled out with certainty.

9. CONCLUSIONS

The present epidemiological study suggests that sugar cane farmers are at higher risk for lung cancer. The risks were particularly increased for workers involved in the preparation of the farm and the post-harvest burning of the farms. The nature of the exposures that could be responsible for the elevated risks is however unclear.

Although elevated risks were obtained for workers involved in the processing of the sugar cane in the mills, such risks were imprecise. Furthermore, the small number of workers and the limited exposure data do not allow the making of definite conclusions. A study of a larger sample of mill workers with exposure measurement particularly for crystalline silica, PAHs, BAS fibers and asbestos during both the processing period and the maintenance period would give more information on the possible risks for lung cancer in this population.

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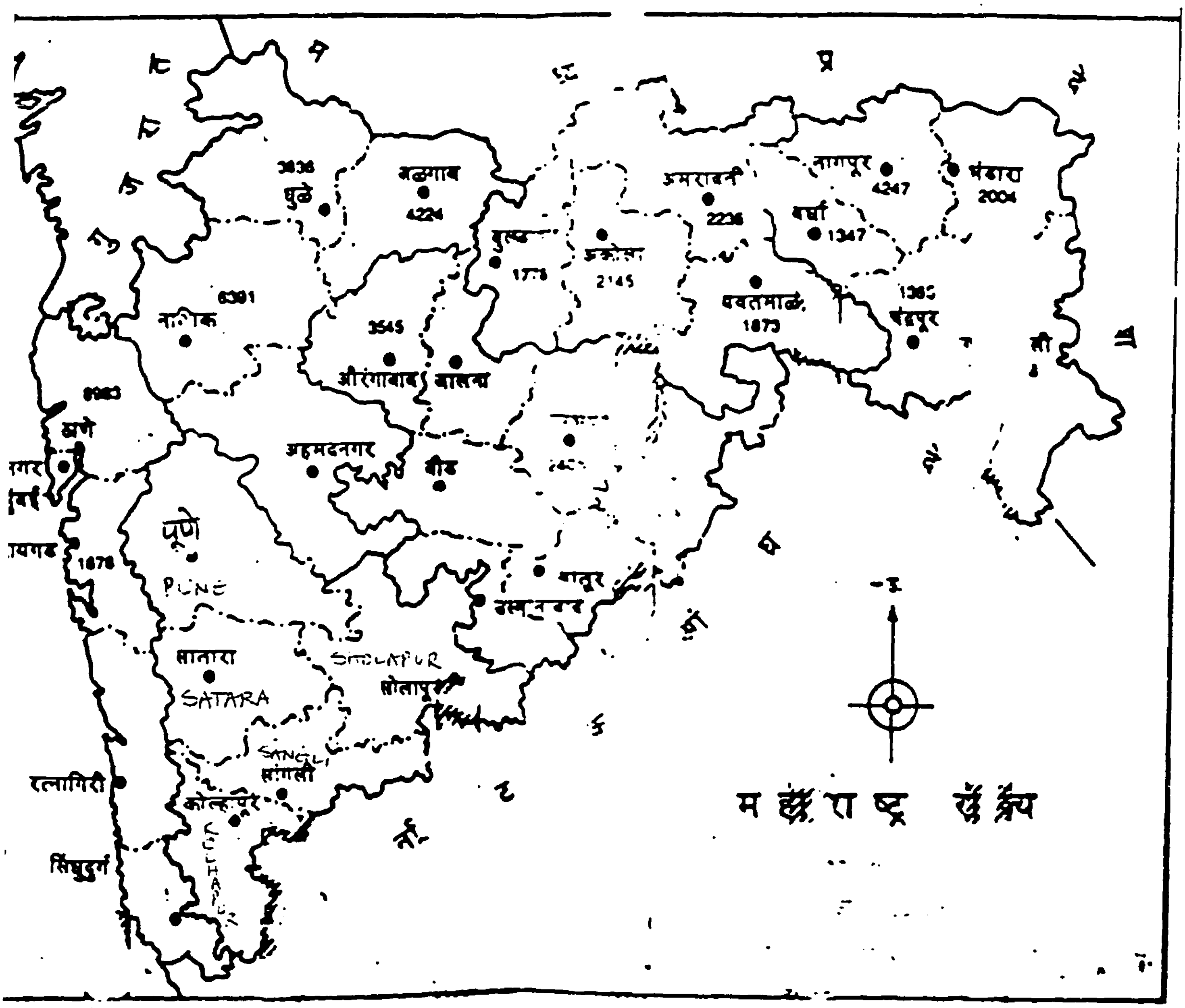
APPENDIX 1

Map showing the study population

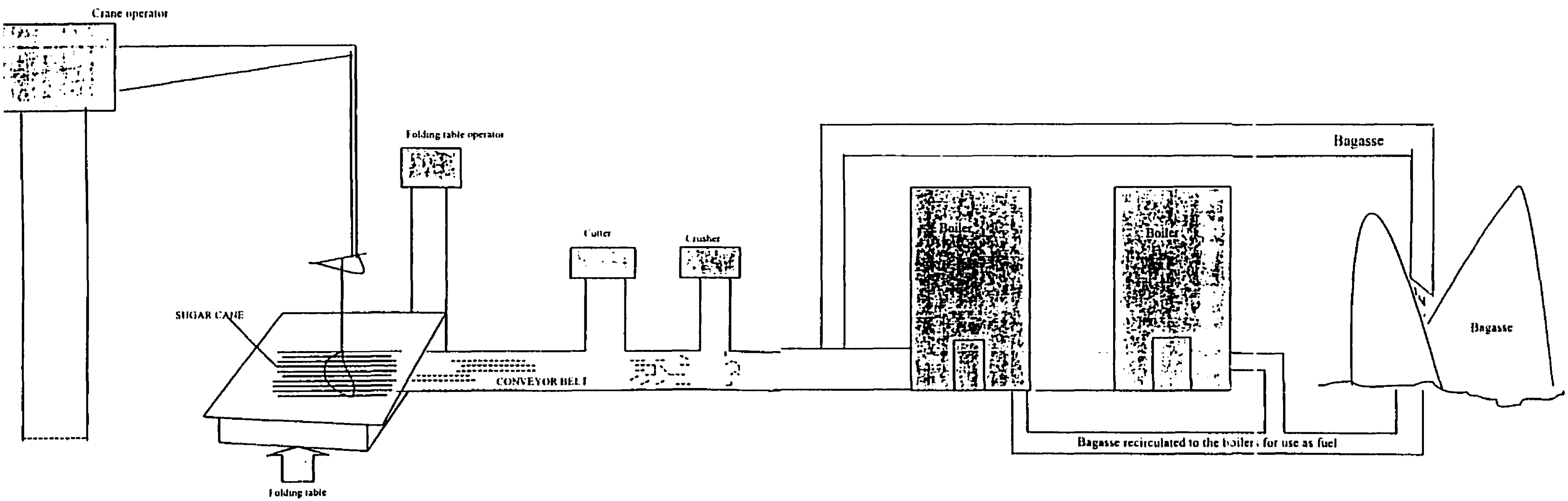


STUDY POPULATION

1. सातारा = SATARA
2. सांगली = SANGLI
3. पुणे = PUNE
4. कोल्हापूर = KOLHAPUR
5. सोलापूर = SHOLAPUR

APPENDIX 2

Schematic presentation of the activities involved in the processing of the sugar cane in the sugar mills


Crane operator
Folding table operator
SUGAR CANE
Folding table
Cutter
Crusher
CONVEYOR BELT
Boiler
Boiler
Bagasse
Bagasse
Bagasse recirculated to the boilers for use as fuel

APPENDIX 3

Questionnaire

A STUDY OF THE RISK FOR LUNG CANCER AMONGST SUGAR CANE FARMERS AND PROCESSING WORKERS IN INDIA

1. Status of patient : Case[1] Control[0] ____________

2. Case Number : ____________
   If control, nb of corresponding case ____________

3. Diagnosis of case / control :

   ____

4. Place of interview : ______________________

5. Date of interview : ______________________

6. Interview given by : Case / Control / Relative ______________

SECTION 1 : SOCIO-DEMOGRAPHIC, PERSONAL AND FAMILY HISTORY

SOCIO-DEMOGRAPHIC

1. What is your name? ______________________
   last name first name middle name

2. Write the sex of the patient? ______ male[1] ________ female[2] 2 ☐

3. What is your date of birth? (if not known, note age)
   ____
   day month year
   ______ age in years 3 ☐

4. What is your present place of residence?
   ____
   ____
   ____

5. For how many years have you lived here? ______ years 5 ☐

6. In which place have you lived the longest? (if the response is similar to Q 4, write down the same address)
   ____
   ____
   ____

7. For how many years have you lived here? ______ years 7 ☐

8. Are you married? ______ yes[1] ______ No[2] 8 ☐

9. What level of education have you had? 9 ☐
   ______ none[1]
   ______ upto primary[2]
   ______ upto secondary[3]
   ______ upto college[4]
   ______ post graduate[5]
   ______ NR[99]

SECTION 1 (CONTD) : HABITS

SMOKING

10.	Have you ever smoked? If Yes, ask	________ Yes[1] ________ No[2] **(Q22)**	☐☐ 10
11.	What do/did you smoke?	________ cigarettes[1] ________ bidis[2] ________ both cigarettes & bidis[3] ________ others (specify) ________ [4] ________ NA[88]	☐☐ 11
12.	Do you currently smoke daily? If Yes, ask	________ Yes[1] ________ No[2] **(Q17)** ________ NA[88]	☐☐ 12
13.	On average how many do you smoke per day?	________ number per day ________ NA[88]	☐☐ 13
14.	For approximately how many years have you smoked?	________ years ________ NA[88]	☐☐ 14
15.	Ever since you started, have you ever stopped smoking?	________ Yes[1] ________ No[2]	☐☐ 15
	If yes,		
16.	On each occasion for how long did you stop?	1.________ months 2.________ months 3.________ months	☐☐ 16

ASK THE FOLLOWING QUESTIONS TO ALL THOSE WHO RESPONDED NO TO Q 12, OTHERWISE GO TO Q 22

17.	At what age did you start smoking?	________ age[1] ________ DK[77]	☐☐ 17
18.	At what age did you stop smoking?	________ age[1] ________ DK[77]	☐☐ 18

19. When you stopped smoking on average,how many did you smoke daily? ________ per day DK[77]

20. During the time you smoked did you ever stop?
________ Yes[1]
________ No[2] (Q22)

IF YES

21. On each occasion for how long did you stop? 1. ________ 2. ________ 3. ________
(months)

PAST HEALTH HISTORY

22. Have you ever been diagnosed of the following conditions?
a. TB Yes[1] No[2] DK[77]
b. Pneumonia Yes[1] No[2] DK[77]

IF YES

23. At what age was it diagnosed? a. ________ b. ________

24. Has anyone in your family ever been diagnosed of lung cancer? Yes[1] No[2] DK[77]

IF YES, CONTINUE, OTHERWISE GO TO Q28

25. What was your relationship with him/her?
________ brother[1]
________ sister[2]
________ father[3]
________ mother[4]
________ DK[77]

SECTION 1 : PAST HISTORY (CONTD)

26. At what age was the cancer diagnosed? ________ age[1] ________ DK[77] ☐☐ 26

27. Did the person with cancer ever smoke daily? Yes[1] No[2] DK[77] ☐☐ 27

SECTION 2: WORK HISTORY

28. Before your illness did you work in any job paid or unpaid? Yes[1] No[2] NR[99] ☐☐ 28

IF YES, ASK, OTHERWISE, GO TO PAGE 10: EMPLOYMENT IN SUGAR FARM....

29. Beginning with the most recent job, list all the jobs held so far

JOB	START YEAR	END YEAR
1.		
2.		
3.		

IF FARMING WAS LISTED AS ONE OF THE JOBS GO TO PAGE 8, AFTER ASKING THE FOLLOWING QUESTIONS FOR ALL OTHER JOBS.

JOB : (put nb from above)

a. What was the name of the company/organization/institution? ________ DK[77] ☐☐ a

b. In which department did you work in? ________ DK[77] ☐☐ b

c. What was your job title? ________ DK[77] ☐☐ c

d. What were your major activities during the job? ________

SECTION 2 : WORK HISTORY (CONTD)

e. During this job were you ever exposed to

dusts Yes[1] No[2] DK[77]
fumes Yes[1] No[2] DK[77]
smoke Yes[1] No[2] DK[77]
solvents Yes[1] No[2] DK[77]

IF YES,

f. On average, how often in the year were you exposed?

dust ________ months
DK[77] NA[99]
fumes ________ months
DK[77] NA[99]
smoke ________ months
DK[77] NA[99]
solvents ________ months
DK[77] NA[99]

g. How often during the month were you exposed?

dusts ________ hours/day
________ hours/week
________ hours/month
________ DK[77] NA[99]
fumes ________ hours/day
________ hours/week
________ hours/months
________ DK[77] NA[99]
smoke ________ hours/day
________ hours/week
________ hours/month
________ DK[77] NA[99]
solvents
________ hours/day
________ hours/week
________ hours/month
________ DK[77] NA[99]

JOB : (put nb from above)

a. What was the name of the the company/organization/ institution? DK[77] ________

b. In which department did you work in ? DK[77] ________

SECTION 2:WORK HISTORY(CONTD)

c. What was your job title? DK[77] ____________

d. What were your major activities during the job? ____________

e. During this job were you ever exposed to

- dusts Yes[1] No[2] DK[77]
- fumes Yes[1] No[2] DK[77]
- smoke Yes[1] No[2] DK[77]
- solvents Yes[1] No[2] DK[77]

IF YES.

f. On average, how often in the year were you exposed?

- dusts ________ months DK[77] NA[99]
- fumes ______ months DK[77] NA[99]
- smoke ______ months DK[77] NA[99]
- solvents _____ months DK[77] NA[99]

g. How often during the month were you exposed?

dusts
- _____ hours/day
- _____ hours/week
- _____ hours/month
- _____ DK[77] NA[99]

fumes
- _____ hours/day
- _____ hours/week
- _____ hours/month
- _____ DK[77] NA[99]

smoke
- _____ hours/day
- _____ hours/week
- _____ hours/month
- _____ DK[77] NA[99]

Solvents
- _____ hours/day
- _____ hours/week
- _____ hours/month
- _____ DK[77] NA[99]

SECTION 2: WORK HISTORY(CONTD)

JOB - (put nb from above)

a. What was the name of the company/organization/ institution? ________________ ________________ DK[77]

b. In which department did you work in? DK[77]________________

c. What was your job title? ________________ DK[77]

d. What were your major activities during the job? ________________ ________________ ________________ ________________

e. During this job were you ever exposed to

dusts Yes[1] No[2] DK[77]
fumes Yes[1] No[2] DK[77]
smoke Yes[1] No[2] DK[77]
solvents Yes [1] No[2] DK[77]

IF YES,

f. On average, how often in the year were you exposed?

dusts ______ months DK[77] NA[99]
fumes ______ months DK[77] NA[99]
smoke ______ months DK[77] NA[99]
solvents _____ months DK[77] NA[99]

g. How often during the month were you exposed?

dusts
______ hours/day
______ hours/week
______ hours/month
______ DK[77] NA[99]

fumes
______ hours/day
______ hours/week
______ hours/month
______ DK[77] NA[99]

smoke
______ hours/day
______ hours/week
______ hours/month
______ DK[77] NA[99]

solvents
______ hours/day

SECTION 2 : WORK HISTORY (CONTD)

__________ hours/week
__________ hours/month
__________ DK[77] NA[99]

ASK THE FOLLOWING QUESTIONS TO ALL THOSE WHO GAVE FARMING AS THEIR JOB IN Q 29, PAGE 4, OTHERWISE GO TO Q 30, PAGE 9.

a. What kind of crop did you farm?

sugar cane[1]
rice[1]
wheat[3]
jowar[4]
bajra[5]
DK[77]
NA[99]
other[6] (specify) __________

IF THE RESPONSE TO a WAS SUGAR CANE FARMING, GO TO Q 30, PAGE 9. OTHERWISE CONTINUE...

b. Were you ever involved in

1. preparation of the field before sowing — Yes[1] No[2] DK[77] NA[99]
2. sowing the crop — Yes[1] No[2] DK[77] NA[99]
3. harvesting the crop — Yes[1] No[2] DK[77] NA[99]
4. other activity (specify) — Yes[1] No[2] DK[77] NA[99]

IF YES, ASK THE FOLLOWING QUESTIONS FOR EACH OF THE ABOVE ACTIVITIES.

ACTIVITY

a. For how many days in a year are you involved in this activity?

________ days/year
DK[77] NA[99]

b. During this activity are you exposed to dusts?

all the time[1]
most of the time[2]
sometime[3]
never[4]
DK[77]
NA[99]

SECTION 2 : WORK HISTORY (CONTD)

ACTIVITY

a.. For how many days in a year are you involved in this activity?

_______ days/year
DK77 NA99

b. During this activity are you exposed to dusts?

all the time1
most of the time2
sometime3
never4
DK77
NA99

ACTIVITY

a. For how many days in a year are you involved in this activity?

_______days/year
DK77 NA99

b. During this activity are you exposed to dusts?

all the time1
most of the time2
sometimes3
never4
DK77
NA99

EMPLOYMENT IN A SUGAR CANE FARM, SUGAR MILL OR IN GUR MANUFACTURING

30. Were you ever employed in a

1. Sugar cane farm	Yes1 No2 DK77 NA99
2. Sugar mill	Yes1 No2 DK77 NA99
3. Gur manufacturing factory	Yes1 No2 DK77 NA99

IF YES, COMPLETE THE NEXT PART, OTHERWISE GO TO Q 31, PAGE 15

SECTION 2: WORK HISTORY EMPLOYMENT IN A SUGAR CANE FARM

1. EMPLOYMENT IN A SUGAR CANE FARM

1.	During which years and for how many years were you involved in this farming?	_____ ____ _____ (eg. 1956 to 1980) ___________ years DK77 NA99	☐☐
2.	During your work were you involved in		
a.	preparation of the crop before sowing	Yes1 No2 DK77 NA99	☐☐
b.	Cutting the crop	Yes1 No2 DK77 NA99	☐☐
c.	burning the field after cutting	Yes1 No2 DK77 NA99	☐☐
d.	transporting the crop	Yes1 No2 DK77 NA99	☐☐
e.	other activity (specify)	Yes1 No2 DK77 NA99	☐☐

IF THE RESPONSE IS YES TO ANY OF THE ACTIVITIES, ASK THE FOLLOWING, OTHERWISE GO TO PAGE 11, EMPLOYMENT IN A SUGAR MILL.....' IF APPLICABLE, ELSE TO PAGE 14, EMPLOYMENT IN GUR....., ELSE TO PAGE 15, Q 31.

ACTIVITY a :

a.	How many days in a year were you involved?	_____ days/year DK77 NA99	☐☐
b.	During this activity were you exposed to any dusts?	all the time1 most of the time2 sometimes3 never4 DK77 NA99	☐☐

ACTIVITY b:

a.	How many days in a year were you involved?	_____ days/year DK77 NA99	☐☐
b.	During this activity were you exposed to any dust?	all the time1 most of the time2 sometimes3 never4 DK77 NA99	☐☐

SECTION 2: WORK HISTORY (CONTD) EMPLOYMENT IN A SUGAR CANE FARM

ACTIVITY c:

a. How many days in a year were you involved?	______ days/year DK[77] NA[99]	☐☐
b. During this activity were you exposed to any dust?	all the time[1] most of the time[2] sometime[3] DK[77] NA[99]	☐☐

ACTIVITY d:

a. How many days in a year were you involved?	______ days/year DK[77] NA[99]	☐☐
b. During this activity were you exposed to any dust?	all the time[1] most of the time[2] sometime[3] never[4] DK[77] NA[99]	☐☐

2. EMPLOYMENT IN A SUGAR MILL

1. When and for how many years were you employed here?	______ (eg.1956 to 1980) ______ years DK[77] NA[99]	☐☐

SECTION 2: WORK HISTORY (CONTD) : EMPLOYMENT IN SUGAR MILL

2. In which department were you employed in?
   ______ administrative[1]
   ______ engineering[2]
   ______ alchohol[3]
   ______ other (specify)
   DK[77]

3. What was your job title?
   ______ title
   DK[77]
   NA[99]

4. During your job were you ever involved in:

a. unloading the sugar cane — Yes[1] No[2] DK[77] NA[99]

b. crushing/cutting the cane — Yes[1] No[2] DK[77] NA[99]

c. handling bagasse — Yes[1] No[2] DK[77] NA[99]

d. cleaning and maintenance of machinery used for processing the cane — Yes[1] No[2] DK[77] NA[99]

e. other activity (specify) — Yes[1] No[2] DK[77] NA[99]

IF THE REPONSE IS YES TO ANY OF THE ACTIVITIES IN Q4, ASK THE FOLLOWING QUESTIONS FOR EACH SUCH ACTIVITY, OTHERWISE GO TO PAGE 14, EMPLOYMENT IN GUR ...... IF APPLICABLE , ELSE TO Q 31,PAGE 15

ACTIVITY a.

1. For approximately how many years have have been involved in this activity?
   ______ years
   DK[77]
   NA[99]

2. For approximately how many days in a year have you been involved in this activity?
   ______ days/year
   DK[77]
   NA[99]

3. During this activity were you exposed to dusts?
   all the time[1]

SECTION 2: WORK HISTORY (CONTD) EMPLOYMENT IN A SUGAR MILL.

most of the time[2]
sometime[3]
never[4]
DK[77]
NA[99]

ACTIVITY b.

1. For approximately how many years have you been involved in this activity?

   ________ years ☐
   DK[77]
   NA[99]

2. For approximately how many days in a year have you been involved in this activity?

   ________ days/year ☐
   DK[77]
   NA[99]

3. During this activity were you exposed to dust?

   all the time[1] ☐
   most of the time[2]
   sometimes[3]
   never[4]
   DK[77]
   NA[99]

ACIVITY c.

1. For approximately how many years have you been involved in this activity?

   ________ years ☐
   DK[77]
   NA[99]

2. For approximately how many days in a year have you been involved in this activity?

   ________ days/year ☐
   DK[77]
   NA[99]

3. During this activity were you exposed to dust?

   all the time[1] ☐
   most of the time[2]
   sometime[3]
   never[4]
   DK[77]
   NA[99]

SECTION 2: WORK HISTORY (CONTD) WORK IN A GUR MANUFACTURING FACTORY.

Activity d :

1. For approximately how many years have you been involved in this activity? ________ years
   DK[77]
   NA[99]
   ☐☐ [1]

2. For approximately how many days in a year have you been involved in this activity? ________ days/year
   DK[77]
   NA[99]
   ☐☐ [2]

3. During this activity were you exposed to dust?
   all the time[1]
   most of the time[2]
   sometime[3]
   never[4]
   DK[77]
   NA[99]
   ☐☐ [3]

3. EMPLOYMENT IN A GUR MANUFACTURING FACTORY

1. When and for how long did you work there? ________ period
   ________ duration
   DK[77]
   NA[99]
   ☐☐ [1]

2. How often in a year did you work there? ________ mths/yr
   DK[77]
   NA[99]
   ☐☐ [2]

3. What were your main activities during the job?

a. ____________________
b. ____________________
c. ____________________
d. ____________________

4. During these activities were you exposed to dust
   all the time[1]
   most of the time[2]
   sometime[3]
   never[4]
   DK[77]
   NA[99]
   ☐☐ [4]

SECTION 2 : WORK HISTORY (CONTD).

Q.31. During any of your jobs were you required to

a.	insulate furnaces	Yes[1] No[2] DK[77] NA[99]	☐☐
b.	repair ships	Yes[1] No[2] DK[77] NA[99]	☐☐
c.	do construction work	Yes[1] No[2] DK[77] NA[99]	☐☐
d.	maintain boilers	Yes[1] No[2] DK[77] NA[99]	☐☐
e.	manufacture cement sheets	Yes[1] No[2] DK[77] NA[99]	☐☐
f.	manufacture refractory bricks	Yes[1] No[2] DK[77] NA[99]	☐☐
g.	do pipe fittings	Yes[1] No[2] DK[77] NA[99]	☐☐

IF THE RESPONSE IS YES TO ANY OF THE ACTIVITIES IN Q 31, ASK THE FOLLOWING Q'S OTHERWISE GO TO SECTION 3, PAGE 16.

ACTIVITY : ________ (Put nb from above)

1. For approximately how many months were you involved in this activity? ________ months DK[77] NA[99] ☐☐

2. For approximately how many hours per day were you involved in this activity? ________ hrs/day DK[77] NA[99] ☐☐

3. During these activities were you exposed to dust ☐☐
   all the time[1]
   most of the time[2]
   sometimes[3]
   never[4]
   DK[77]
   NA[99]

ACTIVITY: ________ (put nb from above)

1. For approximately how many months were you involved in this activity? ________ months DK[77] NA[99] ☐☐

SECTION 2: WORK HISTORY (CONTD)

2. For approximately how many hours per day were you involved in this activity?

   _______hrs/day
   DK77 NA99

3. During these activities were you exposed to dust

   all the time1
   most of the time2
   sometimes3
   never4
   DK77
   NA99

ACTIVITY **(put nb from above)**

1. For approximately how many months were you involved in this activity?

   _______ months
   DK77 NA99

2. For approximately how many hours per day were you involved in this activity?

   _______ hrs/day
   DK77 NA99

3. During these activities were you exposed to dust

   all the time1
   most of the time2
   sometime3
   never4
   DK77
   NA99

SECTION 3: INDOOR ENVIRONMENT HISTORY

32. Which of the following fuels have you ever used for cooking in the house?

   dried sugarcane1
   cow dung2
   gober gas3
   coal4
   wood5
   kerosene6
   DK77
   NA99
   none7

IF ANY OF THE ABOVE FUELS WERE USED ASK THE FOLLOWING, OTHERWISE GO TO SECTION 4, PAGE 17

1. For approximately how many years have you used this fuel? ________ years
DK77
NA99 [1]

2. Do you use it
all the time1
most of the time2
sometimes3
never4
DK77
NA99 [2]

3. Did cooking in the house produce a lot of smoke? Yes1 No2 DK77 NA99 [3]

33. Have you ever used chemicals to kill pests in your house? Yes1 No2 DK77 NA99 [33]

IF YES,

34. How often do/did you use them? ________ / year
NA99 DK77 [34]

SECTION 4:

SECTION 4:
In which catogory does the income of your family from all sources (rupees) fall in?

< 5000 per year1
5000 to 10000 per year2
10000 to 20000 per year3
20000 to 40000 per year4
40000 to 60000 per year5
> 60000 per year6

INSTRUCTIONS FOR FILLING THE QUESTIONNAIRE

Covering page:

Fill in this information before you start the actual interviews. Note down if the patient is a case or control, if it is a control then note down down the number of the corresponding case for which this control has been selected. Note down the complete histological diagnosis of the patient (ex: well differentiated squamous cell carcinoma of the lung). Note down the place of interview (Nargis Dutt Cancer Hospital, Barshi), the date of interview and by whom the interview was given by the patient (case or control) or by the relative of the patient.

Page 1: Section 1: Socio demographic......

Questions 1 to 27, seek information on the social, demographic, personal, past and family history of the patient.

Q1. Write down the name of the patient begining with his last name.
Q2. Write down the sex of the patient
Q3. Ask the patient his date of birth, if not known write down his approximate age
Q4. Ask the patient his present place of residence. It is likely that the patient has come only for the purpose of treatment and is staying temporarily in the area where the hospital is. In that case ask him where he **'usually stays'**. Note the complete mailing address so that if necessary he could be contacted.
Q5. Note down the number of years he has lived in his usual place of residence
Q6. Ask the patient where he has resided for the longest time. It could be a place besides his usual place of residence. In that case, take down the address. If he has stayed the longest in his usual place of residence, write down **'same as Q 4'**
Q7. If the response to Q6 was other that of Q4, note down the duration of stay. Otherwise write down the number of years mentioned in Q5
Q8. Ask the patient if he is married
Q9. Note down the level of education of the patient. Upto primary is from Grade 1 to Grade 4, upto secondary is from Grade 5 to Grade 9, upto College is Grade 11 to Grade 12, post graduate will include B.A, BSc,M.A,MSc etc. If the patient does not respond, tick NR (no response)

Page 2

Q10. Ask if the patient has ever smoked. If the response is yes, ask the next question, if the response is no, go to **Q 22, page 3**
Q11. Ask what he or she smoked. If something besides cigarettes of bidis were smoked, tick 'others' and write down what was smoked.
Q12. Ask if he or she currently smokes everyday. If yes, ask the next question, otherwise go to **Q 17, page 2**

If the patient has not worked anywhere at all, which is very unlikely, then go to **page 10 and ask questions from the section: employment in a sugar cane farm**

Q 29. It is likely that patients may have worked in more than one job. Begining with the most recent job, note down all the jobs held so far with the year the job was started till the year the job was ended.

If farming was listed as one of the jobs done by the patient, first ask the next questions for the other jobs held (if any) and then go to page 8 and ask the questions from 'what kind of crop did you farm.......'. If no other jobs were held, go directly to page 8.

Questions a to g are questions pertaining to each job held. Put down the number of the job from above and then ask the following questions

a. Note down the name of the company, organisation or institution where this job was held
b. Note down the department (if any) in which this job was held
c. Note down the job title during this job if any (eg: superviser, wireman, painter etc)
d. Note down the major activities carried out during this job. Write them down briefly
e. Ask the patient if during this job there was any exposure to dusts, fumes, smoke or solvents. If there was exposure to any of the four, ask **questions f and g**, otherwise go to next job.
f. Note down on an average, how often in the year, the patient was exposed
g. Note down on average how often during the month, the patient was exposed

For any other job held, fill in the job number and ask the questions. If no other jobs were held go to **page 8 to the questions on farming activities**

Page 8: Questions on farming activities.....

If the patient mentioned farming as one of his jobs held so far in Q28, ask the following questions, otherwise go to Q30, page 9

a. Ask the patient what kind of crop did he farm. If he was involved in sugar cane farming, go directly to **Q30, page 9,** if any other crop, then ask the next questions
b. Ask the patient if he was involved in the
1. preparation of the field before sowing the crop. Activities before sowing include, cleaning the field of grass and ploughing the field
2. sowing the crop
3. harvesting or cutting the crop

Q13. Note down the average number of cigarettes/bidis/anything else, smoked per day
Q14. Note down the number of years he or she has been smoking
Q15. Ask the patient if he or she has ever stopped smoking in between. If yes ask the next question. If no go to **Q 22, page 3**
Q16. On each occassion the patient stopped smoking note down for approximately how long he or she had stopped

Q17 to Q22 are for 'past smokers', ie all those who are not currently smoking, but did smoke in the past and responded 'no' to Q12.

Q17. Note down the age when the patient started smoking. If he does not remember, tick **DK (dont know)**
Q18. Note down the age when the patient stopped smoking

Page 3

Q19. Ask the patient the average number of cigarettes/bidis/anything else he or she smoked per day at the time he or she stopped
Q20. Ask the patient if he or she had stopped smoking in between. If yes ask the next Question, otherwise go to **Q22, page 3.**
Q21. On each occassion the patient stopped, note down the amount of time it was stopped in months.
Q22. Ask the patient if he ever had Tuberculosis or Pneumonia. If yes ask the next question, otherwise go to **Q24, page 3.**
Q23. Note down the age of the patient when he was diagnosed of either T.B or pneumonia
Q24. Ask the patient if anyone in the family was ever diagnosed as having lung cancer. If yes, ask the next question, otherwise go to **Q28, page 4**
Q25. Note down the relationship of the patient with the person who had the cancer
Q26. Note down the age of the person when his or her cancer was diagnosed
Q27. Ask whether the person who had the cancer ever smoked.

Page 4. Section 2: Work history

Question 28 to 31 take down details of the employment history of the patient

Q28. Ask the patient if, prior to the illness,he or she worked anywhere, either with or without pay. Many of the patients may be self employed on their own farms and may say no to this question. If they have not worked anywhere ask them specifically if they ever worked on farms. This is more so in the case of housewives, who say they have not worked anywhere, but actually have worked on the farms, either their own or some one else's.

4. any other activity, related to farming the patient was involved in. Specify the activity

If the patient was involved in any of the above activities, ask the following questions for each of the activity

Put the number of the activity in the activity row

a. Ask for how many days in a year the patient was involved in this activity
b. Ask if during this activity the patient was exposed to any dust. Tick the appropriate category

Page 9

Question 30 seeks information on whether the patient was ever involved in sugar cane farming, work in a sugar mill or a gur manufacturing unit

Q30. Ask if the patient was ever involved in work in either of
1. Sugar cane farm
2. Sugar mill
3. Gur manufacturing factory

If the response is yes to any of the 3, complete the next part, if no, then go to **Q31, page 15.**

Page 10

1. Employment in a sugar cane farm

1. Ask during which years and for how many years the patient was involved in this farming
2. Ask the patient if he was involved in
a. Preparation of the field before sowing (include activities such as cleaning the field and ploughing)
b. Cutting the crop
c. burning the field after cutting (in sugar cane farming after 3 crops have been grown on the same field, the field is then burnt and a new crop is sown)
d. transporting the crop to the cane factory
e. Any other activity. Specify the activity

If the patient had been involved in any of the activities, ask the next questions for each such activity.

2. Employment in a sugar mill

Ask the following questions to all those who said they had worked in a sugar mill in Q30

1. Ask during which years and for how long the patient was employed here
2. Note downt he department the patient worked in
3. Note the job title if any
4. Ask if during the job the patient was ever involved in

a. unloading the sugar cane
b. crushing or cutting the cane
c. handling bagasse
d. cleaning and maintenance of machinery used for processing the cane
e. any other activity, specify the activity

If the patient had been involved in any of the activities, the following questions are to be asked for each such activity

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Ask the next questions to all those who mentioned having worked here in Q30

1. Note down when and for how long the patient has worked here
2. Note down how often in the year the patient worked here
3. Note down the major activities in brief
4. Ask if during these activities, the patient was ever exposed to dusts. tick the appropriate category

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Q 31: In this question the patient is asked whether during any of his jobs held so far, he had to...

a. Insulate furnaces
b. repair ships
c. do construction work
d. maintain boilers
e. manufacture cement sheets
f. manufacture refractory bricks
g. do pipe fittings

If the response to any of the above was yes, then the following questions are to be asked for each such activity

Activity: Put the number (a to g) from above and ask the questions

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32. Ask the patient which of the given fuels he or she has used in the house for cooking. Note that more than one fuel could have been used
33. Ask if the patient had ever used any chemical to kill insects in the house. If yes ask the next question, otherwise go to **Section 4.**
34. Ask the patient how often he or she uses them

Section 4: Note down the category in which the income of the patients family falls in from all sources annually.

Abbreviations

NR: No response
NA: Not Applicable
DK: Dont Know
nb: Number
T.B: Tuberculosis

Criteria for selection of controls

For every case of lung cancer interviewed, **3 other cancer cases (ie. besides lung cancer)** should be interviewed. These other cancer cases referred to as **controls** should meet the following criteria:

1. They should be of the same sex as the case of lung cancer i.e if the case of lung cancer was male than the controls for that case should also be male

2. They should be around the same age as the case of lung cancer i.e if the case of lung cancer is around 50 years than the controls should be between 40 to 60 years old

3. They should be from the same area of residence **(district)** as the case of lung cancer i.e if the case of lung cancer is from Sholapur district, then the controls should also be from Sholapur district

Example of procedure for selecting controls

On July 25, 1996 I have interviewed a case of primary lung cancer coming at the radiotherapy department for treatment. The case was male, aged 60 years and from Satara district. From the list of patients coming for treatment of other cancers at the department, I select 3 other cancer cases. 2 of them were oesophageal cancers and 1 was of stomach cancer. Their ages were 55, 65 and 62 years respectively. All of them were from Satara district.

Cancer		**Age**	**Sex**	**Area of Residence**
Case:	Primary lung cancer	60	M	Satara
Control 1:	Oesophageal cancer	55	M	Satara
Control 2:	Oesophageal cancer	65	M	Satara
Control 3:	Stomach cancer	62	M	Satara

Note: It is possible that all the 3 controls meeting the above criteria may not be found on the same day the case. In that case, controls could be selected on the subsequent days.

APPENDIX 4

Typical letter showing granting of permission for the study

APPENDIX 5

Letter showing funds received for the study