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A HOSPITAL BASED CASE-CONTROL STUDY ON RISK FACTORS FOR LUNG CANCER AMONG THAI MALES

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จาก
บัณฑิตวิทยาลัย มหิดล

UMA NATH DEVKOTA

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FACULTY OF GRADUATE STUDIES

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ABSTRACT

A hospital based case control study was conducted at the National Cancer Institute, Bangkok in 1992 to determine the risk factors for lung cancer among Thai males. A total of 333 cases were selected from the medical records of thai males aged 30 years and over with cytologically and or histologically lung cancer, admitted and registered at National Cancer Institute, during the year 1985 to 1990. A total of 345 non cancer controls matched by age were selected also from medical records during the same period. All the necessary information were

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translated from Thai to English and recorded on a recording form which included socio-demographic variables, smoking habits, eating and drinking habits, occupation, use of snuff and past history of pulmonary tuberculosis.

Logistic regression analysis was used to calculate odds ratios adjusted for the effects of other variables. Significant risk factors were: smoking (OR=5.2, 95% CI=2.9-9.4), education (none OR=10.5, 95% CI=3.9-28.0, primary OR=6.6, 95% CI=3.1-13.8, secondary OR=2.9, 95% CI=1.3-6.7), laborer (OR=3.6, 95% CI=1.8-7.0), agriculture (OR=1.9, 95%CI=1.2-3.2), drinking foreign whisky (OR=2.1, 95%CI=1.1-4.0), eating poultry (OR=3.2, 95% CI=1.9-5.3) and past history of pulmonary tuberculosis (OR=2.4, 95%CI=1.1-5.1).

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CHAPTER I

INTRODUCTION

Cancer is a generic term for a wide variety of malignant neoplasm that may result in deleterious effect on the host due to their invasive and metastasizing character. The word, "cancer" means crab or claw like and actually came in to popular usage because the cancer tissue spreads out in resemblance to the claws of a crab as a part of its invasive, destructive action and ultimately will cause death in a large percentage of the cases (1,2,3).

Cancer is a frightening illness because its cause until up to now is still unknown, its treatment can involve great discomfort and it's cure is also uncertain. With an aging world population and increased exposure to carcinogenic hazards, chemical, radiological and virological, cancer has become and will continue to be an increasing public health problem and it is no respecter of persons in term of age, sex, wealth and so forth (4).

Among cancer, lung cancer is a world wide problem, but it's incidence is highest in the industrialized countries. Although the incidence rate vary from country to country, depending partly on the availability of health care and the

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adequacy of demographic system in each country. Lung cancer is the most common cancer not only in Southeast Asia but in many of the developed countries in Europe and America. It ranks first or second as the cause of cancer death in men in many countries. The incidence levels for the Southeast Asian region as a whole are approximately of the same level as in Japan and lower than in Europe, North America and Australia. With in the region Singapore chinese have the highest risk (5).

Table 1. Frequency of Lung cancer in Southeast Asian countries (5).

Country	Male %	Female%	Both sex%
Myanmar	15.5	8.0	11.5
Indonesia	18.1	5.4	10.8
Malaysia	10.6	3.8	7.3
Philippines	19.9	6.1	12.6
Singapore	23.2	5.0	8.7
Thailand	12.8	5.0	8.7

Source: Southeast Asian Journal of Trop Med & Hygiene (1985).

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In Great Britain, United States (blacks) and Finland, the annual age adjusted incidence rate among males exceeding 100 per 100,000 population. In United States primary lung cancer represent about 15 percent of all cancer cases (22% in males and 8% in females). However the incidence is comparatively low in China, India and several Latin American and African countries where rates are near or below 25 per 100,000 (6). From various epidemiological data it has been found that there is an increasing occurrence of lung cancer throughout the world and the trend in mortality is also increasing, following by about 20 years a parallel trend in cigarette smoking (6).

In United States during the period 1950 to 1975 the age adjusted rates for white males increased steadily from $24.6/10^5$ during 1950 to $58.6/10^5$ during 1970, and $89.6/10^5$ and $14.4/10^5$ for black men and black women respectively. In 1980 about 117,000 persons had cancer of the lung in United States, nearly twice as many as in 1968. The number of deaths in the United States from lung cancer in 1975 has been estimated at 81,000 i.e., approximately 222 per day and 9 per hour. If current trend continue, it is projected that 295,000 new cases of lung cancer will occur in the year 2000 (8). In Great Britain, lung cancer increased 50 fold in men from an age standardized death rate of about $2/10^5$ in 1911-15 to over $100/10^5$ in 1970 (Doll and Peto, 1976) (6).

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Table 2. Lung cancer incidence among male in selected countries, 1970 (7).

Annual Age Adjusted Rate (EuropeanStandard) /10^5 Population.				
<25	25 - 49	50 - 74	75 - 99	>100
Puerto Rico Iceland India Singapore (Malaya,Indian) China Nigeria	Israel US (Hispan) US(Utah) Spain Norway Sweden Japan Brazil Colombia	Poland Cuba Yugo- slavia Hungary Canada	Us(White) New Zealand Germany Switzer- land Singapore (Chinese)	UK Finland US (black)

Source: Cancer Incidence in 5 Continents,(Water House et al.1976)

For the lung cancer, death rates are essentially within one order of magnitude. Scotland, England, Wales and Finland have the highest incidence of lung cancer, while the United States ranks 10th and Mexico ranks 37th among the 40 countries surveyed (8).

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Table 3. Death rates (deaths per 100,000 population) for lung cancer in selected countries (8).

Country	World ranking	Male (%)	Female (%)
Scotland	1	78.1	11.1
England-Wales	2	69.7	10.7
Finland	3	61.0	3.9
Netherland	5	53.6	3.4
Germany	9	42.1	5.1
USA	10	40.2	6.8
Canada	18	34.5	5.1
France	24	27.7	3.7
Japan	32	14.0	4.9
Mexico	37	7.3	4.1

Data from Silverberg E, Holleb AI: cancer statistics, 1974 world wide epidemiology.

Lung cancer is predominantly a disease of aging with risk increasing from age 50 years with a peak incidence in the 6th and 7th decade. The Cancer Control Branch of the United States public health services has stated that the risk of lung cancer is highest at age 55 to 70 year.

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Lung cancer tends to be more common in urban than rural areas in virtually all parts of the world. Although people in cities tend to smoke more than those on farms or small urban (6). An inverse association between the lung cancer and socio-economic status, and education has been observed in several studies. The poorest classes are the most severely affected, mainly unskilled laborers are affected, with skilled workers affected to a lesser extent. Low incidence of lung cancer has been observed among certain religion and ethnic groups. It is low among Jews and high in American Indians and Japanese due to low tobacco consumption. Highest rates are seen in natives Hawaiians and blacks (6).

From various studies it has been found that 80% of the lung cancer are due to smoking. But the rising incidence of lung cancer among non smokers points to the role of other environmental factors. Many occupations related to high incidence of lung cancer than rate expected in general population has been identified. The real causation is exposures to various carcinogens (such as asbestos, radon, arsenic, silica, etc.) during the working process. There are certain occupations (miners, sheet metal workers, welders, stone workers, textile workers, brick layers etc.) which carry high risk for the lung cancer and are identified as high risk occupations (10).

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Lung cancer problem in Thailand

Cancer is an important public health problem in Thailand. The acute infectious diseases have been declining in number and severity, where as non infectious diseases have been steadily increasing.

Among these, cancer of all sites are now emerging as the third major cause of death in the Thai people (11). In 1977 the incidence rate of cancer from all causes was 12.6 per 100,000 population with death rate of 4.2 and in 1981 the incidence rate of cancer from all causes increased up to 31.0 per 100,000 population with death rate of 23.4 (11).

In 1988 cancer was the third major cause of death for Thai people with a death rate of 18.7 per 100,000 population, according to I C D Basic Tabulation list, 9th Revision 1982-1986 (12).

Among cancer of all site, lung cancer is becoming more and more of public health importance in Thailand, especially among males because of its increasing trend in incidence rate. In 1971 total number of lung cancer cases were 224 (4.88%) and in 1982 it increased up to 1490 (9.13%) (13).

In 1978 lung cancer incidence rate for all regions was 1.15/100,000 population which increased to 3.05/100,000

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population in 1982. In 1978 incidence rate for Bangkok metropolis was 1.48/100,000 population and in 1982 it increased up to 5.83/100,000 population (13).

g to the National Cancer Institute data (1985), lung cancer was second (12.2%) among the 10 leading sites of cancer in males and 6th (4.7%) in females. But in 1990 it climbed to the first place (19.3%) among males and 4th (3.2%) among females. Age specific incidence rate for lung cancer in male is 10.4/100,000 population and female is 3.6/100,000 population (14). The incidence rate in males starts increasing at the age of 55 years (35.5) and reaches its peak at the age of 70 and over (72.1) (15). Comparing the incidence rate of lung cancer among the four regions of Thailand, the central region including Bangkok has the highest incidence of 16.8 per 100,000. Whereas the incidence rates of north, the north east and the south region are 15.8, 6.2 and 9.1 per 100,000 respectively (15).

With regard to the lung cancer treatment, only 2% of all cases admitted at Siriraj Hospital between 1967 to 1985 could be effectively treated as ordinary health. Almost all lung cancer cases in Thailand have a very short life time after diagnosis because it has a long latent periods, possibly as long as 30 years. The probability of surviving 5 years after the resection of a squamous cell carcinoma is 70%. Post operative radiation has no effect on the survival.

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The overall 5 years survival for adenocarcinoma and large cell carcinoma of the lung is about 9%. In small cell carcinoma, resection combined with adequate chemotherapy and/ or radiation, the 5 years survival is 25% (16).

Table 4. The top 10 leading site of cancer in male and female.

Male			Female		
Site	Cases	%	Site	Cases	%
ALL SITES	789	100	ALL SITES	1,326	100
Lung	152	19.3	Cervix Uteri	444	33.5
Oral cavity	105	13.3	Breast	330	24.9
Liver	99	12.5	Oral cavity	106	8.0
Nasopharynx	46	5.8	Lung	43	3.2
Colon&Rectum	46	5.8	Colon&Rectum	37	2.8
Larynx	35	4.4	Liver	36	2.7
Oesophagus	32	4.1	Uterus	34	2.6
Lymphoma	31	3.9	Ovary	33	2.5
Skin	27	3.4	Skin	30	2.3
Brain	24	3.0	Brain	25	1.9

Source: Annual Report, National Cancer Institute. 1990.

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FIG.1 TREND OF CANCER PATIENTS, 1969-90

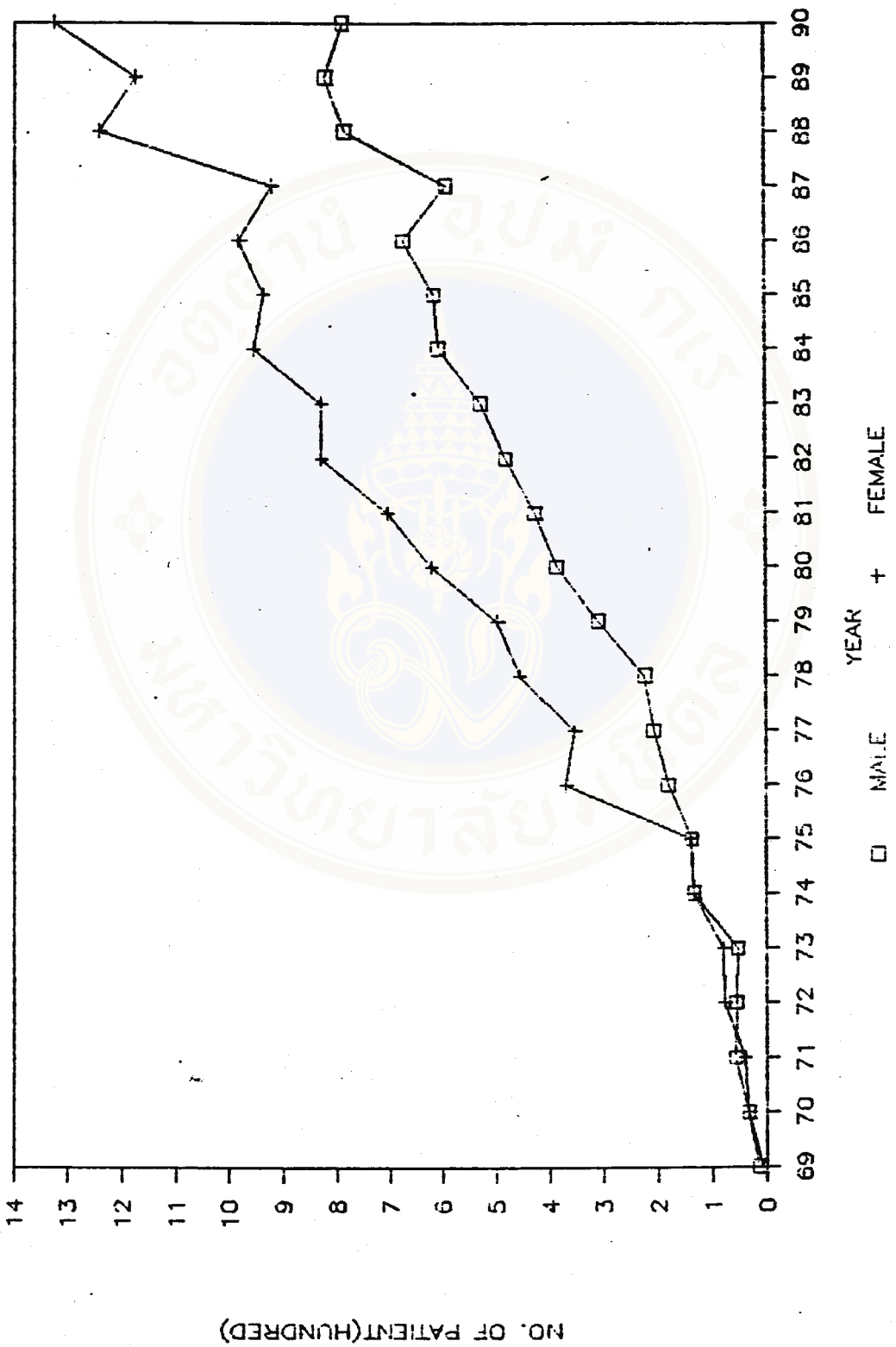

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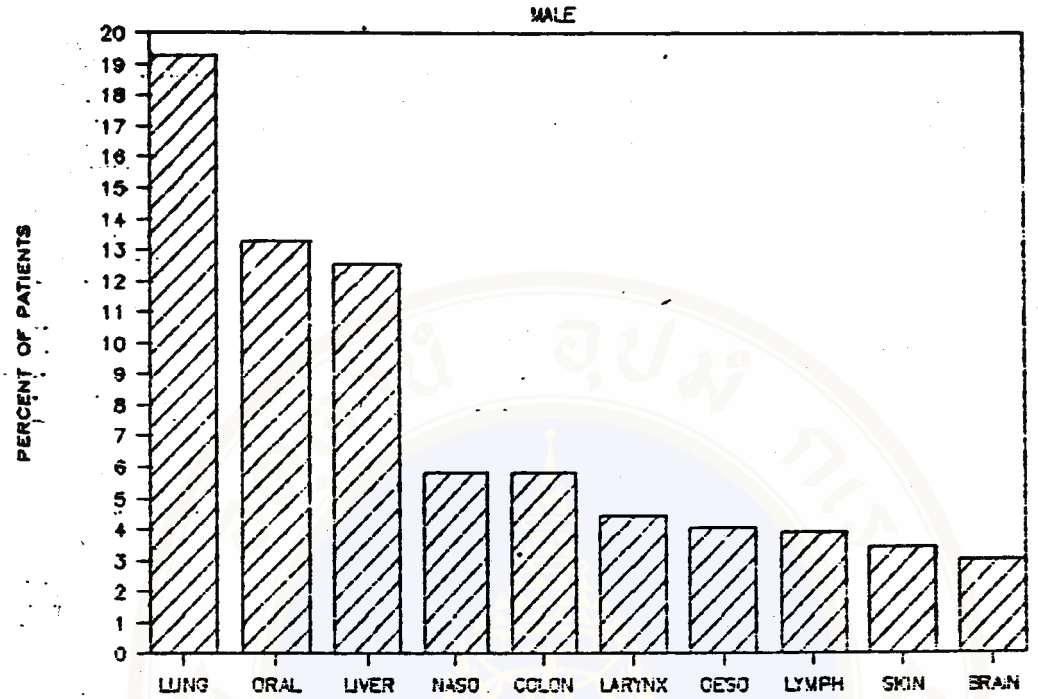
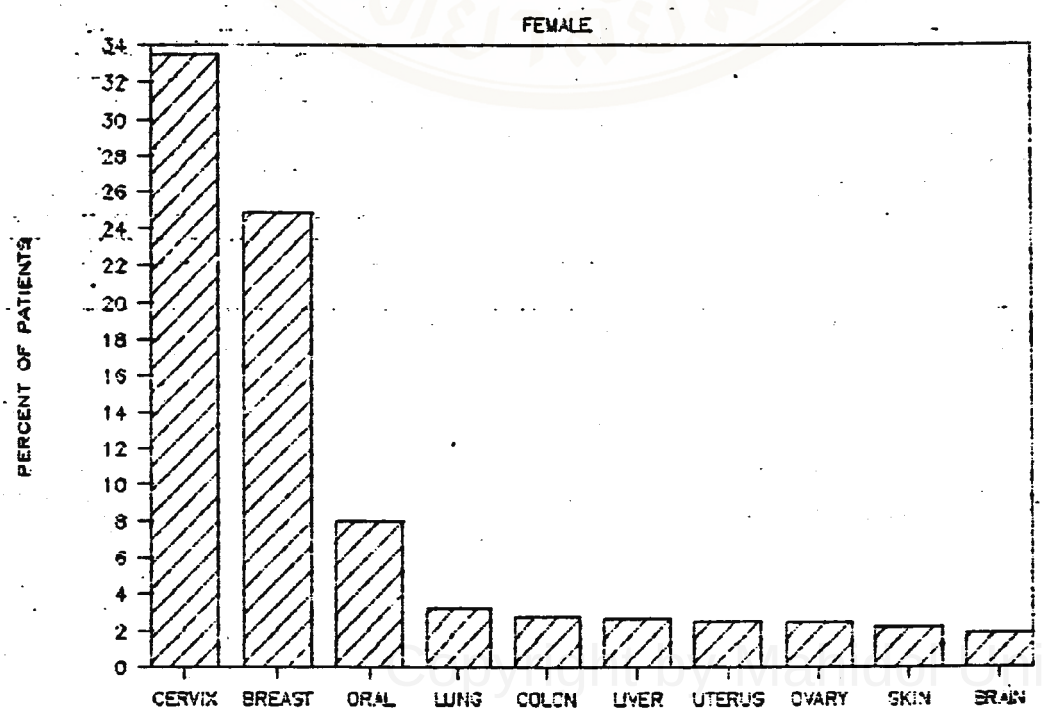
Fig.2 LEADING SITE OF CANCER





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Literature review

Various factors associated with lung cancer have been identified, many epidemiologic studies support the hypothesis that lung cancer is associated with many factors, although several epidemiologic studies have proved that cigarette smoking is the main factor of the lung cancer, by far occupation must be an important factor in this regard also (13). Occupational exposure to various chemical agents are usually heavy and extend over a relatively long period of time with carcinogenic effect on lung. The industrial environment contains chemicals and physical hazards which increase the workers risk of developing various kinds of cancers and lung cancer is perhaps the fore most among these (17).

It is believed that other causes of lung cancer may be various kinds of air pollution, such as urban pollution, industrial pollution, mining and ionizing radiation etc. The change in the nature and amount of environmental contaminants and with the development of new industries, changes in mode of transportation and type of fuels, many of these factors apply as well to the pathogenesis of lung cancer (10).

Occupational lung cancer occur predominantly in males, since they come in contact with industrial carcinogens more

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frequently than females. The first realization that contact with materials in the work environment could cause malignant disease was Percivall Pott's observation of an unusually high frequency of scrotal cancer among London chimney sweeps in 1775 (17).

In 1879, Harting and Hesse identified pulmonary cancer as an occupational disease among metal miners in Central Europe apparently the first instance of an occupationally induced tumor of this organ system. Between 1930 and 1950 there was increased awareness of occupational environments associated with high risk of respiratory cancer. During this period, nickel refining, coal carbonization process, arsenic, chromates and asbestos were implicated as respiratory cancer hazards (17). In the case of asbestosis, suspicions were first aroused when an unusually high frequency of lung cancer appeared at autopsy among asbestos workers dying of asbestosis (17).

An analysis of occupations reported on death certificates between 1921 and 1932 in England and Wales identified several groups of coal carbonization and by products workers to be at high risk of lung cancer. These findings were later confirmed by conventional epidemiologic studies (17).

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To date, most of the known occupational causes of lung cancer have been identified through epidemiologic observations with subsequent confirmation by laboratory studies. Coal carbonization process (eg, coke ovens) liberates a multitudes of chemicals (including polycyclic aromatic hydrocarbons, some of which are carcinogenic in experimental animals). Several reports suggests that exposure to chromic acid mist in chromium plating operations may be associated with an unusual frequency of respiratory cancer. Mineral oil, in the form of cutting oils is related to cancer of the lung and digestive organs among workers exposed to mists arising from machining operations (17).

With the proliferation of epidemiologic studies of different occupational groups during the last 10 to 15 years, many industrial populations have been shown to be at high risk for certain forms of cancer. The foundry industry is a particularly interesting. Since early reports of an unusual frequency of respiratory cancer among foundry workers and metal grinders, iron oxide has been considered a possible etiological agent. However there are new data to suggest a link with polycyclic aromatic hydrocarbons present in certain casting process (Tola et al, 1979) (17).

In a case control study on lung cancer and occupation in New Mexico males in 1980-1982, it was found that welder

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were at a higher risk of developing lung cancer with OR=3.2 (95% CI=1.4-7.4) after adjusting for age, ethnicity and smoking. After stratified with type of industry it was found that welders working in manufacturing, construction, petroleum and gas transmission, iron and steel foundries and welding repairing shops were at significantly increased risk for lung cancer. The OR for those working in shipyard was increased but not significantly (18). Welders are exposed to a variety of substances that are produced during the welding process such as oxides of iron, zinc, lead and chromium and the gases carbon monoxide, nitrogen oxide and ozone (19). In a study, Standard Mortality ratio for welders was 137 ($P<0.05$) (17,18). In another case control study the relative risk of 7.67 ($P<0.01$) after adjusting for smoking was found among welder (17) (18). In another study Registrar General (1978) found relative risk of 1.51 ($P<0.01$) in welders. In another study relative risk of 1.37 ($P<0.05$) and 1.36 ($P<0.05$) were found in welders (17) (18).

According to one study "Occupational differences in rates of lung cancer", it was found that roofer, dental lab technician, decorators, photographers, non automobile mechanics, electricians, bar and restaurant managers, janitors, asbestos workers, heat treater, bartenders, cooks, taxi and truck drivers, painters, plumbers, auto repair and welders have a higher risk of lung cancer (20).

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In another case control study in Sweden, it was found that, after adjusting for smoking, plumber and electricians had OR of 1.8, mechanics had OR of 1.5, OR for concrete and asphalt workers was 2.2, underground miners had OR of 2.7. In the same study it was found that farmers, forest workers, carpenters, railroad workers had low odds ratio (21).

According to a French case control study, the risk of lung cancer was significantly lower for professionals, technical and related workers (RR=0.59, P=0.0005) and administrative and managerial workers (RR=0.68, P<0.02). By contrast, the RR was significantly higher for production and related workers, transport equipment operators and laborers (RR=1.24, P<0.008) (21). An excess risk of borderline significance was found for agricultural, animal husbandry, forest workers, fisherman and hunters (RR=1.22, P<0.07). A significant or borderline significant excess risk of lung cancer was found for farmers(RR=1.24, P<0.06), miners and quarrymen (RR=1.8, P<0.04), sheet metal workers(RR=1.51, P<0.08), plumber and pipe fitters(RR=1.8, P<.04) and motor vehicle driver (RR=1.42, P<0.01) (22).

In another case control study in Shanghai, a significantly increased risk of lung cancer was found for employment in agricultural production (OR=1.6, CI=1.0-2.2), in chemical industry (OR=1.7, CI=0.9-3.1). This group included

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workers in soap detergent, perfumes and cosmetic working. A borderline increased risk was found among workers in food and beverage manufacturing, (OR=1.6, CI=0.7-3.5), printer and other related worker(OR=1.5, CI=0.6-3.5), metal smelting and treatment workers (OR=1.2, CI=0.7-1.7), construction workers (OR=1.4, CI=0.8-2.5) (23).

In a case control study in Italy, the odds ratio greater than 1.0 was found among the workers in transportation, agriculture, construction and metal workers. The occupation of taxi driving has an odds ratio marginally greater than 1.0. The risk for lung cancer among brick layers using fire brick and other refractory material was elevated (adjusted OR=6.5, CI=2.1-20.9) (24).

In one study increased risk were associated with employment in shipbuilding, construction and lumber/ wood industries particularly among workers with repeated exposures to asbestos or wood dust. Increased risk was also found for uranium mining workers (OR=2.1, CI=1.1-3.7) painter (OR=2.7, CI=0.8-8.9) and welders (OR=3.2, CI=1.4-7.4) (25,26).

In a survey of cancer and occupation in young and middle ages men an increased risk of lung cancer was found in the leather industry (RR=2.6, CI=1.2-6.0), in building laborers (RR =1.7, CI=1.0-2.9), and other construction workers

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(RR=1.8, CI=1.0-3.0), in bakers and pastry cooks (RR=3.6, CI=1.3-10.4) and in cooks (RR=2.5, CI=1.2-5.1) (27).

According to a study in Washington state among Orchardists, it was found that there was an increased mortality from lung cancer due to prolonged use of insecticide lead arsenate. Arsenic in its trioxide form is a well known human lung carcinogen. Mortality was 4.6 times higher for Orchardists who were smokers than for those who were nonsmokers (28).

Agriculture and farming has an increased risk of lung cancer. The International Agency for Research on cancer has concluded that several chemicals and processes widely used on farms are carcinogenic. Recent studies have shown that the increased risk in this occupation is due to frequent exposure to herbicides, grains and diesel fumes (22, 23, 29).

According to data on occupation and causes of death by the Central Bureau of statistics of Norway (1976) and by Borgan and Kristoffersen (1986), waiters and bartenders had a higher mortality rates from lung cancer than all other occupational groups (observe 67 death Vs 43.66 expected) with SIR=153. Since waiters smoke significantly more than the general population (Central Bureau of Statistic, 1987) and this presumably explains their excess risk of lung cancer (30)

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From different studies it has been found that butchers in meat industry are at higher risk of lung cancer possibly due to infection by carcinogenic papilloma virus, exposure to polycyclic hydrocarbons and nitrites in the preservation of meat. People who were exposed to recently slaughtered meat or worked with warm meat had highest risk (SMR=184). The excess of death was greatest at least 10 years after first exposure. Increased mortality due to lung cancer was observed among the workers in meat packing plants SMR=1.88, P<0.005) due to exposure to nitrosamine and fumes from labelling and wrapping of meat. It has been claimed that the environment of a slaughters house is favorable to the transmission of human papilloma virus not only from hand to hand but also through aerosol dispersion to the respiratory tract (31) (32).

Exhaust of diesel and gasoline engines contains Benzo(a)pyrene and other polycyclic aromatic hydrocarbons (PAH) and professional drivers are exposed to these carcinogens. In many studies professional drivers were found to be having slightly increased risk of lung cancer. But since drivers were heavier smokers and when stratified with smoking the increased risk was not statistically significant (33). Smoking drivers in an upper age group (70 and over) had a higher relative risk of lung cancer, where as in a lower age group (under 70) no significant increase was found (33). In a cohort analysis of London Transport employee, an increased

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mortality rate for lung cancer among drivers was not observed (33).

In a case control study unadjusted odds ratio for bus driver (OR=5.2, CI=0.8-36.0) and truck driver (OR=1.4, CI=0.7-2.6) when stratified by smoking there was no significant effect (34). After smoking adjustment, excess in lung cancer risk (although not statistically significant) was found in the Roswell Park data for bus taxicab and truck drivers (34). In the Third National Cancer Survey Interview an excess of lung cancer was found among truck drivers (35).

Lung cancer is one of the major effects of exposure to high doses of ionizing radiation. Epidemiological mortality studies of iron ore miners have been conducted in Great Britain, Sweden and the USSR. Most of these survey shown an increased risk of lung cancer which may be as high as 12 times predicted, it is generally attributed to exposure to the miners to radon daughters. The excess of mortality from primary lung cancer is found to be statistically significant for miners between 50-80 years old (PMR between 2 and 3). Lung cancer mortality is associated with the duration of under ground work. The PMR for lung cancer increases with the duration of work under ground and reaches a value of 4.24 for those who worked under ground for more than 30 years and remained even after adjustment for smoking (36). An increased

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risk of lung cancer, particularly of the small cell anaplastic type, has been established among uranium miners and quantitatively related to the inhalation of radon daughters products. Among uranium miners with highest exposures (>3,700 working level months), the smoking adjusted risk of lung cancer is about 20 folds. There has been some suggestion that radon acts synergistically with cigarette smoking to enhance the risk of lung cancer (6).

During the past 20 years and excess risk of lung cancer has been found in bakers and cooks. For a skilled bakers employed in retail bakeries, the SMR is 178(P=0.00008). For the small group of skill bakers employed in hotels and restaurants the SMR is 543(P=0.00002) and for independent bakers the SMR is 146(P=0.007). In a study in England and Wales bakers and pastry cooks were found to have an excess mortality risk due to lung cancer (SMR=128). Polycyclic aromatic hydrocarbons (PAH) which is formed through pyrolysis in the baking ovens is supposed to be carcinogen. Micro organisms as Aspergillus flavus, Aspergillus parasiticus, Aspergillus nidulans may be found in grains, bread and bakery mould can produce aflatoxin and sterigmatocyst in which are both potent carcinogen (37).

Lung cancer is related to various jobs within the rubber factory. In one study the crude relative risk of lung

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cancer for curing and inner tube workers was 3.3 and after adjustment for smoking the RR remained 3.2 (CI=1.3-8.2). The SMR for lung cancer for curing and inner tube workers were higher than for the other groups (38). Increased risk of lung cancer among copper smelter workers has been reported in various studies. The contributing risk factor is supposed to be higher exposure to arsenic and sulphur dioxides. In one study SMR with light exposure to arsenic was 183 ($P<0.05$). Mortality for lung cancer was greatest in workers with high and medium arsenic exposures, elevated risk were also associated with work for 25 years or more in areas of the smelter with low exposures who arsenic (40).

Smoking

Smoking is the most important etiological factor for the lung cancer. In all countries, the increased incidence of lung cancer follows the increase in cigarette smoking. In 1920 and 1930 clinical observation and an alarming increase in lung cancer incidence raised some suspicion that smoking might be a causal factor. In 1950, case control studies in USA and Great Britain (Doll and Hill, 1952, Wynder and Graham 1950) supported the link and the evidence became conclusive through surveys of large cohorts of smokers (6).

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The first comprehensive reviews of the effect of smoking on lung cancer were published in 1962 and 1964 by the Royal college of Surgeons of London and the Surgeon General of the United States. Both case control studies and cohort studies has conformed the strong association between cigarette and lung cancer (RR=3-13 in smoker compared to nonsmoker). The risk of cigarette smoking and lung cancer is a dose response relationship, that the risk increased with the number of cigarette smoked per day, age at which smoking began, inhalation of cigarette smoke and tar content. It has been found that consumption of 20 cigarette per day for 20 years has a risk of 30 times more than non smoker (6).

Hammond and Horn reported the death rate in lung cancer per 100 thousand as 3.4 in the male nonsmoker, 59.3 for 10 to 20 cigarette daily, and 217.3 for 40 or more cigarette daily. The risk of developing lung cancer is proportional to the quantity of tobacco consumed. Cigarette are the chief hazards. The risk is not nil for pipe smoker or cigar smoker, although the risk is 3 times and 10 times less, respectively than cigarette smokers (41). With equal consumption, other factors influencing the risk are, inhalation of the smoke, which is more pronounced in cigarette smoker than cigar or pipe smoker, earlier inhalation of smoking, speed of combustion and number of puffs per cigarette, the habit if keeping a cigarette in the mouth or relighting a stubbed out

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cigarette, the length of the butt, and associated alcoholism (41).

In addition in 1966 the study of Kahn showed that adults aged 45-75 were suggested that a 10 years difference in age of starting smoking between ages 15 and 25 for any level of smoking, effectively accounted for as great a difference in the risk of lung cancer. The magnitude of the effect of smoking duration is as great as the effect of a smoking 10-20 cigarettes per day and 21-31 cigarettes per day at age 55-64 (42). Lung cancer risk is lower in those smoke manufactured and filter cigarettes compare to hand rolled and non filter. Light tobacco has lower risk than dark tobacco. There is a significant increase of risk of cigarette smokers beyond a tar exposure (TE) of 501 (Calculation of TE includes amount of consumption, duration and tar yields of all cigarette brands ever smoked.

Over 1200 substances have been counted in cigarette smoke, which contains both initiators (polynuclear aromatic hydrocarbons such as benzo(a)pyrene, formed by pyrosynthesis) and promotor(phenol and derivatives). Numerous radioactive elements may also be found (polonium-210, carbon-14, radium) as well as many contaminants(arsenic, nickel, molds, additives) (41). The direct toxic effect consists of changes in bronchial elimination process: the mucociliary apparatus is

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damaged and the macrophage are affected, thus making the bronchial tree more vulnerable to other forms of aggression (41). Cessation of smoking induces a return to a normal bronchial epithelium and the risk of lung cancer becomes identical to that of non smoker's after of an average of 13 years. In a prospective survey of British doctors, Doll and Pike found a 25% reduction in the mortality rates due to lung cancer in 12 years during which the number of cigarette smoker decreased by almost 50% with in this group (41). Induction time for cancer related to cigarette smoking has been calculated to be approximately 30 years (41).

Through a systematic study of the bronchial epithelium of smokers, three characteristics were noted: loss of bronchial cilia, basal epithelial hyperplasia, and nuclear abnormalities. The occurrence of all these three types of changes together was never seen among specimens from non smokers and was seen in 9.3% of histological sections from men who smoked 1 to 2 packs of cigarettes a day, in 11.4% of sections for those who smoked 2 or more packs a day, and in 15.0% of sections for those who died of lung cancer (41).

Cell types and smoking

Histologically lung cancer has been divided broadly in to following types.

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1. Squamous cell carcinoma.
2. Adenocarcinoma.
3. Large call carcinoma.
4. Bronchioloalveolar carcinoma.

Data from 1000 lung cancer patients (Siriraj Hospital 1967-1982) showed the following results.

Large cell carcinoma	28.6%
Adenocarcinoma	28.1%
Squamous cell carcinoma	24.7%
Small cell carcinoma	12.5%
Mixed type of adenocarcinoma and squamous cell carcinoma	0.2%
Others	5.9%

There was a difference in cell type between lung cancer patients who were smoker and non smokers.

	SMOKER (805)	NON SMOKER (195)
Large cell	30.1	22.5%
Small cell	14.8	3.1%
Squamous cell	27.2	14.4%
Adenocarcinoma	20.0	53.3%
Mixed type	0.2	-
Others	5.7	6.7%

Kreyberg has demonstrated the rate of tobacco smoking chiefly in squamous cell carcinoma and to a lesser degree in

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oat cell carcinoma (type I). Tobacco has little if any influence on adenocarcinoma and bronchioloalveolor cancer (type II). In non smoker, the predominant cell type is adenocarcinoma. Thus cigarette smoking is reputed to be responsible for 95% of squamous cell carcinoma and 90% of oat cell carcinoma. Squamous cell carcinoma is rarely encountered in non smoker (41).

These data indicates that adenocarcinoma is more common in nonsmokers where as large cell and squamous cell carcinoma are more common in smokers (RR=4.3-27 for squamous cell carcinoma derived for smoker and 1.3-1.9 for adenocarcinoma).

Asbestos

Asbestos has now become a universally recognized carcinogen since the 1st reports dating back to 1935. Over the past 25 years epidemiologic evidence has shown that the risk of lung cancer is higher among workers in various asbestos industries, including miners and miller, textile, insulation, shipyard and cement workers (41). Lung cancer is the major asbestos related disease. Because of its carcinogenic potential and widespread distribution in many industries, asbestos is the agent generally considered to pose

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the largest carcinogenic threat in the work place.
Although exposures are usually to mixed forms of asbestos, all fiber types (crysotile, amosite, crocidolite, anthophyllite) are though to increase the risk of lung cancer. Differences in physical properties and chemical composition of the various types of asbestos indicates that there is a difference in their carcinogenic potential. Men exposed to chrysotile asbestos have a respiratory cancer mortality rates 2.4 times higher than controls, where as those exposed to a combination of chrysotile and crocidotile asbestos have a mortality rates 5.3 times higher than controls. For amosite asbestos the death rate due to respiratory cancer is more than 10 times higher than in controls (41). In most studies the risk of asbestos induced lung cancer is characterized by a latent period of 20 years or longer between start of exposure and onset of the disease. Another characteristics of asbestos induced lung cancer is its synergistic relation with cigarette smoking (41). A recent survey of 276 lung cancer death among insulation workers revealed relative risk of about 5 following asbestos exposure alone, and 50 following combined exposure. Other groups who are exposed to asbestos include clothing ironers, dry wall workers, electricians and plumber (6).

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Polycyclic hydrocarbons

An elevated risk of lung cancer has been reported in several occupational groups heavily exposed to polycyclic aromatic hydrocarbons (PAH). Excessive mortality from lung cancer among gas workers and implicated coal carbonization products has been reported. In Japan, excessive mortality from lung cancer was observed in a group of workers from a gas generator plant (6). In USA, Cloyd (1971) (6) reported the mortality among steel workers and found that men in the coke plant had a risk of lung cancer 2.5 times greater than other steel workers. The excess mortality was confined to men working at coke ovens, reaching 10 folds among those employed five or more years at the top of the ovens. PAH are probably responsible for the excess risk of lung cancer among roofers exposed to asphalt and pitch (6).

Chromium

Since 1948, several studies have shown an excess of lung cancer among workers in the chromate producing industry. An excess of lung cancer has also been found in the chrome pigment industry, among chromic platers, workers producing ferrochromium alloys and spray painters using chromium pigments (6).

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Arsenic

It has been found that workers who handled arsenic in the manufacture of pesticides and herbicides are at higher risk of developing lung cancer. Elevated mortality from lung cancer has been described also in various mining groups heavily exposed to arsenic (6).

Other exposures

Several industrial exposures are suspected as causes of lung cancer. In 1958 epidemiologic studies showed an excess risk of lung cancer among workers in a nickel refinery. Some surveys of the vinyl chloride industry indicate an association with lung cancer. An excess mortality from lung cancer has been reported among workers exposed to beryllium An increase in lung cancer has been reported in some studies of metal workers exposed to ferric oxide dust (6).

Air pollution

Pollutants in the urban air have long been suspected in the etiology of lung cancer. Statistical evidence shows that the lung cancer is commoner in towns than in rural areas and that it's incidence is closely correlated with the degree of atmospheric pollution. It is commonest in large towns with

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an atmosphere heavily polluted by industrial and domestic smoke and by the fumes from internal combustion engines. The carcinogenic agents liberated in the combustion of coal includes benzopyrene and arsenic and the concentration of the former in the air of large town, up to 5 g per 100 cubic meter of air, is such that under normal weather conditions about 0.5 g may be inhaled in 12 hours. The amount is greater in winter than in summer and may be increased almost ten folds in foggy weather (41). The major source of pollution are motor vehicle exhaust (including diesel engines), residential and commercial space heating, oil and coal fired power plants and industrial emissions (6).

In 1977, Doll summarized the association between lung cancer and air pollution. Comparing the 1966 to 1967 mortality rates for lung cancer in 24 countries, it was pointed out that lung cancer was consistently more common in urban areas than in rural areas (43).

In 1975, Brian and others, investigating the association between lung cancer and air pollution during 1968-1972 in South Central Los Angeles County, found that the mortality rates of lung cancer was higher in higher air pollution than in lower air pollution region (44).

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Previous infections

The possible relationship between pulmonary tuberculosis and the subsequent development of lung cancer has attracted attention for several decades. There have been numerous clinical reports of concurrent lung cancer and pulmonary tuberculosis. Some epidemiologic investigations have suggested that pulmonary tuberculosis patients are at significantly increased risk of lung cancer (44).

In a case control study in Shanghai, a significant 50% elevation in the risk of lung cancer, adjusted for cigarette smoking, among persons who had a history of pulmonary tuberculosis. Among those diagnosed with pulmonary tuberculosis with in the past 20 years, the risk exceeded 2.5 folds(RR=2.5). No relationship was found between lung cancer risk and the type of tuberculosis therapy, including isoniazid (44). In many cases pulmonary tuberculosis occur concomitantly with lung cancer and this might be accounted for by a lowering of immune defense mechanism. More over the mean age of TB patients has increased from 49 to 61 years and this might explain the association with lung cancer. However, apart from the problems raised by scar cancer, antituberculous drugs may be directly responsible. In animals, isoniazid is a potent carcinogen and induces pulmonary adenoma in mice. The major metabolite of isoniazid in man (1-acetyl-2-isonic-

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otionoylhydrazine) greatly increases the incidence of lung tumors in mice (44).

It has been reported that personal history of chronic bronchitis or emphysema is associated with increased risk of developing lung cancer(OR=2.0; 95% CI=1.4-2.8 after adjusting for cigarette smoking) (45).

In one study Peter-Golden M, reported that those persons having systemic sclerosis are at higher risk of developing lung cancer (RR=16.5) (46).

Scar cancers of the lung

Feiedrich and Rossle were the first to report a series of pulmonary carcinoma which were found closely associated with previously formed lung scars and established "scar cancer". Among the scar incriminated are old infarcts, gun shot wounds, stab wounds, metallic foreign bodies and granulomatous infections such as tuberculosis. In most of the cases scar cancer belong to adenocarcinomas (44) (47).

Dietary habits

During the past few years, there has been considerable interest in the relationship of dietary habits and lung cancer

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risk. Many studies has been done to prove this relationship. In a case control study of 569 lung cancer patients and 569 control patients admitted to Rosewell Park Memorial Institute indicated that consumption of whole milk 3 or more times daily increased lung cancer risk compared to those never drink whole milk (OR=2.14) (after controlled for cigarette smoking, vit. A intake, education level). The same frequency of intake of reduced fat milk was associated with a significant protective effect (OR=0.54) (48). But in another case control study a strong negative association between lung cancer risk and milk consumption was found. A low rate of lung cancer among individuals with high milk consumption, the estimated odds ratio between consumption of 4 or more glasses a day and less than 1 glass a day being 0.32 (p=0.01) was found (49).

Dietary cholesterol has been found to be positively and significantly associated with lung cancer risk after adjusting for age, ethnicity, pack year of cigarette smoking,and occupational exposure to lung carcinogen. The OR for the persons taking 1000 to more than 3500 mg of dietary cholesterol per week was 1.65 to 3.50. The oxidation product of cholesterol are known to be carcinogenic and mutagenic. Furthermore, at least one investigation has found that cholesterol feeding increases the incidence of lung adenocarcinoma in mice (50). In one study a significant elevation of risk for lung cancer were associated with greater

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frequency of consumption of animal fat sources ie., porkchops, ham and pork sausage (51).

The relative risk for level of repeated coffee and tea consumption all have confidence intervals which includes 1.0. Similarly , infrequent beer and wine intake do have point estimates of risk for which the confidence intervals exclude 1.0 but the relative risk for reported consumption beyond 4 times weekly does not appear to be elevated or reduced (51).

In various case control studies, vitamin A has been found to be having a strong and significant negative effect on lung cancer risk. Carotin was specific mostly for squamous cell carcinoma and small cell carcinoma. Intake of vitamin A from fruits and vegetables(carotene) has been found to be much more strongly associated with reduced cancer risk (49) (50) (51).

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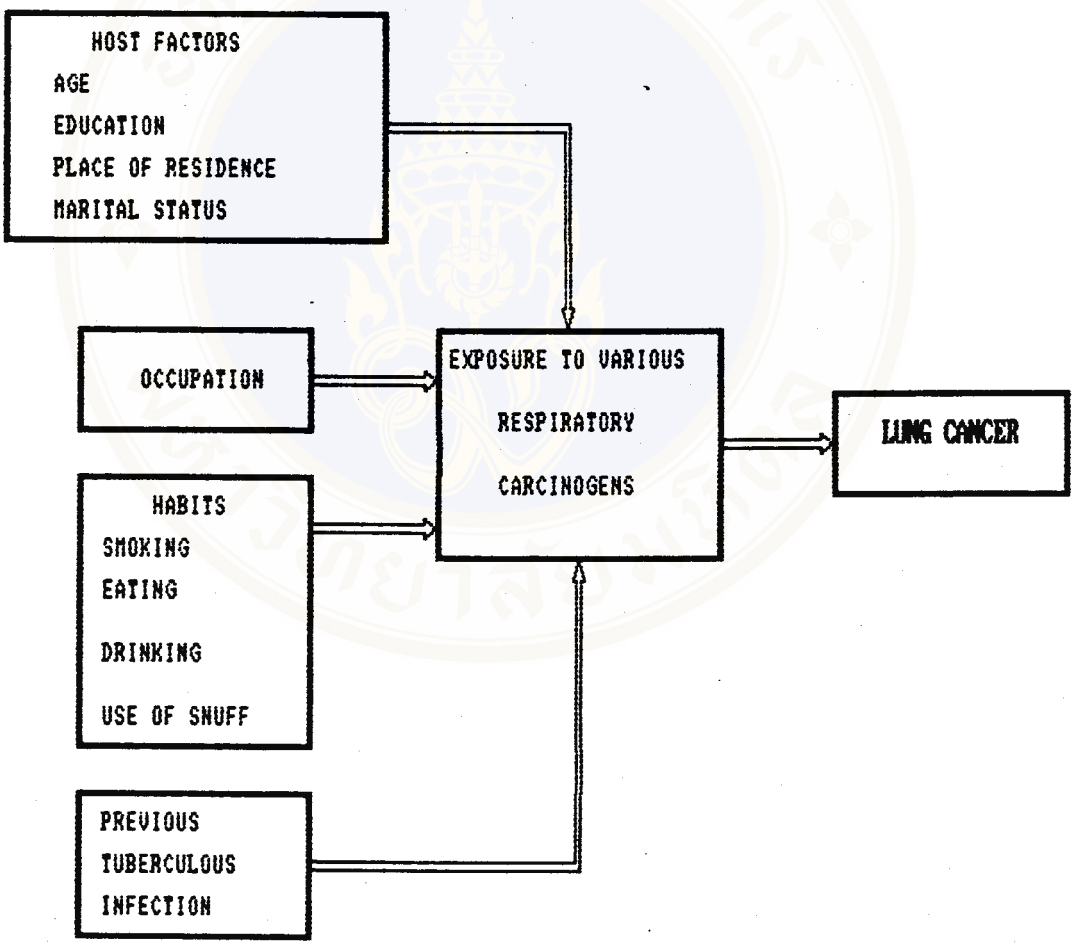
CONCEPTUAL FRAME WORK.



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CHAPTER II

OBJECTIVES

General objectives.

To identify the risk factors for lung cancer among Thai males.

Specific objectives.

1. To determine and compare the demographic and socio economic characteristics of lung cancer among cases and controls (age, place of residence, education, occupation, and marital status).

2. To determine and compare behavioral characteristics of lung cancer among cases and controls (smoking, drinking, eating habits and use of snuff).

3. To determine the frequency of different cell types in lung cancer cases.

4. To determine frequency of different cell types among smokers and non smokers in lung cancer cases.

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5. To determine and compare the frequency of previous tuberculous infections in lung cancer cases and controls.

6. To determine the association of lung cançer and the different demographic, socioeconomic and behavioral characteristics.

7. To identify potential confounders and interactions among independent variables.

Hypothesis.

1. The odds of having lung cancer is higher among those involved in certain occupations than rate expected in general population (like agriculture and farming, welding, painting, mining, asbestos related industries, in construction, meat industry).

2. The odds of having lung cancer is higher among smokers than non smokers.

3. The risk of developing lung cancer is inversely related to education.

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4. The risk of developing lung cancer is higher among those who have had previous infection of pulmonary tuberculosis.

5. The risk of developing lung cancer is higher among those whose place of residence is near to some factory.

6. The risk of developing lung cancer is higher among certain behavioral characteristics such as use of snuff, consumption of beverages (coffee, beer, whisky) consumption of milk, pork, fatty food, poultry.

Significance of research

There is no question that the use of cigarette is the major preventable cause of lung cancer. Despite this knowledge, there is still much to be learned about the chain of causation in lung cancer. Better understanding of other possible risk factors may lead in to a better understanding of the patho-physiology of this important disease and more importantly, to improve preventive strategies.

Though Thailand basically an agricultural country, is approaching very rapidly towards the process of industrialization with opening of more and more new industries. As a result of this, people in Thailand are being

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employed in large numbers in various occupations such as in textile industry, meat industry, mining, construction, transportation services etc. At the same time they are also exposed to various chemicals, fumes, dust, radiation, and other occupational hazards. Various epidemiological studies have proved that workers in various occupations in various industries are at higher risk of developing lung cancer due to prolonged and continuous exposures to various carcinogens. In order to reduce the incidence rate of lung cancer in Thailand it is necessary to identify those occupations which has more risk for developing lung cancer. One of the aim of this research is to find out those occupations which has more risk for the lung cancer among Thai males in hope to help future researcher or health planner for future epidemiological study or for health policy and prevention programs for this disease. After identifying those high risk occupations, what could be done as a preventive measure to reduce the risk for the lung cancer among the workers in those occupations, would be a further research area in this field. Apart from smoking and occupation, certain eating and drinking habits of an individual may also contribute as a risk factor for lung cancer. Another aim of this research is to find out if there is any significant association between lung cancer and foods and beverages. If any such association would be established then it would be possible to reduce the risk of lung cancer by avoiding those foods and beverages from ones diet.

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CHAPTER III

MATERIALS AND METHODS

Study Design

A hospital based case control study design was applied to this study.

Study Area

This study was conducted at the National Cancer Institute, Bangkok, Thailand. This Institute is situated at the center of the Bangkok city and accessible to the general population.

Study population

Cancer patients admitted and or registered at the National Cancer Institute, Bangkok, Thailand, during the period 1985 to 1990.

Case

A case was an adult Thai male aged 30 years and over with a diagnosis of lung cancer, admitted and

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registered at National Cancer Institute, Bangkok, during the period 1985 to 1990.

Inclusion criteria

1. Must be a primary lung cancer case.
2. Cytologically and or histologically confirmed.
3. Must be a Thai National.
4. Aged 30 years and over.

Control

A control was an adult Thai male aged 30 years and over, not suffering from cancer and registered in the out patient of National Cancer Institute, Bangkok, as a case for routine general check up during the period 1985 to 1990.

Sample size estimation

Sample size was calculated by using the following formula: (42)

$$n = \frac{[Z_{1-\alpha}\sqrt{2P_2(1-P_2)} + Z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}]^2}{(P_1-P_2)^2}$$

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Where,

n = Sample size

P_1 = Proportion exposed among cases

P_2 = Proportion exposed among controls

Z = Standard normal deviate

For sample size calculation agriculture was considered as an exposure of interest. The result from a pilot study showed that proportion of lung cancer cases involved in agriculture was 31%, and 68% of the population was employed in agriculture in Thailand. From literature it was found that a minimum odds ratio of 2 would be considered as a public health significance (41). On these assumption P_1 was calculated by the following formula:

The ratio for case : control was 1:1

$$P_1 = \frac{(OR)\ P_2}{(OR)\ P_2 + (1 - P_2)}$$

$$P_1 = \frac{2 \times 0.68}{2 \times 0.68 + (1 - 0.68)}$$

$P_1 = 0.8$

$P_2 = 0.68$

level of significance = 0.05

power of the test = 90%

value of Z (at α =0.05) = 1.96

value of Z (at β =0.1) = 1.282

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$$n = \frac{\left(1.96\sqrt{2*.68(1-.68)} + 1.282\sqrt{.8(1-.8)+.68(1-.68)}\right)^2}{(0.8-0.68)^2}$$

$$n = 300$$

But in this study the sample size was increased by 15% to give allowance for some records where information were not usable. Thus number of subjects in each group were = 345

Method of data collection

This study was relied totally on the information recorded from patient's medical record. Following variables were included in the study and necessary information from patient medical record were transferred to a data recording form. This procedure was intended to simplify and facilitate data processing and coding.

Since the medical records were written in Thai language, necessary help from a translator was taken to translate the necessary information from Thai to English.

Following variables were included in the study

1. Age.
2. Region.
3. Smoking status.
4. Smoking duration.
5. Smoking type.
6. Drinking habits.
7. Eating habits.
8. Education.
9. Marital status.
10. Occupation.
11. Place of residence
12. Use of snuff.
13. Previous Tuberculous infection.

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Sampling technique

Case

Cases for the study were selected by the process of systematic random sampling with a random start. In National Cancer Institute, all the lung cancer patients were entered in a card, "cancer notification form", and it was found that the total number of male cases of primary lung cancer from 1985 to 1990 were 848 (N) and the required number of samples for the study were 345 (n).

So the sampling interval was:

$$\frac{N}{n} = \frac{848}{345} = 2.46$$

During sampling procedure, all of the "cancer notification form" belonging to males were separated from females and then by the process of systematic random sampling every second and then third record, for the first and second case which satisfied the selection criteria were selected as a case. So every second and third record in a alternate fashion was selected as a case. This was to make sure that every record had an equal chance of being selected. The random start was between number 1 and 3. Some selected case did not satisfy the selection criteria during sampling procedure so they were excluded and the immediate succeeding record which satisfied the selection criteria were included. This procedure was followed until all 345 cases had been selected.

Control

Controls were selected from among the patients who consulted in N.C.I. on the same year (1985-1990) when the case

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was diagnosed as lung cancer. For every case selected one control was selected and matched according to age of the case within the age group of <35, 35-44, 45-54, 55-64 and >64.

Records, from where the controls were selected, were filed yearly in to groups starting from 01 to 99, and each groups were records of each patient belonging to that group. For each case selected, One group of records was selected in that particular year for the selection of control. The process of selecting a group of records for each particular year was by simple random sampling using random table. Each group of records consisted of records of both males and females and around 70% of these were of female. To select the controls, each record was examined and the first male record which qualified as a control was selected. When no appropriate control was selected in this group of records then a replacement was done using the same process to select another group of records. This process was followed until all 345 controls had been selected.

Data preparation

Data were coded, edited, and entered in microcomputer using DBASE IV software. Further editing and cleaning was done prior to analysis.

Data analysis

Data were analyzed by using Epi Info software package version 5. Both descriptive and inferential statistics were computed and interpreted.

Descriptive statistics

- frequency/ proportion

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- mean and standard deviation
- t test

Inferential statistics:

- Chi Square

A chi square test and its corresponding P value was computed to determine the association between the disease and the exposure and comparing the X^2 value with df=(r-1) (c-1) for the 5% level of significance. If the calculated X^2 value is greater than tabulated value then one may conclude that it is unlikely that the difference in risk between the group with and the group without the characteristics is a result of chance, at a probability level of 0.05.

$$X^2 = \frac{(n - 1)(ad - bc)^2}{n_1 \; n_0 \; m_1 \; m_0}$$

Odds ratio

To measure the strength of association between the disease (lung cancer) and the exposures odds ratio and its 95% confidence interval was computed.

	case	control	
exposure	a	b	m_1
no exposure	c	d	m_0
	n_1	n_0	n

OR = The ratio of the odds of having the disease with the risk factor present (a/b) and with the risk factor absent (c/d).

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$$OR = \frac{ad}{bc}$$

Its 95% confidence interval was calculated by following formula. If the value of confidence interval cover 1 then it is not significant.

$$OR * \exp\left[+/- 1.96 \sqrt{(1/a)+(1/b)+(1/c)+(1/d)}\right]$$

Stratified analysis

After performing crude analysis, stratified analysis was done to identify and adjust the effects of possible confounders and to screen the variables for logistic regression analysis. This process was done by using Epi Info5 software.

The factors which were considered to be potential confounder were:

1 Age	7 Marital status
2 Region	8 Previous TB infection
3 Smoking status	9 Drinking habits
4 Smoking duration	10 Eating habits
5 Smoking type	11 Use of snuff
6 Education	12 Place of residence

Logistic regression analysis

Logistic regression analysis was done by using MULTLR software to control for confounders simultaneously to determine any interactive effect of different variables.

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Log (odds of getting lung cancer) = $B_0 + B_1x_1 + B_2x_2 \ldots\ldots B_kx_k$

b_0 = baseline regression coefficient

$b_1b_2\ldots\ldots b_k$ = regression coefficient of each corresponding regressor variable

$x_1x_2\ldots\ldots x_k$ = set of values for regressor variables

k = number of regressor

To assess interaction, cross product term such as $b_{ij}x_i*x_j$ was added to the equation. The antilog of each coefficient was taken to get adjusted odds ratio.

Limitations

Data collected were the information recorded in medical records in National Cancer Institute, Bangkok. Therefore the validity and reliability of this research would depend on how valid and reliable were the information recorded.

For example, smoking history was not recorded in detail and specific details of occupational exposure of carcinogens, exact nature of occupation, amount of beverages drank by the patients were not recorded.

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CHAPTER IV

RESULTS AND DISCUSSIONS

RESULTS

Descriptive characteristics of the sample

The comparison of various socio-demographic characteristics between lung cancer cases and controls in National Cancer Institute, (NCI) Bangkok, 1985-1990 were shown in Table 5, 6 and 7. The characteristics included age, education, region, marital status, occupation and residence near factory. The results of the comparison of various socio-demographic characteristics between cases and controls for each variable mentioned above were as follows:

Age.

The percentage distribution of age in cases and controls were almost similar. The age group more than 64 years was the largest group in cases (40.5%) while in controls the age group 55-64 years represented the largest group (36.8%). In cases, the age group 55-64 years and 45-54 years represented the second and third majority with 33.6% and 19.2% respectively while among controls the age group more than 64 years and 45-54 years represented the second and third biggest

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group with 35.4% and 20.3% respectively. Other groups were very few and quite similar in distribution (Table 5, Fig 3).

Education.

The level of education in cases and controls were not similar. Primary education contributed the major group both in cases and controls though the percentage distribution was higher among the cases (65.5% and 37.4% respectively). Among the cases no education was the second largest group comprising 13.8%, while among controls above secondary and secondary education were the second largest group (28.7% and 28.4% respectively). In cases, above secondary education was the least to represent the group (7.5%) while in controls no education was the least to represent (5.5%). (Table 5, Fig 4).

Region.

Central region dwellers represented the major group both in cases and controls with 72.9% and 67.2% respectively and southerners represented the lowest group with 2.4% and 2.8% respectively. Other regions were small in number and similar in percentage distribution (Table 5, Fig. 5).

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Table 5. Comparison of various socio-demographic variables between lung cancer cases and non lung cancer controls in NCI, Bangkok, 1985-1990.

Variables	Case N	(%)	Control N	(%)	χ^2 (df)	p value
1. Age Years						
<35	7	(2.1)	7	(2.1)		
35 - 44	15	(4.5)	19	(5.5)		
45 - 54	64	(19.2)	70	(20.3)	2.13	0.71
55 - 64	112	(33.6)	127	(36.8)	(4)	
>64	135	(40.5)	122	(35.4)		
Mean (SD)	60.9	(11.1)	59.3	(11.0)		
2. Education						
No education	46	(13.8)	19	(5.5)		
Primary	218	(65.5)	129	(37.4)	98.6	<0.001
Secondary	44	(13.2)	98	(28.4)	(3)	
Above secondary	25	(7.5)	99	(28.7)		
3. Region						
Central	243	(72.9)	232	(67.2)		
Northeast	29	(8.7)	48	(13.9)		
North	19	(5.7)	20	(5.7)	4.99	0.28
South	8	(2.4)	10	(2.8)	(4)	
East	34	(10.2)	35	(10.1)		
4. Marital status						
Single	15	(4.5)	12	(3.4)		
Married	276	(82.8)	310	(89.8)		
Separate	7	(2.1)	3	(0.8)	9.02	0.28
Widow	33	(9.9)	17	(4.9)	(4)	
Divorce	2	(0.6)	3	(0.8)		
5. Residence near factory						
Yes	32	(44.4)	40	(55.6)	0.61	0.43
No	296	(49.3)	304	(50.7)	(1)	

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DISTRIBUTION OF CASE AND CONTROL BY AGE

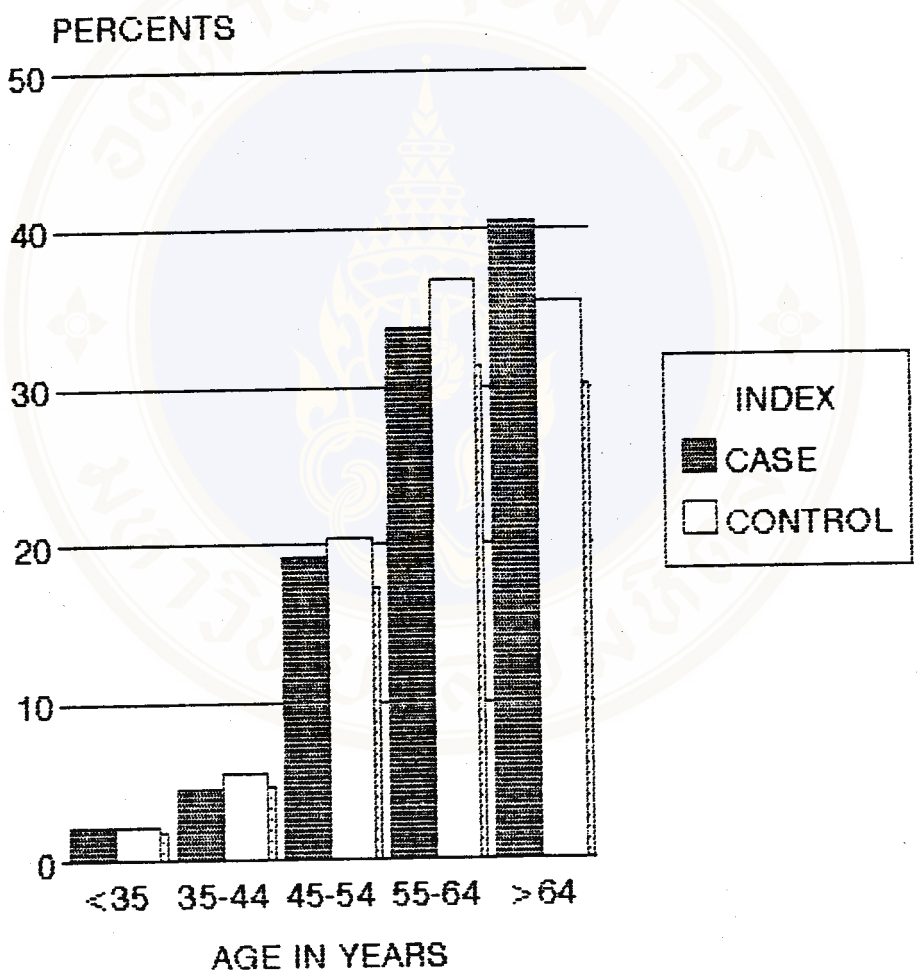

FIG. 3

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DISTRIBUTION OF CASE AND CONTROL BY EDUCATION

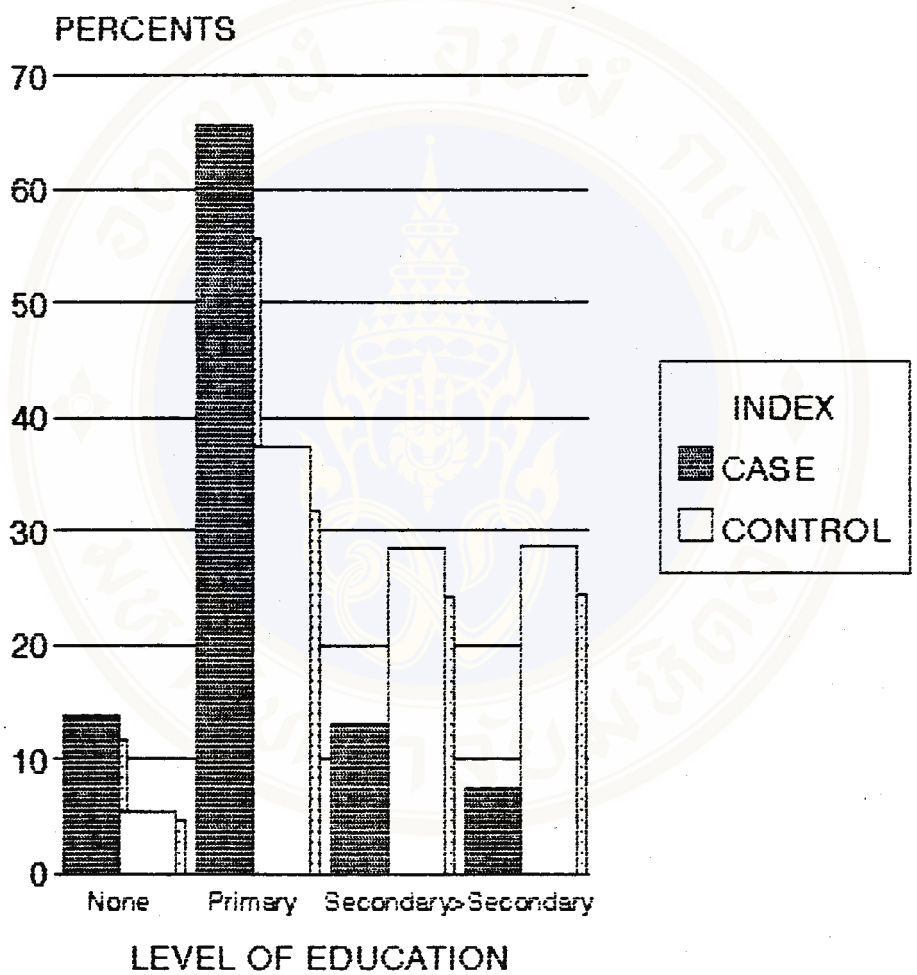

FIG. 4

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DISTRIBUTION OF CASE AND CONTROL BY REGION

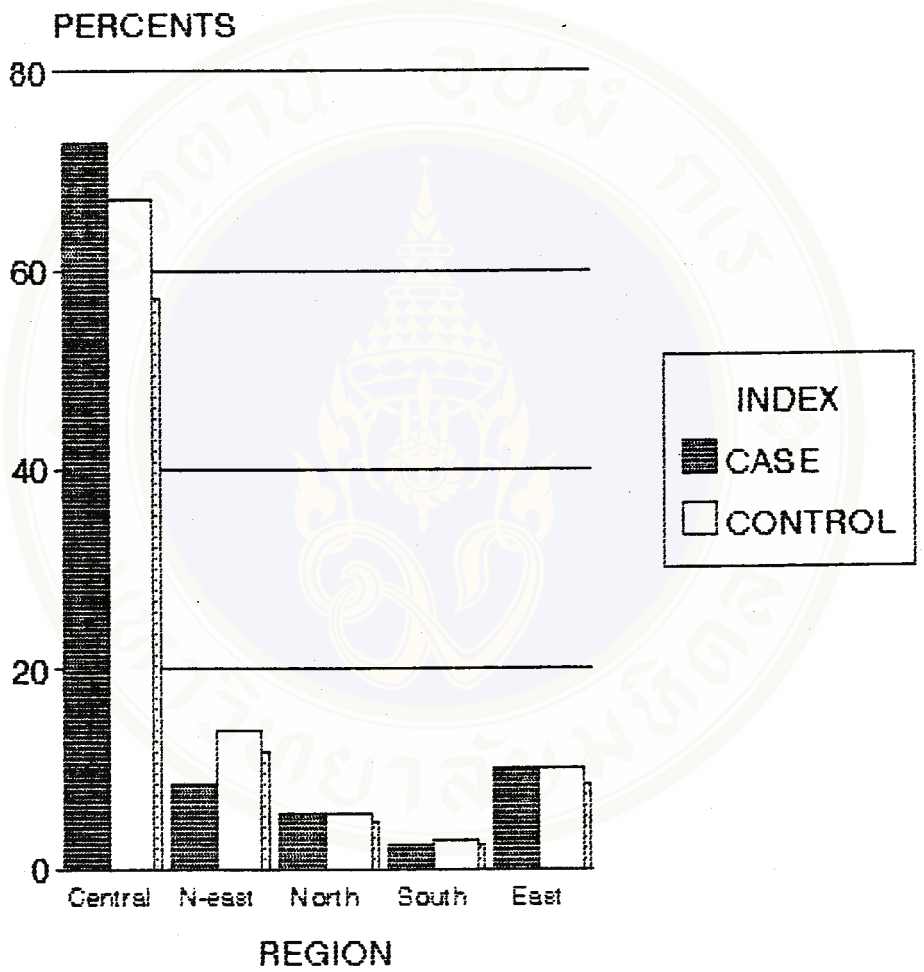

FIG. 5

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DISTRIBUTION OF CASE AND CONTROL BY MARITAL STATUS

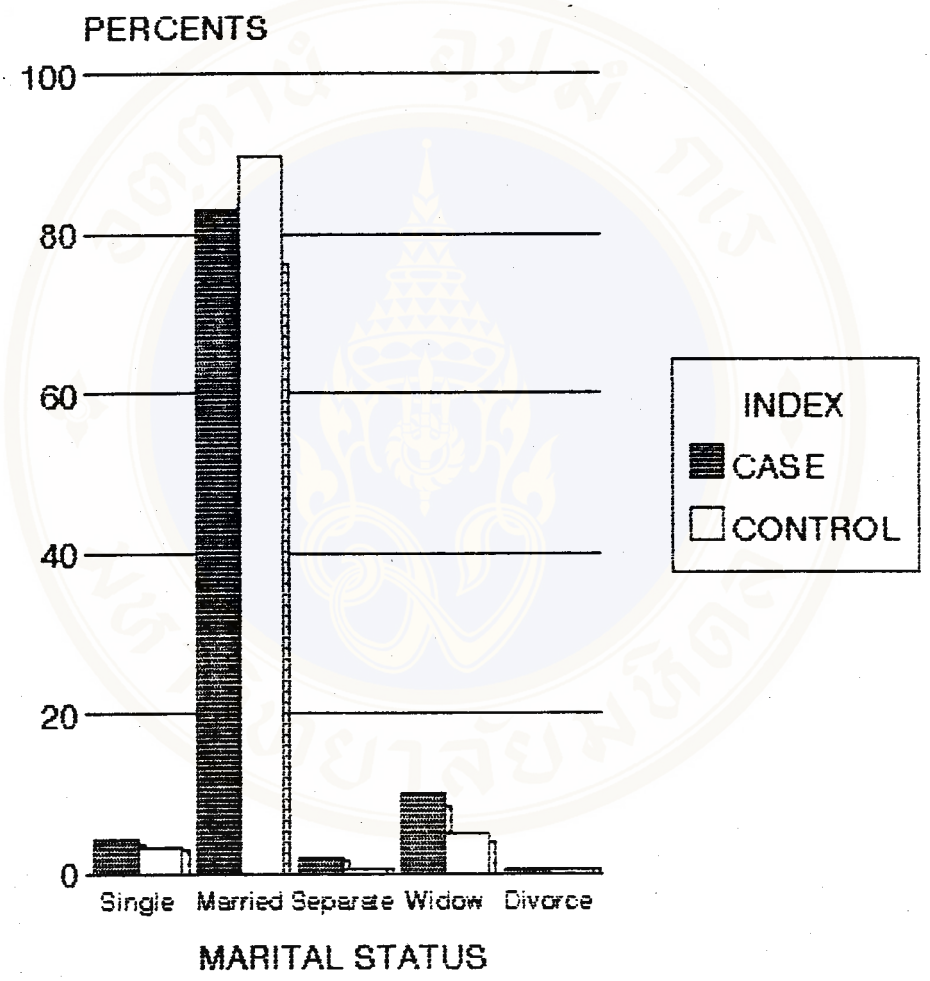

FIG. 6

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Marital status.

Most of the samples in this study were married (82.8% of cases and 89.8% of controls). The smallest group was divorce group with 0.6% of cases and 0.8% of controls. Other groups were very few and quite similar (Table 5, Fig. 6).

Residence near factory.

Among cases, 44.4% of the subjects had their residence near a factory while among controls 55.6% had their residence near a factory (Table 5).

Occupation.

There was a great difference in distribution with regard to current and past occupation among cases and controls. For present occupation, agriculture formed the major group among the cases (40.2%), among controls government officials was the major group (28.0%). Laborer and merchant formed the second major group among cases with 21.7% and 15.8% respectively. But among the controls merchant and agriculture formed the second major group (26.2% and 24.1% respectively). Other occupations were few in number and similar in percentage distribution (Table 6, Fig.7).

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Table 6. Comparison of present occupation between lung cancer cases and non cancer controls in NCI.

Occupation	Case N (%)	Control N (%)	p value*	OR (95% CI)
1. Agriculture	102 (40.2)	59 (24.1)	<0.0001	2.10 (1.41-3.15)
2. Carpenter	2 (0.8)	4 (1.6)	0.441**	0.48 (0.06-3.04)
3. Driver	22 (8.7)	8 (3.3)	0.011	2.80 (1.16-6.99)
4. Govt.official	23 (9.1)	68 (28.0)	<0.0001	0.26 (0.15-0.44)
5. Laborers	55 (21.7)	20 (8.1)	<0.0001	3.10 (1.74-5.55)
6. Merchant	40 (15.8)	64 (26.2)	0.004	0.53 (0.33-0.84)
7. Military	3 (1.2)	6 (2.5)	0.330**	0.47 (0.09-2.16)
8. Teacher	6 (2.4)	14 (5.7)	0.098	0.47 (0.17-1.26)
9. Others	1 (0.4)	1 (0.4)	1.00**	0.96 (0.03-35.29)

* p-value of Chi-square test.

** p-value of Fisher exact test.

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Table 7. Comparison of past occupation between lung cancer cases and non cancer controls in NCI.

Occupation	Case N (%)	Control N (%)	p value*	OR (95%CI)
1. Agriculture	40 (25.5)	182 (24.0)	0.137	1.54 (0.84-2.83)
2. Carpenter	6 (3.8)	1 (0.8)	0.130**	5.21 (0.61-116.22)
3. Driver	9 (5.7)	3 (2.3)	0.142	2.61 (0.63-12.46)
4. Govt.official	18 (11.5)	52 (39.4)	<0.0001	0.20 (0.10-0.38)
5. Laborers	32 (20.4)	14 (10.6)	0.023	2.16 (1.05-4.49)
6. Merchant	31 (19.7)	11 (8.3)	0.006	2.71 (1.24-6.02)
7. Military	9 (5.7)	9 (6.8)	0.704	0.83 (0.29-2.37)
8. Teacher	5 (3.2)	13 (9.8)	0.776	1.19 (0.33-4.42)
9. Others	7 (4.5)	5 (3.8)	0.019	0.30 (0.09-0.93)

* p-value of Chi-square test.

** p-value of Fisher exact test.

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DISTRIBUTION OF CASE AND CONTROL BY OCCUPATION (CURRENT)

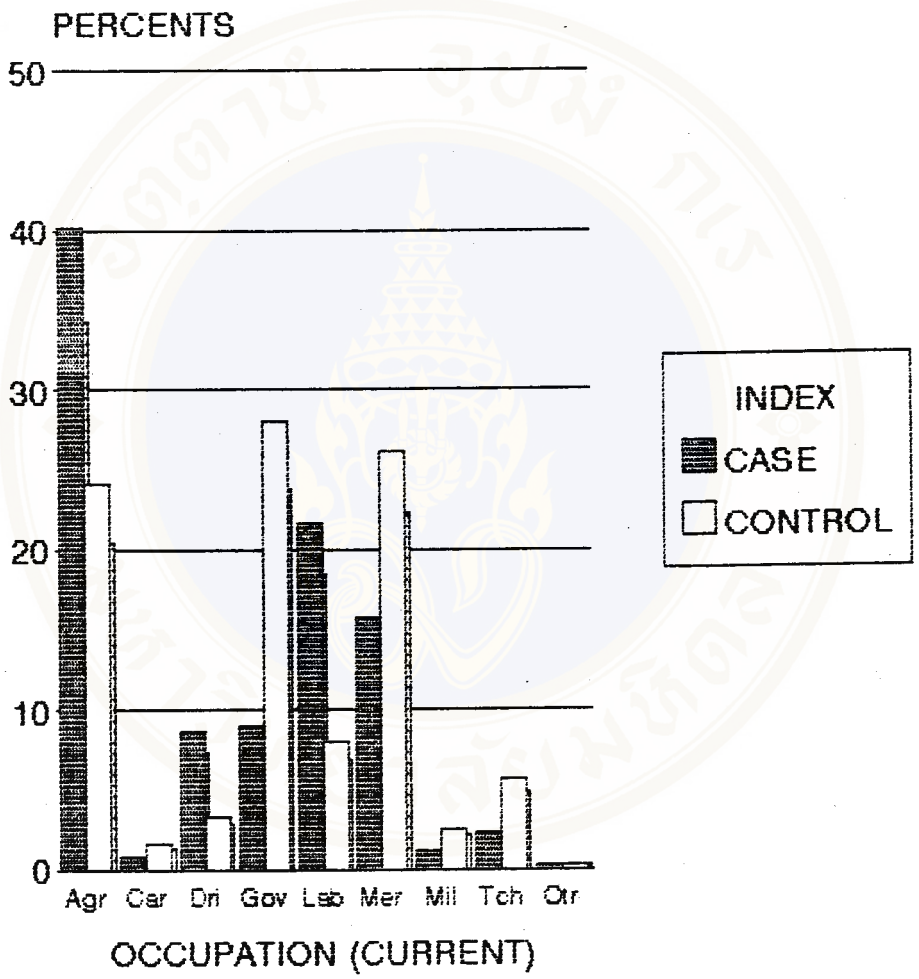

FIG. 7

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DISTRIBUTION OF CASE AND CONTROL BY OCCUPATION (PAST)

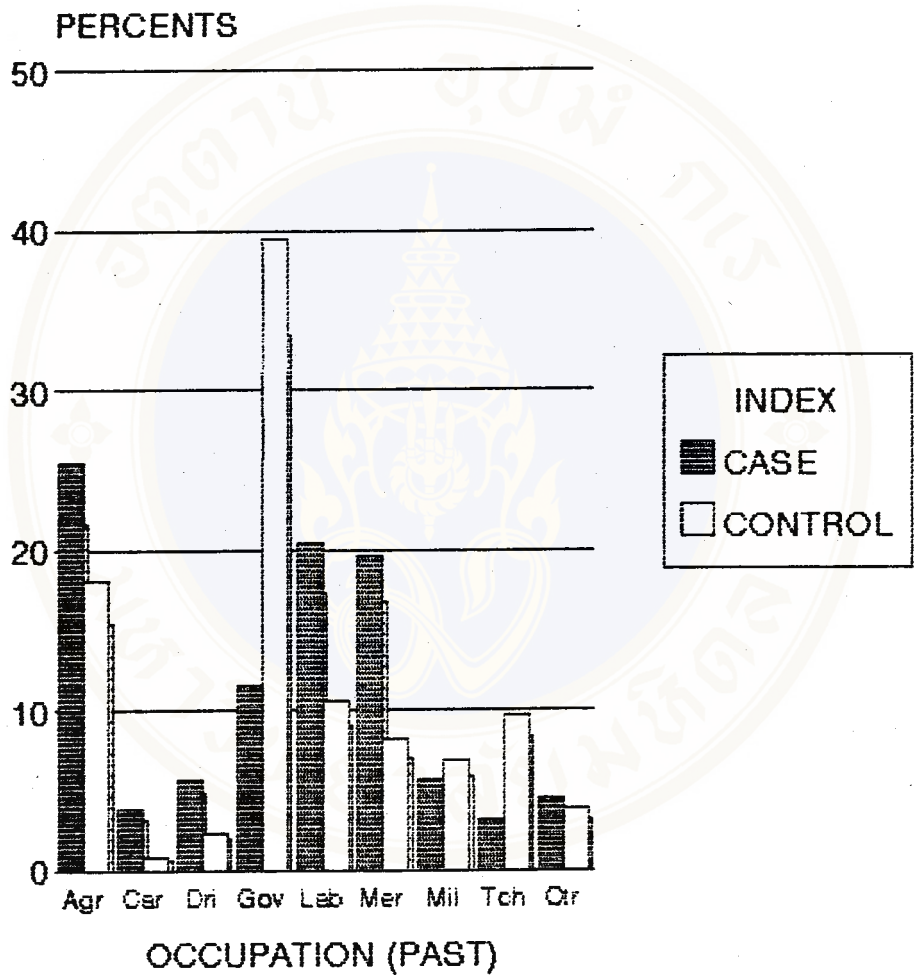

FIG. 8

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For past occupation, agriculture represented the largest group among cases (25.5%) but among controls it was the government official which represented the largest group (39.4%). Among cases merchant formed the second largest group (19.7%) but for controls agriculture formed the second largest group (18.2%). Other groups of occupation were small in number and quite similar in percentage distribution (Table 7, Fig 8).

General characteristics of cigarette smoking.

Features of cigarette smoking were investigated by estimating the risk associated with various exposures to cigarette consumption. For the comparison of cigarette smoking between cases and controls, type of smoking, cigarette smoked per day, duration of smoking and age started smoking were taken into consideration and were analyzed separately. As shown in Table 8, the smokers formed the major group both among cases and controls (89.5% and 58.6% respectively). However the percentage of smokers among cases was higher than controls. The difference was statistically significant. For the type of smoking it was found that 55.7% of the cases and 34.3% of the controls smoked cigarette with out filter. Among cases only 17.3% smoked cigarette with filter where as among controls 35.8% smoked cigarette with filter.

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Table 8. Comparison of smoking habit between lung cancer cases and non cancer controls in NCI.

Variables	Case N (%)	Control N (%)	p** value	OR (95%CI)
1.Smoking status				
Smoker	298 (89.5)	202 (58.6)	<0.0001	6.03 (3.91-9.33)
Non smoker*	35 (10.5)	143 (41.4)	-	1.00
2.Type of smoking				
Cigar	10 (3.4)	7 (3.4)	<0.0001	5.84 (1.8-18.5)
Pipe	16 (5.4)	11 (5.4)	<0.0001	5.94 (2.3-15.2)
Cheroot	54 (18.2)	43 (21.1)	<0.0001	5.13 (2.8-9.2)
No filter	165 (55.7)	70 (34.3)	<0.0001	9.63 (5.9-15.7)
Filter	51 (17.3)	73 (35.8)	<0.0001	2.85 (1.6-4.9)
Non smoker*				1.00
3.Cigarette per day				
<10	43 (14.5)	41 (20.2)	<0.0001	4.2 (2.3-7.8)
10-20	202 (68.0)	147 (72.4)	<0.0001	5.6 (3.5-8.8)
>20	52 (17.5)	15 (7.5)	<0.0001	14.1 (6.8-29.8)
Non smoker*				1.00

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Table 8. (cont.)

Variable	Case N (%)	Control N (%)	p** value	OR (95%CI)
4.Duration of smoking.				
<10 years	5 (1.7)	12 (5.9)	0.34	1.70 (0.5-5.6)
10-20	52 (17.5)	39 (19.2)	<0.0001	5.43 (3.0-9.8)
>20	240 (80.8)	152 (74.9)	<0.0001	6.45 (4.1-10.0)
Non smoker*				1.00
Mean SD	42.2 (23.1)	59.4 (34.8)		
5.Age started smoking (years).				
<16	60 (20.2)	23 (11.3)	<0.0001	10.6 (5.5-20.5)
16-25	212 (71.4)	152 (74.9)	<0.0001	5.7 (3.6-8.9)
>25	25 (8.4)	28 (13.8)	<0.0001	3.6 (1.8-7.3)
Non smoker*				1.00
Mean SD	27.8 (24.9)	52.9 (38.8)		

* Base line for computation for odds ratio

**p-value of Chi-square test.

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DISTRIBUTION OF CASE AND CONTROL BY SMOKING STATUS

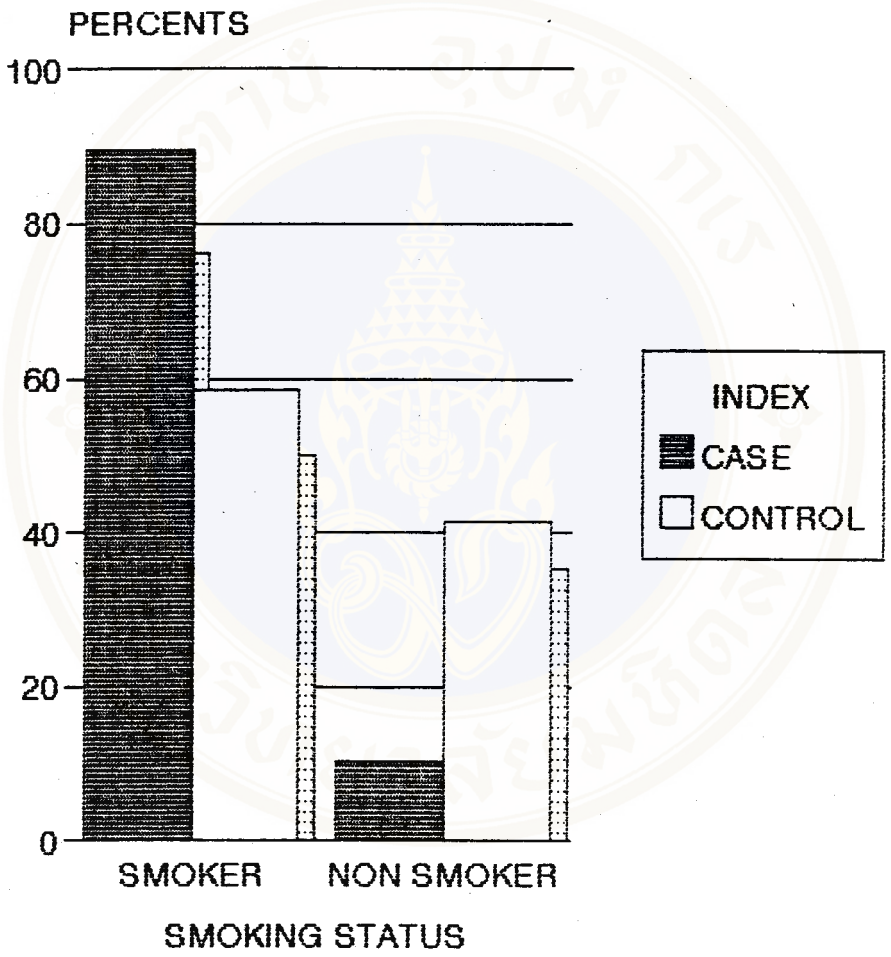

FIG. 9

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DISTRIBUTION OF CASE AND CONTROL BY TYPE OF SMOKING

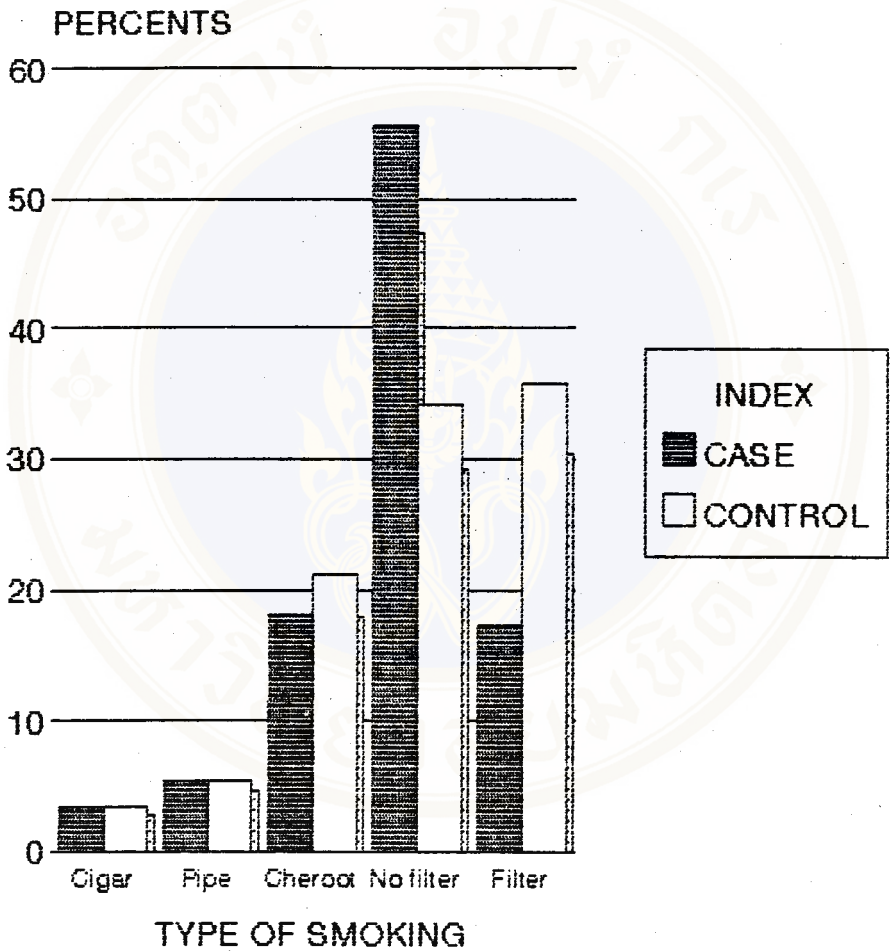

FIG. 10

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DISTRIBUTION OF CASE AND CONTROL BY AMOUNT OF SMOKING

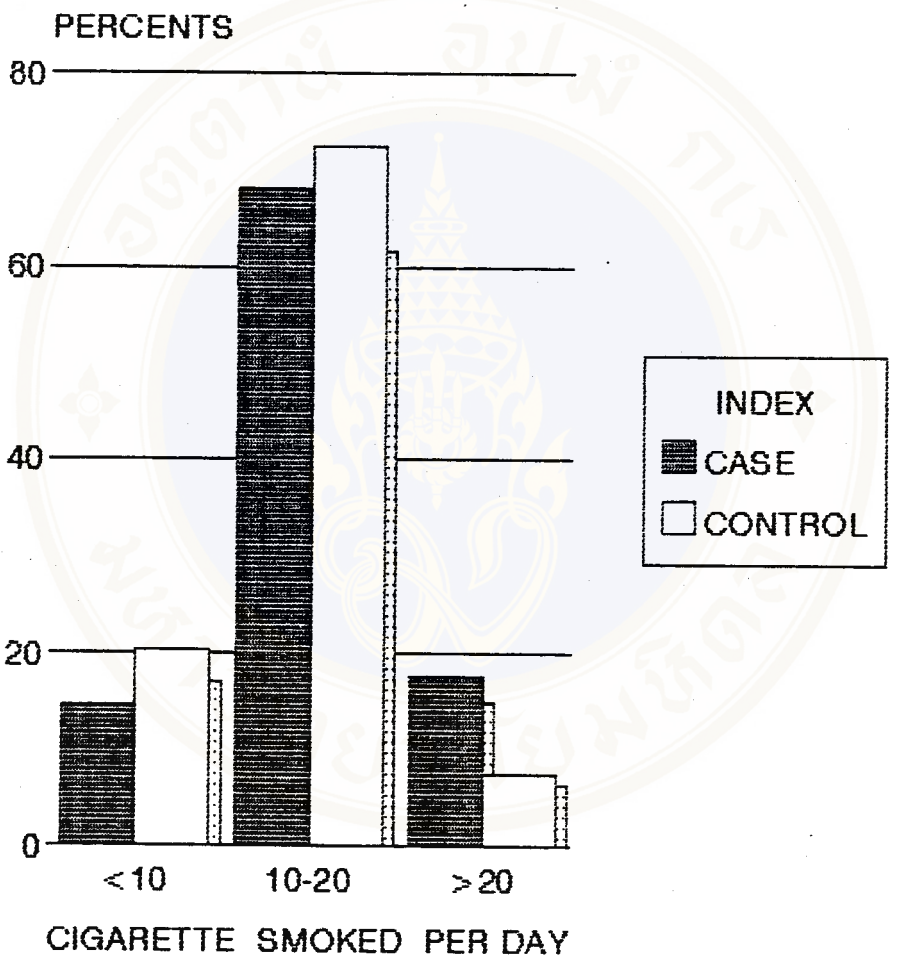

FIG. 11

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DISTRIBUTION OF CASE AND CONTROL BY DURATION OF SMOKING

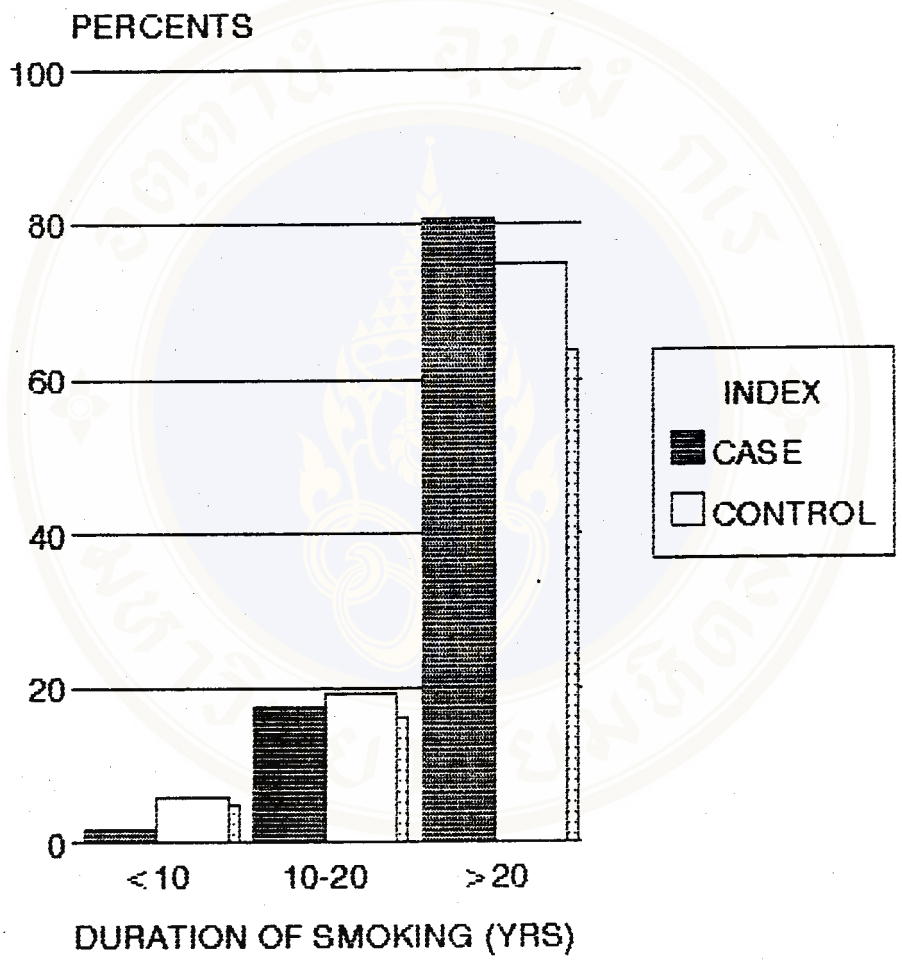

FIG. 12

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DISTRIBUTION OF CASE AND CONTROL BY AGE STARTED SMOKING

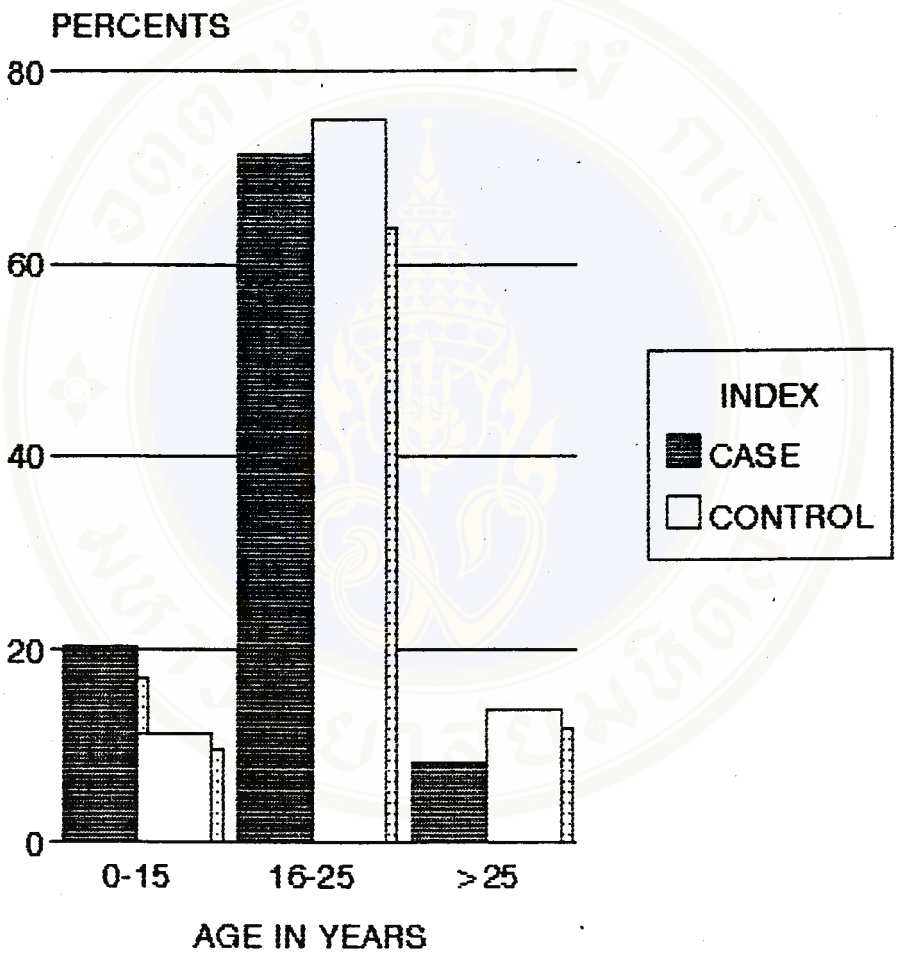

FIG. 13

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Other types of smoking were few and similar in distribution (Table 8). When cigarette smoked per day was considered it was found that the group with 10-20 cigarette per day was the major group both in cases and controls (68.0% and 72.4% respectively) though the percentage distribution was slightly higher among controls. Cigarette smoked more than 20 per day was more than double in cases than controls (17.5% and 7.4% respectively) where as cigarette smoked less than 10 per day was more in controls than in cases (20.2% and 14.5% respectively) (Table 8).

When duration of smoking was taken in to account it was found that cigarette smoking for more than 20 years was the major group both in cases and controls (80.8% and 74.9% respectively). Smoking duration between 10-20 years was the second largest group both in cases and controls with 17.5% and 19.2% respectively. Smoking cigarette for less than 10 years was 1.7% only among the cases and 5.9% among the controls (Table 8).

When the age started smoking was considered it was found that the age group 16-25 was the largest group both in cases and controls (71.4% and 79.9% respectively). In the age group <16 years there were 16.2% among cases and 11.3% among controls. Similarly in the age group of >25 years there were 8.4% among cases and 13.8% among controls (Table 8).

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General characteristics of behavioral habits and history of pulmonary tuberculosis.

In table 9, a comparison of eating and drinking of specific food items, use of snuff and history of tuberculosis among cases and controls were summarized. Regarding the regular drinking of coffee among cases and controls there was not a much difference. Among cases 43.9% and among the controls 56.1% used coffee regularly. But there was a great difference in drinking beer among cases and controls. 74.5% of the cases regularly drank beer while only 25.5% of the controls used it. There was also a great difference in the regular use of whisky (native) and whisky (foreign) among the cases and controls. Among the cases 75.3% regularly used whisky (native) where as only 24.7% of the controls regularly used it. For the whisky (foreign) 64.1% of the cases regularly used it while 35.9% of controls used it regularly.

There was not a big difference regarding the use of milk, pork, eggs and fatty food among the cases and controls (Table 5). But there was a difference in eating poultry among the cases and controls. Among the cases 59.7%ate poultry regularly where as in controls 40.3% used it. Regular use of snuff was almost similar in both cases and controls.

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There was a difference in the history of previous pulmonary tuberculous infection in cases and controls. In cases 62.8% had pulmonary tuberculosis in the past while in controls only 37.2% had history of pulmonary tuberculosis.

Cell types and lung cancer.

In Table 10, frequency distribution of cell types among lung cancer cases were summarized. Most of the cases of lung cancer belonged to squamous cell carcinoma and adenocarcinoma (39.0% and 28.2% respectively). There was a difference in cell type between lung cancer cases who were smokers and non smokers. Adenocarcinoma was more common in non smokers (42.9%) where as squamous cell carcinoma was more common in smokers (39.6%) (Table 11). These results coincide with the results derived from 1000 lung cancer patients at Siriraj Hospital in 1967-1982.

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Table 9. Comparison of behavioral characteristics and pulmonary tuberculous infection between lung cancer cases and non cancer controls in NCI.

Variable	Case N (%)	Control N (%)	p value*	OR (95% CI)
1. Drinking coffee (yes/no)	75 (43.9)	96 (56.1)	0.13	0.75 (0.52-1.09)
2. Drinking beer (yes/no)	35 (74.4)	12 (25.5)	<0.001	3.26 (1.59-6.82)
3. Drinking whisky native (yes/no)	61 (75.3)	20 (24.7)	<0.001	3.64 (2.08-6.45)
4. Drinking foreign whisky (yes/no)	66 (64.1)	37 (35.9)	<0.001	2.06 (1.30-3.27)
5. Consuming milk (yes/no)	130 (55.6)	104 (44.4)	0.01	1.48 (1.06-2.07)
6. Eating pork (yes/no)	233 (52.5)	211 (47.5)	0.01	1.48 (1.06-2.07)
7. Eating poultry (yes/no)	182 (59.7)	123 (40.3)	<0.001	2.18 (1.57-3.01)
8. Eating eggs (yes/no)	158 (55.8)	125 (44.2)	<0.001	1.59 (1.15-2.19)
9. Eating fatty food (yes/no)	159 (51.3)	151 (48.7)	0.29	1.17 (0.85-1.61)
10. Use of snuff (yes/no)	49 (45.4)	59 (54.6)	0.38	0.83 (0.54-1.29)
11. Tuberculous infection (yes/no)	49 (62.8)	29 (37.2)	0.01	1.88 (1.12-3.16)

* p-value of Chi-square test.

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Table 10. Frequency of cell types among lung cancer cases in NCI (1985-1990).

Cell type	No. of cases	percent
1. Adenocarcinoma	91	(28.2)
2. Squamous cell carcinoma	126	(39.0)
3. Large cell carcinoma	45	(13.9)
4. Small cell carcinoma	43	(13.3)
5. Mixed type of adeno and squamous cell	4	(1.2)
6. others	14	(4.3)
Total	323	(100.00)

Table 11. Frequency of cell types among smokers and nonsmokers in lung cancer cases in NCI (1985-1990).

Cell type	Smoker N (%)	Non smoker N (%)
1. Adenocarcinoma	76 (26.4)	15 (42.9)
2. Squamous cell carcinoma	114 (39.6)	12 (34.3)
3. Large cell carcinoma	40 (13.9)	5 (14.3)
4. Small cell carcinoma	41 (14.2)	2 (5.7)
5. Mixed type of adeno and squamous cell	4 (1.4)	-
6. Others	13 (4.5)	1 (2.9)
Total	288	35

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Blood group and lung cancer.

In Table 12 comparison of blood groups between lung cancer cases and non cancer controls were shown. There was not much difference in blood group distribution among cases and controls and were equally distributed except in blood group B where there was a slight increase in percentage distribution among controls when compared to cases (42.1% and 37.4% respectively). It means that blood group has no association with the occurrence of lung cancer.

Table 12. Comparison of blood group in lung cancer cases and non cancer controls in NCI (1985-1990).

Blood group	Case N	Case (%)	Control N	Control (%)
1. A	47	(20.6)	59	(19.4)
2. B	85	(37.4)	128	(42.1)
3. O	83	(36.4)	95	(31.3)
4. AB	13	(5.7)	22	(7.2)
Total	228		304	

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FREQUENCY OF CELL TYPES AMONG LUNG CANCER CASES

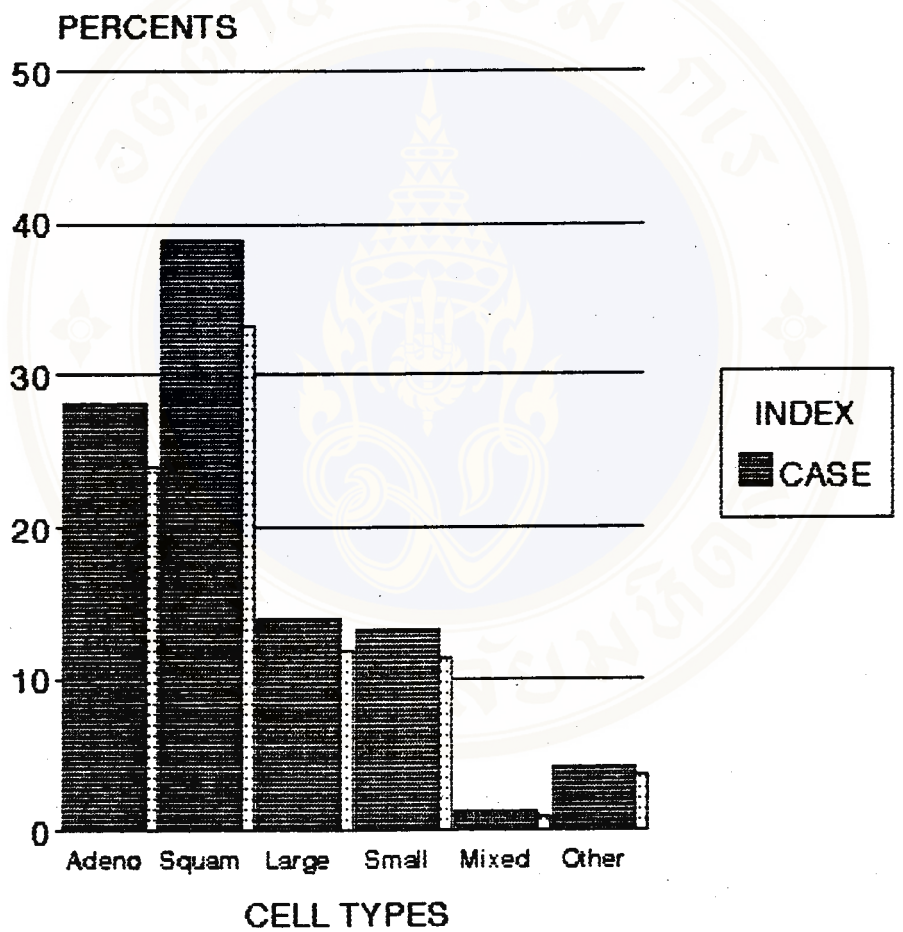

FIG. 14

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FREQUENCY OF CELL TYPES BY SMOKING STATUS

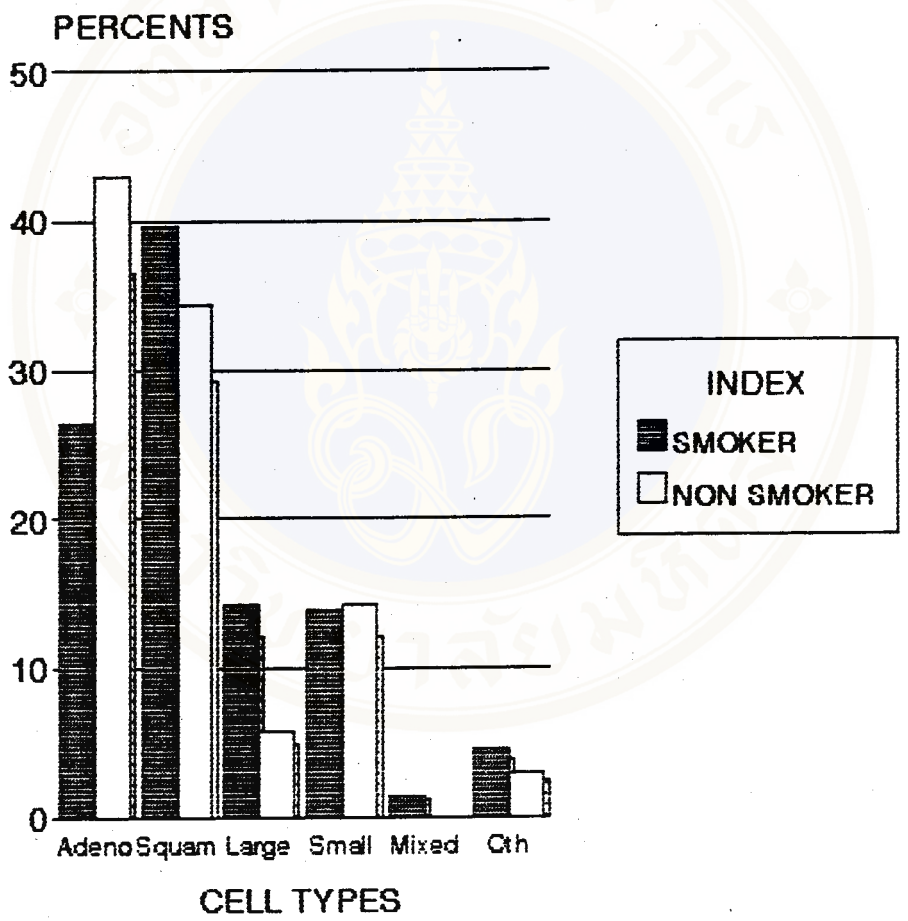

FIG. 15

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DISTRIBUTION OF CASE AND CONTROL BY BLOOD GROUP

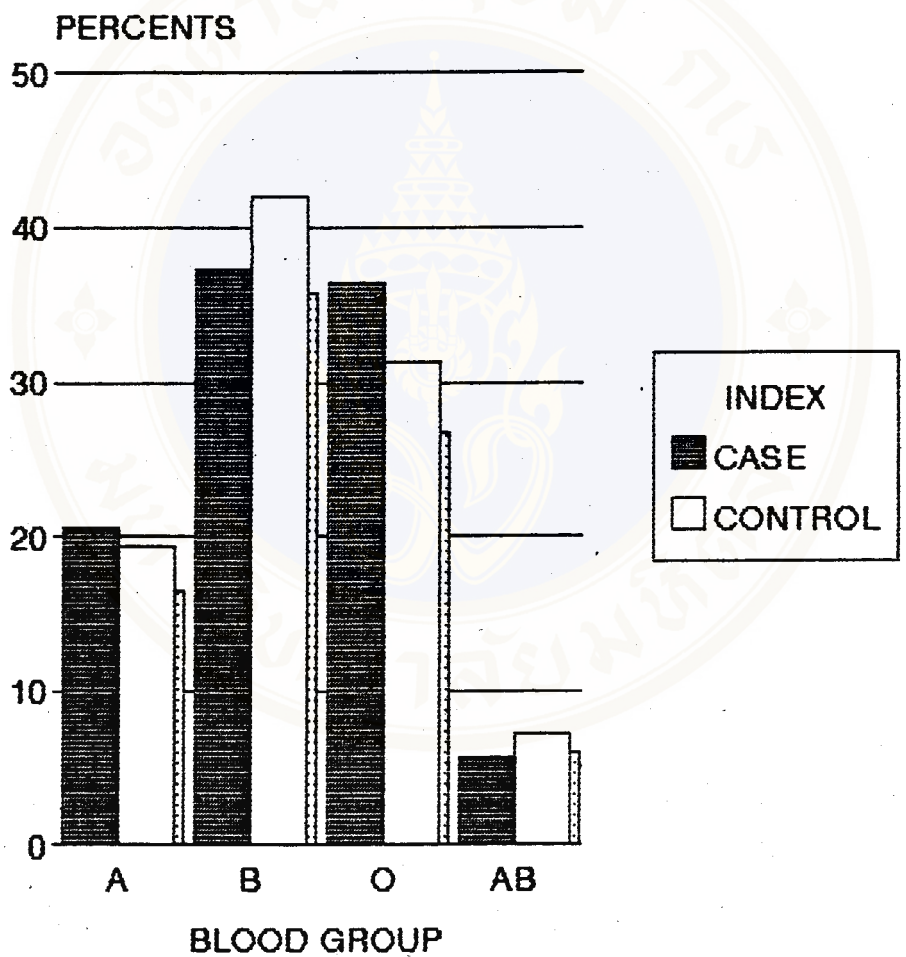

FIG. 16

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The association and effects of various factors in the development of lung cancer.

A Chi-square test and it's corresponding P-value was computed to determine the association between lung cancer and the socio-demographic factors and were summarized in the Table 5. Only education was found to be significantly associated with lung cancer development (P<0.001). The OR was significantly higher when no education was compared with education above secondary (OR=9.59, 95% CI=4.5-20.5). Similarly when primary education was compared with education above secondary the OR was still significant (OR=6.69, 95%CI=3.9-11.3). But when secondary education was compared with above secondary education it's 95% CI included 1.0 though the OR was significant (OR=1.78, 95%CI=0.97-3.27).

Other factors such as age, region, marital status and residence near factory did not show significant association with lung cancer occurrence.

Percentage distribution of cases and controls by present and past occupation with OR and it's 95% CI were shown in Table 6 and 7. For present occupation, agriculture (OR=2.10, 95% CI=1.41-3.15), driver (OR=2.80, 95% CI=1.16-6.99) and laborers (OR=3.10, 95% CI=1.74-5.55) were found to be significantly associated with lung cancer development.

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Similarly for the past occupation only merchant was found to be significantly associated with lung cancer development (OR=2.71, 95%CI=1.24-6.02). When average year at work among cases (mean=27.3, SD=12.8) and controls (mean=35.5, SD=12.5) for agriculture was compared there was a significant difference between two groups ($p<0.05$). Similarly for laborer there was a significant difference ($p<0.05$) in average year at work among cases (mean=22.6, SD=9.7) and controls (mean=27.7, SD=10.2).

The association between smoking and lung cancer was highly significant (OR=6.03, 95% CI=3.91-9.33) (Table 8). It meant that those who were smoker would have 6 times more risk for developing lung cancer compared to non smokers. Not only the smoking but the type of smoking was also significantly associated with lung cancer occurrence. Smoking cheroot when compared to non smoker had a significant association with lung cancer occurrence (OR=5.1, 95%CI=2.8-9.2) (Table 8). It meant that those who smoked cheroot would have 5 times more risk for developing lung cancer compared to those who never smoked cigarette. Similarly smoking without filter when compared with non smoker had a significant association with lung cancer (OR=9.3, 95% CI=5.9-15.7). It meant that those who smoked cigarette with out filter would have more than 9 times more risk for developing lung cancer compared to those who never smoked cigarette. Similarly the OR for cigar, pipe and filter

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smoking compared to non smoker were 5.84,95% CI=1.8-18.5, 5.9, 95% CI=2.3-15.2 and 2.8, 95% CI=1.6-4.9 respectively (Table 8). From the figure 14 a clear cut dose response relationship can be seen between the type of smoking and the risk of developing lung cancer.

Amount of cigarette smoked per day also had a significant association with lung cancer development. Smoking cigarette more than 20 per day when compared to non smoker had a significant association with lung cancer (OR=14.4, 95% CI=6.8-29.8). It meant that those who smoked more than 20 cigarettes per day would have 14 times more risk for developing lung cancer compared to those who never smoked cigarettes. Similarly the OR for cigarette smoking <10 and 10-20 per day was 4.2, 95% CI=2.3-7.8, 5.6, 95% CI=3.5-8.8 respectively (Table 8). In figure 15 a dose response relationship has been shown between amount of smoking and the risk of developing lung cancer.

Duration of smoking also had a significant association with lung cancer. Smoking cigarette for more than 20 years when compared to non smoker had a significant association (OR=6.4, 95% CI=4.1-10.0). It meant that those who smoked cigarettes for more than 20 years would have nearly 6 times more risk for developing lung cancer compared to those who never smoked. Similarly the OR for smoking cigarette <10 and

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10-20 years was 1.7, 95% CI=0.5-5.6 and 5.4, 95% CI=3.0-9.8 respectively (Table 8). In figure 16 a dose response relationship has been shown between duration of smoking and the risk of developing lung cancer.

Similarly age started smoking had a significant association with lung cancer. Smoking cigarette at an early age of less than 16 years when compared to non smoker had a significant association (OR=10.6, 95% CI=5.5-20.5) (Table 8). It meant that those started smoking before 16 years of age would have almost 10 times more risk for lung cancer compared to those who never smoked. Similarly the OR for age started smoking >25 and 16-25 years was 3.6, 95% CI=1.8-7.3 and 5.7, 95% CI=3.6-8.9 respectively (table 8). Figure 17 shows the dose response relationship between age started smoking and risk of developing lung cancer.

After performing the crude analysis, the factors considered to be significantly associated with lung cancer occurrence were as follows: cigarette smoking, education, agriculture, driver, laborers, merchant, drinking beer, drinking whisky native, drinking whisky foreign, drinking milk, eating pork, eating poultry, eating eggs and past history of pulmonary tuberculosis.

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This association might be influenced by confounding factors. So in order to get the real association between various exposures and the lung cancer the potential confounders must be controlled. Cigarette smoking is considered to be the most important confounding factor. So all significant factors were stratified with smoking and were summarized in Table 13. The occupation driver, was no more significant after adjusting for the effect of smoking (OR=2.34, 95% CI=0.98-5.60). Similarly eating pork became insignificant after adjusting for the effect of smoking (OR=1.40, 95% CI=0.99-1.96) (Table 13).

Thus after adjusting for the effect of smoking following factors were found to be significantly associated with lung cancer development: education, agriculture, laborer, merchant, drinking beer, drinking whisky native, drinking whisky foreign, eating milk, eating poultry, eating eggs, and history of pulmonary tuberculosis.

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DIFFERENT ODDS RATIOS AND TYPE OF SMOKING IN LUNG CANCER

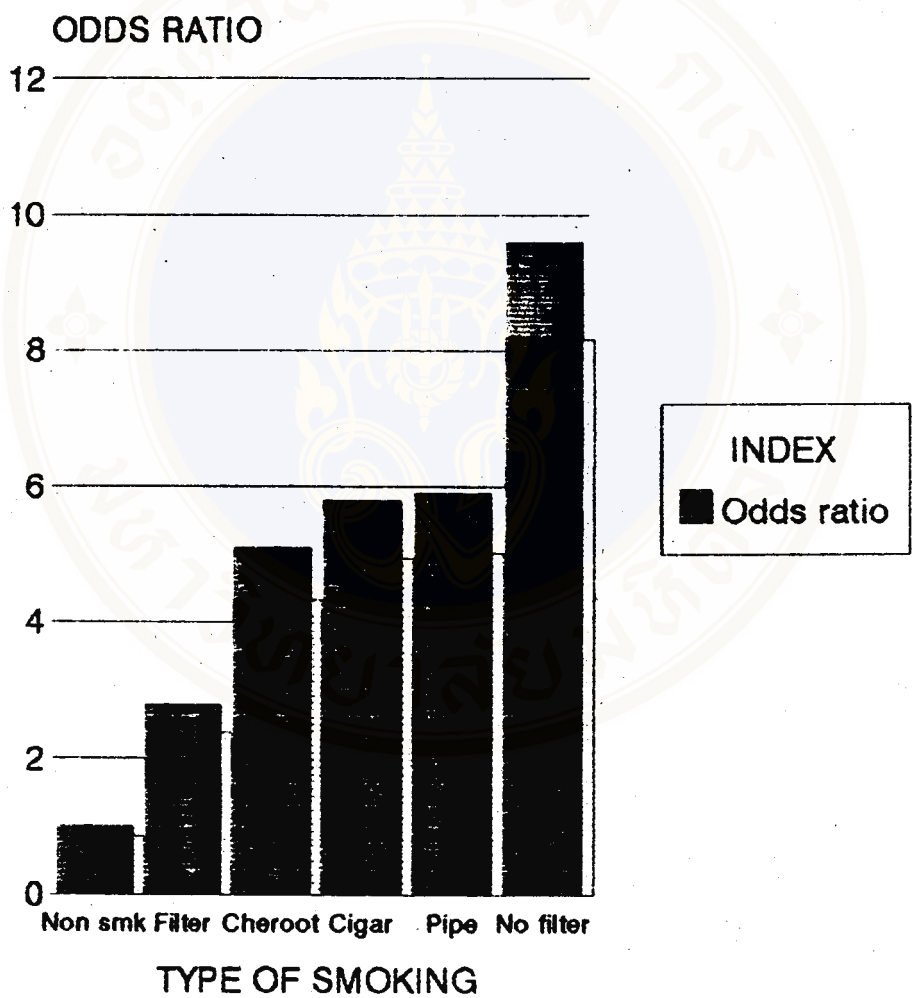

FIG.17

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DIFFERENT ODDS RATIOS AND AMOUNT OF SMOKING IN LUNG CANCER

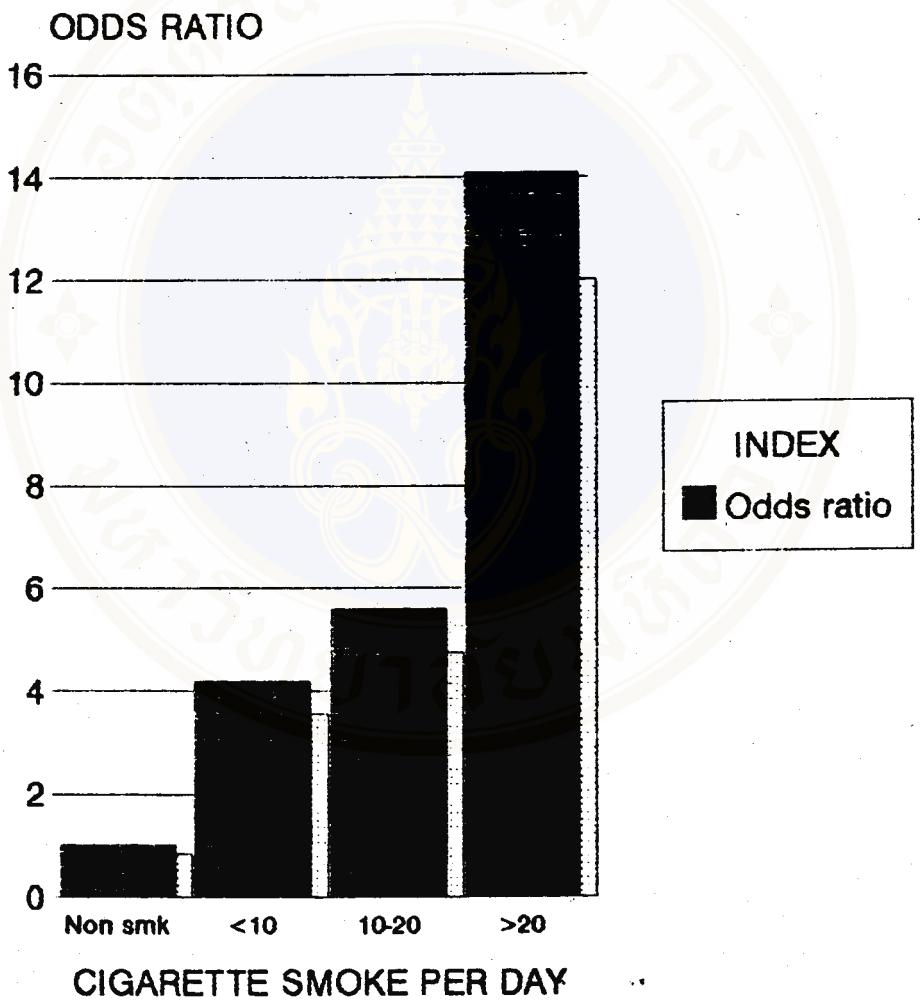

FIG.18

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DIFFERENT ODDS RATIOS
AND DURATION OF SMOKING IN LUNG CANCER

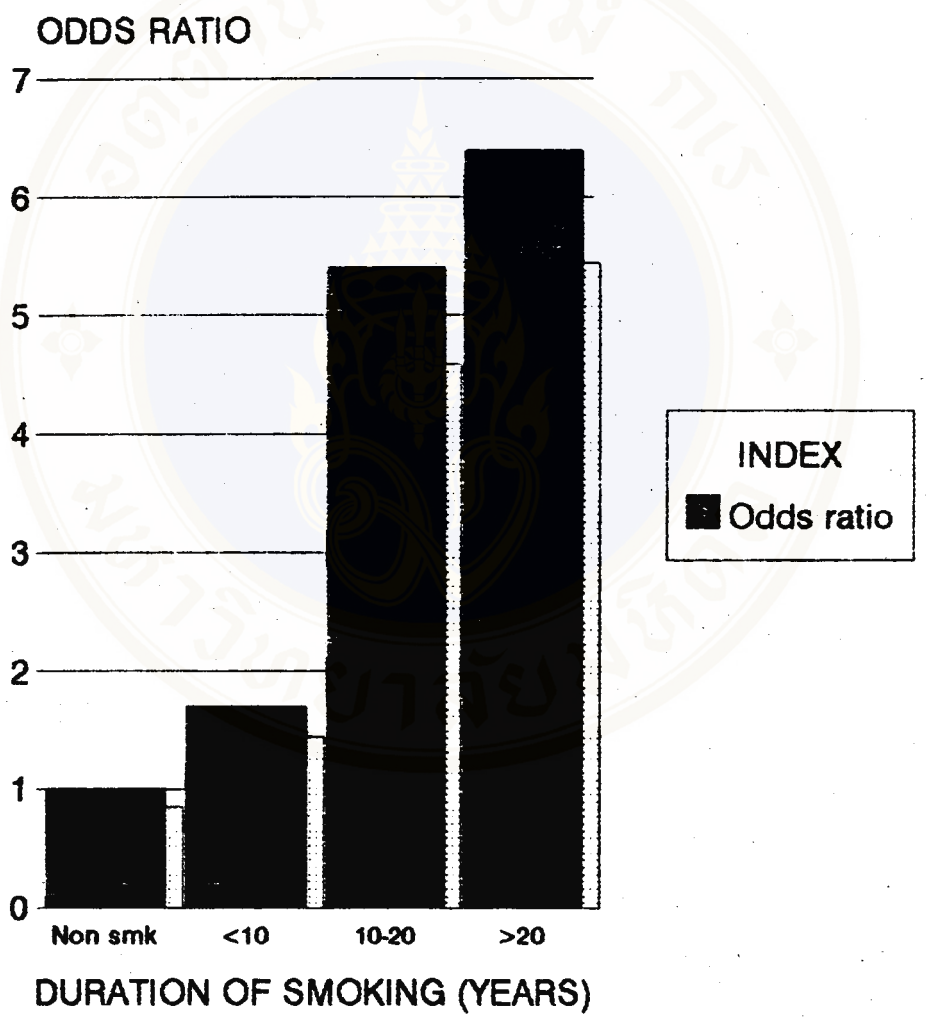

FIG.19

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DIFFERENT ODDS RATIOS
AND AGE STARTED SMOKING IN LUNG CANCER

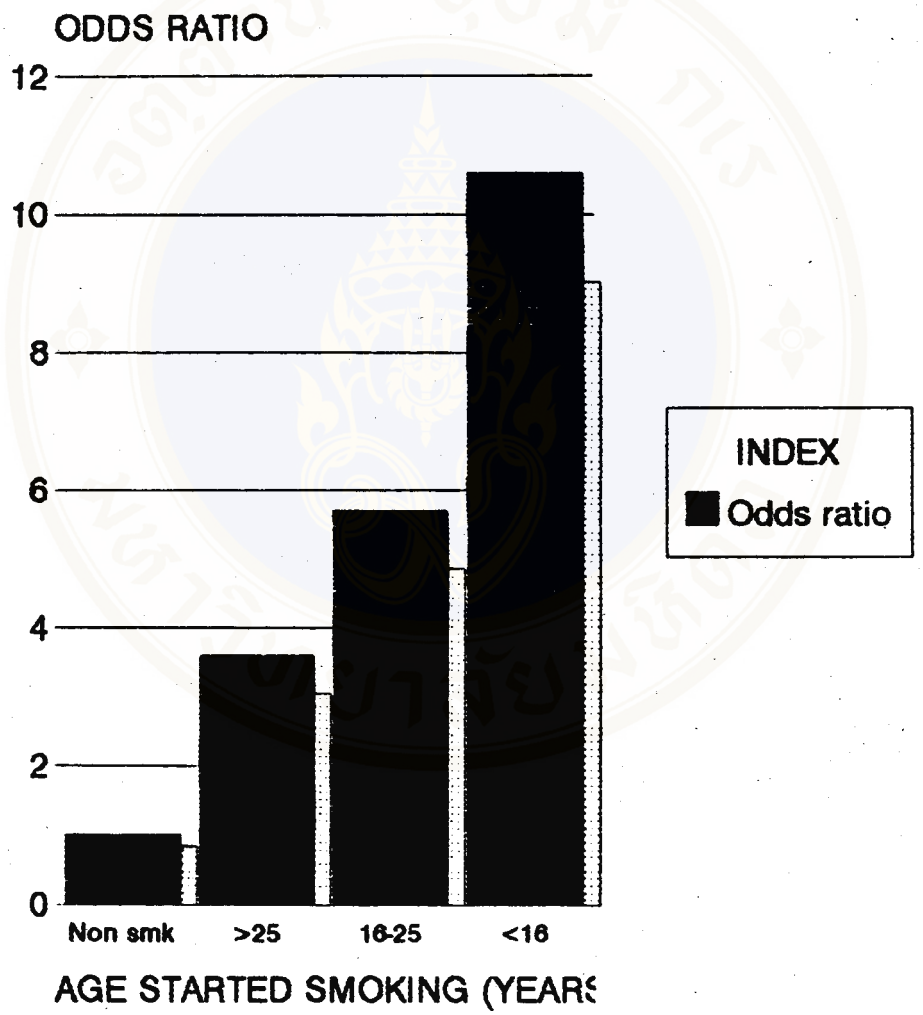

FIG.20

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Table 13. Association between lung cancer and significant exposures after adjusting for the effect of smoking

Exposure	Crude OR (95% CI)	Adjusted OR** (95% CI)	p* value
1. Education			
1.None	9.5 (4.5-20.5)	10.5 (3.9-28.0)	<0.0001
2.Primary	6.6 (3.9-11.3)	6.6 (3.1-13.8)	<0.0001
3.Secondary	1.7 (0.9-3.2)	2.9 (1.3-6.7)	<0.0001
2. Agriculture (yes/no)	2.10 (1.41-3.15)	1.76 (1.18-2.64)	<0.006
3.Driver (yes/no)	2.80 (1.16-6.99)	2.34 (0.98-5.60)	0.078
4. Laborers (yes/no)	3.10 (1.74-5.55)	3.07 (1.72-5.47)	<0.0001
5. Merchant (yes/no)	2.71 (1.24-6.02)	4.21 (1.87-9.48)	<0.0001
6. Drinking beer (yes/no)	3.26 (1.59-6.82)	2.80 (1.36-5.79)	0.007
7. Drinking local whisky (yes/no)	3.64 (2.08-6.45)	2.74 (1.59-4.73)	<0.0001
8. Drinking foreign whisky (yes/no)	2.06 (1.30-3.27)	1.62 (1.03-2.55)	0.045
9. Consuming milk (yes/no)	1.48 (1.06-2.07)	1.63 (1.16-2.30)	0.007
10. Eating pork (yes/no)	1.48 (1.06-2.07)	1.40 (0.99-1.96)	0.917
11. Eating poultry (yes/no)	2.18 (1.57-3.01)	2.42 (1.73-3.37)	<0.0001

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Table 13. (cont.).

Exposure	Crude OR (95% CI)	Adjusted OR** (95% CI)	p* value
12. Eating eggs (yes/no)	1.59 (1.15-2.19)	1.72 (1.23-2.39)	<0.001
13. TB infection (yes/no)	1.88 (1.12-3.16)	1.96 (1.15-3.35)	0.018

* P-value of M-H Summary Chi-square **Adjusted for smoking

A Logistic regression analysis was done to calculate odds ratios adjusted for the effects of other variables simultaneously and were summarized in Table 9. Using logistic regression analysis, drinking beer (OR=1.2, 95%CI=0.5-3.0), drinking local whisky (OR=1.5 95% CI=0.7-3.2), consuming milk (OR=1.3, 95%CI=0.6-1.8) and consuming eggs (OR=0.9, 95%CI=0.5-1.5) were no more significant. At the same time no interactive effect of different variables were found. By logistic regression analysis, the significant risk factors associated were: smoking, education, agriculture, laborer, drinking foreign whisky, eating poultry and past history of pulmonary TB infection and were summarized in Table 14.

To choose the model for prediction of risk for lung cancer, log likelihood estimate for each model were used. Eleven models were constructed, adding one variable at a time.

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Out of 11 variables, 7 variables were invariably significant in the models and the log likelihood ratio for each model were significant. .Maximum log likelihood for each model was calculated. Log likelihood ratio for model with 7 variables to model with 11 variables was not significant, using Chi-square distribution at 4 degree of freedom. Model with 11 variables was not significantly different from the model with 7 variables. So the model for prediction of risk for lung cancer includes: smoking, education, agriculture, laborers, drinking whisky foreign, eating poultry and past history of pulmonary TB and summarized in table 15.

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Table 14. Association between lung cancer and exposures after adjusting for the effects of other variables simultaneously.

Exposures	OR1 (95% CI)	OR2 (95% CI)	p** value
1. Education			
1. None	9.5 (4.5-20.5)	10.5 (3.9-28.0)	<0.0001
2. Primary	6.6 (3.9-11.3)	6.6 (3.1-13.8)	<0.0001
3. Secondary	1.7 (0.9-3.2)	2.9 (1.3-6.7)	0.008
4. > Secondary *	1.00	1.00	
2. Smoking (yes/no)	6.0 (3.9-9.3)	5.2 (2.9-9.4)	<0.0001
3. Agriculture (yes/no)	2.1 (1.4-3.1)	1.9 (1.2-3.2)	0.006
4. Laborer (yes/no)	3.1 (1.7-5.5)	3.6 (1.8-7.0)	<0.0001
5. Drinking beer (yes/no)	3.2 (1.5-6.8)	1.2 (0.5-3.0)	0.590
6. Drinking local whisky (yes/no)	3.6 (2.0-6.4)	1.5 (0.7-3.2)	0.207
7. Drinking foreign whisky (yes/no)	2.0 (1.3-3.2)	2.1 (1.1-4.0)	0.011
8. Consuming milk (yes/no)	1.4 (1.0-2.0)	1.1 (0.6-1.8)	0.634
9. Eating poultry (yes/no)	2.1 (1.5-3.0)	3.2 (1.9-5.3)	<0.0001

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Table 14. (Cont.)

variable	OR1 (95% CI)	OR2 (95% CI)	P** value
10. eating eggs (yes/no)	1.5 (1.1-2.1)	0.9 (0.5-1.5)	0.887
11. His. of TB (yes/no)	1.8 (1.1-3.1)	2.4 (1.1-5.1)	0.014

OR1=Unadjusted

OR2=Adjusted for other variables simultaneously

* Baseline for computation of odds ratio

** p-value from wald statistics

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Table 15. Association between lung cancer and various significant risk factors after Logistic regression analysis.

Exposures	Coefficient	p value	OR** (95% CI)
1. Education			
1. None	2.3908	<0.0001	10.9 (4.1-28.9)
2. Primary	1.9663	<0.0001	7.1 (3.4-14.8)
3. Secondary	1.1644	0.004	3.2 (1.4-7.2)
4. > Secondary *			
2. Smoking	1.7099	<0.0001	5.5 (3.0-9.9)
3. Agriculture	0.7112	0.004	2.0 (1.2-3.3)
4. Laborer	1.2815	<0.0001	3.6 (1.8-6.9)
5. Whisky foreign	0.8665	0.004	2.3 (1.3-4.3)
6. Poultry	1.2206	<0.0001	3.3 (2.1-5.3)
7. His of TB	0.8816	0.017	2.4 (1.1-4.9)
8. Constant	-4.0845	<0.0001	

* Base line for computation of odds ratio

** Adjusted OR after controlling the effect of other variables

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Table 16. Variables and coefficients in logistic regression models.

Variable	coefficient model 1	model 2
1.Education		
None	2.3603	2.3908
Primary	1.8921	1.9663
secondary	1.0944	1.1644
>secondary*		
2.Smoking	1.6595	1.7099
3.Agriculture	0.6871	0.7112
4.Laborer	1.2993	1.2815
5.Whisky(foreign)	0.7825	0.8665
6.Chicken	1.1800	1.2206
7.History of TB.	0.9037	0.8816
8.beer	0.2397	
9.Whisky(native)	0.4589	
10.Milk	0.1218	
11.Eggs	-0.0361	
Log-likelihood estimates =	-253.6488	-254.9194
Likelihood ratio =	182.8763	180.3350
p-value = (log-likelihood test)	<0.0001	<0.0001

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Discussion

From the results of the analysis of these data it was shown that the risk factors for lung cancer among Thai males are almost similar to those identified in several previous studies in western countries.

Smoking and lung cancer

The present investigation has conformed the strong association between cigarette smoking and lung cancer(OR=6.03, 95%CI=3.9-9.3 in smokers compared to nonsmokers) (Table 8) and coincide with the results published in 1962 and 1964 by the Royal College of Surgeons of London and the Surgeon General of the United States (6). In 1971, Public Health Service (USA) summarized 35 case-control and 8 cohort studies dealing with this issue and indicated an elevated relative risk (RR) for lung cancer among smokers (6).

In this study it was found that not only the smoking but the type of smoking, duration of smoking, amount of smoking and the age at which smoking started had a significant association with lung cancer development. Lung cancer risk was relatively higher in those who smoked non filter, cheroot, cigar and pipe compared to filter (Table 8) and coincides with the results from Benhamou S et al, 1985;Vutuc C 1982 and

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Wynder, 1992 (54). In figure 17 a dose response relationship between type of smoking and risk of lung cancer has been shown. The possible explanation for this diminished risk is that the filter cigarettes do have reduced level of tar and nicotine and the carcinogenic polynuclear aromatic hydrocarbons (eg. benzo[a]pyerene) are found in cigarette tar. Increased risk of lung cancer were also associated with pipe and cigar smoking but were of a lower order of magnitude than the risk seen with non filter. It has been suggested that pipe and cigar smoke is more irritant than cigarette so less smoke is inhaled in pipe and cigar smoking than cigarette smoking (6).

From the result it was confirmed that the amount of smoking and lung cancer had a dose response relationship and shown in the figure 18. Smoking cigarette more than 20 per day had 14 times more risk of developing lung cancer compared with non smoker (OR=14.1, 95%CI=6.8-29.8) (Table 8) and coincide with the results from Speizer F 1983, Lucin Israel and Philippe Chahinian 1976 and Wynder EL, Mabuchi K 1972. This result also coincide with the results from Hammond 1972, Doll and Peto 1976, Khan 1966, that the risk of lung cancer increases with the amount of cigarette smoked per day (6).

Those who started smoking below the age of 16 years had nearly 11 times higher risk to develop lung cancer

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compared to non smoker (OR=10.6, 95% CI=5.5-20.5) (Table 8) (Figure 20). Similarly those who smoked cigarette for more than 20 years had 6 times higher risk to develop lung cancer compared to non smoker (OR=6.45, 95% CI=4.1-10) (Table 8) (Figure 19).

The biological plausibility of smoking being linked to develop lung cancer, based on much evidence that cigarette smoking adversely affects ciliary action and the movement of the mucous blanket. Through a systematic study Auerbach et al; quantified three characteristics in the bronchial epithelium of smoker. The cilia in smokers are alleged to be shorter than in nonsmoker, basal epithelial hyperplasia and nuclear abnormalities. Thus in smokers the mucociliary apparatus is damaged and the macrophage are affected thus making the bronchial tree more vulnerable to other forms of aggression. Island of squamous epithelium are said to occur in the region of bronchial division. Some evidence to indicate that cigarette tar may accumulate around the distal margins of such island and suggest that these form the foci for the carcinogenic effect of tobacco (Crofton and Douglas 1981) (55).

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Past history of pulmonary tuberculosis and lung cancer.

In this study it was found that pulmonary tuberculosis in the past had a significant association with lung cancer occurrence (OR=2.4, 95%CI=1.1-4.9) (Table 14) and confirms numerous clinical reports of lung cancer arising from TB scar (Auerbach et al., 1979; Bakris et al., 1983) (45).

Some epidemiologic investigations have suggested that TB patients are at significantly increased risk of lung cancer (45). This result also coincide with the results of the largest cohort study of 64000 TB patients in Canada where a 1.5 fold excess risk of lung cancer was found in patients with TB. Other cohort studies in Australia, Denmark and Israel has revealed 2 fold lung cancer risk among TB patients. In one study Zheing, 1987 found RR >2.5 for TB in development of lung cancer after adjusting for the effect of smoking (45).

The precise mechanism, how the TB causes lung cancer is yet to be discovered. But it has been claimed that TB infection may act as a promoting or late stage event in the carcinogenic process. The chronic TB inflammatory process potentiates the effects of other carcinogenic exposures, traps the carcinogens in scar tissue or enhance abnormal cellular proliferation and growth (45).

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It has been claimed that anti tuberculous drugs may be responsible for the lung cancer. In animals isoniazid is a potent carcinogen and induces pulmonary adenomas in mice. The major metabolite of isoniazid in man (1-acetyl-2-isonic-otionoyl hydrazine) greatly increases the incidence of lung cancer tumor in mice (55).

Eating poultry and lung cancer.

In this study eating poultry regularly was found to be significantly associated with lung cancer occurrence (OR=3.2, 95%CI=2.0-5.0). Eating poultry regularly is a good source of animal fat which in term increases cholesterol level in body. In a study it was found that dietary cholesterol was positively and significantly associated with lung cancer risk after adjusting for age, ethnicity, pack year of cigarette smoking and occupational exposures to lung carcinogens (51). Results of this study coincide with results of one study by M Curtis, 1989 in Rosewell Park Memorial Institute, USA, in which a significant elevation of risk for lung cancer was associated with greater frequency of consumption of animal fat (RR=2.12, 95%CI=1.12-4.00) for those who use animal fat sources (50).

The exact mechanism how cholesterol acts as a carcinogen is not understood. But it has been claimed that

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oxidation products of cholesterol are known to be carcinogenic and mutagenic. Furthermore, at least one investigation has found that cholesterol feeding increases the incidence of lung adenomas in mice (51). In some studies it has been found that subjects dying from lung cancer had higher mean serum cholesterol level than survivors (51). It has been suggested that rich dietary fat and cholesterol intake might saturate the macrophage with lipid in the lung thus impairing defense against carcinogens and increasing the risk of lung cancer.

In view of our findings the association of eating poultry (dietary fat and cholesterol) and lung cancer clearly deserves further investigation.

Level of education and lung cancer.

A strong and significant association between lung cancer and education was observed in this study. The OR for those who had no education was significant when compared to those who had above secondary education (OR=11.7, (95% CI=4.5-30.8). Similarly those with primary and secondary education had their OR=8.8, 95%CI=4.3-18.0 and OR=3.2 95% CI=1.4-7.3 respectively as compared with above secondary education. It meant that there was an inverse association between lung cancer and education. These results coincide with the results from Devesa and Diamond 1983, in a study of 20,868 lung

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cancer cases. Similar results were seen in studies by Graham et al., 1960, Seidman, 1970; Williams and Horm, 1977 (6). This association may be an indirect association. Since the people who has low education or no education are exposed more to the risk factors during their jobs. Low educated people may be not much aware of their health, may be they smoke and drink more than highly educated people.

Drinking foreign whisky and lung cancer

In this study drinking whisky foreign (alcohol) was also a significant risk factor for lung cancer after controlling for smoking, education, laborer, eating poultry and past history of pulmonary TB (OR=2.3,95%CI=1.3-4.3) (Table 15). The biological plausibility of the relationship between alcohol drinking and lung cancer is not clear. However, as Brown and Campbell (1961) stated, the type of life led by a heavy drinker tends to cause vitamins or other nutritional deficiencies, especially vit A which are likely to favor in the development of lung cancer (56). Major physiological role of vitamin A is to control cell differentiation. Since loss of cell differentiation is a basic feature of cancer, there is a ample reason to suspect that intake of vitamin A may be related to cancer incidence. In a study in Norway men where vitamin A consumption was above average had less than half the rate of lung cancer of men whose consumption was below

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average (57). Excessive alcohol consumption causes hepatic injury leading to low tissue level of vitamin A in individuals with regular consumption of alcohol. In one study K Gunnar, B Erik and JG John, reported a higher than average lung cancer rates among individuals with low index of vitamin A among regular alcohol intake (57).

It has been found that the metabolism of alcohol produces acetaldehyde which is a carcinogen. Alcohol when consumed in large quantities, appears to act synergistically with inhaled cigarette smoke to increase the risk for respiratory tract cancer (57).

Laborer and lung cancer

The results of this study has revealed that there was a significant association between occupation laborer and occurrence of lung cancer (OR=3.6, 95%CI=1.8-6.9) and coincide with several studies done else where. The major groups of laborer included in this study were laborer in construction, laborer in textile factory and general laborer. This result coincide with the results of Third National Cancer Survey (TNCS) where an elevated risk for lung cancer was found among construction laborers. In the same study the odds ratio for lung cancer in men working in textile mills was 2.6 and agreed with the results of the US Vital Statistics Study (35). In

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another study in Northeast Florida, an elevated risk associated with construction laborers was found to be associated with lung cancer (RR=1.4) even after adjusting for smoking (25). Odds ratio greater than 1.00 after adjusting for smoking were also found in studies in Italy, Shanghai and France for laborer in construction (24) (23) (22).

Asbestos, silica and dust has been a suspected agent, although polycyclic hydrocarbons appears to be involved in some categories of work such as roofers. Over the past 25 years epidemiologic evidence has shown that lung cancer is the major asbestos related disease (Lemen et al, 1981) (6).

Agriculture and lung cancer

In this study results on the association between lung cancer and agriculture was significant (OR=2.0, 95%CI=1.2-3.3) With increasing use of arsenical insecticides, herbicides and various chemicals by agricultural workers, the increased risk of developing lung cancer observed in this study is consistent with some previously reported results elsewhere. In a case control study in France an excess risk of lung cancer was observed in agriculture (RR=1.22) after adjusting for the effects of smoking (22). In Shanghai the odds ratio for agriculture after adjusting for smoking was marginally significant (OR=1.6, 95%CI=1.0-2.6) (23).

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The odds ratio more than 1.00 was observed in a case control study in Italy for agriculture (24). The possibility that pesticides may contribute to risk among agricultural workers was suggested by raised rates of lung cancer observed among pesticide applicators in the United States and Europe (28). In one study among orchardist in Washington State (1968-1980) it was found that there was an increased mortality for lung cancer due to prolonged use of insecticide (28). The International Agency for Research on cancer has concluded that agriculture and farming has an increased risk of lung cancer and several chemicals and processes widely used in farms are carcinogenic. Recent studies have shown that the increased risk in this occupations due to frequent exposures to herbicide (P=0.054) grains (P=0.015) and diesel fumes (P=0.005) (21) (22) (28).

In arsenical insecticide and herbicide the suspected causative agents are dichlorodibenzodioxin, trichlorodibenzodioxin (Cancer risk and prevention) and arsenic in it's trioxide form is a well known human lung carcinogen. As a result of exposure to these pesticides and herbicides there is induction of enzymes which may lead to the conversion of relatively inactive compounds to more metabolically active carcinogens (58). The possibility that farmers may be more prone to the development of lung cancer as a result of lung dysfunction due to chemical inhalation and

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the known carcinogenicity of many of the substances to which they are exposed needs to be adequately explored.

Recommendations

From the results of this study and many other studies it has been established that smoking is the biggest contributing risk factor for lung cancer. So intensive campaign against smoking and alcohol drinking should be incorporated in health education programs through the primary health care system, school, community leaders and other appropriate channels as part of comprehensive health awareness campaign to reduce the incidence of lung cancer. Specific measures should be taken to discourage continuation of the cigarette smoking and alcohol drinking habit among smokers and drinkers and adoption of the habit among nonsmokers and non drinkers, the majority of smokers and drinkers are aware that smoking and drinking are health hazardous but probably most remain unaware of the relative magnitude of the hazards involved.

Through health education programs and other appropriate channels people should be encouraged to change their behavioral pattern about eating and drinking habits. People should be encouraged to reduce fat intake in their diet and at the same time investigations about the specific

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carcinogen in fat should be made.

The results from this study can be used as a basis for preventing and protecting the high risk group by identifying the specific group who are involved and exposed to the carcinogens whenever possible. The results can be used as a guide line for further research study for better control of the disease.

It is necessary to improve the methods of data extraction from patient in order to facilitate this type of research in future.

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CHAPTER V

CONCLUSION

In order to determine the possible risk factors for lung cancer among Thai males, a hospital based case control study was conducted at the National Cancer Institute (NCI), Bangkok in 1992. A total of 333 lung cancer cases and 345 non cancer controls were selected for the study. The cases were selected from medical records of Thai males aged 30 years and above with cytologically and or histologically confirmed lung cancer admitted and registered at NCI, during the year 1985-1990. Cases were selected by the process of systematic random sampling with random start. For every case selected one control was selected and matched by age with in the age group of <35, 35-44, 45-54, 55-64 and >64. The controls were also selected from medical records of Thai males aged 30 years and above not suffering from cancer and registered in the out patient of NCI as a case for routine general check up during the same period.

All the necessary information were translated from Thai to English and recorded on a recording form. The variables included in the study were socio-demographic variables, smoking habit, eating and drinking habits, occupation, use of snuff and past history of pulmonary

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tuberculosis.

Among the socio-demographic factors only education was significantly associated with lung cancer ($p<0.001$). In education those with no education had higher risk compared to those with above secondary education (OR=10.5, 95%CI=3.9-28). Those with primary education had OR=6.6, 95%CI=3.1-13.8, with secondary education OR=2.9, 95%CI=1.3-6.7, after controlling for the effect of other variable simultaneously.

For occupation, agriculture and laborers were found to be significantly associated with lung cancer after adjusting for the effect of other variables simultaneously (OR=1.9, 95%CI=1.2-3.2 and OR=3.6, 95%CI=1.8-7.0 respectively) Smoking was highly significant after adjusting for the effects of other variables simultaneously (OR=5.2, 95%CI=2.9-9.4). Smoking cigarette with out filter (OR=9.6, 95% CI=5.9-15.7), with filter (OR=2.8, 95% CI=1.6-4.9), pipe (OR=5.9, 95% CI=2.3-15.2), cigar (OR=5.8, 95% CI=1.8-18.5) and cheroot (OR=5.1, 95% CI=2.8-9.2) were significant when compared to non smoker. Smoking cigarette more than 20 per day was significant (OR=14.1, 95% CI=6.8-29.8) when compared to non smoker. Smoking cigarette less than 10 per day (OR=4.2, 95% CI=2.3-7.8) and 10-20 cigarette per day (OR=5.6, 95% CI=3.5-8.8) were also significant. Similarly duration of smoking for more than 20 years when compared to non smoker was significant

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(OR=6.4, 95% CI=4.1-10.0), smoking for 10-20 years (OR=5.4, 95% CI=3.0-9.8) was also significant compared to non smoker. Similarly age started smoking before 16 years was significant (OR=10.6, 95% CI=5.5-20.5), compared to non smoker. Similarly for 16-25 years (OR=5.7, 95% CI=3.6-8.9) and >25 years (OR=3.6, 95% CI=1.8-7.3) the odds ratios were significant compared to non smoker.

For eating and drinking habits, drinking foreign whisky and eating poultry regularly were significant after controlling for the effect of other variable simultaneously (OR=2.1, 95%CI=1.1-4.0 and OR=3.2, 95%CI=1.9-5.3 respectively). Past history of pulmonary tuberculosis was also significantly associated with lung cancer (OR=2.4, 95%CI=1.1-5.1) after adjusting for the effect of other variables simultaneously.

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" APPENDIX A"

DATA RECORDING FORM

1. Patient ID No. [ ][ ][ ][ ][ ][ ][ ]	
2. Serial No.	( )( )( )1-3
3. Age.	( )( ) 4-5
4. Residence by province.	
(0) central (1) north (2) east	( ) 6
(3) northeast (4) south	
5. Marital status.	
(0) single (1) married (2) widow	
(3) separate (4) divorce	( ) 7
6. Education.	
(0) no education (1) primary	
(2) secondary (3) vocational	( ) 8
(4) college (5) Graduates	
7. Occupation.	
present.....no. of yrs.	( )( )( )( )9-12
past.....no. of yrs.	( )( )( )( )13-16
8. Smoking status.	
(0) never (1) ex smoker	
(2) current smoker	( ) 17
9. Age started smoking.....no. of yrs.	( )( )18-19
10. Duration of smoking.....no. of yrs.	( )( )20-21

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11. Type of smoking. ;

(0) pipe (1) cigar (2) cheroot ;

(3) with filter (4) with out filter ; ( ) 22

12. Cigarette smoked per day ;

(0) < 10 (1) 10-20 ;

(2) > 20 ; ( ) 23

13. Has the patient used a regular snuff ;

(0) no (1) yes ; ( ) 24

14. Regular consumption of following ;

beverages. ;

(0) no (1) yes ; ( ) 25

(1) coffee.....cup per day ; ( ) 26

(2) beer..... cup per day ; ( ) 27

(3) whisky native.....cup per day ; ( ) 28

(4) whisky foreign.....cup per day ; ( ) 29

(5) mixed drink.....cup per day ; ( ) 30

15. Do you eat following. ;

(0) rarely/never (1) weekly ;

(1) milk [ ] [ ] ; ( ) 31

(2) pork [ ] [ ] ; ( ) 32

(3) poultry [ ] [ ] ; ( ) 33

(4) eggs [ ] [ ] ; ( ) 34

(5) fatty food [ ] [ ] ; ( ) 35

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16. Have you ever had Tuberculosis :

(0) no (1) yes : ( ) 36

17. Place of residence near any factory :

(0) no (1) yes : ( ) 37

(1) cement (2) steel : ( ) 38

(3) tire (4) zinc :

(5) chemical (6) textile :

(7) gasoline (8) fish sauce :

(9) others :

18. How long do you stay :

in that residence.....yrs : ( )( ) 39-40

19. Distance of factory from :

residence(nearest)....Km : ( )( ) 41-42

20. Cell types (for cases only) : ( ) 43

(1) adenocarcinoma :

(2) squamous cell carcinoma :

(3) large cell carcinoma :

(4) small cell carcinoma :

(5) mixed type of adeno and squamous :

cell carcinoma :

(6) others :

21. Blood group : ( ) 44

(1) A (2) B (3) O (4) AB :

22. Sample (1) Case (0) Control : ( ) 45

Date...../...../.....

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" APPENDIX B"

OPERATIONAL DEFINITIONS

Cancer

Cancer is an abnormal new growth of tissue which grows independently of the rest of the body and serves no useful purpose and ultimately will cause death in a large percentage of the cases. So the word cancer is a generic term that encompasses all malignant tumors.

Lung cancer

According to the international classification of disease (W.H.O.1977) it includes cancer of, trachea, bronchus, and lung with histological confirmation.

Primary lung cancer

Primary lung cancer refers to the cancer originating primarily from the trachea, bronchus, and lung tissue.

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Case

A case is an adult Thai male aged 30 years and above with a diagnosis of lung cancer, admitted and registered at NCI, Bangkok, during the period 1985 - 1990.

Control

A control is an adult Thai male aged 30 years and above and not suffering from cancer and registered in the out patient of NCI, Bangkok, as a case for routine general check up during the period 1985-1990.

Occupation

Any activity that a person usually do for a living. For the purpose of classification in this study the largest occupation that the person was engaged to, will be the one that will be considered for the study. However, the minor occupations will be noted.

Classification

(1). Agriculture

It includes activities primarily engaged in production of crops, nurseries, greenhouse, fruit and vegetable farming, and animal husbandry.

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(2). Mining and quarrying

It includes underground and surface mines, quarries, and wells and all supplemental activities for dressing or beneficiating ores and other crude materials, such as crushing, screening, washing, cleaning, milling, smelting etc.

(3). Carpenter

(4). Driver

(5). Government officials

(6). Laborers (Construction laborers, laborers in textile, general laborers and others).

(7). Merchants

(8). Military & police

(9). Teacher

(10). Others

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"APPENDIX-C"

MULTIPLE LOGISTIC REGRESSION BY UNCONDITIONAL AND CONDITIONAL METHODS

CUTPOINT	TERM	COEFF.	S.E.	Z-SCORE	P-VALUE	O.R.	LOWER	UPPER	REF.CATEG
1.00	EDU(2)	1.1644	0.4133	2.8173	0.0048	3.204	1.425	7.203	BASELINE
2.00	EDU(3)	1.9663	0.3726	5.2773	0.0000	7.144	3.442	14.830	BASELINE
3.00	EDU(4)	2.3908	0.4973	4.8078	0.0000	10.922	4.121	28.948	BASELINE
SINGLE	SKM	1.7099	0.2973	5.7514	0.0000	5.529	3.087	9.901	
SINGLE	AGRI	0.7112	0.2492	2.8542	0.0043	2.036	1.250	3.319	
SINGLE	LAB	0.8665	0.3053	2.8381	0.0045	2.379	1.307	4.327	
SINGLE	WFGN	0.8665	0.3053	2.8381	0.0045	2.379	1.307	4.327	
SINGLE	CHICK	1.2206	0.2289	5.3330	0.0000	3.389	2.164	5.308	
SINGLE	HISTB	0.8816	0.3704	2.3802	0.0173	2.415	1.168	4.990	
	CONSTANT	-4.0845	0.4816	-8.4814	0.0000				

LOG-LIKELIHOOD (CYCLE 1)= -345.0869
LOG-LIKELIHOOD (CYCLE 6)= -254.9194

-2*MAXIMIZED LOG-LIKELIHOOD= 509.8388

TEST	STATISTIC	D.F.	P-VALUE	VARIABLE
SCORE	150.1432	9	0.0000	
LIKELIHOOD RATIO	180.3350	9	0.0000	

CRITERIA AND MODEL-BUILDING CHARACTERISTICS:

ANALYSIS (LIKELIHOOD)	UNCONDITIONAL
TOLERANCE	0.0000010000
CONVERGENCE	0.0000100000
ITERATIONS	15
CONFIDENCE LEVEL	95%
RECORDS IN ANALYSIS	498
ERROR OR WARNING MESSAGES ...	NONE
TIME (SECONDS)	22.850

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CUTPOINT	TERM	COEFF.	S.E.	Z-SCORE	P-VALUE	O.R.	LOWER	UPPER	REF.CATEG
SINGLE	SKM	1.6595	0.3000	5.5318	0.0000	5.257	2.920	9.464	
1.00	EDU(2)	1.0944	0.4155	2.6340	0.0084	2.987	1.323	6.745	BASELINE
2.00	EDU(3)	1.8921	0.3745	5.0526	0.0000	6.633	3.184	13.819	BASELINE
3.00	EDU(4)	2.3603	0.4975	4.7444	0.0000	10.595	3.996	28.091	BASELINE
SINGLE	AGRI	0.6871	0.2511	2.7362	0.0062	1.988	1.215	3.252	
SINGLE	LAB	1.2993	0.3359	3.8684	0.0001	3.667	1.898	7.083	
SINGLE	BEER	0.2397	0.4459	0.5375	0.5909	1.271	0.530	3.045	
SINGLE	WNAT	0.4589	0.3642	1.2598	0.2077	1.582	0.775	3.231	
SINGLE	WFGN	0.7825	0.3108	2.5175	0.0118	2.187	1.189	4.021	
SINGLE	MILK	0.1218	0.2560	0.4759	0.6341	1.130	0.684	1.866	
SINGLE	CHICK	1.1800	0.2577	4.5979	0.0000	3.254	1.964	5.392	
SINGLE	EGGS	-0.0361	0.2561	-0.1410	0.8879	0.965	0.584	1.593	
SINGLE	HISTB	0.9037	0.3703	2.4404	0.0147	2.469	1.165	5.101	
	CONSTANT	-4.0416	0.4846	-8.3410	0.0000				

LOG-LIKELIHOOD (CYCLE 1)= -345.0869
LOG-LIKELIHOOD (CYCLE 6)= -253.6488

-2*MAXIMIZED LOG-LIKELIHOOD= 507.2975

TEST	STATISTIC	D.F.	P-VALUE	VARIABLE
SCORE	152.4297	13	0.0000	
LIKELIHOOD RATIO	182.8736	13	0.0000	
LIKELIHOOD RATIO	6.3536	1	0.0117	HISTB

CRITERIA AND MODEL-BUILDING CHARACTERISTICS:

ANALYSIS (LIKELIHOOD)	UNCONDITIONAL
TOLERANCE	0.0000010000
CONVERGENCE	0.0000100000
ITERATIONS	15
CONFIDENCE LEVEL	95%
RECORDS IN ANALYSIS	498
ERROR OR WARNING MESSAGES ...	NONE
TIME (SECONDS)	31.420

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