The discipline of epidemiology encompasses the evaluation of screening. Screening was one of those approaches which was a hope for control of lung cancer. However, we have learned that the biology of lung cancer is not with us.

The 3 large US trials have demonstrated conclusively no mortality reduction, either from 4-monthly chest x-ray examinations with sputum cytology, compared to normal care, or sputum cytology used in addition to chest x-rays on a 4-monthly basis. Some doubt still remains on the effectiveness of annual chest x-rays used alone, but at the moment, screening for lung cancer cannot be recommended as public health policy. However, in other presentations, we learned of other applications for screening as an aid to etiologic research and as a means of identifying groups that need to be placed under special surveillance. Sputum cytology was used in this context in British Columbia, and has identified a group of aluminum pot-room workers with increased frequency of dysplasia with a relative risk of about 3.5 restricted to those who had worked for 20 years in the process. We also learned in a poster session how sputum cytology is being used for surveillance of individuals being entered into a trial of chemoprevention, those exposed to asbestos in Tyler, Texas. However, we also had a warning. We were told that regression of abnormalities identified in sputum cytology is not unusual, and we must remember that in other context, cytologic abnormalities, for example in the cervix uteri, have been well demonstrated to come and go.

Cytology has not been fully evaluated as a route to identifying groups on whom one should concentrate for prevention. We must remember that in the clinical trials the sensitivity of sputum cytology in detecting lung cancer was not anything like as great as had been originally hoped.

Turning to descriptive epidemiology, various posters and papers were presented describing the amount of lung cancer in different parts of the world, with very high male to female sex ratios in Libya, a falling sex ratio in North America and Europe, with the rise of lung cancer in women, to a female excess in parts of southern China. In general, as exemplified by sophisticated modelling approach from Canada, the rise in lung cancer follows a rise in smoking in the same sex group in the same population 30 or so years earlier. In some areas, the rises have been surprisingly rapid as exemplified by the situation in Italy, and the dramatic rise in lung cancer in women in North America in the last 15-20 years, already overtaking breast cancer as the most important cause of death from cancer in women.

In the United States mapping of lung cancer rates has been productive in identifying areas of higher risk, especially in the coastal regions of the southeast, now known to be associated with asbestos use in shipbuilding in WW II. In British Columbia, a similar situation appears to apply. Development work is ongoing in the United States on a mathematical model to refine the information gained from such maps.

However, overshadowing all this is the increase in lung cancer as a major world disaster. It has been estimated that in 1975 there were just under 600,000 cases of lung cancer diagnosed in the world. In 1985 we now estimate there will be in excess of 1,000,000. In the year 2000 the total will not be far short of 2,000,000, and this increase will have occurred largely during the time period when we knew the major cause.

Turning to the occupational area of analytic epidemiology, we have heard how identification of a lung cancer hazard in a steel foundry in Hamilton, Ontario led to the use of the Ames test for mutagenicity as a means of identifying the high risk work areas, especially the risk to the crane drivers working directly over the fumes arising from the molds into which the steel was poured. Then we heard how use of these same tests to evaluate alternative binding agents in the molds has led to an introduction of what is expected to be much safer work practices. This is truly an example of a multidisciplinary approach to cancer control.

However, a chance remark that the probable load of lung cancer in Canada was greater from exposure to alpha radiation in homes in certain areas of the country than from uranium mining, led to some excitement, especially when we were reminded that the joint effect of smoking and alpha radiation was to multiply the risks of each. This concern that in cold countries with increasing attention to insulation, alpha radiation may be seeping in from basements, especially when there is direct contact with earth, was reinforced by a report of a study from Stockholm where an approximate doubling of risk to lung cancer from exposure to radiation coming into the ground floor of houses and apartment blocks from a glacial escarp or from outcrops of granite, was estimated as a result of a case control study. There was some reassurance from the information that the proportion of lung cancer cases attributable to such exposure in this group was only 4%, yet we can expect many more studies to evaluate this problem in North America and Europe in the future, as well as refinement of the work in Sweden, where a possible hazard was identified several years ago.

However, among the more interesting reports were 2 from China which pointed to indoor pollution from the burning of coal as a major factor in the etiology of lung cancer in certain areas, especially in women. In these largely rural areas, coal is burned in pits in the center of houses, and chimneys are rarely present. The coal burns continuously, and is the source of heat for both warmth and cooking. The rise in lung cancer seen in these areas seems to be anecdotally related to the replacement by coal of wood for heating. Exposure to carcinogens has been estimated to be very high from this and women, clearly exposed more than men, have the greater exposure, thus explaining a female excess of lung cancer in at least one of these areas. This extreme form of local air pollution is probably the best evidence we will get that such exposures can increase the risk of lung cancer, yet it appears that already steps have been taken to ameliorate the problem, a problem that in 1 of the 2 areas described is already being superseded by the effects of smoking, a process which, in China, has resulted in a major smoking-related epidemic of lung cancer in males in Shanghai and which, by the turn of the century, will have spread throughout most of that highly populous country.

China is a world leader in the production of tobacco, an unenviable position, which can at least in part be related to the fact that until very recently Chinese scientists were...
denying that tobacco is a major cause of lung cancer. They were misled, as have been many others, by their failure to recognize the overwhelming importance of the duration of tobacco smoking as the major determinant of a population's risk of the disease.

In the area of investigation of smoking, we had 1 report on the effects of passive smoking from Japan, utilizing the cohort being followed by the Radiation Effects Research Foundation in that country. Risk from passive smoking in spouses was increased by 50% with the risk increasing with the intensity of smoking in the spouse. There was also an indication of an additional effect from occupational exposure to passive smoking. It was important to have this report from Japan as it largely confirms the earlier report from Dr. Hirayama, who unfortunately could not be present at this meeting. Hirayama has maintained that the close social contact at homes of Japanese couples, what he calls the honeymoon effect, has made it much easier to demonstrate an effect of passive smoking in that country, whereas it has been more difficult in North America and Europe, (except possibly in Greece). Although the adverse effect here may be less than in Japan, there probably is an effect, and this can be used to advantage in our efforts to control such exposures.

In the clinical epidemiology area, there were several posters relating to prognostic factors. Nearly all showed the prognostic value of performance status, but 1 from Australia also showed an important independent effect of Feinstein's index.

There were also some studies looking at second primary tumors. It seems clear that we need to do something to stop smoking in people who are surviving from lung cancer.

Finally, I should like to revert to cancer control related to smoking. The problem of smoking has overshadowed this meeting, and in many respects has been its conscience. We have been reminded of the economic influence. We have been reminded that as members of the Association, we may not have recognized the full effect, and in fact a little surprisingly 25% of members of the Association in Japan did not agree that smoking was the major important factor in lung cancer. Our responsibility in this regard, however, is extremely important. Imagine the problem of 2,000,000 lung cancer deaths each year in the world, in the next century. A city the size of Toronto wiped out each year. However, we are making progress. Smoking rates have been falling in men in some countries, and at ages under 55 in the United Kingdom, the United States, Canada, and, I believe, Australia, lung cancer rates are now stable or even falling. The challenge is to extend this gain to women, and even more so by legislation, by example, and education to the countries of the third world.

**Update in Pathology**

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Pathology is the bridge between the laboratory and the clinic. Changing therapy leads to changing pathology, and classification is the method of providing a substitute for clinico-pathologic correlations. Nomenclature is therefore necessarily interim and has to be modified as it becomes biologically and clinically meaningful to do so. Classification systems are never perfect, but like all language, differentiate and specify. Lung cancers represent a continuum with an infinite number of points, which we recognize as overlapping circles when we attempt to quantitate the various features expressed. At the minisymposium it was agreed that light microscopy and the WHO classification remain the core and mainstay of the system and are the most important tools in the pathologist's bag. If well done, they have predictive and therapeutic value. The more tissue one has to examine, the better the appraisal of the whole tumor. After all, a sugar maple is distinguished from a Norway maple by its shape, its leaf, its keys, not by a section of its xylem and phloem, but we often have only a piece of leaf to look at.

Over the past several years, we have learned from clinical trials and detailed histologic comparisons that there is no difference in response to therapy or survival between small cell carcinomas of classic oat cell type and polygonal or spindle-shaped small cells, as long as the nuclei remained typical. On the other hand, when a significant number of large cells was intermingled with the small cells—judged by prominent nucleoli and perinucleolar clearing—there was a poorer response to therapy. These differences corresponded with what was emerging in laboratory cultures as classic small cell, variant small cell, and multipotential subtypes. Therefore, when your pathology panel met at Gleneagles, Scotland a year ago, we arrived at a decision to reclassify the small cell carcinoma group into classic small cell, small cell-large cell, and combined small cell, eliminating the terms oat cell and intermediate cell, since the latter term was too comprehensive and confusing. We do not recommend changing the WHO nomenclature until after the next revision committee, but that those currently using it, divide the intermediate group into those with and without more than about 1% large cells. This has been published in a letter (Yesner R. Classification of lung cancer histology. *N Engl J Med* 1985; 312:652-53) and will be followed by a paper to be sent to *Cancer*.

We have known for 20 years that all lung cancers are epithelial, of endodermal origin, and exist in a dynamic spectrum, which often alters with time and therapy. We have also known for many years that all lung tumors produce ACTH, although greatest in the small cell group and therefore have a neural flavor. These observations have been abundantly fleshed out at the plenary presentation, minisymposia, and poster sessions of this convention. If there has been a single theme that has emerged strongly, it is the heterogeneity of lung tumors, both within and between categories. This heterogeneity has been stressed in light microscopic studies by Roggli et al in a 1,000 slide study of 100 tumors, read by 5 pathologists using WHO criteria, in which only 34% homogeneity was found. Even more striking perhaps was the fact that only about ¼ the previous biopsies accurately represented the whole tumor. It has been stressed in EM studies by Mackay, showing great variations in 31 carcinoids, and even the presence of myoepithelial cells in some of these tumors. It has been stressed in overlapping adenocarcinoma types, and in the immunocytochemistry studies of Linnoll et al, who found multiple NE markers in 40% of their adenocarcinomas and 20% of their large cell