presumably through removing the causative antigens which may proliferate in humid environment.

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REFERENCE
1 Miyagawa T, Ochi T, Takahashi T. Hypersensitivity pneumonitis with antibodies to Cryptococcus neoforms. Clin Allerg 1978; 8:501-09

To the Editor:

I appreciate the comments of Dr. Lee and his colleagues with regard to our article on summer-type hypersensitivity pneumonitis. As they pointed out, recurrence of symptoms in the next season is one of the characteristic features of this disease. Then we use the word remission instead of cure, when patients become asymptomatic. Such recurrence in the following summer season was observed in approximately one third of our patients.

Fundamental prevention of this disease centers on protecting patients from exposure to antigenic substances, as Dr. Lee with his colleagues pointed out, through improving housing environment to remove causative antigens. As we reported, remodeling of houses where patients lived introduced complete remission after episodes of four consecutive seasons.1

As to causative antigen of summer-type hypersensitivity pneumonitis, Dr. Lee described that the sera of his patients showed positive anti-cryptococcal antibody. The method of detecting antibody was not described here; however, I suppose it was the indirect immunofluorescent technique, and was not conventional agar immunodiffusion. Findings of rarity of precipitins against cryptococcal antigen, negative provocative inhalation, and difficulty in finding wild Cryptococcus strain in the environment where patients live raise questions as to causative antigen.

Recently, Shimazu et al2 reported that Trichosporon cutaneum was highly separated from the environment where patients lived and precipitins were detected against this antigen in the patients' sera; the possibility of the causative antigen in this disease was speculated upon.

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REFERENCES

Screening for Lung Cancer

To the Editor:

Melamed et al recently reported the results of periodic screening for lung cancer in high risk men (Chest 1984; 86:44-53). This elegant, randomized study with concurrent controls compared 4,968 men receiving four-monthly sputum cytologic examinations plus annual chest x-ray examinations with 5,072 men receiving only annual chest x-ray examinations.

For the first time they were able to estimate a lead time of three years in the cytologically screened group because this group had a small excess of cancers detected at the outset and this excess was eliminated when the cumulative incidence in the control group caught up three years later. This lead time was confirmed by a better survival rate in the cytologically screened group during the first six years after diagnosis, but thereafter, the survival rate became the same in both groups. In addition, cytologic screening had no impact on population mortality rates for lung cancer during five to eight years of follow-up. A similar failure has been reported for the Johns Hopkins Lung Project.1

This disappointing result of cytologic screening was not applied, and rightfully so, to periodic radiographic screening because the study was not designed to examine the latter modality. Although the authors admitted this in their discussion, they went on to recommend annual chest film screening because the five-year survival rate for lung cancer in both groups was 35 percent compared to less than 10 percent in the general population.

This recommendation is not warranted for several reasons. First, one cannot justifiably compare cancer cases in a largely compliant group of periodically screened men with largely unscreened cases in the general population for at least the reason that radiographic screening has its own lead time.

Second, three earlier studies on semiannual radiographic screening had disappointing results.2,3 While it is true that only one of those three studies was controlled, that of Brett,4 his results showed no statistically significant advantage in case survival rate or population mortality rate in the screened group. Admittedly, Brett's cases were small in number and the observation period was short, but the lack of screening impact has been essentially confirmed by the Mayo Lung Project.5 This investigation was similar to the Memorial Sloan-Kettering study except that four-monthly cytologic screening was accompanied by four-monthly radiographic screening, the controls got no screening at all, and the follow-up period has been longer. The lung cancer population mortality rate was essentially the same in both groups: 2.2/1,000/year (51 cases) in the screened group and 2.3/1,000/year (54 cases) in the control group.

Third, Melamed et al have not considered a very high risk of second lung cancers (42/1,000 person-years) among the radiographically occult lung cancer cases, an incidence rate almost ten times higher than the incidence rate among men at risk of a first lung cancer in the Mayo Lung Project.6 This high risk of second cancers was also associated with a high inoperability rate and a low survival rate. Taken in conjunction with the multifocal nature of lung cancer described more than two decades ago by Auerbach et al,7 the uncomfortable thought arises that perhaps periodic cytologic screening leads to the diagnosis and treatment of some cases whose "cancers" may not have been destined to become a clinical problem before a clinically important cancer took over the picture.

Such a possibility is inherent in all screening for cancer, and its recognition raised concern at an international workshop8 that the basic index of screening efficacy should be the population mortality rate rather than the case survival rate. If we do not reduce the death rate in a screened group, have we really accomplished anything? It may well be that a five to eight year follow-up period is too short to demonstrate an impact of periodic screening on the population lung cancer mortality rate. Further follow-up may clarify this matter, but as yet, there is no basis for routine radiographic screening of high risk populations for lung cancer because "the numerator of the cost-benefit ratio is high and the denominator is low."9

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CHEST / 87 / 2 / FEBRUARY, 1985 273

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To the Editor:

Dr. Weiss participated in one of the first systematic studies of periodic screening as a potential means of controlling lung cancer, the Philadelphia Pulmonary Neoplasm Research project. His reports of that work have become a classic source of reference. We thank him for his kind comments on our own study.

We agree with Dr. Weiss that rigorous statistical proof of the value of periodic radiographic screening is lacking. We would strongly support a study to obtain that proof if we believed it possible to deny chest x-ray films to a randomized, high-risk "control" population with their informed consent. In the absence of irrefutable proof, we note the following even more evidence of value in periodic screening: a shift to earlier stage disease at diagnosis, an increase in the proportion of cases that are resectable, and better survival in the screened compared to the general population. We certainly see no justification for a change from the present medical practice of recommending annual chest x-ray examinations for asymptomatic, high-risk individuals. A decision to do otherwise, as we have noted, is a decision not to treat lung cancer for cure since the symptomatic patient is essentially incurable.

The proportion of early-stage lung cancer detected in our population, the percentage of cases resectable, and the length of survival all are greater than in the three early studies referred to by Dr. Weiss. Operative mortality today for treatment of lung cancer by lobectomy at Memorial Hospital is 2 percent,7 well below the 10-20 percent mortality of lung cancer surgery 20 years ago reported by Dr. Weiss.4 Thus, we are seeing better radiographic detection and better treatment today than was the case 20 years ago.

Patients who have had one lung cancer are at higher risk of another, as Dr. Weiss notes. In our population the risk of a new, second lung cancer following complete resection of a first is about fivefold the initial risk of lung cancer for the entire population. There were 12 men with multiple lung cancers among the 291 who have developed the disease at this writing. Three had two synchronous cancers. Nine of the 166 men who were treated by complete resection of their first cancer have since developed a second primary lung cancer (metachronous cancers). Based on a calculation of time at risk, we have an incidence rate of 16 per 1,000 person years for new primary second lung cancers after complete resection of the first. Five of the nine second primary cancers were resectable, and two of the five men treated by a second resection are alive and free of carcinoma six years and three years following resection of their second cancers. We find that very impressive.

However, we agree with Dr. Weiss and with the consensus of the UICC International Workshop on screening in cancer,4 in which he participated, that the basic index of screening efficiency should be population mortality, not case survival rate. We have reported the mortality rate from lung cancer in our population, but do not have a comparable population of unscreened, cigarette-smoking men with which they can be compared. There are other statistical approaches to solve this dilemma. The most promising, we believe, is through mathematical modeling based on the kind of precise, hard data available to us from the New York Lung Cancer Screening Program. We are presently engaged in deriving such a model from our data, and hope to use that model to show the effects of radiographic screening at various different frequencies, for populations that receive treatment of varying efficacy. It is our hope that we will have Dr. Weiss' critical comments on that effort when it is ready for formal presentation.

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References

2 Melamed MR, Flehinger BJ. Screening for lung cancer (editorial). Chest 1986; 82:3-6