This joint statement is presented on behalf of Dr. Joseph H. Ogura, Dr. Alden H. Miller, Dr. George A. Sisson and Dr. Harold G. Tabb. Dr. Joseph H. Ogura is Professor of Otolaryngology at Washington University, St. Louis, Missouri and Associate Otolaryngologist at the Barnes Hospital Group in St. Louis. Dr. Alden H. Miller is Head of Department and Clinical Professor of Surgery, Department of Otolaryngology at the University of Southern California, School of Medicine, and Head of Department of Otolaryngology at Los Angeles County General Hospital and Childrens Hospital, Los Angeles, California. Dr. George A. Sisson is Clinical Professor of Otolaryngology at the State University of New York, School of Medicine, Syracuse, New York, and Chief of the Department of Otolaryngology at Community-General Hospital at Syracuse. Dr. Harold G. Tabb is Professor and Chairman, Department of Otolaryngology, Tulane University, School of Medicine, New Orleans, Louisiana and Senior Visiting Surgeon at Charity Hospital of Louisiana at New Orleans.

Further data concerning each of the participants are contained in summaries submitted with this statement.

We understand that this Committee is interested in receiving information relating to possible health problems associated with cigarette smoking. It has come to our attention that the Advisory Committee to the Surgeon General reported that cigarette smoking is a significant factor in the causation of laryngeal cancer in the male. This finding is of special interest to us as physicians whose specialty is the treatment of diseases of the larynx and related areas of the nose, mouth and throat. Each of us has devoted years of practice to the diagnosis and surgical treatment of cancer of these
areas. Our total experience comprises in the neighborhood of 3000 cases of cancer of the larynx and adjacent areas. We naturally have great interest in any observations or judgments concerning the possible cause of cancer in this part of the body. However, it is our opinion that the discussion of the problem of laryngeal cancer in the Report of the Surgeon General's Advisory Committee represents an inadequate review and evaluation of the pertinent data and that the conclusion is open to question on a number of grounds.

The Committee's conclusion is essentially based on its interpretation of statistical data showing an association between cigarette smoking and cases of cancer of the larynx. While we have noted a similar association in our cases, we are also aware of other facts which indicate that the association may not have causal significance.

The Vital Statistics of the United States pertaining to the behavior of laryngeal cancer in the population at large reveal an increase in the number of deaths from this disease among white males over the past three decades which is much smaller than might be expected on the basis of growth in population and the increase in the number of people now living to an age when laryngeal cancer tends to occur. Although no official figures for the United States on the number of new cases each year exist, we find no indication of any appreciable increase in the number of cases seen from year to year. If cigarette smoking were a significant factor in the causation of laryngeal cancer, we would, at least, expect to find a large increase in mortality or frequency of the disease over the past three decades corresponding to the increase in cigarette consumption. We regard the absence of such an increase as significant evidence inconsistent with the asserted
role of cigarette smoking.

As the Report of the Surgeon General's Advisory Committee indicates, laryngeal cancer is a disease which occurs predominantly in men. It also notes that the ratio of males to females with cancer of the larynx was 6.3 to 1 thirty years ago as compared to 10.8 to 1 today. Our experience supports the observation that the proportion of males to females among larynx cancer patients has been rising over the years. Since women now represent a larger proportion of the smoking population than they did thirty years ago, it is difficult to explain this phenomenon on the basis that smoking is a significant factor. No adequate explanation has been advanced for the large and increasing preponderance of this disease in males. Some have suggested that hormonal factors may be important, but at this time we simply do not know.

We find not infrequently cases of cancer of the larynx in men and women who have never used tobacco in any form which indicates, at least, that tobacco is not a necessary factor. Very little attention is given in the Report to the possible importance of other factors frequently found in association with laryngeal cancer. It is noted in this Report (p. 211) that "... other factors may play a significant role in the production of laryngeal cancer, such as alcohol and inadequate nutrition." In our view this is a highly pertinent observation and some attempt should have been made to evaluate the significance of these factors. We know from our experience that many patients with laryngeal cancer are heavy drinkers. The association with alcohol in some series of cases may be higher than the association with tobacco. Very often a patient has a history of both heavy drinking and heavy smoking. Inadequate nutrition is also likely to
be part of the clinical picture. The variety in the case histories of patients with cancer of the larynx may be a good indication that some factor which remains undiscovered may eventually be found to be the true cause. Further, if tobacco, alcohol or inadequate nutrition are important in producing cancer of the larynx, we have yet to understand how they operate and why it is that cancer does occur in the absence of any or all of these factors. Our present knowledge would indicate that it is premature to incriminate any of the present suspects.

Another matter not sufficiently dealt with in the Advisory Committee's Report is the question of why cigarette smoke should appear to be specifically related to cancer of the larynx but not to cancer of adjacent parts of the throat. Very little attention is given to the differences in cancer arising in various parts of the relatively small area of the mouth, throat and respiratory passages, although these parts are all exposed to cigarette smoke.

Statistical studies of laryngeal cancer, such as those relied on by the Committee, seldom define with precision the location of the various cancers which may be included within the broad term "laryngeal cancer." Because of this, the importance of such data is difficult to evaluate. When clinicians study problems in relation to cancer of the oral cavity and throat they find it necessary to define precisely the location of the cancer since the clinical behavior of cancers at different sites in and near the larynx differs greatly. The exact definition of site is also important when analyzing case histories since a variety of different factors may appear to be important according to whether the cases studied are, say, cancer of the epiglottis, cancer of the tonsil or cancer of the vocal cord. Careful analysis may show that alcohol use or malnutri-
tion may appear to be important as to one site, chronic infection or syphilis as to another, a sex factor or irritation as to still another. The degree of association with smoking may vary greatly from study to study according to the type of cases which are included in or excluded from the category of laryngeal cancer.

There are other curious phenomena noticed in connection with cancer in various parts of the throat which appear inconsistent with the theory of cigarette smoke carcinogenesis.

We can all agree that a case of cancer of the trachea or windpipe is extremely rare and yet this structure is directly in the path of inhaled smoke. The trachea lies immediately below the larynx and should be similarly affected by smoke.

Cancer does occur at the base of the tongue and on the tonsil. Both of these structures are in close proximity to the larynx. Yet it is curious that cancer at these sites occurs more frequently in women than in men. One might infer that because of this sex distribution it is unlikely that smoking is an important factor in producing cancer in these locations.

In heavy cigarette smokers, we often see deposits of tobacco condensate in the vestibule of the nose which remain there over long periods of time. Yet we have never seen cancer develop in this location.

Cancer of the upper end of the esophagus was, until a few years ago, much more common in women than in men. Recently it has been noticed that this ratio is changing and today we find as many cases in men as in women. We know that some part of the cigarette smoke is dissolved in the saliva and swallowed. Inhaled smoke particles are also carried up from the lung in the mucus and swallowed.
It has been hypothesized that this explains the statistical association between smoking and esophageal cancer. It is difficult to account for the changing sex ratio for cancer of the upper end of the esophagus on the basis of this hypothesis. Assuming that women are particularly susceptible to cancer in this location, if smoke condensates are the responsible agent we would have expected the ratio in favor of women to persist or even to increase with an increasing proportion of women taking up smoking. Furthermore, if swallowed tobacco condensates produce cancer, it is difficult to account for the fact that stomach cancer has decreased remarkably in recent times.

It is worth noting that there is no experimental evidence of the production of laryngeal cancer by tobacco smoke or condensates. Dr. Ogura has observed that some families appear to be predisposed to cancer of the larynx and adjacent areas, but no study of the possible genetic basis of this disease has been undertaken to date.

In conclusion, we would say that the attempt to assign causal significance to any one factor that appears with high frequency in case histories is not the way to make a scientific determination of the cause of a disease as complex as cancer. Such information raises many subjects for consideration and further exploration, but no definite statements concerning the cause of cancer of the larynx should be based on such data alone. We believe that it has yet to be proved that cigarette smoke is a causal factor in laryngeal cancer. While we do not say that the evidence to date rules out smoking as a possible factor, we feel that the Advisory Committee's conclusion would have been on a sounder scientific
footing if the inconsistent and contradictory evidence had been more fully evaluated and the conclusion had been reached that a statistical association between cigarette smoking and laryngeal cancer in the male may have been demonstrated, but it remains to be proved whether the relationship, if any, is one of cause and effect.

Joseph H. Ogura, M.D.
Alden H. Miller, M.D.
George A. Sisson, M.D.
Harold G. Tabb, M.D.