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AETIOLOGY OF CANCER OF THE
LARYNX

Air-borne substances carcinogenic to the bronchi are not necessarily carcinogenic to the larynx simply because they have to pass the larynx before they can reach the bronchi. None of the industrial causes of lung cancer are known to be causes of laryngeal cancer, and it would not be surprising if the carcinogenic effect of smoking was also restricted to the mucosa below the bifurcation of the trachea. That this should be so may even be inferred from the sharp contrast in the trends of the death rates from bronchial and laryngeal cancers. For the mortality from laryngeal cancer has remained practically constant in Britain over the last forty years, while the mortality from bronchial cancer and the consumption of cigarettes have both rapidly increased. It is therefore difficult to interpret the observation, now made by five groups of investigators, that cancer of the larynx and the smoking of tobacco are closely associated.¹⁻⁶ E. L. Wynder, I. J. Bross, and E. Day⁵ found that the smoking habits of men with laryngeal cancer were similar to those of men with lung cancer in all important respects save one. Non-smokers were found in one out of 209 men with laryngeal cancer (0.5%), in one out of 132 men with lung cancer (0.8%), and in 22 out of 209 men with other diseases (10.5%), who had been selected to be of the same age and social background as the men with laryngeal cancer. The proportions of men smoking 35 or more cigarettes a day were respectively 28%, 25%, and 11%. The difference between the two types of cancer lay in the method of smoking; for, while 94% of the smokers in the lung-cancer group smoked cigarettes, the proportions in the laryngeal and control groups were significantly lower (86% and 82%).

¹ Levin, M. L., Goldstein, H., and Gerhardt, P. R., *J. Amer. med. Ass.*, 1950, **143**, 336.

² Sadowsky, D. A., Gilliam, A. G., and Cornfield, J., *J. nat. Cancer Inst.*, 1953, **13**, 1237.

³ Sanghvi, L. D., Rao, K. C. M., and Khanolkar, V. R., *British Medical Journal*, 1955, **1**, 1111.

⁴ Blümlein, H., *Arch. Hyg. (Berl.)*, 1955, **139**, 349.

⁵ Wynder, E. L., Bross, I. J., and Day, E., *Cancer*, 1956, **9**, 86.

⁶ ———, *J. Amer. med. Ass.*, 1956, **160**, 1384.

⁷ U.S. Public Health Service, Federal Security Agency, *Cancer Mortality Series*, 1-10. Public Health Service Publ. Nos. 13, 65, 67, 112, 126, 152, 178, 216, 217, 244, Washington.

⁸ Registrar-General of England and Wales, *Decennial Suppl.*, 1931, Part 2a, *Occupational Mortality*, 1938, H.M.S.O., London.

⁹ Ahlbom, H. E., *Acta radiol. (Stockh.)*, 1937, **18**, 163.

¹⁰ Jacobsson, F., *ibid.*, 1951, **35**, 1.

¹¹ Curwen, M. P., Kennaway, E. L., and Kennaway, N. M., *Brit. J. Cancer*, 1954, **8**, 181.

Why then has cancer of the larynx not increased in incidence like cancer of the lung? There can be no doubt that it has not, but the difference in the behaviour of the two types of cancer may not be as great as has been thought from comparison of the death rates. Mortality data can give a reasonably accurate picture of the incidence of lung cancer because the fatality of the disease is so great; but they may not provide an accurate picture of the incidence of laryngeal cancer, because the fatality is substantially lower, and it has moreover decreased in recent years. In the U.S.A., for example, a study of cancer morbidity in nine areas has shown a 75% increase in the incidence of laryngeal cancer between 1937 and 1947, while the corresponding mortality increased by only 42%.⁷ Thus the incidence of laryngeal cancer may have increased in Britain, even though the mortality in Britain has remained steady.

Again, it seems possible that laryngeal cancer may be related to all types of smoking, whereas lung cancer may be related only to cigarette smoking. If this should prove to be so, it would be understandable that the incidence of laryngeal cancer should increase only slightly in comparison with the incidence of lung cancer; for in Britain, as in many other countries, the recent change in smoking habits has consisted largely in a change-over to cigarettes, and the actual annual consumption of tobacco has risen comparatively little. But the evidence is not conclusive, and it is not altogether consistent. D. A. Sadowsky and his colleagues found, for example, that the relationship between laryngeal cancer and smoking was characteristically a relationship with cigarette smoking.²

Finally, the possibility may be considered that some other environmental factor which contributes to the production of laryngeal cancer has become less prevalent and so has, to some extent, cancelled out the effect produced by the increase in tobacco consumption. Such a factor might be alcohol, which has long been thought to play some part in the aetiology of the disease. In the study of occupational mortality produced by the Registrar-General after the 1931 Census it was shown that innkeepers, barmen, and waiters had a high mortality from laryngeal cancer⁸; and Wynder, Bross, and Day have now carried the evidence a stage further by showing that a greater proportion of men with the disease than of the control patients have been accustomed to heavy drinking.^{5, 6} Since heavy drinkers tend to be heavy smokers, it was not easy to disentangle the effect of one habit from that of the other, but by study of the differences in alcohol consumption within groups of men of similar smoking habits it could be shown that there was no

association between the disease and the drinking of wine, beer, or moderate quantities of spirits, but that the consumption of seven or more tots of spirits a day might increase the risk of the disease by some 5- or 10-fold. Clearly, if this is so, the great reduction in excessive spirit drinking which has taken place in Britain during the last fifty years may have gone some way to countering the effect of other factors tending to produce an increase in incidence. In short, so many variables have to be considered about which knowledge is as yet fragmentary that it would be unjustifiable to conclude from vital statistics alone that there is anything necessarily contradictory in the observations that lung and laryngeal cancers are both produced, to some extent, by tobacco.

Clarification of these and other problems may, perhaps, be obtained when it is more fully appreciated that cancer of the larynx is not one disease but consists of a group of diseases having, in all probability, different aetiologies. In mortality data (and many hospital data) cancer of the vocal cords and other "intrinsic" cancers are classed with "extrinsic" laryngeal cancer, most cases of which might more accurately be described as cancer of the hypopharynx. Wynder and his co-workers found that the relationship with pipe and cigar smoking was particularly strong for cancer of the extrinsic larynx, and this distribution may possibly explain the difference between their results and those obtained by Sadowsky and his team. It was also found that the association with alcohol was much stronger for cancer of the extrinsic larynx than for cancer of the intrinsic larynx. Wynder suggests that alcohol may exert its effect through the associated nutritional deficiency which may accompany excessive drinking of spirits, and he compares the cases developing in heavy drinkers with the cases of cancer of the hypopharynx which has been common in northern Sweden and is believed to be associated with the Patterson-Kelly (or Plummer-Vinson) syndrome of iron-deficiency dysphagia.^{9 10} It is possible that differences in the aetiology of cancer of intrinsic and of extrinsic origin may also account for the peculiar finding that cancer of the larynx in men is commoner in the big towns, while in women it is commoner in the country.¹¹ The majority of male cases are of intrinsic origin, while the reverse is true of female cases, so that the finding could perhaps be explained if cancer of the cords were characteristically an urban disease while cancer of the hypopharynx were characteristically rural.

Neither of the most recent studies show any evidence that tuberculosis or syphilis play any part in the production of the disease,^{4 5} but it would seem that, in some few cases, cancer may be preceded by chronic laryngitis, pachydermia, or perhaps by papillomas or polyps. While all chronic benign lesions of the larynx should clearly be watched carefully, it would seem

that the most immediate hope of prevention lies in education of the public about the probable carcinogenic effect of some of their daily habits.

VACCINATION AGAINST TUBERCULOSIS IN CHILDHOOD

The investigation¹ by a committee of the Medical Research Council into the prophylactic effect of B.C.G. and vole-bacillus vaccine has shown that if all previously uninfected adolescents in Britain were vaccinated the incidence of the disease in young people from the age of 15 up to 17½ years, and probably up to at least 19 years, might be reduced by about one-half. This would be a substantial contribution to the control of tuberculosis, and there is now no justification for any local health authorities to refrain from putting into operation the permissive scheme² of the Ministry of Health for the vaccination with B.C.G. of schoolchildren in their fourteenth year. One of the main disadvantages of mass vaccination in adolescence is the substantial proportion of children—as many as 40% in the Medical Research Council's investigation—who are found to be positive reactors to tuberculin and who form a large group in which tuberculosis cannot be prevented by prophylactic vaccination. It is therefore urgently necessary to decide whether protection should not be offered at an earlier age, perhaps even at birth, before children have had a chance to acquire tuberculous infection naturally.

In 1954 the numbers of notifications of tuberculosis of the meninges and central nervous system in England and Wales were 212 at ages 0-4, 221 at ages 5-14, and 134 at ages 15-24 years. The corresponding figures for respiratory tuberculosis were 1,347, 2,799, and 9,553, and for other forms of tuberculosis 357, 1,225, and 1,065.³ If it is assumed that vaccination will reduce the incidence of tuberculosis by 50%, then, so far as numbers are concerned, the largest reduction of cases—up to about 5,000 of pulmonary tuberculosis—would be achieved by arranging that protection was most effective between the ages of 15 and 24. This is the purpose of the present permissive scheme. To halve the number of tuberculous infec-

¹ *British Medical Journal*, 1956, 1, 413.

² Ministry of Health Circular, 1953, No. 22/53.

³ *Registrar General's Statistical Review of England and Wales for the Year 1954*, 1955, H.M.S.O., London.

⁴ Aronson, J. D., and Palmer, C. E., *Publ. Hlth Rep. (Wash.)*, 1946, 61, 802.

⁵ Stein, S. C., and Aronson, J. D., *Amer. Rev. Tuberc.*, 1953, 68, 695.

⁶ Aronson, J. D., and Aronson, C. F., *J. Amer. med. Ass.*, 1952, 149, 334.

⁷ Leading article, *Med. Offr.*, 1955, 94, 320.

⁸ Leading article, *Manchester Guardian*, December 24, 1955.

⁹ Guld, J., Magnus, K., Tolderlund, K., Biering-Sørensen, K., and Edwards, P. Q., *British Medical Journal*, 1955, 2, 1048.

¹⁰ Gaisford, W., *ibid.*, 1955, 2, 1101, 1164.

¹¹ Wallgren, A., *Acta paediat. (Uppsala)*, 1955, 44, 237.

¹² *Nord. Med.*, 1956, 55, 21.

¹³ Daniels, M., Ridehalgh, F., and Springett, V. H., *Tuberculosis in Young Adults*, 1948, H.M.S.O., London.

¹⁴ Palmer, C. E., and Shaw, L. W., *Amer. Rev. Tuberc.*, 1953, 68, 462.

¹⁵ Jarman, T. F., *British Medical Journal*, 1955, 2, 1235.