

LARYNGEAL CANCER AND BETA-CAROTENE:  
COULD THE ASSOCIATION BE DUE TO CONFOUNDING BY VITAMIN C?

D.E.M. MACKERRAS

Numerous studies have shown that a high intake of foods rich in beta-carotene is associated with a reduced risk of lung and laryngeal cancer. However, as many foods rich in beta-carotene are also good sources of vitamin C, could these results be due to confounding by vitamin C?

As many of these studies used un-validated short food frequency questionnaires to measure dietary intake, it is difficult to interpret their findings, especially when they are contradictory. The validity of a dietary questionnaire is related to which foods are included, not to its length. The following is suggested as one method which may be useful for assessing the content validity of such questionnaires when comparing the results of studies.

Tables showing the foods contributing to total intake and variation in intake of nutrients in the US (Block et al. 1985; Byers et al. 1985) were used to evaluate questionnaires from two studies of diet and laryngeal cancer, one from Buffalo, New York (Graham et al, 1981) and the other from Houston, Texas (Mackerras et al, 1988). The Buffalo questionnaire, which included 28 food types, captured only about 25% of total vitamin A intake but at least 45% of the variability in intake. The Houston questionnaire, which included 42 foods types, captured 78% and 99% of total intake and variability in vitamin A intake respectively. However, only 17% and 36% of total vitamin C intakes were captured by the Buffalo and Houston questionnaires respectively. Neither questionnaire included orange juice which contributes 26.5% of total vitamin C intake and 38% of the variability in vitamin C intake in the US.

These results indicate that these studies measured vitamin A/carotene intakes more accurately than vitamin C intakes as regards both absolute intake and the ranking of individuals. Thus although an association between vitamin C intake and risk of laryngeal cancer was found in the Buffalo study, this could have been a reflection of the high vitamin A content of the few vitamin C-containing foods on the questionnaire. Moreover, poor measurement of vitamin C intake would result in residual confounding by vitamin C even intake after including it in a model with carotene intake. Therefore, the question of whether a relationship exists between vitamin C intakes and laryngeal cancer remains unanswered by these studies.

These results illustrate the importance of measuring potential confounding variables as carefully as the factor of primary interest. They are also a warning against literal interpretation of the level of nutrient intake calculated using a short questionnaire.

BLOCK G., DRESSER C.M., HARTMAN A.M., CARROLL M.D. (1985). Am. J. Epidemiol. 122: 13.

BYERS T., MARSHALL J., FIEDLER R., ZIELEZNY M., GRAHAM S. (1985) Am. J. Epidemiol. 122: 41.

GRAHAM S., METTLIN G., MARSHALL J., PRIORE R., RZEPKA T., SHEDD D. (1981) Am. J. Epidemiol. 113: 675.

MACKERRAS D., BUFFLER P.A., RANDALL D.E., NICHAMAN M.Z., PICKLE L.W., MASON T.J. (1988). Am. J. Epidemiol. 128:980.