Depts. of Microbiology and of Obstetrics and Gynecology, Chicago Medical School, Chicago, Ill.

Cancer in Twins: Concordance or Discordance?

L. Keith, E. Brown

Although published reports of cancer in twins are not numerous, there are case reports of concordance in a variety of tumors in twins. Cancer of the breast is most frequent; concordance has also been noted in uterus, gonads, eyes, stomach and rectum. In general, these reports tend to support the theory that genetic factors operate either in the concordance of cancer or in the site of the specific tumors. The significance of concordance remains in doubt, however. Reported study groups are not comparable because the materials and methods are disparate. In many reviews the methods of zygosity determination are questionable. The fact that not all cases of cancer in twins are reported introduces a constant source of bias. The following review illustrates this well.

In 1940, Madge T. Macklin reviewed the publications of tumors in MZ and DZ twins and concluded that tumors affected MZ twins far more than both members of a DZ pair. She observed concordance in tumor type, site, and age of onset, as more frequent in MZ than DZ twins. She later (1947) reexamined the same material and some additional twin pairs and concluded that MZ twins have identical tumors far more frequently than DZ twins. She emphasized that rare types of tumors were genetically determined.

In 1948, Busk et al reported on a series of 185 twin study pairs from the Danish Cancer Registry; they concluded that (1) there was a tendency toward a higher incidence of cancer in partners of MZ than of DZ cancerous twins; (2) these deviations from expected values were not considered statistically significant; and (3) there was a tendency for tumors in MZ twins to affect corresponding organs in both partners, this being not the case in DZ twins.

Nine years later, Nielsen and Clemmesen (1951) had observed 336 study pairs, but believed that their material did not warrant conclusions regarding the tendency for tumors to occur at the same site in twins who were concordant for cancer. They

actually observed a slightly greater tendency for tumors to occur at concordant sites in DZ than in MZ twins at that time.

In 1956, Harvald and Hauge reported on a series of 1900 pairs of twins from the Institute of Human Genetics of the University of Copenhagen. They studied 212 twin pairs in whom cancer had occurred; cancer concordance was not considered significantly different between MZ and DZ pairs. In a later communication, Harvald and Hauge (1958) reported on 345 twin pairs more than 40 years of age, in whom the low rate of concordance in general was striking, notwithstanding a statistically significant difference between the MZ and same-sexed DZ groups.

Three years later, Hauge and Harvald (1961) reported on 6300 pairs of twins. There were 652 twin pairs with malignant growths, of which 141 pairs were MZ and 511 DZ. The conclusion drawn from this larger study was that the rate of concordance for malignant growths in general was higher in MZ than in DZ pairs, both of same or different sex. Applied to tumor sites, however, these differences were not statistically significant. Hauge and Harvald tentatively concluded that genetic factors could be considered only of limited importance in the development of malignant growths, and suggested that if differences existed between MZ and like-sexed DZ pairs for concordance of malignant growths, such differences were small and less important than nongenetic factors.

In a final publication concerning 6893 twin pairs, among which were 1038 cases of cancer, Harvald and Hauge (1963) concluded that statistically significant differences were not found between the concordance rates in MZ and DZ like-sexed twin pairs for all types of malignant growths when pooled together. Harvald and Hauge suggested a diversity in the population with regard to cancer which was not determined genetically to any significant extent.

Jarvik and Falek (1962) regretted the lack of statistically representative twin data on cancer for the US. They believed that their study group of 1603 index twins was suitable for such analysis. They used 47 senescent index twin pairs, of which 24 pairs were MZ, 15 same-sexed DZ, 7 opposite-sexed DZ, and 1 unclassified. In this group, a concordance rate for cancer of 25% was arrived at for MZ twins, vs. 6.7% for DZ same-sexed twins. Jarvik and Falek concluded that, in view of the difference in concordant rates, the genetic elements in cancerogenesis were operative.

Osborne and DeGeorge (1964) studied 152 twins and a group of 13910 single-born patients as controls. The essential difference between them was the large percentage of twin-born males with diagnosis of benign neoplastic diseases (1.94% benign vs. 1.14% malignant neoplasia). This difference was not found in females. The conclusions, however, were that the total cancer experience of twins did not differ from that of the single-born. They questioned genetic conclusions regarding cancer based on studies of concordance and discordance among twins.

In 1940, v. Verschuer and Kober observed a greater tendency to concordance in site and type of tumor in MZ than in DZ twins. The material was reexamined by v. Verschuer (1956) after the study group had enlarged somewhat. He concluded that, although the occurrence of cancer appeared equal in the MZ and DZ groups,

site concordance was greater in MZ than DZ twins. v. Verschuer believed that hereditary predisposition to cancer was nonspecific, and in some instances, not at all important.

In 1964, Spranger and v. Verschuer examined the same material and concluded that certain trends were evident after a 25-year observation period: (1) the general cancer concordance in MZ twins was not significantly different from that of DZ twins; (2) specific concordance (same type and site) in MZ twins was more than double that of DZ twins (0.138 vs. 0.055). Spranger and v. Verschuer were of the opinion that the genetic influence was not so much one of tumorogenesis but rather of tumor localization.

Reviews from Italy underscore the differing opinions. The numbers of twin pairs available to study will doubtless increase proportionately to the burgeoning population. The future of twin studies is fairly clear. Some authors have expressed inability to draw conclusions from their own limited material. Even when thousands or more pairs of twins are studied, the breakdown by sites and types of tumors gives small numbers for consideration. Review of many publications from the same institution often shows conclusions which change according to the period of observation.

The following deductions may be drawn from the literature.

Agreement generally prevails that MZ twins have higher concordance rates for cancer than DZ twins. The exact genetic influence on concordance remains doubtful. Published reports of cancer among twins note concordance in a variety of tumors. Genetic factors appear to operate either in the concordance of the cancer or in the site of the specific tumors. A genetic propensity toward inheritance of certain diseases, including cancer, may exist. A genetic origin of tumors in homologous twins is possible. Tumors, including type, site, and age of onset, affect MZ twins more than both members of a DZ pair. On the other hand, genetic factors could be only of limited importance in the development of malignant growths. Nongenetic factors often seem more important.

We agree with the suggestion of Gedda and Milani-Comparetti (1966) that computerized permanent twin registers should be established for prospective study and follow-up of large twin populations.

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Louis Keith, M.D., The Chicago Medical School, 2020 West Ogden Avenue, Chicago, Ill. 60612, USA.