Eur J Cancer Clin Oncol, Vol. 23, No. 3, pp. 343–345, 1987.
Printed in Great Britain

0277–5379/87$3.00+0.00

Sounding Board

The Concept of Viral Etiology of Cancer and Allied Diseases with Particular Reference to Cancer of the Colon

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CANCER of the colon recently raised considerable public interest and has been widely discussed in news media. Among the discussions reviewing its nature, possible etiology, diagnostic procedures and treatment, no mention has been made of the possible viral etiology of this neoplastic disease, although familial incidence of cancer of the colon has long been recognized.

Practically all tumors, leukemias and lymphomas thus far investigated in many cold blooded and warm blooded animal species, have been found to be caused by transmissible viruses. This refers to tumors, lymphomas and leukemias in fish, chickens, mice, rats, cats, hamsters, cattle and non-human primates [1]. Rather than speculate on a different etiology of the same disease in humans, it would appear more reasonable to assume that tumors, lymphomas and leukemias in humans are also caused by transmissible viruses. At least certain forms of leukemia and lymphomas, [2] as well as hepatocellular carcinoma [3] in humans, have already been documented to be caused by transmissible viruses.

If we accept the concept of viral etiology of cancer and leukemias as a working hypothesis for humans, we would have to accept, as a logical consequence, the fact that, as in all other virus-caused diseases, the law of obligate communicability would also apply to cancer and leukemia. It would then follow, that cancer, leukemia, or lymphomas do not develop "spontaneously", as a result of either mutation or of an obscure influence of other non-specific factors, but, as in the case of polio or smallpox, each case of cancer or leukemia could be traced to another case of the same disease, caused by the same virus, transmitted from one host to another.

One of the principal differences in epidemiology between neoplastic, and common, communicable diseases, is their transmission pattern. Communicable diseases, such as common cold, mumps, smallpox, or measles, are transmitted from one host to another within the same generation, and the incubation periods are, as a rule, very short, usually not exceeding days or weeks. On the other hand, oncogenic viruses causing neoplastic diseases very often are transmitted "vertically" from parents to offspring, from one generation to another [4]. The latency period elapsing between infection with the viral agent and the development of tumors is usually very long, and may exceed, in certain species, several years, perhaps even decades in humans. The difficulty in following the host-to-host transmission of oncogenic viruses is increased by the fact that many of these viruses remain latent in their carrier hosts, causing no symptom of disease; only a fraction of virus carriers develop tumors or lymphomas. The activating factors changing the hitherto latent virus into a deadly, tumor-inducing agent, may be intrinsic or extrinsic; some of the intrinsic fators may be hormonal or of other chemical nature, often related to aging. Many of the activating factors, however, are unknown, giving the impression that the tumors develop "spontaneously". Among the extrinsic carcinogenic factors, are exposure to ionizing radiation, smoking of cigarettes, pipes or cigars, exposure to asbestos and a variety of carcinogenic

Accepted 22 September 1986.

chemicals in factories, mines, chemical industries and oil refineries, exposure to carcinogenic chemicals present in food, water and polluted air, etc. Intake of large doses of estrogenic hormones, cortisone, or certain immunosuppressive drugs may also have a carcinogenic effect.

Long latency periods usually precede the development of tumors or leukemia. Mice inoculated shortly after birth with either mouse leukemia virus, or mammary carcinoma virus remain in good health until they reach middle age; they then develop leukemia or mammary carcinoma, respectively; a few develop lymphomas or tumors earlier, others later, and some escape disease, even though they carry and transmit the virus. Why this long latency period? What prompts the development of tumors? Similarly, following exposure of rats or mice, respectively, to total body X-ray irradiation, the latency period elapsing between the irradiation and the development of tumors, or leukemia, in the irradiated animals is usually 11–14 months, which represent approximately middle age for these species.

Vertically transmitted oncogenic viruses will cause tumors or lymphomas, as the case may be, only here and there among members of certain susceptible and virus-carrying families. The majority of members of the same families will escape disease and live out their lifespan without developing tumors. This form of transmission of pathogenic agents may result in the development of disease in a spotty manner, imitating genetic inheritance and may confuse the unaware observer.

Although an accidental occurrence of tumors in more than one member of the same family must be considered, numerous "cancer families" have been reported having such a striking incidence of tumors, that a mere chance could be reasonably excluded. This refers particularly to cancer of the colon. As an example, a case was described in a male patient, who, over a period of 30 years, had three primary carcinomas of the colon. In five generations of the same family, 13 members, including the patient's brother, developed carcinomas; 10 of these tumors were carcinomas of the colon [5]. Similar striking reports of familial incidence of breast cancer or cancer of the kidneys, have been also reported. Although most cancer patients seem to represent sporadic cases, the number of recorded cancer families is considerable. Studies on cancer families have been limited, with only few exceptions, to two or three successive generations. There is no reason to doubt that a similar high incidence of tumors did, or will, occur in either preceding, or succeeding, generations. Other families, on the contrary, have very few tumors, or practically no record of cancer, through several successive generations. Attempts to follow vertical transmission of oncogenic viruses in humans are very difficult because most of the patients do not know what happened to their grandparents or great-grandparents, or their ancestors' siblings. Studies of vertical transmission of oncogenic viruses can be performed in a clear manner on certain animal models, particularly on mice, which have a lifespan of 18–24 months. Several family lines in mice have been established and observed for more than 50 successive generations. In such inbred animal models, vertical transmission of certain virus-caused tumors can be clearly observed. This is the case for leukemia and lymphomas, as well as for mammary cancer in mice. In a "high leukemic" Ak inbred line, over 90% of mice develop leukemia in each generation. In another inbred line of mice, such as C3H, a similar high incidence of mammary carcinomas is observed in females of each successive generation. Vertical transmission of leukemogenic viruses in mice was directly demonstrated when cell-free extracts prepared from embryos removed from healthy pregnant females of the Ak inbred line induced leukemia, following inoculation into newborn mice of a non-leukemic inbred line [6]. Similar experiments cannot be carried out readily on animal species which have a relatively long lifespan, such as cats, dogs or cattle.

On the basis of fundamental experiments carried out on animals, we can only assume, as a working hypothesis, a similar pattern of vertical transmission of oncogenic viruses in humans. The familial incidence of cancer and leukemia in certain families of humans is consistent with such a theory.

The concept of viral etiology of cancer offers certain practical conclusions that can be helpful for the prospective patient. Cancer of the colon represents one of the forms of cancer which, when detected early, can be completely removed; in such cases, the chance of a cure is reasonably good. Accordingly, individuals in whose siblings or parents or other family members on either maternal or paternal side, there were cases of cancer of the colon, should be checked regularly, particularly after they reach middle age, for early detection and prompt removal of cancer or precancerous lesions.

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