

50 Years Ago in CORR

Heredity as a Factor in Malignancy

H. Winnett Orr MD CORR 1956;8:142–146

The role of genes in cancer has been known for many decades. Snow, in an article in 1885, raised the question in the title of his article [4] and noted the widespread belief in the notion at the time:

I think I may reasonably assert that to this query an unhesitating answer in the affirmative would be returned by nearly the whole of the medical profession, the exceptions being few and far between. Now, if the question were purely theoretical, no great harm could be done by the persistence of a belief in heredity; but, as it appears to me that this opinion leads to the most important practical results, and is productive of enormous mischief, I venture to solicit from the profession a reconsideration of their attitude in the matter; and, should they withhold their assent from the conclusions I now endeavour to bring before them, at any rate not to regard the current theory as of indisputable authority, until they have thoroughly and dispassionately sifted the circumstances of as many individual cases in ordinary practice as they possibly can. For I am convinced that it is the difficulty of securing direct personal knowledge of the facts, that so greatly obscures our views on this and similar topics; amid in all such it is of the highest

importance (I need hardly point out) to distrust all merely hearsay evidence, and to make ourselves as cognisant as possible of a patient's family history, independently of the patient's own statements [4].

Snow noted the difficulty of scientifically proving any such relationship, and even the deleterious effect of the public believing so, since many patients might assume a fatalistic attitude and avoid treatment:

I can, in extenuation, plead only my conviction: 1. That the belief in heredity is derived merely from popular tradition, and is wanting in any sound basis of scientific proof: 2. That extremely practical issues are involved, and that the views now prevalent lead to disastrous results [4].

Snow did not totally discount the notion in some particular tumors, but his article clearly documents the widespread belief of the role of heredity (and by extension, genes). (While the concept of genes had been proposed by Mendel, the Danish botanist Wilhem Johanssen coined the term "gene" in 1909 to describe the fundamental units of heredity [1].)

By the 1950s, some role of heredity in the occurrence in some tumors was well established, although the role was unclear. The concepts of genes had just been described by Watson and Crick in

1953 [5–7], and the required techniques were not available. (Amplifying genes to analyzable quantities was conceived by Kary B. Mullis in 1983, and published in 1985 [3]. Dr. Mullis won the Nobel prize in 1993 for his techniques, which revolutionized the world of genetic analysis.) Nonetheless, observational and animal studies had unquestionably established a role of genetics.

Dr. Orr, in 1956, reviewing some of the animal experiments, commented, "It seems to me that the very extensive (and expensive) research now under way has had too little to say about the factor of heredity" [2]. He wondered whether and how evolution might be using cancer as a strategy:

"But when we consider that one of the finest manifestations of civilization is the perpetuation, the protection and the care, for years, of those whom nature would permit to fall by the wayside because they have cancer, we may well wonder whether all the misery and suffering, for the well and the sick, can possibly be in the interest of evolution in its better sense, and for the ultimate improvement of the human race" [2].

In this month's issue of CORR, a number of authors explore genetic mechanisms possibly associated with or causing malignancies. Concepts and research techniques have evolved

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dramatically in the last 15–20 years, allowing researchers to study the effects of a single gene on cell function, or the likelihood of a single or a group of genes being associated with very specific forms of malignancy. Further, it is likely in the foreseeable future the presence or absence of certain readily identifiable genes will predict the natural history of the malignancy and likelihood of recurrences or metastases.

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