

has now been removed. Commissioner Schmidt has indicated that when the audit of the UGDP study by the Biometrics Society is published [Feb 10 issue of JAMA.—Ed], the FDA will move swiftly and forcefully to order labeling of the sulfonylureas and phenformin to reflect the results of the UGDP study. He anticipates that this action will discourage future indiscriminate use of the drugs.

If the drugs are used in the future, it would be prudent for the physician

to have the patient sign an informed consent agreement indicating that he has been informed of the possible hazards associated with such drugs and that he accepts the full responsibility for the effects of such therapy.

For physicians who are concerned about the consequences of discontinuing the use of oral hypoglycemic agents by their patients, there is a reassuring precedent for such action. Four years ago, in the wake of the UGDP report, oral agent therapy was

abandoned at Grady Hospital, involving 1,500 patients. Eighteen months later, the blood glucose levels of 60% of these patients were satisfactorily controlled on diet therapy alone. Since 1972, the emphasis on diet therapy and weight reduction has been intensified, and during the last year insulin therapy has been discontinued in all patients who are above ideal body weight.

Additional Readings

A study of the effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes. University Group Diabetes Program. *Diabetes* 19(suppl 2):747-830, 1970.
Effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes: IV. A preliminary report on phenformin results. University Group Diabetes Program. *JAMA* 217:777-784, 1971.

Prout TE: Adverse effects of the oral hypoglycemic drugs. In *Proceedings of the Eighth Congress of the International Diabetes Federation*. Amsterdam, Excerpta Medica, 1974, pp 612-623.
Hurwitz D, McCuiston AC: Tolbutamide: A double-blind study of its effect in diabetes. *N Engl J Med* 257:931-933, 1957.
Lev-Ran A: Trial of placebo in long-term chlorpropamide-treated diabetics. *Diabetologia*

10:197-200, 1974.

Weinsier RL, Seaman A, Herrera MG, et al: Diet therapy of diabetes: Description of a successful methodologic approach to gaining diet adherence. *Diabetes* 23:669-673, 1974.

Davidson JK, Goldsmith MP: *Diabetes Guidebook: Diet Section*. Columbus, Ga, Litho-Krome Co, 1971.



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Carcinoma in Early Life

[Walter L. Bierring, MD, pp 1295-1298]

Carcinoma is usually regarded as the malignant tumor of later life, having its legitimate age limit at 35, though it is most frequently met with after 40 years of age.

With increasing study of the malignant neoplasms, age is gradually losing its hold as a criterion of difference between sarcoma and carcinoma, the former being found at almost any age, while carcinoma is beginning to be noticed more frequently during the earlier decades of life.

Carcinoma in early life often has a slow course, and like that of later years may be latent for a considerable length of time. That cancer in early life is becoming more frequent is very evident; whether it keeps pace with the general increase in carcinoma will be difficult to determine.

Certainly a collective study of the statistics reveals the unfortunate fact that the mortality rate of carcinoma is on the increase. Roswell Park calls attention to the statistics of New York State, showing 2,363 deaths in 1887 against 4,456 in 1898. In England and Wales, where careful records are kept, the rate of occurrence of cancer has increased from 1 in 5,646 population in 1840 to 1 in 1,306 in the year 1896, an increase of five times in fifty years. This increase can hardly be ascribed as due to improvements in methods of diagnosis, for rather the reverse is the case, since many cases that were formerly diagnosed as cancer are now properly classified where they belong in other lists.

While the etiology of cancer remains obscure, there is but little hope that the future will offer any abatement in this progressive increase. As careful observation continues to note the occurrence of carcinoma in the earlier decades of life, there is removed from the list of predisposing causes, the influence of age.

It has been an attractive explanation to attribute to the lessened physiologic resistance in connective tissue the rôle of permitting atypical proliferation of epithelium beyond its normal limits. With

advancing age the submucous, subcutaneous and interstitial connective tissues undergo atrophic changes, while the covering or lining epithelial elements seem to retain their usual vitality. When glands reach the limit of their functional rôle in the organism, the danger from carcinoma is most marked, while it diminishes again when complete atrophy has taken place. When cancer occurs thus in the developing decades of life, the above influences can hardly be considered.

In the entire field of pathology, no subject has proved more alluring to physician and investigator than the etiology of carcinoma. It was no wonder that the development of bacteriologic methods gave a mighty impetus to the search for an etiologic agent, the result of which is well known. Numerous forms of cell inclusions—cancer bodies—have been observed and variously interpreted.

As yet it is evident that the real cause of carcinoma has not been demonstrated. Perhaps it will be necessary to completely modify our culture methods. Perhaps our optical aids are inadequate in magnifying power, but unless the light comes soon, the 19th century will close with the genesis of cancer as much a mystery as when the century began.