of the reactions which are discussed. Photochemistry has been beset by apparent conflicts in experimental results more than most branches of chemistry. This is due to difficulties in experimental technique and to a lack of appreciation of all the variables which can effect the course of a photochemical reaction. The chief criticism of this book lies in the fact that most of the data are presented without an adequate attempt at critical evaluation. This leads all too often to the feeling that there are unresolvable differences of opinion in the interpretation of the data.

The parts of the book which deal with the biological effects of radiation are useful. Much of this material seems never to have been brought together in one place before. Lethal action, therapeutic effects, rickets and Vitamin D, and photosynthesis are among the subjects covered.

"The Chemical Action of Ultraviolet Rays" should be extremely valuable to any worker who wishes a handy reference book covering the field comprehensively. As already indicated any such comprehensive survey of the literature of a field is always of service.

W. ALBERT NOYES, JR.
UNIVERSITY OF ROCHESTER

SOCIETIES AND MEETINGS

NORTH CAROLINA ACADEMY OF SCIENCE

THE fortieth annual meeting of the North Carolina Academy of Science was held at Chapel Hill on April 25 and 26. The meeting was unusually well attended and an exceptional program was provided. The peak of attendance was approximately 300 and more than 80 papers were presented in the various scientific fields. The North Carolina Section of the American Chemical Society met at the same time and place with probably 75 attending to hear the 15 papers offered.

An innovation at the meeting was the setting aside of a definite time for demonstrations. This proved very successful for papers which were presented formally, as well as for those which consisted of the demonstration only.

The Poteat award was conferred on Miss Alma Whiffen, of the University of North Carolina, for her paper on "The Role of Chytrids in Cellulose Decomposition." The American Association grant for research went to Drs. C. H. Lindsley and N. Rosen for a study of the "Zeeman Effect in the Palladium Spectrum." Mr. John M. Stewart, a student of the Alamance High School, was awarded the project prize of $20.00, while the forestry essay prize of $20.00 was divided between William Anderson, of the Hayesville High School, and Omega Rice, of the Dorland-Bell School at Hot Springs.

A meeting was held for high-school teachers and sponsors of high-school science clubs. A program of especial interest to them was provided.

The university gave the academy a dinner, which was followed by the address of the president of the academy, Dr. J. L. Stuckey, on "Man and Minerals." The Elisha Mitchell Scientific Society entertained the academy after the address.

The committee reports were presented in mimeographed form, and these along with the treasurer's preliminary report was adopted. The secretary reported that about 80 members had been added to the roll during the year.

The following officers were elected for the ensuing year: *President,* R. E. Coker, of the University of North Carolina; *Vice-President,* C. N. Warfield, of the Woman's College of the University of North Carolina; *Secretary-Treasurer,* B. Cunningham, of Duke University (continues); *New Member of the Executive Committee,* D. B. Anderson, North Carolina State College; *New Members of the Research Grants Committee,* C. F. Korstian, Duke University, and J. N. Couch, of the University of North Carolina.

A more detailed report of the meeting will appear in the *Journal of the Elisha Mitchell Scientific Society.*

BERT CUNNINGHAM,
Secretary

SPECIAL ARTICLES

THE BIOTIN CONTENT OF TUMORS AND OTHER TISSUES

THE search for significant differences between the metabolism of normal and malignant cells has long occupied the attention of those concerned in a biochemical approach to the tumor problem. Of particular interest in this respect are substances of vitamin or enzyme nature, which in relatively minute amounts exert powerful regulatory influences on the growth of tissues. One of the more recently studied and most active of these compounds is biotin, or vitamin H, which is already known to be essential for the vital functions of many micro-organisms[1,2,3,4,5] and higher

[1] F. Kögl and B. Tonnis, *Zs. phys. Chem.,* 242: 43, 1936.
[2] P. M. West and P. W. Wilson, *Enzymologia,* 8: 152, 1940.
[3] R. Nilsson *et al., Ann. Landw. Hochschule Schwedens,* 7: 301, 1939.
[4] E. E. Snell and R. J. Williams, *Jour. Am. Chem. Soc.,* 61: 3594, 1939.

animals.[6,7] In the present note some preliminary observations on the relative abundance of this growth factor in various tissues are presented, without any attempt to suggest the possible implications of such findings.

Assays for total biotin were made on acid-hydrolyzed tissues by a microbiological method based on the specific requirement of *Rhizobium trifolii* (Wisconsin strain 205) for this factor.[2,3] Details of the procedure will appear elsewhere. Results are expressed in terms of pure biotin, by standardization of the method with the crystalline methyl ester kindly supplied us by Dr. Vincent du Vigneaud.

Since embryos share with most tumors the property of rapid growth it was of interest, before proceeding with an analysis of the latter, to discover whether or not embryonic organs differ appreciably in biotin content from the corresponding structures in the adult. The levels for the same organ from several different adult Wistar rats on a stock laboratory ration were found to be remarkably uniform. Individual organs of the same animal, however, differed widely in the amount of growth factor contained, each apparently possessing an amount peculiar to itself. With a series of biotin values for normal rat organs established, estimations were made on full-term rat embryos and the results compared. The following data, expressed in micrograms of biotin per gram of dried tissue, are typical of several experiments:

Skin:	adult	84 mγ	; embryo	1061 mγ
Muscle:	"	191 "	; "	2150 "
Lung:	"	289 "	; "	1350 "
Brain:	"	772 "	; "	1945 "
Heart:	"	1890 "	; "	1610 "
Kidney:	"	2273 "	; "	707 "
Liver:	"	3393 "	; "	2030 "

It will be seen that in the embryo, skin and skeletal muscle, which make up the greater part of the total body weight, contain amounts of biotin greatly in excess of those found in the corresponding adult organs. Lung and brain present a similar contrast, the data for the four together suggesting that in association with the rapid growth of the embryo there are increased demands for biotin. Heart, kidney and liver, however, which in the adult are notably rich in biotin, show lower levels in the embryo. This we can not explain at present, but it seems possible that in the adult these tissues represent storage depots, thereby complicating a comparison of this kind.

The types of tumor suitable for biochemical study are decidedly limited by the difficulty of obtaining satisfactory normal control tissues. The ideal materials would be a tumor involving only a single variety of cell and a corresponding normal tissue of similar purity and cellularity. A neoplasm approaching these requirements is the Shope rabbit papilloma. By careful dissection it is possible to obtain normal adult rabbit skin as a control which, although not pure epithelium, nevertheless on microscopic examination was found to contain no more connective tissue than the tumor. Analysis of such materials yielded the following results:

Domestic rabbit:	adult	skin	98 mγ	; papilloma	396 mγ
"	"	:	"	"	63 "	; "	300 "
Wild	"	:	"	"	119 "	; "	458 "
"	"	:	"	"	178 "	; "	440 "

Domestic rabbit embryo skin was assayed for comparative purposes and found to contain 531 mγ biotin per gram in contrast to a level of 14 mγ in the skin of the mother.

Other tumors of epithelial origin, obtained from human sources, have also been found distinctly richer in the growth substance than adjacent normal tissue. In carcinomas of the gastro-intestinal tract the controls consisted of normal mucous membrane dissected away from underlying tissues; in carcinomas of the lung, normal lung had to be used, though it is admittedly not so suitable a control as those for the other tumors. Examples of representative assays are:

Carcinoma	of sigmoid	787 mγ	; control	284 mγ
"	" rectum	444 "	; "	102 "
"	" lung	502 "	; "	151 "
"	" lung	352 "	; "	145 "

The figures for 4 bone sarcomas averaged 202 mγ as against 1.2 mγ per gram of organic matter from the adjoining normal bone, but we are sceptical as to the value of these findings since the neoplasms were so much more cellular than the mother tissue.

All diagnoses were confirmed microscopically.

Primary carcinoma of the liver, readily induced in rats by feeding p-dimethylaminoazobenzene,[8] is a tumor well suited to biochemical study. In such animals the biotin level of the liver adjacent to the neoplasms was found to be normal, while the carcinomas themselves, unlike the other tumors examined, were decidedly poorer in this factor; *e.g.*, controls 3671 and 3190 mγ, tumors 1905 and 812 mγ of biotin, respectively. This discrepancy can not be explained by the presence of necrosis, for all visible necrotic material was removed.

It seems significant that in every case studied the biotin level of the tumor deviated sharply from the normal adult values in the same direction as that of the corresponding embryo tissues. One might ask whether this result represents a difference in metabolism shared by tumor and embryo, or whether it represents a change common to all tissues in which cells

[5] J. R. Porter and M. J. Pelczar, *Jour. Bact.*, 41: 173, 1941.

[6] P. György, *Jour. Biol. Chem.*, 131: 733, 1939.

[7] P. György, *et al.*, SCIENCE, 91: 243–245, 1940.

[8] Riojun Kinosita, *Trans. Soc. Path. Japonicae*, 27: 665, 1937.

are actively dividing. The former seems more likely at present, for the biotin content of rat liver vigorously regenerating after partial hepatectomy,[9] or of the pregnant human uterus, was found not to differ from that of the same tissues in a non-hyperplastic state.

We are indebted to the following gentlemen for a generous supply of material: Drs. Robert P. Hill, James W. Jobling, Homer D. Kesten, John G. Kidd, Richard E. Shope, Charles M. Steer, Fred Stewart, Arthur Purdy Stout and Benjamin P. Watson.

PHILIP M. WEST
WILLIAM H. WOGLOM
DEPARTMENT OF CANCER RESEARCH,
COLLEGE OF PHYSICIANS AND SURGEONS,
COLUMBIA UNIVERSITY

THE PRESERVATION BY FREEZING AND DRYING IN VACUO OF THE MILK-INFLUENCE FOR THE DEVELOPMENT OF BREAST CANCER IN MICE[1]

THERE is an active influence in the milk of lactating females of strains of mice having a high incidence of carcinoma of the mammary glands which promotes the development of this type of cancer.[2] This influence is usually obtained by nursing but may also be transferred by the transplantation of splenic tissue[3] and by the feeding of milk secured from females of cancerous strains. The milk was given to animals after they had been weaned.[4] The amount of milk given may have influenced the incidence and the average age at the time of the appearance of the tumors. Macerated liver from mice of cancerous strains failed to affect the incidence of breast tumors.

This report considers the feeding of lyophilized tissue of spontaneous mammary carcinoma. The tissue was prepared by Dr. G. Burroughs Mider, research fellow, National Cancer Institute, while at the University of Rochester, as follows: The spontaneous tumors were removed under aseptic conditions, finely minced with a knife and placed in tubes. The tissue was frozen immediately at −72° C. and dried *in vacuo*. At the completion of the process the tubes were sealed with a blow torch.

Thirty cc of water was added to 10 cc of the lyophilized tumor-tissue and filtered (filter paper). The filtrate was placed before the mice in small dishes: 10 cc for each 5 mice or 2 cc per mouse. The animals had been without water for about 18 hours.

The mice which received the filtrate were representatives of the Ax strain[2, 5, 6] and were from 4 to 5 weeks of age. The mice of this line are descended from a female (No. 38432) of the A strain which had been fostered from birth by a female of the CBA or X stock (low breast cancerous strain). The incidence of breast cancer in breeding females of the Ax strain has been 3.1 per cent. (292 mice), average tumor age 13.9 months and average non-tumor age 17.2 months. Over 90 per cent. of the breeding females of the A stock develop mammary cancer,[5, 6] whereas few (4.9 per cent.) of the females of the A strain kept as virgins became cancerous.[7]

Six of the 10 mice of the Ax strain which consumed the filtrate of the lyophilized tumor-tissue have developed breast tumors (12.4 months), one was missing at 12 months of age and three are living at 17.5 months. These mice were used as breeders.

DISCUSSION

As has been reported the females of the Ax strain are genetically of a constitution in which breast tumors may be expected to develop if they are nursed by females which have the active influence in their milk and are used as breeders.[8]

The ten experimental animals were the progeny of three females. Two of the three mothers have had other progeny which have been continued as breeders, and they and their descendants number 24 mice. As none of these mice has developed breast tumors it is improbable that the mice which received the filtrate of the lyophilized tissue were subjected to an active influence in the milk of their maternal parent or that the influence developed *de novo*.[5]

The voluntary method of feeding the material did not insure that each mouse consumed the same amount, as some might have taken very little. Whether or not the age of the animals at the time they developed tumors may indicate the amount taken is problematical, as great age differences in the time of tumor development are also common among the controls, even for mice of the same litter.

The technique used in the preparation of the lyophilized tumor-tissue was similar to that described by others to preserve the viruses of other diseases.[9] Thus, the results obtained in the present experiment with a small number of animals suggest that the active influence in the milk of females of strains of mice having a high incidence of breast cancer may be a virus.

SUMMARY

The development of spontaneous breast cancer in

[9] George M. Higgins and Reuben M. Anderson, *Arch. Path.*, 12: 186, 1931.

[1] Preliminary report.

[2] J. J. Bittner, SCIENCE, 84: 162, 1936. Reviewed in footnote 8.

[3] *Idem, Pub. Health Rept.*, 54: 1827, 1939.

[4] *Idem, Proc. Soc. Exper. Biol. and Med.*, 45: 805, 1940.

[5] *Idem, Cancer Research*, 1: 113, 1941.

[6] *Ibid.*, 1: 115, 1941.

[7] J. J. Bittner, *Pub. Health Rept.*, 54: 1113, 1939.

[8] *Idem, Jour. Nat. Cancer Inst.*, 1: 155, 1940.

[9] J. G. Wooley, *Pub. Health Rept.*, 54: 1077, 1939.