

Book Reviews

THE ADRENAL CORTEX IN ADAPTATION TO ALTITUDE, CLIMATE, AND CANCER. By Edward S. Sundstroem and George Michaels [formerly Giragossintz]. *Memoirs of the University of California*. Vol. 12. University of California Press, Berkeley and Los Angeles. 1942. VIII + 410 pages; 125 illustrations. Price \$4.00.

After two preliminary chapters on the method employed and the response of normal rats to low atmospheric pressure, the authors take up its effect on tumors of various sorts.

At 300 and 360 mm. definite damage was found in transplantable tumors of five different strains. Not only was growth slower and necrosis more extensive than under normal conditions, but complete regression was much more common. This occurred, also, among strains in which it is ordinarily rare and that resist successfully most other therapeutic measures. But with commendable caution the authors interpret these effects merely as manifestations of the tendency to self cure possessed in greater or less degree by all neoplasms in this group.

The few spontaneous growths used were chiefly mammary adenocarcinomas of the mouse. Exposed to pressures of 260 and 420 mm. they were not quite so easily affected, though the results are described as not wholly discouraging. Other experiments suggested that carcinogenesis in animals with a cancerous heredity might, perhaps, be a little delayed.

The development of tar cancer in mice (the synthetic carcinogenic hydrocarbons were not yet available) appeared to be somewhat slower under the treatment, and the tumors may have been a little less malignant, but on the whole the process was not greatly affected.

What slight damage was done to the tumor cell is ascribed to cooperating deficiencies in oxygen and the hormone of the adrenal cortex.

A wealth of charts illustrate the book, together with a few drawings, photographs, and photomicrographs, and an adequate bibliography is supplied.

The authors do not lack the faculty of self criticism and to the reviewer, as to them too, no doubt, the results, at least so far as tumors are concerned, seem to fall far short of what their enormous industry justly deserved.

WILLIAM H. WOGLOM

ATLAS OF OVARIAN TUMORS. By Gemma Barzilai, M. D. Grune & Stratton, New York. 1943. 261 pages; 58 plates. Price \$10.00.

This book represents a new form for the presentation of material on gynecologic pathology. The chief emphasis is placed on histologic description and on photomicrographs and colored plates. These have been exquisitely reproduced and offer what is perhaps the finest source available of pictures of ovarian tumor pathology. By the evident intent of the author references to the literature and clinical aspects have been reduced to a minimum. Here then is a work devoted to the description in minutest detail of the varying structure of ovarian neoplasms.

According to the author the photomicrographs are based upon material used to illustrate her lectures in Padua, and represent slides from her own collection as well as from material placed at her disposal in Vienna, Istanbul, and Milan.

The classification follows what is gradually coming to be an accepted pattern, with some changes in arrangement and emphasis and some new terms. Granulosa cell and theca cell tumors, perhaps logically as tumors of the specific ovarian structures, have been elevated to the head of the list. There follow the arrhenoblastoma and a tumor that the author cautiously terms a "virilizing lipoid tumor." The concept of derivation from specific embryonal structures or from a one-sided development of a teratoma is given considerable stress and is applied to the majority of the ovarian tumors. One term new to most American gynecologists is the "endosalpingioma," the tumor usually designated a serous, papillary cystadenoma. The morphologic similarity of the epithelium of this growth to that of the tube is made impressive by the author's detailed consideration of its histology. She suggests also that a less differentiated epithelial tumor of the ovary, which she calls the "seroanaplastic carcinoma," may be the malignant form of endosalpingioma.

The reviewer remains unconvinced that the morphologic similarity of this ovarian tumor to the tubal epithelium justifies the term endosalpingioma and somewhat doubts the wisdom of attempting to change the nomenclature now in use. This reservation, however, does not detract from Dr. Barzilai's contribution in drawing attention to the suggestive cellular structure of these neoplasms.

The atlas should serve as at least a partial answer to the need for a dependable work with illustrations of all types of ovarian tumors with which the pathologist may compare the daily material of his laboratory. The painstaking study that has gone into the text and the beauty of the illustrations will make this a desirable volume for the library of the gynecologist also.

HOWARD C. TAYLOR, JR.

BIOCHEMISTRY AND MORPHOGENESIS. By Joseph Needham. Cambridge University Press, London. 1942. XVI + 787 pages; 328 illustrations. Price £2.12.6d.

Apart from its vast general significance, this book should prove of the greatest value to students of cancer on account of the author's characteristic treatment of various subjects relating to oncology. While it will amply repay reading and rereading *in toto*—as indeed it must be studied if the whole plan is to be appreciated—it contains a contents list, with a decimal classification, that is sufficiently detailed to guide the specialist in more particular topics.

Describing the origins of the notion of morphogenetic stimuli, Needham shows how, as early as 1858, Virchow developed this conception in relation to the production of specific types of tumor in man, and how the subject was further advanced by Billroth (1890), who attributed such effects to chemical substances elaborated by the stimulating organism, whether insect, worm, or bacterium. These matters are more fully considered in what Needham modestly calls a digression on the interesting and somewhat neglected subject of gall formation in plants.

Among other morphogenetic stimuli, the primary organizer of amphibian development has special relevance to the tumor problem, although Needham recognizes that this is not apparent at first sight (since evocator substances are concerned with specific differentiation and not with

general growth), and that much must depend on the extent to which the individuation field persists into the adult condition. If the capacity for regeneration is a suitable measure of such persistence, the mammalian individuation field has been wholly lost during development. (Concerning neoplasms in reptiles, anurans, and urodeles, it may be noted that a convenient summary is provided in Table 21, page 241.)

These qualifications aside, the chemical nature of the evocator must clearly be a matter of special interest. Needham admits the tendency in certain quarters, and quotes Spemann in this regard, to dismiss the whole induction effect as unspecific, an attitude that he deplors as a counsel of despair. But is not this tendency largely justified, inasmuch as neural tube inductions have been obtained following implantation of agents as diverse as 1,9-dimethylphenanthrene, methylcholanthrene, "styryl blue," 3,4-benzpyrene, anthracene, sitosterol, pregnandiol, and squalene, apart from fatty acids and nucleoproteins? Of course the author makes it perfectly clear that neural inductions can be brought about by a wide variety of chemical fractions and pure or relatively pure substances, and that the question which of these, if any, is identical with the primary evocator occurring in the dorsal lip of the blastopore, remains unanswered: "The question is rendered particularly difficult owing to the presence of the natural substance in masked condition in the very tissue on which alone the activity of a chemical substance can be tested." But one may perhaps be allowed to differ rather strenuously from Needham when he asserts that studies of dosage "apart from the direct evidence from solubility, etc.," indicate that the natural evocator is a steroid substance. The evidence he puts forward is that the only substance so far shown to act in concentrations "of the vitamin or hormone order" is a polycyclic hydrocarbon, actually an endosuccinate of 1,2,5,6-dibenzanthracene. This evidence is surely insufficient to warrant any such conclusion, even if we admit, as is suggested, that many of the other types of substance that have given positive results have probably done so by unmasking the natural evocator.

In a section on organizer excess and anomalous competence, Needham passes to the problem of teratomas. While appreciating the vastness of the literature, he regards a good deal of it as marked by unscientific speculation, inaccurate description, and errors of logic. Good individual cases, as, for example, some described by Willis and by Barnard, are selected to show the parallelism between teratomas and the chaotic distribution of tissues that is seen when the individuation field in a young embryo is thrown out of gear. While normal induction of the primary axis in an embryo involves both evocation (the stimulus of a chemical substance) and individuation (the regional differentiation of the axis so induced), a dead piece of organization center probably carries the evocator but not the individuation field. Hence it might be expected that the implantation of dead organizer should elicit the appearance of chaotically arranged structures, "always provided that the individuation field of the host was not sufficiently strong to control and order the newly appearing differentiations." It is not entirely clear to the reviewer to what extent this explanation is a true advance, or to

what extent merely a restatement on the basis of analogy, however sound. One must nevertheless freely acknowledge the provocative value of the concept itself; namely, that the phenomena of teratoma formation are due to a failure of the individuation field, at some point early in development, to control the action of evocating substances. The subject is further discussed not only in its relation to spontaneous teratomas but also to the Michalowsky-Bagg teratomas induced by injection of zinc chloride into the testes of the fowl. It is interesting that Needham gives credit for the first application of organizer phenomena in teratoma research to Budde (*Beitr. z. path. Anat. u. allg. Path.*, **75**:357. 1926), who attributed these tumors to what he called an *abgesprengter Organisator*, in a paper written very shortly after that of Spemann and Mangold (*Arch. f. Entwicklngsmechn. d. Organ.*, **100**:599. 1924).

Proceeding to homoigenetic induction (the power acquired by part of an embryo, at the same time as it is determined for a certain differentiation, to induce another of the same kind) the author elaborates what he believes is a formal analogy between this process and the propagation of these types of cancer transmissible by cell-free extracts. But here the analogy is surely much less happy. In particular, there is no positive evidence at present available to support his hypothesis that the Rous agent is a specific hydrocarbon-protein complex, and a great deal that is hardly consistent with such a view. Needham closes his account of organizers and cancer with a quotation from J. B. S. Haldane: "Until it is shown that differentiation is due to gene mutations, it seems reasonable to regard carcinogenesis as anomalous differentiation rather than mutation." This sentence, he believes, provides the justification for the discussion of cancer phenomena in a book on chemical embryology.

Most of the topics remaining, apart from a short account of hereditary tumors in *Drosophila* and various fishes, have a less specific or direct bearing on cancer but are nevertheless of the most profound significance. Thus an excellent account is given (Fig. 205) of the possible relationships, natural and experimental, between the nucleus and cytoplasm in development. This raises among other problems that of parthenogenetic merogony, in which phenomenon E. B. Harvey has demonstrated the possibility of segmentation and even blastula formation, in the complete absence of either paternal or maternal chromatin, in echinoderm eggs. Reference is also made to the question whether cleavage rate in echinoderms is a function of the cytoplasm or the nucleus, in an account of A. R. Moore's experiments with the cross *Dendraster* ♀ × *Strongylocentrotus* ♂, and with the fertilization, either by *Dendraster* or *Strongylocentrotus* sperm, of nucleate and nonnucleate fragments obtained by microdissection; in every case the cleavage rate was that characteristic of the cytoplasm.

The last part of the book, which deals with morphogenetic mechanisms, contains a good fundamental description of the dissociability of, or incompatibility between, the processes of growth and differentiation, referring among other authors to von Bertalanffy, who postulated a causal relationship between rising differentiation and falling specific growth rate, and to both Peter and Lauche,

who were led to conclude that "a cell which is working does not divide, and a cell in mitosis is not working."

A later section deals with the degree to which growth and differentiation are reversible, and whether in reversal they show the same phenomenon of dissociation. Needham indicates that there is no true dedifferentiation in the regression of planarians, as studied by F. R. Lillie in 1900 in *Planaria dorocephala*; starvation of this organism produces a reduction in size to less than that at hatching, but the only morphological changes that occur are slight alterations of the proportions of the parts. The association of dedifferentiation with "degrowth" has, however, been long recognized among ascidians; for example, in the work of Julian Huxley on regression in *Clavellina*. Even here, however, the regressive changes were not looked on by Huxley as reversions to stages passed through in embryogenesis, and "no ascidian tadpole makes its appearance when an ascidian dedifferentiates." The regression is far from being a true reversibility, and is rather an assumption of the cuboidal or spherical shapes, *i.e.*, a condition requiring the least amount of energy for maintenance.

A parallel section deals with the dissociability of growth and metabolism (fermentation and respiration). Starting with the early observations of Warburg on the inhibition of cleavage (but not of respiration) of sea urchin eggs by hypertonic sea water and phenylurethane, it gives an account of many examples illustrating the disengagement of these processes in different types of developing embryonic cells, and unicellular organisms, under the influence of such agents as quinine, iodoacetate, heightened CO₂ tension, and irradiation with x-rays. For tumor tissue, the work of Crabtree with β - and γ - radiation is mentioned, but not that of Boyland (*Biochem. J.*, **33**:618. 1939), on the dissociation of growth and metabolism in spontaneous mammary tumors of the mouse as shown through the inhibition of growth by chemical means.

At the conclusion of a section on heterauxesis, Needham introduces the "sense of duration" and the general notion of "physiological time" as a factor in embryonic events, drawing attention to the contributions of Lambert and Teissier, among others, who proposed as a fundamental law of biology that homologies exist between animals in time as well as in space. "Mouse time must bear the same, or a similar, relation to elephant time as mouse spatial magnitudes to elephant spatial magnitudes. Indeed, unless the time factor is brought into account, we may understand morphological similarity, but we can never hope to understand physiological, still less embryological, similarity." The ratio borne by the latent time of carcinogenesis to specific life span is probably a special case, to which such considerations can be usefully applied.

Finally, under the section on protein metabolism there is included a description of the growth-promoting factor in its relation to cultivation *in vitro*, the healing of wounds, recovery from injury, and the growth of tumors.

The book is provided with a glossary of special terms. Only few pertain directly to cancer, and although the list makes no legislative claims at least one definition, that of metastasis as the "spontaneous dispersion of a tumor from its original site in the body to other sites," has an archaic ring and should be improved. One is

pleased to see that a list of terms the use of which is not recommended, and which in the author's words deserve their *requiescat*, includes "blastogen" and "blastomogen" (for carcinogen).

A bibliography containing several thousand references is supplied, together with animal, plant, gene, and general indexes. The last is not a sufficiently good guide to individual compounds, and a separate chemical index might have been provided with advantage.

To conclude, it is obvious that in spite of limitations in regard to particularities, and these are perhaps not altogether avoidable, the book is one of the first importance for general biology and all its branches. This is not less so because of the breadth of vision that it exemplifies and inculcates, which is so desirable and indeed necessary in the proper study, among the other subjects with which the work deals, of the cancer problem in all its varied aspects.

ALEXANDER HADDOW

CANCER OF THE UTERUS. By E. Hurdon. Oxford University Press, London. 1942. XII + 188 pages.

A few months before her death in 1941 Dr. Elizabeth Hurdon, late Medical Director of the Marie Curie Hospital, London, left the manuscript of this book in the hands of Dr. L. Martindale and Professor S. Russ, who have arranged its publication and contribute a preface. A short introductory chapter deals with those general aspects of the cancer problem (incidence, nature and causation, hereditary and other predisposing factors) that have clinical implications for the specific topic. Cancer of the uterus (of cervix and corpus) is then considered in its clinical pathology, pathological histology with special reference to tumor grading, and clinical history and diagnosis. So far as concerns the histological classification of uterine cancers and the relation between cell type and radiosensitivity, the findings are stated to be based mostly on the work of Dr. Helen Chambers. After a definition of the four anatomical stages of carcinoma of the cervix, the relative values of surgical and radiation treatment are discussed, and a statistical review compares the results obtained from surgery, from surgery and radiotherapy combined, and from radiotherapy alone.

An account is given of the general principles of radiation therapy, the factors conditioning such treatment, and the clinical and histological effects produced. Separate chapters are devoted to clinical technic and to the use of intracavitary radiation. In the latter are described the method and results of dosage calculations, the details of technic employed at the Marie Curie Hospital, the spatial distribution of radiation, and the clinical importance of physical data; acknowledgments are made to Professor W. V. Mayneord for revision of this section. Other chapters deal with the closer evaluation of the results of radium treatment, with cancer of the cervix in pregnancy, and with multiple neoplasms associated with cancer of the uterus. The scope of the work is considerably wider than is indicated by the title since other subjects, such as endometriosis, cancer of the vagina and the vulva, and the treatment of uterine hemorrhage arising from causes other than cancer, are also covered. The book is provided with subject and author indexes and a bibliography.

ALEXANDER HADDOW