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THE PROBLEMS OF CANCER.

By E. F. BASHFORD, M.D.

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I.—*The Extent of the Field which has been Investigated in Regard to Cancer and its Relation to the Pessimistic Views Entertained in Regard to the Ultimate Results of the Investigation of Cancer.*

OUR knowledge of malignant new growths is all but limited to a recognition of the facts which present themselves for investigation in pathological laboratories, obtaining their material from the *post-mortem* or operating theatres of hospitals in the most civilized portions of the world. The material thus obtained has been extensively investigated, from the purely histological standpoint, to a great extent also in co-relation with clinical observations. It is, perhaps, generally conceded that further advances in these directions will not be easy of attainment, and that by these paths alone the problems of cancer will not be solved.

With the materials occurring in hospitals other lines of inquiry, especially biological, bio-chemical, the conditions of growth of cancerous tissue as distinct from the problem of the genesis of malignant new growths, have been hardly touched upon, except in a purely speculative fashion, and in the latter direction to a degree out of all proportion to the meagreness of the facts accumulated.

Speculation in regard to the nature and genesis of malignant new growths has roamed over the full field of biological science and the actual facts constituting our definite knowledge of cancer have been drawn from what by comparison is a singularly limited field, namely, that accessible to the microscopical and other histological methods of the pathological anatomist, for clinical observations have hardly

contributed much to the hypothetical discussions of the nature of cancer.

It would seem to be advisable to endeavour to interchange the disproportions existing between the fields from which the facts and the theories of cancer have been drawn, so that instead of speculations from many fields being founded, as at present, upon the few facts of cancer ascertained from its occurrence among the more educated of mankind, facts from a very extensive biological inquiry, embracing not only all races of men, but, so far as possible, the entire animal kingdom, will be focussed upon the condition which is of so much interest to us at present.

Probably in the disproportions of the fields from which the theories and the facts of cancer have been drawn is to be found the explanation of the standstill to which cancer investigation has come since Virchow's classical work has been followed to its logical results. In this disproportion we have possibly also the cause of the prominence obtained by views, which, had the facts of cancer been founded upon a wider basis, would never have had devoted to their attempted establishment the amount of labour which has been conferred upon them. On the other hand, the apparent hopelessness of endeavouring to elucidate the problems of malignant new growths would not have been magnified to such an extent had this disproportion not existed.

Obviously, it behoves those devoting attention to the problems of cancer to endeavour to adjust the inequality, which has been pointed out, in the hope that when the facts of cancer as a general and comparative biological problem, as distinct from a problem of human pathology only, have been placed upon a basis commensurate with the extent of its ramifications in man and animals, the pessimism now prevailing, not without justification, will, with the attainment of this adjustment, disappear.

In amplification of what is implied by endeavouring to regard cancer not merely as a problem of human pathological anatomy, but as a problem of much greater extent, some matters may be alluded to which, if of a speculative nature, seem to indicate the importance of regarding cancer from the standpoint of a comparative biological problem, even at this early stage.

The following aspects of some problems associated with the study of cancer are referred to in the hope that the attention of those having opportunity of making observations may be directed to them.

II.—*The Theoretical Aspects of a Comparative Biological Study of the Nature of "Cancer."*

Biological investigations will probably ultimately form a very important aspect of any research into the nature of cancer, for the problems of malignant new growths are more likely to be elucidated by a general biological investigation, than by mere attention to the conditions obtaining in man, especially in view of the limitations to which investigations in human beings are subject.

At the outset it is necessary to be certain that the new growths occurring in a long series of domestic animals are absolutely identical in nature and consequences with the benign and malignant new growths of man. In regard to the occurrence of "cancer" among wild animals, we have less positive evidence, owing, possibly, to the difficulty of obtaining information of the kind required.

There can be no doubt that some, if not all, forms of malignant new growths occurring in man and animals are identical in nature. It is a matter of very far-reaching importance that the types of malignant and benign new growths are reproduced in very divergent species of animal with such marked similarity in the minute histological details characteristic of the type of new growth. The features characteristic of a type of new growth in man are reproduced in other mammalia with a degree of similarity not found in any other diseased condition to which man and animals are mutually subject.

The reaction of the tissues of different mammalia, due to the presence of any known identical parasitic organism, is more or less characteristic for each species, and the uninitiated would scarcely fail to pronounce tissue reactions due to the action of the same parasite—tubercle, diphtheria, etc., on different species of animal as entirely distinct conditions. The benign and malignant new growths of man and animals are not distinguished by any such characteristic difference, so that one has no hesitation when shown typical conditions presenting themselves, for example, in the liver of the frog, dog, horse, and man, in at once pronouncing them to be exactly analogous processes.

The exhaustive and comparative study of "cancer" in animals in all its features, clinical, pathological, biological, with particular regard to the distribution throughout the higher and lower animals, will probably

lead to results of the greatest importance. Malignant new growths or certain types of them might be found to be limited to certain orders, or characteristic distinguishing features be discovered for the new growths of different orders, for example, mammals, birds, reptiles, etc.

The crucial problems of cancer can all be attacked by a study of the conditions in animals, some can alone be approached in animals, and only with them will it be possible to perform experiments bearing on the etiology, pathology, prevention, and attempted cure. In this connexion it may be mentioned that absolutely incontrovertible evidence for or against many prevalent conceptions of the nature and cause of cancer would be obtained, and the questions of parasites, heredity, diet, injury, influence of tobacco pipes, etc., would be definitely settled.

In statistical inquiries the importance of taking account of the age and sex-distribution of a population in determining the relative incidence of cancer has long been recognized. The possible importance of the study of age-incidence as a feature in a general biological inquiry has not hitherto had attention drawn to it.

In this connexion the ideal to be desired is a series of observations so extensive that the age at which the maximum incidence of cancer occurs for each species, and the liability to attack of the various organs can be ascertained. It might thus be possible to define the comparative incidence throughout the animal kingdom, and to ascertain whether or not the maximum incidence in each species, or perhaps in each organ, had a relation to a definite stage in the life cycle of each species. We are, however, only likely to accomplish the compilation of data for the mammalia represented by our common domestic animals. The attainment of even so much would be of the very greatest value.

The length of the human life cycle has been a great impediment to the solution of many problems which can easily be investigated in short-lived animals, for example, the study of heredity, and particularly with regard to the fulfilment of the requirements of Galton's law.

The length of the life cycle in the different species proved to suffer from cancer varies greatly. Cancer in animals occurs as in man, especially in the aged. Old age in the domestic animals is, however, attained at 14 to 20 years, or less. It is obvious, therefore, that identical manifestations first presenting themselves in any number in mankind after 40 years of age, and in the common domestic animals at 14 to 20 years, must pass through the latent non-manifest stages in a much shorter period in the latter. It may be that this latent period

will be found to be in strict proportion to the life duration, and be different and definite for each species just as much so as the gestation period.

The fact that such pronounced variations occur in the periods within which identical processes manifest themselves in man and in different species of animals would indicate the important dependence of the development of malignant new growths on circumstances innate in each species of organism, and on the biological laws peculiar to and controlling the growth of each species of animal.

Domestic animals, with the exception perhaps of pet dogs and cats and horses, are not frequently allowed to attain old age; the vast majority are put to death at an early stage in life. The total number reaching the most favourable age for the development of cancer is small. It has of course been asserted that cancer in domestic animals is the result of contact with man. I am not at present concerned with the possibility of the transmission of cancer from one individual to another, but would only point out that man's responsibility in regard to domestic animals may, for all we know to the contrary, be limited to the provision of opportunities for reaching the cancer age. Among wild animals also, in the absence of artificial assistance for the maintenance of life in the struggle for existence, the same factor may enter, and, together with the difficulty of making observations, contribute to the rarity with which the condition is met with among them.

A comparative study of the age-incidence of cancer among domestic and wild animals of varied species will certainly give comprehensive information on the relation of the incidence of cancer to the rapidity with which maturity is attained. Light may also be thrown on the reasons underlying the higher cancer-rate of later life.

For the same reason, exact observations on the age-incidence in the males and females of differing races of mankind among whom also maturity is arrived at, at varying ages, is desirable. A comparison of the age-incidence of cancer in men as contrasted with that in women who attain maturity more rapidly, might also be of value, for example, in India, where puberty is attained at an early age, and the child-bearing period stated to be over at, or about, the thirtieth year.

In the classification of "tumours" no marked advance has been made since Virchow, and on the basis of experience limited to mankind is not likely to be easy of attainment; but with the assistance of the extensive study of tumours in mammalia and other animals, it is

reasonable to suppose that an advance would take place and a comparative natural classification be evolved.

Another specific problem—namely “deciduoma malignum,” or “chorion-epithelioma”—seems to require consideration from the comparative biological standpoint, and to be more than a problem, merely of interest to obstetricians. It appears to be of great theoretical importance, and therefore it is much to be desired that those who have the opportunity will search for its possible occurrence, or for analogous processes in other mammalia among those with deciduate and non-deciduate placentae.

In cases where animals die after abortion or abnormal gestation, it would be very desirable if a necropsy could be made, and attention particularly directed to the uterus in order to discover, if possible, in other mammalia, anything analogous to the “deciduoma malignum” of mankind. If in any case an abnormal condition be detected, search should be made for secondary deposits in other organs.

It is only fair to point out that in indicating the extensive nature of the field of inquiry thus marked out, it has not been forgotten that the difficulties in attempting to carry it out will be very great indeed. It will involve the co-operation of workers in many professions, and in many trades and fields of scientific inquiry, and years of patient observation. A difficulty met with in mankind presents itself in animals in augmented form; cancer in animals is only likely to be recognized during life if it be situated on the visible, readily accessible, portions of the body; cancer of the internal organs is only likely to come rarely under observation, viz. at necropsies. Among aborigines it is probable that reliable data regarding cancer will be very difficult to obtain, except in those instances where there has been much contact with the white man.

A comparative study of the facts relating to the incidence of “cancer” in the animal kingdom would certainly enable us to orientate ourselves to an extent not likely to be attained through any other line of investigation. It is undesirable at present to speculate whether or not a common biological law applicable to the whole question, or a series of biological laws would be revealed.

Perhaps what has been stated may suffice to show that the prevailing pessimistic views as to the hopelessness of investigating cancer are unjustified in the face of what still remains to be done in this problem. Owing to the fact that cancer has hitherto been considered a subject which concerned only medical men, we are only at the very beginning

of the work before us—surely the most inopportune occasion on which to regard it as hopelessly beyond our powers. For the accomplishment of the work to be done it is too much to require the mere medical man to do all in an investigation which extends far beyond the province of medicine into those of general biology, ethnology, zoology, and embryology. Is it too much to hope that workers in these fields will appreciate the importance of their share in attempts to ascertain the cause and nature of the malignant new growths of man and animals? What is most needed at present is a definition of the distribution of the various types of malignant new growths throughout the animal kingdom.

In conclusion, I should like to add that the ideas forming the basis of the above remarks have taken on a more definite form in consequence of much discussion with Dr. J. A. Murray.

