necropsies have been made, and I have examined the records of all the cases of malignant disease of the pancreas. In the following table I have included all the cases in which malignant disease was primary in the pancreas, and I have classified them into those in which secondary growths were present and those in which secondary growths were not present.

Table showing Number of Cases described as Primary Carcinoma of the Pancreas in the Post-mortem Theatre of Guy's Hospital from 1861 to 1901, both Inclusive, and Classified into those with and those without Secondary Deposits.

Year.	Number of Cases of Malignant Disease of Pancreas with Secondary Deposits.	Number of Cases of Malignant Disease of Pancreas without Secondary Deposits.	Year.	Number of Cases of Malignant Disease of Pancreas with Secondary Deposits.	Number of Cases of Malignant Disease of Pancreas without Secondary Deposits.
1901	3	2	1880	3	1
1900	4	0	1879	2	1
1899	3	1	1878	3	1
1898	1	0	1877	0	0
1897	1	0	1876	1	0
1896	8	0	1875	0	0
1895	3	0	1874	2	0
1894	2	0	1873	1	0
1893	2	0	1872	0	0
1892	3	1	1871	1	1
1891	1	0	1870	0	0
1890	1	0	1869	0	0
1889	2	0	1868	0	0
1888	1	0	1867	0	0
1887	2	1	1866	0	0
1886	2	1	1865	0	0
1885	0	0	1864	0	0
1884	1	0	1863	0	0
1883	0	0	1862	0	0
1882	0	0	1861	0	0
1881	4	0			

It is quite clear that the cases in which secondary deposits were present cannot be regarded as examples of chronic pancreatitis, but I have examined both the clinical and *post-mortem* reports of each case which is entered in the *post-mortem* records as malignant disease of the pancreas, but in which no secondary deposits were present. The first occurred in 1871. The account of the *post-mortem* says: "The duodenum was found to be puckered and contracted, its calibre just admitting the little finger. There was a growth situated posteriorly, and connected with the head of the pancreas." There was no histological examination, but from the description we probably have here an example of new growth. The case which occurred in 1878 showed an ulcerated fungating growth. Dr. Goodhart made a histological examination of the pancreas of the case which occurred in 1879, and pronounced it to be carcinoma. With regard to the case which presented itself in 1880 the head of the pancreas contained a hard scirrhus-like mass with a quantity of colloid material in it, so this can hardly have been an instance of chronic pancreatitis, a histological examination was made in this case. The necropsy made in 1886 showed that the head of the pancreas was surrounded, and involved in a soft fleshy-pink growth..... The common bile duct could not be traced into the duodenum; it appeared to end in the growth. This does not suggest pancreatitis. The description of the *post-mortem* of the case that died in 1887 reads more like pancreatitis than the others, for a large cubical mass of what appeared to be growth was found in the head of the pancreas, but the patient was never jaundiced, and it is doubtful if chronic pancreatitis could kill apart from jaundice. It is true that Opie⁷ has recorded four cases of chronic interlobular pancreatitis associated with persistent vomiting, and the patient under consideration had persistent vomiting, but in Opie's cases something else serious enough to cause death was present, for the first died after an operation for premature labour and had pulmonary haemorrhage, the second had carcinoma of the uterus, the third had mitral disease, and the fourth malignant disease. But at the necropsy on the woman who died at Guy's Hospital in 1887 nothing to explain death was found beyond the tumour of the pancreas, which had caused contraction of the duodenum. The case, however, that died in 1892 does read very much as though it was a case of chronic pancreatitis. Therefore I publish it in full by the kind permission of Dr. Frederick Taylor.

A. A. W., male, aged 42, a travelling accountant, was sent to the hospital by Dr. Bisshopp, of Tunbridge Wells, on account of jaundice. He was admitted under Dr. Frederick Taylor, April 21st, 1892. There was no

evidence of alcoholism or syphilis. He first noticed jaundice with itching in November, 1891; soon his motions became quite white. He has not wasted.

On Admission.—He was deeply jaundiced, suffering much from itching. His liver was uniformly enlarged, extending to 3 in. below the ribs. There was no pain. The urine was loaded with bile, but otherwise healthy. The motions were very white, and he had some diarrhoea.

May 2nd. He first complained of pain over the liver, which had remained the same size as since admission. May 12th. He had lost 7 lb. since admission. May 16th. Much diarrhoea, motions dark, liver thought to be smaller. May 23rd. Motions white again. May 31st. Vomiting had set in; stomach appeared dilated. Had lost 6 lb. more. The sickness continued; he had much abdominal pain, and gradually became weaker, and soon died. At the necropsy the body was deeply jaundiced. The head of the pancreas was hard and much enlarged, and the pancreatic ducts and bile ducts were much dilated. The gall bladder was normal. There were no gall stones or secondary deposits anywhere. Histologically the pancreas showed increase of embryonic connective tissue. An adjacent lymphatic gland was also examined histologically and found healthy.

The case which died in 1899 was examined histologically and found to be a columnar-celled scirrhus carcinoma and the two remaining cases, which occurred in 1901, were certainly not chronic pancreatitis for one was an example of suppuration in connexion with a growth and the other was proved histologically to be a carcinoma. If from these 10 cases described in the report of the necropsy as examples of carcinoma of the pancreas without secondary deposits we deduct those histologically examined (four in number), and the case in which there was a fungating ulcerating growth and the one in which there was suppuration in connexion with a growth and which cannot therefore have been an example of the kind of pancreatitis we are considering, we have six in all to deduct, leaving only 4 cases out of 19,000 necropsies which could by any possibility be chronic pancreatitis. One almost certainly was, but in each of the other three there was some evidence that they were not, so that it was very unlikely that they were all examples of chronic pancreatitis. Hence we see that chronic pancreatitis is excessively rarely a fatal disease, probably not being responsible for more than one or two out of nineteen thousand deaths and certainly not being responsible for more than four. Thus from this point of view also the question of the necessity, except very rarely, of operation is raised. Further experience alone can give us the correct answer. It will be noticed that no cases of carcinoma of the pancreas occurred in the decade from 1860-1870 that cannot be due to any error of observation for during that period the necropsies were being made by Sir Samuel Wilks and Dr. Moxon.

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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 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.

THE second Congress of Italian Pathologists will be held at Florence on October 5th, 6th, and 7th.

AN EXPERIMENTAL EXAMINATION OF MESENTERIC GLANDS, TONSILS, AND ADENOIDS,

WITH REFERENCE TO THE PRESENCE OF VIRULENT TUBERCLE BACILLI.

BY

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THE experiments were primarily undertaken with a view to determine the presence or absence of virulent tubercle bacilli in the mesenteric glands of young children by an examination of suitable *post-mortem* material. The results, it was hoped, might furnish additional data with reference to the importance of the digestive tract as a channel for the entrance of tubercle bacilli into the system. The methods adopted were as follows:—The mesenteric glands on their removal at the necropsy were placed in a mixture of equal parts of glycerine and normal saline solution and conveyed to the laboratory. The material was tested in every instance by means of inoculation experiments. For this purpose a new method of procedure was adopted. The glands were freed as far as possible from the glycerine mixture, and were then disintegrated in a mechanical contrivance devised by Mr. Rowland for the purpose. It was considered that the method employed would facilitate the detection of the tubercle bacilli, and that it presented advantages over an ordinary emulsification, or a microscopic examination of the glands by the usual methods. If the organisms are sparse in number their physical presence may at times be overlooked. A thorough disintegration of the gland material will, on the other hand, tend to expose any organisms imbedded in recesses of the tissues and thus increase the chances of a successful inoculation experiment. In this respect the method appeared to us to approach more nearly to the conditions of an absolute test, and to be, therefore, the best adapted to the special purpose in view. The trituration of the glands was continued until the disintegration was so complete that a pulpy mass sufficiently fluid to be injected by means of a hypodermic syringe was obtained.

The disintegrating process lasted from half an hour to one hour, and every precaution was taken to carry it out under aseptic conditions, and to prevent any undue heating of the material. Of each gland thus treated, one half was injected subcutaneously, and the other half peritoneally into a guinea-pig. At the end of six to eight weeks any animals which had survived that period were killed and examined. The results were only considered positive in those cases in which tubercle bacilli were detected by microscopical examination of the lesions present in animals.

The *post-mortem* notes of the cases were furnished by the pathologist who had made the examination, and our thanks are due particularly to Dr. Cecil Bosanquet, to Dr. Fennell, and to Dr. Nabarro, whose aid rendered the investigation possible.

The *post-mortem* findings and the general results of the inoculation experiments are contained in the accompanying table. It only therefore, remains for us to give the inferences we have drawn from the results obtained. The total number of cases upon which the present paper is based is 28. We had hoped to increase the number, but unexpected difficulties arose in the way of procuring further material. The results, however, appear to be of sufficient interest to justify their being put on record.

The material examined was obtained as far as possible from cases of five years of age and under, as it is in such cases that a food infection would be most likely to occur. Only 2 cases were above 5—the one being about 6 and the other about 8 years of age. As regards sex, 16 were males, 9 females, and in 3 the sex was unrecorded. The examination for virulent tubercle bacilli was made irrespective of disease.

In none of the pathological reports was mention made of the detection of intestinal lesions. In the 28 cases the *post-mortem* diagnosis was as follows: Acute milinary tuberculosis, 1; general tuberculosis, 4; tuberculous meningitis, 2; tuberculous broncho-pneumonia, 1; non-tuberculous or suffering from other diseases, 20. There was, therefore, existent tuberculous disease in 8 of the cases.

The animal inoculation experiments showed that virulent tubercle bacilli were present in the mesenteric glands in 10 of the 28 cases, 18 having given negative results. Of the