SOME REMARKS UPON AN ANALYSIS OF 5,000 CASES OF DEATH FROM MALIGNANT DISEASE.*

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LAST year, when preparing the Report of the Committee appointed by this Branch to inquire into the influence of locality on the prevalence of malignant disease, I had the opportunity of analysing more than 5,000 cases of death from the various forms of cancer. The various reports received by the Committee contained also in many instances facts of great interest connected with the subject of cancer. In this paper I wish to extend the analysis of these cases somewhat further than I was able to do in the Committee's report, and to point out what seem to be some legitimate deductions from the analysis and from the facts recorded.

First, as to the proportion of cases occurring in the two sexes. Of 5,000 cases, 1,837 were males and 3,018 females (in 145 the sex was not stated). At first sight these figures seem to show a very marked and special susceptibility on the part of the female sex to malignant disease, namely, in the proportion of about 62 per cent. to 38 per cent. But the great preponderance of female cases on examination is seen to be due to the very great frequency with which cancer attacks the uterus and female breast. Of all the female cases it is found that in 40 per cent. it is one of these two organs which is affected, so that we may look upon the excess of female cases as due to the fact that the female is the unfortunate possessor of these two special organs, and not as an indication of a generally greater tendency to cancer in the female.

The fact is that if all the cases of malignant disease occurring in organs peculiar to either sex be excluded—that is, if the sexual peculiarities of both sexes be eliminated—the inequality is reversed, and the male is found to be the more often affected in the proportion of about 53 to 47 per cent. This small excess of some 6 per cent. may and probably does arise from the fact that many of what we may call the predisposing causes of cancer come much more frequently into operation in the male than in the female. Of these I need only mention trauma and syphilis. While speaking of the relation of sex to cancer, it is interesting to note that while a remarkable and steady increase in the general cancer mortality is noted to have occurred during the last thirty years, this increase is by far the more noticeable in males than in females. The last decennial report of the Registrar-General states that since the period between 1861-70 the increase of mortality from cancer has been as great as 78 per cent. among males, while that among females has been 42 per cent.; in other words, the increase among males has been nearly double that among females. Why is this?

It is no doubt true that the statistical increase is not all a real increase, but due chiefly to increased care and skill in diagnosis, in which case an answer at once suggests itself. We have just seen that in 40 per cent. of all the female cases it is in the uterus or breast that the disease occurs. Here increased care or skill in diagnosis would make little or no difference, as few are likely to fail to diagnose cancer of the breast or uterus in its final stages. It is quite otherwise in the case of cancer of the stomach and pylorus, which accounts for more than a quarter of all the male cases, since it is just here that increased skill in diagnosis would have most influence in increasing the number of cases certified as "cancer."

That there are other reasons is probable, but this I think is undoubtedly the most important. Another reason which acts by tending to reduce the total female mortality from cancer is the great advance in the surgical treatment of cancer of the uterus and breast, by which many lives which two decades ago would have been doomed are now saved. The following table shows the percentages in which the various organs are affected in males, females, and persons.

On referring to this table, it will be noticed that in the following organs and situations cancer is far more common in the male than in the female, namely: tongue, bladder,

oesophagus, jaws, face, mouth, limbs, lips, and stomach. In the majority of these situations the male is more liable to injury or chronic irritation than is the female.

Table showing the percentage in which the various Organs are Attacked in Males, Females, and Persons.

Organ.	Persons.	Male.	Female.
Uterus	15.50	—	24.0
Stomach and pylorus	15.00	28.00	11.0
Liver and gall bladder*	14.40	16.70	13.0
Breast	11.00	—	17.8
Rectum	7.00	10.80	5.8
Intestine	5.40	7.00	4.5
Oesophagus	2.80	5.80	1.0
Limbs	2.08	3.30	1.5
Bladder	2.06	4.25	0.7
Tongue	2.00	4.40	0.5
Face (including eye, nose, ear, and parotid gland)	1.83	3.00	1.3
Neck	1.80	2.80	1.3
Jaws	1.60	3.00	0.8
Omentum and mesentery	1.20	—	—
Thorax	1.20	1.80	0.8
Pancreas	1.00	1.30	0.8
Lips	0.70	1.30	0.3
Kidney	0.55	—	—
Pharynx	0.54	1.40	—
Mouth	0.45	1.00	0.2

* The large majority of these cases certified as cancer of the liver are secondary to intestinal, uterine, or ovarian primary growths, and are not primary cancer of liver.

It also will be noticed that a very large proportion of all the deaths from cancer in the male are due to cancer of the stomach and pylorus. It is, indeed, remarkable that, including the liver—in which the disease was probably for the most part secondary to some primary intestinal growth—about three-fourths of all the cases of cancer in the male occur in the alimentary tract.

With regard to the frequency with which the various forms of cancer occur at varying ages, the two following diagrams, with curves drawn for the four organs or situations most frequently the site of primary growths will be of interest:

Diagram A, showing how many out of each hundred cases of cancer of stomach, rectum, mamma, or uterus occur in each decade.

* Read before the Birmingham and Midland Counties Branch of the British Medical Association.

Diagram B, showing proportional liability of each decade to cancer of the stomach, rectum, breast, and uterus. These curves are calculated on the number of persons surviving in each decade, so that they show how increasing age affects the individual liability to these forms of cancer.

Diagram B, which is the more interesting, shows that after the third decade the individual liability to cancer of the stomach, breast, or rectum increases in direct proportion to the increasing age up to the seventh decade (71-80), and then declines, while the liability to cancer of the uterus starting in the third decade rises rapidly, and again in direct proportion to the increasing age, but only to the fifth decade (51-60), and then somewhat slowly declines.

It will be seen that the liability to cancer of the stomach between the ages of 51 and 60 is exactly one-half what it is between the ages of 71 and 80, the liability to cancer of the breast a little less than one-half, and that to cancer of the rectum only one-third.

These facts teach us that although up to a certain age increasing years, with presumably decreasing cell vitality, render the individual increasingly liable to cancer, this is only true up to a certain point. There comes a time beyond which increasing age renders the individual less, and not more, liable to cancer. It looks as though a certain amount of vitality or activity in the special cells of these organs were necessary, or at least most suitable, for the production of cancer, and that when this vitality was diminished beyond a certain point a greater stimulus was needed before a malignant tumour could be started.

It is of interest also in this connection to note how much earlier this stage is reached in the uterus than in the three other cases. Here the maximum liability is reached immediately after the cessation of functional activity, and the later years of life are associated with a considerably lessened liability to cancer of uterus. Do the facts which have been collected by the Committee throw any light upon the possible causation of cancer?

The conclusions of the Committee were as follows;

1. Certain more or less well-defined areas exist in which the mortality from cancer is markedly above, and others in which it is markedly below, the average for England and Wales.
2. Although age and sex incidence undoubtedly influence this variation, in some cases considerably, they only account for a small proportion of it.
3. That owing to the great difficulty of diagnosis in many cases of internal cancer the death-rate from cancer is probably at present underestimated.
4. Contamination of the soil or subsoil for long periods with decomposing organic matter is very probably a factor in the production of a high death-rate from cancer.
5. A damp, ill-drained, waterlogged soil of whatever geological formation is more frequently associated with a high cancer death-rate than is a dry well-drained soil.
6. There is abundant evidence of the existence of groups of houses in which cancer is found with marked frequency; and some evidence which tends to show that second and third cases occur in the same house with greater frequency than can be accounted for by mere coincidence.
7. Cancer occurs more frequently in old than in new houses and districts.
8. There is some evidence suggesting that under certain circumstances

cancer may possibly be transmitted from one person to another in constant close association.

Although the evidence collected by the Committee does not, of course, disclose the nature of the exciting cause or causes of cancer, it points, I think, very strongly to the existence of some definite exciting cause or causes.

The following may be mentioned as some of the more certain predisposing causes:

1. Prolonged local irritation, due to various causes, setting up local inflammatory changes in the irritated tissue.
2. The immediate or after-effects of direct and sudden injury, whether mechanical, thermal, or chemical.
3. Syphilis and possibly other constitutional diseases which are associated with local tissue changes.
4. The tissue degenerations of advancing years varying with the age.
5. Individual proclivity.
6. The presence of foetal remnants or "cell rests."
7. (According to the Committee's report) the residence in the neighbourhood of a sodden and sewage-soaked soil.

Now all these predisposing causes, except possibly the last, resolve themselves into conditions in which the resisting power of the individual cells have most probably been reduced. At any rate the vitality of the cells or their power of specialisation has been interfered with.

It is just in such a condition that the invasion of a parasitic organism might be expected to have most chance of success. And as the existence of some external exciting cause is necessary in order to explain the known facts in the large majority of new growths, one can hardly refrain from suggesting that these various predisposing causes are simply conditions which prepare the soil for the advent and growth of some essential exciting cause, possibly a parasitic organism.

But if such germ exist, how does it gain entrance into the body? How does it reach the tissue in which by its influence or growth a malignant tumour is subsequently formed? This may take place in one or more of the following ways:

1. Absorption from the intestinal tract.
2. Absorption from the respiratory tract.
3. Direct inoculation (a) through abrasion of skin or mucous membrane, (b) by the bites of blood-sucking insects.

The great frequency with which malignant disease occurs in the various portions of the intestinal tract or on those portions of the surface skin most exposed, to injury would suggest that a definite local inoculation does sometimes take place; and indeed there is strong presumptive evidence of this in many cases. For instance, how often in the case of surface epitheliomata do we get the history of a small neglected abrasion which "would not heal," followed later on by the formation of a definite growth. In connection with this it is interesting to remark that in going through the statistics collected by the Committee, it was noticed that in a remarkable number of the cases of surface epitheliomata recorded the patients were agricultural labourers, just the persons most subject to such conditions.

Instances of apparent direct inoculation might be multiplied indefinitely by examples taken from the lip, tongue, scrotum, etc., or by the power of an epithelioma (of the vulva, for instance) to start a second growth by direct contact.

A second mode of direct inoculation which should be considered is the possible conveyance of the "essential germ" into the blood or the tissues through the agency of blood-sucking insects, such as gnats, midges, horseflies, mosquitos, fleas, and bugs. In the light of the established connection between malaria and the mosquito, this should merit serious consideration.

Although no doubt a large number of cases of cancer might fairly be attributed to a local inoculation, there are many in which such local inoculation cannot be assumed, but in which the germ, if it exist, must have been conveyed through the blood. Here the germ may have been absorbed from a wound without affecting the tissues locally, or from the broken or unbroken surface of the mucous membrane of the alimentary or respiratory tracts. We have of course no direct evidence of this taking place in any of these cases; but the rarity of primary malignant disease of the lungs and its frequency in the stomach would lead us to expect that it is through the

alimentary rather than the respiratory tract that such entrance is obtained.

A remarkable and striking instance of a malignant growth (round-celled sarcoma) following directly upon a blow came under my notice not long ago. A farmer and his servant returning one night from a horse fair, where they had concluded a rather sharp bargain with some gipsy dealers, were attacked by the latter, who thought they had been cheated. In warding off a blow aimed at his master, the man received a heavy stroke from a cudgel upon his right arm just below the shoulder. The result was a large hæmatoma, which after five weeks was still as large as a hen's egg. After this time the swelling ceased to diminish, but, on the contrary, began to get larger again. It was at this stage that I first saw the man, and found an elastic swelling in the position of the hæmatoma, but which felt exactly like a soft growth. Later on I sent the man to the General Hospital, Birmingham, where he came under the care of Mr. Barling, who made an exploratory incision and a diagnosis of sarcoma. Amputation at shoulder-joint followed, but unfortunately there was a recurrence some months later. The growth proved to be a soft, round-celled sarcoma.

Other instances in which a malignant tumour followed directly upon an injury might be quoted, but it would be hard to find a clearer example than the foregoing.

In going through the reports received by the Committee from the various districts, it was noticed that in a number of instances second cases were mentioned as having occurred among those in close constant association with an earlier case. Dr. Law Webb's report contains an example of this, which will serve to illustrate this point. In a series of cases, A., B., and C. living near each other, A. died of cancer of the uterus; B., who waited upon A. in A.'s last illness, died of epithelioma of the mouth. A woman who waited on B. died of cancer of the breast. A man lodging with A. died of epithelioma of the larynx. C., who lived near A. and B., died of epithelioma of the mouth, and his son, also, some time later of epithelioma of the mouth.

The following case came under my own observation not long ago: A man suffering from cancer of the rectum was nursed after colotomy during the last six months by his daughter, aged 38. After his death she left home, and went to live in another neighbourhood. Some eight months later she came under my care with symptoms suggesting partial intestinal obstruction. Two months later the obstructive symptoms became pronounced, and nodules appeared in the skin of the abdomen. She died shortly after of a growth involving the descending colon. Are these cases mere coincidences, or do they indicate the existence of a definite contagion, though perhaps one of a very low degree of infective power? Time and careful observation, and recording of observed facts alone, will answer this question; meanwhile we are bound to keep an open mind.

NOTE.

¹ A condensed analysis of these 5,000 cases appeared on pp. 40-41 of the Report referred to (*A Contribution to the Ætiology of Cancer*. Hall and English, Birmingham).

ERYTHEMA MULTIFORME AND VACCINATION.

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In the *Scottish Medical and Surgical Journal* (April, 1901) I published a short note, with an illustration, of a case of Erythema Multiforme closely resembling Small-pox. The difficulty of diagnosis was considerable, but we were greatly aided by the fact that the patient had been successfully vaccinated four weeks previously. It did not occur to me to connect the vaccination with the skin eruption. Since then four other cases have come under my observation, all of them recently vaccinated, and all showing features which seem to make it certain that the vaccination was causally related to the eruption. Curiously, with one exception all occurred in persons more or less directly connected with the medical profession—doctors, students, or nurses.

My second case was that of a Queen's nurse, whose hands presented an absolutely typical picture of erythema iris. On questioning her, however, I found that the legs were also

affected, and that the eruption spread up the arm beyond the usual limitation of erythema iris. When she removed her dress the vaccination lesions presented an appearance quite out of keeping with the time which had passed since the operation was performed. Although a month had elapsed the scabs were still moist, and they were surrounded by a raised erythematous patch of the same character as the eruption elsewhere.

The other cases were possibly not so perfect in their mimicry of the real disease, but having become familiar with the condition I had no difficulty in recognising them. All presented certain features in common; all were vaccinated with glycerinated lymph, and in all of them the early course of the vaccination was uneventful. In three of the five cases there was nothing more than a slight feeling of *malaise*. The eruption developed always on the hands and the face, but on other parts as well. At the same time the vaccination area showed evidence of fresh activity. In two cases the scabs had fallen off, and apparently all was over, but coincident with the eruption fresh vesicles developed on the part, just as if the patient had again been vaccinated. The course of the erythema was uneventful, the eruption rapidly disappearing.

I have since discovered that I had overlooked a reference to this condition, which was incidentally mentioned in a discussion at the meeting of the American Dermatological Association last summer, which was published under the heading "Bullous Dermatitis in Children." In the discussion, Bowen of Boston gave notes of five cases following vaccination. He noticed the tendency to appear on the backs of the hands and feet and on the face, and he suggested that the condition was allied to dermatitis herpetiformis. White of Boston drew attention to the fact that the lesions appeared on regions most exposed to autoinfection. Corlett had noted bullous eruptions appearing after vaccination, but had regarded them as closely related to impetigo. It is interesting to note that he had stated he had never observed the eruption after the use of glycerinated lymph. Gilchrist mentioned a case occurring at the Johns Hopkins Hospital, where a diagnosis of herpes iris had been made; the temperature in that case rose to 103° F. One of the lesions was excised, and sections suggested the presence of a toxin circulating in the blood. Other cases of erythema following very shortly after vaccination were referred to. These are obviously not the cases which have come under my care. Many of the American observers noted, as I did, that the vaccination wound had entirely healed before the eruption appeared; and I certainly incline to adopt the suggestion of Gilchrist that a toxin is produced which, circulating in the blood, produces, as many toxins do, that form of erythema which we know as erythema multiforme, and especially that variety described as erythema iris. I have heard of two other cases apparently similar, but it seems incredible that there have not been many more, and it would be interesting to know whether any particular stock of lymph is especially liable to be followed by such an eruption.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, ETC.

A CASE OF HÆMATEMESIS OCCURRING IN THE COURSE OF APPENDICITIS.

It was with much interest that in the *BRITISH MEDICAL JOURNAL* for February 23rd I read a short account of the communication made by Professor Dieulafoy (Paris) before the Académie de Médecine, reporting 6 cases in which hæmatemesis occurred in the course of appendicitis. A case exactly similar in every respect, except that there was a previous history of gastric ulcer, has lately come under my notice; and as the subject is one of considerable importance, I have ventured to submit the following notes:

D. B., aged 19, had two years previously suffered from what was considered to be gastric ulcer, unaccompanied, however, by any signs of hæmatemesis. From this she completely recovered, and from that time until February 8th, 1901, she enjoyed very good health with absolutely no symptoms indicative of any gastric trouble. On the afternoon of this