

THE NATURAL DURATION OF CANCER.

BY

W. S. LAZARUS-BARLOW, M.D., F.R.C.P.,

AND

J. H. LEEMING, M.D.

(From the Cancer Research Laboratories, the Middlesex Hospital.)

In every instance where the value of a method of treatment in disease is under consideration a basis of comparison derived from observations in which no special treatment is applied is necessary. Sometimes, as in the case of acute intestinal obstruction and operation, or in that of diabetic coma and insulin, the comparison is sharply defined between life and death within a few hours. More frequently the question resolves itself into the less dramatic inquiry whether the given treatment relieves suffering or prolongs life, and periods of weeks or months are involved. Further, the matter is of importance for indicating whether the method of treatment is intrinsically sound, and therefore further advantage may be anticipated from increased attention to technique, or is intrinsically unsound and should be abandoned.

Such a provision of "controls" as a basis of comparison is of more than normal importance in cancer, where the question of "cure" or complete recovery is particularly uncertain. It may be quite impossible to promise cure in any individual case, and yet it may be fully permissible to indicate that, from consideration of a large number of cases, a given line of treatment is associated, on an average, with prolongation of life. And if such prolongation of life be accompanied by relief of symptoms, the method by which these two benefits are attained is not merely an advantage as it stands, but calls for additional research in order to magnify those advantages.

With a view to providing such controls for researches upon cancer treatment in general, and treatment by radiations in particular, we have analysed the records of the Middlesex Hospital over a period of forty years (1883-1922) and present the results of the inquiry in tabular form.

The natural duration of the disease in each case has been taken as that period which elapsed between the date of reputed onset as determined from the patient's history and the date of death. Cases in which operation was performed other than palliative (for example, tracheotomy, colostomy) have been excluded, and the same is true with regard to experimental lines of medical treatment (for example, soamin, trypsin, and amylopsin), but it was impossible to exclude purgatives, analgesics, and drugs of like simple character, nor was it considered necessary.

In a few instances where the patient had been discharged from hospital at his own request and the actual date of death was not known, a computation was made of the possible survival by careful consideration of the state of the patient on discharge; and lastly, where the reputed onset was unusually long or short, the case was reconsidered, and if there was reasonable cause for doubt was discarded entirely, otherwise it was retained.

In many instances where the reputed onset was separated by a long period from the date of admission it appeared probable that a pathological but non-malignant condition passed imperceptibly into malignancy. Such cases were found most frequently in the breast and cervix. In the breast a lump may have been recognized for many years prior to admission, but occasionally it is expressly noted that at some later date the mass took on increased growth. When such a statement was found in the records this later date was regarded as that of the onset of the cancer, otherwise the earlier date was utilized. Similarly in the case of the cervix it is often impossible to be certain whether the first symptom noted by the patient is due to changes at the menopause or to cancer. Hence it is probable the mean durations given in the table are somewhat over-estimated for cancer of the breast and for cancer of the cervix about the menopause. Nevertheless, it appears certain that some cases of malignant disease last for a very long time. In the notes we have examined we have found one case of cancer of the cervix which lasted eighteen years from reputed onset to death, and fourteen of these

years were spent in the hospital under constant observation. Another case of malignant disease of the pelvic bones was a patient in the cancer ward for over fifteen years, and many records of the local condition are found in the notes. The reputed onset in this case was ten years before admission. Both patients were admitted with clinical signs of undoubted cancer, died in the hospital, and autopsies were made. In spite of the unusual duration we felt that neither case could be regarded as non-cancerous.

Naturally it is desirable that such basic figures should not emanate from the experiences of a single institution, and we have reason to believe that values calculated on identical lines are being prepared by the Cancer Hospital, the Christie Hospital, Manchester, and the Glasgow Royal Cancer Hospital. When these have been obtained fairly reliable figures indicating the natural duration of cancer at the principal primary sites should be available for Great Britain.

The average durations were calculated for decennial age periods in all cases, but only such figures are given in Table I as are derived from a reasonable number of cases,

TABLE I.—Natural Duration of Cancer at Certain Primary Sites Calculated on Age at Reputed Onset.

Site.	Age.	Sex.	No. of Cases.	Natural Duration in Months.			Percentage of Cases below Mean.
				Mean.	Maximum.	Minimum.	
Breast	Under 25	F.	1	24.0	—	—	—
	25-34	F.	15	36.0	196	3	80.0
	35-44	F.	42	32.0	112	5	64.3
	45-54	F.	61	39.2	186	2	68.8
	55-64	F.	60	40.7	210	3	70.0
	65-74	F.	44	44.3	169	11	63.6
	75 and over	F.	20	36.1	64	12	50.0
Cervix	Under 25	F.	3	13.0	17	6	33.3
	25-34	F.	96	18.6	100	5	60.4
	35-44	F.	295	21.4	126	3	66.1
	45-54	F.	316	21.4	120	3	66.1
	55-64	F.	150	22.4	130	6	62.7
	65-74	F.	49	24.9	223	4	69.4
	75 and over	F.	7	11.3	21	5	57.1
Tongue and mouth	Under 25	M.	1	17.0	—	—	—
	25-34	M.	7	9.1	16	3	42.9
	35-44	M.	33	15.8	52	4	63.6
	45-54	M.	70	16.9	54	3	61.4
	55-64	M.	74	15.8	75	4	68.9
	65-74	M.	33	15.5	60	3	69.7
	75 and over	M.	7	16.3	37	3	57.1
Rectum	Under 25	M.	3	9.0	12	3	33.3
	25-34	M.	10	14.5	35	4	60.0
	35-44	M.	19	22.6	69	6	68.4
	45-54	M.	39	20.1	54	4	64.4
	55-64	M.	59	21.2	86	4	67.8
	65-74	M.	38	25.2	56	4	68.4
	75 and over	M.	4	24.0	38	6	50.0
Rectum	Under 25	F.	1	16.0	—	—	—
	25-34	F.	14	23.9	122	3	78.6
	35-44	F.	19	16.7	34	3	52.6
	45-54	F.	47	26.3	67	4	63.8
	55-64	F.	62	26.8	73	7	54.8
	65-74	F.	22	26.4	63	6	59.1
	75 and over	F.	8	32.0	109	10	62.5

When figures from the additional sources mentioned above have been obtained it may be possible to separate other primary sites on a decennial basis. For the present such averages as are derived from a small number of observations are given (Table II) as general means and only divided into males and females.

It is obvious that no detailed examination of the results is called for, but two facts seem to emerge: (1) that the earlier the age of onset the shorter the total duration of the untreated disease, and (2) that the natural duration of cancer at one and the same primary site is longer in the female than in the male.

In the case of cervix, breast, rectum (male and female), and tongue and mouth (male), where sufficiently large numbers were available, the cases were divided into two equal periods of twenty years—namely, 1883 to 1902 and 1903 to 1922—in order to determine whether the natural duration of the disease had undergone a change during later years. The differences were as follows: for breast, rectum

TABLE II.—Mean Natural Duration of Cancer at Various Primary Sites.

Site.	Sex.	No. of Cases.	Natural Duration in Months.			Percentage of Cases below Mean.
			Mean.	Maximum.	Minimum.	
Lip	M.	19	18.3	42	7	63.2
Tongue and mouth	M.	225	15.9	75	3	65.8
Tongue and mouth	F.	18	17.4	37	6	66.7
Cheek	M.	29	13.4	27	3	48.3
Cheek	F.	7	12.0	31	6	57.1
Pharynx	M.	32	11.8	26	3	56.7
Pharynx	F.	6	15.8	34	7	40.0
Larynx	M.	44	14.0	40	3	55.8
Larynx	F.	11	14.0	37	4	70.0
Tonsil	23 M., 2 F.	25	14.2	42	3	48.0
Neck	M.	36	9.4	37	3	51.4
Neck	F.	7	13.0	26	3	40.0
Parotid	1 M., 3 F.	4	14.5	19	11	50.0
Thyroid	3 M., 2 F.	5	8.6	13	3	50.0
Oesophagus	M.	63	12.1	51	2	66.1
Oesophagus	F.	11	19.4	56	2	36.4
Stomach	M.	61	16.5	60	3	65.6
Stomach	F.	58	17.2	50	3	58.9
Colon	M.	32	16.0	51	2	53.3
Colon	F.	45	19.2	98	2	58.1
Rectum	M.	172	20.4	86	3	61.6
Rectum	F.	173	25.9	122	3	59.9
Peritoneum	1 M., 7 F.	8	19.4	53	4	62.5
Prostate	M.	17	15.4	46	6	66.6
Penis	M.	8	21.4	52	10	57.1
Testicle	M.	3	26.0	37	5	33.3
Scrotum	M.	3	23.0	29	15	33.3
Cervix	F.	916	21.3	126	3	66.6
Corpus uteri	F.	28	24.2	88	5	42.9
Ovary	F.	22	15.1	38	3	57.1
Vagina and vulva	F.	57	22.1	181	5	72.7
Bladder	M.	22	26.9	101	2	71.4
Bladder	F.	18	15.2	44	4	55.5
Kidney	8 M., 9 F.	17	15.1	51	3	63.2
Liver and gall bladder	M.	7	13.0	26	7	60.0
Liver and gall bladder	F.	23	10.8	44	2	54.5
Pancreas	5 M., 8 F.	13	11.2	36	3	69.2
Breast	F.	243	38.4	210	2	59.3
Skin	11 M., 9 F.	20	19.4	39	2	60.0
Bones—short	33 M., 20 F.	53	22.5	311	2	71.7
Bones—long	10 M., 5 F.	15	14.1	27	2	46.6
Muscle (sarcoma)	2 M., 1 F.	3	14.0	35	8	66.6

(male) and rectum (female) the mean duration was 9 to 13 per cent. greater during the second period than during the first, for tongue and cervix 1 to 5 per cent. less.

One final observation is necessary. The values in Table I are computed from the ages at reputed onset of the disease. Obviously, if this date were accurately known, the values would be absolute. But, since it is an uncertain factor, it must of necessity be reflected in the "natural duration." At primary sites, where cancer normally runs a rapid course, probably little difference obtains whether age at reputed onset or age at admission to hospital is employed. But in the breast, where many cases last a long time, such is not the case. For this organ the same series of 243 cases was

compared under the two methods. The values obtained were as follows:

Age.	25-34.	35-44.	45-54.	55-64.	65-74.	75.
At reputed onset	36.0	32.0	39.2	40.7	44.3	36.1
At admission	19.2	31.1	32.0	41.2	46.2	45.2

It is seen that, although the tendency of the disease to last longer as it occurs later in life is apparent under both methods of calculation, noteworthy differences obtain in several of the decennial age periods. And since age at admission is relatively of little interest, age at reputed onset has been adopted in all cases.

SPLENECTOMY IN A CASE OF SPORADIC ACHOLURIC JAUNDICE.

BY

E. J. FOULDS, M.B., CH.B.,

HOUSE-SURGEON, MANCHESTER ROYAL INFIRMARY.

In view of the somewhat variable results of splenectomy in acholuric jaundice the following case may be of interest:

A girl, aged 18, was admitted to the Manchester Royal Infirmary on November 19th, 1923, on account of chronic jaundice and attacks of abdominal pain. She was a healthy child until the age of 4, when jaundice was first noticed. She had been continuously jaundiced for fourteen years, though the intensity of the jaundice had varied somewhat from time to time. There was no history of clay-coloured stools or itching of the skin. As long as she could remember she had been subject to attacks of pain in the epigastrium and left hypochondrium. These attacks lasted a few hours at a time, were of considerable severity, and had become increasingly frequent of late. No history of any similar condition in any relative could be obtained.

The patient, a fairly well nourished girl, was jaundiced with a deep golden yellow colour of the skin and sclerotics. There was considerable enlargement of the spleen below the costal margin and slight enlargement of the liver. Bile was present in the blood serum, but not in the urine. The urine was bright pink, from the presence of urobilin, and the faeces a brick-red colour. The absence of obstruction in the bile ducts was confirmed by van den Bergh's reaction (indirect). The fragility of the red corpuscles was increased, haemolysis occurring with N/25 salt solution, whereas normal red cells haemolyse with N/35 saline. A blood count before operation showed:

Red corpuscles	3,056,000 per c.mm.
Haemoglobin	52 per cent.
Colour index	0.85
White corpuscles	9,400 per c.mm.
Polymorphs	69.6 per cent.
Lymphocytes	21.2 "
Large mononuclears	7.4 "
Eosinophiles	1.8 "

X-ray examination of the gastro-intestinal tract and gall-bladder region was negative. The Wassermann reaction was negative.

Operation.

On November 24th, 1923, Mr. Morley made a median incision above the umbilicus. The gall bladder and cystic duct were found to be filled with small soft pigment stones, but no stones were found in the common bile duct, which was not dilated. The spleen, which was four times its normal size, was not adherent, and was easily removed. The gall bladder was opened and the pigment stones removed. A tube was left in the gall bladder for ten days.

After-History.

Convalescence was uneventful. A week after the operation the jaundice, which had persisted for fourteen years, had vanished. A blood count on December 10th (seventeen days after operation) showed that the red corpuscles had risen from 3,056,000 to 5,048,000 per c.mm. and the haemoglobin from 52 to 78 per cent.

At the present time, seven months after the operation, the patient is perfectly well, and has remained entirely free from jaundice.

Histological Examination of Spleen.

Dr. G. E. Loveday reported as follows: "The sections show no obvious increase in the connective tissue stroma. The most marked feature is the general distension and patency of the sinuses. The tissue between the sinuses is infiltrated with blood, and the appearance suggests congestion rather than haemorrhage. The ordinary cells of the pulp are consequently scattered. The endothelium of the sinuses shows proliferation. The endothelial cells of the Malpighian bodies are not particularly proliferated, and the outline of Malpighian bodies is rather less defined than usual in some instances."

I am indebted to Mr. John Morley, under whose care the patient was admitted, for permission to publish these notes.