SURGICAL TREATMENT OF CARCINOMA OF THE CERVIX*

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I propose to confine my remarks to the results I have obtained by Wertheim's operation. I shall not touch upon the technique of the procedure, for those interested in the subject will find it fully discussed in two recent publications of mine to which I would refer them.^{1 2}

RESULTS ON BASIS OF FIVE YEARS' FREEDOM FROM RECURRENCE

Between May, 1907, and May, 1927, I performed the operation 339 times. The results are as follows:

Died of the operation	...	...	...	52
Lost sight of before 5 years	...	...	...	11
Died other disease before 5 years	...	...	...	9
Died recurrence before 5 years	...	...	...	135
Well 5 years after operation	...	...	...	132
				339

The operative mortality rate is 15.3 per cent. The relative cure rate is 38.9 per cent., or, deducting the twenty cases that were lost sight of or died of other disease before five years, 41.3 per cent.

Glandular Invasion.—Of the 339 cases malignant invasion of the regional glands was present in 143 (42 per cent.). The following table gives the results obtained from this group.

Regional Glands Invaded				
Died of the operation	...	...	...	31
Lost sight of before 5 years	...	...	...	5
Died other disease before 5 years	...	...	...	2
Died recurrence before 5 years	...	...	...	71
Well 5 years after operation	...	...	...	34
				143

These figures contrast markedly with those obtained from the group of cases in which the regional glands were not involved.

Regional Glands Not Invaded				
Died of the operation	...	...	...	21
Lost sight of before 5 years	...	...	...	6
Died other disease before 5 years	...	...	...	7
Died recurrence before 5 years	...	...	...	64
Well 5 years after operation	...	...	...	98
				196

It will be noted that in the gland-invaded group the operative death rate is 21.6 per cent., whilst in the non-invaded group it is only 10.7 per cent. Further, the relative cure rate of the gland-invaded group is only 23.7 per cent., or, with deductions, 24.6 per cent. as against 50 per cent., or, with deductions, 53.5 per cent. in the non-invaded group. The presence of growth in the regional glands about halves the chance of cure.

Absolute Five-Year Cure Rate.—I reckon my operability rate at 63 per cent. The 339 cases tabulated may therefore be regarded as a selection out of 538 cases originally presenting themselves for treatment. The absolute cure rate is thus 24.5 per cent., or, with deductions, 25.4 per cent.

RESULTS ON BASIS OF TEN YEARS' FREEDOM FROM RECURRENCE

My experience shows that five years' freedom from recurrence is only a 90 per cent. cure, for about 10 per cent. of all recurrences take place between the fifth and

tenth years after the operation. From 1907 up to May, 1922, I had performed the operation 227 times. The results are as follows:

Died of operation	...	...	...	37
Lost sight of before 10 years	...	...	...	18
Died other disease before 10 years	...	...	...	11
Died recurrence before 10 years	...	...	...	92
Well 10 years after operation	...	...	...	69
				227

The operative death rate is 16.3 per cent. This is higher than that in the comparable table in the five-year statistics because my operative mortality was higher in my earlier years. The relative cure rate is 30.3 per cent., or, deducting the twenty-nine cases lost sight of or died of other disease, 34.8 per cent.

Glandular Invasion.—Of the 227 cases malignant invasion of the regional glands was present in 93, or 40.9 per cent. The following table gives the results obtained from this group:

Regional Glands Invaded				
Died of operation	...	...	...	21
Lost sight of before 10 years	...	...	...	4
Died other disease before 10 years	...	...	...	2
Died recurrence before 10 years	...	...	...	46
Well 10 years after operation	...	...	...	20
				93

In contrast to these figures the next table shows the results obtained from the group of 134 cases in which the regional glands were not invaded:

Regional Glands Not Invaded				
Died of operation	...	...	...	16
Lost sight of before 10 years	...	...	...	14
Died other disease before 10 years	...	...	...	9
Died recurrence before 10 years	...	...	...	46
Well 10 years after operation	...	...	...	49
				134

As in the five-year statistics so in the ten-year—the operative death rate of the gland-invaded group is much higher than that of the non-invaded (22.5 per cent. as against 11.9 per cent.). The relative cure rates also are very different—21.5 per cent., or, with deductions, 22.7 per cent., as against 36.5 per cent., or, with deductions, 44.1 per cent. This again shows how very markedly the chances of cure are lessened if the regional glands are malignant.

Absolute Ten-Year Cure Rate.—Reckoning my operability rate as 63 per cent., the 227 cases dealt with on the ten-year basis may be regarded as a selection out of 360 cases originally presenting themselves for treatment. The absolute cure rate is therefore 19.1 per cent., or, with deductions, 20.8 per cent.

PRIVATE CASES

When Comyns Berkeley and I began to do the operation in 1907 no one else in our circle was performing it, nor had radium made its appearance on the scene, so that we had the free run of the out-patient departments both at Middlesex Hospital and at Chelsea Hospital for Women, and there was no difficulty in keeping an accurate count of all the cases seen by us. In the years 1907–11 112 cases were presented to us, and out of these we operated on seventy, or 63 per cent. After 1911 it became increasingly difficult to keep such a count, because not only had our colleagues begun to do the operation, but I had been translated from the out-patient department, whilst Middlesex Hospital (to which, on account of its incurable cancer wards, an undue proportion of advanced cases had always been sent) became known as a radium centre, and the number of these cases became so increased

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that the patients presenting themselves there no longer constituted a fair sample of the cases of carcinoma of the cervix in the community at large. We therefore gave up the futile task, and in all our subsequent communications continued to reckon our operability rate at 63 per cent.

There is, however, one group of cases wherein I can with perfect accuracy give the proportion on which I operated—namely, those whom I saw for the first time in my consulting room in private practice.

Between 1910 and May, 1927, I saw at my house 133 women suffering from carcinoma of the cervix, and of this number I operated on 109, or 82 per cent. The results obtained are as follows:

Patients Seen Privately				
Died of operation	...	...	...	10
Lost sight of before 5 years	...	...	...	2
Died other disease before 5 years	...	...	...	1
Died recurrence before 5 years	...	...	...	51
Well 5 years after operation	...	...	...	45
				109

The operative death rate of this group of cases is 9.1 per cent., the relative cure rate (without deductions) 41.2 per cent., and the absolute cure rate 33.8 per cent. It may be argued that this group represents a number of specially picked cases in whom the average advancement of the disease was less than ordinary. The gland involvement rate does not support this suggestion, for of the 109 cases the regional glands were malignant in 41, or 40 per cent., which is only fractionally below the general average. The lower operative mortality is due to the fact that these women, owing to their better social and financial position, were in a less deteriorated state of health than the average patient.

DEATH RATE OF THE OPERATION

The operative mortality of Wertheim's operation in the past was, and often still is, held up as a reproach against it, although for many years now my death rate has been no greater or less than that of certain other operative procedures the performance of which excites no criticism. I have succeeded in diminishing it to a figure which is considerably below that of prostatectomy. Between 1907 and the end of last year I had performed the operation 428 times, and the following table shows how the operative death rate has fallen:

First	100 operations, 20 operative deaths:	20 per cent.
Second	100 " 13 " "	13 "
Third	100 " 16 " "	16 "
Last	128 " 12 " "	9 "

CONCLUSION

According to approved custom I have carried my percentages into decimals, but such meticulousness has little real value, for the figures dealt with are far too small to be beyond the vagaries of chance. A run of good luck puts them up a cipher or two, a run of bad luck puts them down. We can better express the utility of the operation by saying that by its means we can cure (meaning by that term survival for five years) two out of every five patients operated on and one out of every four patients seen.

If we go further and desire to use the term "cure" in its complete sense, we must frame our statement on the ten-year basis, and say that the operation cures one out of every five patients seen and one out of every three patients operated on.

This general statement applies not merely to my own figures, but also to the results published by those other surgeons who have performed the operation on a large

scale and kept count of their patients' after-histories. Moreover, it is a fixed result incapable of material improvement unless the average period elapsing between the incidence of the disease and the time when the patient presents herself can be shortened—which seems to me very unlikely. It might be thought that the marked reduction in operative mortality would be reflected in the end-results, but it is to be remembered that the bulk of the patients dying as the result of the operation are in an advanced stage of the disease, so that of those who now escape operative death only a small proportion escape death by recurrence. Finally, I would emphasize that the cures effected by the operation are obtained from only a proportion of the cases seen by the surgeon. Besides those he selects for operation, a considerable surplus remains out of every hundred seen by him. These inoperable cases are treated by radiation. As a group they are in an advanced stage of the disease, but, nevertheless, a certain small proportion can be salvaged by these means, and this number must be added to the number of operative cures when estimating the total achievement.

REFERENCES

- ¹ *Lancet*, February 8th, 1930, p. 277.
- ² *Australian and New Zealand Journ. of Surgery*, June, 1931.

B. DIPHTHERIAE, GRAVIS AND MITIS

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Anderson, Happold, McLeod, and Thomson, in 1931, described two forms of diphtheria bacilli, *gravis* and *mitis*, the former being associated with the severest cases of diphtheria with a characteristic clinical picture and a high death rate, the latter with milder attacks and a lower death rate. The main bacteriological characteristics of *gravis*, *mitis*, and *intermediate* forms were as follows:

Gravis ferments starch and glycogen; pellicle and granular deposit in broth; grey or grey-black colony on chocolate tellurite medium.

Mitis does not ferment starch or glycogen; uniform turbidity in broth; black colony (often partial inhibition of growth) on chocolate tellurite.

Intermediate does not ferment starch or glycogen; granular growth in broth.

Twelve strains which Professor McLeod kindly sent us behaved culturally in our hands exactly as he described; nine were typical *gravis* and three typical *mitis*.

IMMUNOLOGICAL EXPERIMENTS

Our first interest was in the immunological implications, for the suggestion arose from this work that the ordinary therapeutic antitoxin was relatively ineffective against infection with the *gravis* bacillus. In order to investigate this point we carried out animal experiments with "typical" *gravis* and *mitis* strains, which were either sent to us by Professor McLeod or isolated by ourselves.

Response to Antitoxin

Gravis and *mitis* strains were injected subcutaneously into groups of guinea-pigs, each guinea-pig receiving 60,000 million bacilli. After various intervals, twenty