CANCER OF THE BREAST: END-RESULTS*

MASSACHUSETTS GENERAL HOSPITAL 1921, 1922 AND 1923

BY ROBERT B. GREENOUGH, M.D., AND GRANTLEY W. TAYLOR, M.D.

HEREWITH is presented the fourth of a series of reports on the end-results of treatment of cases of cancer of the breast at the Massachusetts General Hospital covering all cases which entered the Hospital in the calendar years 1921, 1922 and 1923.

The first report of the series[1] was published in 1907, and covered the years 1894 to 1904. In this first report a three-year minimum period was employed, as was customary at that time (although the average period of observation after operation was nearly seven years), and untraced cases were omitted from consideration.

In 1921 another report (Number two) was published[2] recording the results in the series of cases which entered the hospital in the period from August, 1911 to April, 1914. In this series the five-year minimum period was adopted for end-results. At this time also a formula was devised for recording end-results in cancer cases which was designed to give a complete and balanced account of all cases entering the hospital in a given period, in order that the figures obtained in one hospital might more fairly be compared with those of another institution. This report covered a period during which, by spe-

*Read before the New England Surgical Society, September 29, 1933, at Boston.

cial assignment, almost all cases of breast cancer were allotted to the care of the surgeons who presented the report.

In 1926, a third report was published[3] giving the results in the cases of carcinoma of the breast for the years 1918, 1919 and 1920. In this series again a five-year minimum end-result period was employed, but untraced cases were omitted from consideration. In this report the employment of prophylactic x-ray treatment as an adjunct to surgery was discussed, and the significance of the histological grading of breast cancer was presented.

The current report (Number four) covers all of the cases of breast cancer which were admitted to the Massachusetts General Hospital in the calendar years 1921, 1922 and 1923, two hundred and thirty-eight in number. Twenty-three of these cases were in the private ward and from the attending surgeons, data sufficient for classification and end-results were not obtainable. Nine were reëntries (duplicates) and two cases, although entered as cancer, were proved by pathological examination not to be cancer at all. One case received no treatment and six died of causes other than cancer before the lapse of the five-year period[4]. These cases have been deducted from the 238, leaving 197 cases for study, of which 177 were primary cases and 20 recurrent after previous operation.

In the following tables and discussion, the term "Cure" applies to a case which had pathologically proved cancer of the breast, and which has shown no evidence of a recurrence for a minimum period of five years after operation. Cases which died within the five-year period without evidence of recurrent disease are omitted as inconclusive. Cases which died after five years without evidence of disease are included as "cures". Cases which died after five years

TABLE I

		1894-1904	1911-1914	1918-1920	1921-1923
A.	Total Entries	613	115	175	238
B.	Omit reëntries (duplicates)	80	8	7	9
B. i	Omit not carcinoma			2	2
C.	Omit recur. from previous op.	65	4	15	20
C. i	Omit private ward cases (no data)			17	23
C. ii	No treatment				1
D.	Cases available for study of operability, mortality	468	103	134	183
E.	Radical operations	360	74	100	148
F.	Incomplete operations	56	20	24	20
G.	No operation	52	9	10	15
H.	Operative deaths	15	0	4	5
I.	Operative mortality	3.6%	0	3%	3%
J.	Operability—rad. ops.	77%	72%	75%	80%
K.	Operability—all ops.	89%	91%	91%	91%
M.	Omit untraced	38	5	23	0
N.	Omit died within 5 yrs. without recurrence	2	3	4	6
O.	Primary cases for end-result data	428	95	107	177
P.	Radical operations	320	69	76	145
Q.	Incomplete operations	56	17	21	17
R.	No operation	52	9	10	15
S.	No. cases—alive and well	64	22	21	50
T.	No. cases died without recur. (over 5 yrs.)	7	1	0	6
U.	No. 5 yr. "cures"—all ops.	71 (3 yrs.)	23	21	56
V.	No. 5 yr. "cures"—rad. ops.	67 (3 yrs.)	22	21	52
W.	% 5 yr. "cures"—all ops.	19%	27%	21%	35%
X.	% 5 yr. "cures"—rad. ops.	21%	32%	27%	36%
X. i	% 5 yr. "cures"—rad. ops. IABC Group			30%	36%
Y.	% 5 yr. "cures"—glds. not inv.		56%	54%	62%
Y. i	% 5 yr. "cures"—glds. involved		24%	23%	21%
Z.	% cases remaining free from local recurrence after radical operation	1894-1904 52%	1911-1914 69%	1918-1920 58%	1921-1923 78%

with recurrent disease are classified as failures.

The classification of cases adopted by the American College of Surgeons has certain definite advantages for recording the degree of development of the disease, and the 197 cases of this series have been tabulated in that form.

The No. 1 indicates primary cases; No. 2 indicates recurrence after radical operation, and No. 3 indicates recurrence after incomplete operation. The letters indicate the extent of disease, as follows:

A. Process confined to the breast, axillary nodes not involved.
B. Axillary nodes doubtful.
C. Axillary nodes involved.
D. Supraclavicular nodes involved.
E. Remote metastases.
F. Other breast involved.

This tabulation shows five-year "cures" in 29 per cent of all cases entering the hospital. It includes primary and recurrent cases, those

TABLE II

	Cases	Cures	Per Cent
1 A Group—Axilla not involved	50	31	62
1 B Group—Axilla doubtful	2	2	
1 C Group—Axillary nodes involved	111	23	21
1 A B C Group—Operable Cases	163	56	34
1 D Group—Supraclavicular Nodes involved	6	0	
1 E Group—Remote metastasis	7	0	
1 F Group—Other breast involved	1	0	
1 D E F Group—Inoperable Cases	14	0	
Total Primary Cases	177	56	32
2. Recurrent after Radical Operation	11	0	
3. Recurrent after Palliative Operation	9	0	
Total All Entries	197	56	29

treated by operation, whether radical or palliative; and those not operated on at all; a salvage of nearly one in three of all cases. One hundred and seventy-seven primary cases, including advanced and inoperable cases, gave 32 per cent five-year successes, and primary cases of the so-called operable class (no disease evident beyond the axilla) gave 34 per cent cures. In the early favorable cases (axillary glands not found to be diseased on pathological examination) the five-year "cures" are 62 per cent.

There were one hundred and forty-five radical operations in this series, by which is understood the removal of the whole breast, the skin over the breast, both pectoral muscles, the axillary contents to the clavicle, and the deep fascia from sternum to latissimus and from clavicle to epigastrium. These radical operations yielded fifty-two or 36 per cent five-year "cures".

The clinical criterion of operability has been a tumor movable on the chest wall with at most small movable axillary metastases. We have gradually narrowed the field of operability in the course of the years covered by these reports. Skin nodules, large or fixed axillary nodes, a swollen arm, and supraclavicular fullness have been recognized as contraindications to operation. Routine preoperative x-ray study of the bones and chest for determination of the presence of remote metastases was not followed in all cases of this series although it has since then come into general use. Care in history and examination of the patient, and clinical alertness in interpreting backache or dyspnea have gradually become more common.

The so-called "inflammatory" type of carcinoma of the breast is now generally recognized as not curable by operation. The development of effective palliative treatment in the form of radiation has made us less willing to recommend

operation in poor risk patients. These factors alone even without consideration of such improvements in operative technique as we believe developed prior to this period, should entitle us to show progressive improvement in our cures by operation in successive series of cases. It is probable that with greater attention to these factors, many of the deaths which occur within the first six months after operation could be avoided.

The figures for the percentage of five-year "cures" from radical operation in operable cases (1A—1B—1C—A. C. S. Classification) for the previous series are presented for comparison.

TABLE III

1904 (3 yrs.)	1914 (5 yrs.)	1920 (5 yrs.)	1923 (5 yrs.)
16%	32%	30%	36%

It is of interest to note that during the three-year periods ending in 1914 and 1923, Breast Cancer was a special assignment, while in the 1904 and 1920 series, cases were distributed over the regular surgical services.

There were seventeen incomplete or palliative operations in this series with four five-year "cures" or 23 per cent. In fifteen cases no operation was attempted and the patients were given x-ray treatment. None of these patients survived five years. While the fact is already well established it is to be emphasized that nothing short of the complete radical operation can be expected to give the patient the chance to which she is entitled to be cured of cancer of the breast.

The classical measurement of the degree of extension of cancer of the breast is the involvement of the axillary lymph nodes as shown by

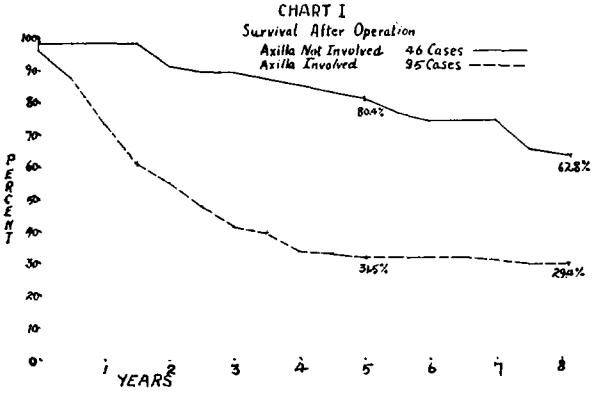
pathological examination of the tissue. The clinical estimate of axillary involvement is, however, erroneous in a considerable proportion of cases. Thus in this series 16 out of 50 in the 1-A group were thought on clinical examination to have involved axillary nodes, which were proved on pathological examination to be free from disease (32%). On the other hand 24 out of 111 (22%) showed no clinical evidence of enlarged nodes, although on pathological examination after removal, cancer proved to be present.

It is true also that cancer in certain regions of the breast, notably the median hemisphere and the upper inner quadrant, may extend to the internal mammary chain of nodes within the chest, or directly to the supraclavicular nodes, before reaching those in the axilla. In spite of these inaccuracies, however, the involvement of axillary nodes is still our most valuable measure of the extent of the disease.

In this series there were 50 cases in the 1 A group (axillary nodes not involved) with 31, or 62 per cent five-year cures. There were 111 cases in the 1 C group (axillary nodes involved) with 23, or 21 per cent, five-year cures. The six cases in which the supraclavicular nodes were enlarged gave no cures (in spite of one attempt to dissect the supraclavicular region), and the cases of remote metastases, and the one case of bilateral involvement were also failures. The postoperative survival of the 1 A and 1 C cases is shown in chart I.

We have some reason to doubt the accuracy of clinical data as regards the duration of cancer of the breast. In the present series of cases preoperative duration of over two years was arbitrarily reduced to two years. On this basis, the average preoperative duration for 107 cases treated by radical operation was found to be 8.2 months. Of this number 78 were failures, with an average preoperative duration

of 9.1 months. There were 29 five-year cures with an average preoperative duration of 5.7 months. Among the cured cases, however, there were at least three patients who reported a preoperative duration of two years or more. In a previous series (1918-1919-1920) it was found that in 39 cases with greater than the average duration there were 10 cures (26%), while in 52 cases with less than the average duration there were 12 cures (23%). In the present series the average preoperative duration in the



1 A cases (nodes not involved) was 7.2 months. The cures in this group averaged 6.2 months' duration, and the failures 8.7 months' duration. The average preoperative duration in the 1 C group (axillary nodes involved) was 8.7 months. The cures in this group averaged 5.7 months, and the failures 9.3 months. In view of these figures we must admit that however important the duration of the tumor may be in the individual case, its value in group prognosis is limited.

It is frequently suggested that cancer of the breast has a much graver prognosis in young women than in older women. When our cases

are divided into two groups, those over 50 years of age, and those less than 50 (the approximate mean age of the group) it is found that the cures are respectively 34.5 per cent and 32.8 per cent. In a series as small as this one, the difference is not significant. When the cases are divided into three groups, however, those under 45 years of age, those from 45-60 inclusive, and those over 60, the percentage cures are respectively 22.2 per cent, 40 per cent and 45 per cent. About half the cases fall into the middle group, and roughly a quarter each into the young and old groups. These figures therefore do emphasize strikingly the relatively greater gravity of the disease in younger women.

The pathological classification of breast cancer as to the degree of malignancy as indicated by the cellular architecture and histology has been followed out in this series of cases. The criteria on which the grading was done have been described elsewhere[5]. Since the original report we have been obliged to give consideration to an additional factor, "infiltration". This is a condition found occasionally even in cases of relatively pure adenocarcinoma or medullary growth, in which the tumor cells in one place or another have broken out from their elsewhere typical conformation and have infiltrated the fat and fibrous tissue in the neighborhood in columns of a more scirrhous type. This appearance we regard as a marked step in de-differentiation, and thus an indication of high malignancy. The present series yielded 122 cases of radical operations with known five-year results, of which the microscopic slides were obtainable for review. The examination of these slides was made by Dr. H. F. Hartwell and Dr. R. B. Greenough. The grading was done without knowledge of the end-results, and in only five cases were there serious differences of opin-

ion between the two observers; and these were readily composed on further study and discussion.

The results are shown in table IV, which presents also the percentages of cures from the previous series for comparison.

TABLE IV

DEGREE OF MALIGNANCY IN RELATION TO CURES

	Cases	Cures	Per Cent	'18, '19, '20 Series Per Cent
Axilla Not Involved				
Grade I	8	8	100	82
Grade II	29	17	59	43
Grade III	5	0	0	0
Axilla Involved				
Grade I	1	1	100	50
Grade II	42	13	31	31
Grade III	37	1	3	0

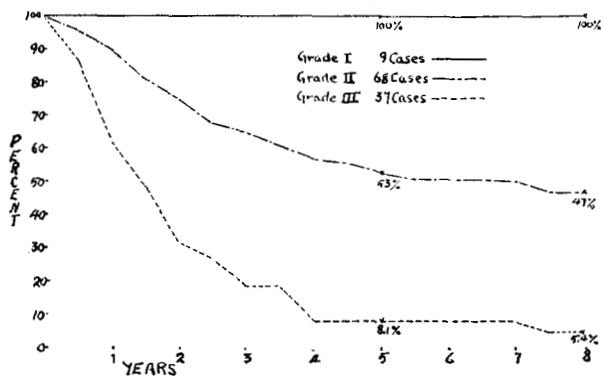
The grade of malignancy in relation to the duration of postoperative life is shown in chart II.

In this series the number of low-grade tumors is lower than in the previous series. The percentages, however, are not materially different. One notable exception exists to the general rule, namely, the single case in the Grade III, I C group which is alive and well, now nine years after operation. This case has been reviewed and discussed, but shows so great a degree of pleomorphism and so complete a degree of de-differentiation that it is impossible to grade it other than as a highly malignant tumor.

The application of this classification of the degree of malignancy of a breast cancer to the prognosis of the individual case must be made with considerable reservation. We must recognize that every case of breast cancer is ca-

pable of causing the death of the patient. Again the extent of the disease is of the greatest significance. Other things being equal, however, we may say that a tumor of low-grade malignancy does not extend so widely nor so promptly from the point of origin, and thus the opportunity for successful removal is greater than in the middle group, and far, far greater than in tumors of high malignancy. That 42 out of 122, or 34 per cent of this series fell in the high-grade group indicates that a very considerable number of cases of cancer of the breast are still beyond the hope of surgical relief. However, unless our present idea of the origin of cancer as a local process is incorrect, there

CHART II
Survival After Operation



is no reason why earlier and earlier recognition of the disease should not give us more and more cures even in the cases of high-grade malignancy.

The significance of the grading for prognosis may be considered also from the viewpoint of preoperative duration of the disease. It will be noted that all the Grade I cases were cured and that with one exception all the Grade III cases

were failures. The average preoperative duration for both groups was the same, namely eight months. The Grade II cases without axillary involvement presented an average duration of 5.3 months in the cured cases, and of eight months in the failures. The Grade II cases with axillary involvement averaged 4.6 months in the cured cases and 10.3 months in the failures.

Axillary metastases were present at the time of operation in 11 per cent of Grade I cases, 70 per cent of Grade II cases, and 90 per cent of Grade III cases.

An attempt was made to determine the possible danger of exploratory incision in cases of doubtful diagnosis. Definite exploration of the tumor was made in 27 cases, including a few in which several days elapsed between simple mastectomy and radical operation. This group presented 15 cures (55.5%). It should be realized that cases in which exploration is indicated are in general very early cancers, and that the curability is high in this group. Certainly the figures give no ground for supposing that exploration is prejudicial to cure. We are strongly of the belief, however, that exploration or excision of a doubtful breast tumor should never be undertaken unless facilities for a frozen section diagnosis, and for the completion of the radical operation at the same sitting, are available.

In addition to radical operation, 125 cases received either preoperative or postoperative prophylactic x-ray therapy. These cases gave 48 or 38 per cent five-year cures. The 13 cases which did not have x-ray therapy yielded only four, or 31 per cent cures. The relatively small number of cases in the latter group makes this percentage difference of little or no significance.

Only 11 cases received preoperative x-ray therapy, with nine failures and two successes. Seven

of these cases also received postoperative x-ray therapy.

Virtually all the x-ray cases were treated either by Dr. G. W. Holmes at the Massachusetts General Hospital, or by Dr. L. B. Morrison of Boston. During this period Dr. Holmes was using a Waite and Bartlett machine, 5 milliamperes, 16 inch distance, 3 mm. aluminum filter, 80 K.V., later equipped with boosters to yield 200 K.V. Dr. Morrison used an Acme machine, 140 K.V., 12 inch distance. For preoperative treatment 1 erythema dose was given. For postoperative treatment usually two erythema doses were given in one series of 12 to 14 weeks.

It is regrettable that opportunity for comparison of similar series with and without prophylactic radiation is not available at this time. With the data available, however, we are forced to admit that prophylactic x-ray treatment gave slightly better five-year results in this series than in the previous series, and that the improvement in the end-results of this series may well be due in part at least to the more general use of x-ray. It should be noted, however, that in the 1918-1919-1920 series the I A cases (glands not involved) formed only 25 per cent of the whole series, while in the present group the percentage of I A cases has risen to 28. Final conclusions in regard to the value of prophylactic x-ray, therefore, are scarcely justified from these statistics.

SUMMARY AND CONCLUSIONS

1. A consecutive series of cases of cancer of the breast entering the Massachusetts General Hospital in the years 1921-1922-1923 is reported with the five-year end-results.

2. In comparison with previous series, the percentage of five-year cures has gradually in-

creased since 1904. Greater care in estimation of the operability may be expected to increase the percentage of five-year cures.

3. Twenty-nine per cent of all cases entering the hospital are free from disease more than five years, and 36 per cent of the cases of radical operation are free from disease more than five years.

4. The extent of the disease as determined by pathological examination of the tissues removed at operation is of the greatest importance in prognosis.

5. The preoperative duration of the tumor as recorded by the patient is of relatively little value in prognosis.

6. Cancer of the breast in young women is less curable than cancer in older women.

7. The histological grading of the degree of malignancy of the tumor is of great importance in prognosis, but it must be considered in connection with the extent of the disease and with other factors affecting the prognosis.

8. Tumors pathologically of high-grade malignancy metastasize early to the axillary lymph nodes and elsewhere.

9. Exploratory incision or excision of a breast tumor, properly performed, does not prejudice the chance of cure.

10. Prophylactic x-ray therapy was employed almost as a routine in this series, and the improved results in the series may be in part due to this treatment.

11. Further reduction of the mortality from cancer of the breast depends today chiefly upon further education of the public and of the profession to regard seriously and to treat promptly and properly any abnormality of the breast.

NOTE: The writers acknowledge gratefully the assistance of Dr. Charles E. Dumas of Boston in

reviewing the radiation therapy given in these cases, and of Dr. Harry F. Hartwell in the study and grading of the pathological material.

REFERENCES

1 Greenough, R. B.; Simmons, C. C., and Barney, J. D.: The results of operations for cancer of the breast at the Massachusetts General Hospital from 1894 to 1904. Surg. Gynec. & Obst. 5: 39 (July) 1907.

2 Greenough, R. B., and Simmons, C. C.: End-results in cancer cases. Cancer of the breast. Boston M. & S. J. 185: 253 (Sept.) 1921.

3 Greenough, R. B.: Carcinoma of the breast. Results of treatment 1918-1919-1920. Am. J. Roentgenol. 16: 439 (Nov.) 1926.

4 No. 2, age 66. Died strangulated hernia, 21 mos.
No. 31, age 76. Died heart disease (autopsy), 55 mos.
No. 68, age 75. Died cerebral hemorrhage, 26 mos.
No. 118, age 74. Died myocarditis, 14 mos.
No. 162, age 87. Died cardiorenal, 44 mos.
No. 177, age 47. Died carcinoma stomach, 14 mos.

5 Greenough, R. B.: Varying degrees of malignancy of cancer of the breast. J. Cancer Research. 9: 453 (Dec.) 1925.

Printed in the U. S. A.