

# FACTORS INFLUENCING PROGNOSIS IN CARCINOMA OF THE BREAST \*

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THERE are many excellent articles in the literature concerning the prognosis of carcinoma of the breast. Many surgeons have studied this from the clinical viewpoint and many pathologists have attempted to estimate the prognosis upon an histologic study of the tumor. There have been very few reports correlating clinical and pathologic study.

A clinical classification is presented. The histologic classification of Haagensen is used. It is hoped that these classifications may be used in future studies at larger hospitals and clinics. In this way we may learn the prognosis of cases of certain extent and microscopic type. Thus we may determine, for example, that a carcinoma of the breast with only pectoral gland metastasis of a comedo carcinoma type results in a certain percentage of cures. This is much more satisfactory than stating that one surgeon cures 35 per cent of his cases while another cures only 25 per cent. The former surgeon probably sees earlier stages of the disease due to caring for a more intelligent class of people.

A standard method of study of these cases, giving both clinical and microscopic types and stages of the disease, should have approximately the same results if treated similarly. After finding these results, the value of various forms of treatment can be better determined.

This study is based upon a careful review of 60 cases of carcinoma of the breast cared for in private practice at Immanuel Hospital by my father, B. B. Davis, and myself, also upon 23 cases at the University of Nebraska Hospital treated by various surgeons. In both groups the study begins at the earliest date that microscopic sections of the tumors were kept for record. This began at Immanuel Hospital in 1922, and at the University of Nebraska Hospital in 1927. No cases are included that were admitted for treatment later than 1932, so that there are at least four years intervening since they were first seen. I have personally reviewed the histories, studied the microscopic sections and obtained reports of their present condition. No effort is being made to prove any certain fact but the study is made merely to see what the results have been. It is realized that this series of cases is far too small to justify one in drawing very definite conclusions from them.

In the operable cases the treatment was radical mastectomy by one of the standard methods, removing the breast and dissecting out the axilla, with re-

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removal of the lymph nodes there. Exception was made in only three cases. In these a simple mastectomy without axillary dissection was performed. In addition to radical mastectomy, postoperative roentgen-therapy was carried out in ten cases and preoperative radiation in three. In recent years I have used preoperative radiation much more frequently. Recurrence has usually been treated by irradiation and occasionally by local excision.

TABLE I  
BREAST CASES

Hospital	Cases Studied	Benign Microscopically	CARCINOMA				
			Primary Operable			Recurrent	
			Total	No.	Per Cent	No.	Per Cent
Immanuel 1922-1932 (private cases)....	60	6	51	51	94	3	6
University 1927-1932.....	23	2	19	15	71	2	9
Totals.....	83	8	70	66	88	5	7

TABLE II  
PRIMARY BREAST CARCINOMA  
OPERABLE CASES  
*Results—November, 1936*

Hospital	Total	Operated	Results Known	WELL				DEAD				Total	
				No.	Per Cent	Carcinoma Deaths		Operative Deaths		Other Causes		No.	Per Cent
						No.	Per Cent	No.	Per Cent	No.	Per Cent		
Immanuel..	51	51	41	12	29	25	61	2	5	2	5	29	70
University.	15	14	13	4	31	8	61	1	7	0	0	9	69
Total...	66	65	54	16	30	33	61	3	6	2	3	38	70

In the early years of the study, six cases in the Immanuel Hospital series were diagnosed on their records as carcinoma which, on study of the sections, I believe were benign. Four of these I know to be well but have not been able to follow-up the other two. The diagnosis in 54 cases was carcinoma, checked either by microscopic section or by death from metastases. Fifty-one of these cases were operated upon. I know the results in 41, 12 of which are well now, which is a period of four to 14 years after operation. This is 29

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per cent of the traced cases. The percentage of five-year so-called cures is actually higher as several of the cases reported as dead were well for longer than five years. Besides this, two cases had operative deaths and two died of causes unrelated to the carcinoma.

Of 13 traced University Hospital cases, four, or 31 per cent, are now well. In the combined series I know the results in 54 out of 65 operated cases. Of the 54, 16 cases, or 31 per cent, are well while 33 cases, or 61 per cent, are dead as a direct result of the carcinoma. The other eight deaths were not due to carcinoma itself.

The average age of the patients upon admission was 53½ years. The youngest proved case was 28. Most of the cases previously diagnosed carcinoma, but which I consider benign, were of the younger age groups. The oldest case was 80.

TABLE III  
AGE INCIDENCE

Age	Immanuel				University				Total			
	No.	Unknown	Result		No.	Unknown	Result		No.	Unknown	Result	
			Well	Dead			Well	Dead			Well	Dead
20-29..	0	0	0	0	1	0	0	1	1	0	0	1
30-39..	5	0	1	4	1	0	0	1	6	0	1	5
40-49..	12	4	5	3	9	2	1	6	21	6	6	9
50-59..	23	2	5	16	5	0	1	4	28	2	6	20
60-69..	9	3	1	5	3	0	1	2	12	3	2	7
70-79..	3	1	0	2	2	0	1	1	5	1	1	3
80.....	1	0	0	1	0	0	0	0	1	0	0	1
Age not stated.	1	1	0	0	0	0	0	0	1	1	0	0
Totals..	54	11	12	31	21	2	4	15	75	13	16	46

It is seen that 61 cases, or 81 per cent, were between the ages of 40 and 69. The series is inconclusive in proving any age group more malignant than the others. A much larger series of cases is needed.

Chart 1 indicates that the private cases came for treatment somewhat earlier than the University Hospital cases. In the former, 16 were operated upon within a month of the time of the first symptom. In the University Hospital series only two presented themselves that early and one of those was admitted for trouble other than the carcinoma of the breast, which was discovered in the course of the routine physical examination. Thirty-six, or 67 per cent, of the private cases were seen within two months of the onset. During the same length of time only five, or 24 per cent, of the University Hospital cases were admitted. In another series of 60 cases at the University

Hospital which was reviewed two years ago it was found that 50 per cent had had symptoms for over one year before admission.

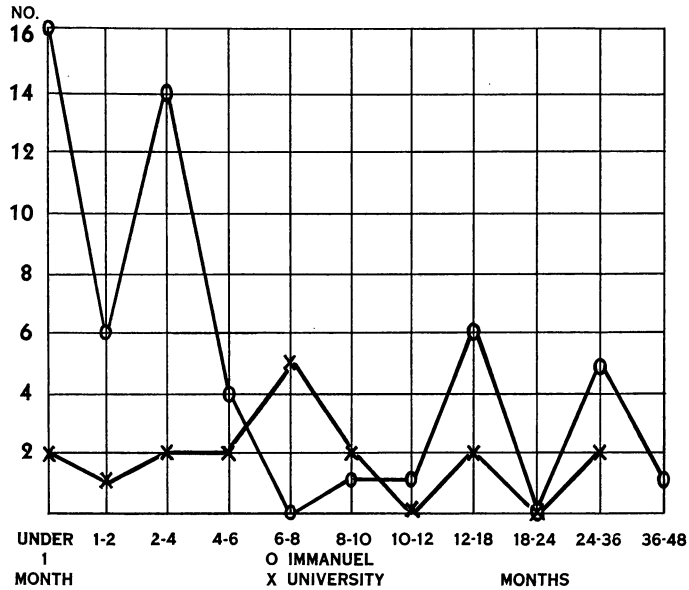


CHART 1.—Showing duration of tumor previous to admission.

Chart 2 shows that 75 per cent of the cases still well were operated upon within six months of the onset and 25 per cent between six and 12 months. There was not a single cure in cases of one year or over. This proves very

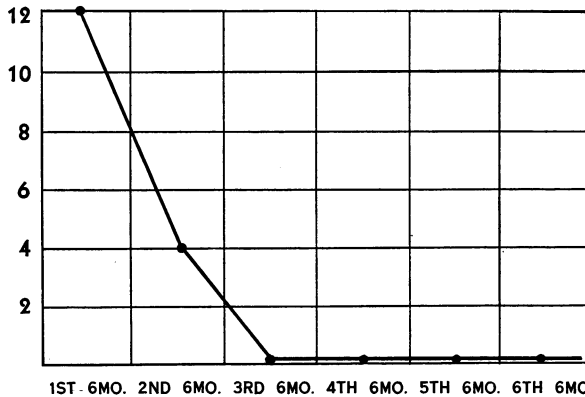


CHART 2.—Shows the precipitant decrease of favorable prognoses, predicated upon the duration of the disease previous to admission.

conclusively that early diagnosis and treatment are very essential in the cure of carcinoma of the breast. The question of the advisability of surgery for cases of long duration is raised.

Aside from the duration of disease, a knowledge of the extent of it is im-

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portant in determining prognosis. For this purpose the following clinical classification is presented:

- P\*1—Early, nonadherent tumor without metastasis
- P 2—Tumor adherent to skin or fascia without metastasis
- P 3—Tumor with only pectoral node metastasis
- P 4—Tumor with general axillary node metastasis
- P 5—Tumor involving pectoral fascia with axillary node metastasis
- P 6—Large bulky tumor
  - (a) Without axillary node metastasis
  - (b) With axillary node metastasis
- P 7—Tumor with skin metastasis
- P 8—Tumor with bone metastasis
- P 9—Tumor with intrathoracic metastasis
- P10—Tumor with several types of distant metastases
- P11—Bilateral breast tumor
- P12—Carcinoma during pregnancy or lactation
- R 1—Local recurrence in scar
- R 2—Metastasis to skin
- R 3—Axillary involvement
- R 4—Distant recurrence
  - (a) Bony
  - (b) Intrathoracic
  - (c) Cerebral
  - (d) Abdominal

\*P = Primary. R = Recurrent.

Of the primary classes, the first six, and possibly the last two, may be operable. Class 7 may possibly be made operable by preoperative irradiation. Classes 8 to 10 inclusive are distinctly inoperable and palliation only can be considered.

TABLE IV  
CLINICAL CLASSIFICATION OF BREAST CARCINOMA

	Immanuel	University	Total
P*1.....	24	1	24
P 2.....	1	5	6
P 3.....	9	2	11
P 4.....	10	4	14
P 5.....	0	0	0
P 6a.....	0	0	0
P 6b.....	5	2	7
P 7.....	0	1	1
P 8.....	0	1	1
P 9.....	0	0	0
P10.....	1	2	3
P11.....	0	0	0
P12.....	1	0	1
Not stated.....	0	1	1
Totals.....	51	19	70

\* P = Primary

Most of the recurrent cases are inoperable, with the possible exception of those occurring in Class I, *i.e.*, local recurrence. With adequate radical mastectomy this is rare.

As the private cases were seen sooner after the onset, the clinical class in general is lower than in the University Hospital cases. Forty-four cases, or 86 per cent, of the Immanuel Hospital cases were of one of the first four clinical classes, while only 12 cases, or 63 per cent, of the University Hospital cases were in these classes.

TABLE V  
PERCENTAGE OF CURES DEPENDING UPON CLINICAL EXTENT

	Total	Well		Dead		Unknown	
		No.	Per Cent	No.	Per Cent	No.	Per Cent
P 1.....	25	10	40	10	40	5	20
P 2.....	6	3	50	3	50	0	0
P 3.....	11	2	18	6	55	3	27
P 4.....	14	0	0	13	93	1	7
P 5.....	0	0	0	0	0	0	0
P 6a.....	0	0	0	0	0	0	0
P 6b.....	7	1	14	4	57	2	29
P 7.....	1	0	0	1	100	0	0
P 8.....	1	0	0	1	100	0	0
P 9.....	0	0	0	0	0	0	0
P 10.....	3	0	0	3	100	0	0
P 11.....	1	0	0	1	100	0	0
P 12.....	0	0	0	0	0	0	0
?.....	1	0	0	0	0	1	100
Totals.....	70	16	23	42	60	12	17

Table V shows that the cures decrease rapidly when gross metastases are found in the axilla.

While Types P1 and P2, which are the cases with no demonstrable axillary metastases, give at least 40 to 50 per cent of cures, even low axillary metastases result in only 18 per cent now reported as well. There is only one case now well in which the cancer had spread to the other axillary nodes. This raises the question of the advisability of very thorough dissection of the central and infraclavicular groups of axillary nodes lying along the course of the axillary vein. If the results are so poor, may it not be better to leave these high axillary nodes and so decrease the number of cases of postoperative swelling of the arm? A larger series of cases would be necessary to decide this question.

Histologically I am using the classification of Haagensen. It considers: (1) The manner of growth of cells; (2) cell morphology; and, (3) the reaction of the stroma. In detail it is as follows:

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TABLE VI  
HAAGENSEN'S HISTOLOGIC CLASSIFICATION

Manner of Growth of Cells

- (1) Papillary: Origin in a cyst formed in a duct
- (2) Comedo: Growth mainly within ducts
- (3) Plexiform: Growth in plexiform strands
- (4) Adenoid arrangement of cells

Cell Morphology

- (5) Size of cells
- (6) Size of nuclei
- (7) Variation in size and shape of nuclei
- (8) Hyperchromatism of nuclei
- (9) Number of mitoses
- (10) Secretory activity of cells
- (11) Clearness of cytoplasm

Reaction of Stroma

- (12) Fibrosis
- (13) Hyaline degeneration
- (14) Lymphocytic infiltration
- (15) Gelatinous degeneration
- (16) Invasion of lymphatics

Let us now consider the manner of growth of cells. The results in the cases under consideration are as follows:

	Total	Well		Dead		Unknown	
		No.	%	No.	%	No.	%
(1) Papillary.....	2	0	0	2	100	0	0
(2) Comedo.....	15	5	33	7	47	3	20
(3) Plexiform.....	37	9	24	22	60	6	16
(4) Adenoid.....	8	3	38	4	50	1	12
Totals.....	62	17	27	35	57	10	16

Two died of shock of operation. Two died of other disease.

Different parts of the same tumor may be of quite different histologic types. Even in a single microscopic section there may be several types very distinctly represented. In following Haagensen's classification with four types, depending upon manner of growth of cells, we found two distinct types in nine cases, three types in three, and all four types in one case. We classified these cases in the prevailing type from the sections studied. Therefore, histologic grading is definitely subject to error.

How does the growth of cells histologically affect each of these classes?

CLASS PI—EARLY NONADHERENT TUMOR WITHOUT METASTASES

	Total	Well	Dead	Unknown
Papillary.....	0	0	0	0
Comedo.....	10	4	3	3
Plexiform.....	9	3	5	1
Adenoid.....	3	2	0	1
Not stated.....	3	1	2	0
Totals.....	25	10	10	5
Per cent.....		40%	40%	20%

## CLASS P2—TUMOR ADHERENT TO SKIN WITHOUT METASTASES

	Total	Well	Dead	Unknown
Papillary.....	0	0	0	0
Comedo.....	1	1	0	0
Plexiform.....	5	2	3*	0
Adenoid.....	0	0	0	0
	—	—	—	—
Totals.....	6	3	3	0
Per cent.....		50%	50%	

\* One was an operative death

## CLASS P3—TUMOR WITH ONLY PECTORAL NODE METASTASES

	Total	Well	Dead	Unknown
Papillary.....	1	0	1*	0
Comedo.....	1	0	1	0
Plexiform.....	5	2	1	2
Adenoid.....	3	0	2†	1
Not stated.....	1	0	1	0
	—	—	—	—
Totals.....	11	2	6	3
Per cent.....		18%	55%	27%

\* Had local excision; 1 yr., 9 mos. later, radical mastectomy. Died 12 yrs. after first operation.

† One died of cerebral hemorrhage suddenly several years after operation.

## CLASS P4—TUMOR WITH GENERAL AXILLARY NODE METASTASES

	Total	Well	Dead	Unknown
Papillary.....	0	0	0	0
Comedo.....	2	0	2	0
Plexiform.....	10	0	9*	1
Adenoid.....	2	0	2	0
	—	—	—	—
Totals.....	14	0	13	1
Per cent.....			93%	7%

\*(1) One died of shock four days after operation. (2) One died of apoplexy 1 yr. after operation. (3) Had tumor for 2 yrs. before operation and died 5½ yrs. after onset.

In Classes 5 and 6a there were no cases.

## CLASS P6B—LARGE BULKY TUMOR WITH AXILLARY NODE METASTASES

	Total	Well	Dead	Unknown
Papillary.....	0	0	0	0
Comedo.....	0	0	0	0
Plexiform.....	6	1*	3	2
Adenoid.....	1	0	1†	0
	—	—	—	—
Totals.....	7	1	4	2
Per cent.....		14%	57%	29%

\* Age 51, tumor 1 yr. Very large ulcerating mass with bulky axillary metastases. Had considerable adenoid type also. Performed simple mastectomy only, postoperative roentgenotherapy. Still well 12 yrs. after onset.

† Died four days postoperative of shock.



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CLASS P7—TUMOR WITH SKIN METASTASES

One case, 6 mos. duration, roentgenotherapy only. Died 9 mos. from onset. No microscopic section.

CLASS P8—TUMOR WITH BONE METASTASES

One case, 2 mos. duration, roentgenotherapy to spine. Died 4 mos. after onset. No microscopic section.

CLASS P10—TUMOR WITH SEVERAL TYPES OF DISTANT METASTASES

	Total	Well	Dead
Papillary . . . . .	0	0	0
Comedo . . . . .	0	0	0
Plexiform . . . . .	1	0	1
Adenoid . . . . .	0	0	0
No section . . . . .	2	0	2
	—	—	—
Totals . . . . .	3	0	3
Per cent . . . . .			100%

CLASS P11—BILATERAL BREAST TUMOR

Case, age 42. Second breast operation—radical mastectomy. Five years before had first radical mastectomy of other breast. Died 7 yrs. after onset.

An interesting fact in the above study is that, while both cases of a papillary carcinoma, which is usually considered not highly malignant, died, they each lived a considerable time. The case in private practice, age 50, had a tumor for two years before treatment, and it had invaded the pectoral lymph nodes. This case lived 12 years. The case at the University Hospital, age 55, also had a tumor for two years before treatment with invasion of all the axillary nodes. She was given preoperative roentgenotherapy followed by a radical mastectomy. She lived 5 1/3 years from the date of onset. In both of these cases the ultimate death may be attributed to the delay in institution of treatment. This series of cases, again, is too small from which to draw definite conclusions.

Using the above classification, Haagensen divided the cases histologically into three grades :

(I) When papillary or comedo, when adenoid arrangement of cells was marked, when gelatinous degeneration was present, or if lacking any of these preceding characteristics, when variation in the size and shape of the nuclei was slight and there were but few mitoses.

(II) All others.

(III) Highly malignant tumors. Absence of adenoid arrangement, marked variation in the size and shape of nuclei, and numerous mitotic figures. If any two of these three present—Grade 3.

What are the results in the various grades in each clinical class considered separately?

## CLASS P1—EARLY NONADHERENT TUMOR WITHOUT METASTASES

	Total	Well	Dead	Unknown
Grade 1 . . . . .	11	7	1	3
Grade 2 . . . . .	6	1	3	2
Grade 3 . . . . .	5	1	4	0
Unknown . . . . .	3	1	2	0
	—	—	—	—
Totals . . . . .	25	10	10	5
Per cent. . . . .		40%	40%	20%

## CLASS P2—TUMOR ADHERENT TO SKIN WITHOUT METASTASES

	Total	Well	Dead	Unknown
Grade 1 . . . . .	1	1	0	0
Grade 2 . . . . .	3	0	3*	0
Grade 3 . . . . .	2	2	0	0
	—	—	—	—
Totals . . . . .	6	3	3	0
Per cent. . . . .		50%	50%	

\* One was an operative death.

## CLASS P3—TUMOR WITH ONLY PECTORAL NODE METASTASES

	Total	Well	Dead	Unknown
Grade 1 . . . . .	5	1	3*†	1
Grade 2 . . . . .	4	1	1	2
Grade 3 . . . . .	1	0	1	0
Not stated . . . . .	1	0	1	0
	—	—	—	—
Totals . . . . .	11	2	6	3
Per cent. . . . .		18%	55%	27%

\* Had local excision; 1 yr., 9 mos. later, radical mastectomy.  
Died 12 yrs. after first operation.

† One died of cerebral hemorrhage, suddenly, several years after operation.

## CLASS P4—TUMOR WITH GENERAL AXILLARY NODE METASTASES

	Total	Well	Dead	Unknown
Grade 1 . . . . .	5	0	5*	0
Grade 2 . . . . .	3	0	3	0
Grade 3 . . . . .	6	0	5	1
	—	—	—	—
Totals . . . . .	14	0	13	1
Per cent. . . . .		0%	93%	7%

\* Tumor for 2 yrs. before operation, died 5½ yrs. after onset.  
One died of apoplexy 1 yr. after operation. One died of shock 4 days after operation.

## CLASS P6B—LARGE BULKY TUMOR WITH AXILLARY NODE METASTASES

	Total	Well	Dead	Unknown
Grade 1 . . . . .	1	0	1*	0
Grade 2 . . . . .	1	0	1	0
Grade 3 . . . . .	5	1	2	2
	—	—	—	—
Totals . . . . .	7	1	4	2
Per cent. . . . .		14%	57%	29%

\* Died of shock 4 days postoperative.

The result of summarizing the statistics noted in the preceding tabulations, relative to the question of grading, is appended.

	No.	Total		Well		Dead		Unknown	
		Cent	No.	Cent	No.	Cent	No.	Cent	
Grade 1.....	23	100	9	39	10	44	4	17	
Grade 2.....	17	100	2	12	11	65	4	23	
Grade 3.....	19	100	4	21	12	63	3	16	
Unknown.....	4	100	1	25	3	75	0	0	

It is to be noted that we obtain distinctly better results in Grade 1 than in Grades 2 and 3. Unexpectedly, the results are a little better in Grade 3 than in Grade 2. This would probably not be true for a large series.

SUMMARY

(1) A method of study is presented to determine the prognosis in carcinoma of the breast. This considers both the clinical extent of the carcinoma and the histologic study.

(2) A new clinical classification depending upon the extent of the growth is discussed.

(3) The histologic classification of Haagensen is used.

(4) This study is based on 75 cases of proved carcinoma of the breast.

(5) The most important factors in determining prognosis are delay in institution of treatment and the extent of the disease.

(6) The histologic classification seems to be of less importance than the clinical study, but has a definite value.

(7) No attempt has been made to determine the value of various forms of treatment.

(8) It is realized that this series of cases is quite small. It is hoped that this method of study may be adopted at larger clinics so that a greater number of cases may be followed.