

Section of Pathology

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Histological Grading of Rectal Cancer

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THIS paper will try to answer the question "To what extent is it possible to base prognosis on the histological characters of cancer of the rectum?" We all know that these malignant growths may be very dissimilar in microscopic structure, some being anaplastic and others relatively well differentiated. In reporting on these tumours the pathologist may qualify his description by such expressions as "highly malignant" or "relatively benign". Such terms as these, however, may be used with different connotations by different persons and there is an obvious advantage in the adoption of some fixed standard.

MALIGNANCY GRADES

The system of grading tumours described by Broders supplies such a standard [1, 2, and 3]. It can be applied easily to malignant growths of the adenocarcinoma type provided one bases the judgment on a general survey and not on a single field of the microscope. Actually the decision as to the grade of malignancy is dependent more on the arrangement of the cells than on the relative number of so-called undifferentiated cells. This is shown by the accompanying photomicrographs of typical examples of Grade 1, 2, 3, and 4, tumours and colloid growths (figs. 1, 2, 3, 4, and 5). The essential points are that Grade 1 tumours closely resemble a benign growth and can only be distinguished as malignant because of evidence of invasion. In Grade 2 the tumour cells are less differentiated but grouped in fairly regular acini. There is evidence of more rapid epithelial proliferation in Grade 3, the tumour cells being arranged in irregularly folded rings or clumps. In Grade 4 the malignant cells are very anaplastic and do not form gland-like structures, but pervade the tissues singly or in small irregular clumps.



FIG. 1.—Grade 1.

× 50



FIG. 2.—Grade 2.

× 50

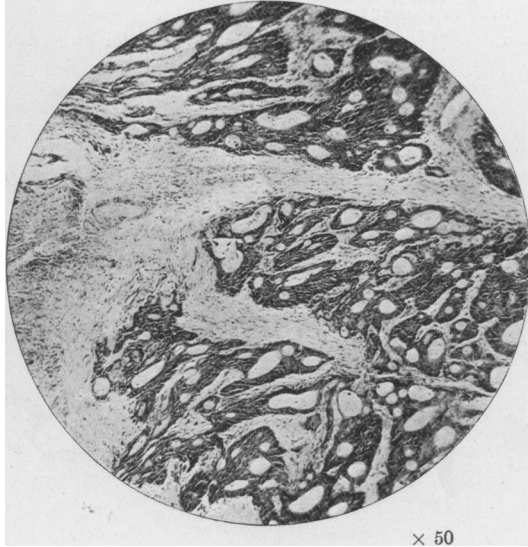


FIG. 3.—Grade 3.

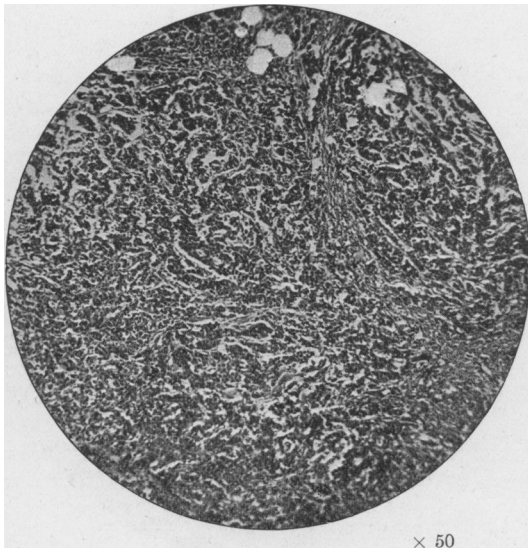


FIG. 4.—Grade 4.

I have graded more than 600 cases of cancer of the rectum and am convinced that this is a natural and practical system of classification. The first 200 of these were graded more than five years ago. These have all been kept in touch with by the follow-up system, and the striking differences in the prospect of survival have

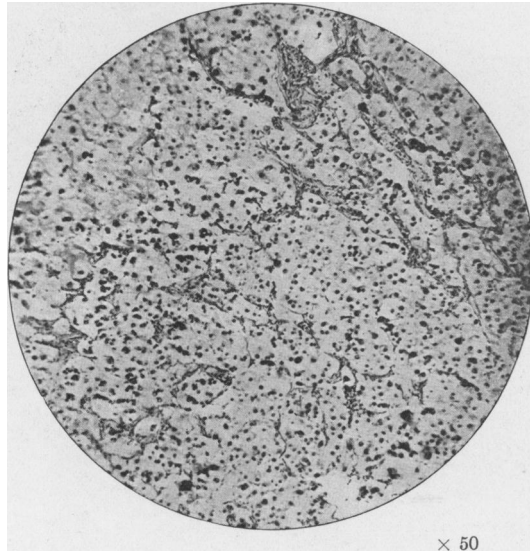


FIG. 5.—Colloid.

made me adopt grading as a routine. I shall refer also to 300 patients who have been followed for three years only, but before discussing these five-year and three-year survival rates I must point out that the distribution of these four different grades is very unequal.

PROPORTION OF HISTOLOGICAL TYPES

On the basis of their histology, cancers of the rectum, with very few exceptions, may be included either in the group of adenocarcinomas or in that of colloid growths. The commonest form of rectal cancer is adenocarcinoma Grade 2; in fact this group includes approximately half the malignant growths of the rectum. Next in order of frequency are Grade 3 (26%) and colloid growths (12%), Grade 1 (6%) and Grade 4 (2%).

These figures are derived from an analysis of operation specimens and it is probable that they do not correctly express the natural distribution of the grades because Grade 1 tumours are sometimes treated by local excision and Grade 4 growths may often be beyond the scope of surgery when first diagnosed.

AFTER-HISTORY OF EACH GRADE

The difference in prognosis between the grades is seen at once by comparing the percentage of deaths which occurred in each grade in the first three years and first five years after operation. Thus the death-rate in the first three years was 20% for

Grade 1, 36% Grade 2, 48% Grade 3, and 66% for Grade 4. The death-rate for the colloid cases was 40% for the same period.

For the five-year period the differences are equally striking, the death-rates being 40% for Grade 1, 56% Grade 2, 76% Grade 3, and 100% Grade 4. The death-rate for colloid growths was 63%.

At first sight these figures would seem to show that the less differentiated types of malignant growths, such as Grades 3 and 4, grow more rapidly and kill the patient more quickly than the better differentiated tumours of Grades 1 and 2, but before accepting this seemingly obvious conclusion, allowance must be made for the extent of spread at the time of operation. We are not watching the natural uninterrupted march of malignant disease. These patients all underwent the operation of excision of the rectum for cancer and in some cases the disease was at an early stage and in others was actually beyond the scope of surgery at the time of operation. Looked at from this point of view, it might be argued that the survivors in each grade

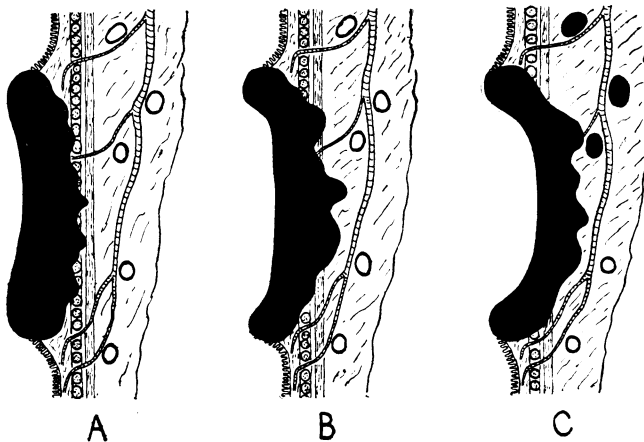


FIG. 6.—A. Growth limited to wall of rectum.
B. Extension of growth to extrarectal tissues but no metastases in regional lymph nodes.
C. Metastases in regional lymph nodes.

simply represent the proportion of cases which were at a curable stage at the time of operation. In other words, these striking differences in the number of deaths in each grade may not be a reflection of the rate of growth of the tumours but simply a measurement of the proportion of patients in each grade who could be cured by the treatment they received.

This is a question which is easily settled because all these tumours were also classified according to extent of spread into A, B, and C cases (see fig. 6).

In A cases the growth was limited to the wall of the rectum, in B cases there was extension by direct continuity to the extrarectal tissues, but no glandular metastases, and in C cases there were metastases in the regional lymph nodes [4]. Experience with this method of classification has shown that the survival rate for A cases on a five-year basis is 93%, for B cases 65%, and for C cases 23% (see Table I).

TABLE I.—RESULTS OF PERINEAL EXCISION ON A FIVE-YEAR BASIS (142 CASES)

Classification of growth	No. of operation survivals	No. untraced and died of other causes	Alive at five years	Percentage of five-year survivals
A	30	2	26	93
B	50	7	28	65
C	62	5	13	23

This overwhelming difference in survival rate makes it necessary to compare the proportion of A, B, and C cases in each grade before drawing any conclusion as to the supposed rate of growth.

DISTRIBUTION OF A, B, AND C CASES IN EACH GRADE

In a long series of cases of cancer of the rectum accepted by surgeons as operable, it has been found that approximately 15% are A cases, 35% B, and 50% C. An analysis of the distribution of A, B, and C cases in each grade shows a great relative increase in the proportion of A cases in Grade 1, and a virtual disappearance of A cases from Grades 3 and 4; on the other hand, the C cases, which form a relatively small fraction of Grade 1 tumours, become the main constituents of Grades 3 and 4 and colloid.

This unequal distribution of A, B, and C cases may provide the chief explanation of the difference in prognosis of the different histological grades. Since the group of Grade 1 tumours contains a relatively high proportion of early cases (A cases) it is obvious that a larger number of patients are cured by operation, and fewer cancer deaths are to be expected in the succeeding three to five years. Similarly since the proportion of advanced growths is so much higher in the groups graded 3 and 4 and colloid, it is only to be expected that these grades will show a relatively poor prognosis.

This is one explanation of difference in survival rate, and probably the chief. It attributes the poor prognosis of Grades 3 and 4 not to more rapid growth of the tumours, but to the fact that these are generally more advanced at the time at which they receive treatment. It is possible also that the more anaplastic tumours do actually grow more rapidly, so that a residual metastasis of this type would kill a patient more quickly than a similar residual metastasis of the better differentiated growths. This question could be answered by comparing the average period of survival of operation cases with extensive glandular metastases. In the present series there are insufficient of such cases in each grade for any trustworthy comparisons, but the records show a few Grade 1 patients who have lived on for more than five years with a local recurrence of the malignant growth. The Grade 3 and 4 patients with local recurrence have generally died within a few months.

SUMMARY

My experience of grading tumours may be summarized in the following three sentences:—

- (1) That grading is a natural and practical method of classifying tumours.
- (2) That if tumours are graded by Broders' method the after-history will show that there is a distinct difference in the survival rate according to the grade.
- (3) That this difference in prognosis is chiefly due to the fact that the more anaplastic tumours are likely to have spread further than the better differentiated growths at the time when they receive surgical treatment.

REFERENCES

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- 2 *Id.*, *M.J. and Rec.*, 1925, 121, 133.
- 3 RANKIN, F. W., and BRODERS, A. C., *Surg., Gynec. and Obst.*, 1928, 46, 660.
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