Reporting colorectal cancer

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SUMMARY Reporting colorectal cancer comprises two phases: the careful collection of pathological data; and the division of patients into groups with differing prognoses. Dukes' classification of rectal cancer was the outcome of this dual approach. It evolved over many years, and full details of its final form were not published until 1958, towards the end of his career. Others modified the classification during its evolution, and numerous rival pathological and clinicopathological systems now exist. The resulting confusion that surrounds the Dukes classification may make it impossible to compare pathological findings and the results of treatment between different centres.

The importance of meticulous dissection and examination of surgical specimens is emphasised and a simple set of recommendations made. It is shown how modern statistical methods may identify pathological variables that have independent clinical importance. On the basis of this information a new system of prognostic categorisation for patients receiving apparently curative surgery for rectal cancer has been developed, which is superior to the Dukes classification in that it can place many more patients into groups with clear prognostic implications.

Although the Dukes classification of rectal cancer is simple to use and enjoys wide popularity, misconceptions abound about its origins and the manner in which modifications have been made over the years, both by Dukes and others. It is astonishing how often both clinicians and pathologists are unable to define the meaning of the Dukes A, B, C categories when pressed to do so. Even the fact that Dukes was a pathologist can come as a surprise to some. The situation has been complicated by the introduction of rival pathological or clinicopathological staging systems: several new or updated classifications have appeared during the past few years and others are being planned. This renewal of interest reflects increasing awareness of the prognostic importance of staging as well as the availability of new treatment modalities, including chemotherapy, immunotherapy, radiotherapy and local excision. Patients must be randomised into equivalent groups if new forms of treatment are to be evaluated. In this paper we try to put the Dukes classification into perspective and appraise it critically. A methodical approach to pathological reporting is important and we emphasise items that are likely to be of prognostic value.

The Dukes classification: historical perspectives

After the First World War interest in survival follow-

ing surgery for rectal cancer was fuelled by rivalry between those who favoured abdominoperineal excision, developed by E Miles of the Gordon Hospital, London, and the proponents of the more conservative operation of perineal excision, performed by JP Lockhart-Mummery of St Mark's Hospital, London. Lockhart-Mummery believed that the types of patients treated by these alternative methods might not be the same. He suggested that rectal cancer should be staged clinically before and during the operation. The results of this attempt at clinical staging were published in 1926,¹ but Dukes remained dissatisfied and so began his work on the extent of spread found in operation specimens. At first he devised a classification into groups: A, B1, B2, C1 and C2. This early classification was incorporated in a paper in which Gordon-Watson was coauthor.² Dukes later modified and simplified the classification into A, B, and C categories when he was able to analyse the follow up data on 215 patients with operable cancer treated by excision of the rectum.³

In his first paper on the A, B, C classification of rectal cancer³ many important and still relevant points were made. Dukes regarded his classification as being of interest in the general pathology of malignant disease and stated that it could be applied to all intestinal cancers. His research, however, was limited to rectal cancer. The method of dissection was

described in detail, and this must be regarded as one of the most essential features of the work. There is little point in applying a pathological classification unless the data on which it is based are collected with meticulous care. The steps described by Dukes are followed to this day: an A case was a growth confined to the rectal wall; a B case was one in which spread in continuity had extended beyond the wall but had not invaded lymph nodes; a C case was one that had formed lymph node metastases. At this time Dukes believed that lymph node metastasis did not occur when growth was limited to the bowel wall, but it is now clear that local spread is limited to the rectal wall in about 5% of C cases. Among the 215 cases of rectal cancer Dukes studied were 38 A cases (18%), 76 B cases (35%), and 101 C cases (47%). This distribution has remained the same at St Mark's Hospital. When the proportion of C cases is found to be lower, one must consider the possibility that the method of dissection described by Dukes was not followed. Dukes foresaw the present interest in screening in his inspired statement made in 1932³: "There is no doubt that the proportion of A and B cases could be increased by earlier diagnosis. The relative proportion of A, B and C cases in the future will provide a delicate indication as to whether or not propaganda for the earlier recognition of malignant disease has been successful in respect of the lower end of the alimentary tract."

The most important aspect of the A, B, C classification was the striking difference in survival after surgery in the three groups. In 1958 Dukes published his research on the spread of rectal cancer and its effect on prognosis, based on the study of 2447 operation specimens collected between 1928 and 1952.⁴ This was not merely an extension of the 1932 paper but contained new and important information. Indeed, this paper represents the culmination of Dukes' research and describes the modification of his classification that is used at St Mark's Hospital today. Dukes described how every possible endeavour had been made to keep in touch with the 2037 operation survivors. Only 28 could not be traced and were assumed to have died. The crude five year survival for all patients treated by surgical removal of the primary tumour was 48.3%, but it was appreciated that crude five year survival was unsatisfactory because of the variation in the age and sex in the groups of patients to be compared. For this reason "age and sex corrected" five year survival was used. Survival figures were based on all operation survivors. No distinction was made between those cases in which the growth was regarded as incompletely removed (palliative operations) and those in which a cure could be hoped for (radical or curative operations). It should be emphasised that the Dukes classification was

designed purely as a pathological staging system for the purposes of comparing spread of disease, as observed in the surgical specimen, with the clinical outcome.

One interesting aspect of the 1958 publication⁴ was the separate consideration of local spread, lymphatic spread, venous spread and tumour grade as discrete variables. It was shown that these variables were interdependent, but it was not then possible to carry out multivariate regression analysis to measure the size of the independent contribution of each variable. Local spread was classified as (i) confined to the rectal wall (none); (ii) starting to invade the extrarectal tissues (slight); (iii) well established in the mesentery (moderate); and (iv) deeply invasive and possibly extending into neighbouring organs (extensive). Corrected five year survival figures for B cases showing slight, moderate, and extensive spread were 89.7%, 80.0%, and 57.0%, respectively. The extent of extramural spread is of importance in the prediction of local recurrence as well as survival. The five year survival figure for no spread was not given, but in a recent though smaller series of patients treated at St Mark's Hospital this was calculated as 97% (regardless of lymph node status).⁵ This confirms how correct Dukes was in avoiding subclassification of spread based on the depth of penetration within the bowel wall. Nevertheless, there is one important reason for recording the depth of intramural spread—namely, to correlate this variable with the risk of lymph node metastasis. This information is of considerable importance in the assessment of locally excised tumours. Dukes and Bussey found the incidence of lymph node metastasis in tumours confined to the rectal wall to be 14.2%, but once slight spread beyond the rectal wall had occurred the figure rose to 43.2%.⁴

In the 1958 paper C cases were divided into C1, in which only the regional nodes contained metastases, and C2 when there was more extensive lymphatic spread to include the nodes at the point of ligation of the blood vessels. Corrected five year survivals for A, B, C1 and C2 cases were 97.7%, 77.6%, 40.9% and 13.6%, respectively. It was shown also that the number of lymph node metastases influenced survival. Groupings of one, two to five, six to 10, and more than 10 positive lymph nodes were associated with corrected five year survivals of 63.6%, 36.1%, 21.9% and 2.1%, respectively.

The Dukes classification: a critique

One must accept that classifications will be changed and improved as new information comes to light. One important reason for staging or classifying tumours is to place therapeutic decision making on a rational basis. Decisions are made at different times for

patients with colorectal cancer: at the time of presentation, following examination under anaesthesia, following local excision of a rectal tumour, or following major surgery. On each of these occasions clinical, or a combination of clinical and pathological information, will be available. One could therefore devise clinical or clinicopathological staging systems that would be tailored to answer specific questions at different stages of clinical management. In this paper we only discuss prognostic pathological classifications based on the examination of surgical specimens.

What are the hallmarks of the ideal system of classification of large bowel cancer and how does the Dukes classification of 1958⁴ measure up to this ideal? In the design of a system of classification it is reasonable to utilise all useful information, whether this relates to the grade, stage, or any other assessable property of the tumour. The term "useful" refers to data that have an independent bearing on any clinically important end point. Statistical methods for assessing the independent value of particular variables were not available to Dukes. Potentially useful data such as the limitation of direct spread to the bowel wall in C cases,⁵ the extent of extramural spread in B and C cases, the number of lymph nodes containing metastatic cancer, and the grade of the tumour could therefore not be heeded, except by the creation of an overcomplex system, which Dukes was anxious to avoid.

Purists might object to the mixing of subjective variables relating to grade and the more objective ones relating to anatomical progression or stage of the disease. If subjective data are shown to have independent worth, however, one is obliged to use these data and hopefully to discover ways of making them more objective. The question as to whether a cancer has spread beyond the reach of the scalpel can be phrased in another and more biological way. One can ask to what extent the cancer has acquired the property to invade blood vessels, travel unhindered via the blood stream to other organs, leave the vessel and continue to grow within and colonise the parenchyma of a distant organ. The metastasising potential of a tumour is obviously of crucial importance in determining clinical outcome. It is our view that the best guide to metastasising potential is provided by a variable that is normally perceived as a reflection of tumour stage—namely lymph node spread. It is obvious that tumour spreads to the liver via the portal vein, yet invasion of extramural veins does not seem to influence survival independently.⁵ On the other hand, the presence of a lymph node metastasis is indicative not only of vascular (or at least lymphatic) invasion, but is proof in itself of the ability of the cancer to colonise sites away from the main growth (at

least lymph nodes). The more aggressive tumours seem to colonise more lymph nodes.^{4,5} One may suggest, therefore, that lymph node metastasis tells us as much about the grade of the tumour as its stage. As grade and stage are intimately related it is unnecessary to analyse them separately.

All classifications should be based on research that has been carried out with meticulous care. Caution should be applied to data generated within multiple centres because the pathological and clinical input will not be homogeneous. If the classification is to be clinically meaningful then it must be linked to carefully collected follow up data. Ideally, the cause of death in non-survivors should be determined at necropsy. These criteria were fulfilled in Dukes' classification of rectal cancer.

It is likely that only three or four discrete variables would form the basis of a prognostic classification of colorectal cancer. It is obviously desirable to perform a small number of important tasks well than to undertake a large number of tasks badly. Some variables are likely to be more important than others. The scoring of variables might therefore need to be weighted to facilitate the stratification of patients into groups with differing prognoses. The final classification should be simple so that the chosen symbols can be readily equated with a clinically important fact or course of action.

There are two main outcomes for patients receiving radical surgery for colorectal cancer. About 50% are cured of their disease, whereas the remainder will die of cancer. The ideal classification should perhaps reflect this simple clinical fact and comprise only two categories. Unfortunately, a group of "don't knows" must persist for the foreseeable future. Although the Dukes classification is simple, only 15% of patients (A cases) can be told that they have an almost certain chance of cure.

Having derived a classification, it would be pointless to commend its general use unless it were accompanied by clear instructions as to what should be recorded and how these data should be derived with minimum effort and maximum accuracy. It is imperative that all terms should be defined clearly and unambiguously. In his publications, unfortunately, Dukes failed to define the limits of the bowel wall, an omission that has generated considerable confusion. At St Mark's Hospital the outer border of the muscularis propria has always been regarded as the outer limit of the bowel wall, both for the rectum and the colon. As Dukes only studied rectal cancer his survival figures for A, B, C1 and C2 categories will not necessarily apply to colonic cancer. In his major papers Dukes included palliative cases in his overall survival analysis, but it is more meaningful to analyse palliative and curative operations separately. An

operation is judged to have been palliative when there is evidence, ideally with histological confirmation, that not all the tumour has been excised. This would include patients with distant metastases and patients in whom excision was judged to be incomplete. Perforation of the bowel (carrying the risk of tumour spillage) has also been used as a criterion of palliative surgery at St Mark's Hospital. Penetration of the peritoneal membrane by tumour cells might be regarded in a similar light. It is important to analyse the various palliative subcategories separately.

Other staging systems

The Dukes classification has at various times been modified by others. The fact that Dukes' name has remained appended to these variants has resulted in a considerable measure of confusion. This has been eloquently highlighted in reference to President Reagan's colonic cancer.⁷ No reason was given for the division of Dukes A cases into A (confined to mucosa) and B1 (confined to submucosa or muscularis propria) by Kirklin *et al.*⁸ Furthermore, we advise against the diagnosis of carcinoma for neoplastic processes that are confined to the mucosa.⁹ The Kirklin modification was changed further by Astler and Coller,¹⁰ who recognised that lymph node metastasis could occur when direct spread in continuity was limited to the bowel wall. They, however, did not show a survival difference for their subcategories of C1 (C cases with direct spread limited to the bowel wall) and C2 (C cases with direct spread beyond the bowel wall). Some recent research has shown that Astler-Coller C1 cases may, in fact, be associated with a relatively good prognosis.⁶

Another modification to Dukes's classification was the addition of a "D" stage to indicate the presence of distant spread.¹¹ A "D" stage has been adopted by the Australian clinicopathological classification¹² and is now commonly used in clinical reports, but, as noted above, palliative surgery encompasses more than being able to show distant metastases. Furthermore, the distribution of A, B, and C cases determined in the laboratory cannot be compared for different centres if a proportion of operable cancers are placed within a D category. It is reasonable to mix clinical and pathological data, but the result will be a muddle if this is achieved in a single step. One's data might first be presented as a pathological categorisation. Subsequently, data may be broken down to show the number of operations within each category that were regarded as palliative, as well as the reasons for this designation. In this way no information will be lost.

Finally, we come to the tumour nodes metastases (TNM) staging system, which has been widely hailed as a logical form of cancer staging that may be applied

to all organs.¹³ It should be noted, however, that "T" does not have uniform meaning. For many sites it refers to the size of the primary growth, but for colorectal cancer it has been adapted to cope with the extent of direct spread in continuity. Unfortunately, most of the T numbers are used up on the description of the extent of spread within the layers of the bowel wall (which has little or no prognostic importance) instead of being applied to the extent of spread beyond the bowel wall. The latter is of considerable clinical importance, particularly in the prediction of local recurrence.¹⁴

The TNM system is not based on research, but is merely a method of encoding pathological and clinical data. The latest version is an improvement on its predecessors,¹³ but is still not comprehensive and does not provide the pathologist with clear definitions and guidelines. The old definition of T2 was vague because the bowel wall was not accurately defined. For this reason the old TNM coding system cannot be translated into the new version. The coding system remains cumbersome and complex and lacks clinical meaning. Recently the American Joint Committee on Cancer¹⁵ translated the numerous encoded TNM categorisations into four stages (I, II, III, IV) which are identical with the A, B, C and "D" stages of the original Dukes classification,³ as modified by Turnbull *et al.*¹¹

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The following account is slanted towards the collection of data that are likely to be of prognostic importance. A workshop on the staging of colorectal cancer was held in 1986 under the auspices of the United Kingdom Coordinating Committee for Cancer Research. The advice given below heeds the recommendations of the workshop (United Kingdom Coordinating Committee for Cancer Research. Recommendations for the staging of colorectal cancer).

Specimens should be received fresh, opened along the antimesenteric border, pinned out on to a cork mat, immersed in formalin and allowed to fix for 24 hours. They should then be unpinned and fixed for a further 24 hours.

LOCAL SPREAD

As noted above the outer limits of the bowel wall and muscularis propria are synonymous. The longitudinal coat of the muscularis propria becomes fragmented in the region of the internal anal sphincter. It is suggested that the outer border of the internal sphincter should be taken as the outer limit of the lower rectum (and anal canal). In cancers confined to the bowel wall it is worth noting whether tumour spread is limited to the submucosa, if only to provide correlations

between depth of invasion and lymph node metastasis. It is important to select blocks which include the maximum extent of extramural spread as well as the deep margin of excision. The extent of extrarectal spread may be measured on the gross specimen and confirmed histologically. Simple extrapolation may be used when the muscularis propria is destroyed by tumour. The deep excision margin may be stained with india ink at the time of dissection to ensure that it is represented within the histological section. Extent of spread into the mesentery or retroperitoneal tissues of colonic resections should be recorded in identical fashion; spread beyond the peritoneal membrane should also be recorded. This may be visible as gross ulceration or as small points of penetration detected microscopically. It is important to appreciate that the serosa is a membrane which includes a connective tissue layer as well as the overlying peritoneum itself, formed of a flattened sheet of mesothelial cells. At St Mark's Hospital extramural spread of 0–5 mm, >5–10 mm, and >10 mm are currently graded as slight, moderate, and extensive, but this choice of figures is arbitrary. Direct spread into adjacent organs such as vagina, bladder, and prostate should be recorded. It is unnecessary to examine the proximal and distal resection margins at the microscopic level unless the margins are close (<3 cm) to the tumour, or the cancer shows either a highly infiltrative pattern of growth, or extensive vascular or lymphatic permeation.

LYMPH NODE SPREAD

All lymph nodes which drain the segment of bowel harbouring a cancer should be dissected out with meticulous care and subjected to histological examination. A knife with a long sharp blade and a heavy handle should be used to cut sections through the well fixed mesentery at 1 mm intervals. A small scalpel will be far less effective. We have not found fat clearance techniques to be of any benefit. On the contrary, fat clearance using graded alcohol solutions and xylene was costly, time consuming, unpleasant and did not lead to the discovery of more lymph nodes.¹⁶ The harvest of lymph nodes, the number of nodes containing metastatic tumour, and the presence of tumour in a lymph node at the point of a high vascular ligature should be recorded. Circumscribed nodules of tumour may be found within the extramural fat without any signs of a residual lymph node. The clinical importance of this observation is unknown at present.

DISTANT SPREAD

Histological proof should always be obtained.

VENOUS SPREAD

This confers little or no prognostic information in the presence of other pathological variables.⁵ The assess-

ment is somewhat subjective, and it is recommended that only invasion of extramural veins with muscular walls should be recorded. This observation may be important in individual cases.

TUMOUR TYPE

Most colorectal cancers are adenocarcinomas. Mucinous carcinomas secrete large amounts of mucus and account for about 10% of cases. Other types are rare and include signet ring cell, large cell undifferentiated, small cell undifferentiated, squamous, adenosquamous, and carcinoid tumours. Tumour typing, at least into adenocarcinoma, mucinous carcinoma, and signet ring cell carcinoma, confers no important independent prognostic information in the presence of other pathological variables.¹⁷ Tumour typing may, however, be of some importance in understanding the aetiology and histogenesis of large bowel cancer.¹⁸

DIFFERENTIATION

Architecture or tubule configuration is the most important indicator of grade of differentiation.⁵ The presence of irregularly folded, distorted, and often small tubules, or the absence of any tubule formation should be the essential hallmarks of poorly differentiated cases. These will represent the grades III and IV categories, as described in detail by Dukes.¹⁸ All other tumours (about 80%) should be recorded as "other". This recommendation reflects the highly subjective nature of grading and poor levels of inter-observer agreement.¹⁹ In view of the current concept of the selection of clones of increasing malignancy it is logical to grade according to the worst area rather than according to the predominant pattern. Tubules at the advancing front of a tumour often seem to be distorted, especially in the presence of inflammation. Cancers should not be downgraded on this account.

LYMPHOCYTIC INFILTRATION

The presence of an inflammatory mantle at the advancing edge of a tumour confers an excellent prognosis that is at least partly independent of other pathological variables.²⁰ Eosinophils, neutrophils, and plasma cells, as well as lymphocytes, are represented within the mantle which follows the contour of the invasive margin of the tumour and may resemble the normal lamina propria. This finding characterises about 20% of rectal cancers and is more common in the earlier stages of the disease.

INVASIVE MARGIN

About 25% of rectal tumours invade in a diffusely infiltrative manner, dissecting between normal structures in a seemingly effortless fashion that is usually unopposed by any form of inflammatory response.

The margins of such growths are difficult to define. This is an unfavourable feature.⁵

A method for stratifying patients into prognostic categories

A most efficient deployment of pathological data can be made by identifying a small number of important variables which influence clinical end points independently. When survival is chosen as the clinical end point the appropriate method of statistical analysis is through the Cox proportional hazards regression model.²¹ A pathological variable will have a lesser or greater independent bearing on survival, the magnitude of which can be computed by multivariate regression analysis. Appropriately weighted scores can then be given to each of the selected variables (based on their regression coefficients) and patients with differing prognoses divided into groups.

Specimens from 379 patients receiving "curative" surgery for rectal cancer were studied and a comprehensive set of pathological variables was subjected to multivariate regression analysis (table 1).²² The collection and recording of these data have heeded the recommendations of the preceding section. The single exception is the division of extent of extramural spread into slight and extensive, which was based on the subjective impression of the pathologist carrying out the dissection and not on measurement. Four variables with an independent influence on clinical outcome were selected by means of multivariate regression analysis: number of lymph nodes with metastatic tumour, character of invasive margin, lymphocytic infiltration, and local tumour spread

Table 1 Pathological variables subjected to multivariate regression analysis

Number of lymph nodes containing metastatic tumour: 0, 1-4, >4
Metastasis in apical lymph node: yes, no
Extent of local spread: none, slight, extensive
Extramural venous invasion: yes, no
Type of tumour: adenocarcinoma, mucinous carcinoma, signet ring cell
Differentiation: poor, other
Character of invasive margin: expanding, infiltrating
Peritumoural lymphocytic infiltration: conspicuous, other

(table 2).²² Distinction between slight and extensive spread beyond the bowel wall was unimportant in the presence of the other selected variables, and this is reflected in the scoring system (fig 1). Fig 1 depicts the selected variables, together with their appropriately

Fig 1 Pathological variables with an important and independent influence on survival shown by multivariate analysis, using the Cox proportional hazards regression model. Scores have been weighted according to regression coefficient associated with each variable; total scores for these four variables are translated into prognostic groups I-IV.

Table 2 Variables selected by multivariate regression analysis

Variable	Regression coefficient	Standard error	Likelihood ratio test	DF	p value
No of positive lymph nodes	0.93	0.14	44.28	1	<0.0001
Invasive margin	0.80	0.21	14.90	1	0.0001
Lymphocytes	1.13	0.35	12.78	1	0.0004
Spread	0.45	0.18	6.58	1	0.01

Table 3 Survival figures for prognostic groups

Group	No of patients (%)	Cancer deaths	Alive	Deaths from other causes	Death from unknown causes	Survival (%)	
						5	10
I	117 (31)	7	52	51	7	96	95
II	119 (31)	23	44	41	11	85	78
III	69 (18)	26	18	16	9	67	60
IV	74 (20)	59	8	5	2	27	18
Totals	379 (100)	115	122	113	29		

Logrank 3 df 181.00; trend 1 df 149.45.

weighted scores and key to prognostic groupings. Fig 2 shows the survival curves and table 3 figures for the prognostic categories. Survival figures for the four new prognostic groups are coincidentally similar to those associated with Dukes A, B, C1 and C2 cases (fig 3). The new prognostic classification is superior to the Dukes classification because more than twice as many patients are allocated to groups which provide a confident prediction of outcome. The new prognostic classification has been shown to be reproducible when tested on a second set of patients.²²

As pathological data are now being tailored for the provision of a cumulative prognosis, the resulting categorisations must approximate to the ideal, given the quality and range of the data on which they are based. It is not possible, however, to reclaim the original pathological data once these have been converted into anonymous scores to derive the cumulative prognostic groupings. This distinguishes the system from the more traditional staging classifications.

Fig 2 Survival curves for prognostic groups in I-IV. Deaths not due to cancer have been omitted.

Role of new laboratory techniques

The histopathologist is now able to complement routine methods of reporting with a wide range of sophisticated special techniques—for example, tumour DNA content may be measured by means of flow cytometry. This technique allows the DNA content of many thousands of cells to be measured with ease and rapidity. Furthermore, nuclear suspensions can be prepared from formalin fixed, paraffin embedded tissues, and this has opened the way for retrospective studies.^{23 24} Flow cytometry, however, is relatively insensitive in as much as a small increase in the amount of DNA or a small population of aneuploid cells with abnormal DNA content may not be resolved. Moreover, the definition of DNA aneuploidy is arbitrary. It is generally agreed that

Fig 3 Distribution of patients stratified according to new prognostic grouping compared with distribution of identical patients classified by Dukes' method. Although prognosis of patients in groups I-IV is similar to Dukes' stages A, B, C1 and C2, respectively, more patients are allocated to groups with a clear cut clinical outcome (stippled segments) by new system of prognostic categorisation. Only 4% of patients are placed into poor prognostic Dukes' C2 category while new prognostic system identifies 20% of patients with comparable prognosis. Furthermore, a greater proportion of patients (31%) fall into "excellent" category, comparable in prognostic terms with Dukes' stage A (17% of patients).

large bowel cancers fall into two groups: those with an obviously aneuploid population; and those in which no aneuploid population can be resolved. About 60% of cancers are obviously aneuploid.^{26 27} Unfortunately, there is disagreement concerning the prognostic importance of this finding. In some studies this was the most important predictor of clinical outcome,²⁸ whereas in others aneuploidy had no bearing on survival whatsoever.²⁹ In a retrospective study of 203 operable rectal cancers carried out at St Mark's Hospital aneuploidy was shown to influence prognosis adversely.³⁰ No clinically useful discrimination between survivors and non-survivors was obtained, however, and although ploidy influenced survival independently, shown by multivariate regression analysis, this contribution was too small to be of clinical value.³⁰ There would seem to be no justification in using flow cytometry routinely for the grading of surgical specimens of colorectal cancer.

Conclusions

The reporting of large bowel cancer comprises two phases. The first is the meticulous recording of pathological data; the second is the derivation of clinically important patient groupings. The Dukes classification of rectal cancer of 1958⁴ represents the culmination of detailed research performed over many years. The groupings are few, can be defined in simple pathological terms, and have important clinical relevance. In these respects the Dukes classification has no rivals, but Dukes lacked the benefit of modern statistical methods that would have allowed him to tailor his data to the prediction of specific clinical end points. A new prognostic classification has been developed from pathological data relating to patients undergoing "curative" surgery for rectal cancer. It permits more patients to be allocated to groups which provide clear insight into the likelihood of cure. Further research is required to find other more objective methods of predicting tumour behaviour.

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