ing that we could not show any prognostic influence for tumour fibrosis.^{2,3} In fact, like them, we showed tumour fibrosis to be an adverse factor, but in our particular model this was not an independent variable.² The important point is that it is not correct to compare their model with ours. Firstly, we were looking only at rectal cancer. Secondly, we broke up Dukes' stage into discrete variables. Considerably more prognostic information is provided by entering the extent of direct spread and number of affected lymph nodes as discrete variables. Although peritumoral fibrosis does not feature in our prognostic model, the observation may be of considerable biological importance. There is growing interest in stromal-epithelial interactions, and further study of the mechanisms of tumour fibrosis may provide new insight into the basis of tumour aggressiveness.

It is gratifying to note that a lack of prominent inflammatory cell reaction (assessed in the same way as our lymphocytic infiltration) confers independent prognostic information when others have reported difficulties with the reproducibility of this variable.⁴ Interestingly, we were unable to show that lymphocytic infiltration confers independent prognostic information for colonic cancer.⁵ In fact, different prognostic models may be required for colonic and rectal cancer. Clearly, a good deal more research is required and there is a need for a comprehensive, prospective, multicentre study of prognostic variables. It should be emphasised, however, that a prognostic classification is unlikely to become widely used unless it is based on a small number of important features.

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Drs Halvorsen and Seim comment:

We unfortunately referred inaccurately to their findings regarding the prognostic influence of tumour fibrosis in rectal cancer.^{1,2} This we regret. As highlighted by Dr Jass, the selection of different patient groups will make any comparison between clinicopathological series difficult. Some additional problems, however, pertain to comparing results from different proportional hazards regression analyses (Cox models) or to multiple regression models in general. First, the choice of variables with possible independent prognostic influence may have substantial impact on the results. Secondly, the variables are often categorised differently by different investigators, as emphasised by Dr Jass. Thirdly, some users of the Cox model prefer to treat the categories of a single variable by assuming "equidistance" between them, whereas others, as we do, prefer to recode the variable categories into dichotomous variables. Fourthly, few authors say anything about the proportionality assumption of the Cox model and the question of whether interaction terms should be included in the model. In a Cox analysis with no interaction terms it is implicitly assumed that each of the independent variables represents an unchanged risk factor, regardless of the values of the other variables, and also that a particular level of a risk factor implies an increase (or decrease) in the hazard rate that is constant throughout the follow up time.

Based on plots of the log minus log survival function,³ we have chosen a Cox model in which the grade and stage related risk factors influence the prognosis equally in the colon and rectum. We admit, however, that significant deviations from such assumptions may be found in data sets with considerably more observations than in our study. So, we agree with Dr Jass that such analysis should take into consideration the question of whether different models are required for colonic and rectal cancer.

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EVA SEIM

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Fine needle aspiration of thyroid nodules

Kendall¹ did not describe adequately the technique he used, merely mentioning that a standard technique was used.^{2,3} Fine needle aspiration is developing rapidly and a standard technique is probably not yet consolidated. To allow other workers to share his experience it would be important to state the size of the needle used, and whether a syringe was used and of what volume.

The author also did not describe the details of the cytospin preparation—for example, what solution was used to suspend the cells, what model of equipment was used, and what was the speed used. There was also no explanation for why direct smears were considered to be unsatisfactory.

The technical aspects are very important as they strongly influence the accuracy of interpretation of the morphology in fine needle aspiration. The standard technique varies from one laboratory to another. Most workers use 22 or 23 gauge needles,^{2,3} but others prefer the 21 gauge needle.⁴ Similarly, some are in favour of the haematoxylin and eosin stain while others prefer the Giemsa stain. I am certain other workers would like to hear his experience in this very important field in diagnostic pathology.

In our laboratory we perform over 2000 fine needle aspirations a year; 634 were on the thyroid in 1988. We use the 21 gauge needles with 10 ml syringes, loaded on a Cameco syringe holder⁵; we use the rehydration technique and haematoxylin and eosin stain for direct smears,⁶ and we prepare cell blocks from direct fixation of the aspirate in 7.5% buffered formalin as a routine.⁶ The rehydration technique gives us excellent results. Among other advantages it also lyses red blood cells without resorting to the use of acetic acid.¹

Kendall was of the opinion that specific diagnosis could not be achieved in most cases in fine needle aspiration of the thyroid. He had difficulty in occasionally distinguishing cellular colloid goitre from neoplasms. We addressed this point specifically in a previous study.⁴ Our experience is that a specific diagnosis can be made in most cases, even in cellular aspirates. For fine needle aspiration to be useful, more attention should be put on the technical aspect of this developing field, so that a specific diagnosis can be offered

whenever possible to allow the surgeon to act accordingly with more precision.

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Dr Kendall comments:

I thank Dr Kung for his interest and am pleased to provide further details of the method. Technically, it is not demanding and produces good morphological detail, but I would not claim any special benefit over the many other methods used.

The aspiration is performed using a 10 ml syringe, 21 gauge (venesection) needle, and a syringe holder (Cameco). The aspirate is drawn gently into the barrel of the syringe by washing through with cytospin collection fluid (Shandon Ltd), the needle removed, and the aspirate expelled into the cytospin fluid. After centrifugation, the cell button is resuspended in 2-3 ml of cytospin fluid. Aliquots (0.5 ml) are then introduced into the cytospin chambers (Cytospin II, Shandon Ltd) and the cells spun on to glass slides (1700 rpm for four minutes). If the aspirate was bloodstained, the cell suspension was treated with excess 1% acetic acid, washed twice with saline, and then resuspended in cytospin fluid. The cell spreads are fixed in 95% alcohol and stained with haematoxylin and eosin and Papanicolaou stains.

Cytospin preparations have, in my view, several advantages over direct smears if immediate reporting is not required. A recent letter to the College Bulletin outlined several points,¹ with which I agree. With regard to

the thyroid, aspirates are frequently contaminated with blood and it was this which led me to abandon direct smears as I found adequate smear preparation difficult.

Regarding specificity of diagnosis, my view is that interpretation of thyroid fine needle should be mainly directed at distinguishing between simple and neoplastic nodules. Precise preoperative diagnosis is an additional refinement if available, as in some cases of papillary carcinoma in my series. Follicular neoplasms, for example, are not in my view susceptible to such precision. Lobectomy is generally regarded as the treatment of choice for differentiated thyroid tumours; hence the practicality of a classification into simple and neoplastic. Poorly differentiated tumours form a third diagnostic group, which is useful to identify as the management may be other than surgical.

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- 1 Howat AJ, Anderson G, Dundas SAC, Harris SC, Underwood JCE. Fine needle aspiration biopsies of breast lesions. *Royal College of Pathologists' Bulletin* 1988;64:19.

Notices

bssc

British Society for Clinical Cytology

Certificate of competence in cytology screening

(Recognised by the Department of Health for entry to the Cytology Screener Grade)

Examination dates and venues:

Thursday November 2, 1989;
University Medical School, Leeds

Saturday November 4, 1989;
Birmingham Maternity Hospital

Closing date for applications:
September 22, 1989

Tuesday February 13, 1990;
Northwick Park Hospital, London

Closing date for applications:
December 29, 1989

Further particulars and application forms from: Dr E McGoogan, Chairman BSCC Examination Committee, Department of Pathology, University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG.

IMLS

Triennial Conference

The 19th Triennial Conference of the Institute of Medical Laboratory Sciences is to be held at the University of Warwick, near Coventry, from 2 to 6 September 1989.

For further information contact John Cairns, Haematology Department, East Birmingham Hospital, 45 Bordesley Green East, Birmingham B9 5ST; Tel: 021-766 6611 ext 4280.

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