way, predispose to certain malignant neoplasias." Although these authors attempt to exclude external causes for suppression of monocyte activity by comparing patients with malignancy with other patients, this may not be sufficient as a control. Monocyte esterase is easily inhibited by several pharmacological and environmental factors. Organophosphates, used as a component in insecticides, are potent inhibitors of monocyte esterase.⁴ Monocyte esterase has been shown to be a useful measure of occupational exposure to organic compounds in plastics manufacturing.⁵ The excess in monocyte esterase deficiency in patients with cancer observed by Markey *et al* could be due to differences in drug exposure compared with patients who do not have cancer. They were able to report familial studies in only 11 esterase negative patients, of which five had cancer and six other conditions, out of a total of 90 esterase negative patients. Attributing esterase deficiency to an inheritable form, therefore, is not definitely known as the cause in most patients in their study. Their results are certainly important, however, and could lead to future studies which might elucidate these questions.

DW ROSS
University of North Carolina,
Chapel Hill,
NC 27599
USA

- 1 Markey GM, McCormick JA, Morris TCM, *et al*. Monocyte esterase deficiency in malignant neoplasia. *J Clin Pathol* 1990;45:282-6.
- 2 Markovic OT, Young DS, Markovic NS. Quinidine-induced inhibition of leukocyte esterases. *Clin Chem* 1988;34:518-24.
- 3 Ross DW, Bishop C, Henderson A, Kaplow L. Whole blood staining in suspension for non-specific esterase and alkaline phosphatase analyzed with a Technicon H-1. *Cytometry* 1990;11:552-5.
- 4 Lee MJ, Waters III HC. Inhibition of monocyte esterase activity by organophosphate insecticides. *Blood* 1980;50:947-51.
- 5 Levine MS, Fox NL, Thompson B, *et al*. Inhibition of esterase activity and an undercounting of circulating monocytes in a population of production workers. *J Occup Med* 1986;28:207-11.

Dr Markey comments:

The Haemalog D automated differential white cell counter, producing as it did, a monocyte count on esterase stained cells and a monocyte count on peroxidase stained cells (screening 10 000 cells on each channel) was an excellent system for identifying monocyte esterase deficiency. It is indeed unfortunate that subsequent improvements to its technology involved relinquishing the esterase channel. The semiautomated method of Ross *et al*, however, which involves the manual staining for esterase of whole blood samples and counting the stained cells on the current Technicon H1 system, should permit confirmation of our results. A peroxidase monocyte count by the H1 must also be recorded for each sample because a low esterase percentage count can occur due to many other reasons, whereas only in esterase deficiency will a low recording on the esterase channel be accompanied by a normal count on the peroxidase channel.

We do not believe that the excess of esterase deficient subjects among cancer patients can be due to differences in drug exposure because treatment regimens for different malignant diseases are reasonably standard for each disease group in this hospital and the radiotherapy centre, yet only a small proportion of any malignant disease group manifest

ted the anomaly. Moreover, of the group of patients with carcinoma, six had not had any chemotherapy or radiotherapy (primary diagnostic beds), while six had (oncology specialist beds). Neither have we any evidence that our subjects' deficiency was acquired as a result of exposure to organophosphates. Levine *et al* (as referred to by Ross) did not report any follow up of their esterase deficient subjects after they had been removed from the plastics production process, but one may reasonably expect recovery of monocyte esterase in newly developing monocytes when organophosphates disappear from the blood stream, as occurred within 14 days of acute organophosphate poisoning in the case reported by Oehmichen *et al*.¹ Fifty of our subjects had confirmatory samples taken over 14 days (mean 17 weeks) following the initial Haemalog D sample and many have had repeat samples since then. None has reverted to positivity. Moreover, we have no evidence of exposure to organophosphates, such as has been reported by Levine *et al*. On the contrary, we have evidence of familial deficiency in nine of 11 families studied (and in one family of three studied in the interim period). At this time we therefore feel that the balance of our evidence is in favour of an inheritable basis for the deficiency in our subjects.

As to our hypothesis that esterase deficiency may predispose to malignant neoplasia, we now have evidence that esterase negative monocytes do not respond to lactoferrin stimulation, with an increase in cytotoxicity for K562 cells, using a modified assay for measurement of monocyte cytotoxicity²; esterase positive monocytes respond vigorously (unpublished observations).

- 1 Oehmichen M, Pedal I, Besserer K, Gencic M. Inhibition of non specific leukocyte esterase activity. Absence of monocyte esterase activity due to phosphoric and thiophosphoric acid ester intoxication. *Int Forens Sci* 1984;25:181-9.
- 2 McCormick JA, Markey GM, Morris TCM. Lactoferrin inducible monocyte cytotoxicity for K562 cells and decay of natural killer lymphocyte (NK) cytotoxicity. *Clin Exp Immunol* (in press).

AgNORs and follicular lymphomas

It was of interest that Cronin and colleagues showed no significant difference between AgNOR scores in follicular hyperplasia and follicular lymphoma.¹ This confirms the results of an original study in this laboratory some three years ago,² where there was no numerical difference in AgNOR score between low grade lymphomas and hyperplastic nodes. The slight trend to higher counts in benign lesions, shown by Cronin *et al*,¹ is to be expected, as in most somatic tissues and neoplasms, and certainly in non-Hodgkin's lymphomas, the interphase AgNOR score has been shown repeatedly to be related to cell proliferation.³ This latter is generally taken to be greater in hyperplastic than malignant (low grade) follicle centres. These observations would presumably only hold true if follicle centre cells are enumerated; unfortunately, this is not made clear by Cronin *et al*. AgNOR scores, however, can discriminate between hyperplastic follicles and high grade (pure centroblastic) follicles. I have examined 10 specimens of reactive follicular hyperplasia and 10 of centroblastic follicular lymphoma using the standard AgNOR sequence² with 3 μ m paraffin wax sections. The latter

had been shown to be of a B cell derivation by means of standard immunophenotyping; eight were detected de novo, and two had arisen by transformation from centroblastic-centrocytic lymphomas. All AgNOR dots, both intra- and extra-nucleolar, were counted in 200 follicle centre cells from each case. The cells were selected at random from all levels of the follicle centres, excluding the mantle zone. The range of values for reactive follicular hyperplasia was from 2.3 to 3.5 (mean 2.85; SD 0.43) AgNOR sites per nuclear profile. In the centroblastic follicular lymphoma specimens the range was from 4.8 to 10.1 (mean 6.12; SD 1.75) (figure). Thus we have yet another example of a malignant transformation carrying with it a higher mean AgNOR score, doubtless as a result of the proliferative overgrowth of neoplastic centroblasts, which themselves have high mean AgNOR counts.

J CROCKER
Department of Histopathology,
East Birmingham Hospital,
Bordesley Green East,
Birmingham B9 5ST

- 1 Cronin K, Loftus BM, Dervan PA. Are AgNORs useful in distinguishing follicular hyperplasia from follicular lymphoma? *J Clin Pathol* 1989;42:1267-8.
- 2 Crocker J, Nar PK. Nucleolar organiser regions in lymphomas. *J Pathol* 1987;151:111-8.
- 3 Crocker J. Nucleolar organiser regions. In: Underwood JCE, ed. *Pathology of the nucleus*. Heidelberg: Springer-Verlag, 91-147.

Dr Cronin *et al* comment:

We thank Dr Crocker for his interest in our small study. Essentially we agree with his comments. The point of our paper was that although we did find a statistical difference between the two groups studied (follicular lymphoma and follicular hyperplasia) the overlap was such that AgNOR counts had no discriminant value as a diagnostic test in the group of patients we examined. As stated in our paper, we confined our study to the centroblastic/centrocytic category of follicular lymphomas; we evaluated cells randomly within follicles, while omitting identifiable macrophages. In our experience (about 80-100 cases of malignant lymphomas a year) pure centroblastic lymphoma is

relatively uncommon and so we chose to study centroblastic/centricytic follicular lymphoma. We accept Dr Crocker's opinion that AgNOR counts may be useful in separating pure centroblastic lymphomas from reactive hyperplasia. We also agree that AgNOR counts reflect proliferative activity.¹

- 1 Dervan PA, Gilmartin LG, Loftus BM, Carney DN. Breast carcinoma kinetics: Argyrophilic nucleolar organizer region counts correlate with Ki 67 scores. *Am J Clin Pathol* 1989;92:401-7.

Pathologists' ability to estimate percentage of luminal occlusion in coronary artery disease

I was most interested to read the letter from Drs Champ and Coghill.¹

In a small study, presented at the Pathological Society in London in January 1985,² we wished to answer three questions:

- (1) How accurate are pathologists in estimating the percentage of luminal occlusion in a coronary vessel?
- (2) What is the extent of variation among different pathologists estimating the same vessel?
- (3) Does the use of a diagram proforma help in the naked eye assessment of coronary artery disease?

Twenty five segments of coronary artery taken at necropsy were selected to provide a range of concentric and eccentric stenoses. These were shown to 15 trainee and consultant pathologists whose experience ranged from two months to over 30 years. No prior warning was given to the participants and each in turn was asked to estimate the percentage area of the lumen which was completely occluded by intimal proliferation (percentage estimate) and to grade this subjectively into mild/moderate/severe stenosis (subjective estimate). Having done this, diagram proformas (figure) were then produced and the pathologist was asked to repeat the exercise. When all the results had been recorded, luminal occlusion was determined by planimetric methods on elastic van Gieson stained sections using a Kontron Videoplan computer (objective measurement). Each of the 25 coronary segments was then assigned to one of the following groups: mild (0 to 30% occlusion), moderate (31 to 69% occlusion), or severe (70 to 100% occlusion) stenosis on the basis of the objective measurements.

We then compared the percentage estimates and the subjective (mild/moderate/severe stenosis) estimates that had been made without the diagrams and with the diagrams to the objective measurements.

Not surprisingly, we found that the path-

ologists were most accurate in their estimations of coronary stenosis of less than 30% and greater than 70%.

The use of a diagram proforma improved the estimation of percentage of arterial occlusion, but the subjective estimate of arterial occlusion was not reproducible within this group of pathologists and was not improved by the use of the diagrams. This was because there was a wide range of values for luminal occlusion which different pathologists considered significant. Comparison of the percentage with the subjective estimates for each pathologist showed a range of 25% to 60% (mean 32%) occlusion for the lowest value in the moderate stenosis category. For the severe stenosis category the lowest values ranged from 40% to 90% with mean of 67% which compares with the degree of stenosis that is generally considered to be of clinical importance.³

We suggested that to improve accuracy and reproducibility among pathologists in the naked eye assessment of coronary artery stenosis:

- 1 Diagram proformas should be used as an aid to assessment.
- 2 One should always try to quote a percentage of luminal occlusion.
- 3 If subjective estimates are used, one should agree on the cut off points for mild/moderate/severe stenosis.

C WOMACK

Department of Pathology
Peterborough District Hospital
Thorpe Road
Peterborough PE3 6DA

- 1 Champ CS, Coghill SB. Visual aid for quick assessment of coronary artery stenosis at necropsy. *J Clin Pathol* 1989;40:887-8.
- 2 Womack C, Lowe JS. Naked eye assessment of coronary arterial stenosis. *J Pathol* 1985; 145:17A.
- 3 Thomas AC, Davies MJ. Post mortem investigation and quantification of coronary artery disease. *Histopathology* 1985;9:959-76.

Consequences of the provision of laboratory services of the National Health Service by commercial firms

I read this article by Shanks with great interest, and I would like to make some comments about it and about the general state of private pathology laboratories.

Many people may not know that J S Pathology is a public company quoted on the stock exchange and that Dr Shanks is the executive director. The laboratory is the largest in the United Kingdom and not attached to any hospital or university department, and is about to move into purpose built premises in North London. The laboratory work is tailored to private medicine and has a low proportion of medical to non-medical staff, and the bulk of the work is biochemistry and haematology with some microbiology, rather a lot of cytology, and little histopathology.

Laboratories of this kind are almost invariably "demand led" whereby the tests are undertaken and interpreted by the clinicians that request them. With few pathologists available for advice, the consequences are that there is no control of the number and nature of the tests that are performed, in contrast to the NHS where pathologists are available for consultation concerning difficult

clinical problems and will give advice on how the laboratory can help. Another result of the "tests on demand" approach is that aggressive drug companies will use these laboratories for promoting their products. The marketing of serum tumour markers is a good example of this.

With the advent of efficient cervical and breast screening programmes and the expansion of private medicine, the private sector must become responsible to those organisations concerned with quality assurance and conform to responsible reporting of tests undertaken so that meaningful national statistics can be compiled. Many people concerned with these projects consider the private sector the "18th Region" from which the feed back at the present time is almost non-existent. Private pathology laboratories through the Independent Health Care Association should be far more aware of these responsibilities and be prepared to cooperate with national data collecting bodies, resisting the temptation to promote indiscriminate cervical screening.

Clinical pathology departments in the NHS have a proud record of providing a service and responsible advice to clinicians concerning the management of their patients. There is a danger that with the commercial factor ruling, laboratories will be established that will indulge only in remunerative pathology practice. There is no doubt that health service laboratories need to increase their efficiency, as we are continually being told in advance of April 1991. I would reverse the concerns Dr Shanks expresses in her final sentence, however, and say that it would be a sad day if the lessons learnt in the NHS were ignored by the private sector rather than the other way around.

PA TROTT
20 Devonshire Place
London W1N 2DH

Provision of laboratory services

Both Whitby *et al*¹ and Shanks² seem to conclude that it is no longer feasible for small to medium sized pathology laboratories to function autonomously. I would agree with this point of view as it seems to be inappropriate for each district general hospital to attempt to provide a comprehensive on-site pathology service. Two questions then arise. First, which tests should be retained locally, and secondly, which laboratory should deal with those tests which are referred out.

In their conclusion Whitby *et al* seem to point the way forward.¹ They propose a plan of action which is similar to the approach we have adopted.³ As part of our business planning we have completed a detailed review of our present working practices. We have now defined our core pathology services which will be retained locally. The aim now is to refine the definition of these services by having detailed discussions with our hospital consultants and general practitioners.

The next step is then to determine how non-core pathology services should be provided. One option is to proceed with a process of competitive tendering for these services. Clearly, the result of this may be that tests are either referred to another distant NHS laboratory or to a laboratory within the private sector. I favour the alternative option