trichrome (deep red) and Mallory phosphotungstic acid hematoxylin (deep blue). In addition, fibrin thrombi were observed in some sinuses. Rickettsiae were not found. In these two patients similar changes were also noted in liver biopsies: granulomas with fibrinoid ring and fibrin thrombi.

Bone marrow changes in Q fever are not surprising because of the systemic distribution of the disease. These lesions, quite similar to those described by Ende and Gelpi, may be explained by the vascular tropism of Rickettsiae. The angiitis could be responsible for the fibrin thrombi and fibrinoid ring. Nevertheless, after biopsies were cut serially we interpreted the lesion portrayed in the inset of Fig. 1 differently than they did. In our opinion the clear central space was not a vestigial vascular lumen but an adipocyte incorporated in the developing granuloma.

As the result of granuloma in Q fever, this disease has to be considered among the possible diagnosis of bone marrow granulomas. Nevertheless, the presence of the singular fibrinoid ring, within or around the granuloma, is a diagnostic aid for the pathologist.

GEORGES DELSOL, M.D.
MICHELE PELLEGRIN, M.D.
JACQUELINE FAMILIADES, M.D.
JEAN CHARLES AUVERGNAT, M.D.
Laboratoire d'Anatomie Pathologique
Centre Hospitalier de Purpan
Toulouse, France

REFERENCES


TdT Activity in B Cell ALL

To the Editor:

It was with great interest that we have read the recent report in this journal by Shaw et al. Some caution, however, appears necessary before concluding an “association of TdT with immature and proliferating blast cells, rather than any specific differentiating pathway to B- or T-cell status.” Early studies by Harrison et al. clearly showed that TdT activity is independent of cell cycle status and thus not higher per se in proliferating cells. Regarding the technique of TdT determination, it ought to be kept in mind that the comparison of an assay for DNA polymerase β in purified form and in a crude cell homogenate could lead to some erroneous conclusions regarding specificity. Furthermore, ethanol and NEM, which were used to inhibit TdT activity, will also inhibit DNA polymerase α, which would be present in high amounts in the homogenate of proliferating cells. It has been reported that ATP specifically inhibits TdT without any effect on other DNA polymerases, and we have found this to be a most useful specificity control in our own studies of TdT levels in leukemia and lymphoma. As mentioned by Shaw et al., the well-documented presence of a receptor for the Fc portion of IgG on some T cells or antibodies directed against the cell surface of the leukemic cells could very well account for the observed binding of IgG to the peripheral blood lymphocytes. It is unfortunate that these studies were carried out in the peripheral blood with only 42% blasts and not on a bone marrow sample. Moreover, an absolute value for the IgG serum spike, labeling of the cells after trypsinization and/or short-term culturing and the use of fluorochrome-tagged monovalent anti-α and F(ab')2 fragments of antibodies, and information about the IgG spike during remission and at relapse would have been helpful to determine the nature of this patient’s leukemia.

ROLAND MERTELSMANN, M.D.
BEN KOZINER, M.D.
MALCOLM A. S. MOORE, Ph.D.
Memorial Sloan-Kettering Cancer Center
New York, N.Y.
REFERENCES


TdT Activity in B Cell ALL: Reply

To the Editor:

We should like to thank Dr. Mertelsmann and colleagues for their helpful comments and to answer them point by point.

With regard to the level of TdT activity in cells of different stages of the cell cycle, changes in the levels of TdT during the development of the chicken have been reported. The activity per gram of thymus increases very rapidly from 0.5 U/g at the first week to 184 U/g at the third week.

Concerning the specificity of the TdT assay, we should like to point out that the TdT activity may be confused with DNA polymerase only when activated DNA is used in the assay. In Table 1 of our paper, we clearly showed that (dA), is the preferred initiator for TdT and that its activity is dependent on the addition of the initiator. To further distinguish the activity, we assayed DNA polymerase purified from L1210 cells under conditions used to assay TdT activity and showed that the DNA polymerase did not incorporate a significant amount of ‘H-dGMP when (dA), was used as the initiator. A combination of NEM and ethanol markedly inhibited the TdT activity when (dA), was used as the initiator. This property has been used by others to distinguish TdT and DNA polymerase activities. The inhibition of DNA polymerase activity by NEM and ethanol can be measured only when activated DNA or synthetic deoxyribo primer templates are used in this assay. We used (dA),, as the initiator in the assay; (dA),, is not utilized by DNA polymerase after all. We wonder if Dr. Mertelsmann and colleagues realized this distinction before commenting on this aspect.

The report showing that ATP inhibits TdT appeared when our paper was in the process of publication. We believe that we used the assay system considered specific for determining TdT activity. Perhaps in the future more and even better distinguishing properties may be forthcoming and should be taken into consideration for future publications. We have one word of caution about the claim that ATP specifically inhibits the cellular DNA polymerases. Those authors used only synthetic primer templates to show that ATP did not inhibit the cellular DNA polymerases. This observation ought to be confirmed with the more common template, activated DNA, to conclude that it is “a most useful specificity control.”

We are obviously aware of the problems involved in being certain that the proliferating cells were B cells and that many of the investigations suggested by Dr. Mertelsmann and colleagues would have been done had it been possible to obtain followup samples. The patient was in an outreach hospital in Connecticut, and the original tests were done on a routine basis because he was not known to be of special interest. It is extremely unlikely that the immunoglobulin
TdT activity in B cell ALL [letter]
R Mertelsmann, B Koziner and MA Moore