Reed-Sternberg cells, lymphocytes, and interdigitating reticulum cell rosettes in Hodgkin's disease

Hodgkin's disease still remains an enigma both in the nature of its malignant cell population and in its polymorphic cellular composition. Recently, several authors have identified the various lymphoid subsets in the different subtypes of Hodgkin's disease.¹⁻³ We investigated lymph nodes partially affected by Hodgkin's disease and focused our attention on the cellular composition of the tumoral areas and the topographical relation between the different cell types and Reed-Sternberg cells, using immunohistochemistry and enzyme histochemistry. Most of our findings agreed with data from published studies.¹⁻³ Two unexpected findings, however, were noted.

In the affected areas we observed a predominance of cytotoxic suppressor T cells, in contrast to the excess of helper T cells reported previously.^{2,3} Moreover, a remarkable number of medium sized non-lymphoid cells was seen in these tumoral areas. On the basis of their morphology (irregular, indented nucleus with finely dispersed chromatin, pale eosinophilic cytoplasm with long projections), immunophenotype (OKIa⁺, BA1⁺, OKT9⁺, OKM1⁻, S₁₀₀⁺), and enzyme activity (ATPase⁺), these cells corresponded to interdigitating reticulum cells.⁴ These cells were found in a close topographical relation with typical Reed-Sternberg cells. At the ultrastructural level the Reed-Sternberg cells were often surrounded by fine dendritic projections belonging to the adjacent interdigitating reticulum cells.

These projections are most probably responsible for the "membranous" expression on Reed-Sternberg cells of a phenotype similar to the interdigitating reticulum cells on light microscopy.⁵ Hence the histogenetic relation between both cell types, which is based on recent findings,⁵ can be questioned.

A close relation between Reed-Sternberg cells and lymphoid cells, mainly helper/inducer T cells, has already been reported.⁶ Our findings highlight a further aspect—that is, the relation of the interdigitating reticulum cells to the Reed-Sternberg cell and lymphocyte rosette.

A functional role of interdigitating reticulum cells in the activation of T lymphocytes has been suggested.⁷ Moreover, the terminal differentiation of B lymphocytes into plasma cells is controlled by activated T cells.⁸ The Reed-Sternberg/lym-

phocyte/interdigitating reticulum cells rosette might therefore be suggestive of a lymphoid origin of the Reed-Sternberg cell, either an activated T cell or a transformed B cell.

G VAN PARYS
J VAN DEN OORD
C DE WOLF-PEETERS
RITA DE VOS
VJ DESMET

*Department of Pathology,
Laboratorium voor Histochemie
en Cytochemie,
Universitaire Ziekenhuizen,
Katholieke Universiteit, Leuven,
B-3000 Leuven,
Belgium*

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Lymphoid tissue and cyclical endometrium

I learned much about endometrial lymphoid tissue from the article by Morris *et al.*¹ Their findings convincingly showed that endometrial lymphoid tissue is very similar

to mucosal associated lymphoid tissue as seen elsewhere in the body. The authors also suggested that lymphoid tissue in the endometrium "appears to be a unique form of mucosal associated lymphoid tissue which is capable of rapid replenishment after shedding of the stratum functionalis during menstruation." Although this view would undoubtedly receive overwhelming support, I think it is wrong.

Almost all doctors believe that at menstruation the stratum functionalis of the endometrium is shed and the endometrium is then replenished by growth of the stratum basalis. This is what is taught at schools and universities throughout the world; it is what is stated in all standard texts, and it is an attractive and simple explanation for the observed fact that during menstruation endometrial thickness is reduced by 75% and the long tortuous late secretory glands are replaced by the short straight glands of the early proliferative phase. In 1957, however, Bartelmez² showed conclusively, using comparative studies on humans and rhesus monkeys that virtually no tissue is shed during menstruation.² He studied menstruating endometrium by means of reticulin staining and showed that the stroma reduced in thickness by 75% largely due to loss of fluid, with minimal superficial loss of tissue. The postmenstrual stromal reticulin framework was compact while in premenstrual endometrium it was loose and separated. Postmenstrual endometrium was shown to be not stratum basalis but stratum functionalis and compact stratum functionalis. What Bartelmez did not explain was how the long tortuous glands of premenstrual endometrium reverted to the long straight glands of early proliferative phase in endometrium. An explanation for this was provided by us in 1976 and 1977 in our electron microscopic studies of menstruating endometrium.^{3,4} We showed that at menstruation single epithelial cells were removed by the process of apoptosis and ingestion by intraepithelial macrophages, which then migrated back across the epithelial basement membrane into the stroma. I was pleased to note that Morris *et al* found intraepithelial macrophages by their immunohistochemical approach and also to learn that the intraepithelial lymphocytes which we had observed electron microscopically are T lymphocytes.

If the above view of menstruation is correct and very little endometrium is shed, then endometrial lymphoid tissue is not required to be regeneratively unique. I shall be interested to see if conventional