Virchows Arch. A Path. Anat. and Histol. 385, 335–342 (1980)

Virchows Archiv A

The Sternberg-Reed Cell: Mononuclear, Multinucleated or Multilobated?

N. Buyssens and N. Bourgeois

Department of Pathology, University of Antwerp, Wilrijk-Antwerpen, Belgium

Summary. The relationship between mononuclear, multinucleated and multilobated Sternberg-Reed cells was studied by reconstructions done on serial sections 1–2 μm thick. The 21 cells so studied showed the following combinations: 7 were binucleated, but two nuclei were composed of two parts at certain levels; these nuclei we propose to call composite. 8 cells were mononuclear and had composite nuclei and 6 cells were mononuclear and had single nuclei.

Key words: Sternberg-Reed cell – Reconstruction.

Introduction

According to accepted criteria the diagnostic Sternberg-Reed cell is binucleated. The nuclei are often in a mirror image position and contain one or more large inclusion body – like nucleoli. Mononuclear cells with the same characteristics are not considered to be diagnostic.

This study was carried out in order to clarify the relationship between mononuclear, multinucleated or multilobated Sternberg-Reed cells (SRC).

Material and Methods

A representative biopsy of a lymph node of Hodgkins Disease of mixed cellularity was studied. It contained many diagnostic Sternberg-Reed cells (SRC). The node was fixed in Mercuric Chloride/Formalin (B5) fixative and processed in glycolmetacrylate (JB4 Polysciences). 20 step sections of 1–2 μm thick were cut with glass knives on a Sorvall JB 4 microtome and stained with Haematoxylin and Eosin.

Twenty one SRC were traced throughout all the sections and photographed with a 63× immersion objective. The photographs were projected at a final magnification of 8000. The nuclei and the cell borders and other reference structures (small vessels, fibrous septa) were drawn on

Offprint requests to: Prof. Dr. N. Buyssens, Department of Pathology, Building S, University of Antwerp, UIA, Universiteitsplein 1, B-2610 Wilrijk-Antwerpen, Belgium

0340-1227/80/0385/0335/$01.60

transparent paper. These sheets were then superimposed according to the requirements for graphic or plastic reconstruction (Staubesand et al., 1953, Buyssens, 1962). Graphic reconstructions in the plane of the section and perpendicular to this plane were done on 5 cells. A plastic reconstruction of one representative nucleus was carried out. The thickness of the sections is a problem in any reconstruction and although the microtome was set at 1 µm, experience shows that this minimal thickness is only rarely reached and that the sections vary between 1 and 2 µm. We arbitrarily accepted a thickness of 1.5 µm. That this was a realistic figure was supported by the finding that the mean of the largest dimension of the nuclei in the plane of the sections was 14.04 µm and in a perpendicular plane 14.14 µm.

The major difficulty in studies of this kind is the tracing of the nuclei in the whole series with a high power immersion objective. The large binucleated cell is easily recognized, but when it becomes smaller, mononuclear and shows no nucleolus it is very hard to locate in the polymorphous cellular infiltrate of Hodgkins disease: this is particularly true when the nucleus ends and only a vague eosinophilic fragment of cytoplasm is left. In order to allow reconstructions the nuclei must be photographed and drawn in the same general direction and much time and effort is needed for exact orientation of the nuclei in the photomicroscope.

Results

21 cells presenting the accepted morphological features of multinucleated SRC or mononuclear Hodgkin cells were studied. The cells contained a total of 41 nuclei if all the separate nuclei in each section were counted. The following combinations were found:

1) 7 cells were binucleated, and two of the 14 nuclei were composed of two or more separate fragments which at a certain level however formed only one mass: these nuclei we designated as composite. Nuclei forming one mass throughout the series were called single. This does not mean that they have a regular rounded or oval shape: on the contrary they very often display a pronounced tortuosity, deep indentations, structures and pseudopods. It is only by the superposition of the drawings and the comparison with the microphotographs and the sections that a nucleus can be classified with certainty as single or composite.

2) 8 cells were mononuclear but had composite nuclei, which means that in several, not necessarily successive, sections of the series they presented as if there were two nuclei (Fig. 1).

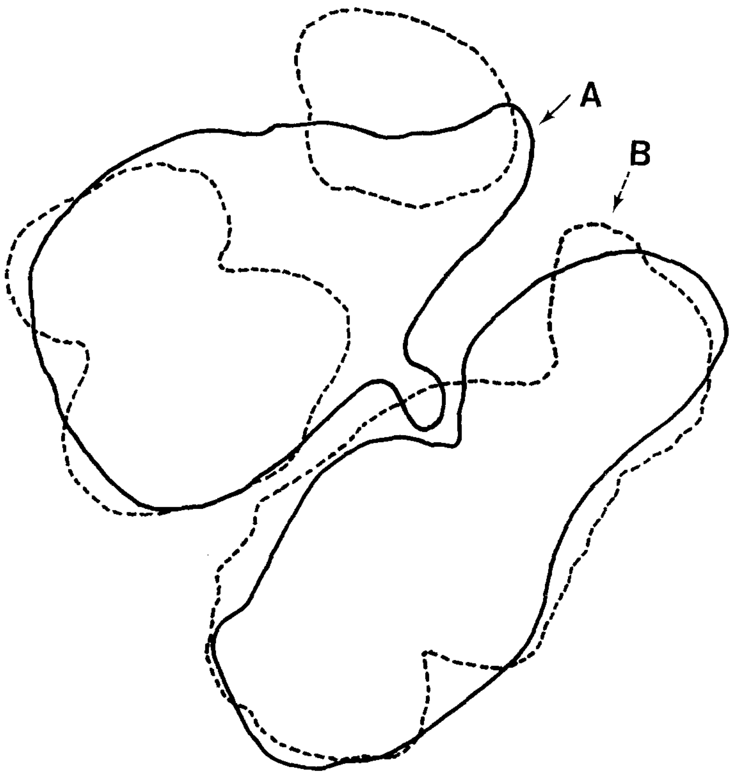
3) 6 cells were mononuclear and had a single nucleus. Since by definition the SRC should be binucleated it may be questioned whether it is justified to include these cells in the study. The reason is that they were morphologically indistinguishable from the "halves" of composite nuclei of group 2, and that when starting the examination one could not predict whether a given nucleus would turn out to split or not into more fragments.

Several morphological features were found regularly:

1) Extreme polymorphism of the nucleus changing from one section to the next. This is illustrated in the plastic reconstruction (Fig. 2).

2) The nucleus very often had a horseshoe shape, but the open end changed from place in each section and this relative rotation could be of the order of 180° (Fig. 3).

3) A considerable number of pyknotic mononuclear or binucleate SRC was found. Sometimes only a part of a nucleus was pyknotic, an example of which



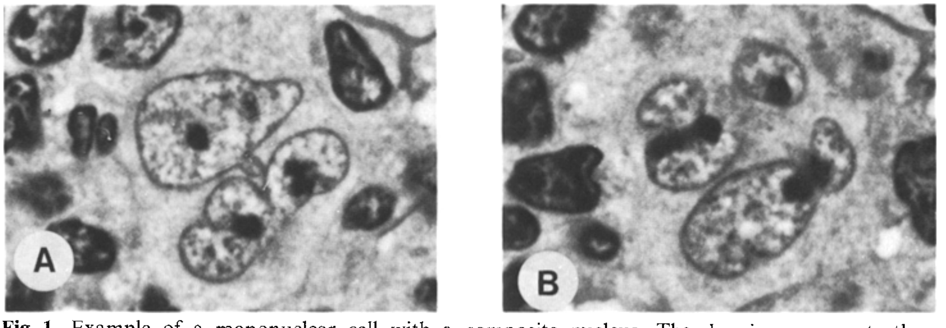


Fig. 1. Example of a mononuclear cell with a composite nucleus. The drawing represents the superposition in the plane of the section of two successive sections and demonstrates that the different fragments belong to one nucleus. Magnification: Drawing ×5,440, microphotographs ×1,650

is shown in Fig. 4: the cell is binucleate, one nucleus is single, the other is composite and part of it is pyknotic.

4) The nucleoli showed extreme variation in number, size and shape. They did not generally extend beyond three sections, very often lying in a stricture and sometimes giving the impression of protruding outside the nucleus. Several nucleoli may be present in one section and none in the next (Fig. 5).

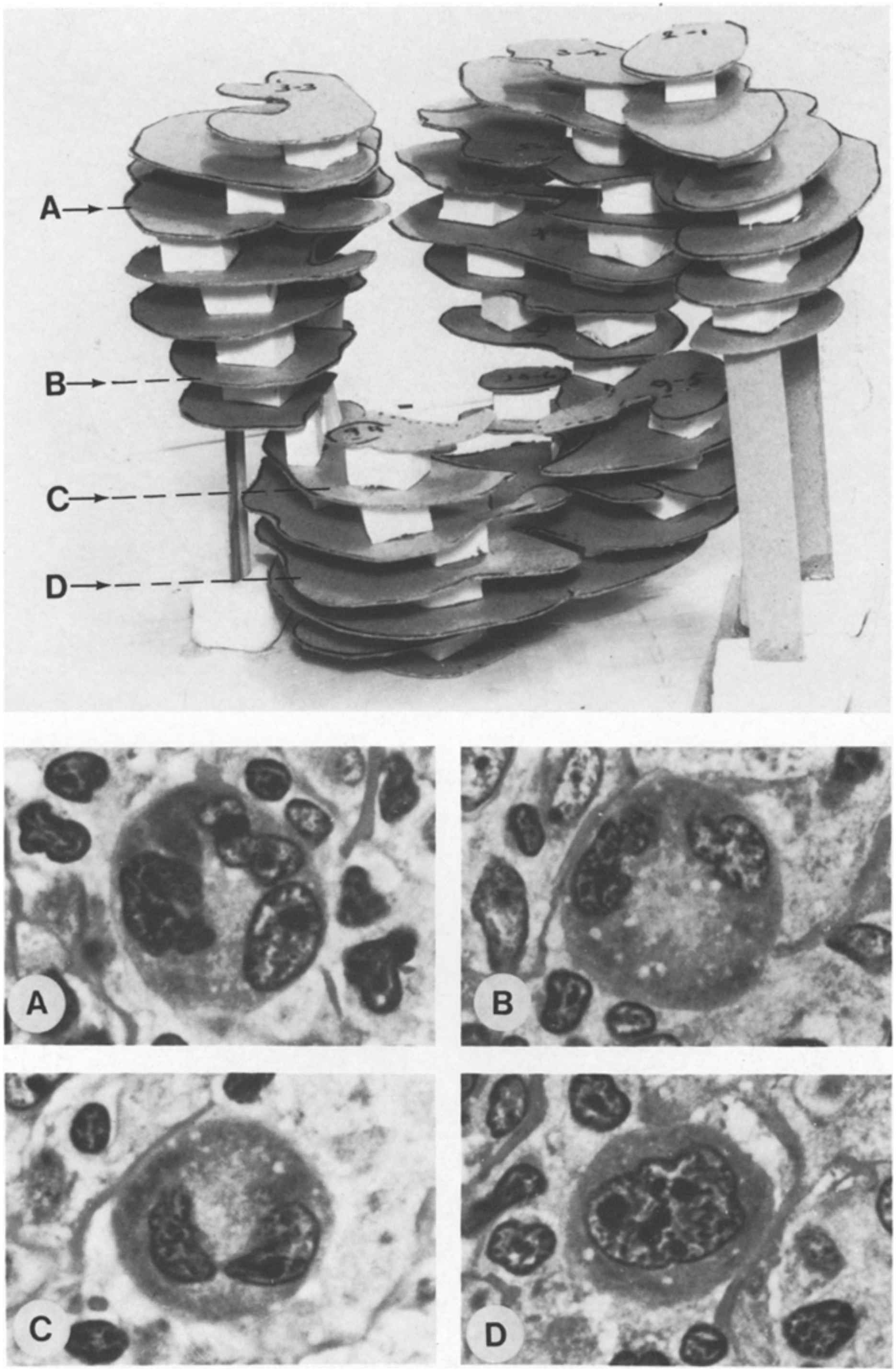
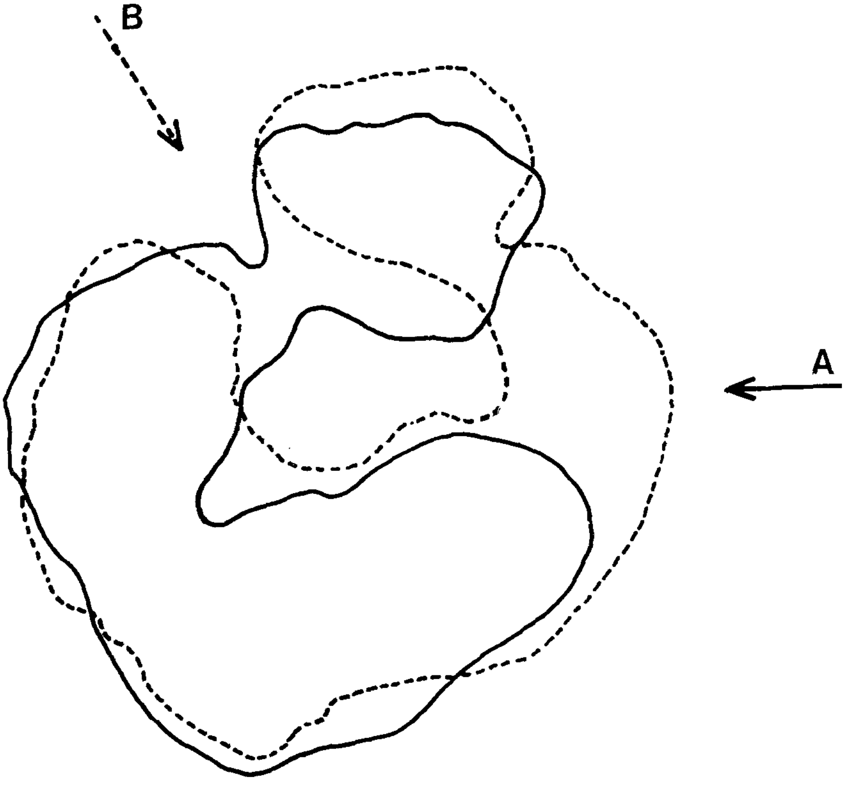


Fig. 2. Plastic reconstruction in cardboard. The lower border of the microphotographs corresponds to the front view of the reconstruction. Example of a monuclear cell with a composite nucleus showing extreme variation in size and shape of the different fragments. Magnification: Reconstruction $\times 4{,}210$, microphotographs $\times 1{,}325$



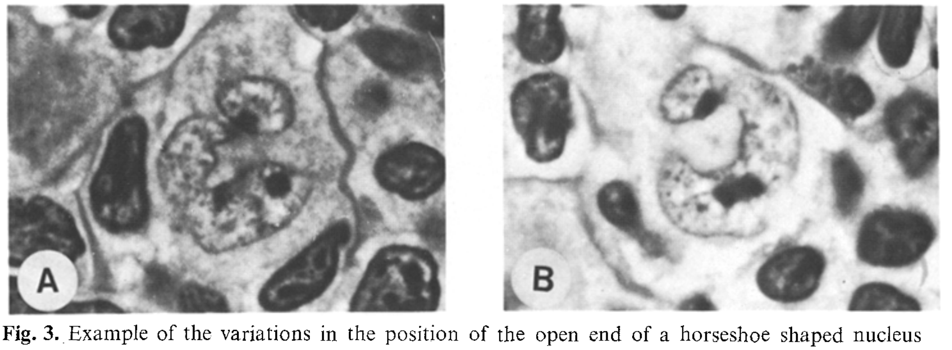


Fig. 3. Example of the variations in the position of the open end of a horseshoe shaped nucleus in two successive sections. The arrows points to the respective open ends. Magnification: Drawing $\times$ 6,150, microphotographs $\times$ 1,650

5) The size of the nuclei was also very variable. From the serial sections it was possible to determine exactly the largest dimension (diameter is not an appropriate term for such irregular nuclei): it ranged from 10 to 27 μm with a mean of 14.04 μm.

6) Mitotic figures in large cells, which because of their size could be regarded as SRC cells, were regularly found. They were, however, abnormal and consisted

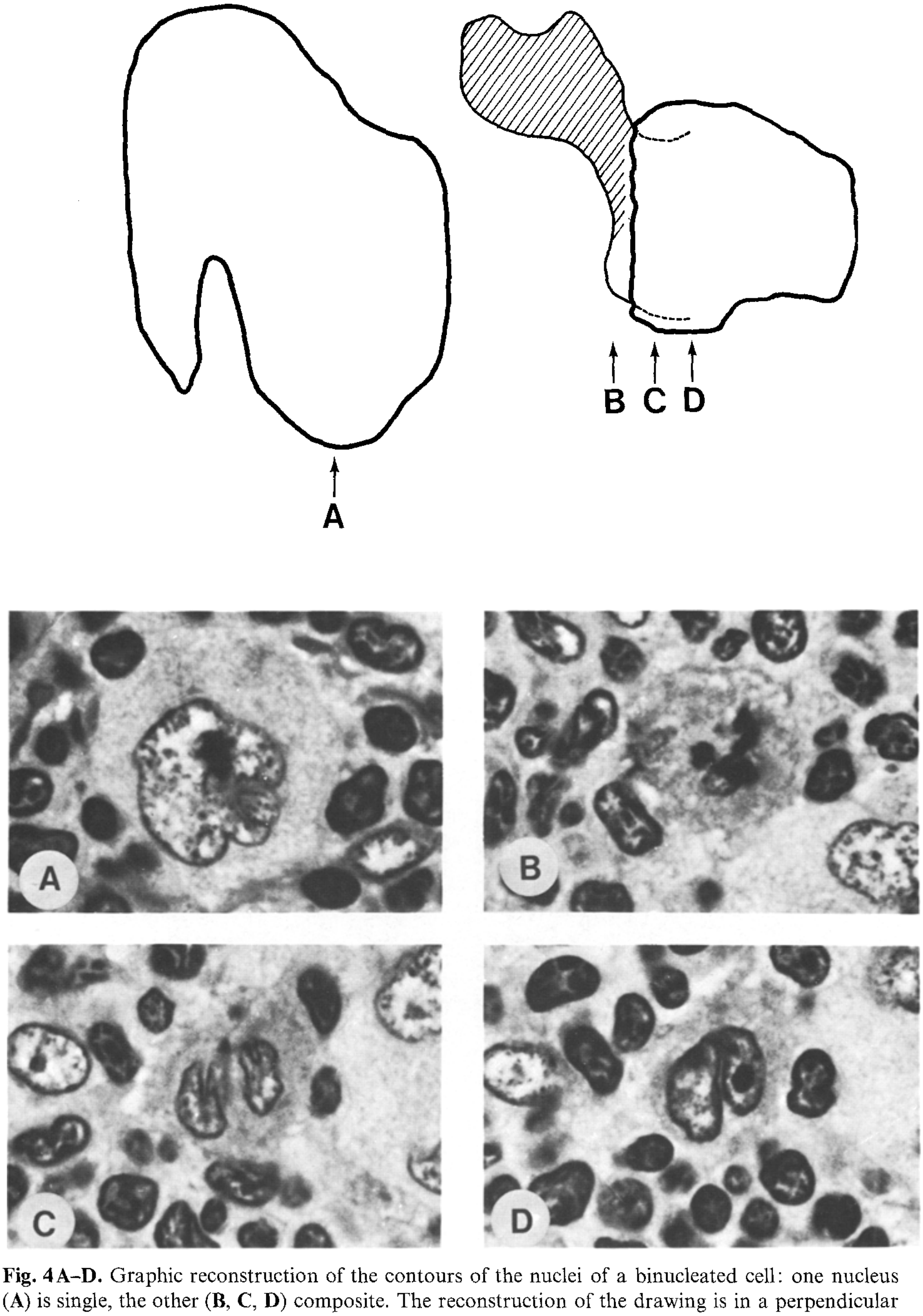


Fig. 4A–D. Graphic reconstruction of the contours of the nuclei of a binucleated cell: one nucleus (**A**) is single, the other (**B**, **C**, **D**) composite. The reconstruction of the drawing is in a perpendicular plane to the sections and the projection plane corresponds to the left border of the drawing and of the microphotographs. The arched zone corresponds to the pyknotic part of the nucleus, illustrated in figure B. Magnification: Drawing $\times$3,480, microphotographs $\times$1,325

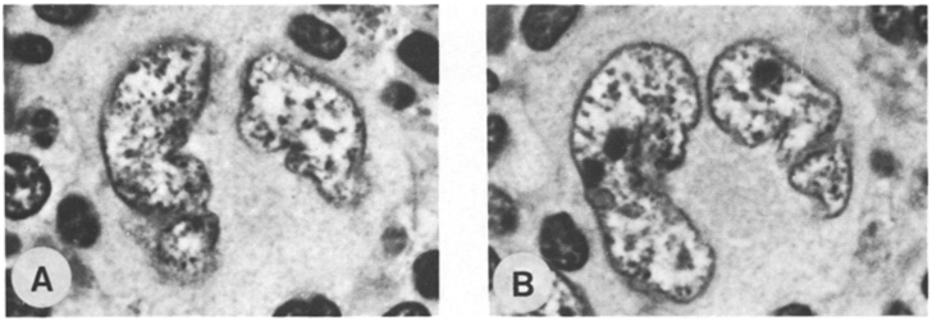


Fig. 5. Two successive sections of a binucleated cell to illustrate the changing pattern of the nucleoli. Magnification $\times$ 1,325

of radiating branches of chromatin comparable to wheel spokes; up to 5 branches were seen in one cell. Cell divisions were not found.

Discussion

Our results show that:

1) There are binucleated and multinucleated SRC, and each nucleus can be single or composite.

2) There are mononuclear SRC with composite nuclei which in certain sections will present as binucleated SRC. This finding confirms the description of Dorfman et al. (1973).

3) There are mononuclear SRC with a single, sometimes very indented nucleus.

The morphological appearance of any of these nuclei may be identical. The presence of nucleoli varies from section to section so that a large nucleus without a nucleolus must be considered as a possible candidate for a SRC.

Lukes (1966) states that the mononuclear type of the RSC is not a reliable basis for diagnosis: this certainly is a safe attitude. It should however be realized that a large single nucleus with or without a nucleolus, when situated in an "appropriate cyto-architectural milieu" (Kadin et al., 1971) is very likely to be part of a SRC. It is often told in tutorials and meetings that it is necessary to make many sections in order to find a "diagnostic" SRC. It would perhaps be more useful to make a short series, 10 or so, of step sections of 4 µm thick, and look for the same cell in the successive sections.

The fact that only a part of a nucleus may be pyknotic indicates that pyknotic nuclei or nuclear fragments stem from the original nucleus of the SRC and that these are not remnants of phagocytosed nuclei. In terms of general biology it is hard to understand how a part of a nucleus looks normal while the other part shows irreversible lethal damage. A possible explanation can be found in the theory of Altmann (1964) on the genesis of the nucleus of the SRC. He observed that in Hodgkins disease the "abnormal" reticulum cells undergo abnormal mitoses because of an insufficient development of the extrachromosomal dividing apparatus (the centriole and the central spindle). Hence groups of chromosomes irregularly scattered in the cytoplasm are formed. Each group becomes surrounded by a membrane and in a further stage these membranes fuse in an irregular fashion, giving as the final result an extremely indented and twisted nucleus. It is therefore concievable that the different parts of such a nucleus may have a certain degree of autonomy and may undergo changes which will not necessarily affect the other segments. We observed abnormal mitoses not accompanied by cell division, which is consistent with the Altmann theory.

References

Altmann, H.W.: Zur Kenntnis der Kerngestalt, des Cytozentrum und der Mitosestörungen in Sternbergschen Riesenzellen. Klin. Wochenschr. **42**, 1117–1122 (1964)

Buyssens, N.: La prolifération des canaux biliaires et la formation de structures tubulaires au cours des affections hépatiques en pathologie humaine et expérimentale. Rev. Belge Pathol. Med. Exp. **29**, 7–116 (1962)

Dorfman, R.F., Rice, D.F., Mitchell, A.D., Kempson, R.L., Levine, G.: Ultrastructural studies of Hodgkin's Disease. Nat. Cancer Inst. Monogr. **36**, 221–238 (1973)

Kadin, M.E., Glatstein, E., Dorfman, R.F.: Clinicopathologic Studies of 117 untreated Patients subjected to laparatomy for the Staging of Hodgkin's Disease. Cancer **27**, 1277–1294 (1971)

Lukes, R.J., Butler, J.J., Hicks, E.B.: Natural history of Hodgkin's disease as related to its pathologic picture. Cancer **19**, 317–344 (1966)

Staubesand, J., Andres, K.H.: Graphische Rekonstruktion zur räumlichen Darstellung präterminaler Gefäße und intravasaler Besonderheiten. Mikroskopie **8**, 111–120 (1953)

Received October 25, 1979