Lymphocyte Compartments in Human Spleen

An Immunohistologic Study in Normal Spleens and Noninvolved Spleens in Hodgkin's Disease

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A panel of monoclonal antibodies directed against T and B lymphocyte antigens was used to analyze the presence and localization of several lymphocyte subsets in 13 normal human spleens (3 of newborns) and 17 noninvolved spleens of patients with Hodgkin's disease. The distribution of cells in the white pulp corresponded with findings in other secondary lymphoid organs, except for the presence of a marginal zone, a unique compartment localized at the border of white and red pulp. The phenotype of the marginal zone cells indicates that it is likely that the marginal zone contains nonrecirculating as well as recirculating B cells, while T cells (of the T helper type) are also represented. Therefore, the notion that marginal zone cells are nonrecirculating IgM^+, IgD^- cells, appears to be an oversimplification. No clear differences were observed between spleens of patients with and without Hodgkin's disease. (Am J Pathol 1985, 120:443–454)

T AND B LYMPHOCYTES and their interactions play an important role in immunity. Therefore, the exact anatomic localization of T and B cells within lymphoid structures is of considerable interest. Studies in a variety of species, including man, have provided evidence for a distinct anatomic compartmentalization of lymphocytes.[1,2] B cells are located predominantly in follicular areas, whereas T cells are found in the paracortical or interfollicular regions of lymph nodes and in the periarteriolar region of the white pulp in the spleen.

The development of monoclonal antibodies, directed against lymphoid cell surface and cytoplasmic antigens has enabled the characterization of various human lymphoid subpopulations. As a consequence of this characterization, it has become possible to analyze the localization and proportion of cell subsets in lymphoid organs.[2–8] Because the spleen is likely to play a specific role in immunity, we decided to study the *in situ* anatomic relationship of immunoregulatory cells in human spleen. Therefore, a series of monoclonal antibodies was used in an immunoperoxidase method on frozen tissue sections. The possible implications of the localization of the different cell subsets in the spleen and their position in relation to one another, will be discussed. Special attention will be given to the marginal zone, a lymphocyte compartment in the spleen lacking in other lymphoid tissues.

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Table 1—Characteristics of the Monoclonal Antibodies

McAb	Antigen MW (daltons)	Reactive with	References
B1	30 K	B cells	13, 14, 15
B2	120/140K	B cells (C3d-receptor)	14, 16, 17
B4	80,40K/120K	B cells	18
BA1	45, 55, 65K	B cells, granulocytes	19
Leu 1	67K	T cells, thymocytes	20, 21
OKT3	19K	T cells, thymocytes	22, 23, 24
Leu 3A	55K	Helper/inducer T cell subset	21, 25
OKT5	33/76K	Cytotoxic/suppressor T cell subset	26, 27
OKT8	33/76K	Cytotoxic/suppressor T cell subset	22, 27
OKT11	55K	T cells (sheep red blood cell receptor)	28
66IIG5	40K	T cells	29, 30
Tac	58 K	The interleukin-2 receptor, present on activated T-cells	31
Leu 7	110K	Large granular lymphocytes, including natural killer cells	32, 33
Leu 11a	50/70K	Natural killer cells, neutrophils, basophils	34, 35
OKT10	37/45K	Thymocytes, some activated T cells, plasma cells	23
OKI1	29K, 34K	HLA-DR antigen	36
Leu 10	29K, 34K	HLA-DC/DS antigen	37
Leu 8	NR	T cells, B cells, granulocytes	34, 38

NR, not reported.

B1 and B2 were a gift of Dr. L. M. Nadler (Dana Farber Cancer Institute, Harvard Medical School, Boston, Mass); BA1 from Dr. T. W. LeBien (University of Minnesota, Minneapolis, Minn; OKT5, OKT10, OKT11 and OKI1 from Ortho Diagnostic Systems (Raritan, NJ); 66IIG5 from Dr. M. van de Rijn (Dana Farber Cancer Institute, Harvard Medical School, Boston, Mass; Tac from Dr. T. A. Waldmann (National Cancer Institute, National Institute of Health, Bethesda, Md); and anti-immunoglobulin monoclonal antibodies from Dr. J. Haaijman, RIV, Rijswijk, The Netherlands. B4 was purchased from Coulter Clone (Hialeah, Fla), Leu monoclonal antibodies from Becton-Dickinson (Mountain View, Calif), and OKT monoclonal antibodies from Ortho Diagnostic Systems.

Because (in rodents) the marginal zone is described to develop after birth,[9,10] three spleens of newborns were studied.

Because of the association of Hodgkin's disease and immunological defects, mainly in cellular immunity,[11,12] noninvolved spleens of Hodgkin's disease patients were included in this study for evaluation of whether changes in lymphocyte subsets could be found.

Materials and Methods

The spleens used in this study were obtained from 10 adult patients with ages ranging from 4 to 62 years. Splenectomy was performed because of trauma. In addition, three spleens of newborns (1 died of a congenital heart defect, and 2 of hyaline membrane disease) were included. Noninvolved spleens of 17 untreated patients with Hodgkin's disease, removed as part of a staging laparotomy, were also studied.

Tissue Preparation

Several tissue blocks of each spleen were snap-frozen in liquid nitrogen and stored at −70 C until use. Cryostat sections were cut at 6 μ and air-dried for 10–15 minutes with a hairdrier. Subsequently, slides were fixed in acetone for 10 minutes at room temperature and washed in phosphate-buffered saline (PBS), pH 7.4.

Monoclonal Antisera

A series of monoclonal antibodies (McAb) was used, which have been subject to several reports and from which the specificities are well defined. The present knowledge of the characteristics of these antibodies is listed in Table 1. The antibodies were used at dilutions considered to be optimal, as determined by previous experiments.

Immunoperoxidase Staining Procedure

A two-step indirect immunoperoxidase technique was used. Serial sections were incubated with 25 μl of the monoclonal reagents for 30 minutes. Control sections of each tissue block were incubated with 25 μl of PBS or with irrelevant monoclonal antibodies. Subsequently, the sections were incubated with 25 μl of a 1:20 dilution of a horseradish-peroxidase-conjugated rabbit anti-mouse immunoglobulin antibody solution (P161, Dakopatts, Copenhagen, Denmark) supplemented with 1% human AB serum, for 15 minutes. Each step was immediately followed by a repeated washing in PBS for 5 minutes. 3-Amino-9-ethylcarbazole (Sigma, St. Louis, Mo), together with H_2O_2, was used as a substrate for the demonstration of peroxidase reactivity according to the method of Graham, et al.[39] After washing in distilled water, counterstaining of the sections was per-

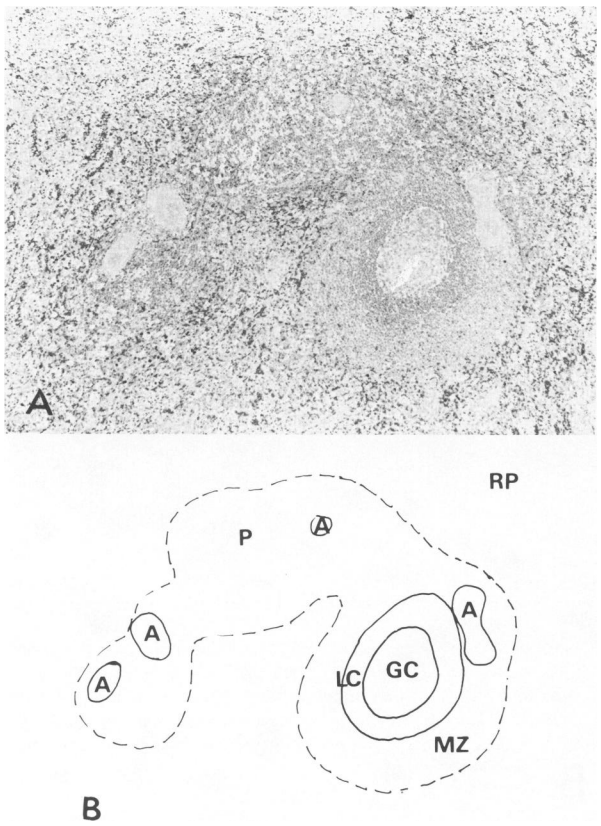

Figure 1A—Giemsa-stained section of spleen. (×56) **B**—Schematic representation of the splenic lymphocyte compartments shown in **A**. *RP*, red pulp; *GC*, germinal center; *LC*, lymphocyte corona; *MZ*, marginal zone; *P*, periarteriolar lymphocyte sheath; *A*, arteriole.

formed by incubation in fresh hemalum for about 30 seconds. The sections were mounted with glycerol–gelatin (Merck, Darmstadt, West Germany).

Double Staining Procedures

Leu 3a/Leu 7 Double Labeling

Sections were incubated with a mixture of Leu 3a and Leu 7 for 30 minutes. Subsequently, the sections were incubated with a mixture of fluorescein-conjugated goat anti-mouse IgG (Cappel Laboratories, Cochranville, Pa), detecting Leu 3a (being of IgG subclass) and rhodamine-conjugated goat anti-mouse IgM (Cappel) detecting Leu 7 (which is of the IgM class).

Leu 1/IgM Double Labeling

After incubation with Leu 1 for 30 minutes, sections were incubated with a mixture of fluorescein-conjugated goat anti-mouse IgG, detecting Leu 1, and rhodamine-conjugated rabbit anti-human IgM (polyclonal, Nordic, The Netherlands) labeling the IgM^+ cells.

Results

A schematic representation of the splenic lymphocyte compartments is shown in Figure 1.

Immunohistology of control sections, incubated with PBS or irrelevant antibodies instead of "specific antibodies," showed only weak, brownish endogenous peroxidase staining of mast cells, eosinophils, and neutrophils. In contrast, the reddish brown staining patterns obtained with the specific antibodies in the different lymphocyte compartments were distinctive, as shown in Figures 2–5 and summarized in Tables 2, 3, and 4. Nevertheless, the evaluation of Ig-positive cells in the red pulp often was hampered by the presence of serum, which was positive for Igs, especially IgG, and, to a lesser degree, IgA.

Plasma cells in general stained for Igs and with OKT10, and not with the anti-B-cell McAb B1, B2, B4, and BA1. In each case, the total number of plasma cells, stained for IgG, IgA, IgM, and IgD was about equal to the amount of $OKT10^+$ plasma cells. Arterioles frequently appeared to be surrounded by a considerable amount of these OKT10- or Ig-stained plasma cells.

Apart from the staining of lymphocytes, OKT8 showed a marked staining of reticuloendothelial lining cells of sinusoids in the red pulp (Figure 5 C and D). OKT 5 showed a similar staining pattern as OKT8 of lymphocytes in the PALS but did not react with the lining cells of the sinusoids.

In an attempt to gain information on the distribution of natural killer (NK) cells, apart from Leu 7, another monoclonal antibody, Leu 11a, was employed. In our study, Leu 11a showed a marked diffuse staining in the red pulp. The only cells that could be discerned were granulocytes. In general, follicles showed no staining, although occasionally a stained cell could be seen.

Compared with adult spleen, the white pulp of the neonatal spleens we studied showed a less demarcated configuration. In the follicles of this white pulp very few germinal centers (GCs) could be observed. Generally, all cells of the follicles were intermediate-sized lymphocytes, and a real marginal zone could not be discerned. B1 and B4 stained almost all cells of the follicles and also several cells in the red pulp (more than in adult spleen). BA1 had a staining pattern similar to that of B1 but showed much stronger reactivity of lymphocytes than in adult spleen. B2 showed staining of dendritic reticulum cells but no staining of lymphocytes.

Staining of few cells was seen for IgG, whereas anti-IgA generally showed no staining. Generally all follicle lymphocytes showed reactivity for IgM. Staining for IgD showed a pattern resembling the IgM staining pattern with respect to intensity as well as number of positive cells. Several plasma cells were stained for IgM and

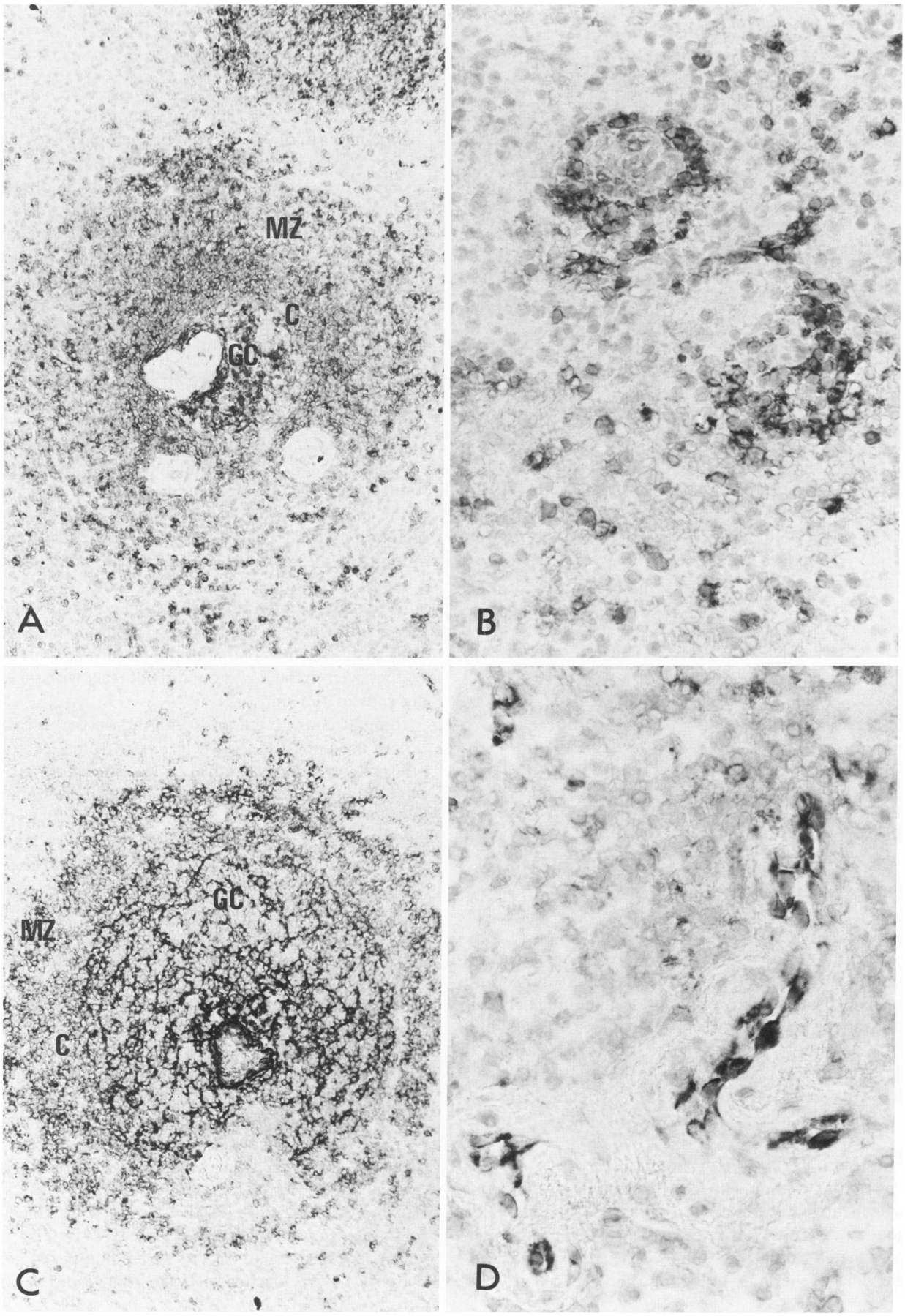

Figure 2A—Spleen section stained with B1. The majority of cells in corona (*C*) and marginal zone (*MZ*) are stained. The germinal center (*GC*) shows staining of a majority of the lymphocytes and also intercellular staining. (×140) **B**—Higher magnification of B1 staining in the red pulp. Part of the B1-positive cells are surrounding small vessels. (×350) **C**—Staining of spleen section with B2. The reactivity of lymphocytes in the marginal zone (*MZ*) is stronger than in the corona (*C*). In the germinal center (*GC*) intense dendritic staining is seen, while no staining of lymphocytes is present. (×140) **D**—Higher magnification of B2 staining of endothelial cells of small vessels in the red pulp. (×560)

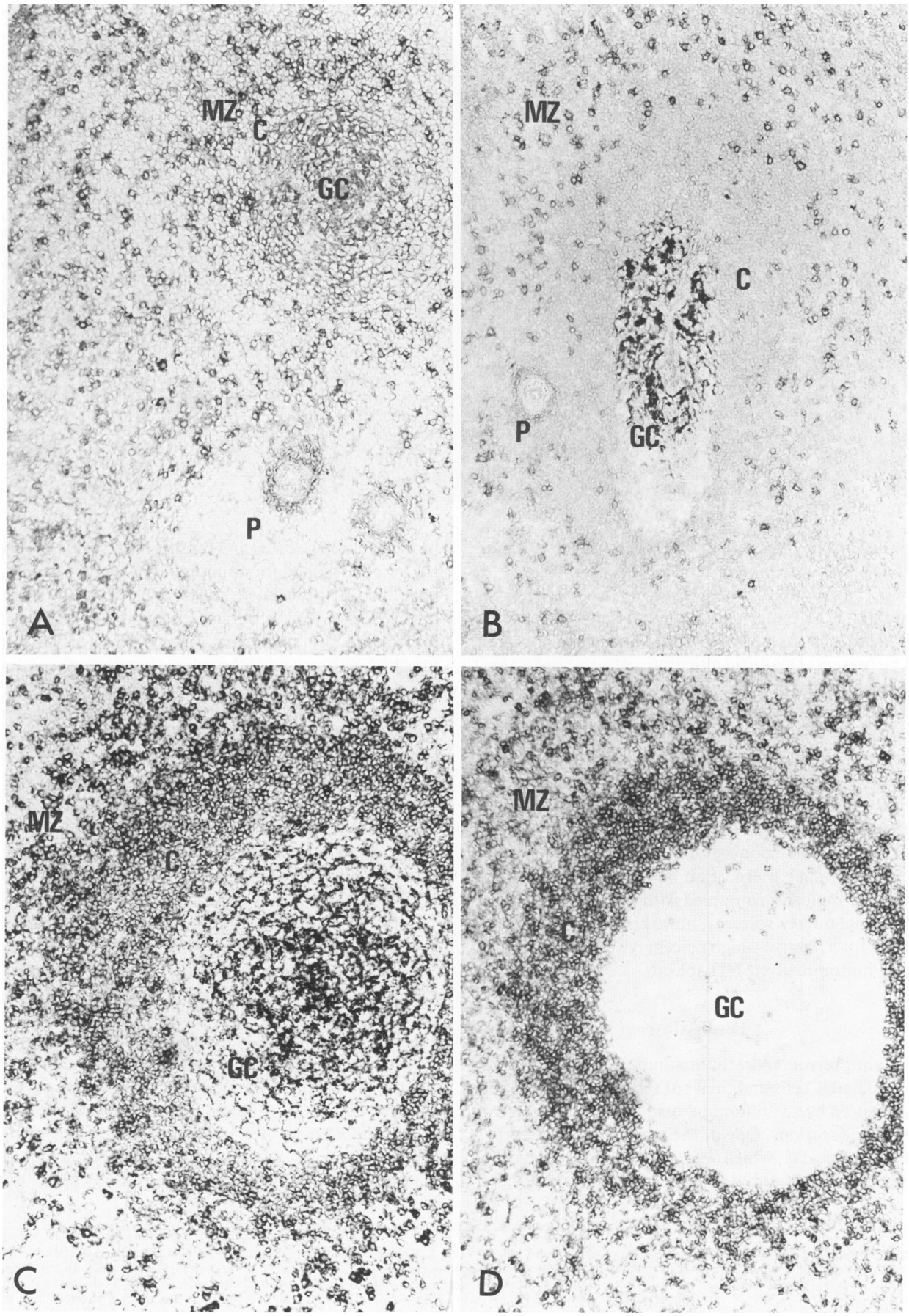

Figure 3—Spleen section stained for IgG (**A**), IgA (**B**), IgM (**C**), and IgD (**D**). Dendritic staining in the germinal center (*GC*) is seen for IgG and more intensely for IgA and IgM. IgD staining of the germinal center shows no reactivity, although rarely some stained cells are seen. Almost all corona lymphocytes (*C*) are stained for IgM and IgD and few for IgG and IgA. In the marginal zone (*MZ*), apart from staining of a majority of the cells for IgM, also several cells show reactivity for IgG, IgA, and IgD. Occasionally a stained cell is seen in the periarteriolar lymphocyte sheath (*P*). (×140)

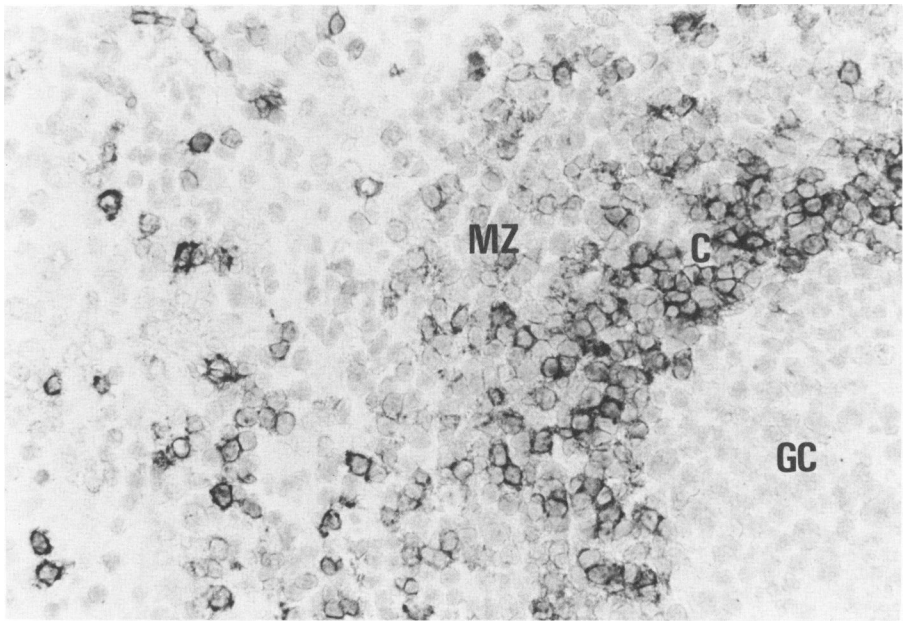

Figure 4—Higher magnification of IgD-staining of marginal zone cells. Note the absence of staining in the germinal center (*GC*), and, apart from the staining in the corona (*C*), the presence of several cells with positive staining (most weakly, few intensely) in the marginal zone (*MZ*). (×350)

OKT10 and few for IgG or IgD. Plasma cell staining for IgA was rarely seen.

OKI1 and Leu 10 showed reactivity in a pattern comparable to the pattern seen in adult spleen. Dendritic reticulum cells as well as interdigitating cells appeared to be present. Dendritic reticulum cells showed no immunoglobulin staining.

Adult and neonatal spleen showed little or no differences in the staining pattern of anti-T-cell McAbs and Leu 8, although the neonatal spleens showed a relatively smaller number of stained cells. No OKT8 staining was observed of the endothelial lining cells of the red pulp sinusoids.

Leu 7 showed staining of very few cells.

The staining pattern of noninvolved Hodgkin's disease (HD) spleens, compared with the staining pattern of normal human spleens, showed no clear differences, except for a relatively high percentage of secondary follicles in noninvolved HD spleens.

Discussion

In the present report the anatomic localization of human B and T cells and their subsets was studied in human spleen by an immunoperoxidase technique on frozen tissue sections. One of the monoclonal antibodies we used, Leu 11a, which was thought to react possibly with a "pan" NK antigen, at least in human peripheral blood,[39,40] showed staining results, indicating that it is not very well suited for immunohistochemical staining of spleen tissue specimens. In general, the results of our investigation were in agreement with the findings in previous reports of normal human lymph nodes and tonsils[2-8] with respect to the splenic lymphocyte corona, GC and periarteriolar lymphocyte sheath (PALS).

In the PALS, traditionally a T-dependent area, few cells were stained for Tac, which indicates a subset of activated T cells.

In the lymphocyte corona population very few cells possessed T-cell antigens. Nevertheless, double immunofluorescence labeling showed that a minority of corona IgM$^+$ B lymphocytes expressed weak Leu 1 reactivity. This Leu 1 reactivity was also observed in B-cell lymphomas,[40,41] as well as in reactive lymph nodes.

In the GC a variable number of cells could be demonstrated with anti-IgG, anti-IgM, and anti-IgA, the presence of which may be the result of heavy-chain class switching, thought to take place in the GC.[42,43] However, the possibility cannot be ruled out that the presence of different heavy-chain class immunoglobulins is (partly) due to B-cell traffic into the follicles from a recirculating pool. Anti-IgD showed in most spleens no GC staining (Figure 3D). This is in agreement with observations in other studies.[2,4,8] The finding of large IgD$^+$ cells in early GC by Hsu and Jaffe[7] could not be confirmed in the studied cases (normal spleens as well

Figure 5—Staining of T-cell subsets in the spleen: with Leu 3A (**A**), with Leu 7 (**B**), and with OKT8 (**C**). In the periarteriolar lymphocyte sheath (*P*), a majority of cells are positive for Leu 3a, a minority for OKT8; and Leu 7 shows generally no stained cells. In the germinal center (*GC*), on the border with the corona (*C*), several stained lymphocytes are seen with Leu 3a and Leu 7. Note the rim of Leu-3a–stained cells (*arrows*) in the middle of the marginal zone (*MZ*). (×140) **D**—Higher magnification of OKT8 staining of the red pulp. The staining of lymphocytes (*arrows*) is stronger than the staining of the sinusoid lining cells. (×350)

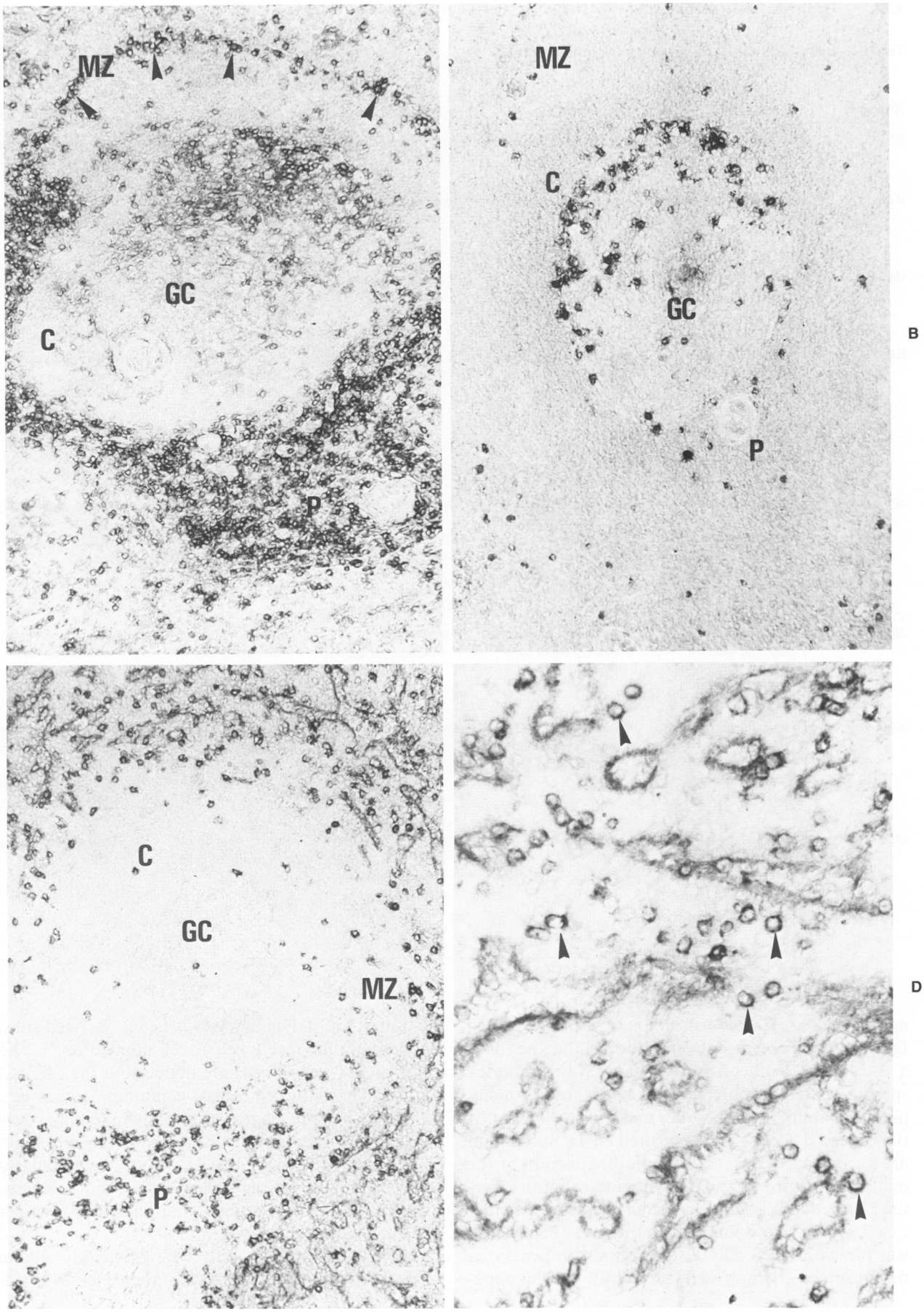
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Table 2—Distribution of B-Cell Subsets in Human Spleen

Antibody	Red pulp	White pulp			
		PALS	Marginal zone	Corona	Germinal center
B1	Few scattered stained cells	Few scattered stained cells	Staining of almost all cells	Staining of almost all cells	Staining of almost all cells; some intercellular staining
B2	Few scattered stained cells	Few scattered stained cells	Staining of almost all cells	Very weak staining of almost all cells; also intense dendritic staining	No staining of GC cells; intense dendritic staining
B4	Few scattered stained cells	Very few scattered stained cells	Staining of almost all cells	Staining of almost all cells	Staining of almost all cells; some intercellular staining, mainly in light zone
BA1	Few scattered stained lymphocytes; variable but generally large amount of stained granulocytes, generally concentrated around follicles	Staining of few large cells with cytoplasmic extensions	Staining of almost all cells	Staining of almost all cells (less intense than B1)	Weak dendritic staining
aIgG	Diffuse background staining; no separate cells can be discerned except for in some cases some plasma cells	Some stained cells, surrounding the arteriole	Outer part: variable amount, but minority of cells stained (less intensely than corona); inner part: hardly any staining	Variable, up to 25% of cells stained	Several cells weakly stained; some dendritic staining
aIgA	Diffuse, nonspecific staining; variable amount of intensely stained plasma cells	No staining, but for some plasma cells	Variable amount of lymphocytes stained	Up to 10% of lymphocytes stained	Some stained cells; intense dendritic staining, mainly in light zone
aIgM	Few scattered stained lymphocytes; variable amount of stained plasma cells	Few scattered stained cells; few stained plasma cells	Staining of large majority of lymphocytes (staining stronger than in corona)	Staining of large majority of lymphocytes	Very intense dendritic staining mainly in central part and towards light zone; few cells in light zone stained
aIgD	Few scattered stained cells; mostly very few stained plasma cells	Few scattered stained cells	Variable amount but up to 50% of lymphocytes weakly stained; few strongly stained cells, mainly in outer part	Strong staining of majority of cells	Generally no stained cells

as noninvolved HD spleens), although rarely a few small IgD^+ cells were observed. Despite the fact that the GC is a B-cell compartment, it also shows T-lymphocyte-specific staining, as observed in previous studies on human and animal lymph nodes and tonsils.[1,3] Most of the observed T cells represent the Leu $3a^+$ subset and are located as a crescentic rim on the junction of the light zone of the GC and the lymphocyte corona (Figure 5A). A double staining procedure demonstrated that Leu 7, which also stains cells in this area (Figure 5B), was present on GC cells, also reactive with Leu 3a, as demonstrated in lymph nodes previously.[33,44] This population of GC T lymphocytes is Leu 8^-, a T-cell subset containing the real T helper cell population.[34,45] Leu 7^+ Leu $3a^+$, Leu 8^- cells are not seen in the early GC reaction or in the centroblast-containing dark zone of GCs, but in later stages, specifically in the light zone, which consists mainly of centrocytes. Therefore, it is likely that the Leu 7^+, Leu $3a^+$, Leu 8^- subpopulation plays a regulatory role in maturation and differentiation of GC cells and not in initiation and development of the GC reaction.

In the red pulp, B cells were frequently situated around small vessels. These cells stained for B1 (Figure

Table 3—Distribution of T-Lymphocyte Subsets in Human Spleen

Antibody	Red pulp	White pulp			
		PALS	Marginal zone	Corona	Germinal center
OKT1	Few scattered stained cells	Majority of lymphocytes stained	Several stained cells mostly located in middle part of marginal zone	Very few stained cells	Several stained cells, crescentic rim of stained cells in light zone on border with corona
OKT3	Similar to OKT1	Similar to OKT1	Similar to OKT1	Similar to OKT1	Similar to OKT1
Leu 3	Few scattered stained cells; faint diffuse reaction with cords of red pulp	Up to 70% of lymphocytes stained	Rim of stained cells in middle part of marginal zone	Few stained cells	Staining of large number of cells in light zone; intercellular staining
OKT8	Several stained cells some inside sinuses	Up to 30% lymphostained	Rarely some stained cells	Rarely some stained cells	Occasionally few stained cells
OKT5	Fewer than OKT8	Similar to OKT8	Similar to OKT8	Similar to OKT8	Similar to OKT8
OKT11	Several scattered stained cells	Majority of cells stained	Similar to OKT1	similar to OKT1	Usually no staining but for thin crescentric rim of some stained cells in light zone on border with corona
66IIG5	Several intensely stained cells, more concentrated around white pulp	Majority of cells stained, mostly less intensely than in red pulp	Several stained cells localized in a pattern resembling that of Leu 3A	Very few stained cells	Several weakly stained cells, similar to OKT1; crescentic rim of stained cells in light zone on border with corona, less intensely staining than in the PALS
Tac	Very few scattered stained cells	Few stained cells	Rarely some stained cells	Rarely some stained cells	Weak staining of a few large cells, probably cytoplasmic

2B), B2, B4, OKI1, IgM, and IgD. Several of the endothelial cells of the vessels were positive for B2 (Figure 2D).

In contrast to the lymphoid compartments discussed so far, which have their equivalents in other lymphoid tissues, the marginal zone does present different features.

Marginal zone cells, mainly intermediate-sized lymphocytes, were in the majority reactive with B1, B2 (Figure 2A and C), B4, BA1, Leu 8, Leu 10, and anti-IgM (Figure 3C) and sometimes with anti-IgA, anti-IgD, or anti-IgG (Figure 3A, B, and D). Expression of B2 is considerably stronger in the marginal zone than in the lymphocyte corona, suggesting that marginal zone cells are more mature than corona cells.[8,14] Relatively weak staining for OKI1 is seen in the marginal zone lymphocytes.

Double staining showed that IgA, IgG, and a small part of IgD were not coexpressed with IgM on the same cells.[46]

The staining patterns of IgG, IgD, Leu 8, and, to a lesser degree, OKI1 and Leu 10 showed differences between an inner and an outer part of the marginal zone with respect to staining intensity and/or amount of stained cells (Tables 2 and 4). A rim of stained cells is seen in the middle part of the marginal zone with Leu 3a (Figure 5A) and 66IIG5, and also, but less clear, with OKT1, OKT3, and OKT11. The entrance of recirculating B cells in the marginal vascular sinus, which drains into the red pulp sinuses, could (partly) be an explanation for the selective presence of IgG^+, IgD^+, Leu 8^+, Leu 10^+, and $OKI1^+$ cells in the outer part of the marginal zone.

MacLennan et al[47] proposed that at least an (IgD^-) part of the marginal zone cells are a distinct functional lineage of nonrecirculating B cells. Nevertheless, a certain amount of (small) IgD^+ marginal zone cells (Figure 4), which represent up to 50% of the cells in the compartment, may be recirculating cells. These cells might be derived from follicular corona as well as from the peripheral blood circulation.

In summary, the marginal zone is a distinct anatomic

Table 4—Staining Patterns of Monoclonal Antibodies, Not T- or B-Cell–Specific

Antibody	Red pulp	White pulp			
		PALS	Marginal zone	Corona	Germinal center
OKI1	Diffuse weak staining; few scattered strong staining cells	Intense staining of several large cells with cytoplasmic extensions; no stained lymphocytes	Variable, up to 50% of cells stained, most of them weakly, a minority intense; staining of dendritic cells, mainly in outer part	Majority of cells stained, most of them weakly, a minority intense; weak staining of few dendritic cells	Staining of generally all cells; partly large dendritic cells; intercellular staining
Leu 10	Few scattered strong staining cells (less diffuse staining than OKI1)	Similar to OKI1	Variable, up to 75% of cells stained; staining of dendritic cells mainly in outer part	Majority of cells stained; weak staining of few dendritic cells	Similar to OKI1
OKT10	Few stained small lymphocytes; variable but generally large amount of stained plasma cells	Few intensely stained plasma cells, surrounding arteriole	No staining	No staining	Weak staining of large majority of GC cells; some strongly stained plasma cells
Leu 8	Several scattered stained cells	Intense staining of large majority of cells	Majority of cells strongly stained, in inner zone less intensely than in outer zone	Majority of cells stained (weaker than in PALS)	No staining
Leu 7	Variable amount of stained cells, usually more concentrated surrounding white pulp	Generally no staining, although sometimes a rare cell can be seen	Generally no staining	Generally no staining	Several intensely stained cells in light zone, mainly on border with corona

lymphocyte compartment in the spleen with unique immunohistologic features and cannot be compared with lymphocyte compartments in other lymphoid tissues. Apart from the described IgM^+, IgD^- nonrecirculating B cells in the marginal zone,[47] some other subsets appear to be present. From our results, it seems likely that also Leu $3a^+$ T cells, and non-IgM^+, IgD^- B cells are located in the marginal zone. Part of these B cells do present a phenotype similar to phenotypes of recirculating B-cell subsets.

The distribution of T- and B-cell subsets in noninvolved HD spleens, compared with normal human spleens, showed no marked differences. An abnormal distribution of T cells as one of the explanations for the defect in cellular immunity of Hodgkin's disease[48,49] could therefore not be confirmed in our study of noninvolved HD spleens.

The T-cell staining pattern in the PALS of neonatal spleen was similar to the pattern seen in adult spleen. Reduced cellular immunity in the newborn, compared with that in adults,[50] is therefore not reflected by differences in the phenotype and distribution of the splenic T cells. Interestingly, in contrast to adult spleen, OKT8 showed no reactivity at all with the reticuloendothelial lining cells of the sinusoids in the red pulp. The relative absence of Leu 7^+ cells is in agreement with low NK activity in newborns.[51]

The B cells in neonatal spleen are of intermediate size, $sIgM^+$, $sIgD^+$, and $B1^+$, relatively strongly $BA1^+$, and $B2^-$. Few cells stained for IgG and generally none for IgA, which is in accordance with findings in peripheral blood of newborns.[50]

Neonatal white pulp B cells are configurated in a folliclelike shape, in which no separate compartments could be discerned. The size and phenotype of the B cells do not correlate with those of B cells of adult splenic marginal zone, corona, or GC and may be an indication that most of the B cells in these spleens are of the early B type. The observation of the absence of adult-type white pulp B-cell compartments indicates that in man the development of these compartments to an adult configuration takes place after birth, as is also observed in rodents.[9,10] Poor response of infants to certain antigens, including polysaccharide antigens on the cell surface of several microorganisms, resulting in increased susceptibility to bacterial infections,[52] could be due to the absence of a functional marginal zone, in view of the supposed function of the marginal zone in the immune response against carbohydrate antigens.[47]

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