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CYTOLOGICAL AND FUNCTIONAL CRITERIA FOR THE CLASSIFICATION OF MALIGNANT LYMPHOMATA

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Summary.—The subtle morphology and functional properties of cells are the best parameters to use for their definition. This is also true for the corresponding tumours, especially malignant lymphomata. In studies of 106 cases of malignant lymphoma we therefore applied as morphological methods haematological staining (Giemsa in sections and imprints) and electron microscopic analysis. As functional criteria we used the nonspecific esterase reaction to define tumours of histiocytes and an estimation of the immunoglobulin content of tissue extracts and single cells to define tumours of B lymphocytes and their derivatives. By combining all of these methods it was possible to propose a new classification.

Whereas not one histiocytic malignant lymphoma ("reticulosarcoma") was found in the series, at least most of the malignant lymphomata investigated seemed to be derived from the B lymphocyte system. The following types are distinguished: (1) Chronic lymphocytic leukaemia; (2) diffuse germinocytoma (malignant lymphoma, lymphocytic, intermediate); (3) germinoblastoma (follicular, follicular and diffuse, diffuse; sclerotic, nonsclerotic) which can show a transition into germinoblastic sarcoma; (4) immunoblastic sarcoma of the B cell type (previously called reticulosarcoma); (5) lymphoplasmocytoid immunocytoma, which may be associated with Waldenstrom's macroglobulinaemia and can show a mixed cellularity; (6) lymphoblastic (paraleukoblastic) sarcoma and leukaemia, which are, at least in most cases, probably neoplasias of germinoblasts.

All of these lymphomata can produce immunoglobulins. Sixty-seven cases showed an Ig increase in the tumour. This was mostly IgM, but sometimes IgG, IgA, IgD and/or IgE. A morphological equivalent of even abnormal Ig secretion is the globular positive (diastase resistant) PAS reaction in lymphoid cells (not in the histiocytes) in paraffin sections, which we found in 43 cases. Only 19 of the 63 cases with an IgM increase in the tumour showed an increase of IgM in the serum. Waldenström's macroglobulinaemia is a facultative symptom of morphologically different malignant lymphomata and should therefore be considered only as a clinical syndrome and not as a nosological entity.

THE BEST WAY to specify a tumour is to combine a subtle cytohistological analysis with the demonstration of a characteristic cellular function which corresponds to the normal function of the cell type involved. This is also true for malignant lymphomata, as a report on our recent lymphoma studies indicates. Previous observations have been reported (Lennert, 1972; Stein, Kaiserling and Lennert, 1972; Stein, Lennert and Parwaresch, 1972). In 106 cases we supplemented detailed morphological analyses of Giemsa stained sections and imprints with electron microscopic investigations. Since the function of histiocytes is reflected in their enzyme pattern, the nonspecific esterase and acid phosphatase reactions were applied. Since it has been shown that immunoglobulin production is the main function of the B lymphocyte system, a study of the Ig content of malignant lymphomata might provide some insight as to the nature of the tumour cells and could yield an answer to the question whether or not the tumours

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are wholly or partly of the B cell type.

We investigated the Ig content on several levels: (1) in extracts of lyophilized tumours; (2) on the surface of suspended cells, light and electron microscopically with the immunoperoxidase technique; (3) in paraffin sections as (diastase resistant) PAS positive inclusions in the tumour cells; and (4) electron microscopically as protein deposits in the cytoplasm of the tumour cells.

For the Ig assays, fresh biopsy material from 106 non-Hodgkin lymphomata was lyophilized, suspended in saline solution, homogenized and centrifuged. The resulting clear supernatant was used for the analyses. The Ig determination was performed with radial immunodiffusion and the Ig content then expressed as a ratio of Ig concentration to albumin. The total protein values were corrected for their haemoglobin contamination. For interpretation the Ig values for the tumour tissue homogenates were compared with those obtained for normal lymph nodes.

Surface Ig was studied with the indirect immunoperoxidase technique described by Avrameas (1969) and modified for light microscopy by Stein and Drescher (1973).

The results from all of these studies compelled us to take a fresh look at our old lymphoma classification and to propose a new one. We would like to present such an attempt here. Thereby we shall disregard plasmocytoma, plasma cell leukaemia and other rare lymphomata.

1. *Chronic lymphocytic leukaemia (CLL) (synonym: malignant lymphoma, lymphocytic, well differentiated)*

CLL is a neoplasia which consists mainly of lymphocytes but always contains some lymphoblasts and prolymphocytes, which are accumulated in proliferation centres and usually exhibit a pseudofollicular pattern. The lymphocytes are totally PAS negative in paraffin sections. Plasma cells do not occur (Fig. 1).

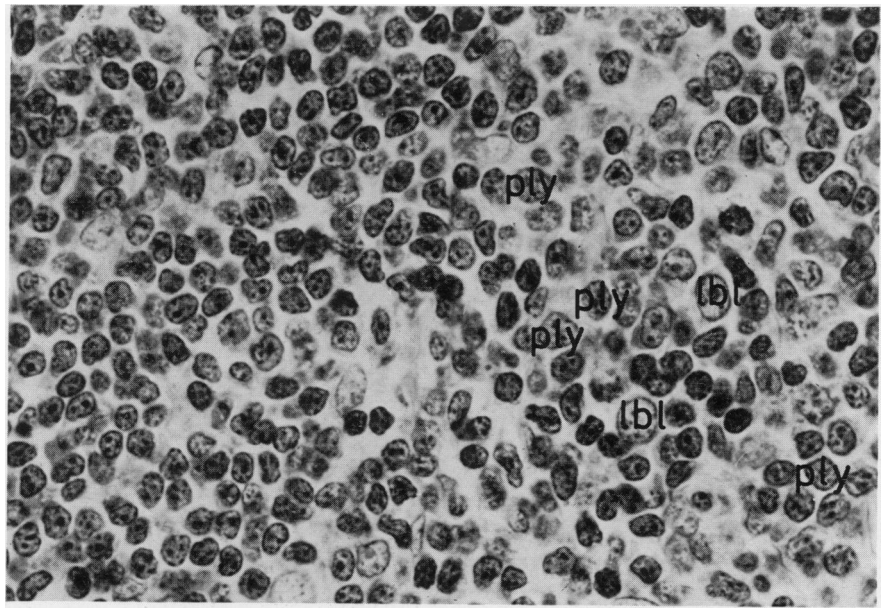

FIG. 1.—Chronic lymphocytic leukaemia. Note some lymphoblasts (lbl) and prolymphocytes (ply) on the right. IgM content 3·6 times normal. Giemsa. ×800.

Fig. 2 shows the IgM values for tissue extracts of 22 PAS negative chronic lymphocytic leukaemias. In this and the following figures the IgM values for the lymphomata are expressed in i.u. IgM/mg albumin, the serum IgM values in i.u. IgM/ml serum. The normal values for both lie within the shaded area. Circles stand for the lymphoma values and squares for the serum values.

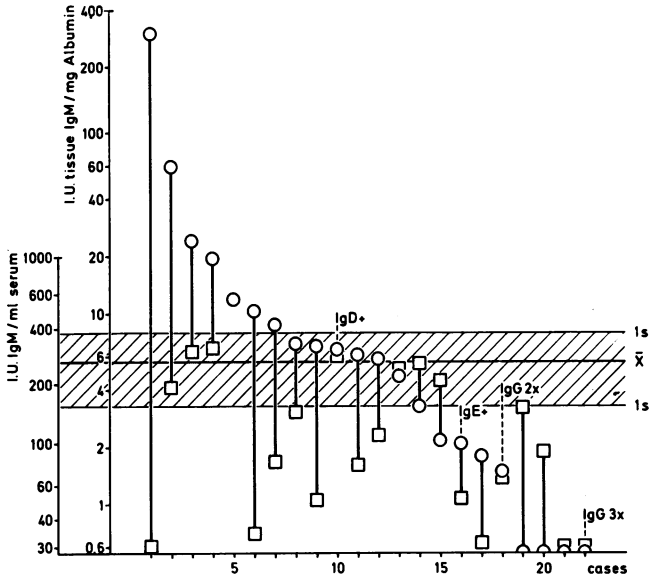

FIG. 2.—IgM values for tissue (○) and serum (□) of CLL.

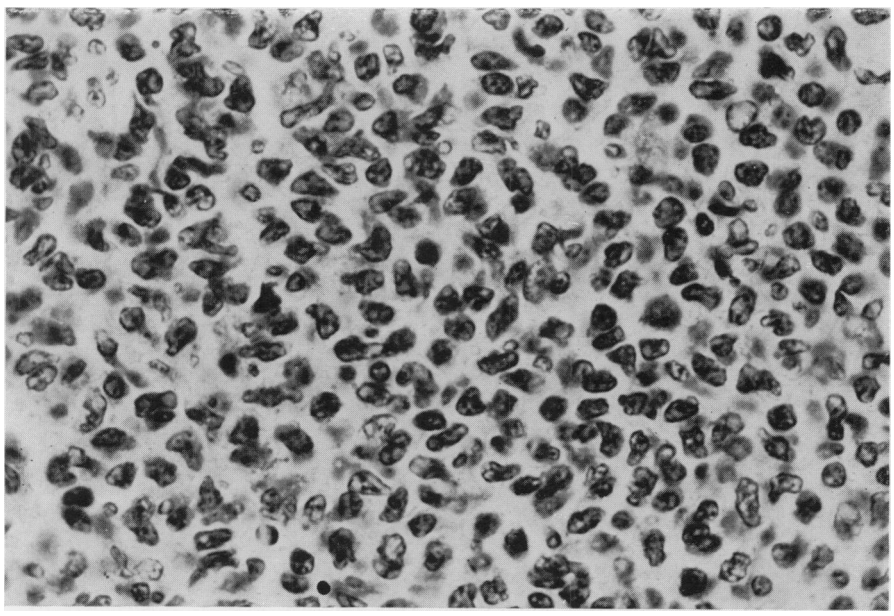

FIG. 3.—Diffuse germinocytoma. Note the polymorphous nuclei. IgM content 0·9 times normal. Giemsa. ×800.

It can be seen that 7 cases showed an increase of IgM in the tumour, whereas no case showed an increase in the serum. The highest value was about 60 times higher than normal In 2 cases we found increases in monoclonal IgG of 3 and 2 times respectively, in one case we found IgD and in another a large amount of IgE. The morphology of this last case was somewhat different from that of the others in that so-called cleaved cells (cf. below) were intermingled with the lymphocytes and lymphoblasts. This case should perhaps be eliminated from the group of CLL.

2. *Diffuse germinocytoma (synonyms: lymphocytic lymphosarcoma; malignant lymphoma, lymphocytic intermediate; follicle centre cell tumour, small cleaved cell type)*

This tumour, which can have a leukaemic blood picture, looks very much like CLL but differs from it in the absence of proliferation centres of lymphoblasts and prolymphocytes (Fig. 3). Above all, the lymphocytoid cells are very different from the lymphocytes of CLL. They are slightly larger and have characteristic nuclei. These are very irregular in shape (not round) and often cleaved. The chromatin is very fine and the nucleoli are very small or not to be seen at all. The cytoplasm is small and only slightly basophilic. It is usually more difficult to recognize the irregularity in the shape of the nucleus in imprints than it is in sections. We often find a few germinoblast-like cells in imprints but normally cannot identify any germinoblasts in sections.

Electron microscopically, the cells are quite similar to the so-called germinocytes of our nomenclature. The nuclei are polymorphous and lighter than those of lymphocytes. The chromatin is more uniformly distributed and not accumulated in clumps. We sometimes find nuclear pockets. In some cases it was possible to demonstrate desmosome connected dendritic reticulum cells, which are highly characteristic of germinal centres. Three cases showed some small plasma cells in between the germinocytes.

In silver stains, there is sometimes a resemblance to primary lymph follicles, albeit for the most part diffuse and with only very few but thick argyrophilic fibres.

This tumour shows a very close relationship to follicular lymphoma. Because we are convinced that it is a lymphoma of the germinocytic type, it has been called diffuse germino*cytoma*. However, we would like to stress that it does not correspond to the follicular lymphoma which we called germinocytoma in our earlier nomenclature (Lennert, 1964). This is now included in the group of germino*blastomata* (cf. below).

Fig. 4 shows the estimated IgM content of 11 cases. Seven showed a slight to moderate increase of IgM (up to 5 times higher than normal) in the tumour but no increase in the serum. After pretreatment with the detergent NP 40, the IgM content of one case was 15 times higher than normal. The blood serum of this case showed a monoclonal increase of IgM. The PAS reaction was negative in the sections of all but one case.

We investigated one case for surface bound antibodies and found IgM/lambda with typical capping. This phenomenon can also be seen at the electron microscopic level.

3. *Germinoblastoma (synonyms: follicular lymphoma; malignant lymphoma, nodular; follicle centre cell tumour, cleaved and non-cleaved)*

In contrast to sections of germinocytoma, those of germinoblastoma always reveal many, or at least some germinoblasts which are more basophilic than the lymphoblasts of CLL (Fig. 5). Typical germinoblasts have several medium-sized nucleoli which are often situated at the nuclear membrane. Together with numerous germinocytes and some dendritic

reticulum cells and macrophages, these cells are organized in germinal centres. However, in some cases of germinoblastoma the growth pattern is diffuse or follicular and diffuse. Furthermore, a special variant of germinoblastoma shows a sclerosing tendency (Bennett and Millett, 1969). Finally, germinoblastoma can transform into a uniform sarcomatous tumour, germinoblastic sarcoma, which

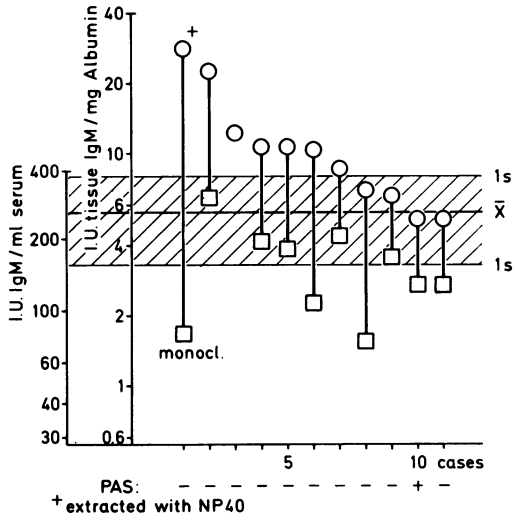

FIG. 4.—IgM values for tissue (○) and serum (□) of diffuse germinocytoma.

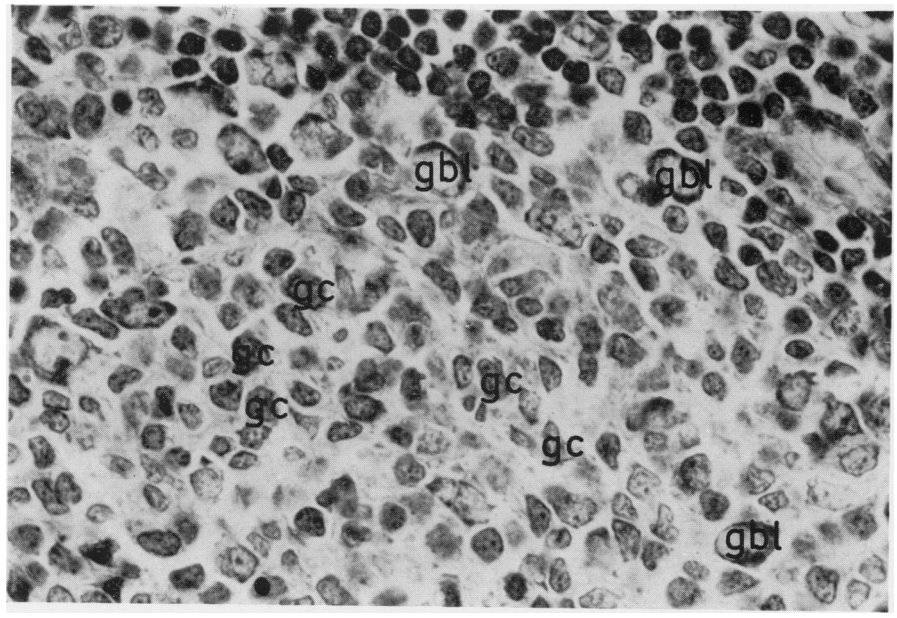

FIG. 5.—Follicular germinoblastoma. Above right note lymphocytic cuff of a germinal centre. Some germinoblasts (gbl) and many germinocytes (gc). IgM content 0·36 times normal. Significant amount of IgE! Giemsa. ×800.

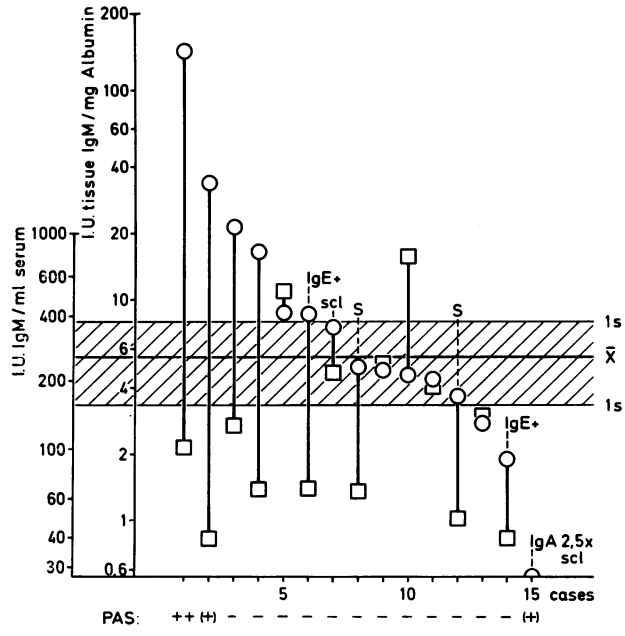

FIG. 6.—IgM values for tissue (○) and serum (□) of germinoblastoma and germinoblastic sarcoma (S). Two cases of the sclerosing type (scl).

sometimes corresponds to so-called Burkitt's tumour. As a rule it shows a diffuse growth pattern. The term germinoblastic sarcoma is used only when a typical follicular lymphoma (germinoblastoma) has been previously diagnosed.

Fig. 6 shows the IgM values for 13 cases of germinoblastoma and 2 cases of germinoblastic sarcoma (S). Two of the 13 germinoblastomata were histologically defined as sclerotic (scl), the others were of the typical follicular type.

Six of the 13 germinoblastomata showed a slight to moderate increase of IgM (up to 11 times higher than normal). Four cases showed normal and 3 cases subnormal values. The IgM values for the 2 germinoblastic sarcomata were normal and subnormal respectively. Two of the typical germinoblastomata revealed a significant amount of IgE in the tumour. One of the sclerotic germinoblastomata showed an increase of 2·5 times the normal amount of IgA.

The serum IgM values were normal in all but 2 cases. One case showed an increase of 3·5 times higher than normal. We do not know whether the IgM increase was monoclonal and shall therefore not take this case into account.

In one case we found many intracytoplasmic and intranuclear PAS positive inclusions, together with a moderate number of atypical plasma cells.

4. *Immunoblastic sarcoma (synonyms: reticulosarcoma; malignant lymphoma, histiocytic type)* (Fig. 7)

This group comprises all tumours which are composed of large cells with moderately to strongly basophilic cytoplasms and large nuclei with prominent nucleoli. The cytoplasm is either large or medium-sized. The nonspecific esterase reaction was negative for the tumour cells of all cases. Electron microscopically, all of the tumours contained a large number of polyribosomes and various

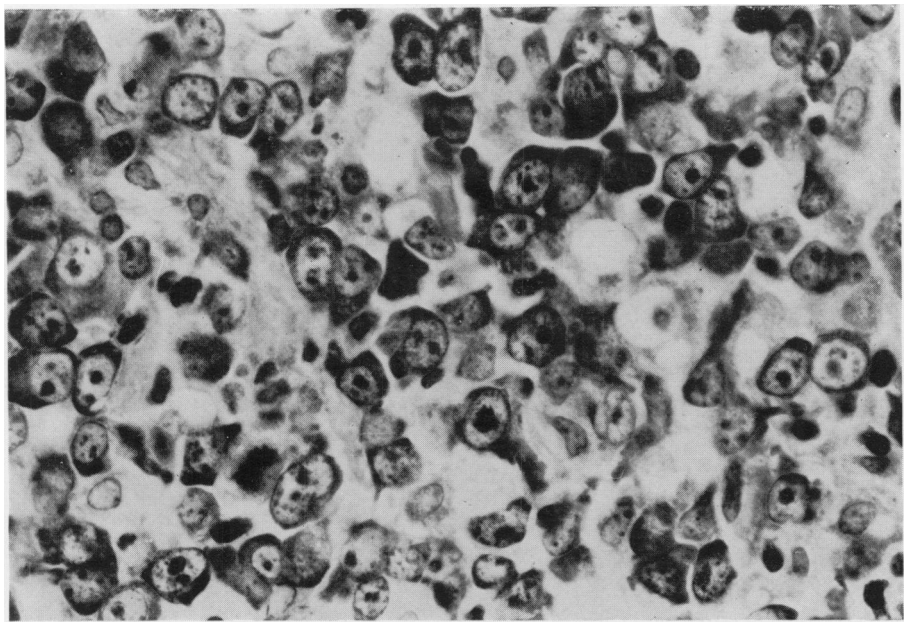

FIG. 7.—Immunoblastic sarcoma. Large, strongly basophilic cells with large nucleoli. IgM content 5·5 times normal. Giemsa. ×800.

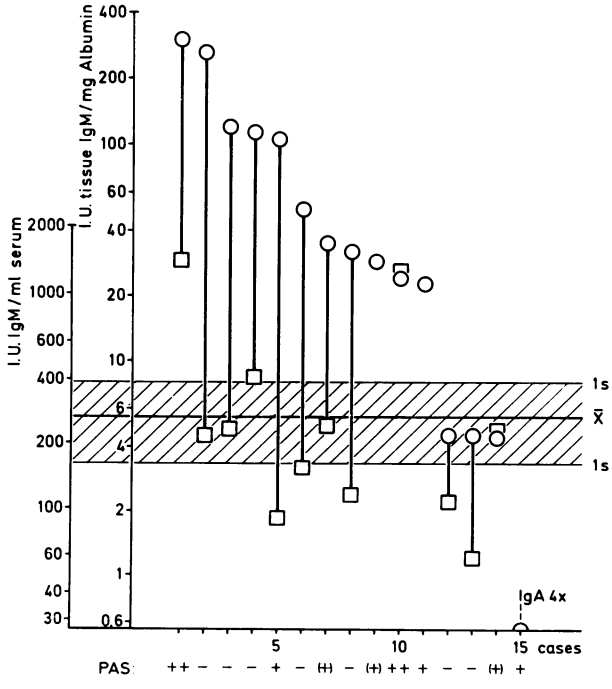

FIG. 8.—IgM values for tissue (○) and serum (□) of immunoblastic sarcoma.

amounts of rough endoplasmic reticulum. This and the IgM increases found in 4 cases led us to call the tumour immunoblastic sarcoma at the meeting in Nagoya, 1971.

Fig. 8 shows the results in 15 cases of so-called reticulosarcoma. Eleven of them revealed an increase in the tumour IgM content of up to 30 times higher than normal. In 3 of these cases there was a monoclonal increase in the serum IgM. The tumour IgM content of the second case was studied twice: 9 months after the first assay the IgM value was reduced to below the norm as a result of the increased anaplasia of the tumour. In 3 further cases, the IgM value lay within the normal range. The last case showed an increase in the IgA content of up to 4 times higher than normal. The PAS reaction revealed a globular and/or diffuse red staining of the tumour cells in 7 cases. Using the immunoperoxidase technique, we were able to demonstrate that the tumour cells of the 2 cases investigated bore surface IgM.

The high incidence of Ig increase in the so-called reticulosarcomata strongly suggests that the tumours of our series were in fact composed of immunoblasts of the B cell type. We therefore call them immunoblastic sarcomata of the B cell type. A positive PAS reaction in sections provides confirmation of the diagnosis.

Although we were not able to find a case with a reduced Ig content, we cannot exclude the possibility and we even assume that a few sarcomata exist that are composed of immunoblasts of the T cell type as well as true reticulosarcomata.

5. *Lymphoplasmocytoid immunocytoma (synonyms: malignant lymphoma, lymphocytic, well differentiated; for some: macroglobulinaemia Waldenström)* (Fig. 9)

This term covers a group of cases which show a great morphological variability. Some correspond to the well-known histological and cytological picture

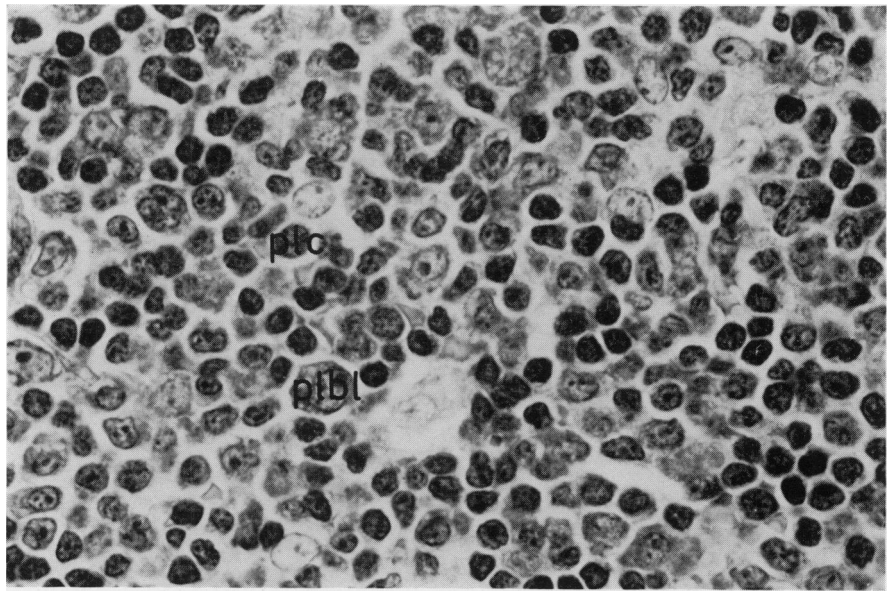

FIG. 9.—Lymphoplasmocytoid immunocytoma. Mixed cellularity. Plasmoblast (plbl), plasma cell (plc), lymphocytes, and lymphoid cells of different size and shape. IgM content 2·9 times normal. Giemsa. ×800.

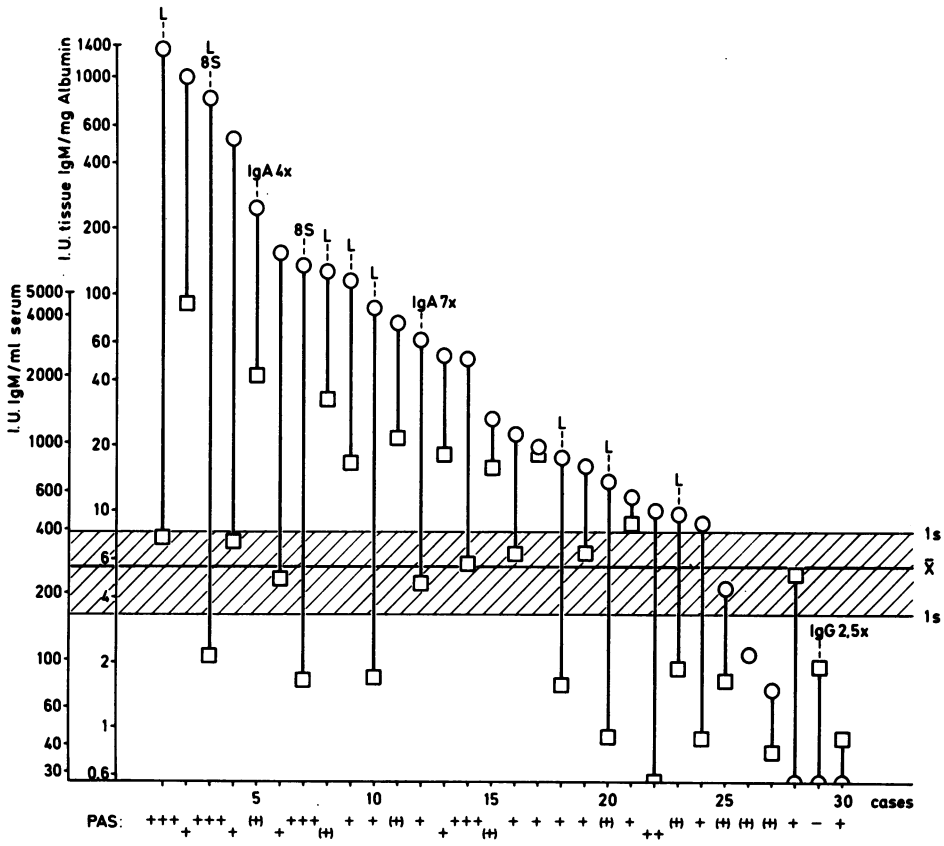

FIG. 10.—IgM values for tissue (○) and serum (□) of lymphoplasmocytoid immunocytoma. L indicates leukaemia. 8 S indicates that the IgM was of the 8 S type.

of macroglobulinaemia (Lennert, 1955). We may eventually have to divide this group into several subgroups. However, for the time being we would like to leave these cases together in one until we have more material.

At the present, lymphoplasmocytoid immunocytoma is diagnosed according to the following criteria:

1. Cytologically there are two main patterns: (a) mainly *lymphocytic*, but usually with at least some plasma cells and sometimes combined with the clinical appearance of chronic lymphocytic leukaemia. This pattern is mostly found in Waldenström's macroglobulinaemia; (b) *mixed cellular* with large basophilic cells (immunoblasts), medium-sized lymphoid or plasmocytoid cells, and small lymphoid or plasmocytoid cells.

2. The growth pattern is always diffuse and not follicular or pseudofollicular like that of CLL. We nevertheless find accumulations of immature cells which can be distinguished from the typical picture of CLL or germinoblastoma.

3. A mostly globular positive (diastase resistant) PAS reaction is usually found in at least some cells in paraffin sections, sometimes in a very large number.

4. About one-third of the cases show a monoclonal increase of IgM in the blood serum.

Fig. 10 shows the results in 30 cases of lymphoplasmocytoid immunocytoma. The letter "L" indicates a leukaemic

blood picture—there were 8 cases—the remaining cases were aleukaemic. The sign " 8 S " indicates 2 cases for which we characterized the extracted IgM as 8 S monomer. The serum of both cases contained reduced amounts of 19 S IgM; 8 S IgM was not detectable. (For details of both cases see Kaiserling, Stein and Lennert, 1973.)

As can be seen, all but 6 cases showed an increase in the tumour IgM. Nine cases also showed increases of IgM in the serum, some of which were proved to be monoclonal. In 2 cases both IgM and IgA revealed a monoclonal increase. The number of PAS positive tumour cells varied markedly from case to case. However, they were found in all but one. It produced IgG instead of the carbohydrate-rich IgM.

The results of the histochemical detection of Ig deposits with the PAS reaction did not fully agree with those from the Ig determination of the saline-extracted tumour tissues, namely in cases 27 and 30. The tissue from these 2 immunocytomata was then re-extracted with a mixture of NP 40 and Na desoxycholate. However, this extraction method did not release any more IgM from the tissue membranes. This indicates either that in some immunocytomata only few cells can produce Ig in significant quantities, or that the detergent is not able to solubilize the PAS positive cytoplasmic inclusions.

In this context, another finding is noteworthy because it can explain a similar one reported by Kim, Heller and Rappaport (1973). Together with Stacher and Lennert (1972) we have seen one case with a slight increase of IgM in the lymphoma but a significant decrease in the serum IgM. Light chains were found in the patient's urine. This suggests that in lymphoplasmocytoid immunocytomata, as in multiple myelomata, a dissociation in the synthesis of light and heavy chains takes place so that the production of heavy chains is impaired whereas that of light chains prevails.

6. *Lymphoblastic (paraleukoblastic) sarcoma and leukaemia (synonyms: malignant lymphoma, lymphocytic, poorly differentiated; ALL; follicle centre cell tumour, non-cleaved)* (Fig. 11, 12)

Whereas the groups 1–5 are morphologically quite well defined, this last group has yet to be adequately understood. The number of cases studied is not yet large enough to provide exact data.

We have designated as lymphoblastic or paraleukoblastic sarcoma and leukaemia those neoplasias which are uniformly composed of small (but somewhat larger than lymphocytes) or medium-sized, moderately to strongly basophilic cells, sometimes intermingled with so-called starry sky cells. Burkitt's tumour has to be included in this group.

Electron microscopically, the small and medium-sized types show the similarities and differences described in Table I. Both contain germinoblast-like cells with numerous polysomes and medium-sized nucleoli often located at the nuclear membrane. The small cell type also shows cells with cleaved nuclei. Only this type has a large number of nuclear pockets. The medium-sized cells of the second type contain small amounts of rough endoplasmic reticulum and are somewhat similar to immunoblastic sarcoma cells. However, they are smaller and look more like germinoblasts than immunoblasts. It should be stressed that the morphological borderline between medium-sized cell lymphoblastic and immunoblastic sarcoma is far from sharp.

The results for 13 cases shown in Fig. 13 show that 7 cases were of the small cell type (Type I) and that 6 consisted of medium-sized cells (Type II). Type I is involved only in children whereas Type II is found mostly in adults, especially those older in age. Type I was usually leukaemic, Type II was not. The PAS reaction was positive in 2 cases each.

The IgM values for the tissue extracts were slightly increased in 3 cases of

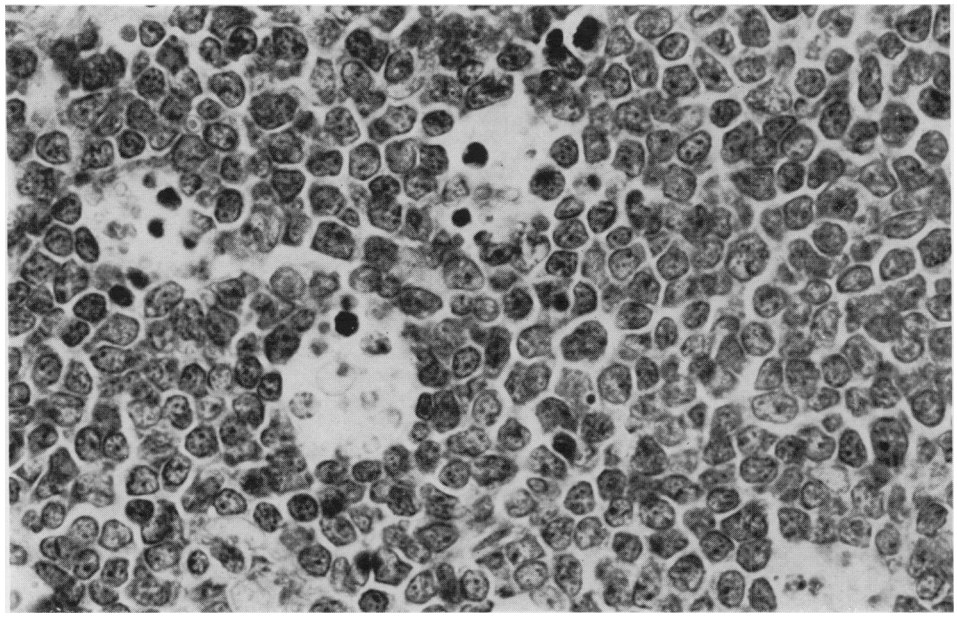

FIG. 11.—Lymphoblastic (paraleukoblastic) leukaemia. Small cell type. 4 starry sky cells. IgM content 0·8 times normal. Giemsa. ×800.

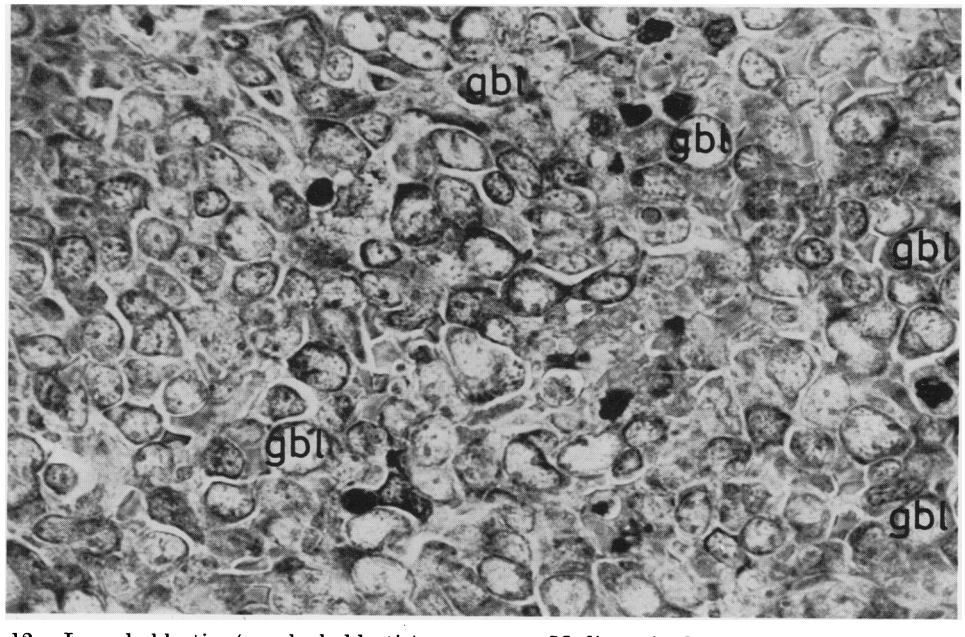

FIG. 12.—Lymphoblastic (paraleukoblastic) sarcoma. Medium-sized to large cells, some with characteristic germinoblastic appearance (gbl). IgM content 10·5 times normal. Giemsa. ×800.

TABLE I.—*Electron Microscopic Differences between the Small and Medium-sized Cell Types of So-called Lymphoblastic Sarcoma and Leukaemia*

	Small cell type	Medium cell type
Nucleus		
shape	Predominantly cleaved	Predominantly round
nucleoli	Multiple	Multiple
	Often at the membrane	Often at the membrane
	Medium-sized	Medium-sized or large
Nuclear pockets	++	(+)
Cytoplasm		
ribosomes	+	(+)
polysomes	(+)	++
rough ER	ϕ	(+)

Type I, once together with a small increase in the serum value. The IgM values for Type II, however, were greatly increased in 3 cases. In one case the tumour extract showed a normal IgM value whereas the serum revealed monoclonal IgM, which was partly the 8 S monomer.

The true nature of these tumours has not been conclusively determined. However, it is probable that at least some are derived from germinal centre cells, as Lukes (1973, personal communication) believes, since the electron microscopic morphology shows some similarities to germinocytes and germinoblasts (nuclear pockets, membrane associated medium-sized nucleoli). Further support for this interpretation of germinoblastic sarcoma lies in the fact that tumours developing from a typical follicular lymphoma (germinoblastoma) may be morphologically identical to Burkitt's tumour.

A final problem is the special lymphoma described by Lukes (1973*a*) which is said to be derived from the thymus and is called lymphocytic, convoluted type. We have seen some cases of this type of lymphoma, but at the present we are faced with contradictory findings and no final conclusions. The only consistent finding seemed to be a cytochemical one: in each case the acid phosphatase reaction showed a solitary focal positivity, which we could not observe in any other lymphoma.

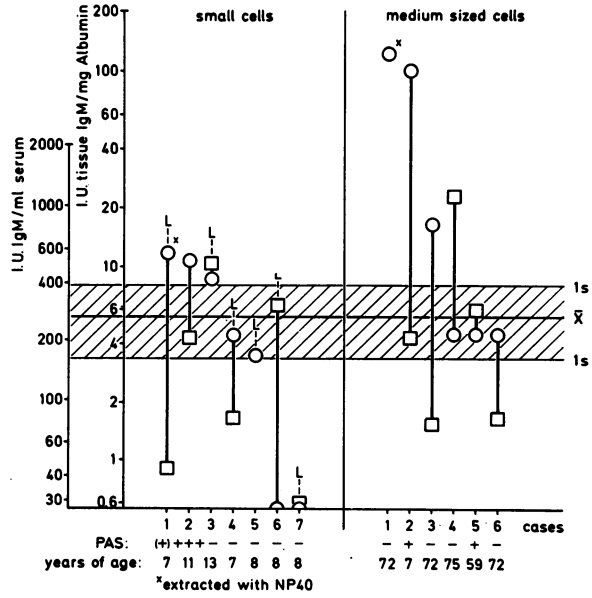

FIG. 13.—IgM values for tissue (○) and serum (□) of lymphoblastic (paraleukoblastic) sarcoma and leukaemia (L).

CONCLUSION

The Ig findings are summarized in Table II, which also contains the data on PAS positivity and the synonyms to our nomenclature. It can be seen that 67, or nearly two-thirds of the cases, showed an Ig increase in the tumour. A biclonal gammopathy was found in 4 cases. As to the type of Ig, the frequency of increase in IgM is quite outstanding whereas IgG and IgA were only rarely increased. This is in contrast to multiple myeloma in which the production of IgG and IgA is most frequent.

It is of interest that IgE was increased in 3 out of the 40 cases investigated. Since it was found in 2 follicular lymphomas and 1 case of "CLL", which showed some similarities to germinal centre cell tumours, a relationship to germinal centres is likely.

Only 19 of the 63 cases with an IgM increase in the tumour also revealed an IgM increase in the serum. This serum increase was not monoclonal in all cases. Two of the cases with no IgM increase in the tissue showed an IgM increase in the serum. One of these serum increases was monoclonal. It therefore seems that there is only a very loose relationship between the tissue and serum Ig values. Furthermore, the monoclonal macroglobulinaemia did not have a unique morphological basis. We found macroglobulinaemia in lymphoplasmocytoid immunocytomata, immunoblastic and lymphoblastic sarcomata, and in diffuse germinocytomata. The clinical *symptom* macroglobulinaemia should therefore not be used as the crucial criterion of a *disease*, *i.e.* Waldenström's macroglobulinaemia. Instead, we should define all tumours with IgM secretion into the blood according to their morphological appearance.

TABLE II.—*Frequency of Ig Increase in* 106 *Malignant Lymphomata. IgM, IgA, and IgG were Estimated in all* 106 *Cases, IgD and IgE in only* 40 *Cases*

Lymphoma	Synonyms	No. of cases	Increase of IgM	IgG	IgA	IgD	IgE	PAS+
CLL	m.l. lymphocytic well diff.	22	7 (0)[1]	2	—	1	1[2]	—[3]
Diff. germinocytoma	m.l. lymphocytic intermed.; lymphocytic lymphosarcoma; FCC-tumour, cleaved	11	7 (1)	—	—	—	—	1
Germinoblastoma	Follicular lymphoma; FCC-tumour, cleaved and non-cleaved	13	6 (2)	—	1	—	2[4]	1
Germinoblastic sarcoma		2	—	—	—	—	—	—
Immunoblastic sarcoma	Reticulosarcoma; m.l., histiocytic	15	11 (3)	—	1	—	—	8
Lymphoplasmocytoid immunocytoma	m.l. lymphocytic well diff.; macroglobulinaemia	30	26[5] (11)	—	2[6]	—	—	29
Lymphoblastic (paraleukobl.), sarcoma and leukaemia	m.l., lymphocytic poorly diff.; ALL; FCC-tumour, non-cleaved	13	6 (2)	—	—	—	—	4
Total		106	63 (19)	2	4	1	3	43

73–4 double producers = 69 cases

[1] In brackets: IgM increase in serum.
[2] Borderline case to germinoblastoma.
[3] The positive cases are included in the lymphoplasmocytoid immunocytomata.
[4] In one case together with an increase of IgM.
[5] In 2 cases 8 S IgM.
[6] Together with an increase of IgM.

The fact that all of the types of lymphoma investigated can show a monoclonal increase of Ig in tissue extracts indicates that they could all be B cell lymphomata, even though an increase cannot always be demonstrated in every case. The more anaplastic a tumour cell is, the less it produces immunoglobulin, which is a sign of functional competence. However, we cannot exclude the possibility that there are also isomorphic lymphomata which truly represent T cell or histiocytic tumours with no Ig increase. Even if the Ig content is increased in a given case, it does not have to be a B cell lymphoma when the Ig is not monoclonal.

B cells can be either secretory or non-secretory. The non-secretory cells—a prototype being the small lymphocyte—have a large amount of Ig *on* the surface, whereas the secretory cells—a prototype being the plasma cell—contain most of the Ig *within* the cytoplasm. Secretory Ig is produced at the outer nuclear membrane and/or the rough endoplasmic reticulum. The production and secretion mechanisms can be disturbed. This results in the storage of Ig in the cytoplasm, which can be easily recognized through a positive, mostly globular, diastase resistant PAS reaction, apparently often situated within the nuclei. However, it should be stressed that the PAS positivity must be localized in the *lymphoid* tumour cells (not in the histiocytes) and that it has nothing to do with that found in imprints of CLL or so-called lymphoblastic leukaemia. This PAS positivity represents glycogen instead and such soluble glycogen deposits are seldom seen in routinely fixed paraffin sections.

As shown in Table II, all types of lymphoma can show a positive PAS reaction. Altogether there were 43 cases, or nearly half of our material. The fact that all kinds of tumours *can* have secretory properties may be explained in two ways. First, we could assume that all types of B cells are basically able to secrete without having to first transform into special secretory cell variants, such as plasma cells. Or we could presume that, due to some defect, lymphoma cells as atypical cells can switch on the secretory mechanism even though they would normally not be able to do this.

We realize that an immunochemical investigation of tissue homogenates alone is a limited technique and that it cannot provide conclusive evidence as to the cell types present. However, we are convinced that our studies are meaningful for the following reasons: In all of the cases we investigated the results from the determination of both Ig in the tissue homogenates and Ig on the cytological level were identical as to the special heavy and light chains present. Similarly there was always concordance between the Ig assays of the blood serum and of the urine concerning the light chain type. Finally, we never found such high Ig values in cases of reactive or inflammatory changes in the lymph nodes: they were never above 1·5 times higher than normal.

In conclusion, this study of the functional properties of lymphoma cells has allowed them to be related to their normal equivalents. This in fact leads to a new understanding of familiar morphological pictures and provides meaningful suggestions for a scientifically based classification above speculation and dogmatic rigidity.

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