TABLE—*Classification of Malignant Lymphomata (Modified from Lukes and Collins 1974a, b)*

- I. Undefined cell type
- II. T-cell types
 - 1. Thymic lymphoma (convoluted lymphocytic)
 - 2. Node based T cell lymphoma
 - 3. Mycosis fungoides and Sezary's syndrome
 - 4. T cell ALL and CLL
 - 5. ? Immunoblastic sarcoma (of T cells)
 - 6. ? Hodgkin's disease
- III. B-cell types
 - 1. Small lymphocyte (CLL)
 - 2. Plasma cytoid lymphocytic
 - 3. Follicular-centre cell (FCC) types
 - (a) small cleaved
 - (b) large cleaved
 - (c) small transformed—Burkitt's lymphoma
 - (d) large transformed
 - 4. Immunoblastic sarcoma (of B cells)
- IV. Histiocytic types
- V. Unclassifiable.

from lymphomata containing neoplastic follicular structures with one exception had surface Ig, and closely resembled follicular centre cells (FCC) ultrastructurally. Similar findings were described in those diffuse lymphomata containing, by light microscopy, cleaved FCC or a mixture of cleaved and transformed FCC. FCC lymphomata made up 58% of the 45 consecutive lymphomata studied. These studies further showed that many lymphomata previously diagnosed as "histiocytic" lymphoma were composed of cells which bore surface Ig, did not have the cytochemical reactions of histiocytes, and were similar to transformed lymphocytes by ultrastructural examination. A complex group of neoplasms of T cell origin, some arising in lymph nodes, was found.

On the basis of these and similar studies of a small number of cases, it seems likely that each sub-population of lymphoid cells may give rise to a distinct neoplasm, and that lymphoid neoplasms may be usefully classified by a combined functional and structural evaluation (Table I). The use of such classifications will significantly improve interchange of information about normal lymphoid populations with information about lymphoid neoplasms. By this approach, relationships between diseases with altered immunological functions and lymphoid malignancies will be more apparent, relationships between lymphoid neoplasms primarily affecting the

marrow and lymphoid neoplasms primarily involving the extramarrow tissues may be established, and perhaps most importantly, lymphoid neoplasms may be used more effectively to study the normal lymphoid apparatus.

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METHODS FOR THE STUDY OF CELL DIFFERENTIATION IN ACUTE LEUKAEMIA

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The aim of the study of cell differentiation in acute leukaemia (AL) is to improve our means of recognizing the different cell types involved in the neoplastic process and to establish a firm basis for a classification of the disease. This may help in the identification of groups that vary in response to treatment and in prognosis, and could lead to improved selection of patients for different types of treatment. Some of the methods used are:

1. Cell morphology

On Romanowsky-stained films. A high standard of film spreading, fixation and staining permits the recognition of already well-differentiated cells in acute myeloid leukaemia (AML); *i.e.* cells containing azurophil granules, Auer rods, etc. Some distinct variants of AML, like promyelocytic leukaemia, may be diagnosed easily from these preparations.

2. Cytochemistry

Myeloperoxidase and nonspecific esterase reactions do help in the assessment of early myeloblastic or monoblastic differentiation in

otherwise undifferentiated cases of AML; this permits their separation from undifferentiated leukaemia (UL) which includes childhood lymphoblastic leukaemia. A positive acid phosphatase reaction in UL has been associated with the presence of T lymphocyte markers in the leukaemic cells (Catovsky *et al.*, 1974).

3. Products released by leukaemic cells

Consistently elevated serum and urine lysozyme (muramidase) concentrations are found in AML with predominantly monocytic differentiation (Perillie and Finch, 1973). This enzyme can also be demonstrated in single cells by a cytochemical test (Catovsky and Galton, 1973). Serum levels of vitamin B₁₂ binding protein (Transcobalamins I and III) seem to parallel granulocytic differentiation in the bone marrow.

4. Immunological markers

These have been dealt with in more detail by previous speakers. Their main application in AL is in the study of the morphologically and cytochemically undifferentiated cell types. The majority of childhood UL cases lack recognizable markers of B and T lymphoid cell differentiation ("null" blasts.) About 20% have been shown to have T-cell markers (Catovsky, *et al.*, 1974; Borella and Sen, 1974; Brown *et al.*, 1974), some of these cases present as a malignant lymphoma. B-cell markers may be found in cases of UL with morphological features resembling Burkitt's lymphoma cells and in adult cases of poorly differentiated lymphoma with blood and bone marrow involvement. Some of the findings in the latter cases show differences from the B-cell markers which are often found in chronic lymphocytic leukaemia.

5. Electron microscopy (E/M)

- (a) Transmission electron microscopy allows a more detailed study of the cell structure, degree of nuclear maturation, presence of cytoplasmic granules, etc. In AL it is of value when used in combination with
- (b) Cytochemical techniques at E/M level: Myeloperoxidase is a specific marker of the early "azurophilic" granules which appear during myeloid differen-

tiation. This enzyme may sometimes be demonstrated in a few cytoplasmic granules and/or in membranous structures of the cell in cases where the same reaction appears negative by light microscopy. Acid phosphatase with a special localization in the structure of the Golgi apparatus has been found in T-lymphoblastic leukaemia (Catovsky *et al.*, 1975).

- (c) Scanning electron microscopy (SEM): Differences in the surface structure of B and T lymphocytes were reported by Polliack *et al.* (1973). Few studies have been reported in AL. We have not observed differences in the surface appearances of T and "null" blast cells in cases of childhood UL (Catovsky *et al.*, 1975).

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EXPRESSION OF SURFACE ANTIGENS IN RELATION TO THE MITOTIC CELL CYCLE

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"... for many years we and others have compared the special biochemical properties of the cancer cell with what we called the corresponding normal cell. The great bulk of these studies utilized the corresponding normal *adult* cell, and we now begin to see how misleading this comparison can be. It is likely that the real comparison ought to be between the cancer cell and a *normal cell growing rapidly*" (Haddow, 1967).

This opinion is enforced by a failure to find *real* phenotypic differences between normal and transformed cells. Innumerable biological properties, originally considered peculiar to tumour cells, have subsequently been shown to be a feature of dividing cells. These include changes in electro-negative charge (Purdom, Ambrose and Klein, 1958; Ben-Or, Eisenberg and Doljanski, 1960), membrane permeability (Cunningham and