Memoranda

HISTOPATHOLOGICAL DEFINITION OF BURKITT'S TUMOUR*

Following clinical and pathological descriptions of a malignant tumour occurring with unusual frequency in African children, the eponym " Burkitt's tumour " was introduced in order to circumvent international semantic differences in the classification and nomenclature of haematopoietic neoplasms and also to honour the man who published the first clinical report. The use of this eponym, however, resulted in considerable confusion, particularly in the wake of numerous publications of cases from many non-African countries. The term has been variously interpreted as referring to a specific morphological entity found only in Africa, to a type of lymphoma seen everywhere but unusually common in Africa, to a clinical or clinical-pathological syndrome, or simply to a large malignant jaw tumour in children. It has even been applied to some animal tumours which have certain similar morphological features.

As interest in epidemiological, etiological, and therapeutic studies of the disease increased, it was considered that a more precise definition of Burkitt's tumour needed to be formulated as a necessary first step to further investigation. In 1964 a plan was devised to collect at a central repository at Villejuif, France, a large amount of representative pathological material and clinical data from a number of African countries as well as from other continents. The material would be circulated among a number of pathologists who, after review, would complete a detailed form listing the histological and cytological characteristics. It was hoped that computerization of the data would indicate essential criteria which in turn would permit a precise histopathological definition. Many difficulties were encountered during the attempted implementation of this plan, however, and it soon became clear that, even if many of the logistical and technical problems were overcome, the programme could not be completed in a reasonable length of time.

When in 1967 the WHO International Reference Centre for the Histopathology of Leukaemias and Other Neoplastic Conditions of the Haematopoietic Cells at Villejuif, re-emphasized the importance of the proper and accurate definition of Burkitt's tumour for inclusion in a new classification in preparation by the Centre, a modified approach was sought.

It had become apparent by this time that most of the confusion about Burkitt's tumour was the result either of semantic differences among international investigators or of inaccurate interpretations by inexperienced observers. It was believed, therefore, that an international consultation among experienced haematopathologists and cytologists with a particular interest in Burkitt's tumour could result in an authoritative definition which would be internationally acceptable. Such a consultation was accordingly organized by WHO in collaboration with the International Agency for Research on Cancer. A particular effort was made to include participants who would represent most of the differing opinions on the subject as expressed in the literature.

TERMS OF REFERENCE AND OBJECTIVES

The following statement of general objectives and specific points to be considered was circulated to and approved by all the signatories of this memorandum.

The purpose of the consultation is to define Burkitt's tumour and to determine its position in the proposed new WHO classification of leukaemias and other neoplastic conditions of the haematopoietic cells.

To meet this general objective, an attempt must be made to answer the following questions:

(1) Does the eponym refer to a lymphoma composed of a specific cell type, a lymphoma with a specific clinical behaviour and/or anatomic distribution, or a combination of these?

(2) If the eponym refers to a specific cell type, what is the most suitable and correct name for this cell?

The answer to, a consensus on, or, if necessary as a last resort, an arbitrary decision on these two basic questions will clarify several other points of contention and confusion which continually arise in respect of the diagnosis and treatment of this tumour.

(3) Does the malignant lymphoma which occurs with high frequency in children of equatorial Africa, and is called Burkitt's tumour, occur also in other parts of the world?

* This memorandum was drafted by C. Berard, G. T. O'Conor, L. B. Thomas and H. Torloni. For complete list of signatories, see pages 606-607.

(4) Is the cell type identical and uniform in all tumours?

(5) Is this same cell type found in other lymphomas or leukaemias which do not exhibit the clinical and anatomic manifestations of the African disease?

(6) Do lymphomas of other cell types sometimes have clinical and anatomic manifestations that are the same as or similar to those of the African disease?

(7) What are the minimum criteria and biological preparations needed for the diagnosis of Burkitt's tumour?

Obviously if the definition includes a combination of morphology and clinical features, a diagnosis cannot be made without both.

It is recognized that existing knowledge and techniques are limiting factors to an adequate understanding of neoplasms of the haematopoietic system, and that the conclusions reached will certainly not represent the final word. However, there is a need to formulate an authoritative definition of Burkitt's tumour which will be acceptable to clinicians and pathologists and which will make possible a more accurate reporting of cases, permit better epidemiological and other studies related to etiology and pathogenesis, and—of the greatest importance—will allow for accurate comparison of therapeutic schedules.

MATERIAL AND METHODS

A planning group met in June 1967 and asked specific participants to provide appropriate case material to serve as the basis for discussion when all the signatories met later in the year. In addition to cases which the contributor believed to be Burkitt's tumour, examples of controversial cases, or those which typified problems of differential diagnosis were sought. Haematoxylin-and-eosin-stained (H&E) sections from 55 selected cases were ultimately circulated to all the signatories, who were asked to complete an accompanying form. This form asked for a specific histological diagnosis or designation and an indication as to whether the given section fulfilled the observer's criteria for a diagnosis of Burkitt's tumour.

In addition to providing the basis for study and discussion of specific cases, it was hoped that this exercise might give information on the following additional points.

(1) Among a group of pathologists experienced in haematopathology, how much agreement is there in terms of classifying a given lymphoma? Can an accurate distinction be made with only H&E sections between a variety of undifferentiated and poorly differentiated tumours?

(2) How well does each pathologist's concept of the histopathology of Burkitt's tumour correlate with the final diagnosis of a case when supplementary material and clinical information are available?

When, in October 1967, the signatories met for discussions, they had before them, in addition to the H&E-stained sections circulated in advance, all pertinent and available clinical data for each of the 55 cases as well as additional sections, imprints, bone marrow and special cytological and histochemical preparations. A number of other cases were also submitted by participants. There was detailed discussion of 24 cases selected to illustrate particular points of interest and to emphasize areas of special difficulty.

On the basis of the material presented and discussed, two of the signatories felt that Burkitt's tumour is a clinico-pathological concept only; they found no significant evidence for the existence of such a tumour in a specific histological or cytological sense and held that the use of the term Burkitt's tumour was warranted only in a general clinical sense. The other 16 signatories, however, were convinced that Burkitt's tumour is, indeed, a pathological entity and, as such, is definable and that its inclusion in morphological classifications is appropriate.

DEFINITION OF BURKITT'S TUMOUR

Burkitt's tumour is a malignant neoplasm of the haematopoietic system and is more specifically designated: malignant lymphoma,[1] undifferentiated, Burkitt's type. The predominant and characteristic cells are undifferentiated lymphoreticular or primitive stem cells showing moderate nuclear and cytoplasmic variations interpretable either as biological variations within the same cell type or as limited differentiation to histiocytic or lymphocytic cell types.

Macrophages are frequently interspersed amid the tumour cells so as to form a so-called " starry-sky " pattern. Although a prominent histological feature, this pattern is not specific to or pathognomonic of Burkitt's tumour.

A consideration of clinical and gross anatomical features follows, together with a description of the component cells of the tumour, methods by which

[1] Malignant lymphoma is a generic term used by most of the signatories for malignant tumours of the lymphoreticular system.

these cells can be characterized, and a discussion of differential diagnoses.

Clinical aspects and gross pathology

Although many clinical features of Burkitt's tumour, particularly the anatomical presentation and distribution, tend to be characteristic, none is pathognomonic and a variety of malignant neoplasms have similar clinical manifestations. In general, clinical and laboratory signs and symptoms are entirely related to the anatomical distribution of the tumour and to its impingement on vital structures.

The principal clinical and gross anatomical features characterizing Burkitt's tumour are as follows:

(1) Predominantly a tumour of childhood; the disease, however, may occur in any age-group.

(2) Rapid onset and rapidly fatal course in untreated cases. (Reference to response to treatment is omitted here as outside the objectives of the consultation.)

(3) Clinical presentation as a rapidly growing solid tumour or tumours which are predominantly extranodal. The disease is usually multifocal and widely disseminated, with involvement of one or more of the following sites:

(*a*) abdominal and/or pelvic viscera,

(*b*) retroperitoneal soft tissues,

(*c*) facial bones and/or long bones,

(*d*) thyroid gland,

(*e*) salivary glands,

(*f*) central nervous system.

Retroperitoneal masses and discrete nodular involvement of the abdominal viscera are found in virtually all cases even when jaw tumours are the dominant manifestation. The kidney, liver, gonads, and endocrine organs are frequently involved. Bilateral ovarian tumours in females at all ages are a particularly characteristic feature of the disease, as also are massive bilateral breast tumours in women of child-bearing age. Tumours in the spleen, mediastinum, and lungs are uncommon and rarely massive. Nodular deposits in the epicardium and myocardium are not infrequent.

There is conspicuous sparing of the peripheral lymph-nodes in most cases but occasional patients may exhibit tumours in one or more of the peripheral chains. Generalized peripheral lymphadenopathy due to tumour is rarely, if ever, found. Massive involvement of mediastinal nodes is likewise uncommon and primary tumour in the thymus has not yet been observed. Involvement of Waldeyer's ring is rare in cases of Burkitt's tumour in Africa but has been reported in the USA and in England.

The frequency of jaw tumours in African cases is definitely related to age, the maximum incidence being at the age of 3 years and falling progressively thereafter. The apparent lower incidence of jaw tumours in cases reported from North America may be due to a difference in the age incidence of Burkitt's tumour in the two continents or possibly to a greater susceptibility of the jaws of Africans to tumour growth.

Involvement of multiple quadrants of the jaw is common and, even when only one tumour is grossly evident, detailed pathological or radiological examination of the remaining quadrants usually reveals other small tumour foci. The tumours appear to begin as small osteolytic foci in the molar or premolar areas, coalescing to form large expanding tumours with displacement and loosening of the teeth. Involvement of bones other than the jaw is much less frequent but may occur as single or multiple tumours.

Paraplegia may be the presenting feature of Burkitt's tumour. This may be due to infarction of the lower thoracic cord as a result of interference with the vascular supply to this region by an expanding retroperitoneal tumour or to meningeal involvement with cord compression. Involvement of the meninges, base of brain, cranial nerves, and even the brain and cord tissue has been recognized recently with increasing frequency.

(4) Absence of significant leukaemic manifestation in the peripheral blood. Although nodular tumour deposits are frequently seen in bones, diffuse infiltration or replacement of the bone marrow by Burkitt's tumour is uncommon except as a terminal or preterminal event and has not been reported in the absence of extensive disease elsewhere. Small numbers of tumour cells may be found in the peripheral blood in advanced cases but a significantly elevated white blood cell count due to those cells and frank leukaemia have not been seen. A leukoerythroblastic reaction may be found in the peripheral blood in cases with bone-marrow replacement.

Histopathology (Fig. 1–6)

Immediate and proper fixation of fresh tissue is essential for the accurate interpretation of histological sections of Burkitt's tumour. Buffered formol is adequate but in the case material examined by the signatories special fixatives containing mercuric

chloride or dichromate usually gave better cytological definition.

The growth pattern of Burkitt's tumour tends to be that of an expanding nodular mass rather than of diffusely infiltrating cells. Encasement of organs and tubular structures by tumour is noted and, particularly in the liver and spleen, parenchymal extension from the capsule occurs along the septa.

Sections of tumour reflect a monotonous overgrowth of undifferentiated lymphoreticular cells with little variation in size and shape. Mitotic activity is high. Macrophages with abundant clear cytoplasm containing tumour cells or cell debris are almost invariably found scattered uniformly throughout the tumour, producing the characteristic " starry-sky " pattern. Supporting stroma and reticulin fibre distribution vary with the tissue invoved. In large tumour masses reticulin is scanty and found as short thin strands between occasional groups of neoplastic cells.

The cohesiveness of the principal tumour cells varies considerably in different portions of the same section and depends largely on fixation. In well-fixed areas they are generally cohesive. Each cell, however, has a narrow rim of cytoplasm which, with haematoxylin and eosin stains, has a degree of amphophilia equivalent to that of plasma cells. Use of an oil-immersion objective usually reveals a few of the cytoplasmic vacuoles that are such a prominent feature of most imprint preparations.

The tumour cell nuclei are also very uniform in size and approximate to that of the nuclei of scattered macrophages. They are usually round but may occasionally be ovoid and show a slight indentation. The nuclear membrane is prominent. The coarsely reticulated chromatin is irregularly distributed in a relatively clear parachromatin. Nucleoli are prominent and are usually 2 to 5 in number.

Cytology (Fig. 7 and 8)

In air-dried Romanovsky-stained imprints of tumour tissue the predominant cells again have very uniform nuclear and cytoplasmic qualities. There is often, however, a variation in cell size—from 10 μ to 25 μ—which is much greater than is usually appreciated in sections but which does not correspond to any apparent maturation. The cytoplasm is moderate in amount, well defined, deeply basophilic and usually contains a number of clear vacuoles 1 μ to 2 μ in diameter. The cytoplasm is non-granular and homogeneous apart from a pale-staining area at the nuclear indentation. In imprints the nuclei may also show more variation in shape than in sections and varying degrees of nuclear indentation are more commonly seen. The reticulated chromatin is more evenly distributed than in sections but the parachromatin remains fairly well defined and 2–5 nucleoli of moderate size are usually visible.

Smears of body fluids are equally useful in characterizing the tumour cells. They are usually very well preserved in such preparations and, when air-dried, their appearance corresponds to that described above for imprints.

Histochemistry and cytochemistry (Fig. 9 and 10)

In both imprint preparations and well-fixed sections the tumour cells show a marked cytoplasmic pyroninophilia that can be abolished by prior digestion with ribonuclease. Although an occasional cell may contain coarse periodic-acid–Shiff (PAS) positive cytoplasmic granules, the majority of tumour cells show no PAS reaction. Coarse cytoplasmic lipid droplets can be demonstrated in a large proportion of the tumour cells in frozen sections and formol-fixed imprints. These droplets stain with neutral fat stains and can be readily extracted with acetone and other lipid solvents. Large amounts of neutral fat can usually be demonstrated in the macrophages interspersed between the tumour cells. Alkaline phosphatase and nonspecific esterase activity is absent in the tumour cells. When very sensitive methods are used, small amounts of acid phosphatase can be demonstrated in the tumour cells and the histiocytes contain large amounts of this enzyme as well as nonspecific esterase.

Ultrastructure [1] (Fig. 11 and 12)

At low magnification the monomorphism of the dominant cells is striking. They are round or oval and have a relatively high nucleocytoplasmic ratio. Scattered macrophages are seen and usually contain phagocytosed cell debris. The ultrastructural features of the typical cells are as follows:

(1) *Nucleus :*

(*a*) The nucleus is round or oval, and shallow irregular indentations are frequently found. Rarely, these indentations are deep and significant-

[1] This section is based on a paper by Professor W. Bernhard, Centre de Recherches sur la Cellule normale et cancéreuse, Centre national de la Recherche scientifique, 94–Villejuif, France, who had been invited to participate in the consultation but was unable to attend.

ly distort the nuclear shape. Projections of the nuclear envelope may appear as satellites or as invaginations of the nucleus. Such changes of the nuclear membrane are not, however, specific for these tumour cells.

(*b*) Chromatin is abundant and clumped at the nuclear envelope and around the nucleoli. The interchromatinic substance is relatively clear, an important characteristic of undifferentiated cells.

(*c*) Nucleoli are quite large and the nucleolonemas are usually visible.

(2) *Cytoplasm :*

(*a*) The cytoplasm is moderate but variable in amount and relatively dense.

(*b*) The most characteristic feature is the large number of polyribosomes.

(*c*) Ergastoplasmic lamellae are rare.

(*d*) Mitochondria are few, large, and have a tendency to polarize.

(*e*) Large inclusions consistent with lipid vacuoles are found in some cells.

As interpreted on the basis of the ultrastructural features, a small percentage of tumours examined by electron microscopy show a definite but very limited degree of lymphatic or reticulum cell (histiocytic) differentiation.

DISEASES RESEMBLING BURKITT'S TUMOUR AND DIFFERENTIAL DIAGNOSIS

Several types of poorly differentiated neoplasms, including metastatic carcinomas, rhabdomyosarcomas, neuroblastomas, retinoblastomas, granulosa-cell tumours and plasmacytomas have been mistakenly diagnosed as Burkitt's tumour. However, the greatest difficulty in differential diagnosis is encountered with certain cases of acute leukaemia and poorly differentiated malignant lymphomas. The histological appearance of H&E-stained sections may be similar to that in Burkitt's tumour. In fact, the similarity may be so great that the differential diagnosis cannot be made on routinely stained sections and can be established only after study of imprints of fresh tumour or by the use of special stains.

This discussion of differential diagnosis is limited to the following four primary neoplastic diseases of the haematopoietic system which may simulate Burkitt's tumour:

(1) acute lymphoblastic leukaemia;

(2) acute myeloblastic leukaemia,

(3) malignant lymphoma, histiocytic type (reticulosarcoma),

(4) malignant lymphoma, poorly differentiated lymphocytic type (" classical " lymphosarcoma).

The differential diagnosis is particularly difficult when one or more of the clinical and/or pathological features listed below are present:

(*a*) the disease presents as a solid tumour either in a lymph-node or in an extra-nodal location, particularly the latter;

(*b*) the peripheral blood picture is not leukaemic;

(*c*) a " starry-sky " pattern is a prominent feature in tissue sections;

(*d*) differentiation or maturation of the tumour cells is not present or not readily apparent in routinely stained sections;

(*e*) the tumour cells contain cytoplasmic vacuoles resembling those in the cells of Burkitt's tumour.

(1) The diagnosis of *acute lymphoblastic leukaemia* (Fig. 13–16) is favoured when:

(*a*) the nuclei are smaller than those of the histiocytes in the same sections;

(*b*) nuclear indentations and clefts are relatively frequent;

(*c*) nuclear chromatin is delicate, and evenly distributed;

(*d*) the nucleoli are small and relatively inconspicuous;

(*e*) cytoplasmic pyroninophilia is not marked;

(*f*) diastase-sensitive, PAS-positive granules are demonstrated in the cytoplasm.

(2) The diagnosis of *acute myeloblastic leukaemia* or " *blastic crisis* " in chronic myelocytic leukaemia (Fig. 17–20) is favoured when:

(*a*) occasional eosinophilic myelocytes, with nuclear features similar to undifferentiated non-granular cells, are found;

(*b*) a nonspecific esterase in the cytoplasm of some of the neoplastic cells is demonstrable by the naphthol-AS-D-chloroacetate method; [1]

(*c*) there is a marked PAS-positivity in the cytoplasm of the maturing abnormal granulocytes.

[1] Leder, L. D. (1964) *Verh. Dtsch. Ges. Path.*, **48**, 317-320.

(3) The diagnosis of *malignant lymphoma, histiocytic type* (reticulosarcoma) (Fig. 21 and 22) is favoured when:

(*a*) the tumour cells have a relatively abundant cytoplasm;

(*b*) there are variations in the staining quality of the cytoplasm, particularly in the pyroninophilia;

(*c*) there is an absence of uniform sudanophilic vacuoles in the cytoplasm (when vacuoles are present they are larger than those in Burkitt's tumour cells);

(*d*) the nuclei are larger and more pleomorphic than those of Burkitt's tumour cells;

(*e*) the nuclear chromatin is relatively coarse and irregularly distributed;

(*f*) the nucleoli are very large and eosinophilic.

(4) A diagnosis of *lymphosarcoma, poorly differentiated*, is favoured when:

(*a*) the nuclei are generally smaller than those of histiocytes in the same sections;

(*b*) considerable variations in nuclear size and shape are evident and there are prominent nuclear indentations and clefts;

(*c*) the nuclear chromatin is coarse and irregularly distributed;

(*d*) pyroninophilia is not marked or is variable from cell to cell.

It should be emphasized that in all the above instances a significant maturation of a portion of the tumour cell population, best appreciated in imprints or bone marrow when involved, is inconsistent with a diagnosis of Burkitt's tumour.

CONCLUSIONS

The responses of the signatories, following the October 1967 consultation, to the questions posed in the statement of objectives cited above (see page 601) showed remarkable agreement. On the basis of these answers and of the substantial agreement that has been outlined in the foregoing pages, the following conclusions are drawn:

(1) The eponym "Burkitt's tumour" is best applied to a malignant neoplasm of the haematopoietic system composed of a predominant and characteristic cell type.

(2) There is little agreement as to the theoretical or potential pathways for differentiation of the principal tumour cells, but most observers believe them to be primitive lymphoreticular elements showing limited degrees of what may be interpretable as slight differentiation.

(3) The Burkitt's tumour, therefore, is most logically classified as a malignant lymphoma, undifferentiated type. Since the question whether there are other types of undifferentiated or stem cell lymphomas distinct from the type under discussion remains unresolved, it seems advisable to make the following designation: *malignant lymphoma, undifferentiated, Burkitt's type.*

(4) Other neoplastic diseases, haematopoietic and non-haematopoietic may have clinical and pathological features resembling Burkitt's tumour.

(5) Although fresh and well-fixed histological sections from surgical material usually provide sufficient cytological detail to make a strong presumptive diagnosis of Burkitt's tumour as defined above, other primitive cell tumours may have a similar histological appearance. Touch preparations, bone marrow, and clinical information, or a combination of these, will allow of definitive confirmation and should therefore be sought in all suspected cases. When the histological preparations are not of the best quality, the additional material is absolutely essential.

(6) Burkitt's tumour as defined above is not limited to Africa and occurs in many parts of the world.

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RÉSUMÉ

DÉFINITION HISTOPATHOLOGIQUE DE LA TUMEUR DE BURKITT

Une réunion internationale, groupant des hématologistes et des anatomo-pathologistes, s'est tenue en octobre 1967 sous les auspices de l'OMS et du Centre international de Recherche sur le Cancer. Le but de cette consultation entre spécialistes était de formuler, sur la base de critères histopathologiques, une définition de la tumeur de Burkitt qui puisse être adoptée à la fois par les cliniciens et par les anatomo-pathologistes. On pouvait en effet espérer qu'une telle définition non seulement permettrait de décrire avec plus de précision les cas de cette maladie, mais faciliterait aussi les études comparatives sur les plans épidémiologique et thérapeutique. Après avoir examiné minutieusement un abondant matériel histologique et cytologique, étudié les données cliniques et discuté un certain nombre de cas typiques, les participants ont adopté le présent rapport et formulé les conclusions ci-après:

1. Le terme « tumeur de Burkitt » (Burkitt ayant été le premier à donner une description clinique de l'affection) s'applique essentiellement à une tumeur maligne du système hématopoiétique dont la structure comporte un type cellulaire prédominant et caractéristique.

2. L'accord est loin d'être fait au sujet des possibilités théoriques et du potentiel de différenciation de ces cellules tumorales principales. Néanmoins la plupart des observateurs les considèrent comme des cellules lympho-réticulaires primitives qui ne montrent que des signes limités de ce que l'on peut interpréter comme un faible degré de différenciation.

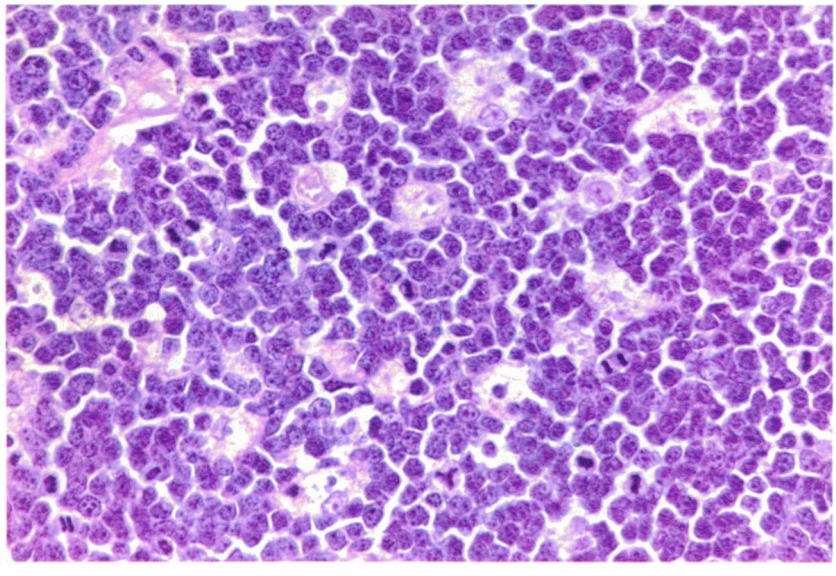
3. Le plus logique est dès lors de classer la tumeur de Burkitt parmi les lymphomes malins de type indifférencié. La question de l'existence éventuelle d'autres types de lymphomes formés de cellules primitives ou de cellules souches n'étant pas résolue, il semble judicieux d'adopter la désignation suivante: *lymphome malin, indifférencié, type Burkitt.*

4. D'autres affections néoplasiques, qu'elles soient ou non d'origine hématopoiétique, peuvent présenter des aspects cliniques et anatomo-pathologiques rappelant ceux de la tumeur de Burkitt.

5. En général, l'examen histologique de coupes récentes et convenablement fixées de matériel prélevé chirurgicalement décèle suffisamment de détails cytologiques pour que l'on puisse poser avec une certitude suffisante un diagnostic présumé de tumeur de Burkitt; cependant d'autres tumeurs formées de cellules primitives donnent parfois des aspects histologiques similaires. L'étude de préparations par empreintes, l'examen de la moelle osseuse et/ou les données cliniques permettent de confirmer le diagnostic et doivent donc être utilisés dans tous les cas suspects. Si les préparations histologiques ne sont pas d'une qualité irréprochable, ce complément d'information est absolument indispensable.

6. La tumeur de Burkitt, telle qu'elle vient d'être définie, n'est pas une affection particulière au continent africain et est observée dans de nombreuses régions du globe.

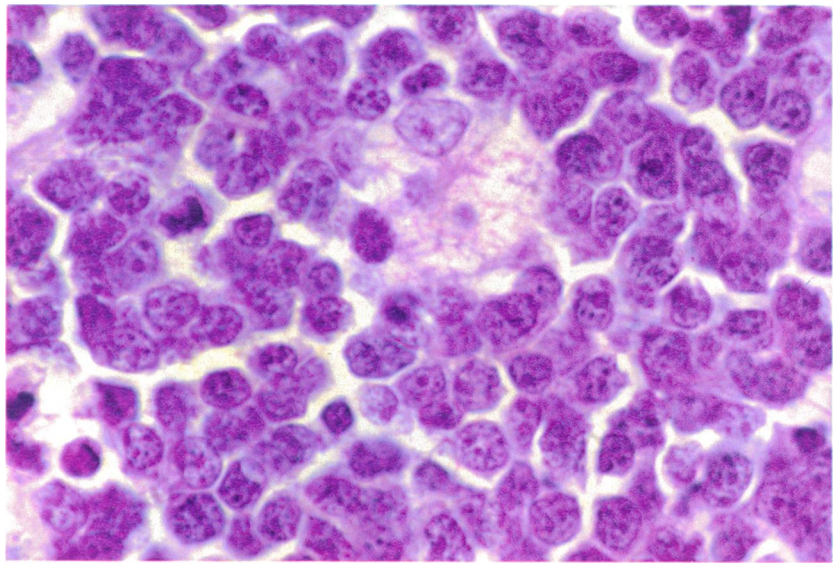
FIG. 1. BURKITT'S TUMOUR



Formalin fixation H&E stain ×400

Section of large tumour from the orbit in a 4-year-old African boy.

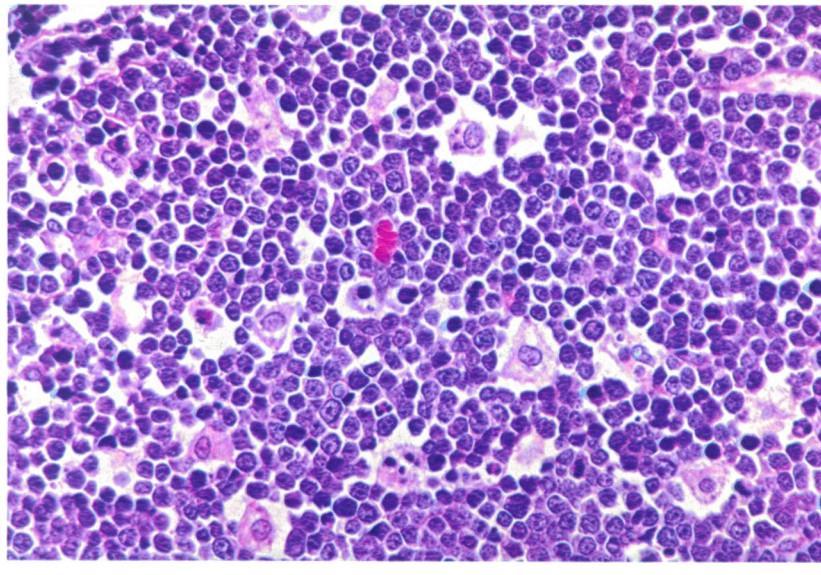
FIG. 2. BURKITT'S TUMOUR



H&E stain ×1000

Same case as Fig. 1.

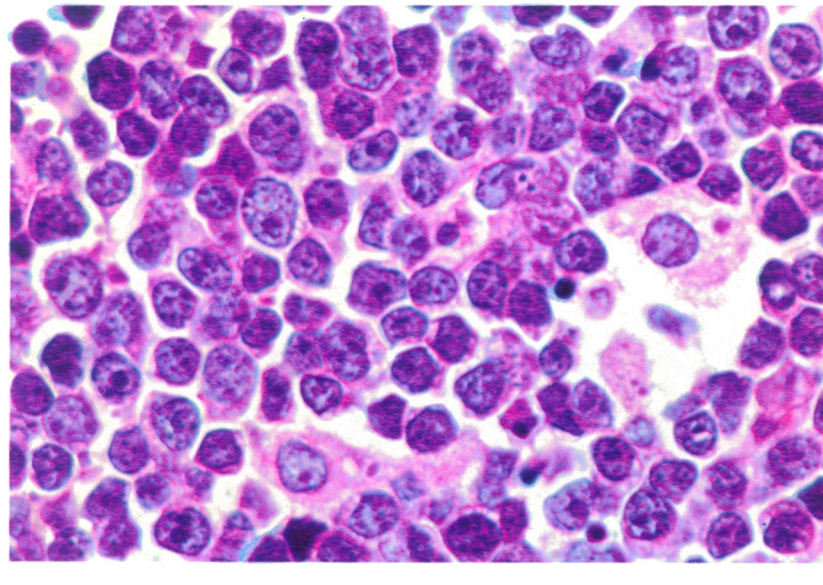
FIG. 3. BURKITT'S TUMOUR



Formalin fixation H&E stain ×400

Section of retroperitoneal mass from a 10-year-old white American boy.

FIG. 4. BURKITT'S TUMOUR

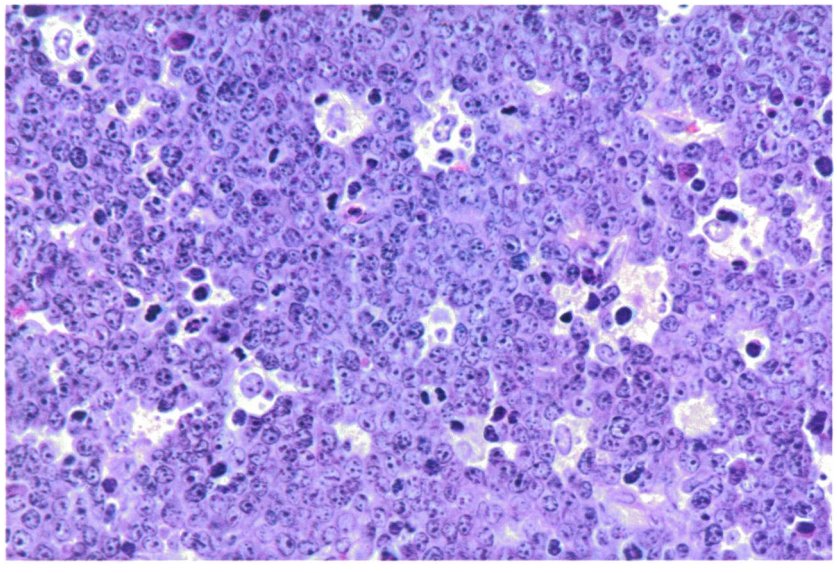


H&E stain ×1000

Same case as Fig. 3.

Note amphophilic cytoplasm containing vacuoles. The small dark nuclei are interpreted as having undergone pyknosis rather than lymphocytic differentiation.

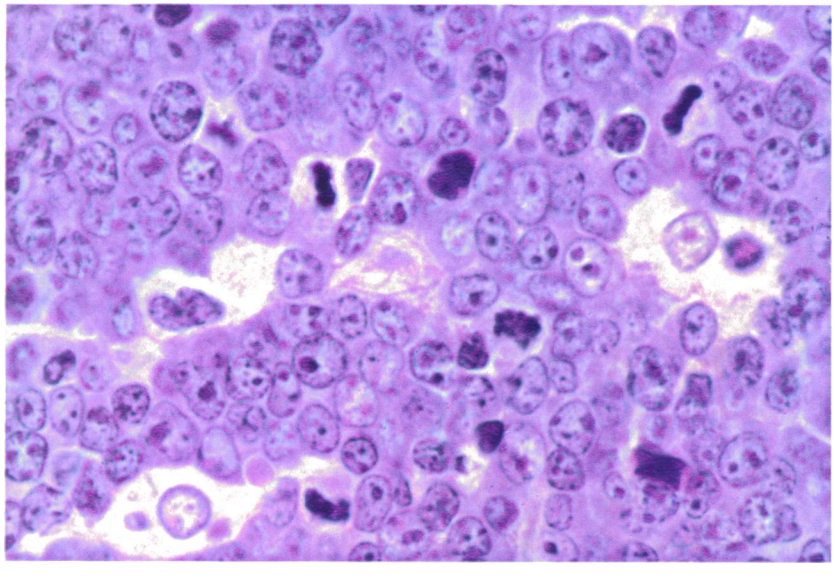
FIG. 5. BURKITT'S TUMOUR



Mercuric-chloride–formalin fixation H&E stain ×400

Section of jaw tumour from a 16-year-old white American boy.

FIG. 6. BURKITT'S TUMOUR

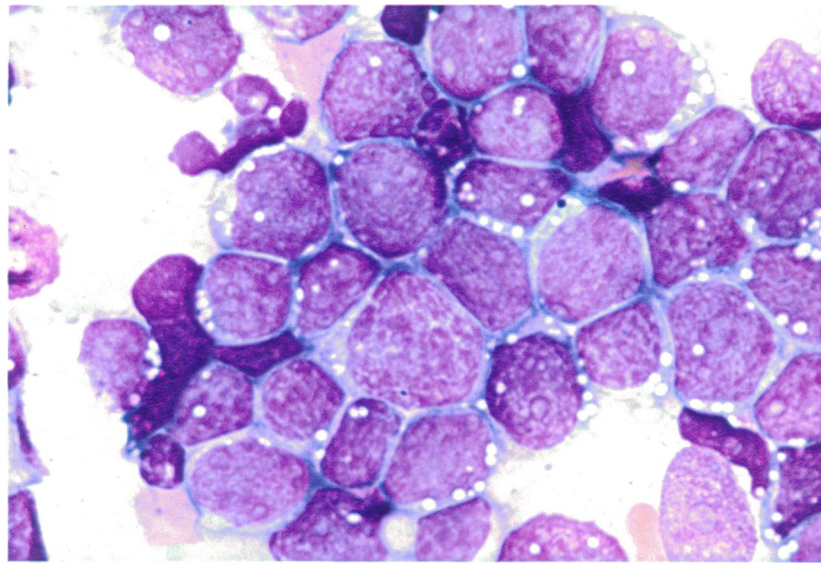


H&E stain ×1000

Same case as Fig. 5.

Note frequent mitoses. The vesicular appearance of the nuclei and the prominence of the nucleoli are characteristic of sections fixed in mercuric chloride or dichromate additives.

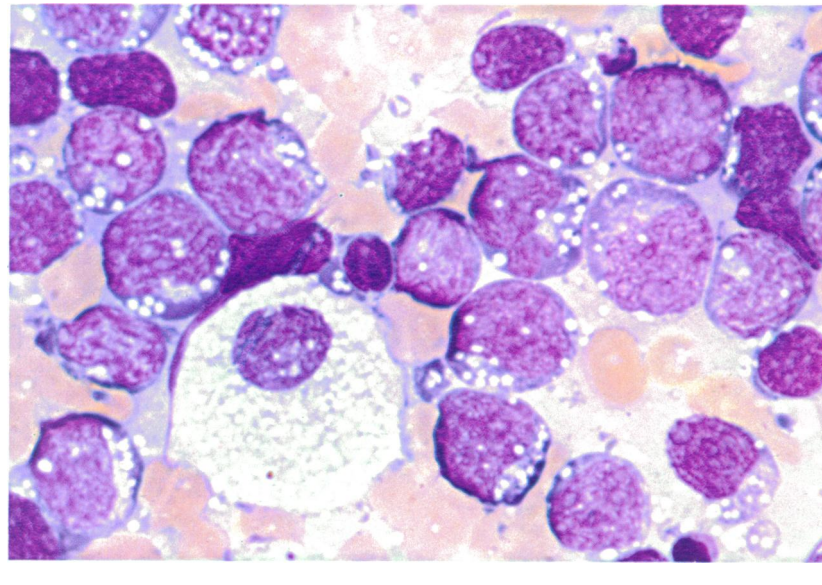
FIG. 7. BURKITT'S TUMOUR



Giemsa stain ×1000

Imprint of involved cervical lymph node from a 3-year-old white American girl who presented clinically with bilateral large ovarian tumours.

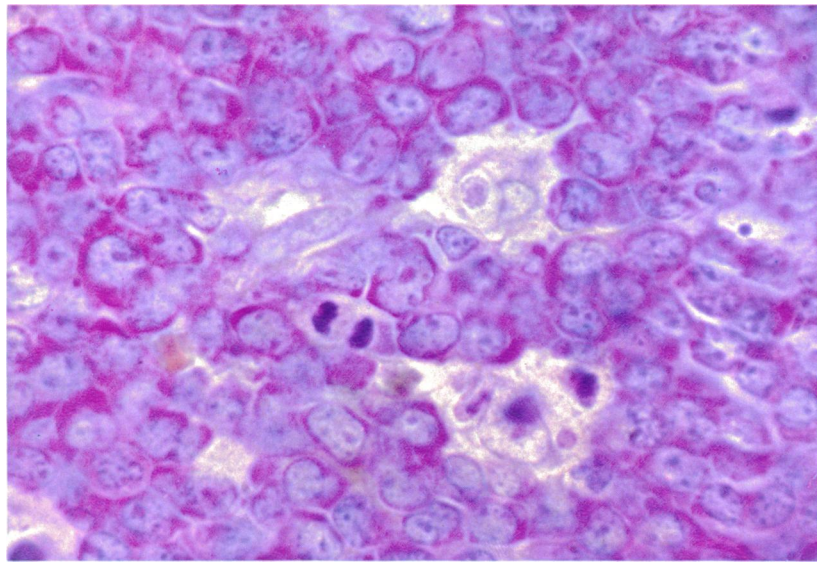
FIG. 8. BURKITT'S TUMOUR



Giemsa stain ×1000

Imprint of jaw tumour from a 4-year-old African girl.

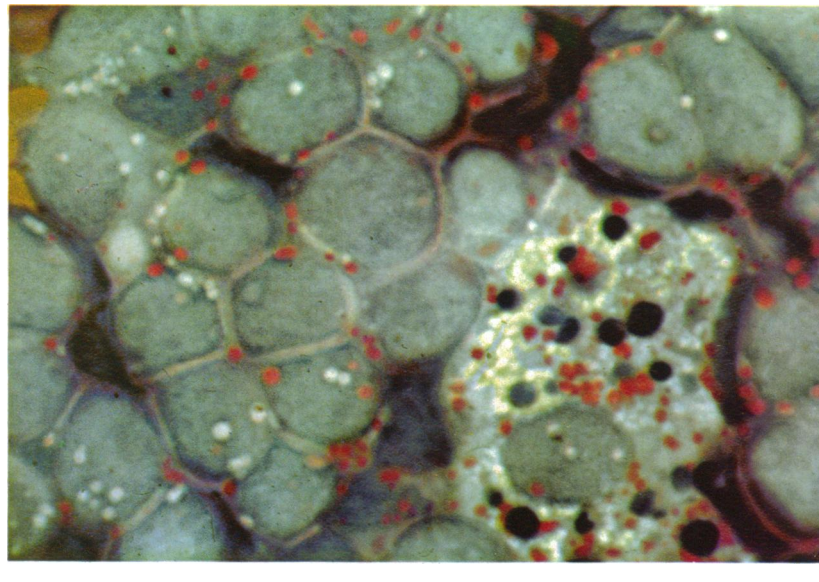
FIG. 9. BURKITT'S TUMOUR



Methyl-green–pyronine stain ×1000

Same case as Fig. 5 & 6.

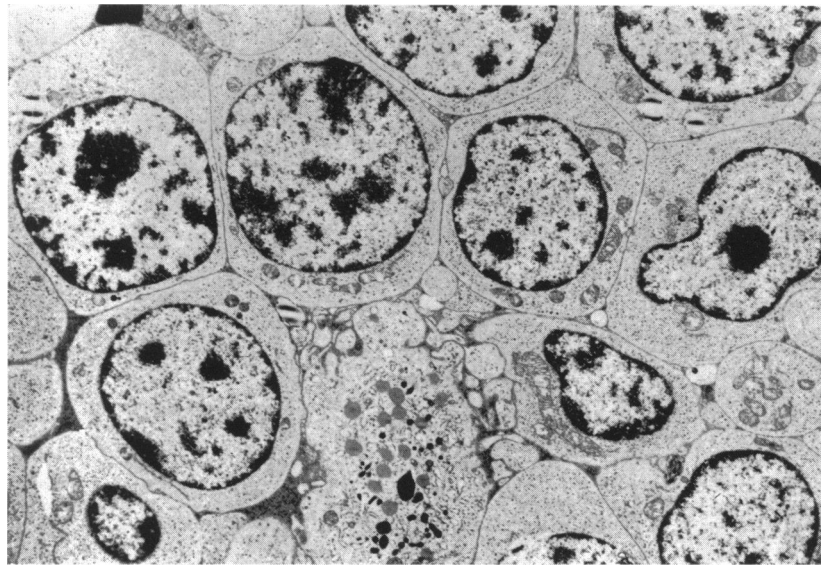
FIG. 10. BURKITT'S TUMOUR



Formalin-vapour fixation Oil Red O stain ×1000

Imprint of breast tumour in a 17-year-old American girl.

FIG. 11. BURKITT'S TUMOUR

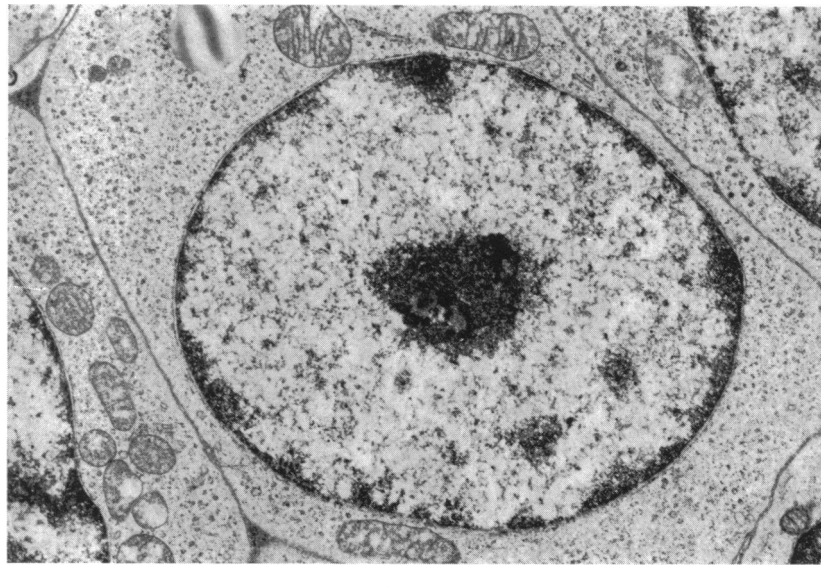


Glutaraldehyde–osmic-acid fixation | Epon-embedded | Uranyl-acetate–lead-hydroxide stain | × 3900

Section of breast tumour in a 17-year-old American girl. Same case as Fig. 10. Electron microscopy.

Tumour cells with " open " nuclei and prominent nucleoli are seen in proximity to a portion of a macrophage having a complexity of cytoplasmic organelles.

FIG. 12. BURKITT'S TUMOUR

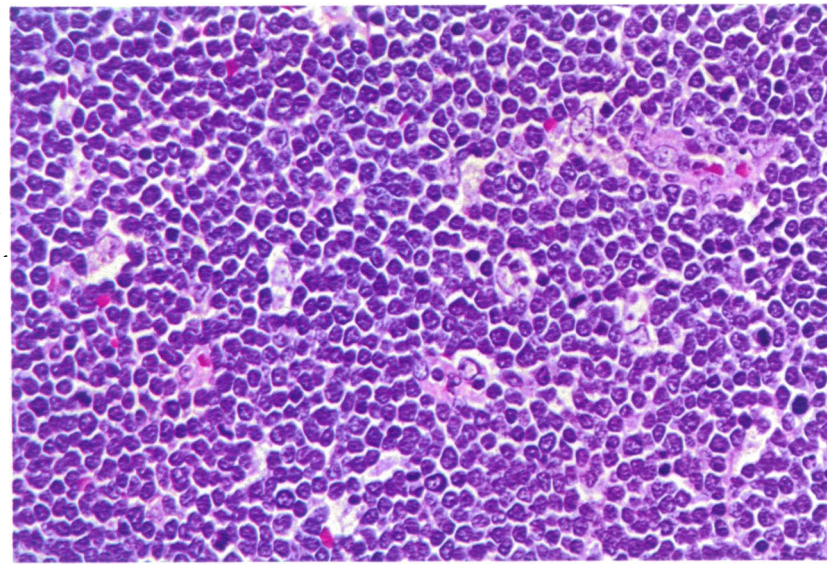


× 11 000

Same case as Fig. 11. Electron microscopy.

Note abundance of polyribosomes and paucity of endoplasmic reticulum in the cytoplasm.

FIG. 13. ACUTE LYMPHOBLASTIC LEUKAEMIA

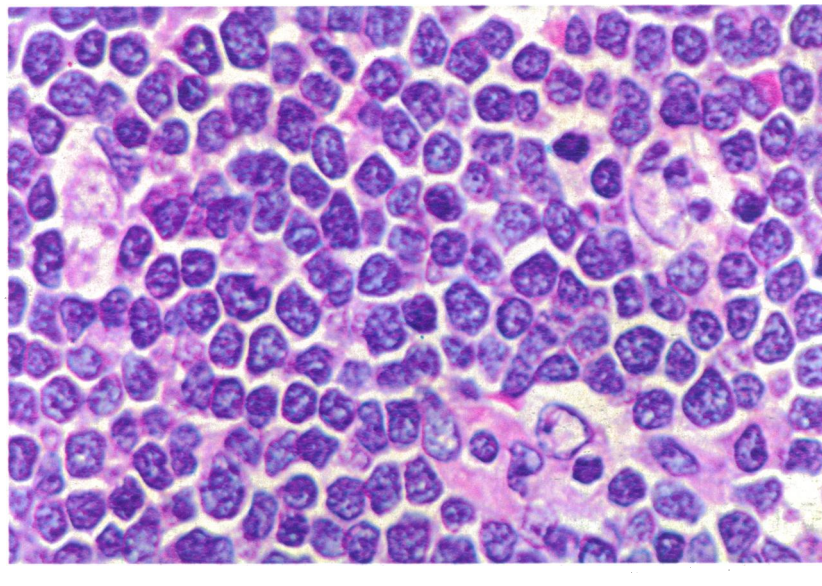


Formalin fixation H&E stain ×400

Section of lymph node from a 20-year-old white male. The white cell count in the peripheral blood was 30 000 with 45 % lymphoblasts. Similar cells replaced the bone marrow.

The " starry sky " pattern is prominent. Note that the tumour cell nuclei are smaller than the nuclei of the phagocytic histiocytes.

FIG. 14. ACUTE LYMPHOBLASTIC LEUKAEMIA

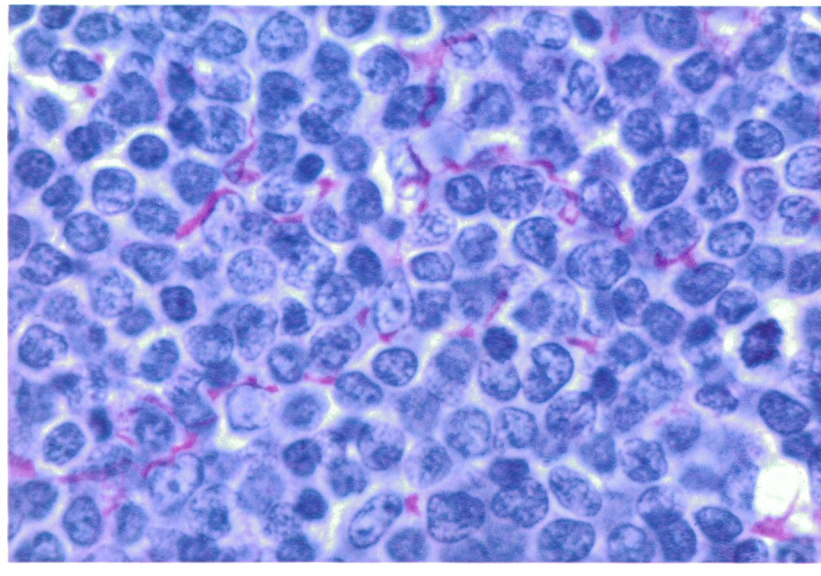


H&E stain ×1000

Same case as Fig. 13.

Note the frequency of nuclear clefts and inconspicuous nucleoli.

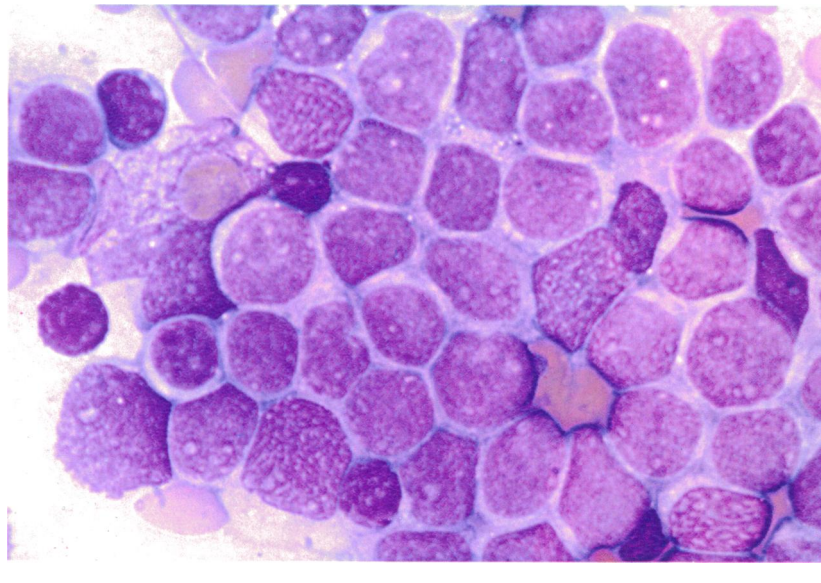
FIG. 15. ACUTE LYMPHOBLASTIC LEUKAEMIA



Formalin fixation H&E stain ×1000

Section of lymph node from a 19-year-old white male who presented with generalized lymphadenopathy and a peripheral white blood cell count of 37 400 with 50 % lymphoblasts. The bone marrow was diagnostic of acute lymphoblastic leukaemia.

FIG. 16. ACUTE LYMPHOBLASTIC LEUKAEMIA

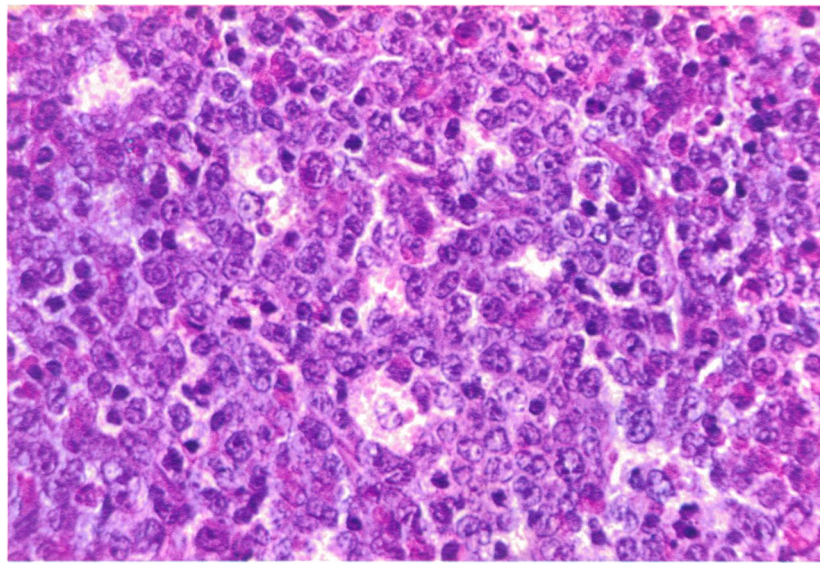


Giemsa stain ×1000

Imprint of lymph node. Same case as Fig. 15.

The cytoplasm is less basophilic than in Burkitt's tumour cells and lipid vacuoles are not a prominent feature. The nuclear chromatin is fine, delicate and evenly distributed.

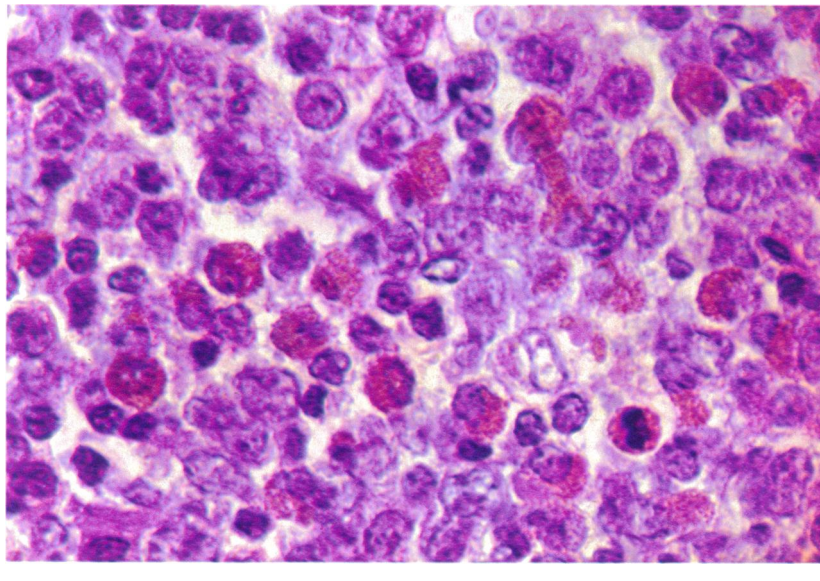
FIG. 17. ACUTE "BLASTIC CRISIS" IN CHRONIC MYELOCYTIC LEUKAEMIA



Formalin fixation H&E stain ×400

Section from lymph node from 20-year-old white female with diffuse replacement of bone marrow and lymph nodes with myeloblastic and immature granulocytic cells. The microscope field illustrates a "starry sky" pattern and a relative uniformity of cell type simulating Burkitt's tumour.

FIG. 18. ACUTE "BLASTIC CRISIS" IN CHRONIC MYELOCYTIC LEUKAEMIA

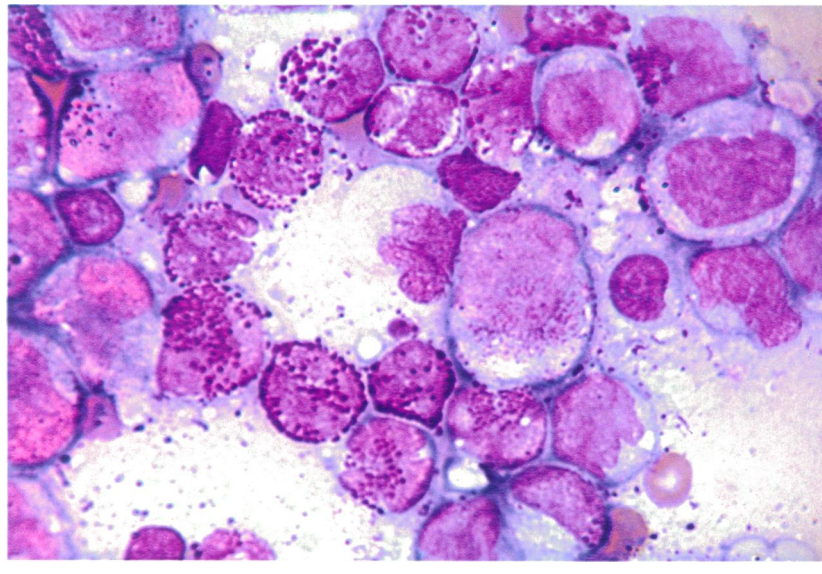


H&E stain ×1000

Same case as Fig. 17.

The numerous eosinophilic myelocytes in this microscope field are characteristic of granulocytic leukaemia.

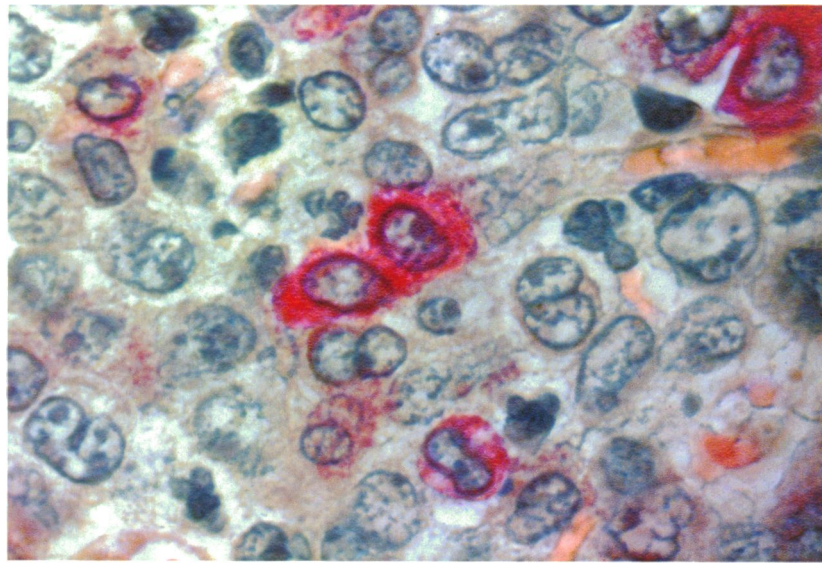
FIG. 19. ACUTE " BLASTIC CRISIS " IN CHRONIC MYELOCYTIC LEUKAEMIA



Giemsa stain × 1000

Imprint of same lymph node as illustrated in Fig. 18.
Specific neutrophilic and basophilic granules are readly apparent in the imprint.

FIG. 20. ACUTE " BLASTIC CRISIS " IN CHRONIC MYELOCYTIC LEUKAEMIA

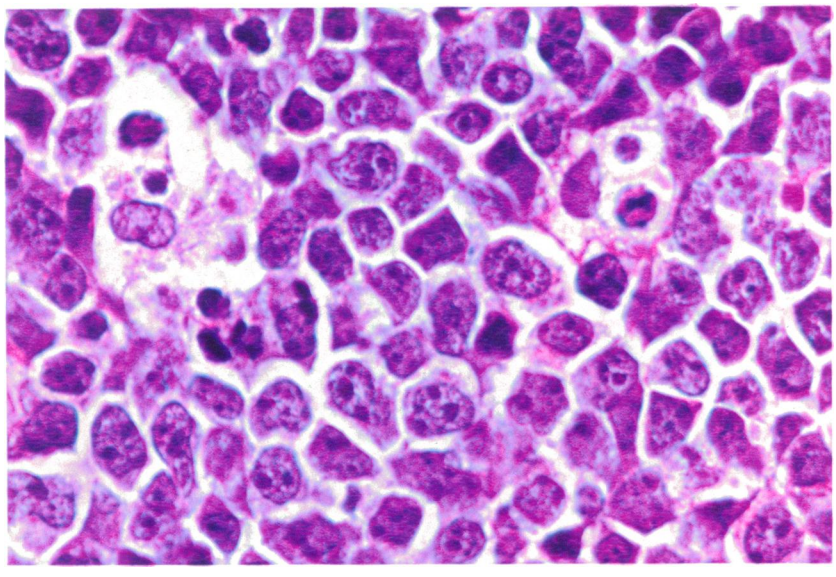


Naphthol-AS-D-chloroacetate-esterase reaction × 1000

Same case as Fig. 17.

The positive esterase reaction in immature neutrophils is characteristic of myelocytic leukaemia. Esterase activity is not found in Burkitt's tumour cells.

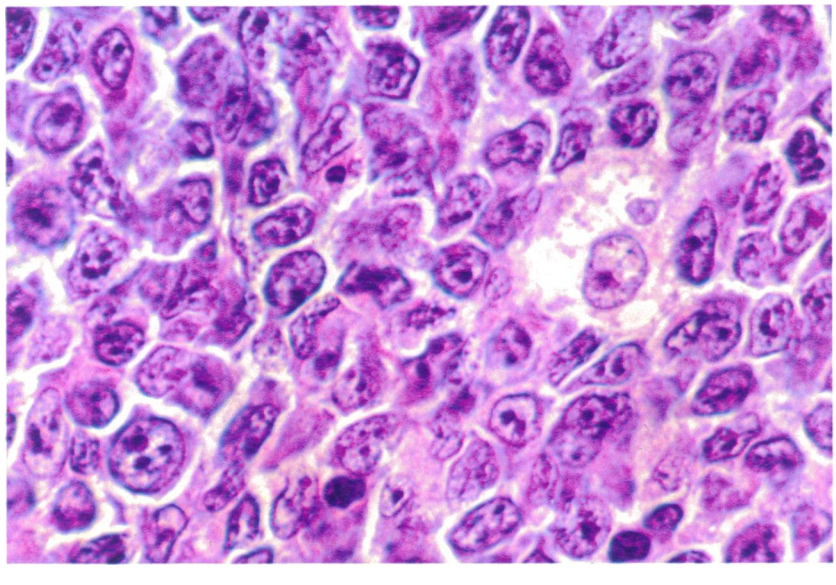
FIG. 21. MALIGNANT LYMPHOMA, HISTIOCYTIC TYPE (RETICULOSARCOMA)



Formalin fixation H&E stain ×1000

Section of cervical lymph node from a 42-year-old white man.

FIG. 22. MALIGNANT LYMPHOMA, HISTIOCYTIC TYPE (RETICULOSARCOMA)

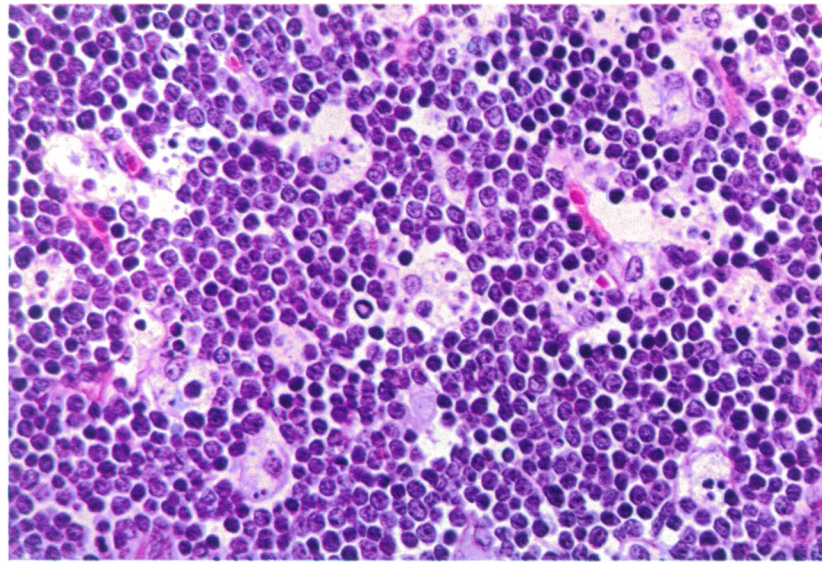


Formalin fixation H&E stain ×1000

Section of enlarged inguinal lymph node from a 49-year-old white man.

In Fig. 21 & 22 the histopathological appearance is similar to that in Burkitt's tumour. Distinguishing features are polymorphism of nuclei, prominence of very large nucleoli and relatively abundant cytoplasm.

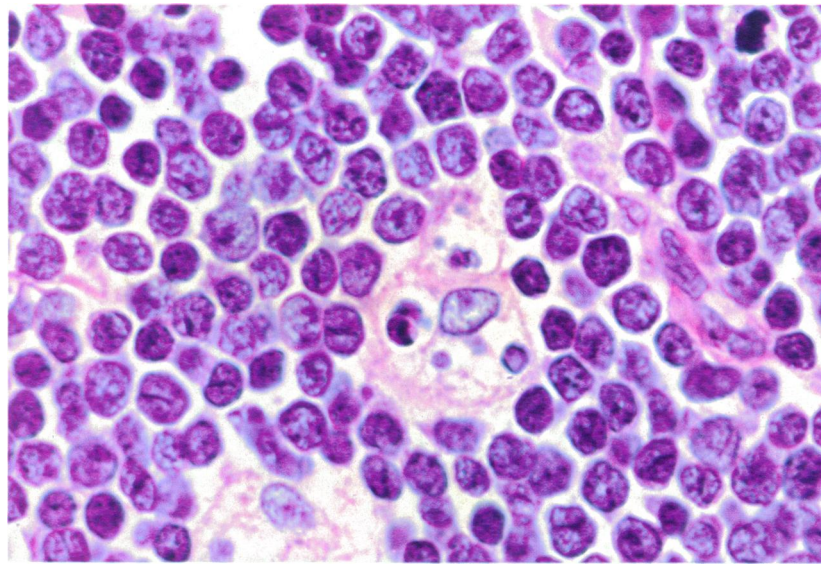
FIG. 23. LYMPHOSARCOMA, POORLY DIFFERENTIATED



Formalin fixation H&E stain ×400

Section from supraclavicular lymph node from a 9-year-old boy with cervical adenopathy and hepatosplenomegaly.

FIG. 24. LYMPHOSARCOMA, POORLY DIFFERENTIATED

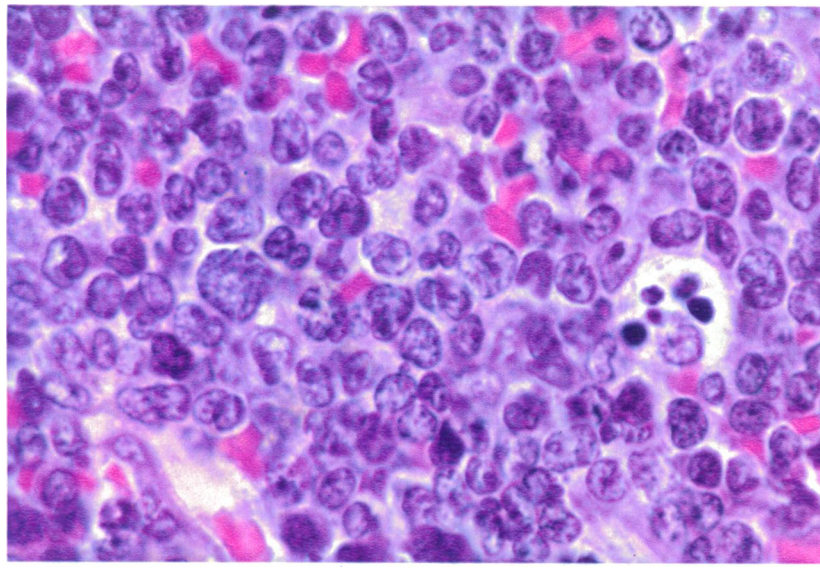


H&E stain ×1000

Same case as Fig. 23.

Note variation in cell size and frequency of nuclear clefts.

FIG. 25. LYMPHOSARCOMA, POORLY DIFFERENTIATED

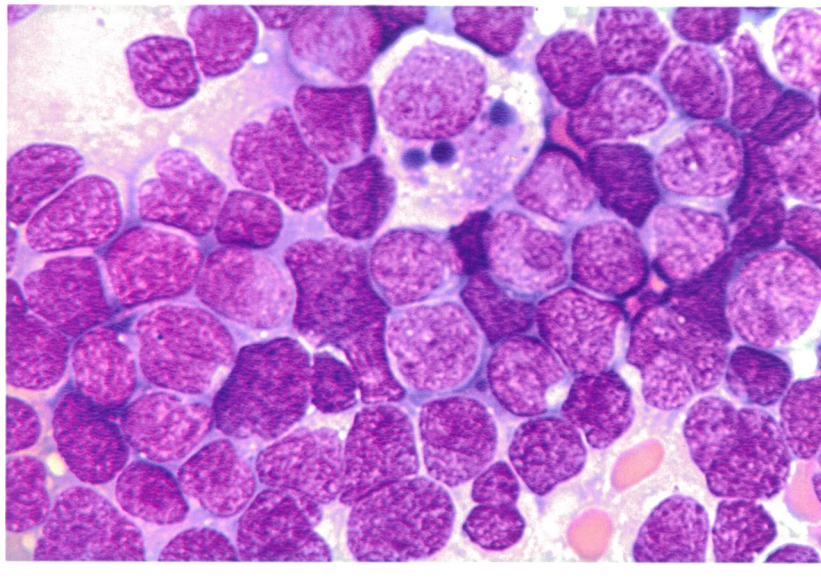


Formalin fixation H&E stain ×1000

Section of axillary lymph node from a 43-year-old white male.

Again the variability in cell size and shape and the prominence of nuclear clefts are important features that distinguish this from Burkitt's tumour. Compare with Fig. 2 & 4.

FIG. 26. LYMPHOSARCOMA, POORLY DIFFERENTIATED



Giemsa stain ×1000

Imprint of same lymph node as illustrated in Fig. 25.

Lymphocytic differentiation is evidenced by scanty cytoplasm. Nuclear polymorphism, frequent nuclear clefts, inconspicuous nucleoli and scanty cytoplasm are characteristics of lymphosarcoma. Most tumour cell nuclei are smaller than the nucleus of the macrophage and cytoplasmic vacuoles are rare. Compare with Fig. 7 & 8.