

Histopathology: disorders of white blood cells

These presentations are to help you identify basic histopathological features. They do not contain the additional factual information that you need to learn about these topics, or necessarily all the images from resource sessions.

This presentation contains images of basic histopathological features of various disorders of white blood cells, lymph nodes and selected anaemias.

Before viewing this presentation you are advised to review relevant histology, relevant sections in a pathology textbook, relevant lecture notes and relevant sections of a histopathology atlas. Note that you do not have to make detailed diagnoses (e.g. of granulomatous inflammation or melanoma) from cytological specimens but you should understand the principles of cytological diagnosis.

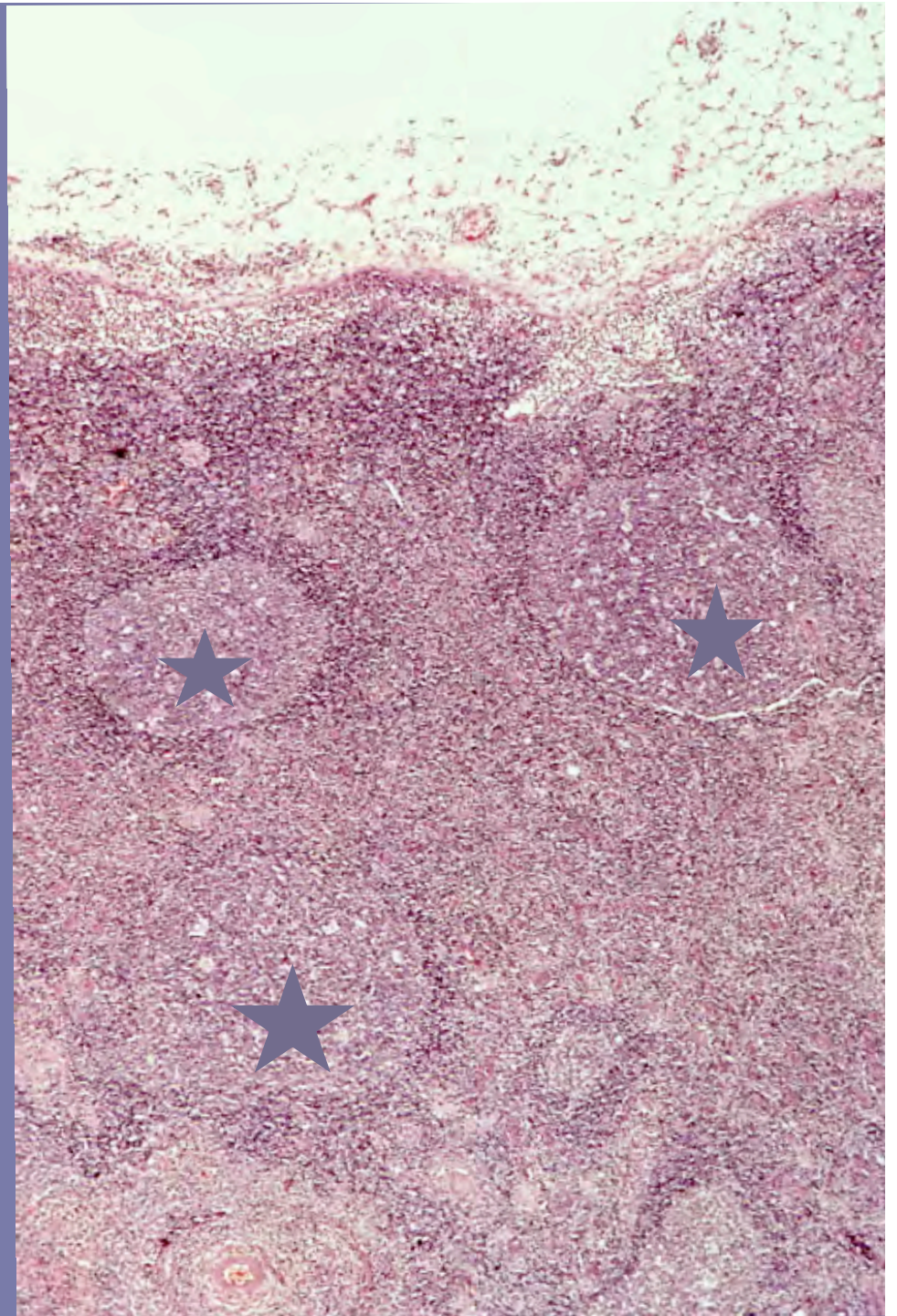
Copyright University of Adelaide 2011

(Med 3 semester 1)

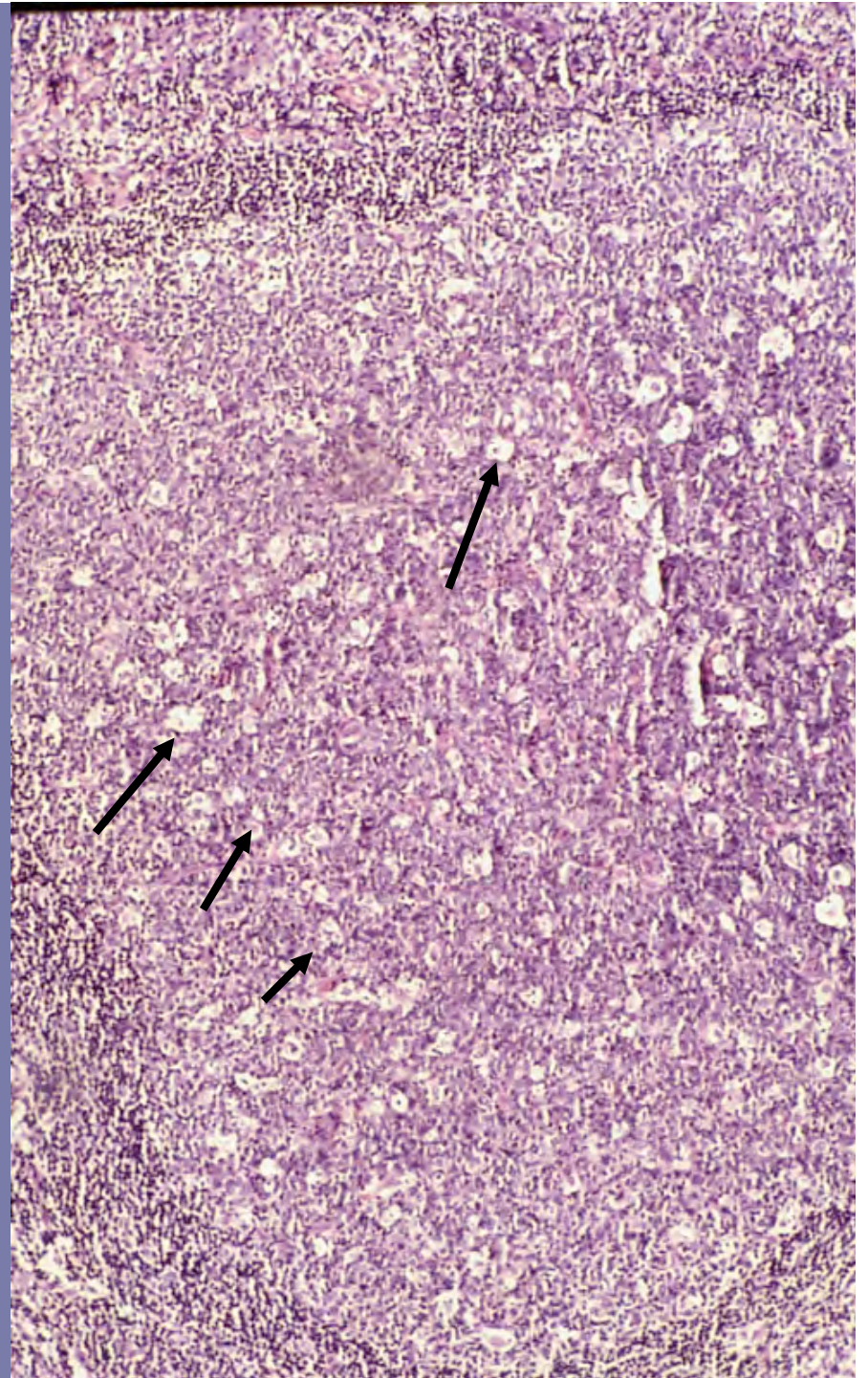
Patterns of reactive lymphadenopathy

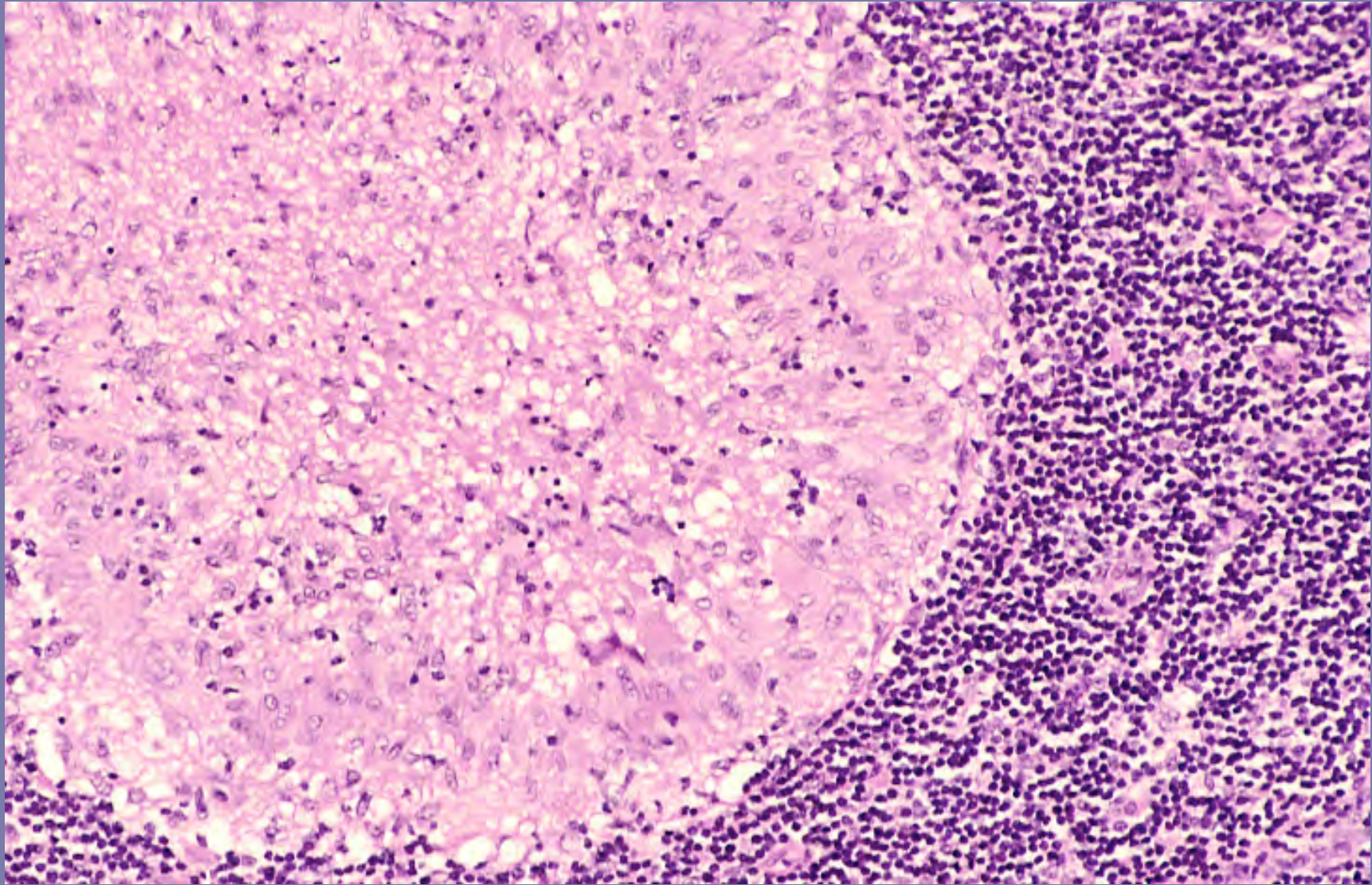
- Acute non-specific lymphadenitis
 - Generally from microbial infection
 - Neutrophil infiltration, oedema, follicular hyperplasia
- Follicular hyperplasia
 - From stimuli that activate humoral immune responses e.g. autoimmune disease, microbial infection
- Paracortical
 - From stimuli that activate cellular immune responses e.g. viral infections, certain drugs
 - Proliferation and activation of T cells
- Sinus histiocytosis
 - Non-specific e.g. nodes draining cancers
 - Increase in macrophages in sinuses
- Granulomatous inflammation e.g. in certain infections, sarcoidosis

Low power view of a reactive lymph node showing germinal centre formation (grey stars) indicating the development of a humoral immune response.



Low-medium power view of a germinal centre. The pale areas (black arrows) are the macrophages containing phagocytosed apoptotic cells (tingible body macrophages). Following appropriate stimulation, B lymphocytes undergo clonal expansion and differentiation into centroblasts, centrocytes then immunoblasts within a germinal centre from where they migrate to the medullary cords where they complete their differentiation into plasma cells. Some become memory B cells.





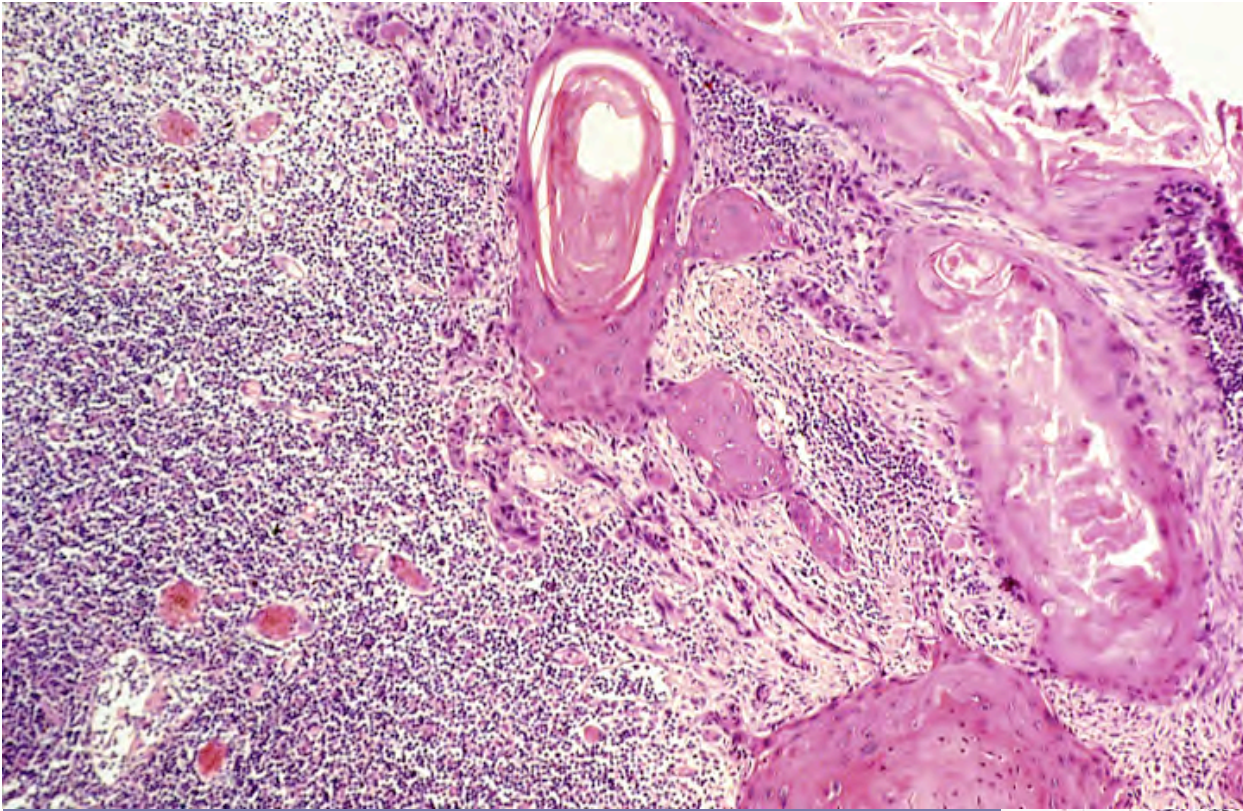
Lymph node (medium power view) with area of necrotising granulomatous inflammation.

Causes of neoplastic lymphadenopathy

- Primary tumours: Hodgkin's lymphoma, Non-Hodgkin's lymphoma
- Secondary tumours (metastases) - more common
 - Carcinomas, melanomas and germ cell tumours readily metastasise to lymph nodes
 - Unlike sarcomas which don't metastasise to nodes so readily
- Leukaemic infiltration

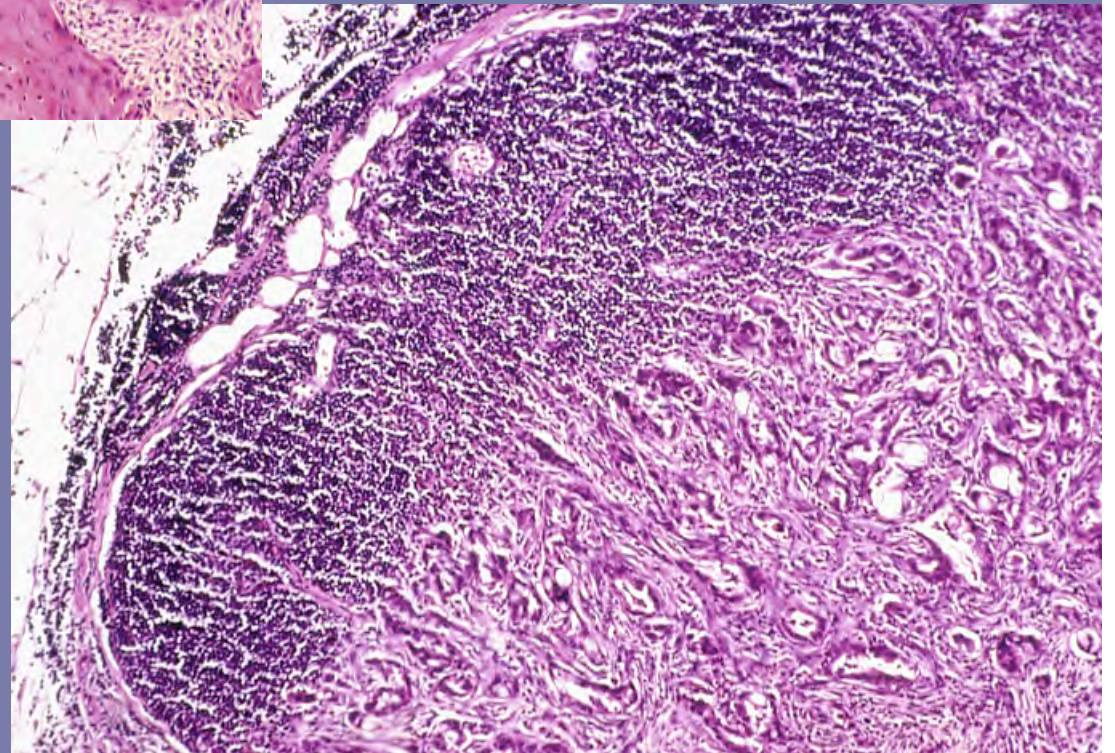
The location of an enlarged node gives important clues about possible causes: neoplastic or reactive. Knowledge of the anatomy of lymphatic drainage is very important clinically.

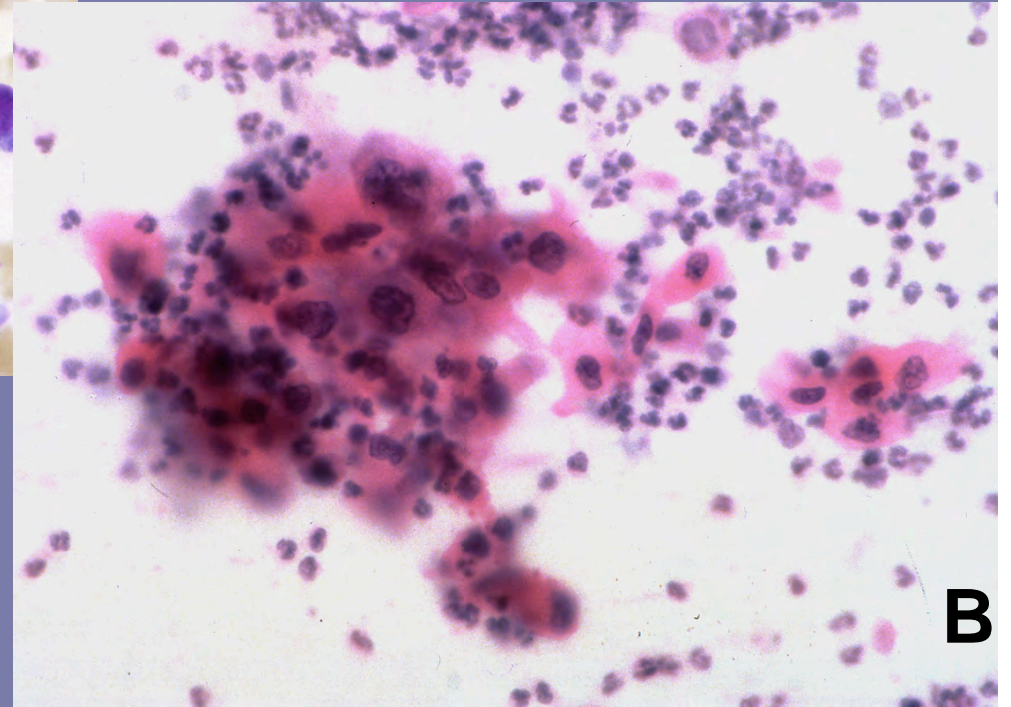
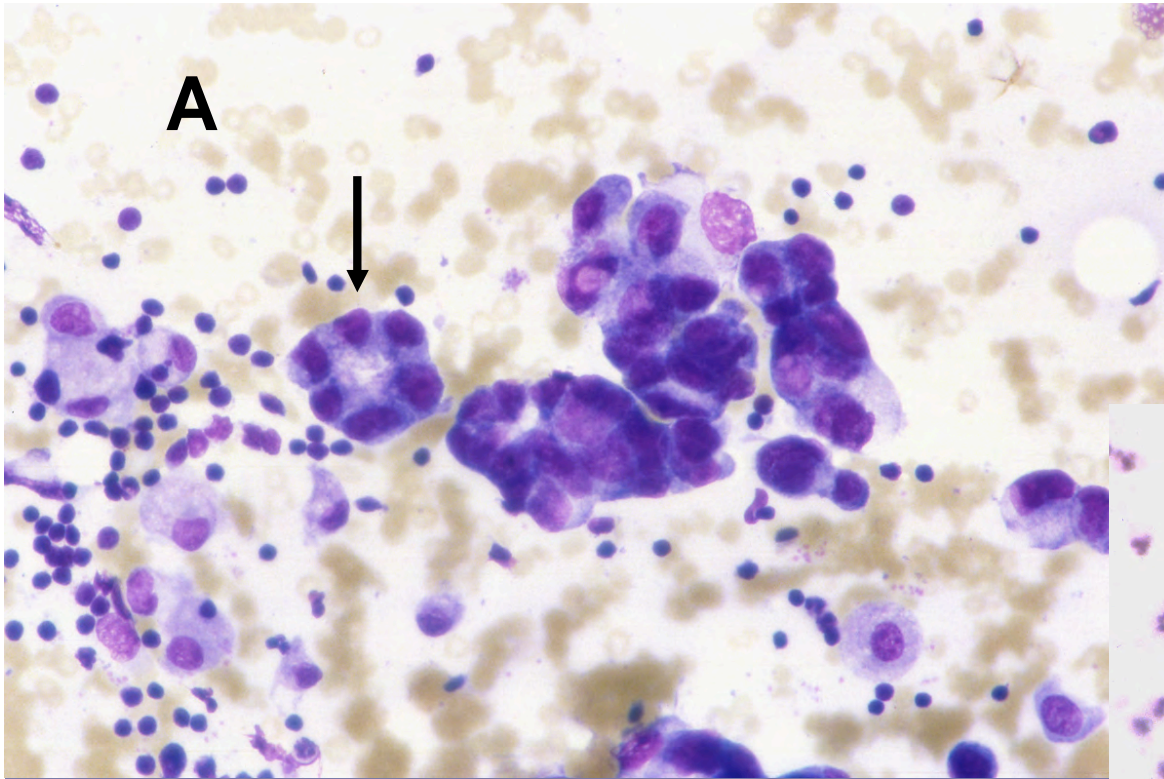
Fine needle aspiration biopsies are commonly performed on enlarged lymph nodes to help ascertain the cause.



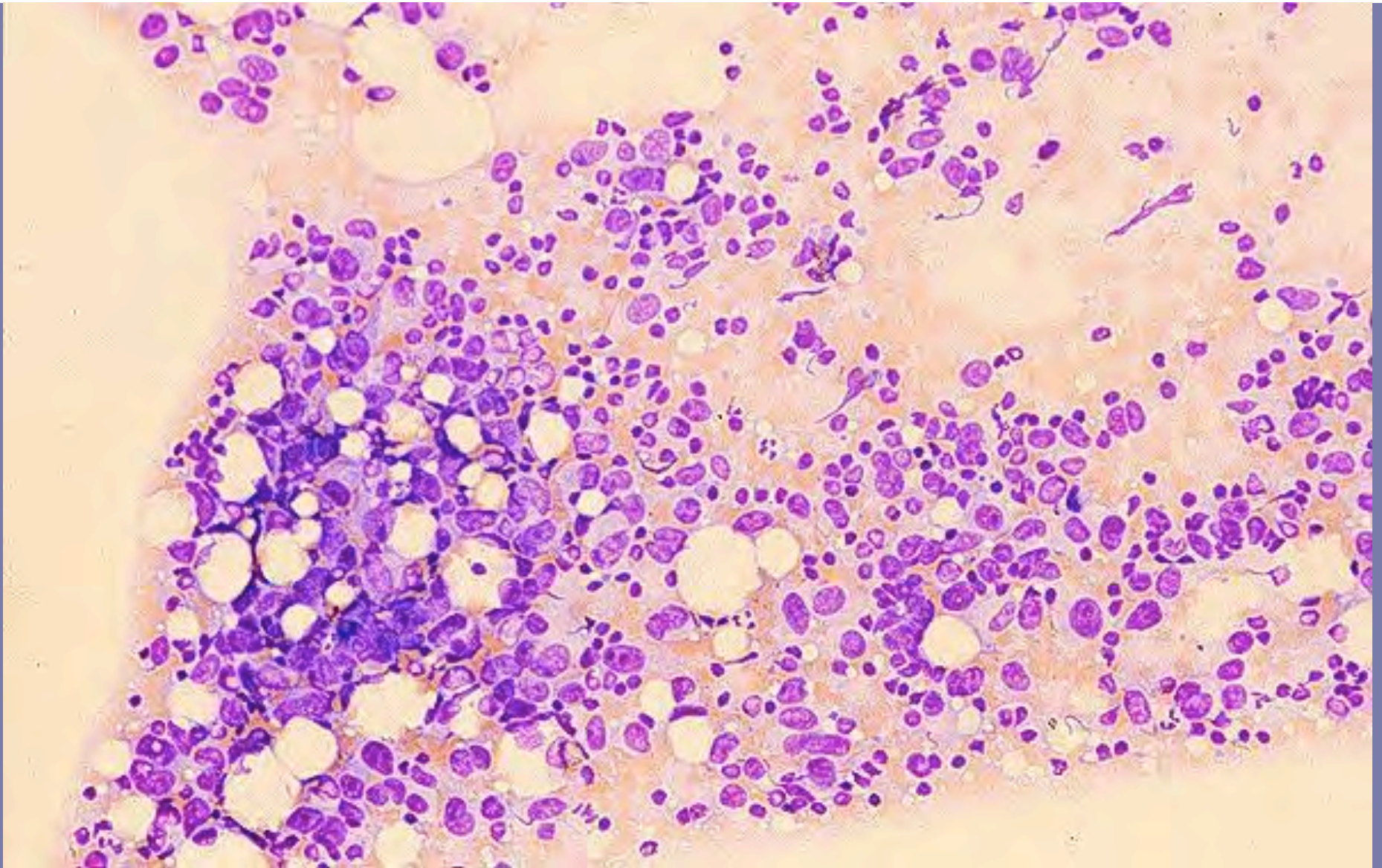
Left: Lymph node containing metastatic squamous cell carcinoma. The abnormal cells in the node show abundant eosinophilic cytoplasm and focal keratin pearl formation indicating squamous differentiation.

Right: Lymph node containing metastatic adenocarcinoma. Tubule formation by the tumour cells here indicates glandular epithelial differentiation.

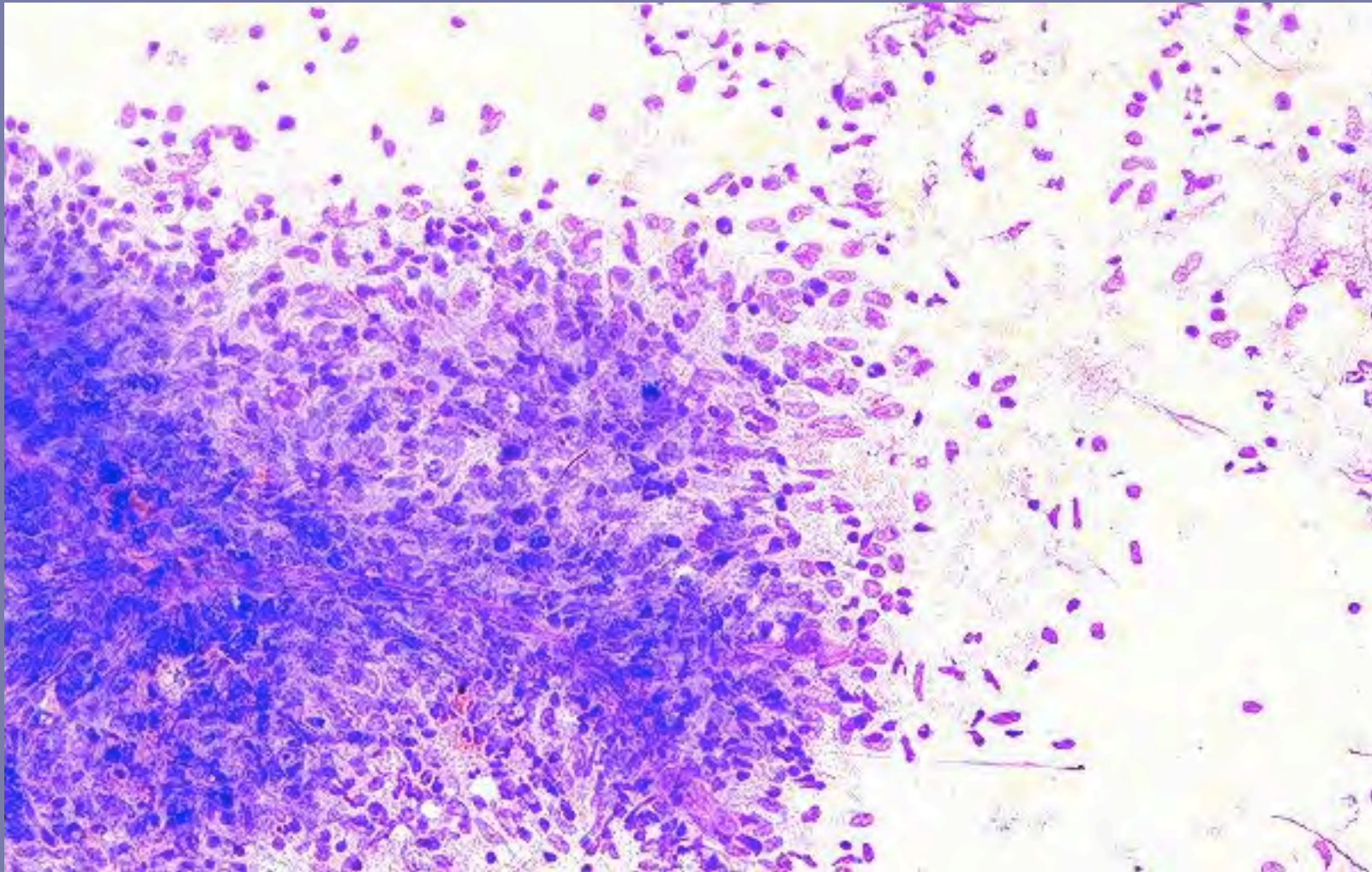




Fine needle aspirates of adenocarcinoma (A, Giemsa stain) and squamous cell carcinoma (B, pap stain) metastatic to a lymph node. Features of malignancy (large nuclei) and glandular (arrow) and squamous (pink staining on the pap stain) differentiation can be seen. Rbcs, lymphocytes and macrophages are in the background in A and neutrophils are in the background in B.



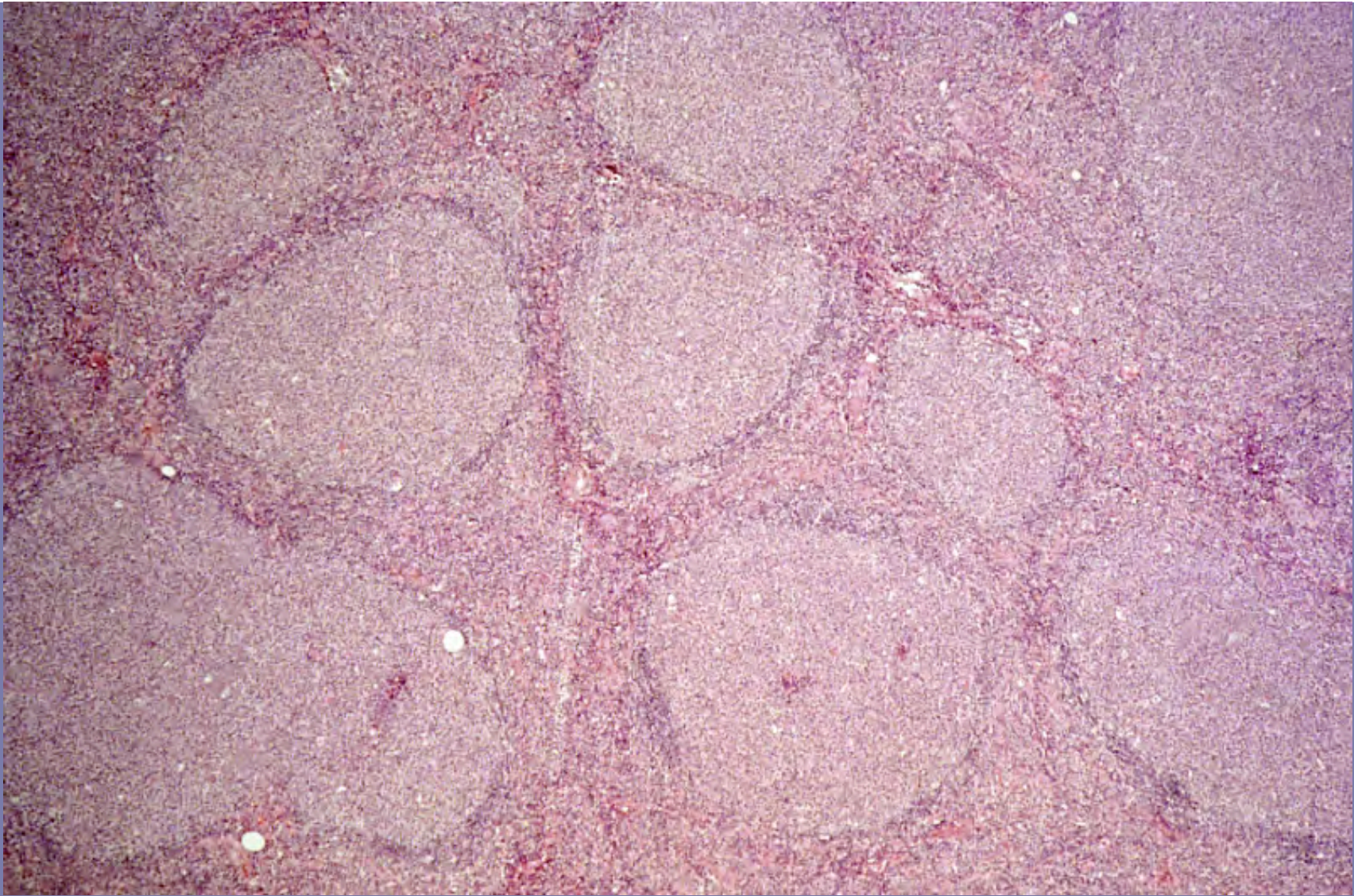
Cytology of a fine needle aspirate of malignant melanoma metastatic to a lymph node. The large neoplastic cells with prominent nucleoli are in a background of predominantly lymphocytes. (Giemsa stain)



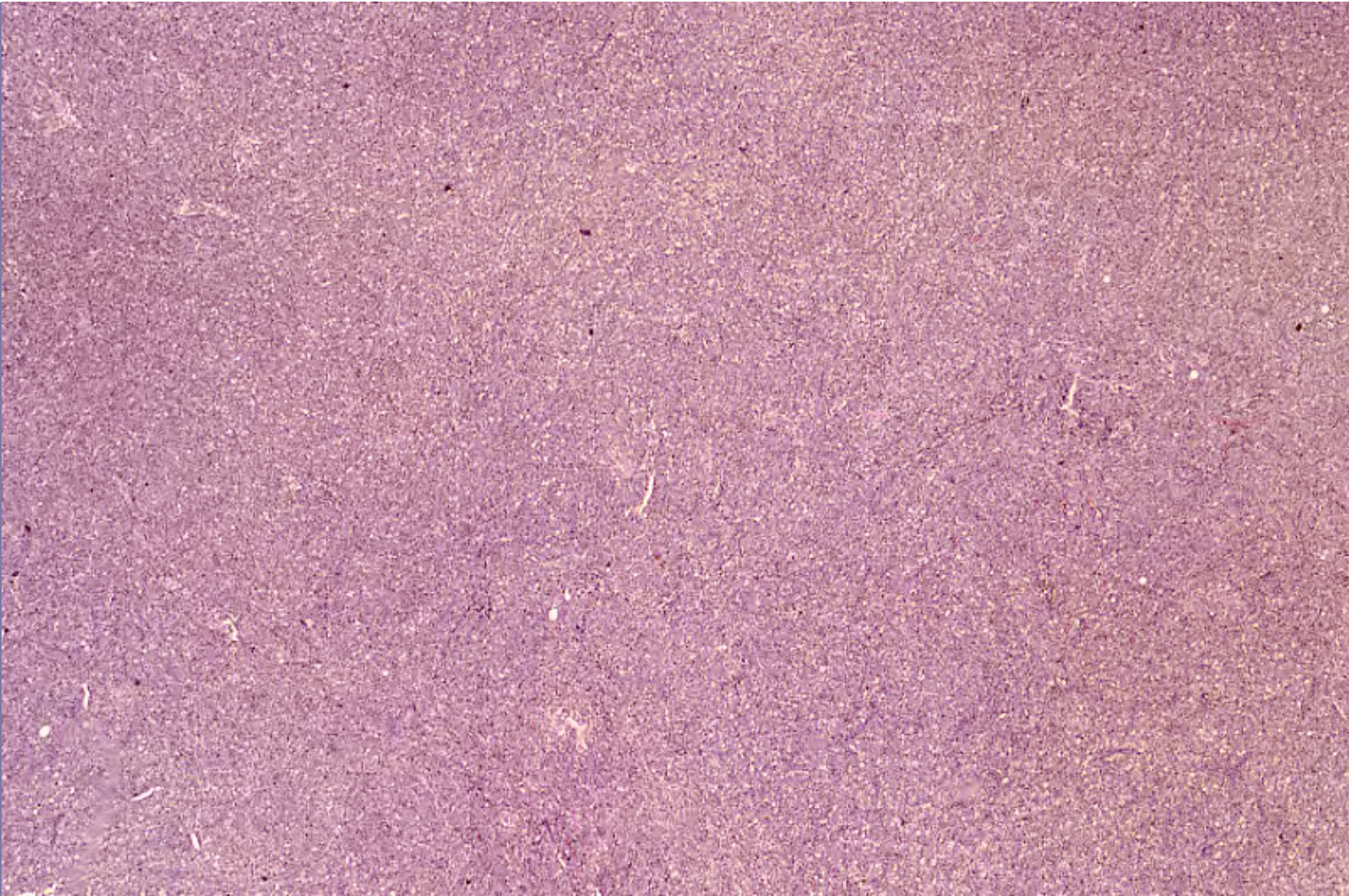
Fine needle aspirate from an enlarged cervical lymph node. In this case there is a large dyscohesive cluster of fairly regular cells with oval nuclei. These are epithelioid macrophages in granulomatous inflammation. (Giemsa stain)

Neoplastic proliferations of white cells (overview)

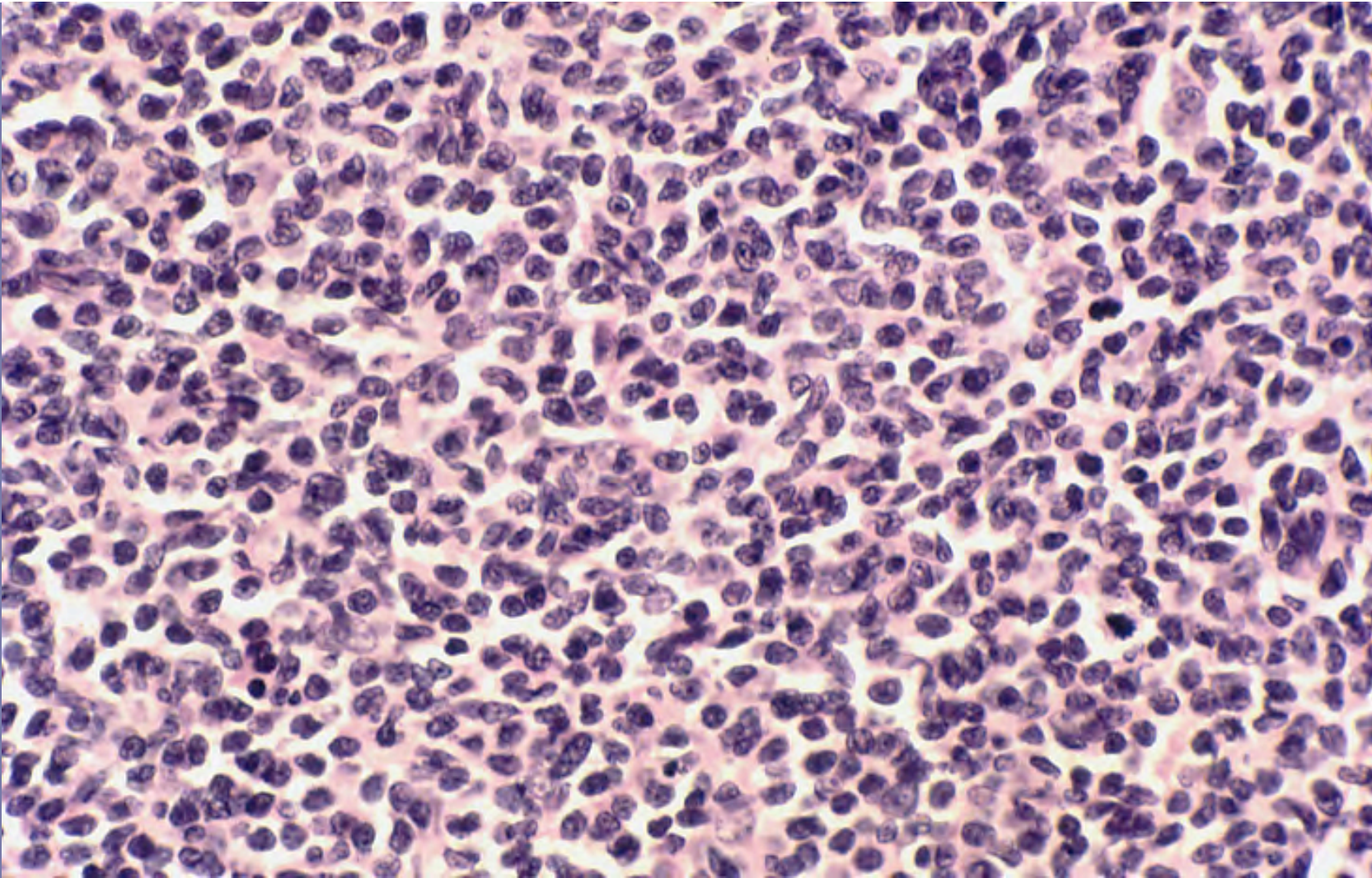
- Lymphoid neoplasms: the phenotype (morphological and immunological) of the neoplastic cells closely resembles that of lymphocytes at particular stages of normal differentiation. The architecture, morphology and immunological features of the neoplastic cells are used in diagnosis and classification.
 - Precursor B cell neoplasms (neoplasms of immature B cells, i.e. show phenotype of developing cells in bone marrow)
 - Peripheral B cell neoplasms (neoplasms of mature B cells)
 - Precursor T cell neoplasms (neoplasms of immature T cells, i.e. show phenotype of developing cells in bone marrow)
 - Peripheral T cell and NK cell neoplasms (neoplasms of mature T cells and NK cells)
 - Hodgkin's lymphoma (neoplasms of Reed Sternberg cells and their variants)
- Myeloid neoplasms
 - Acute myelogenous leukaemias
 - Myelodysplastic syndromes
 - Chronic myeloproliferative disorders
- Histiocytoses



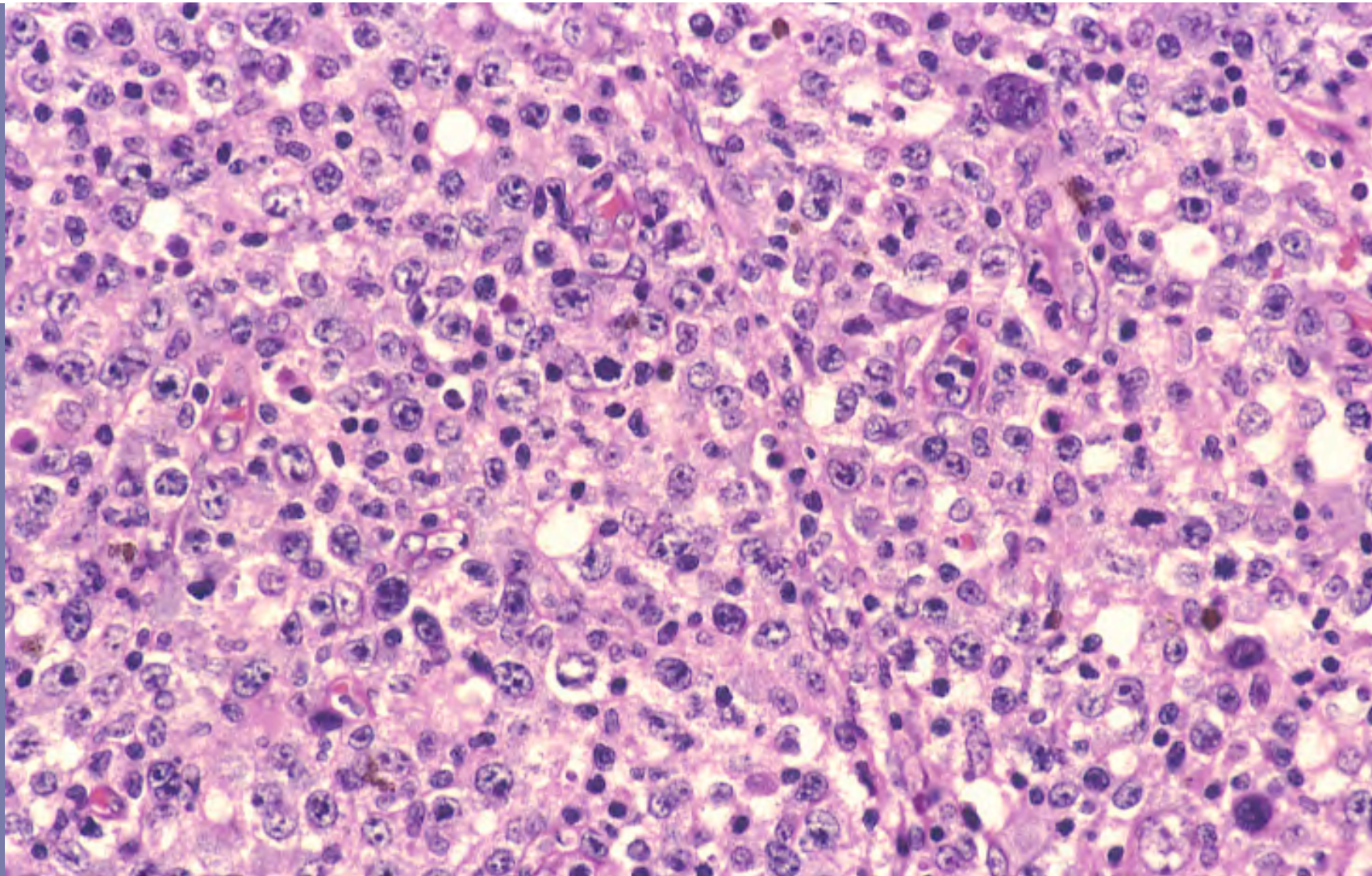
Follicular non-Hodgkin's lymphoma (NHL), low power. The neoplastic cells are of B cell lineage that recapitulate the differentiating B cells within a germinal centre, thus form nodules/follicles.



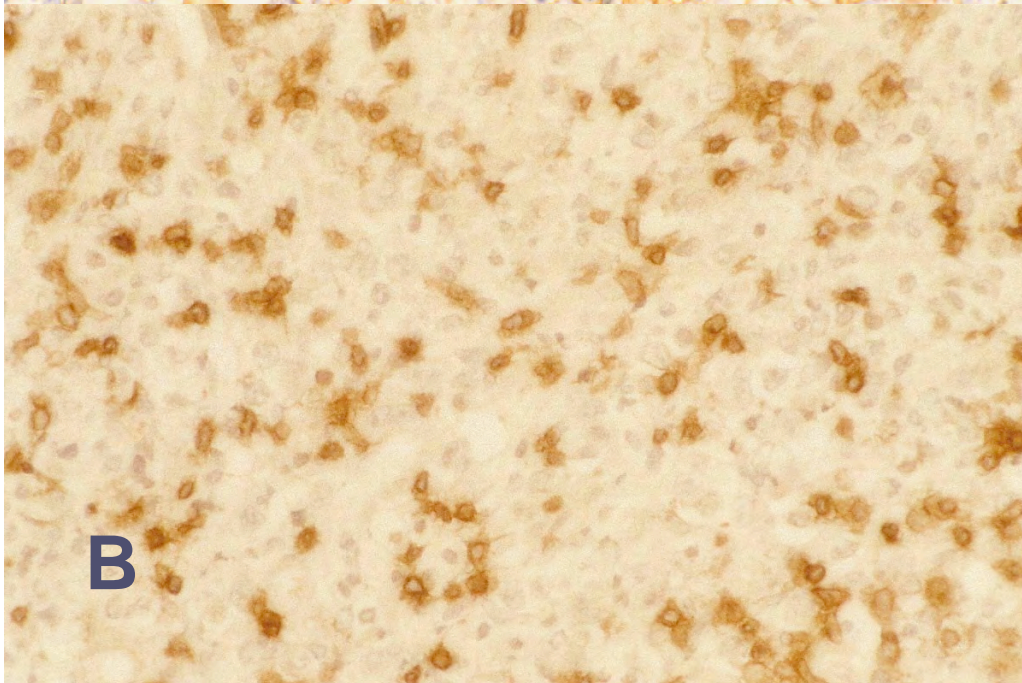
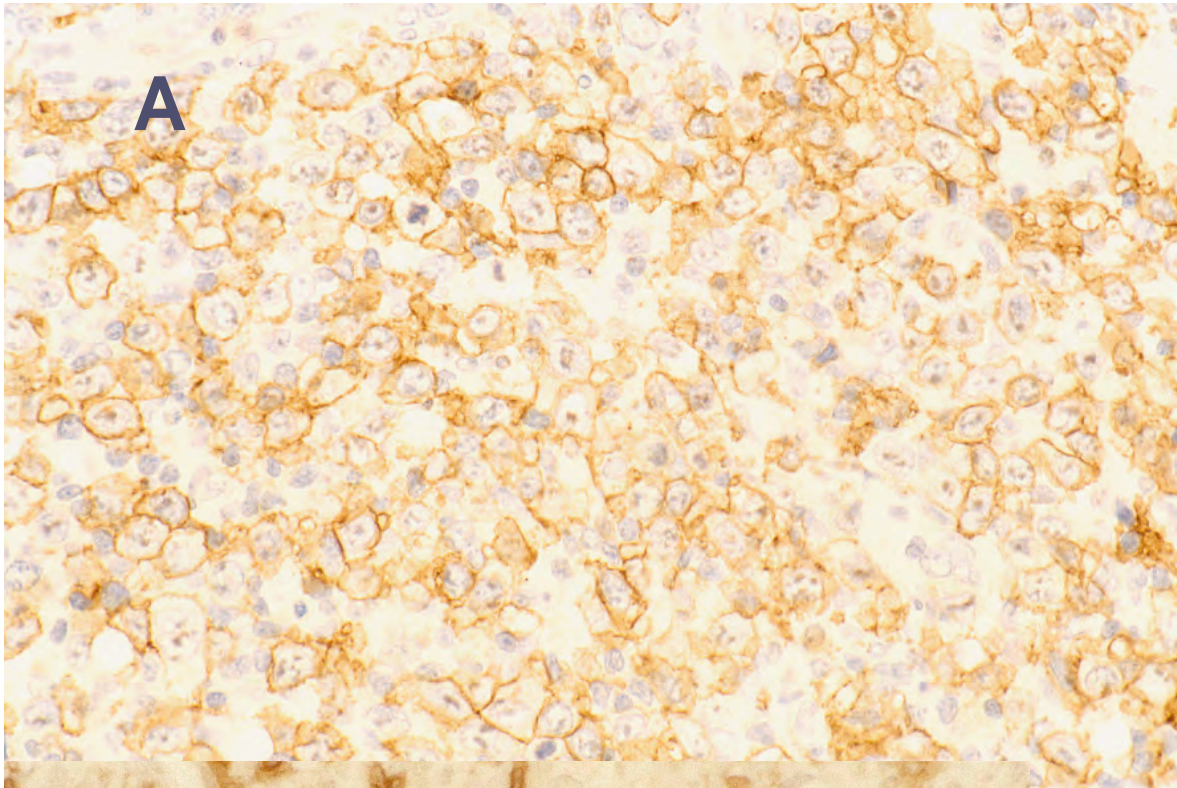
Diffuse non-Hodgkin's lymphoma, low power. There are various types (usually large B cell) that display a diffuse pattern of growth.



Non-Hodgkin's lymphoma, medium power. Small lymphocytes with scant cytoplasm and an irregular 'cleaved' nucleus recapitulating the centrocytes (differentiating B cells) of a germinal centre and typically are the predominant cell type in follicular lymphomas.

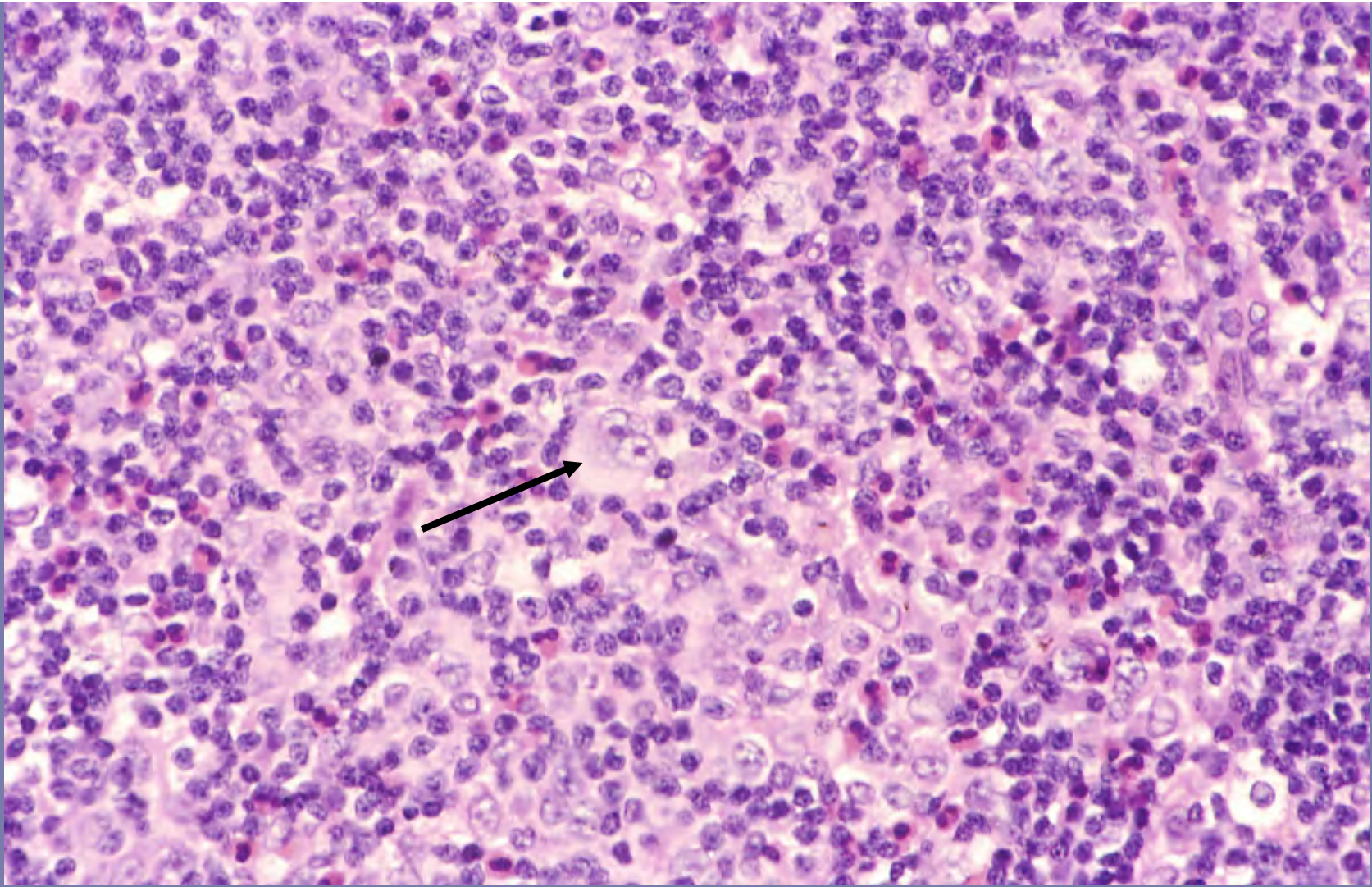


Non-Hodgkin's lymphoma, medium power. Predominantly large lymphocytes with relatively abundant cytoplasm, large vesicular nuclei and prominent, sometimes multiple, nucleoli. These are generally of B cell phenotype and recapitulate centroblasts and immunoblasts in plasma cell differentiation.

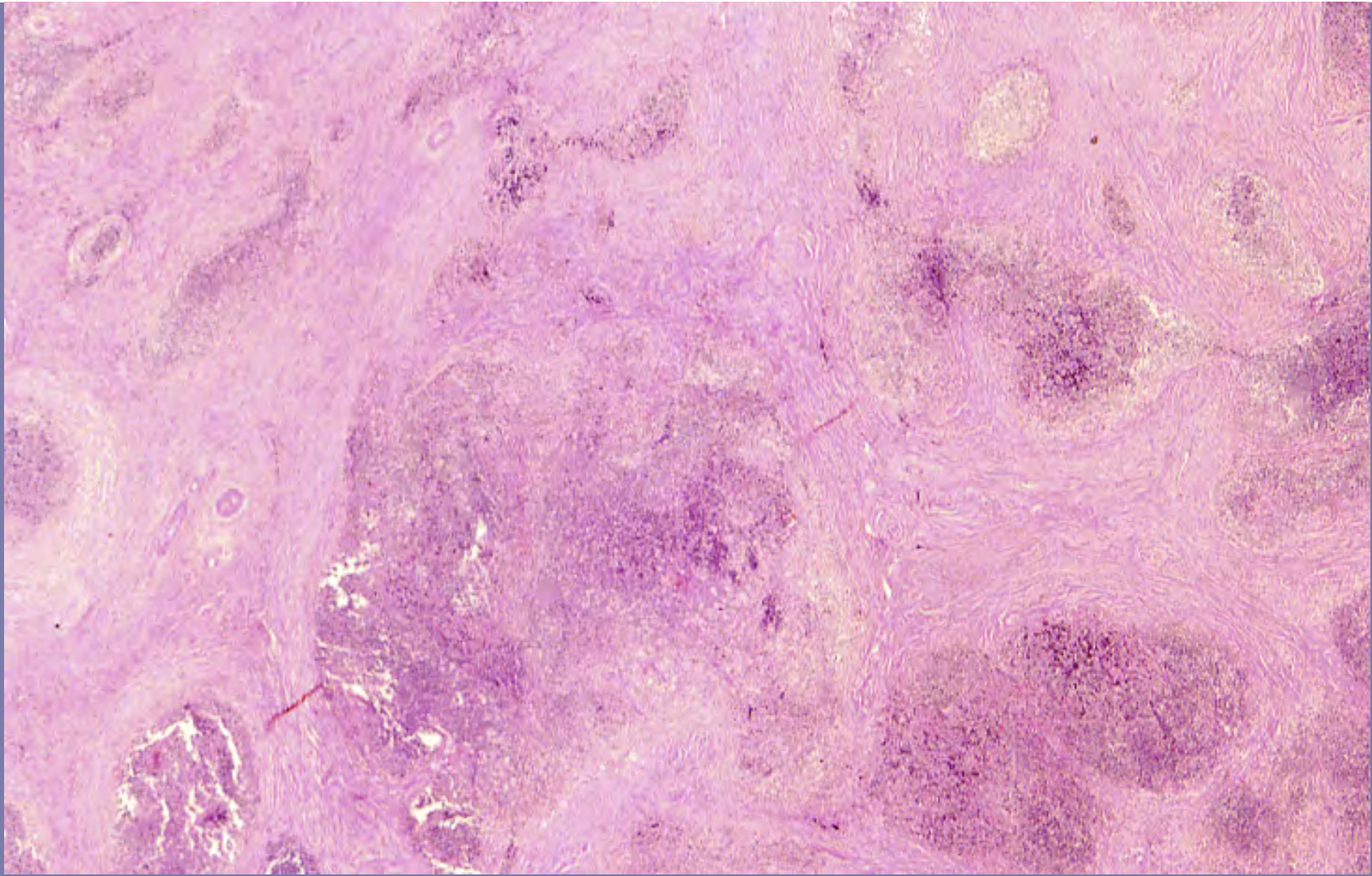


Immunohistochemistry is commonly used in the diagnosis and classification of lymphoid neoplasms. Image A demonstrates a large cell NHL in which the large neoplastic cells show cell membrane staining (brown) using antibody L26 for CD20, an antigen expressed by B cells, confirming their B cell nature.

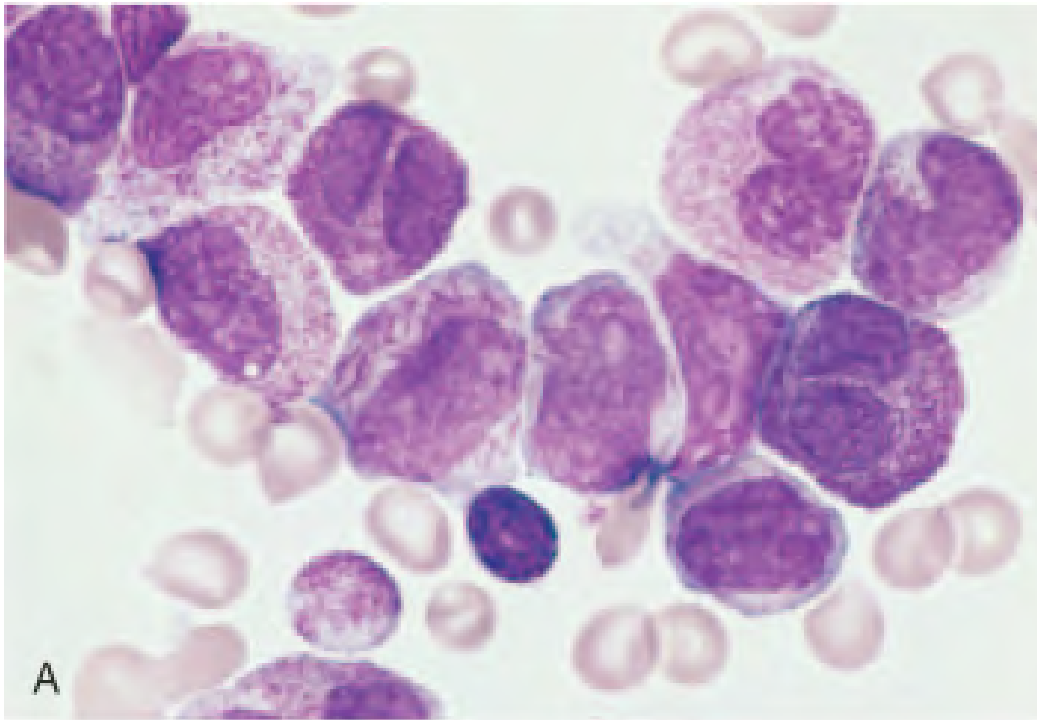
Image B is from the same tumour but these smaller cells show cell membrane staining (brown) for CD3, an antigen expressed by T cells. These cells are non-neoplastic T cells infiltrating the tumour. The large neoplastic cells do not stain. Many other antibodies to numerous other antigens expressed by these cells at various stages of their differentiation can be used to subtype these tumours further if necessary.



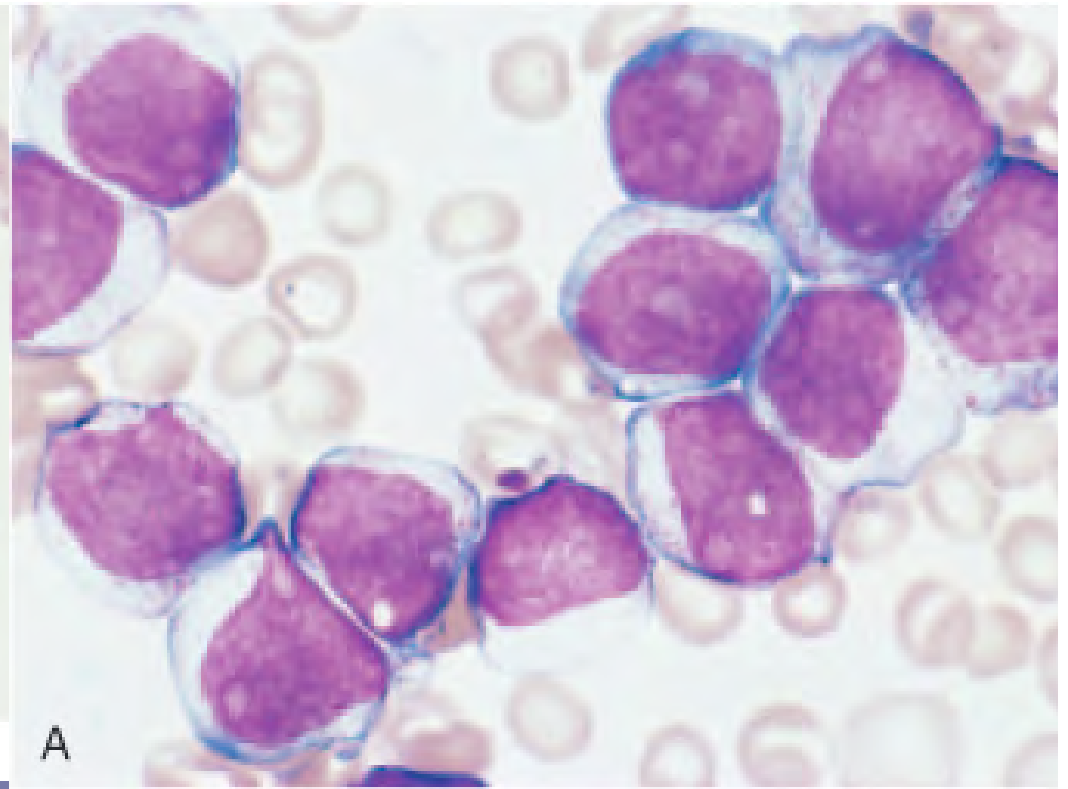
Hodgkin's lymphoma, medium power. The neoplastic cell is the Reed-Sternberg cell, a cell of B lymphocyte origin. There are several morphological variants of Reed-Sternberg cells but the typical cell (black arrow) is large with abundant cytoplasm and a large bilobate nucleus with prominent eosinophilic nucleoli. These neoplastic cells make up only a minority of the tumour cell mass, the majority of the cells being non-neoplastic lymphocytes, plasma cells, eosinophils and macrophages.



Hodgkin's lymphoma, medium power. There are 5 subtypes of Hodgkin's lymphoma. The most common form, the nodular sclerosis type, demonstrated here, typically contains abundant fibrous stroma that divides the tumour into nodules.

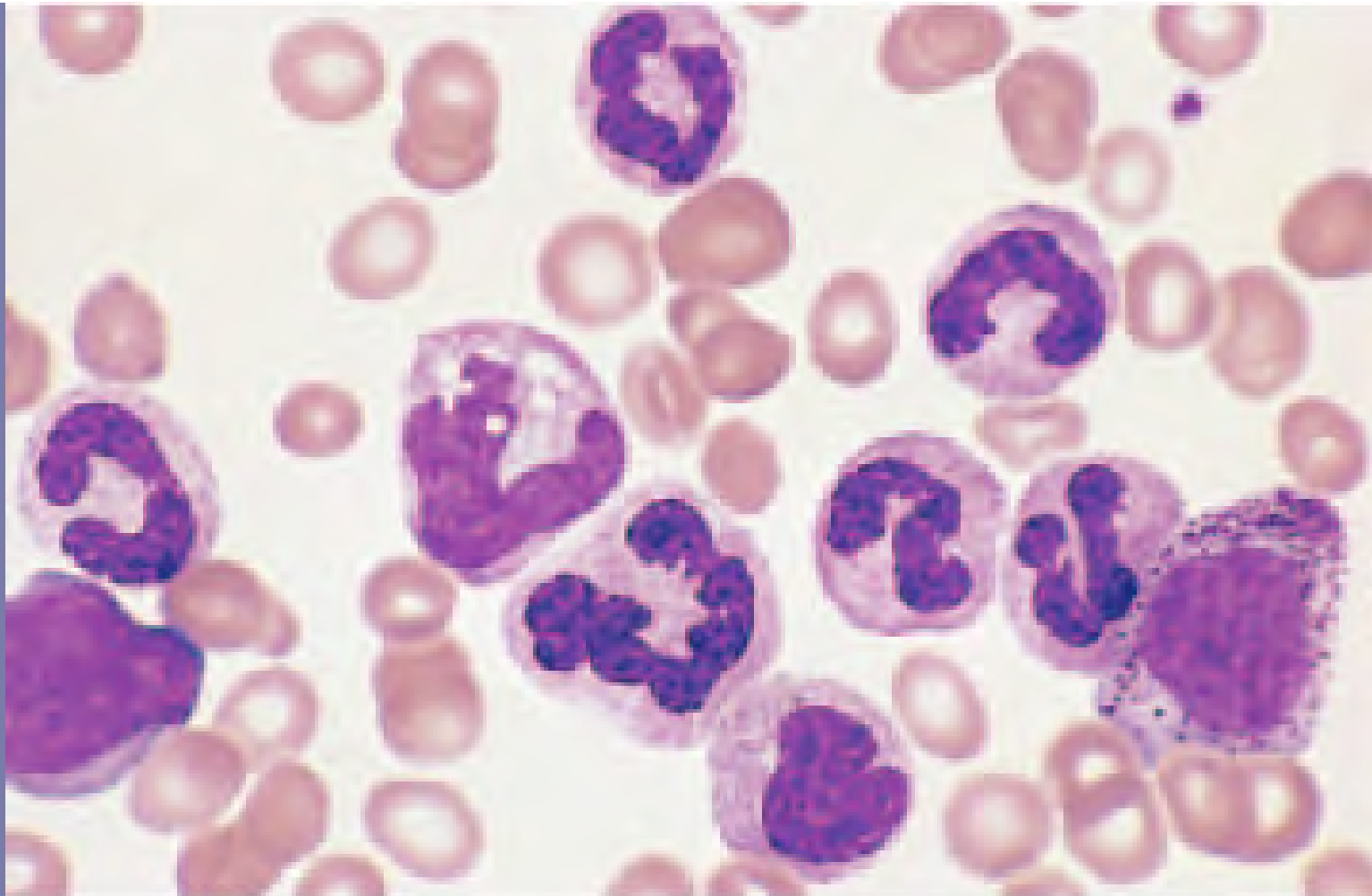


© Elsevier 2005



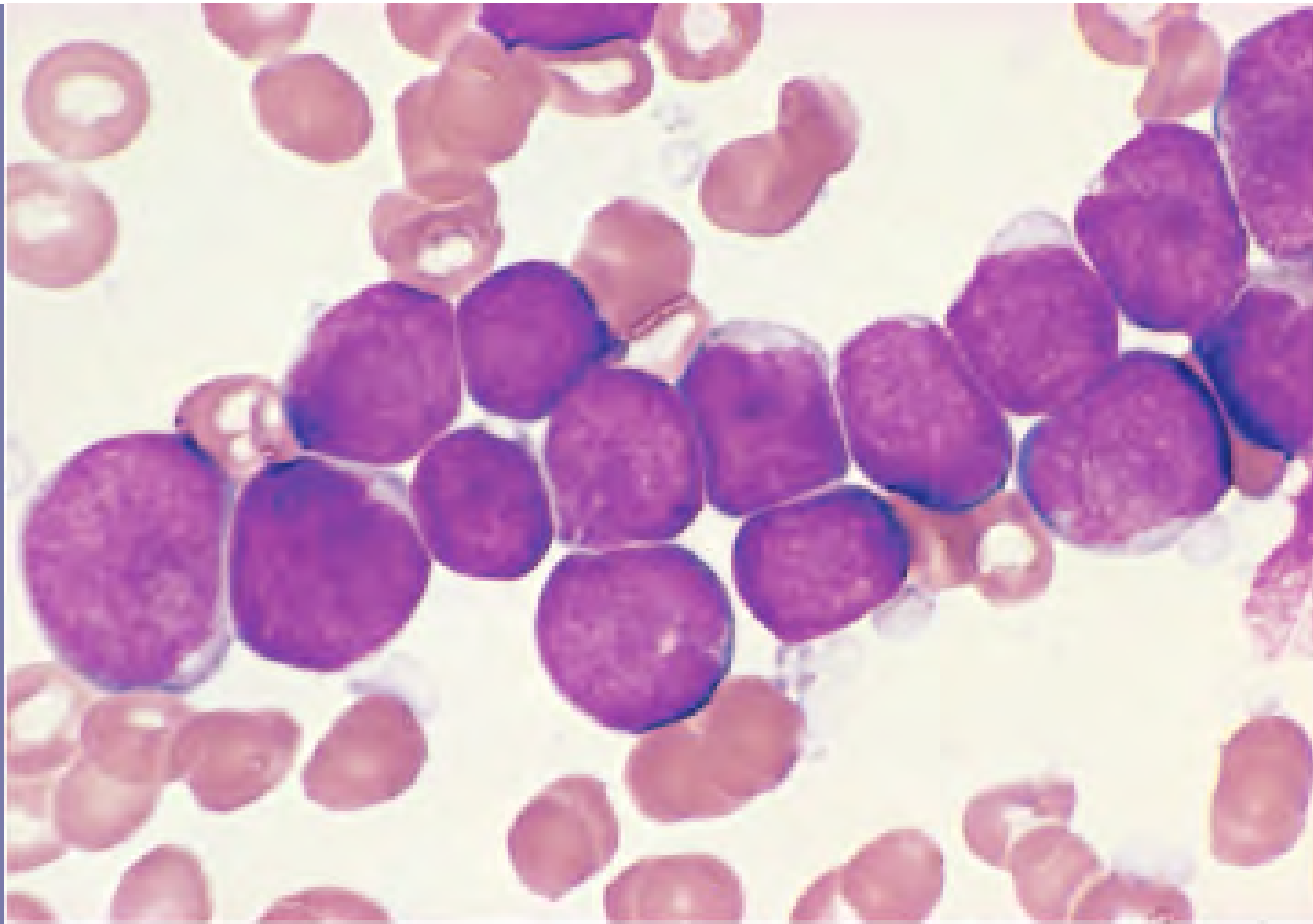
© Elsevier 2005

Acute myelogenous leukemia. Bone marrow aspirate shows neoplastic precursor myeloid cells. The cytoplasm contains azurophilic granules. The immature nuclei contain nucleoli. Depending on the specific type, the nuclei may or may not be indented or bilobate. (From Robbins and Cotran Pathologic Basis of Disease, 7th ed, Elsevier Saunders)



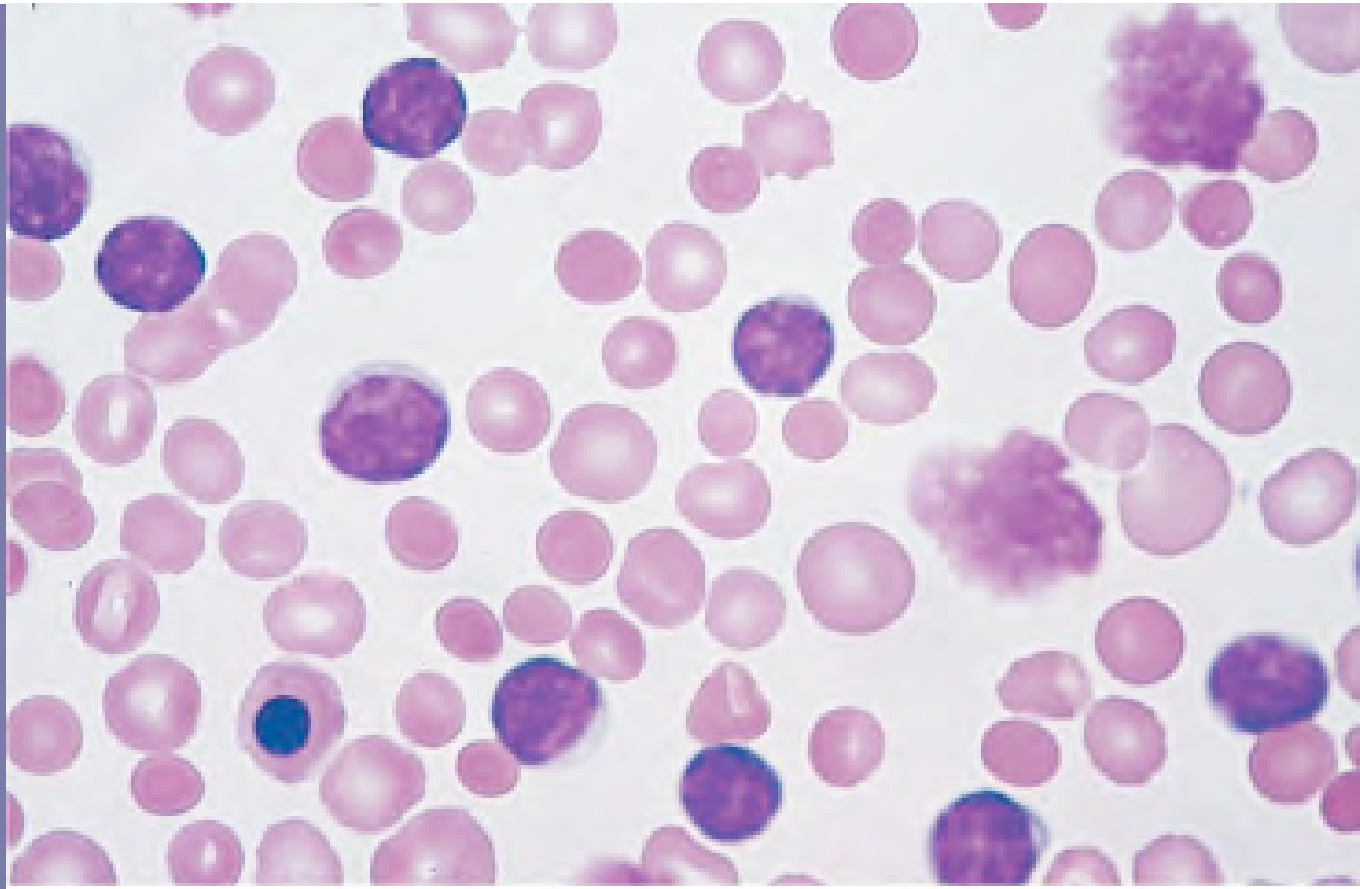
© Elsevier 2005

Chronic myelogenous leukemia. Peripheral blood smear shows many mature neutrophils, some metamyelocytes, and a myelocyte. (From Robbins and Cotran Pathologic Basis of Disease, 7th ed, Elsevier Saunders)



© Elsevier 2005

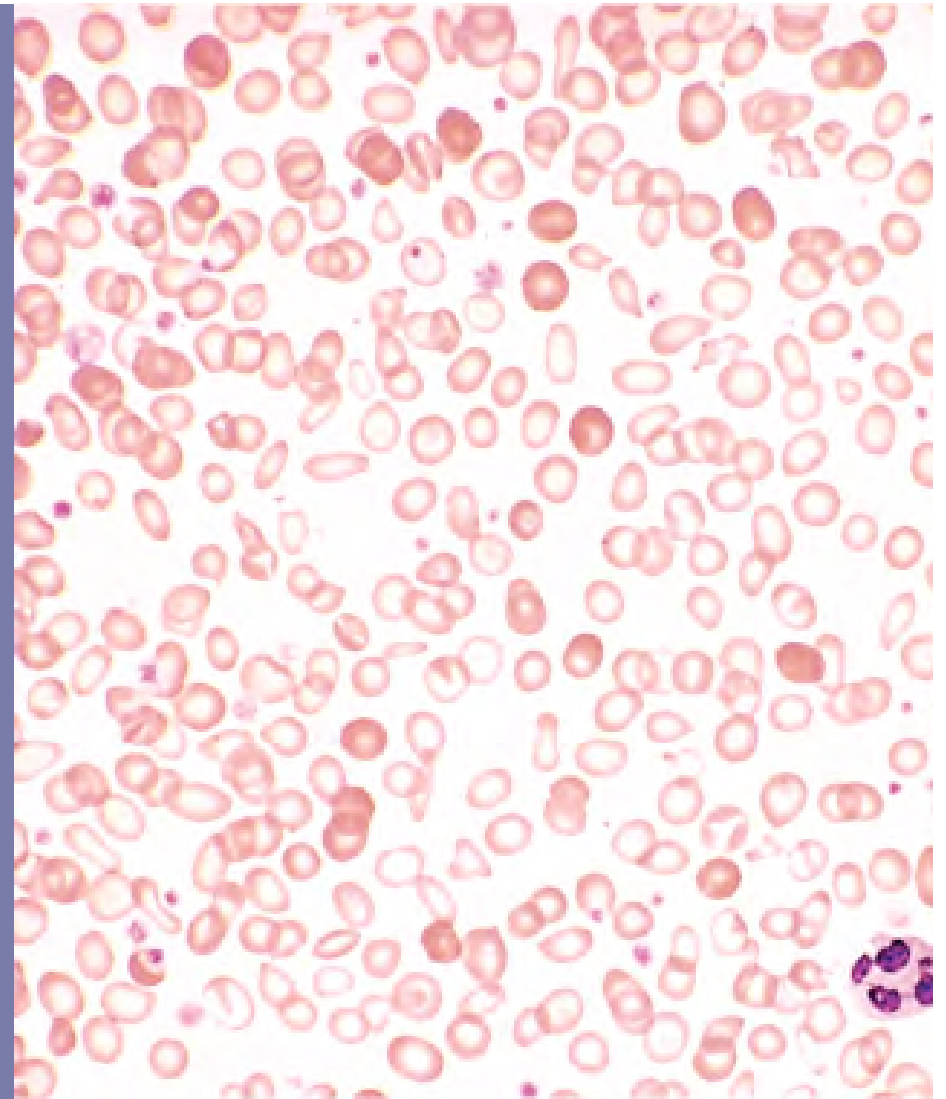
Acute lymphoblastic leukemia/lymphoma. Lymphoblasts with condensed nuclear chromatin, small nucleoli, and scant agranular cytoplasm. (From Robbins and Cotran Pathologic Basis of Disease, 7th ed, Elsevier Saunders)



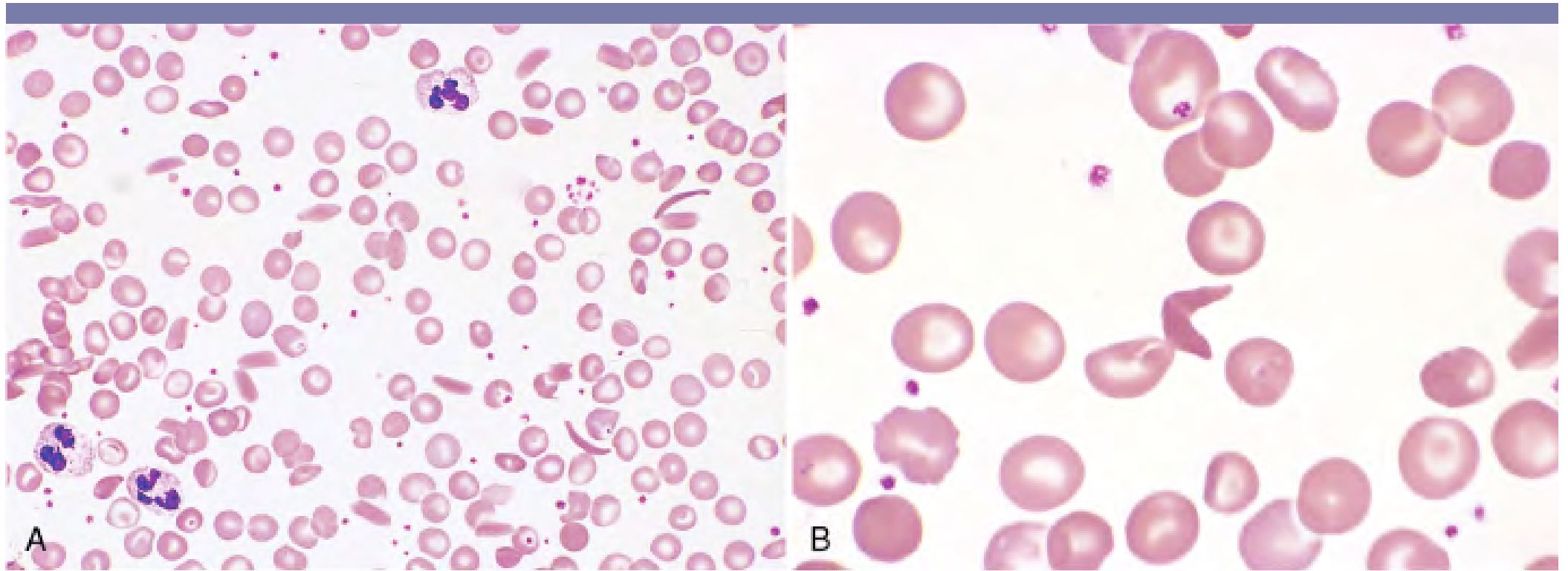
© Elsevier 2005

Chronic lymphocytic leukemia. Peripheral blood smear with many small lymphocytes with condensed chromatin and scant cytoplasm. A characteristic finding is the presence of disrupted tumor cells (smudge cells). A nucleated erythroid cell is present in the lower left-hand corner of the field. (From Robbins and Cotran Pathologic Basis of Disease, 7th ed, Elsevier Saunders)

Selected anaemias: Hypochromic microcytic anemia of iron deficiency (peripheral blood smear). Note the small red cells containing a narrow rim of peripheral hemoglobin. Scattered fully hemoglobinized cells, present due to recent blood transfusion, stand in contrast. (From Robbins and Cotran Pathologic Basis of Disease, 7th ed, Elsevier Saunders)

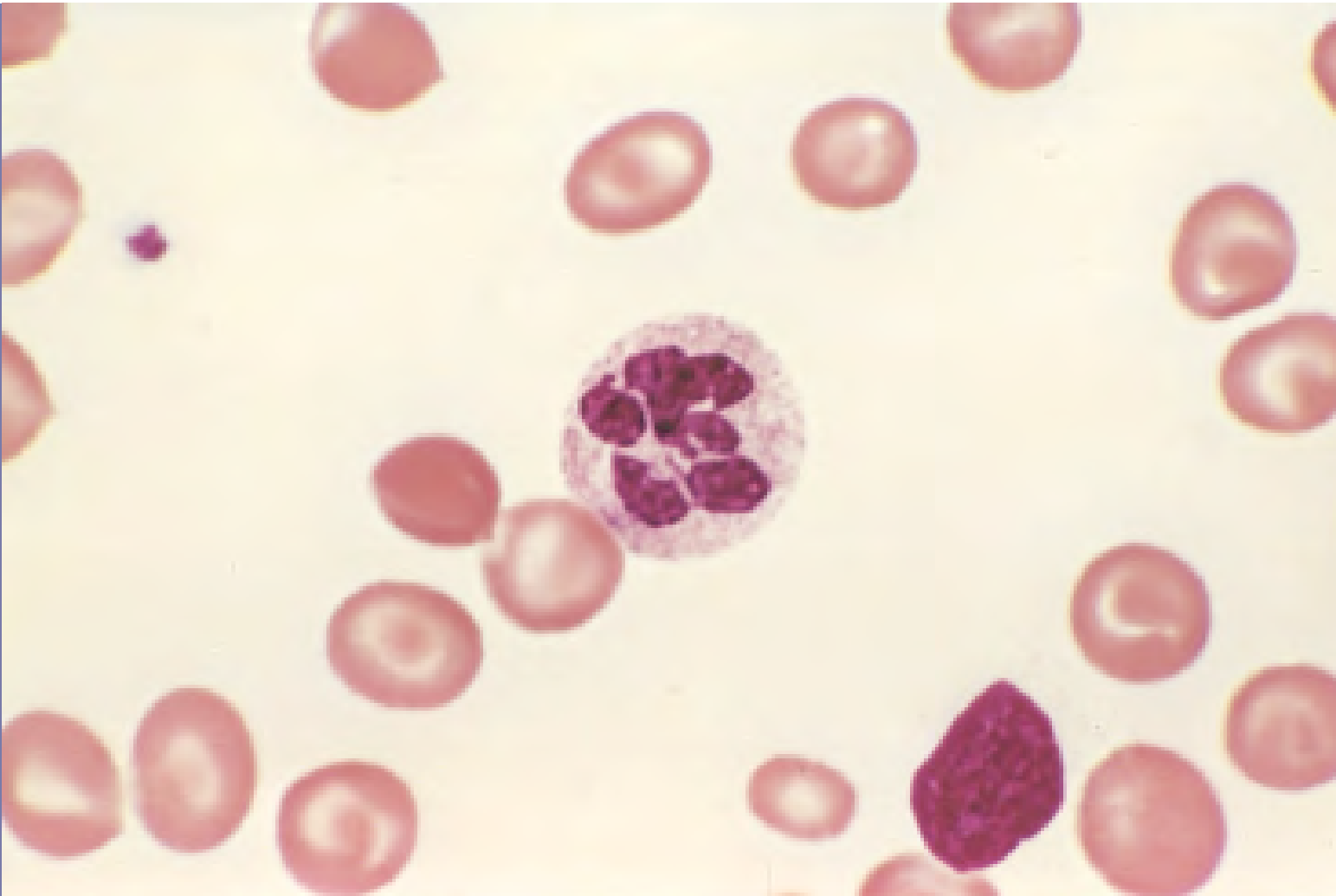


© Elsevier 2005



© Elsevier 2005

Selected anaemias. Sickle cell anemia (peripheral blood smear). *A*, Low magnification shows sickle cells, anisocytosis, and poikilocytosis. *B*, Higher magnification shows an irreversibly sickled cell in the center. (From Robbins and Cotran Pathologic Basis of Disease, 7th ed, Elsevier Saunders)



© Elsevier 2005

Selected anaemias. Megaloblastic anemia. A peripheral blood smear shows a hypersegmented neutrophil with a six-lobed nucleus. (From Robbins and Cotran Pathologic Basis of Disease, 7th ed, Elsevier Saunders)