NZIMLS

THE NEW ZEALAND
INSTITUTE OF MEDICAL
LABORATORY SCIENCE (INC)

STANDARDISED REPORTING OF BLOOD FILM MORPHOLOGY

FOURTH EDITION 2011

OBJECTIVES

AIM:

To provide standard nomenclature and reporting of results in the Haematology Laboratory.

ADVANTAGES:

1. Consistency of reporting where patients' specimens are processed at different sites.
2. Morphologists use terms with clear definitions.
3. Trainees can use standard and commonly understood terminology.

USE:

This document has been prepared to provide clear guidelines for a morphologist to report blood cell morphology. It is not intended as a definitive reporting system but rather as an initial step. Abnormal morphology should be reported where possible with an accompanying interpretative comment. Clinically relevant terminology has been chosen using simple, widely understood words and with reference to available literature.

CONTENTS

GENERAL HAEMATOLOGY

1. The abbreviation for litre will be L.

2. **Red cell parameters**

   The units, multipliers and order of reporting will be as follows:

Red cell count	$x10^{12}/L$
Haemoglobin	g/L
Packed cell volume / Haematocrit	
Mean cell volume	fL
Mean cell haemoglobin	pg
Red cell distribution width	

3. **Mean cell haemoglobin concentration** (MCHC) will be deleted from report forms. It is intended that it will continue to be used within the laboratory for quality control purposes.

4. **Nucleated red cells** will be reported as cell concentration per litre using 10^9 as the multiplier.

5. **Reticulocytes** will be reported as cell concentration per litre using 10^9 as the multiplier.

6. **White cell differential**

   White cell types will be reported as cell concentration per litre using 10^9 as the multiplier.

   The order of white cells will be as follows:

   Blast
   Promyelocyte
   Myelocyte
   Metamyelocyte
   Band neutrophil
   Segmented neutrophil
   Basophil
   Eosinophil
   Monocyte
   Lymphocyte
   Other cell types
   Plasma cell
   Smear cell

7. **Platelet count**

   From 0 to $9x10^9/L$ will be reported as "less than $10x10^9/L$".

BLOOD CELL MORPHOLOGY

INTRODUCTION

Blood cells are subject to many factors which can influence their appearance such as the age of the cell, the dynamics of the blood stream, body function in health and disease and other influences such as drugs and infections.

The following nomenclature list is considered sufficient to describe the observed appearance of individual cells. The presence of abnormal morphology (individual cells and overall appearance) may be associated with certain clinical conditions. Using data from blood cell morphology, laboratory procedures and clinical details, appropriate interpretative comments should be made to assist clinical diagnosis and management. As a general rule the morphologist should review the full blood picture and comment accordingly rather than comment on isolated abnormalities i.e. any single abnormality should be interpreted in the context of the overall picture – morphology, clinical information and laboratory results.

When examining blood cell morphology in the Romanowsky stained blood film it is essential that the film is prepared and examined following the procedure in the method manual in your laboratory.

NOMENCLATURE

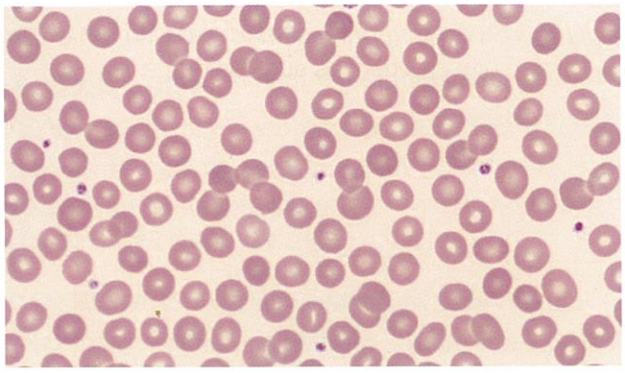
It is recommended that:

Red Cell is used whenever possible instead of erythrocyte.
White Cell is used whenever possible instead of leucocyte.
Platelet is used whenever possible instead of thrombocyte.

ORDER OF REPORTING

The recommended order of morphology reporting is red cell, white cell, platelets.
The recommended order for reporting red cell morphology is size, chromia, shape, inclusions.

NORMAL RED CELL MORPHOLOGY

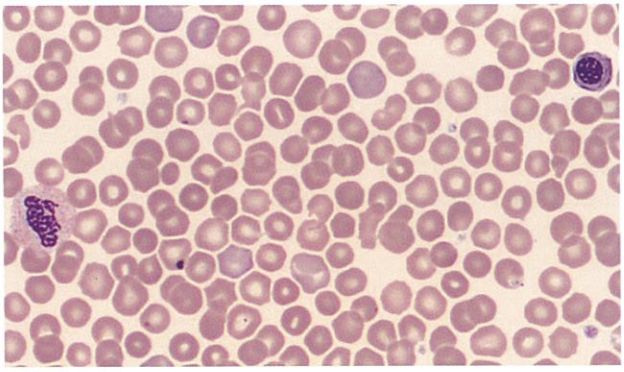


NORMAL ADULT

In well spread blood films the majority of red cells have round smooth contours and have a diameter within a comparatively narrow range of 6.0-8.5 um (mean ± 2 SD). They stain orange-pink with the eosin component of Romanowsky dyes. The staining is darker at the periphery with a pale central area which usually occupies less than 1/3 of the diameter of the cell i.e. normochromic. Up to 0.5% may show faint blue-grey (polychromatic) staining.

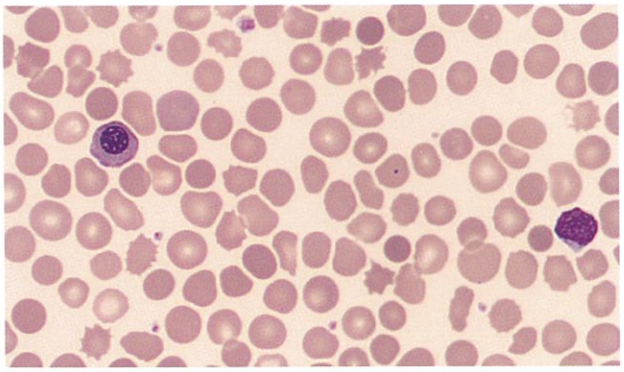
CORD BLOOD FILMS AND CHILDREN'S BLOOD FILMS

The variation in the size, shape and colour of red cells observed in cord blood and children's films are not to be compared with normal adult red cell morphology.



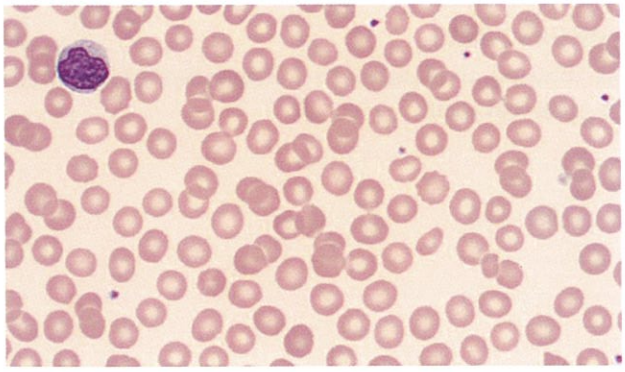
NORMAL CORD BLOOD

The red cells of the term infant are much larger than normal adult red cells with an average diameter of 8.5 um. Up to 5% of the red cells are polychromatic. Variation in cell shape may be seen with up to 60% of red cells exhibiting an irregular contour. Nucleated red cells constitute about 0.1% of the newborns' circulating red blood cells. Values of 0 – 10 nucleated red cells per 100 white cells are typical, and values above 10 – 20 nucleated red cells per 100 white cells are elevated, although these values are highly dependent on the total white cell count.



LOW BIRTH WEIGHT / PREMATURE BABIES

Cord blood and neonatal blood samples from low birth weight babies, premature babies and infants with with hypoxia, cardiac or respiratory problems may show increased variation in red cell size and shape, with increased numbers of polychromatic and nucleated red cells when compared with a cord blood from a normal full term infant. The degree of change is related to gestational age.

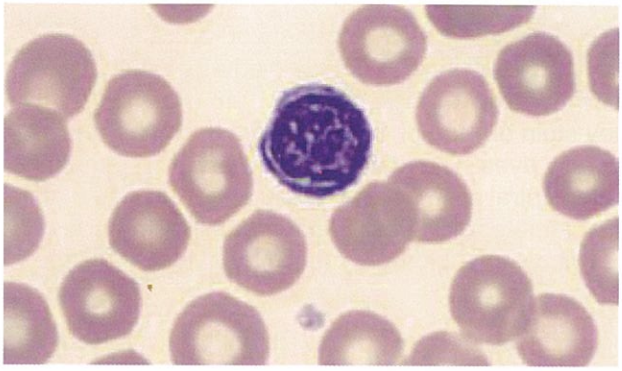


NORMAL CHILDREN

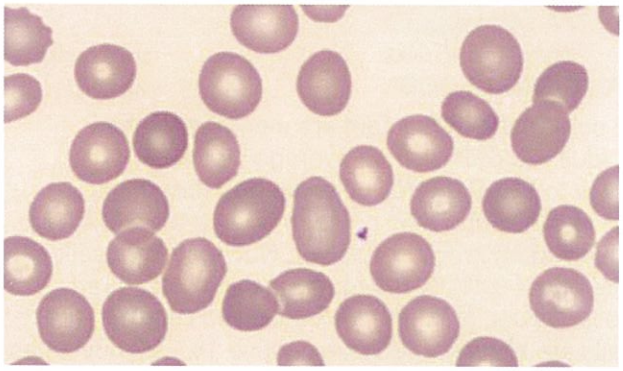
Red cells in children show a wide variation in diameter according to age. This ranges from an average of 8.5 um at birth, to a minimum of 5.0 um during early childhood and reaching adult red cell size when the child is about 12 years old. Refer to the reference ranges in your laboratory.

MORPHOLOGICAL RED CELL VARIATIONS

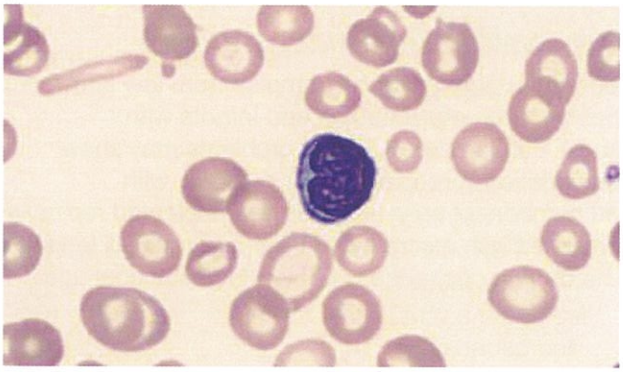
SIZE



MACROCYTE
A red cell with a diameter greater than 8.5 um.
a) Round macrocyte

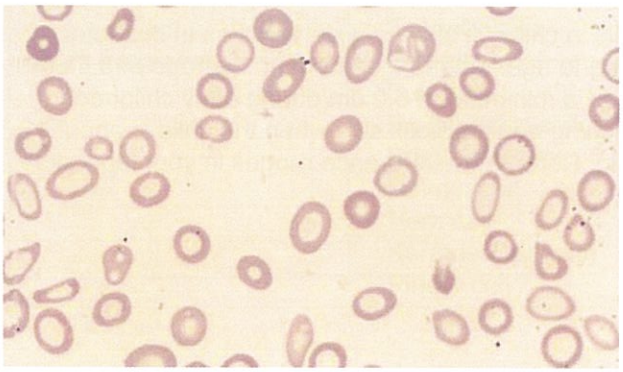


b) Oval macrocyte

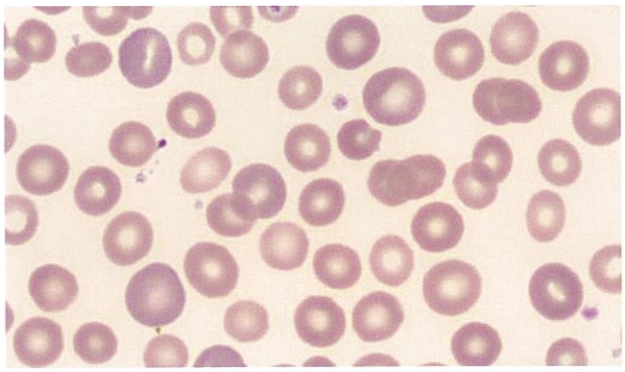


MICROCYTE
A red cell with a diameter less than 7 um.

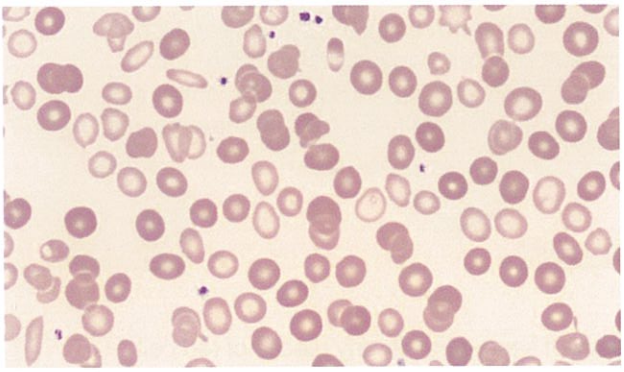
COLOUR



HYPOCHROMIC CELL
A red cell showing an increase in central pallor greater than one third of its diameter.

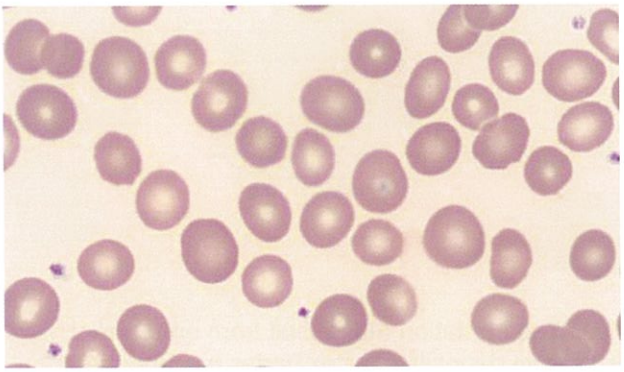


POLYCHROMATIC CELL
A blue-grey staining red cell usually larger than a normal mature red cell.



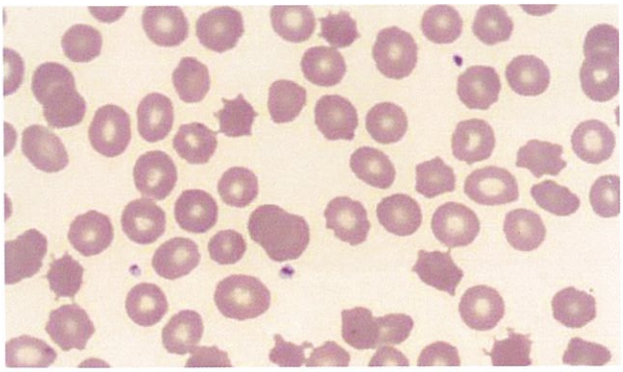
DIMORPHIC POPULATION
Two clearly different populations of red cells usually hypochromic and normochromic but can also relate to size.

Normochromic and hypochromic

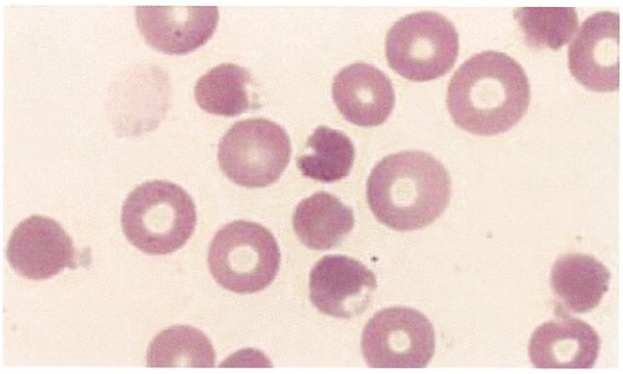


Normocytic and macrocytic

SHAPE

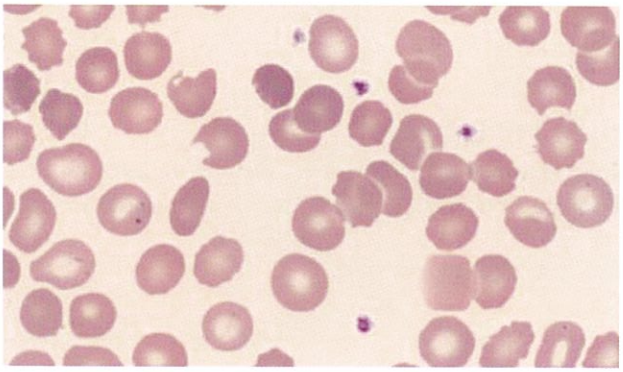


ACANTHOCYTE
Acanthocytes are round, hyperchromic red cells with a small number of spicules (2-20) of variable length, thickness and shape. Some spicules have club-shaped ends.



BLISTER CELL

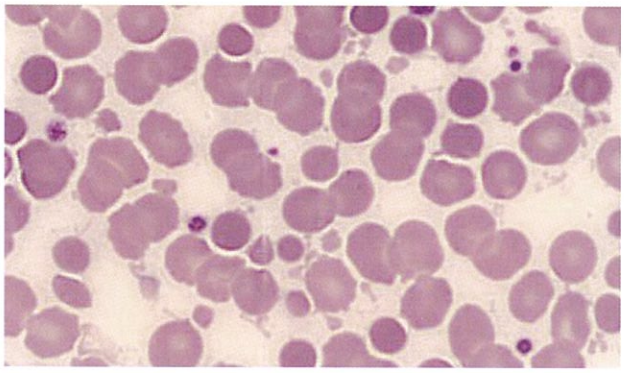
A red cell of variable size and shape in which the haemoglobin appears to have retracted from a portion of the membrane. The haemoglobinised portion appears dense and hyperchromic while the rest of the cell appears empty.



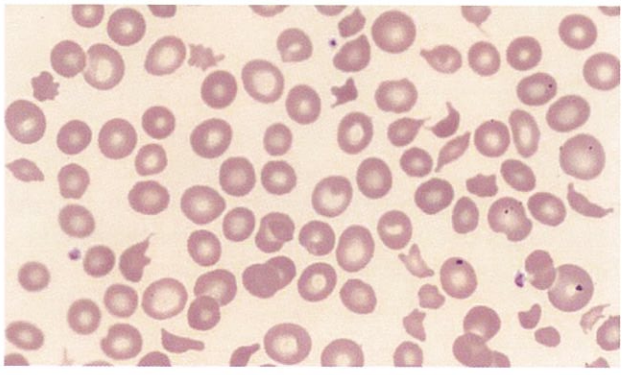
CELL FRAGMENT

An irregular portion of a red cell.

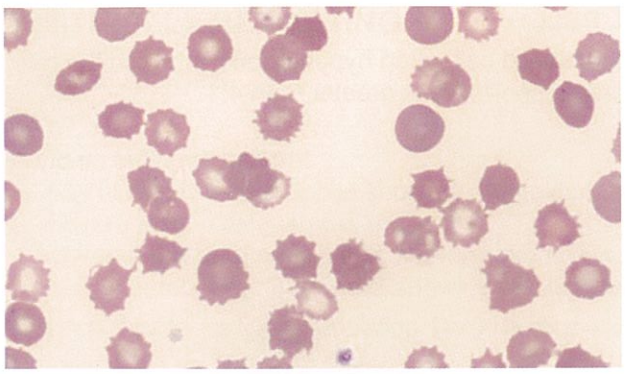
(a) Oxidation of haemoglobin by drugs or chemicals can result in oxidative intravascular haemolysis, Heinz body formation and red cell fragmentation. "Bite" cells are formed when Heinz bodies together with some red cell content are removed from red cells as they pass through the spleen.



(b) In cases of severe burns, tiny pieces of red cell membrane, spherocytes and microspherocytes may be seen

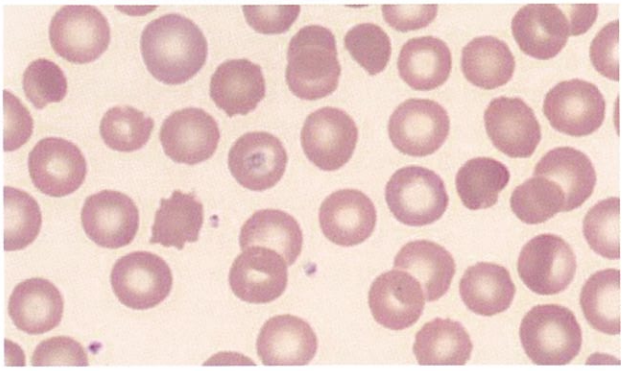


(c) Red cell fragmentation may result from endothelial damage or fibrin deposition in capillaries causing direct physical damage i.e. microangiopathic haemolytic anaemia



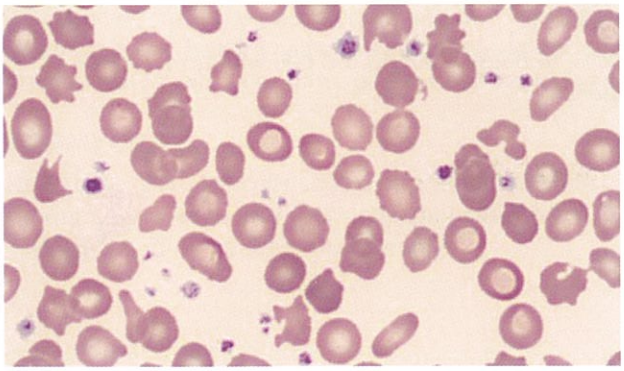
ECHINOCYTES

Red cells which have lost their disc shape and are covered with 10-30 short, evenly distributed spicules.



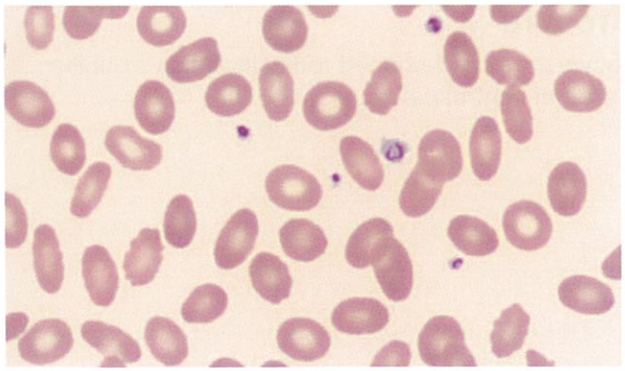
IRREGULARLY CONTRACTED CELL

A red cell lacking central pallor and irregular in shape.



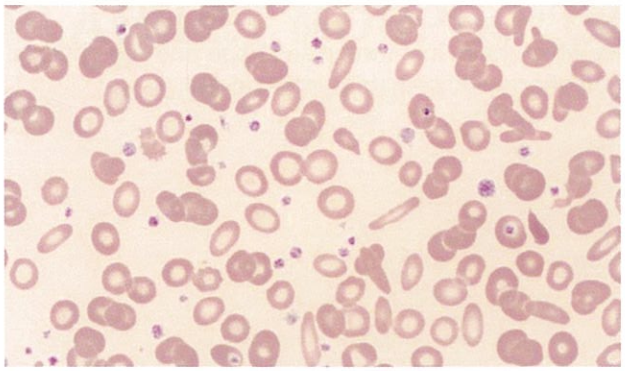
IRREGULAR SHAPED CELL – POIKILOCYTE

A red cell of abnormal shape that cannot be classified as any other cell shape. The presence of poikilocytes of certain specific shapes e.g. spherocytes or acanthocytes may have a particular clinical significance.



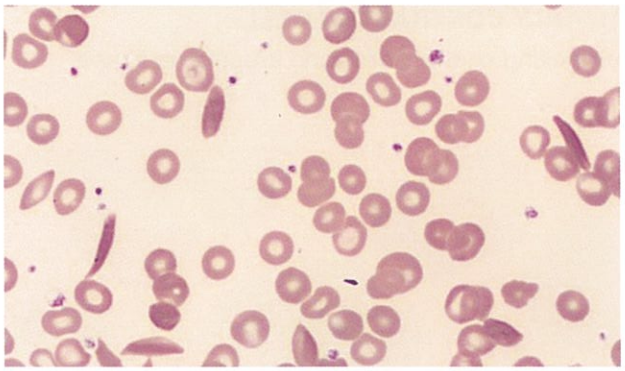
OVAL CELL / ELLIPTOCYTE

An oval or elliptical red cell with a ratio of long axis to short axis between 1.5:1 and 4:1.



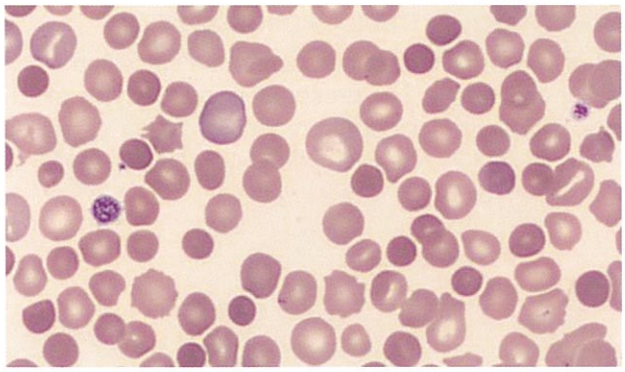
PENCIL CELL

An elongated red cell, often hypochromic, in which the ratio of the long to short axis is greater than 4:1.



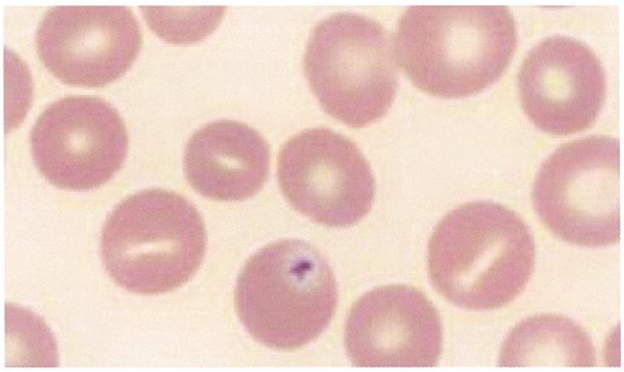
SICKLE CELL

A sickle shaped red cell with long spicules at each end. May be boat shaped with blunted ends.



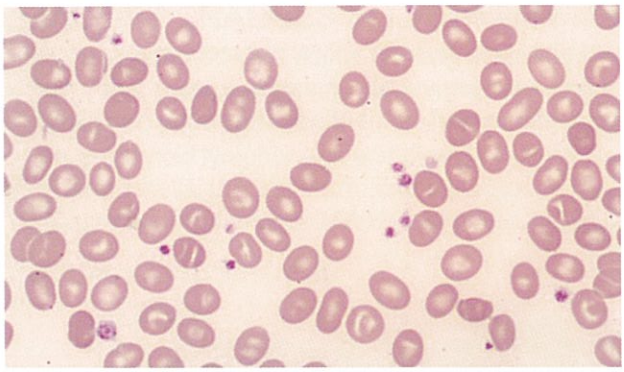
SPHEROCYTE

A spherical, densely staining red cell with an absence of central pallor.



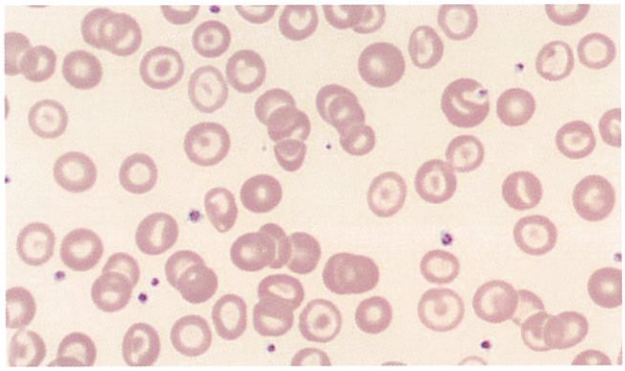
STOMATOCYTE

Stomatocytes are bowl-shaped red cells which exhibit a slit-like area of central pallor.



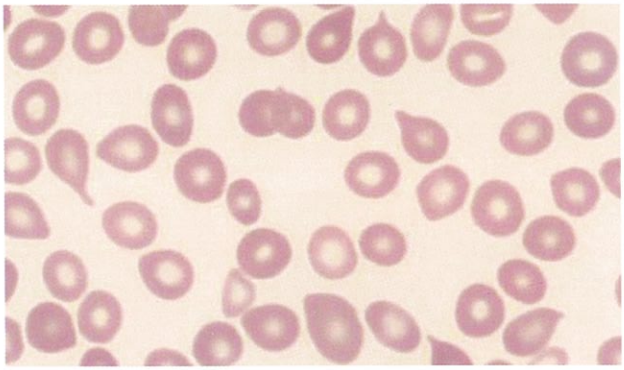
SOUTH EAST ASIAN STOMATO-OVALOCYTES

Red cells are round or oval and include stomatocytes. There is a small population of macro-ovalocytes, many of which are stomatocytic. Stomas may be longitudinal, transverse, V or Y shaped or there may be two stomas per cell.



TARGET CELL

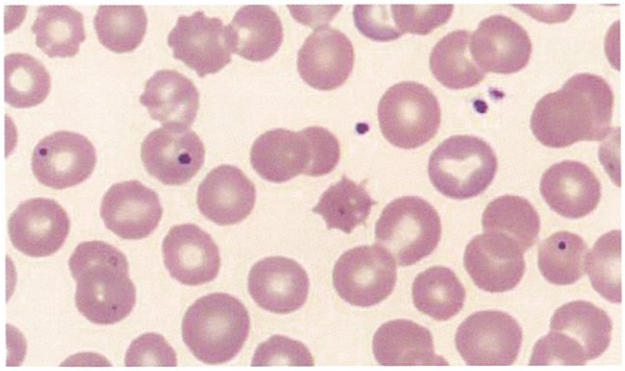
A red cell which has a central area of haemoglobin surrounded by a non haemoglobinised area with a rim of haemoglobin at the periphery of the cell. Target cells can be small or large.



TEAR DROP CELL

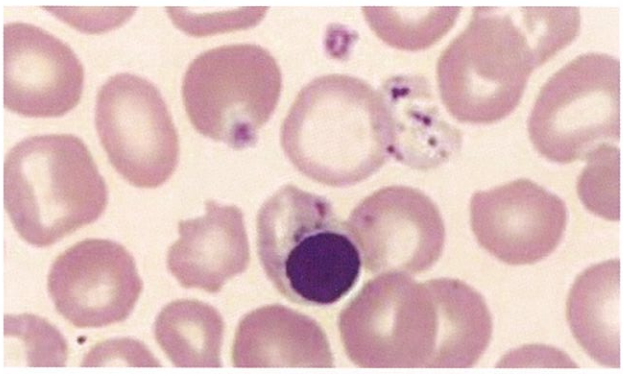
A red cell with a single elongated or pointed extremity.

INCLUSIONS



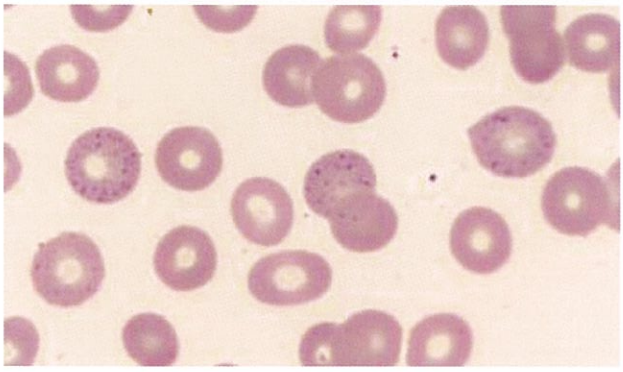
HOWELL JOLLY BODY

A fragment of nuclear material – a round, densely staining, red-violet inclusion about 1 um in diameter. They usually occur singly but occasionally more than one may be present in a red cell.



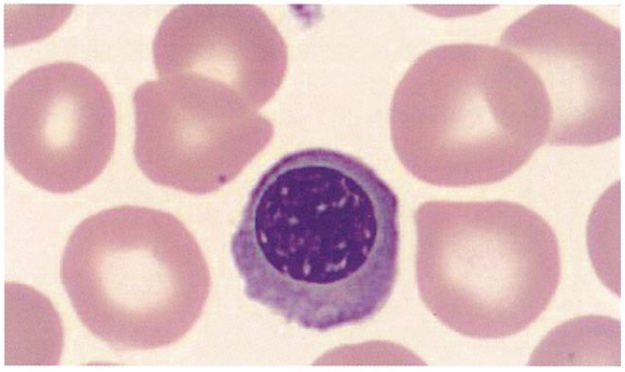
PAPPENHEIMER BODY

A stained blue-black granule which may be present in the red cell singly or more usually in small clusters. They may vary in size, shape and distribution. They stain positively for iron.



STIPPLED CELL

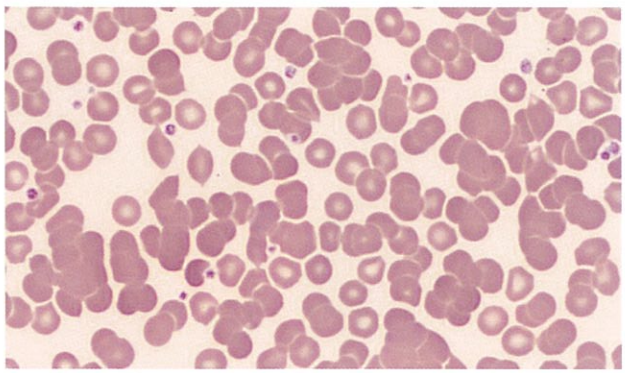
A mature red cell with basophilic inclusions which may vary in size and shape and are usually distributed uniformly throughout the cell. Stippling can disappear if the blood is exposed to EDTA for more than 6 hours.



NUCLEATED RED CELL

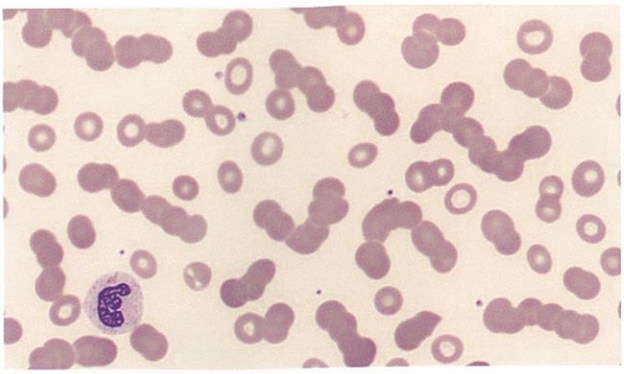
A red cell approximately 8-10 um in diameter which has retained its nucleus. The nucleus is round and stains violet-black. The cytoplasmic staining varies from blue to red-orange depending on the maturity of the cell.

DISTRIBUTION



AGGLUTINATION

Irregular clumps of red cells.

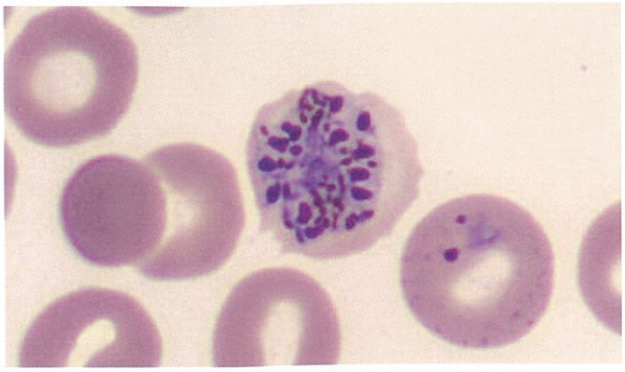


ROULEAUX

Red cells stacked up like a pile of coins.

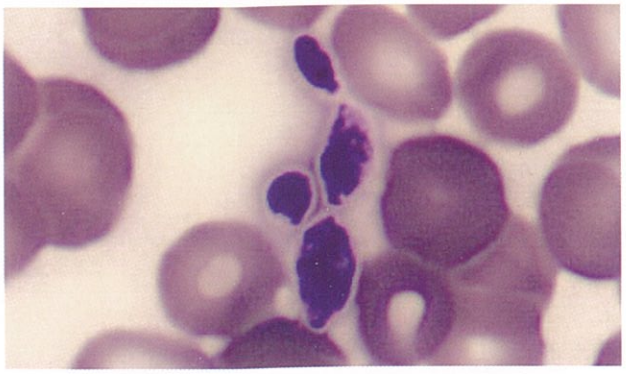
MICRO-ORGANISMS IN RED CELLS AND WHITE CELLS

Micro-organisms may be seen free between or within red cells in patients with bacterial, fungal or parasitic infections.



MALARIAL PARASITES

Trophozoites, schizonts and gametocytes can be detected in Romanowsky stained blood films.



FUNGAL SEPSIS

INTRACELLULAR BACTERIA

Neutrophils and monocytes may contain inclusions that represent phagocytosed material e.g. intracellular organisms (bacteria, fungi, parasites) or cryoglobulin.

STANDARDISED REPORTING ON VARIATIONS FROM NORMAL

RED CELL VARIATION	ADULTS AND CHILDREN > THAN 2 YEARS		CORD BLOOD (FULL TERM)	
	Increased Numbers %	Marked Increase / Numerous %	Increased Numbers %	Marked Increase / Numerous %
Hypochromic cells	2	20	0.5	5
Macrocytes	2	20		
Microcytes	2	20	0.5	5
Oval cells	2	20	0.5	5
Echinocytes	1	10		
Oval Macrocytes	1	10	0.5	5
Pencil cells	0.5	5	0.5	5
Acanthocytes	0.5	5	1	10
Stomatocytes	0.5	5	1	10
Target cells	0.5	5	1	10
Irregular shaped cells	0.5	5	5	20
Polychromatic cells	0.5	2.5	5	20
Tear drop cells	0.2	2.5	1	10
Spherocytes	0.2	2.5	5	10
Cell fragments	0.1	2.5	2	10
Stippled cells	0.2	2.5	0.2	5
Blister cells	0.0	2.5	0.0	5
Sickle cells	0.0	2.5	0.0	5
Howell Jolly bodies	0.0	2.5	0.2	5
Pappenheimer bodies	0.0	2.5	0.2	5

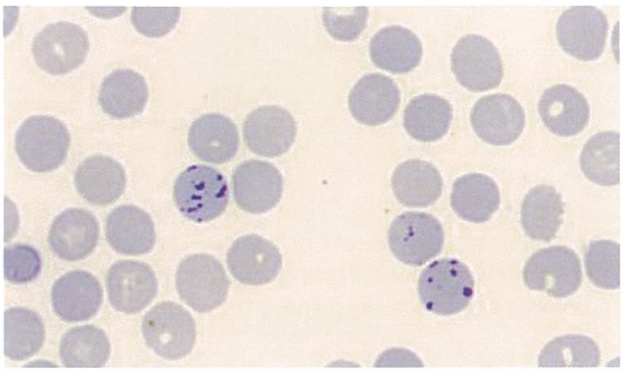
Count the number of red cells per high power field (HPF) e.g. 100x objective with a 10x eyepiece. As a guide line, an average HPF in a normal blood film will contain about 200 cells. An anaemic blood film however, will have closer to 100 cells.

The percentages quoted above may be interpreted as follows:

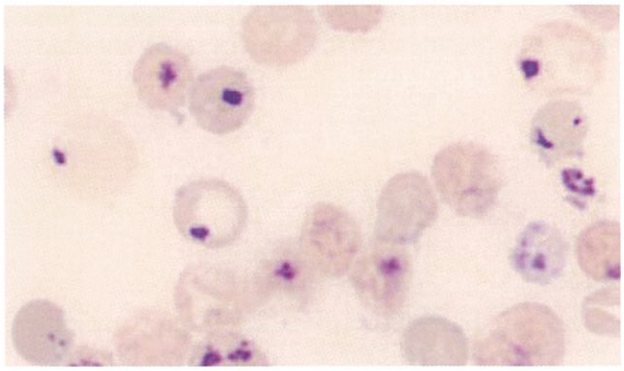
20.0% = 1 abnormal cell in five
10.0% = 1 abnormal cell in ten
5.0% = 1 abnormal cell in twenty
2.5% = 1 abnormal cell in forty
2.0% = 1 abnormal cell in fifty
1.0% = 1 abnormal cell per field of 100 cells
1.0% = 2 abnormal cells per field of 200 cells
0.5% = 1 abnormal cell per 2 fields of 100 cells
0.5% = 1 abnormal cell per 1 field of 200 cells
0.2% = 1 abnormal cell per 5 fields of 100 cells
0.2% = 2 abnormal cells per 5 fields of 200 cells

Nucleated red cells: When the frequency exceeds 1% of the total nucleated cells, they should be reported as concentration per litre. Many cell counters now enumerate the NRBC and will provide a very accurate count as well as making adjustments to the white blood cell count.

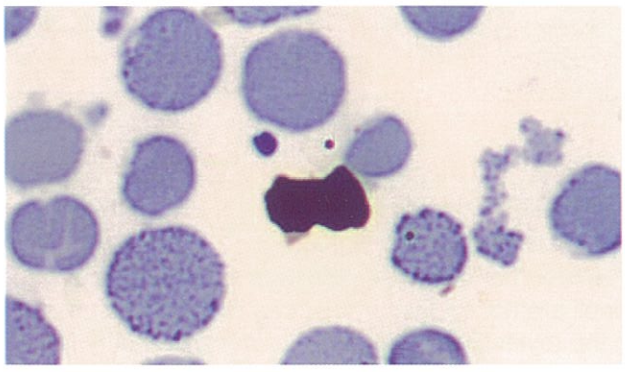
OTHER HAEMATOLOGY STAINS ASSOCIATED WITH RED CELLS



RETICULOCYTE
A supravitally stained red cell which contains two or more discrete blue granules, clumps of granules or a network (reticulum) of granules with connecting filaments. The granules must be within the same focal plane as the periphery of the red cell. They should be away from the edge of the cell to avoid confusion with Heinz bodies which may also be seen in reticulocyte preparations. In Romanowsky stained blood films some of the reticulocytes appear as polychromatic cells. Many of the cell counters provide very accurate reticulocyte counts.



HEINZ BODIES
A supravitally stained preparation using methyl violet or Rhodanile blue. Heinz bodies appear as purple staining inclusions approximately 1-3 um in diameter. They may vary in shape, are usually close to the edge of the cell and more than one may be present in a cell. They are not seen in Romanowsky stained films.



HAEMOGLOBIN H BODIES
Blue-green round inclusions usually less than 1 um in diameter seen after incubation with brilliant cresyl blue. They resemble the surface of a golf ball. The multiple inclusions may vary in size and staining intensity and are usually distributed evenly throughout the red cell.

WHITE CELL MORPHOLOGY

THE MYELOID SERIES

INTRODUCTION

These are guidelines for each stage. The cells are gradually maturing and changing from the myeloblast to the mature granulocyte. With increasing maturity the cell diameter decreases and the nucleus of the neutrophil, basophil and eosinophil precursors become progressively more dense, smaller and multi-lobular. In the Romanowsky stained film the nucleus of the myeloid cell stains red-violet. Maturation of the cytoplasm is characterised by the development of red-violet primary granules. In the mature cells they are less obvious than the secondary or specific granules. The basophil granules stain dark violet with basic dyes (basophilic), the eosinophils stain red-orange with acidic dyes (eosinophilic) and the neutrophil granules stain pale red-violet with a mixture of these dyes (neutrophilic).

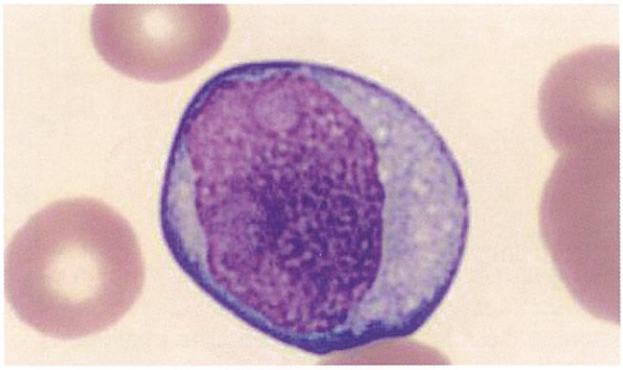
GRANULOCYTE GRANULES

Azurophilic granules
When referring to these granules the term azurophilic will not be used because of its ambiguity of definition and use. Instead, the colour of the granules will be described for each specific cell type.

Primary granules (sometimes called azurophilic)
Appear at the promyelocyte stage.

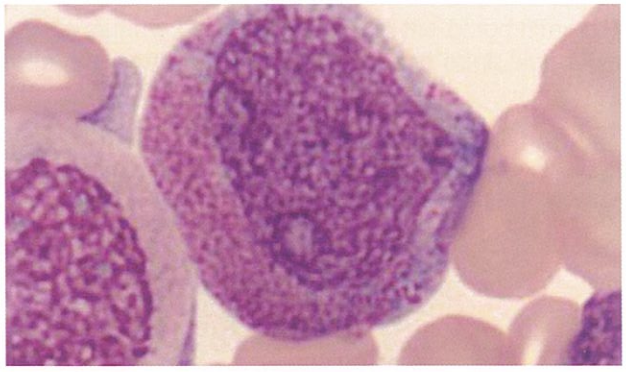
Secondary granules / Specific granules
Appear at the myelocyte stage and predominate in the mature granulocyte.

MYELOID MATURATION (normal)



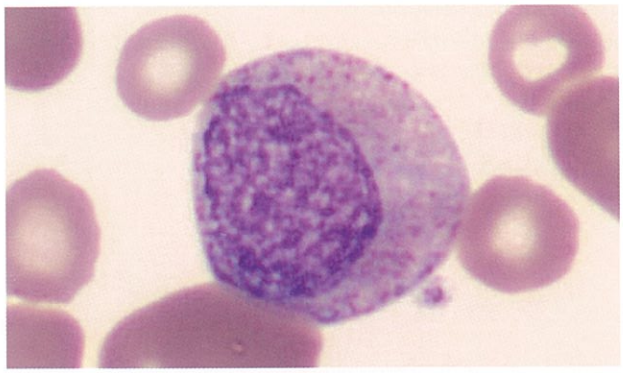
MYELOBLAST

Has a diameter of 15-20 um. The relatively large nucleus is round to oval, with no nuclear peripheral tags or buds. The nucleus has a diffuse chromatin pattern and usually one or more distinct nucleoli. The cytoplasm is scanty and blue, becoming darker at the cell edge. Granules are not usually visible.



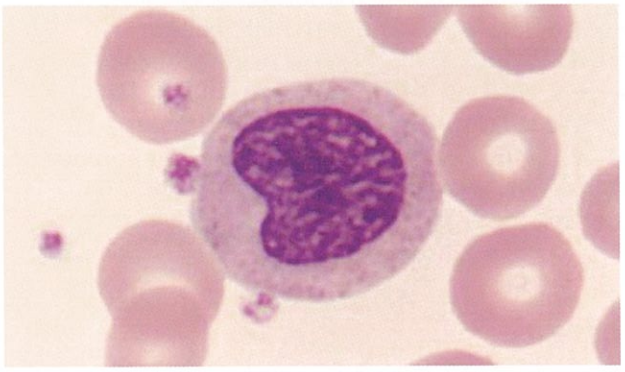
PROMYELOCYTE

Has a diameter of 15-20 um but may be larger. The nucleus is round or oval, the chromatin is coarser and the nucleoli are not so numerous or as well defined as those in the myeloblast. They have more cytoplasm than a myeloblast and consequently a lower nuclear : cytoplasmic ratio. A pale area equating to the golgi zone can be found adjacent to the nucleus. There are a variable number of blue-violet and red (primary) granules. They may appear over the nucleus and increase in number as the promyelocyte matures.



MYELOCYTE

The myelocyte is the same size as a promyelocyte or smaller, approximately 10-18 um in diameter. The nucleus is usually round, oval or slightly indented and may be eccentrically placed. The chromatin shows a moderate degree of coarse clumping. Nucleoli are not usually apparent. The myelocyte has a moderate amount of blue-pink cytoplasm which contains numerous red-violet granules that are scattered throughout and may appear over the nucleus. As the myelocyte matures the secondary granules develop definite neutrophilic, eosinophilic or basophilic characteristics.

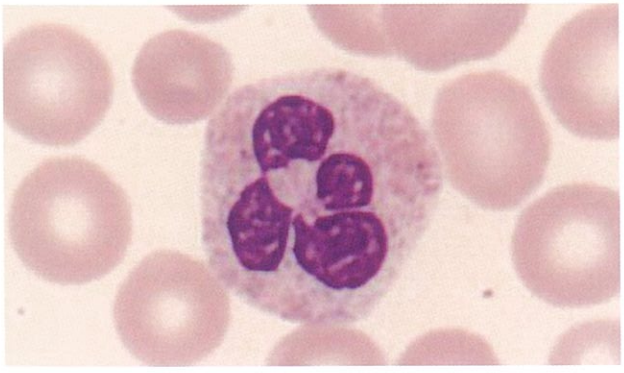


METAMYELOCYTE

The metamyelocyte is smaller than the myelocyte, approximately 10-18 um in diameter. The nucleus is usually indented or kidney shaped. Chromatin strands are coarse but not as deeply stained as in the more mature cells. Nucleoli are not observed.There is a moderate amount of cytoplasm which may occasionally be blue-pink but is usually clearly pink and contains granules that are smaller, stain less deeply and are clearly differentiated as neutrophilic, eosinophilic or basophilic (secondary) granules.

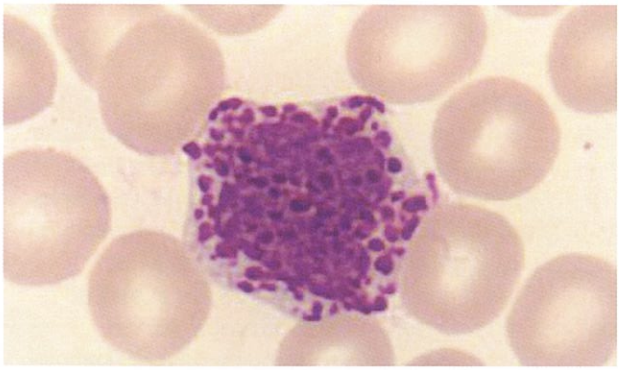
BAND NEUTROPHIL

The band neutrophil is 10-14 um in diameter. The nucleus is nonsegmented or has rudimentary lobes connected by a thick band rather than a thread. At its thinnest part the band should not be less than 1/3 the width of the lobes. Cytoplasm is abundant, pink and contains many small violet-pink neutrophilic granules distributed evenly throughout the cell. Many laboratories do not report band neutrophils on adult patients and this is a well recognised and acceptable practice. Appropriate comments may be made if increased numbers are seen in adult blood films.



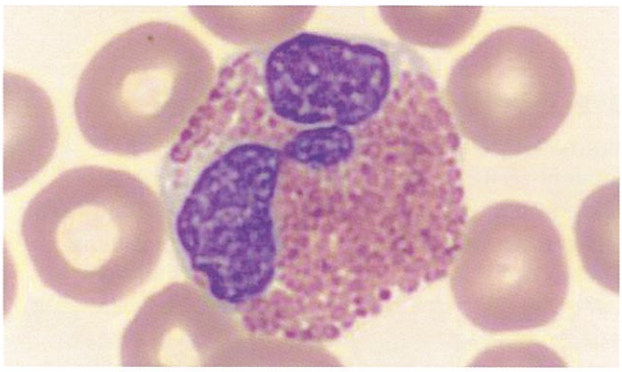
SEGMENTED NEUTROPHIL

A granulocyte that is 10-14 um in diameter.
The nucleus is lobulated with 2-5 lobes connected by a thin thread of chromatin. The chromatin is coarse, stains violet and is arranged in clumps. Small nuclear appendages may be seen. There is abundant pink cytoplasm with many small neutrophilic granules distributed evenly throughout the cell.



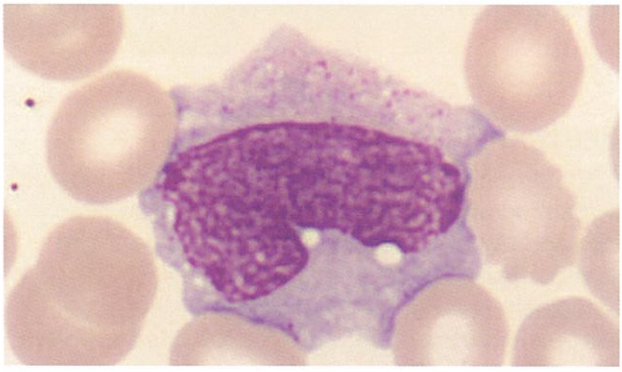
BASOPHIL

The diameter of the basophil is 10-16 um. The nucleus is segmented but often obscured by the purple-black secondary basophilic granules. The cytoplasm is pale blue and abundant. The basophilic granules may vary in number, size and shape. These granules are water soluble and may dissolve on staining and so clear areas in the cytoplasm may be artificially created.



EOSINOPHIL

The diameter of the eosinophil is 12-17 um. The nucleus usually has only 2 lobes. The chromatin pattern is the same as for the neutrophil i.e. it is violet staining and coarsely clumped. Cytoplasm is abundant. The characteristic feature of these cells is the presence of many refractile, eosinophilic (orange) secondary granules in the cytoplasm. They are larger than those in the neutrophil and more uniform in size.

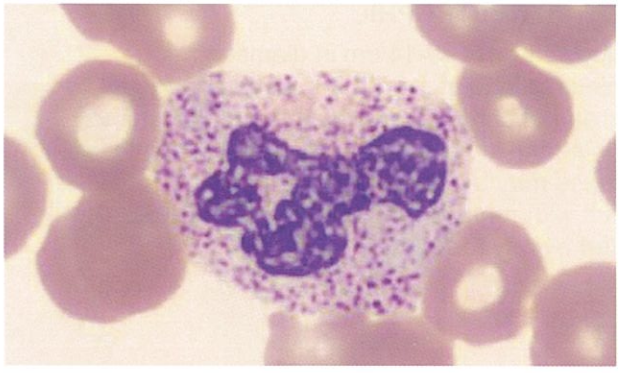


MONOCYTE

This is the largest cell in the peripheral blood, variable in size but usually 15-22 um in diameter. The nucleus may be round, kidney shaped, oval or lobulated and frequently appears to be folded. The chromatin is arranged in fine strands with sharply defined margins. The cytoplasm is light blue or grey and contains numerous fine dust like granules, giving a "ground glass" or opaque appearance. Some cells may contain a small number of larger-red violet granules. Vacuolation may be present. EDTA can cause an increase in vacuolation.

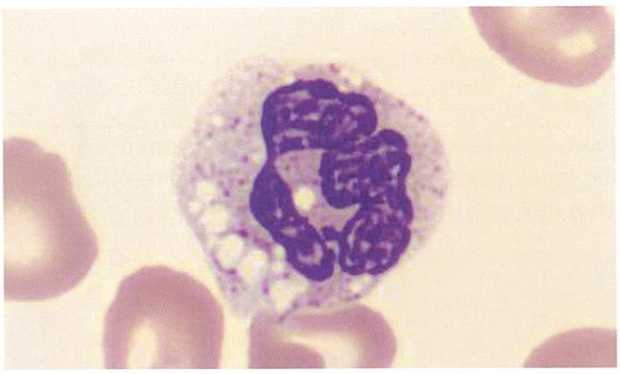
NEUTROPHIL TOXIC CHANGES

Toxic granulation, vacuolation and Dohle bodies are primarily found in infection, but can occur with drugs, tissue damage and other conditions.



Toxic granulation

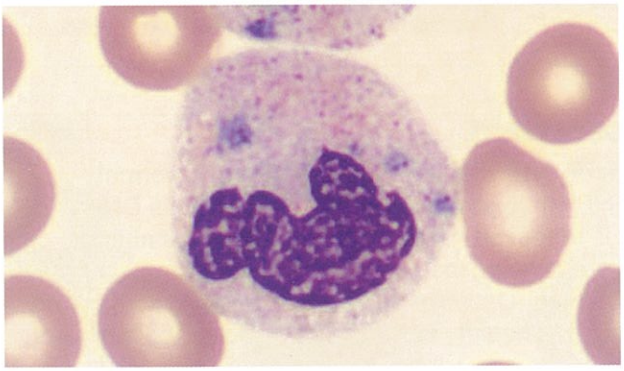
Coarse, dark violet staining, primary neutrophil cytoplasmic granules which occur as a response to infection and inflammation. Hypergranular neutrophils may also be seen in normal pregnancy, cytokine therapy with G-CSF and GM-CSF and in the presence of tissue damage.



Vacuolation

Neutrophil cytoplasmic vacuolation in infection is due to granule fusion with a phagocytic vacuole and release of lysosomal contents to kill bacteria. This vacuolation may appear as "pin hole" vacuolation – small, discrete vacuoles, but the vacuoles may be larger.

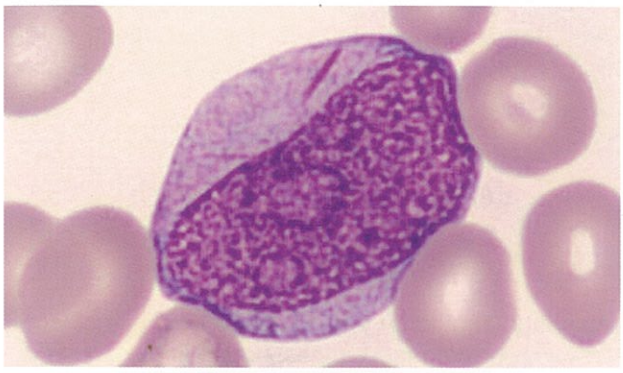
Toxic vacuolation should be distinguished from cytoplasmic vacuolation due to prolonged exposure to EDTA anticoagulant, a storage artefact.



Dohle bodies

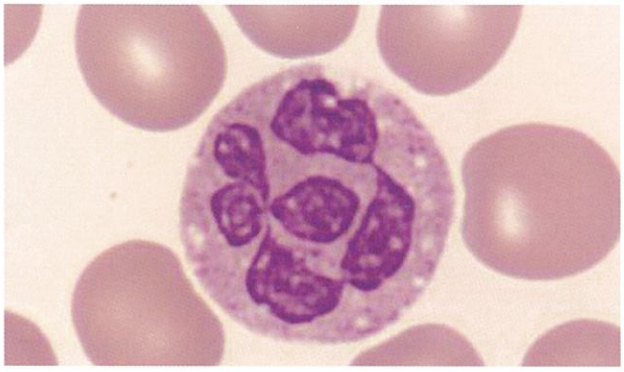
Pale light-blue or grey-blue, single or multiple, cytoplasmic inclusions found near the periphery of the neutrophil. Dohle bodies are also found in pregnancy, burns, cytokine therapy with G-CSF and GM-CSF and some haematological malignancies.

ABNORMAL MYELOID CHANGES



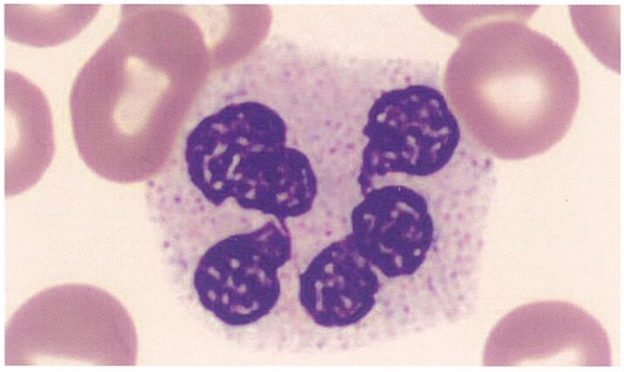
AUER ROD

A sharply defined red rod seen in the cytoplasm of some leukaemic myeloblasts or promyelocytes. There may be several in a cell and may be arranged in bundles (faggots).



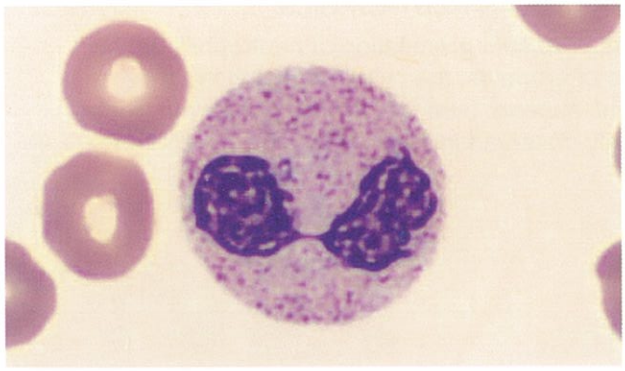
HYPERSEGMENTATION

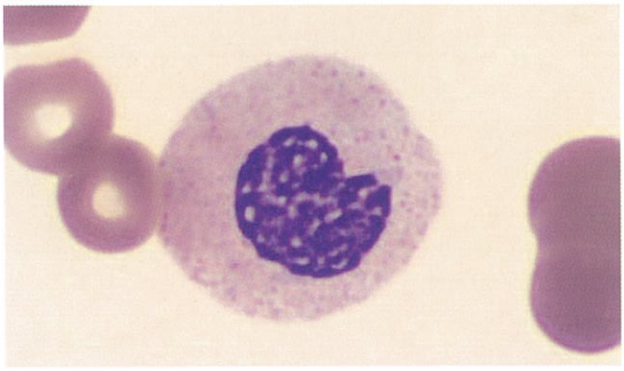
This is an increase in the number of distinct lobes of the mature neutrophil.

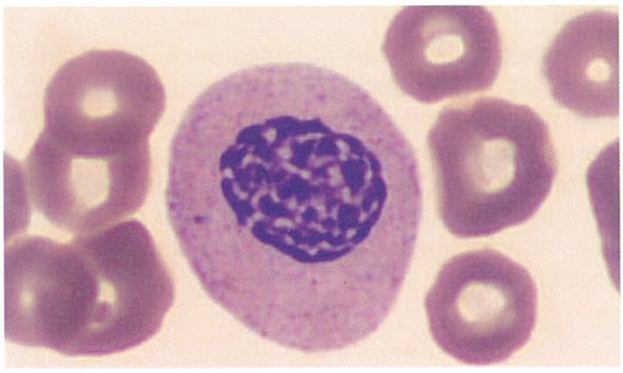


MACROPOLYCYTE

A macropolycyte is about twice the size of a normal neutrophil (15-25 um rather than 12-15 um). Its DNA content is tetraploid rather than diploid, the number of lobes present being increased proportionately. Some may be binucleated. Occasional macropolycytes may be seen in the blood of healthy individuals but increased numbers may be seen in some inherited conditions, G-CSF and cytotoxic drug administration, megaloblastic anaemia, chronic infection and myeloproliferative disorders.

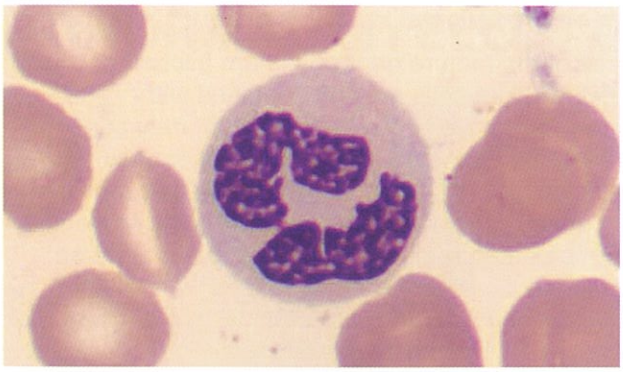






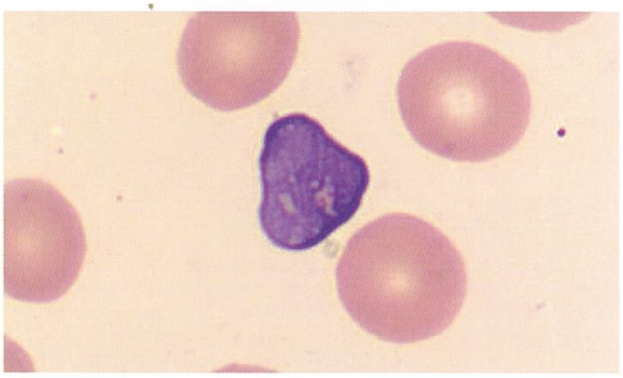
PELGER-HUET ANOMALY

The nuclei of the mature neutrophils are bilobed or round. These Pelger-Huet cells may be confused with myelocytes, metamyelocytes or bands but may be differentiated by their smaller nucleus, condensed nuclear chromatin characteristic of mature neutrophils and the colour of the cytoplasm which has the same pink appearance of mature neutrophils. It is recommended that these cells be reported as mature neutrophils but with a suitable interpretative comment. The Pelger-Huet anomaly may be congenital or acquired.



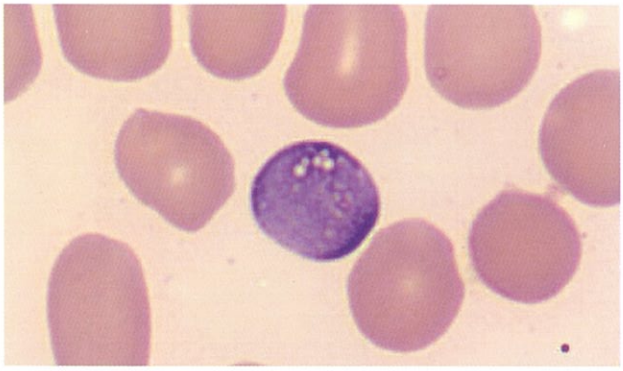
HYPOGRANULAR NEUTROPHILS

Reduced or absent granulation of neutrophils. In the absence of granules, the cytoplasm of the mature neutrophil appears blue-grey. Hypogranulation is most commonly observed in Myelodysplastic Syndromes.



WHITE CELL CYTOPLASMIC FRAGMENTS

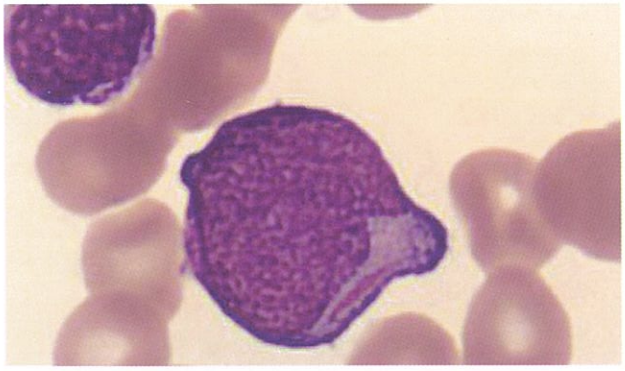
Fragments of cytoplasm derived from leukaemic cells. As these are often of a similar size to platelets, the platelet count may be falsely elevated.

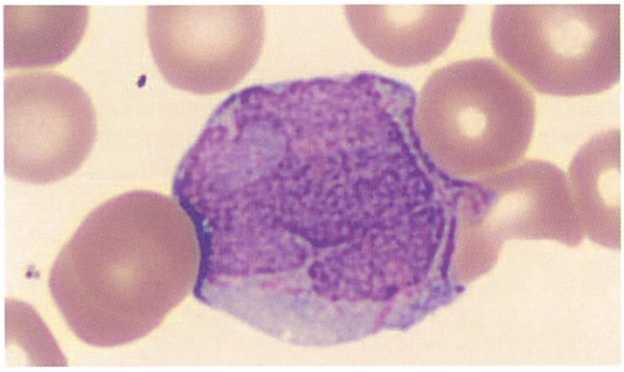


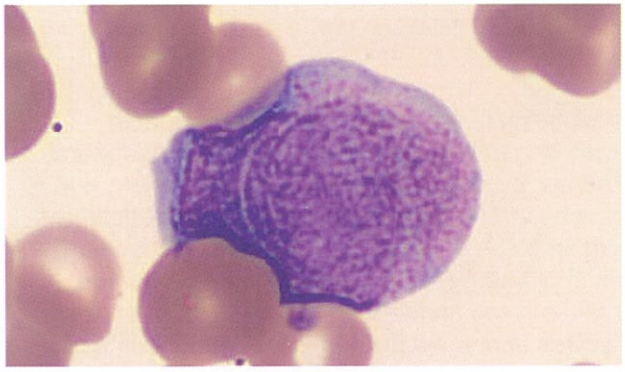
MYELOID LEUKAEMIC BLASTS

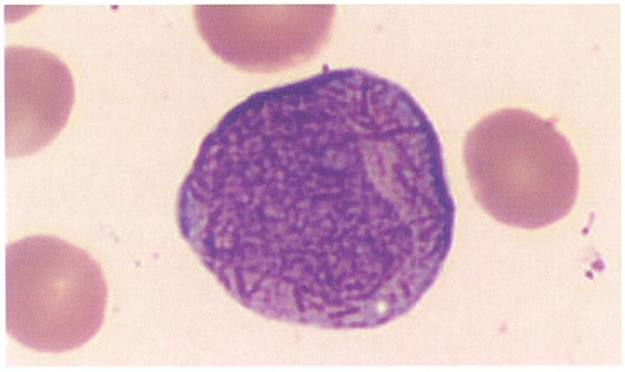
Myeloblasts

Leukaemic myeloid blasts vary in appearance. They can be large or small in size. Some may have a high nuclear: cytoplasmic ratio, uncondensed chromatin and usually one or more prominent nucleoli. Others may have a few red-purple granules and a lower nuclear:cytoplasmic ratio. Blast cells may contain Auer rods. Nuclear and cytoplasmic irregularities may be present e.g. nuclear folding and cytoplasmic blebbing.



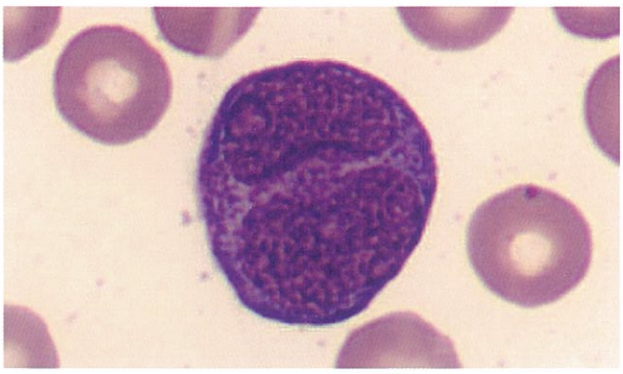






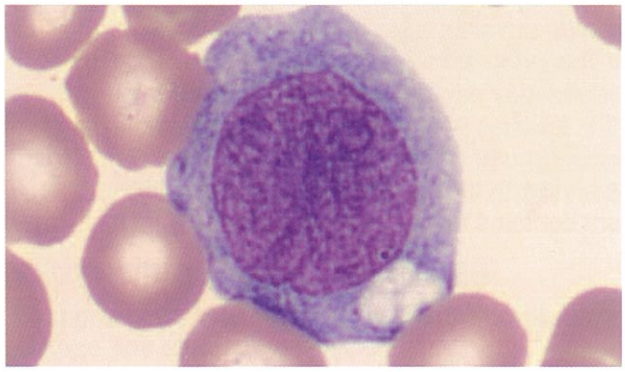
Abnormal promyelocytes in APML

The promyelocytes in the hypergranular variant of APML have nuclei that vary in size and shape and are often bilobed. The cytoplasm is packed with large pink-purple granules and may contain Auer rods. These may be grouped in bundles or "faggots" within the cytoplasm. In the hypogranular or microgranular variant, the nuclear shape is similar to the hypergranular form but the cytoplasm contains few or no granules.



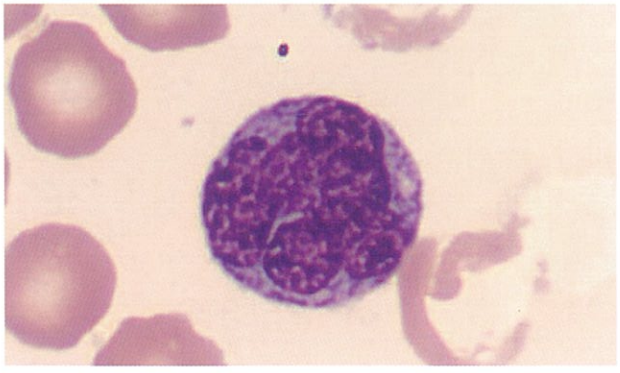
Monoblasts

Monoblasts are larger than myeloblasts. They have rounded nuclei with a fine chromatin pattern and one or two prominent nucleoli. The cytoplasm is basophilic and lacks granules. They are only seen in the peripheral blood in acute leukaemia with monocytic differentiation.



Promonocytes

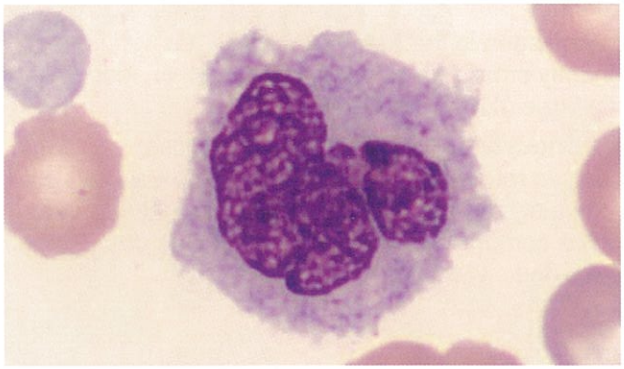
The promonocyte is considered to be equivalent in significance to a monoblast when seen in the peripheral blood. The nucleus has a diffuse chromatin pattern and is indented, lobulated or may have some other irregularity. A nucleolus may be present. The promonocyte is usually 12-18 um in diameter; the cytoplasm is blue-grey and may contain a small number of fine red violet granules. Promonocytes should be distinguished from the immature or abnormal monocytes that are present in reactive conditions and in chronic myeloid neoplasms.



ABNORMAL MONOCYTES

Reactive conditions

Monocytes produced under conditions of bone marrow stress or stimulation e.g. infections, G-CSF administration, show an increased nuclear:cytoplasmic ratio, a more delicate chromatin pattern, nucleoli and increased numbers of vacuoles. Granulation and cytoplasmic basophilia may also be increased.



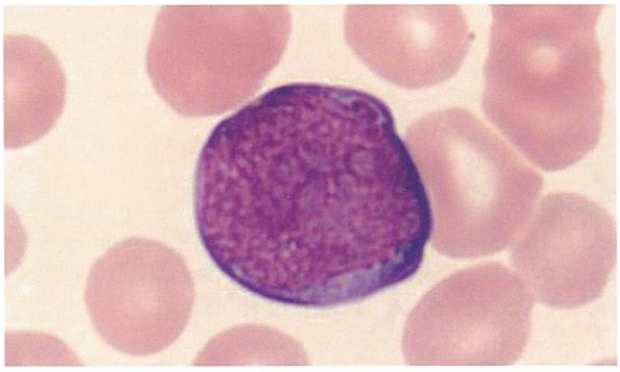
Chronic myeloid neoplasms

The monocytes in chronic myeloid neoplasms such as Chronic Myelomonocytic Leukaemia are generally mature, with unremarkable morphology, but can exhibit abnormal granulation, unusual nuclear lobation or chromatin pattern. These abnormal monocytes are immature, but, in comparison to promonocytes (and monoblasts), have denser chromatin, nuclear convolutions and folds, and a more greyish cytoplasm.

THE LYMPHOID SERIES

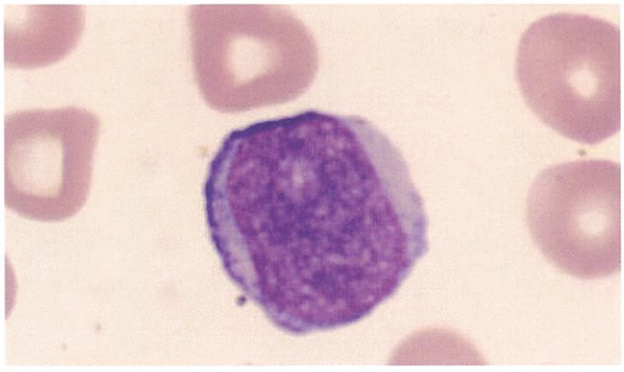
INTRODUCTION

All lymphocytes are derived from a lymphocyte stem cell present in the bone marrow. This lymphocytic stem cell matures through a number of intermediate stages to give rise to B-cell lymphocytes (which mature in the bone marrow), and to T-cell lymphocytes (which mature in the thymus). Because of the complexity of lymphocyte maturation, and the absence of distinguishable morphological characteristics, these intermediate stages will not be discussed in this document.



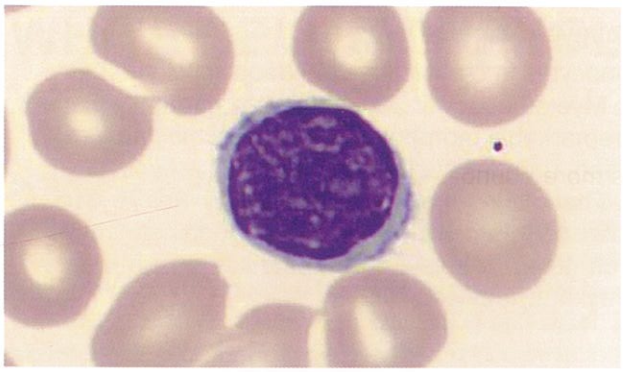
LYMPHOBLAST

The lymphoblast has a diameter of 8-20 um The nucleus is round or oval with fine granular chromatin that is slightly coarser than that found in the myeloblast. The nuclear membrane is well defined and one or more indistinct nucleoli may be present. The cytoplasm is scanty, usually clear blue or deeply basophilic and cytoplasmic granules are absent.



PROLYMPHOCYTE

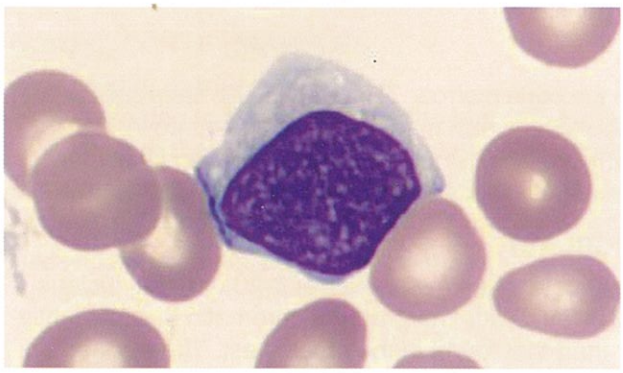
Prolymphocytes are not usually seen in the peripheral blood. The nucleus is round and contains a single prominent nucleolus. It has more cytoplasm than a lymphoblast and the chromatin is more condensed.



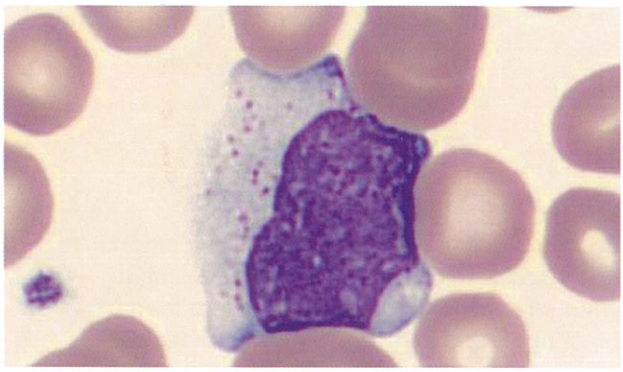
LYMPHOCYTE

Lymphocytes seen in the peripheral blood are predominantly small (10-12 um in diameter), or, less frequently large (12-16 um in diameter).

Small lymphocytes are usually round in outline. The nucleus is round or slightly indented with coarse densely staining chromatin. Cytoplasm is scanty. Small lymphocytes comprise 80-90% of lymphocytes seen in the peripheral blood.



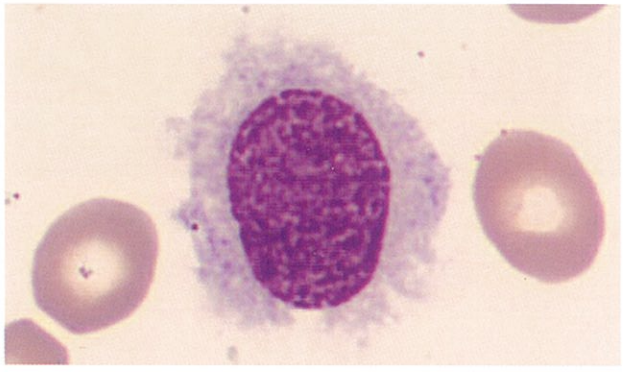
Large lymphocytes are usually irregular in outline. The nuclear chromatin is not as coarse as that seen in the small lymphocyte. Cytoplasm is abundant and tends to be light sky blue in colour.



Large granular lymphocytes are of the same appearance as the large lymphocyte, but the cytoplasm contains quite prominent red-violet granules. They may comprise 10-15% of all lymphocytes seen in the peripheral blood.

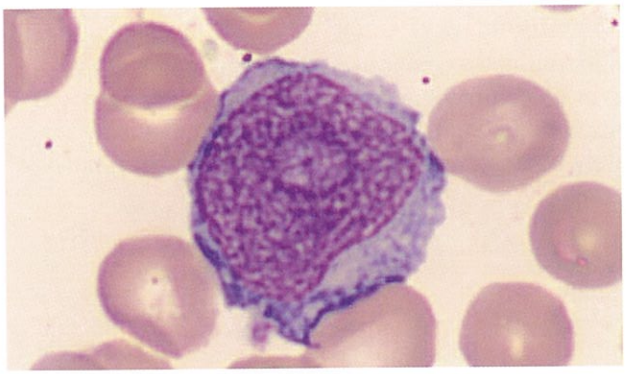
N.B. Lymphocytes predominate in the blood films of infants and children. These lymphocytes tend to be larger and more pleomorphic than those seen in adult blood films.

ABNORMAL LYMPHOID CELLS



HAIRY CELLS

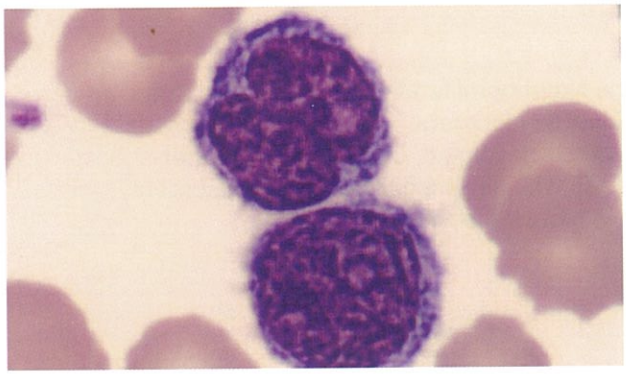
Hairy cell leukaemia is a chronic B cell lineage leukaemia with morphologically distinctive neoplastic cells. They have pale blue-grey cytoplasm with fine hair-like projections.



PROLYMPHOCYTES

Neoplastic B Prolymphocytes

Are larger than the lymphocytes seen in CLL and often show more variation in size. They are predominantly round with round nuclei and weakly basophilic cytoplasm, which is more abundant than CLL lymphocytes. Many have a large and prominent nucleolus. There is moderate chromatin condensation, which is enhanced around the nucleolus giving it a 'vesicular' appearance.



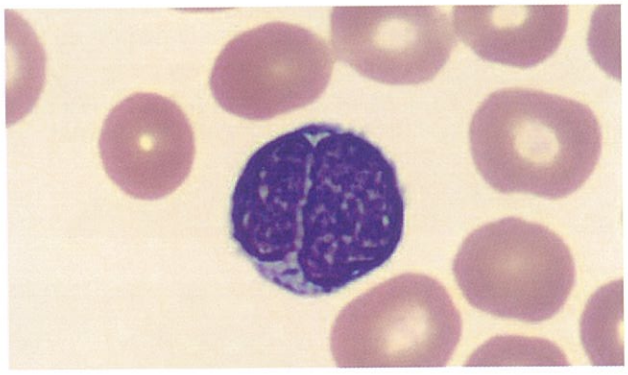
Neoplastic T prolymphocytes

Are smaller and more pleomorphic than B-lineage prolymphocytes. Nuclei are irregular or lobulated. Cytoplasm is often scanty and moderately basophilic. Cytoplasmic blebs may be present. Nucleoli are rarely as large or prominent as B-lineage prolymphocytes.

LYMPHOMA CELLS

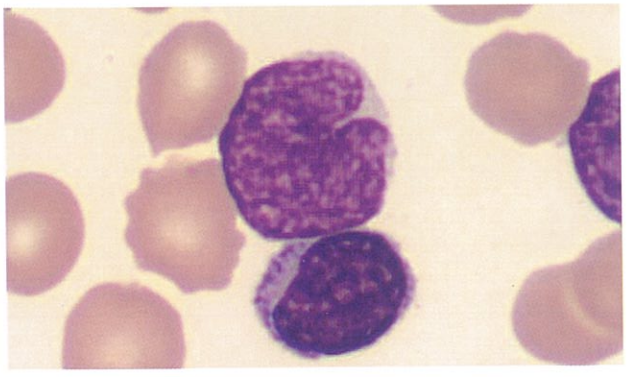
Lymphoma is a neoplasm of B, T or NK lymphocytes and is more often found in tissues other than bone marrow and peripheral blood. Lymphoma may have a leukaemic phase however, in which morphologically abnormal lymphoid cells appear in the peripheral blood. A comprehensive classification of lymphoma is beyond the scope of this document but some specific examples include:

B CELL LYMPHOPROLIFERATIVE DISORDERS



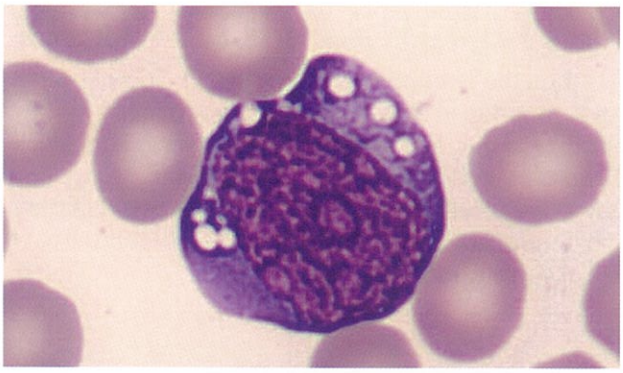
Follicular lymphoma

Lymphoma cells are often small with scanty, weakly basophilic cytoplasm. Some nuclei may show notches or deep narrow clefts. Sometimes the lymphoma cells are larger and more pleomorphic. They may have small but distinct nucleoli and the nuclei have clefts or notches.



Mantle cell lymphoma

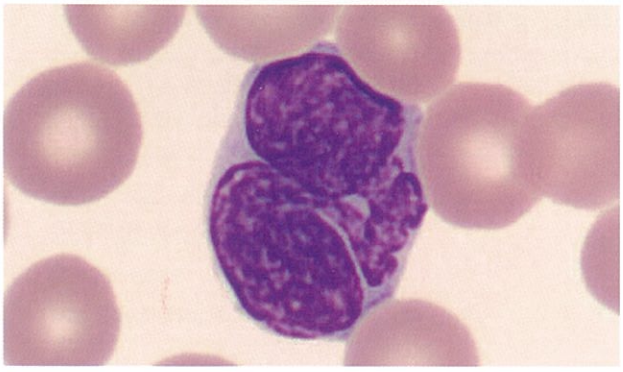
Lymphoma cells vary from small to medium in size. The cells are pleomorphic varying in size and nuclear – cytoplasmic ratio. Chromatin condensation is less than in CLL lymphocytes and some cells appear blastic. Some have cleft or irregular nuclei and a prominent nucleolus.



Burkitt lymphoma

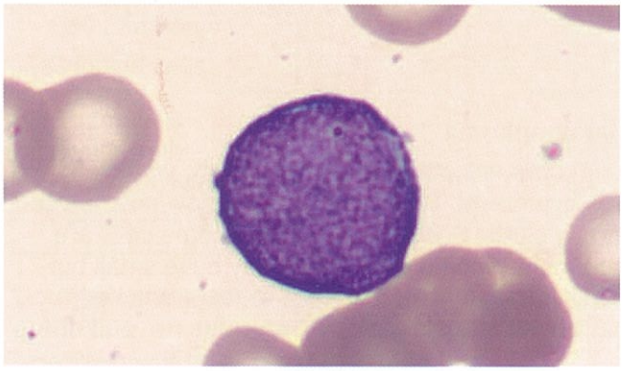
The lymphoma cells are large and the nucleus is round with one or more prominent nucleoli and a dense but finely stippled nuclear chromatin pattern. The cytoplasm is moderately abundant and deeply basophilic with prominent vacuolation.

T CELL LYMPHOPROLIFERATIVE DISORDERS

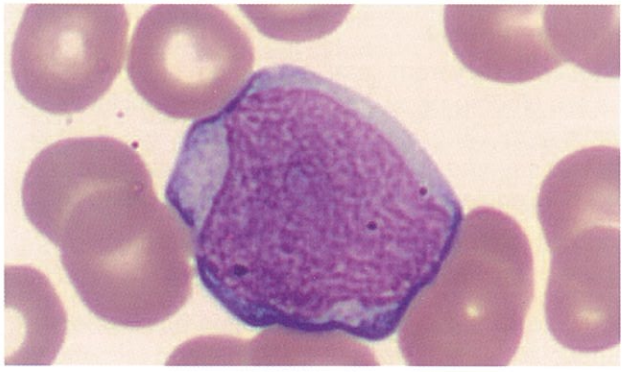


T-lineage lymphoproliferative disorders are less common than B-lineage disorders. The cells are pleomorphic and often have a convoluted, cerebriform or flower-shaped nucleus. As with all lymphoproliferative disorders, precise diagnosis requires immunophenotyping.

LYMPHOID LEUKAEMIC BLASTS



Lymphoblasts range from those with a high nuclear: cytoplasmic ratio, fine to clumped chromatin, inconspicuous nucleoli and scanty basophilic cytoplasm to those that are heterogeneous in cell size and have a nuclear chromatin pattern varying from finely dispersed to coarsely condensed. The nuclear outline may be irregular and nuclear clefting, indentation and folding are common. Nucleoli vary in size and number but are often indistinct.

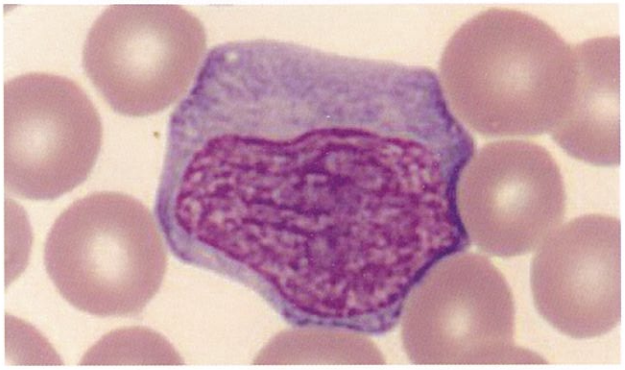


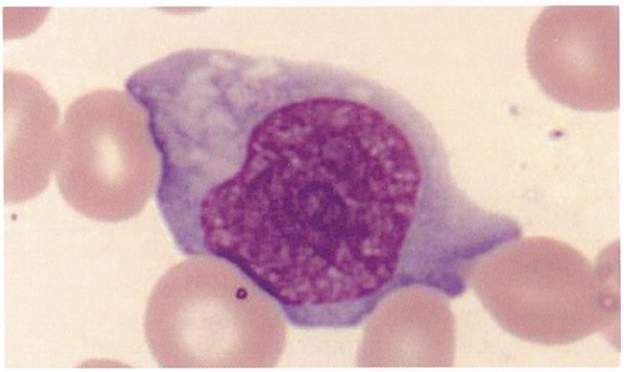
REACTIVE CHANGES IN LYMPHOCYTES

Lymphocytes can respond to viral infections and other immunological stimuli by an increase in number and cytological alterations:

- B lymphocytes can differentiate into plasma cells
- Intermediate stages are also seen and are designated plasmacytoid lymphocytes
- Plasmacytoid lymphocytes and plasma cells may contain abundant globulin inclusions composed of immunoglobulin
- B and T cells can transform into immunoblasts
- Cells showing less specific changes in lymphocyte morphology are termed reactive lymphocytes

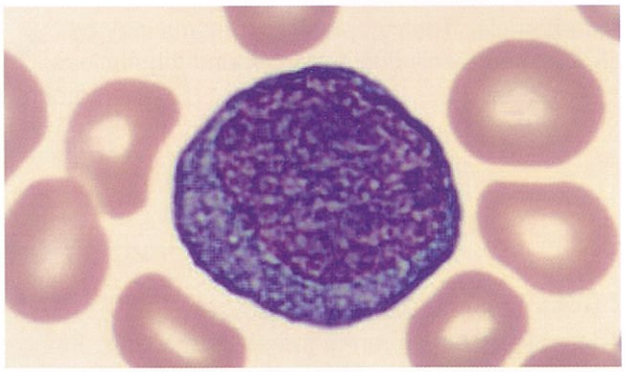
REACTIVE LYMPHOCYTE





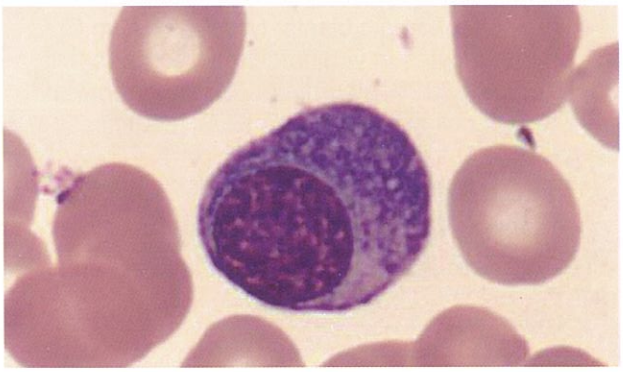
Abnormalities include increased cell size, immaturity of the nucleus including a visible nucleolus and lack of nuclear chromatin condensation, irregular nuclear outline or lobulation, cytoplasmic basophilia or vacuolation, irregular cell outline. The cytoplasm may be abundant and often appears foamy. In staining it ranges from blue-grey to light blue but it may be markedly basophilic especially at points of contact with adjacent cells.

PLASMACYTOID LYMPHOCYTE

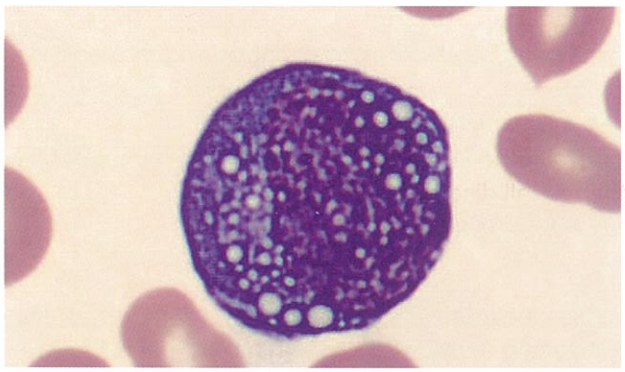


A B-lineage lymphocyte with characteristics intermediate between a mature lymphocyte and a plasma cell. The chromatin is not as condensed as a plasma cell and the nucleus may be slightly eccentric. There is moderate cytoplasmic basophilia.

PLASMA CELL

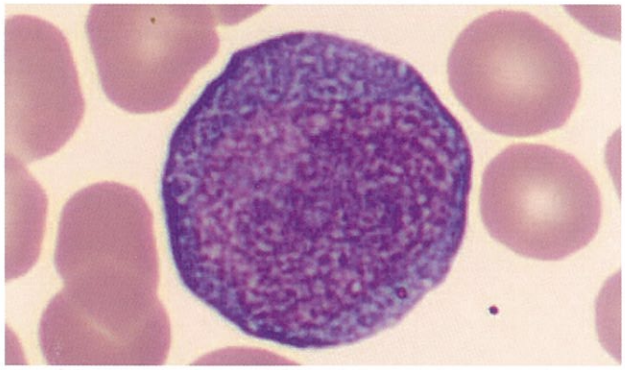


A plasma cell is larger than a normal small lymphocyte (9-25 um), has deeply basophilic cytoplasm, an eccentric round or oval nucleus, coarsely clumped chromatin and a pale golgi zone adjacent to the nucleus. In addition to reactive causes, plasma cells may also be seen in the peripheral blood in neoplastic disorders e.g. plasma cell myeloma, plasma cell leukaemia and related conditions.



MOTT CELL

A plasma cell or plasmacytoid lymphocyte with prominent cytoplasmic vacuoles (Russell bodies). These vacuoles represent dilated endoplasmic reticulum containing secreted immunoglobulin.

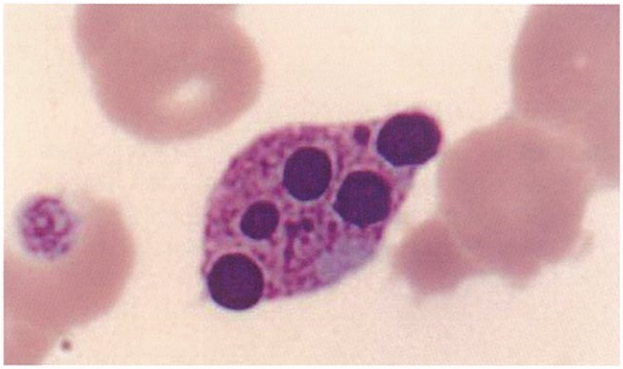


IMMUNOBLAST

Large cells with abundant basophilic cytoplasm and a central prominent nucleolus.

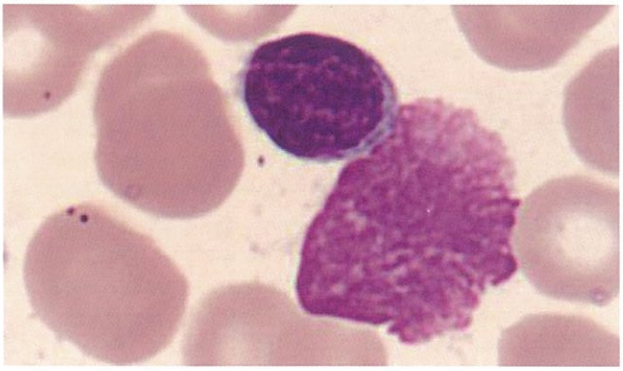
OTHER WHITE CELL CHANGES

Both pyknotic cells and smear cells may be found in degenerative situations e.g. aged blood or toxicity.



PYKNOTIC CELL

This dead cell can be of any white cell type. The structureless nucleus is homogenous, condensed and circular. There is no nuclear bridging present between lobes of segmented nuclei. The cytoplasmic contents may be aggregated and unevenly distributed around the nucleus.



SMEAR CELL

Smear cells result from shearing forces on the cells during the spreading of blood films. They are the disrupted nuclei of fragile cells e.g. leukaemic blasts, lymphocytes in CLL and reactive lymphocytes in viral infections. A repeat film made with one part of 22% albumin added to four parts of blood may prevent cell disruption and allow identification of the fragile cells.

WHITE CELL REPORTING

TOXIC CHANGES

Report as:

1. Toxic changes present:
   Any number of neutrophils showing one toxic feature, other than small discrete vacuolation
2. Severe toxic changes present:
   a) Any number of neutrophils showing more than one toxic feature
   b) Any number of neutrophils showing discrete vacuolation

The individual terms toxic granulation, Dohle bodies and toxic vacuolation may be used to further define the toxic changes.

HYPERSEGMENTATION

Neutrophil hypersegmentation is defined as any neutrophil having 6 or more lobes, more than 5% of neutrophils having 5 lobes and/or more than 20% having 4 lobes, when 100 neutrophils are examined. Neutrophil hypersegmentation, when seen, should be reported as present.

ABNORMAL COUNTS

Where appropriate, in addition to the reported absolute counts, an interpretative comment can be included when cell numbers are increased or decreased: e.g.

Causes of eosinophilia include parasitic infestations, allergy, drug hypersensitivity, skin disease, connective tissue disease and some cases of malignancy.

Causes of neutropenia include drug reactions, infection (especially viral), autoimmune disease, B12/folate deficiency and bone marrow disorders.

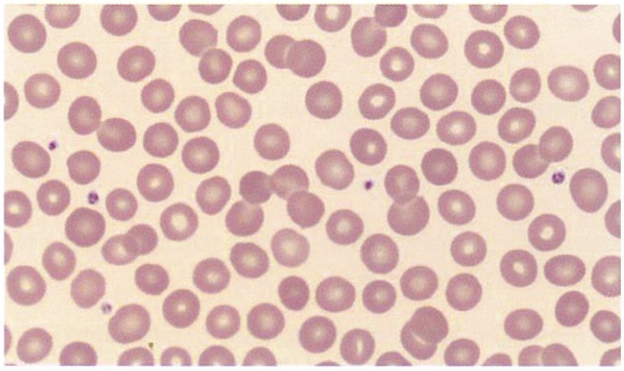
ABNORMAL LYMPHOID CELLS AND REACTIVE LYMPHOCYTES

The ICSH is recommending that **reactive lymphocyte** is used to describe lymphocytes with a benign aetiology and **abnormal lymphocyte** (with an accompanying description of the cells) is used to describe lymphocytes with a suspected malignant aetiology. Cells that can be identified as a particular neoplastic cell type e.g. hairy cells, lymphoma and Sezary cells (based on distinctive morphology and confirmed by cell markers) and plasma cells in plasma cell myeloma or other plasma cell dyscrasias can be included in the differential as that cell class.

SMEAR CELLS

Identifiable disrupted cells should be counted with the category to which they belong e.g. neutrophil, eosinophil or basophil. Smear cells, the nature of which is not clear, should be counted as a separate category and reported when they exceed 5% of nucleated cells present.

PLATELET MORPHOLOGY

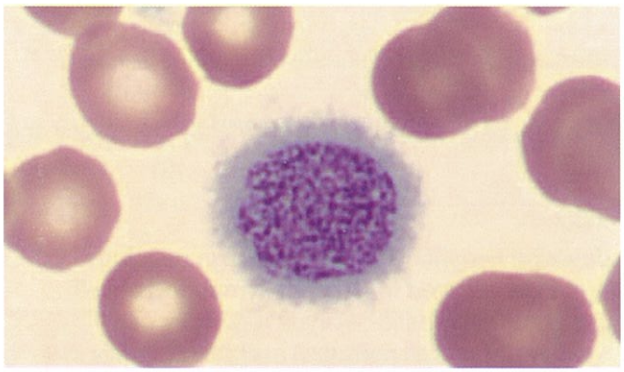


NORMAL PLATELET

A megakaryocyte cytoplasmic fragment, 2-3.5 um in diameter. Shape ranges from round to elongated cigar shaped forms. The clear blue cytoplasm contains red-violet granules which may be dispersed, form a crown around a vacuole or be tightly packed in the centre. Large platelets have a diameter greater than 4 um in diameter.

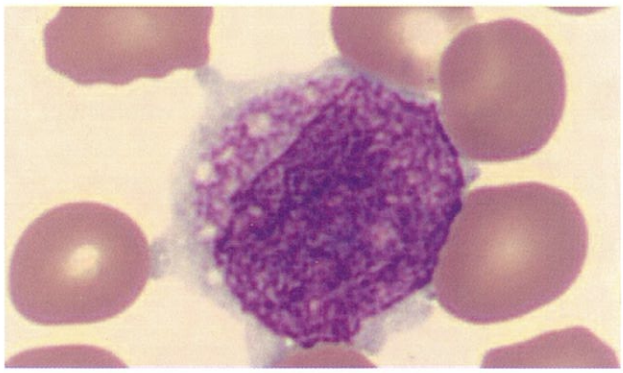
SMALL PLATELETS

Decreased platelet size is less common than increased size but it is a feature of Wiskott-Aldrich syndrome.



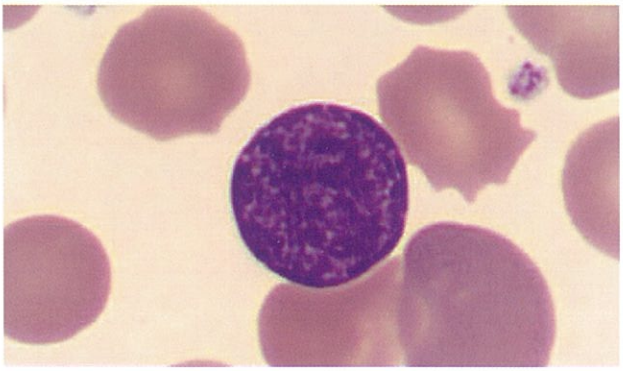
GIANT PLATELET

A platelet with a diameter similar to a normal red cell or small lymphocyte.



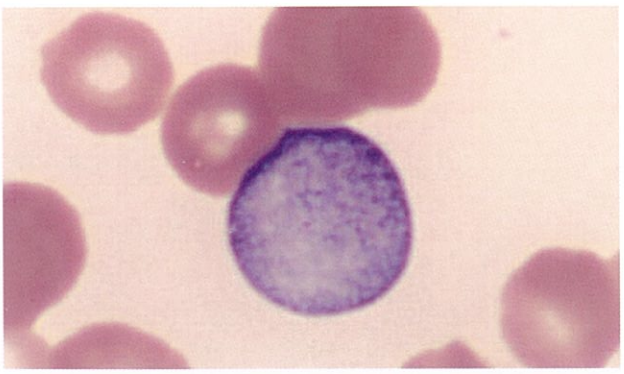
MICROMEGAKARYOCYTE

A small, diploid mononuclear cell no larger than 30 um in diameter. The cytoplasm is weakly basophilic and there may be cytoplasmic vacuolation and a few, or numerous, cytoplasmic granules. Cytoplasmic protrusions or 'blebs' may be present and sometimes platelets appear to be budding from the surface. The nucleus is round or slightly irregular with dense chromatin. Micromegakaryocytes may be seen in the blood of patients with haematological neoplasms e.g. idiopathic myelofibrosis and CML.



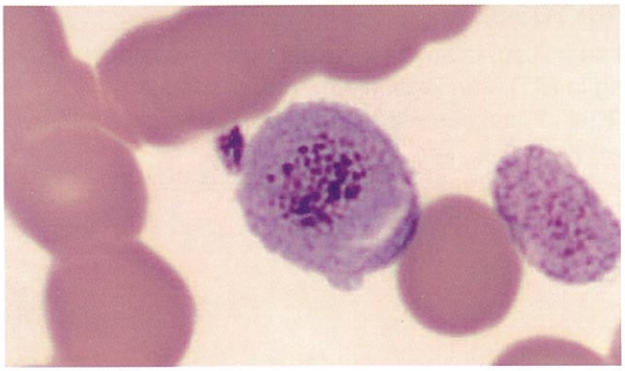
MEGAKARYOCYTE NUCLEAR FRAGMENT

Medium to large bare megakaryocyte nuclei that stain dark purple.



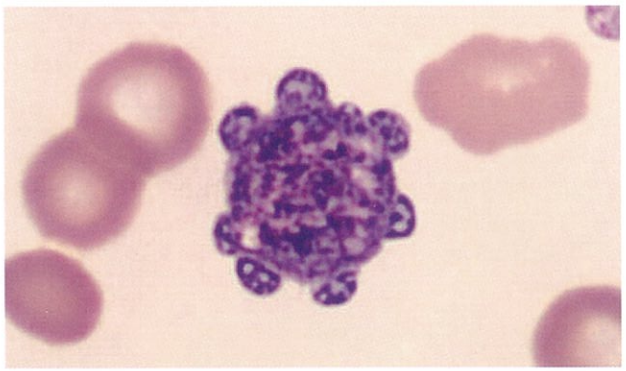
HYPOGRANULAR PLATELET

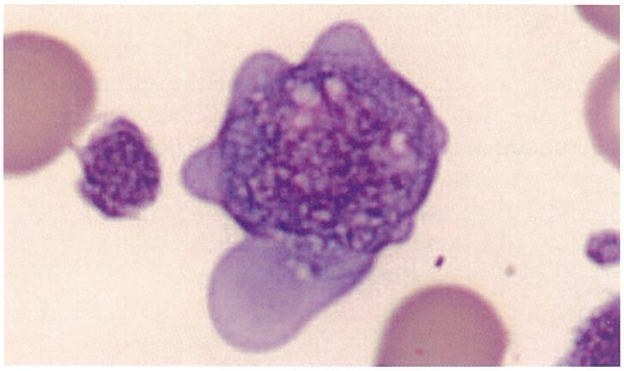
A pale blue-grey staining platelet that lacks the normal red-violet granules. This may be an artefactual change because the specimen has partly clotted or because platelets have aggregated and have discharged some or all of their granules. Alternatively, it may occur as a rare congenital abnormality (grey platelet syndrome) or be a feature of a bone marrow disease such as a myeloproliferative or myelodysplastic disorder.



BIZARRE PLATELET

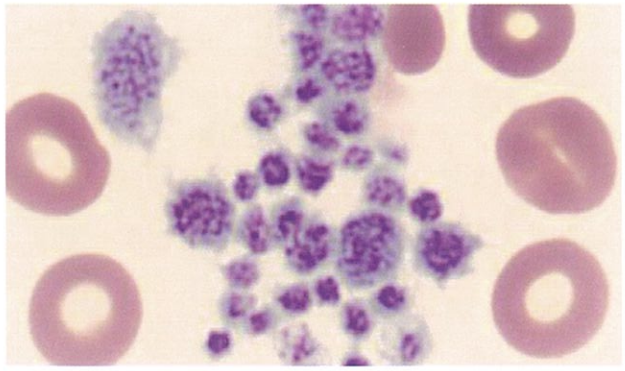
A platelet which shows one or more of the following features: irregular size and shape, pseudopodia or a frilly outline, vacuolation, granules may be absent, scattered or clumped, giving the impression of a nucleus.





PLATELET SATELLITISM AND PLATELET PHAGOCYTOSIS

Platelet satellitism is an in-vitro phenomenon usually occurring in EDTA-anticoagulated blood. Platelets adhere to and encircle neutrophils and some may be phagocytosed.



PLATELET CLUMPING

This is usually an EDTA-antibody mediated artefact. Platelet aggregates occur when blood is collected into EDTA but are absent in-vivo. Collection into a citrate tube often corrects this problem. Because of the different blood to anticoagulant ratio, multiply the citrate tube platelet result by 1.1 to give the correct platelet count.

PLATELET REPORTING

PLATELET COUNT

When the platelet count is abnormal, comment as increased or decreased in addition to the reported platelet count.

PLATELET SIZE

Platelet size is of diagnostic significance particularly when considered in relation to the platelet count.

In a normal person, usually less than 5% of the platelets appear large.

A comment about the presence of small, large and / or giant platelets can be made with an additional interpretative film comment if appropriate.

THROMBOCYTOPENIA AND PLATELET SIZE:

Thrombocytopenia and small or normal sized platelets suggest that the low platelet count is due to bone marrow production failure.

Thrombocytopenia and large or giant platelets suggest that the low platelet count is more likely to be caused by peripheral consumption or destruction of platelets from the marrow. The bone marrow responds by increasing platelet production and early release of the platelets. If the platelet count is low, the presence of giant platelets is clinically significant and should be reported – there may be very few platelets but most of them may be giant.

THROMBOCYTOSIS AND PLATELET SIZE:

Thrombocytosis and normal sized platelets suggest a reactive process e.g. due to infection or inflammation. Thrombocytosis with large or giant platelets is more suggestive of a myeloproliferative disorder although it should be noted that patients with infiltrated bone marrows or myeloproliferative syndromes may have large or giant platelets regardless of the platelet count. In these cases, platelet morphology may also be abnormal with greater than 10% hypogranular platelets. Other peripheral blood features such as the presence of tear drop cells, basophilia and megakaryocyte nuclei may also suggest a myeloproliferative disorder or bone marrow infiltration rather than a reactive process.

APPENDIX A

The following list of synonyms for red cell nomenclature was prepared from the reference texts and cell atlases. Students may encounter these terms in their reading and although this list is not definitive, it will enable them in most cases to cross reference to the appropriate recommended nomenclature. It should be noted that the authors may use the same term to describe different cells. For example the term burr cell may be used by one author to describe an echinocyte while other authors will use the term to describe a cell fragment or acanthocyte.

RED CELLS

RECOMMENDED NOMENCLATURE	SYNONYM	RECOMMENDED NOMENCLATURE	SYNONYM
Red cell	Erythrocyte	Cell Fragment	Poikilocyte
	Normocyte		Prickle cell
	Discocyte		Shistocyte
Macrocyte	Macronormocyte		Schizocyte
	Megalocyte		Thorn cell
Microcyte	Micronormocyte		Triangulocyte
Hypochromic Cell	Anulocyte		Triangular cell
	Leptocyte	Echinocyte	Berry cell
	Pessary form		Burr cell
	Ring form		Crenated cell
Acanthocyte	Acanthoid cell		Desicyte
	Acanthrocyte		Mulberry cell
	Astrocyte		Poikilocyte
	Burr cell		Pyknocyte
	Prickle cell		Pyropoikilocyte
	Pyknocyte		Spiculated cell
	Star cell		Spur cell
	Spur cell		Sputnik cell
	Thorn cell		Star cell
Irregular Shaped cell	Burr cell	Spherocyte	Microspherocyte
	Irregularly contracted cell		Pre-lytic cell
			Spherostomatocyte
	Poikilocyte		Spherical cell
	Pyknocyte	Stomatocyte	Cup cell
	Spur cell		Mouth cell
Oval cell / Elliptocyte	Ovalocyte		Mushroom cap cell
	Bacillary cell		Post box cell
	Cigar shaped cell		Slit cell
	Rod shaped cell		Uniconcave disc
Sickle cell	Drepanocyte		Knizocyte
	Holly leaf cell	Target cell	Codocyte
Blister cell	Puddle cell		Leptocyte
	Eccentrocyte		Mexican Hat cell
Cell Fragment	Bizarre cell	Tear Drop Cell	Dacrocyte
	Burr cell		Poikilocyte
	Fragmented cell		Tadpole cell
	Fragmentocyte		Tennis Racket cell
	Helmet cell		Pear shaped cell
	Horn cell	Reticulocyte	Proerythrocyte
	Keratoschistocyte		
	Pincer cell		

APPENDIX B

WHITE CELL

RECOMMENDED NOMENCLATURE	SYNONYM
Band neutrophil	Juvenile neutrophil
	Non-Segmented neutrophil
	Stab cell
	Staff neutrophil
Segmented neutrophil	Mature neutrophil
	Polymorph
Dohle Body	Amato body
Pelger Huet cell	Pince-nez cell
	Stodmeister cell
Reactive Lymphocyte	Abnormal lymphocyte
	Activated lymphocyte
	Antigenic lymphocyte
	Atypical lymphocyte
	Atypical lymphoid cell
	Atypical Mononuclear
	Downey cell I, II, III
	Glandular fever cell
	Immunocyte
	Immunoblast
	Pfeiffer cell
	Plasmacytoid cell
	Reactive mononuclear
	Reider cell
	Variant lymphocyte
Plasma cell	Abnormal lymphocyte
	Antigenic cell
	Antigenic lymphoid cell
	Atypical plasmacytoid
	Immunoblast
	Immunocyte
	Plasmacytoid cell
	Plasmacytoid lymphocyte
	Turk cell
Smear cell	Bare nucleus
	Basket cell
	Ghost cell
	Smudge cell
Pyknotic cell	Karyorrhexic cell
	Necrobiotic cell
	Senescent cell
	Senile cell

APPENDIX C

Haematology full blood count reference ranges as agreed by the NORTHQAG group. A consensus has not yet been reached on neonatal reference ranges and laboratories are currently using their own stratified ranges between Cord and one month. The neonatal reference ranges included in this table are currently in use at Middlemore Hospital.

N.B. It is not uncommon to see immature granulocytes (band neutrophils, metamyelocytes, myelocytes) and NRBC in neonatal blood films. NRBC usually disappear from the blood by about the fourth day in healthy term babies and, by the end of the first week, most of the myelocytes and metamyelocytes have also disappeared.

	CORD	1 DAY	2 DAYS	1 WEEK	2 WEEKS	1 MONTH	2 MONTHS	4 MONTHS
RBC x 10^{12}/L	3.5 – 5.5	3.5 - 6.0	3.5 - 6.0	3.2 - 6.4	3.1 - 6.0	2.9 – 4.8	3.3 – 4.8	4.0 - 5.3
HB g/L	124 - 192	145 - 225	152 - 228	135 - 215	125 - 205	93 – 158	97 - 130	105 - 136
PCV	0.37 –0.56	0.45 - 0.67	0.45 - 0.67	0.42 - 0.66	0.40 - 0.72	0.27 - 0.46	0.29 - 0.38	0.31 - 0.40
MCV fL	99 - 119	99 -119	98 - 121	90 - 126	88 - 122	89 – 100	72 - 91	69 - 84
MCH pg	32 - 39	31 - 37	30 - 38	28 - 40	28 - 40	28 – 34	24 - 32	22 - 29
MCHC	305 - 345	320 - 360	320 - 360	320 - 360	320 - 360	324 – 364	323 - 361	315 - 353
PLATS x 10^9/L	150 - 400	150 - 400	150 - 400	150 - 400	150 - 400	150 - 650	150 - 650	150 - 575
WBC x 10^9/L	7.3 – 25.8	8.0 - 25.0	8.0 - 25.0	8.0 - 25.0	5.0 - 20.0	5.8 – 13.0	6.6 – 15.0	6.4 - 17.0
NEUTS x 10^9/L	3.1 – 12.0	5.0 - 21.0	1.5 - 9.5	1.5 - 9.5	1.5 - 9.5	0.5 – 3.9	0.8 – 4.7	0.9 – 5.9
LYMPHS x 10^9/L	2.0 – 7.3	2.0 - 11.5	2.0 - 11.5	2.0 - 17.0	2.0 - 17.0	3.7 – 8.0	4.2 – 10.6	3.5 - 11.5
MONOS x 10^9/L	0.3 - 2.6	0 - 2.0	0 - 2.0	0 - 2.0	0 - 2.0	0.5 - 1.5	0.4 - 1.3	0.3 - 1.5
EOS x 10^9/L	0.0 - 1.2	0 - 1.0	0 - 1.0	0 - 0.7	0 - 0.7	0 - 0.9	0 - 0.9	0 - 0.9
BASOS x 10^9/L	0.0 - 0.3	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2
	1-3 YEARS	4-7 YEARS	8-12 YEARS	13-15 YEARS MALE	13-15 YEARS FEMALE	ADULT MALE	ADULT FEMALE	PREG.
RBC x 10^{12}/L	4.0 - 5.4	4.1 - 5.4	4.2- 5.6	4.4 - 5.7	4.0 - 5.35	4.3 - 6.0	3.6 - 5.6	3.4 - 5.0
HB g/L	105 - 140	113 - 145	115 - 145	125 - 160	115 - 150	130 – 175	115 – 155	100 - 145
PCV	0.32 - 0.41	0.33 - 0.42	0.35 - 0.43	0.37 - 0.47	0.35 - 0.44	0.40 - 0.52	0.35 - 0.46	0.30 - 0.44
MCV fL	70 - 86	74 - 87	75 - 90	78 - 93	78 - 93	80 – 99	80 – 99	80 - 99
MCH pg	23 - 29	24 - 29	24 - 30	25 - 31	25 - 31	27 – 33	27 – 33	27- 33
MCHC	317 - 353	319 - 353	315 - 350	315 - 350	315 - 350	320 - 360	320 -360	320 - 360
PLATS x 10^9/L	150 - 500	150 - 475	150 - 425	150 - 400	150 - 400	150 - 400	150 - 400	150 - 400
WBC x 10^9/L	5.0 – 14.5	4.5 - 12.0	4.3 – 12.0	4.2 - 10.0	4.2 – 10.0	4.0 – 11.0	4.0 – 11.0	5.0- 14.5
NEUTS x 10^9/L	1.0 - 7.0	1.5 - 8.0	1.5 - 7.0	1.8 - 7.0	1.8 - 7.0	1.9 - 7.5	1.9 - 7.5	1.9 - 11.0
LYMPHS x 10^9/L	2.0 - 8.0	1.4 – 5.7	1.4 – 4.5	1.4 – 4.0	1.4 – 4.0	1.0 - 4.0	1.0 - 4.0	1.0 - 4.0
MONOS x 10^9/L	0.3 - 1.3	0.3 - 1.0	0.3 - 0.9	0.3 – 0.9	0.3 – 0.9	0.2 - 1.0	0.2 - 1.0	0.2 - 1.0
EOS x 10^9/L	0 - 0.9	0 – 1.0	0 - 0.9	0 – 0.8	0 – 0.8	0 - 0.5	0 - 0.5	0 - 0.5
BASOS x 10^9/L	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2	0 - 0.2
RETICS x 10^9/L						10 - 100	10 - 100	

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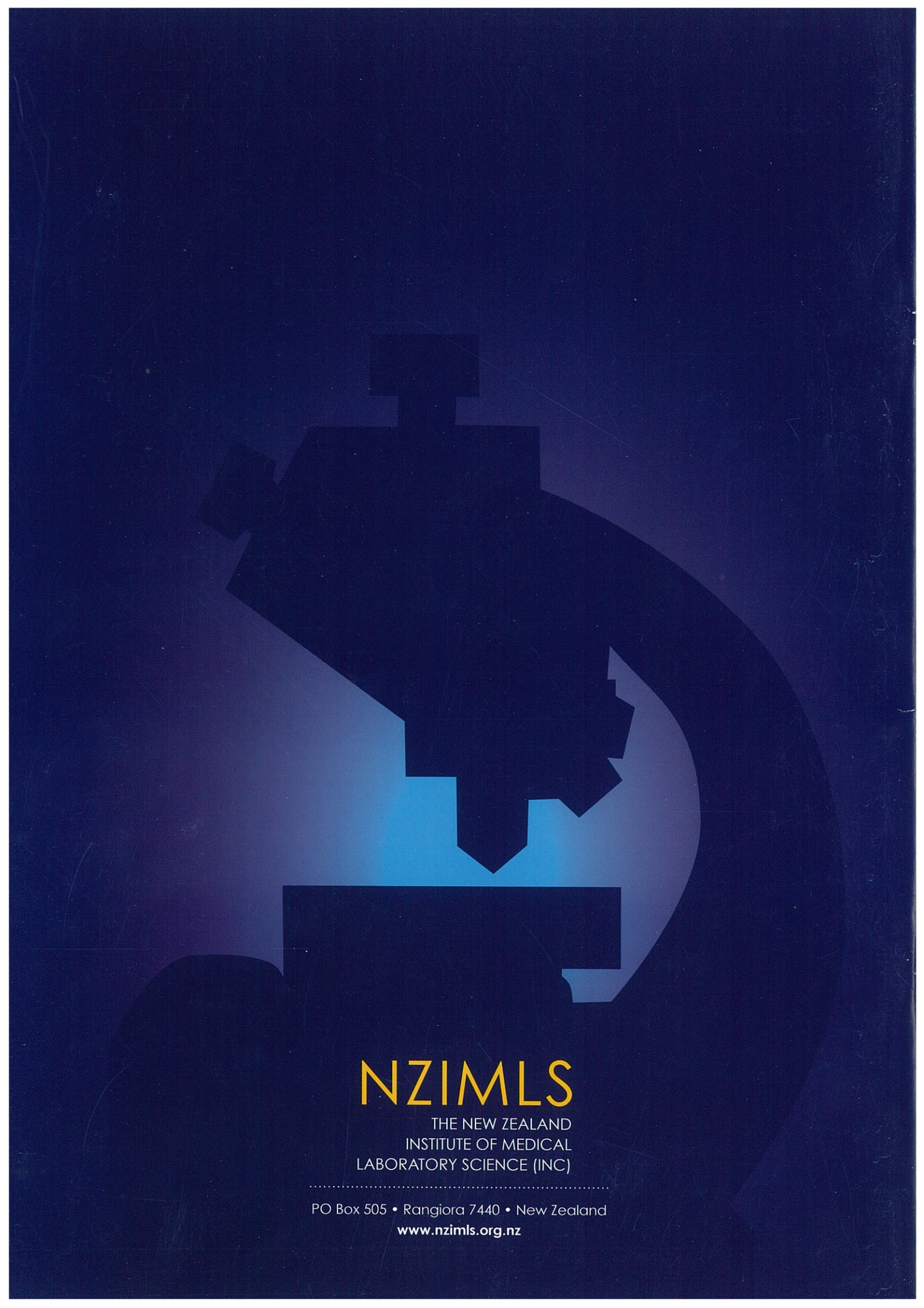

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