علم الفسلجة البشري

قسم تقنيات العلاج الطبيعي

المرحلة الأولى

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العملية النظري / محاضرة ٤

22 Acute leukaemia

Acute leukaemia is a malignant disorder in which haemopoietic blast cells constitute >30% of bone marrow cells. The primitive cells usually also accumulate in the blood, infiltrate other tissues and cause bone marrow failure.

Classification

There are two main groups: acute lymphoblastic (ALL); and acute myeloid (myeloblastic) leukaemia (AML). Rare cases are undifferentiated or mixed. Subclassification of ALL or AML depends on morphological, immunological, cytochemical and cytogenetic criteria (Tables 22.1–22.3).

Aetiology and pathogenesis

The malignant cells typically show a chromosome translocation or other DNA mutation affecting oncogenes and anti-oncogenes (see Chapter 19). AML may follow previous myeloproliferative or myelodysplastic diseases. In childhood B lineage (common) ALL there is evidence that the first event, a chromosomal translocation, may occur *in utero* and subsequent events (? infection) precipitate the onset of ALL.

Incidence

Approximately 1000 new cases (20–25/million population) each of AML and ALL per year in the UK. ALL is the most common malignancy in childhood (peak age 4 years) but also occurs in adults. AML occurs at all ages but is rarer than ALL in childhood, being most common in the elderly.

Clinical features

- Short (<3-month) history of symptoms due to bone marrow failure (e.g. anaemia, abnormal bruising/bleeding or infection). Disseminated intravascular coagulation (DIC) with bleeding is particularly common in AML M3.
- Increased cellular catabolism may cause sweating, fever and general malaise.
- Lymphadenopathy and hepatosplenomegaly are frequent, especially in ALL.
- Tissue infiltration, e.g. of meninges, testes (more common in ALL), skin, bones, gums with hypertrophy (AML M5 or M4) may cause clinical symptoms or signs.

Laboratory features

- Anaemia, thrombocytopenia and often neutropenia.
- Leucocytosis caused by blast cells in the blood usually occurs. Leucopenia is less frequent.
- The bone marrow shows infiltration by blast cells (>30% and often 80–90% of marrow cells).
- Coagulation may be abnormal and DIC can occur, especially with AML M3.
- Serum uric acid, lactate dehydrogenase (LDH) may be raised.
- Morphological analysis (Figs 22.1–22.12, Table 22.1) usually reveals cytoplasmic granules or Auer rods (condensations of granules) in AML. Cytochemical stains are helpful—AML blasts have granules positive by Sudan black, myeloperoxidase and chloroacetate esterase, while monoblasts are positive for non-specific and butyrate esterase. B-lineage lymphoblasts show blocks of positive material with periodic acid–Schiff (PAS) stain, and in T-lineage ALL with acid phosphatase.
- Immunophenotype analysis involves use of antibodies to identify cell antigens (many termed clusters of differentiation or CD, see Appendix 1) which correlate with lineage and maturity (Table 22.2). Other antigens, e.g. TdT, and cytoplasmic immunoglobulin may be also be detected.
- Cytogenetic analysis gives diagnostic and prognostic information (Tables 22.3 and 22.4).

Table 22.1 French–American–British (FAB) classification of acute leukaemia.

Myeloid		Lymphoid	
M0	Undifferentiated by morphology + cytochemistry, myeloid immunophenotype	L1	Small cells, high nuclear/cytoplasmic ratio
M1	Little differentiation, >90% blasts	L2	Larger cells, lower nuclear/cytoplasmic ratio
M2	Differentiated, 30–90% blasts	L3	Vacuolated, basophilic blast cells
M3	Promyelocytic: intensely granular, variant form is microgranular		
M4	Myelomonocytic		
M5a	Monocytic with differentiation		
M5b	Monocytic without differentiation		
M6	Erythroid differentiation, >50% of mononuclear cells are erythroid		
M7	Megakaryoblastic		

* All subtypes have >30% blast cells in the bone marrow.

23 Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is a B-cell clonal lymphoproliferative disease in which lymphocytes accumulate in the blood, bone marrow and often in the lymph nodes and spleen (absolute lymphocyte count $> 5.0 \times 10^9$/L). A disease of older patients (peak age 72), it is the commonest leukaemia in Western countries (over 70 new cases/million population/year in the UK, male/female ratio 2 : 1) but is rare in Asia.

Aetiology and pathophysiology

The cause is unknown. Commonest chromosome changes are trisomy 12, a 13q deletion and deletions of 11q including the ataxia telangiectasia gene. Oncogene mutations or deletions occur which may prevent cells from undergoing programmed cell death (apoptosis).

Clinical features

Stages depend on clinical and laboratory findings (Fig. 23.1).

- Many cases (Stage A) are symptomless and diagnosed on routine blood test.
- Presenting features include lymphadenopathy (typically symmetrical, painless and discrete), night sweats, loss of weight, symptoms of bone marrow failure.
- Spleen is often moderately enlarged.
- Hypogammaglobulinaemia and reduced cell-mediated immunity predispose to bacterial and viral infection.

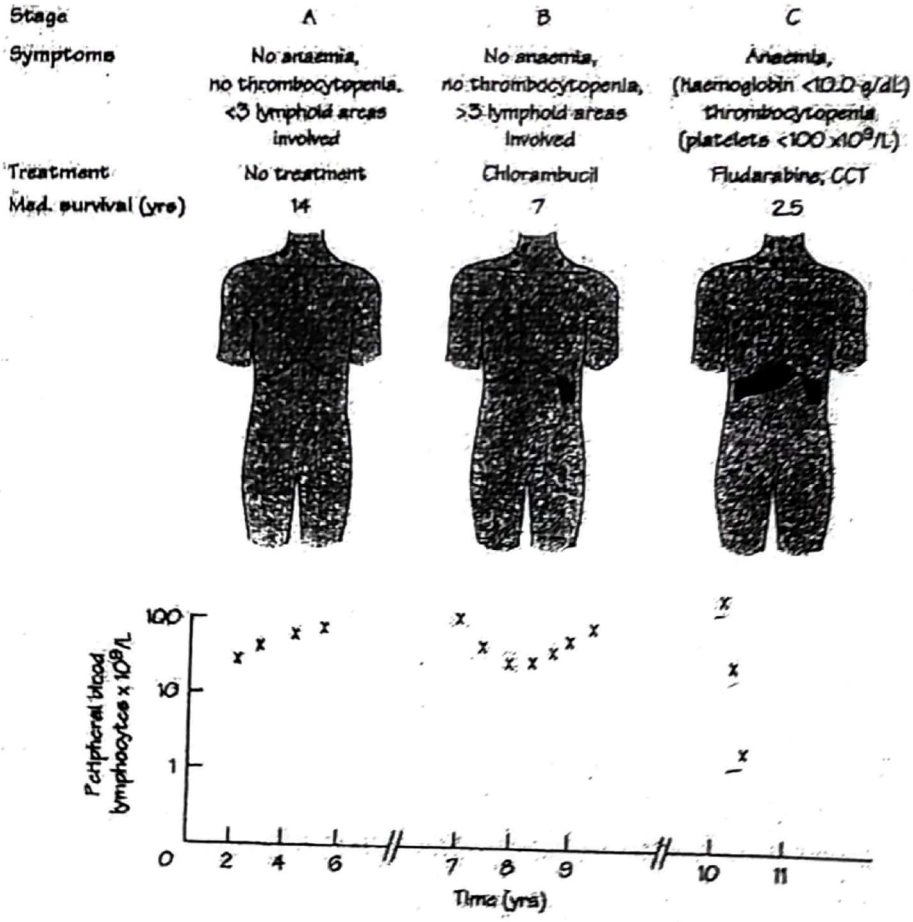


Fig. 23.1 The clinical course of chronic lymphocytic leukaemia (CLL). The Binet staging system evaluates enlargement of the following: lymph nodes, whether unilateral or bilateral, in the head and neck, axillae and inguinal regions; spleen and liver. Stage A patients are usually asymptomatic and do not require treatment. The peripheral blood lymphocyte count may rise progressively. Stage B patients often require treatment (e.g. with oral chlorambucil). Stage C patients will often respond to more intensive therapy (fludarabine, combination chemotherapy (CCT)).

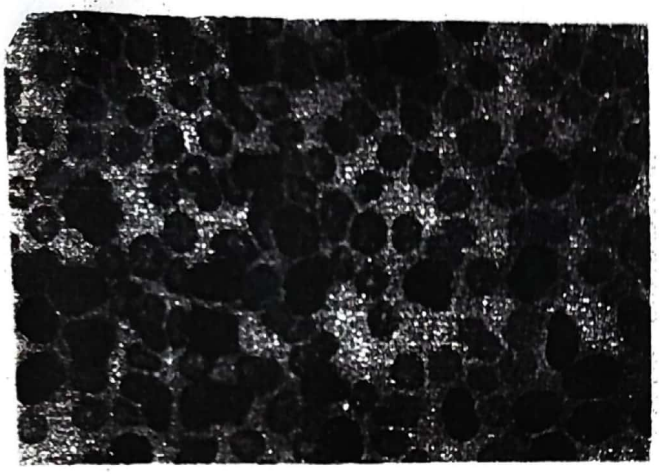
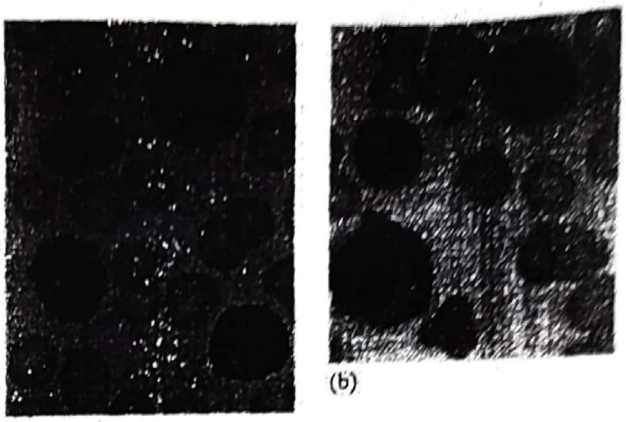


Fig. 23.2 Chronic lymphocytic leukaemia: peripheral blood film showing large numbers of mature lymphoid cells and some 'smear' cells.



(a) (b)

Fig. 23.3 (a) Prolymphocytic leukaemia: blood film. (b) Hairy cell leukaemia: blood film.

Laboratory findings

- Increased peripheral blood lymphocytes (Fig. 23.2 usually 10–30 × 10^9/L at presentation) which are B cells (CD19, CD22 and also CD5 positive).
- They have weak expression of surface IgM which is monoclonal (expressing only κ or only λ light chains).
- Serum immunoglobulins are depressed.
- Anaemia and thrombocytopenia may occur due to marrow infiltration or as a result of auto-antibodies.

Course and prognosis

Patients may present at an early stage and subsequently remain stationary, progress or may present with late-stage disease. Some patients need no treatment for 10 years or more whilst in others the disease follows an aggressive course. Immunoblastic transformation (Richter's syndrome) may be a terminal event.

Treatment

- Observation only for asymptomatic Stage A patients.
- Oral chlorambucil to lower the lymphocyte count and reduce lymph node and spleen size.
- Corticosteroids for bone marrow failure due to infiltration and for autoimmune haemolytic anaemia or thrombocytopenia.
- The purine analogue fludarabine is valuable, either alone or in combination.
- Combination chemotherapy e.g. CHOP (see Chapter 26).
- Support care (Chapter 39).
- Splenectomy or splenic irradiation is useful if the spleen is large and causes symptoms as a result of hypersplenism.

Variants of chronic lymphocytic leukaemia

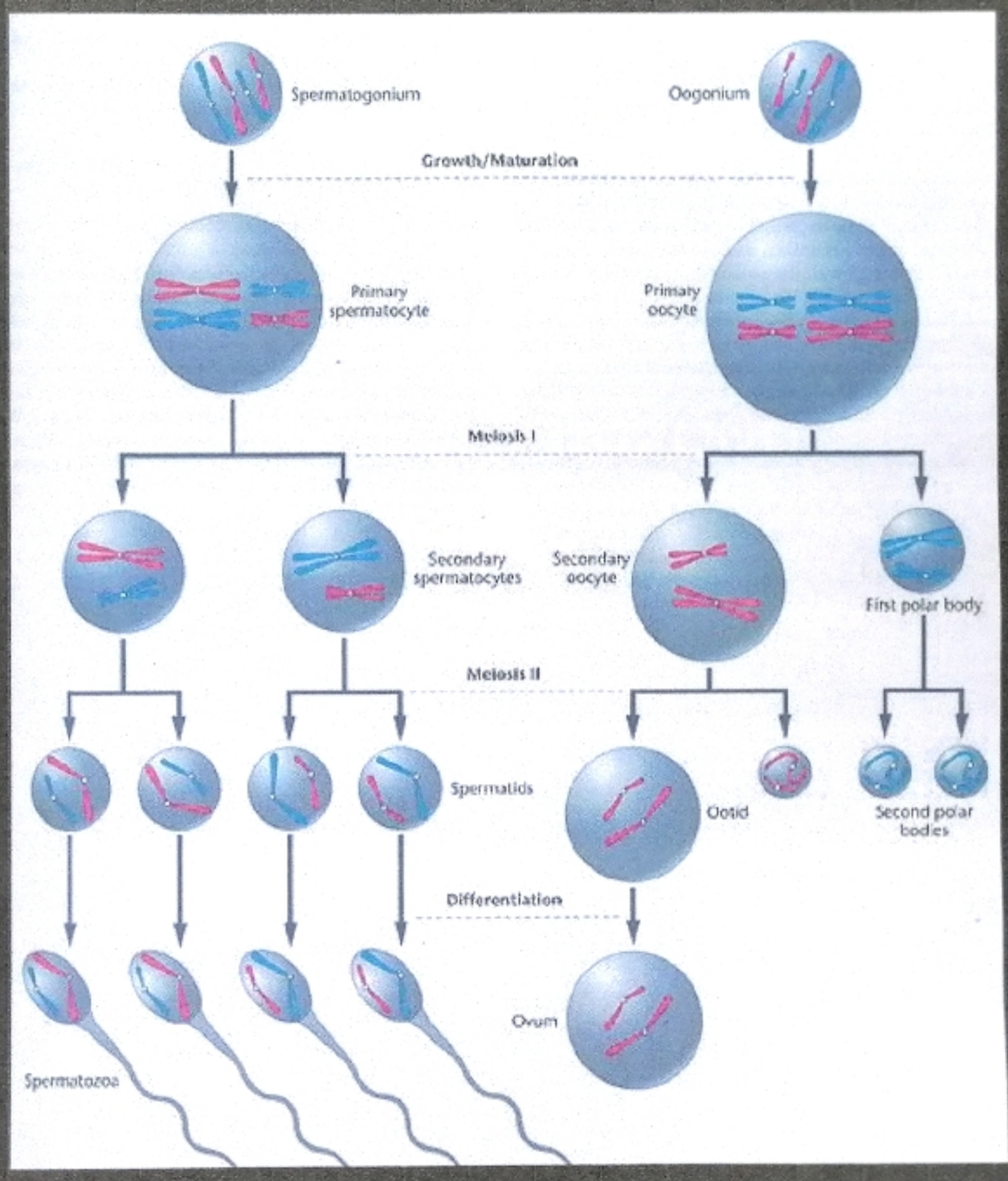
Prolymphocytic leukaemia (PLL, Fig. 23.3a) resembles CLL but usually occurs in older (> 70 years) patients, the white cell count is high and responds poorly to treatment.

Hairy cell leukaemia (HCL, Fig. 23.3b) is rare (male/female ratio of 4 : 1, peak age of 55 years), presents with splenomegaly and pancytopenia. 'Hairy cells' are present in bone marrow and blood. Infections are frequent. They are B cells which stain for tartrate resistant acid phosphatase. Effective treatments include 2-chlorodeoxyadenosine (2-CDA) deoxycoformycin, interferon-α and splenectomy.

T-cell variants of CLL, PLL and HCL are much rarer than B-cell type and are more aggressive.

Gametogenesis

- Gametogenesis: formation of gametes.
- Gametes develop in the gonads (sex cells).
- In males, it is spermatogenesis, formation of sperm.
- In females, it is oogenesis, formation of ova.



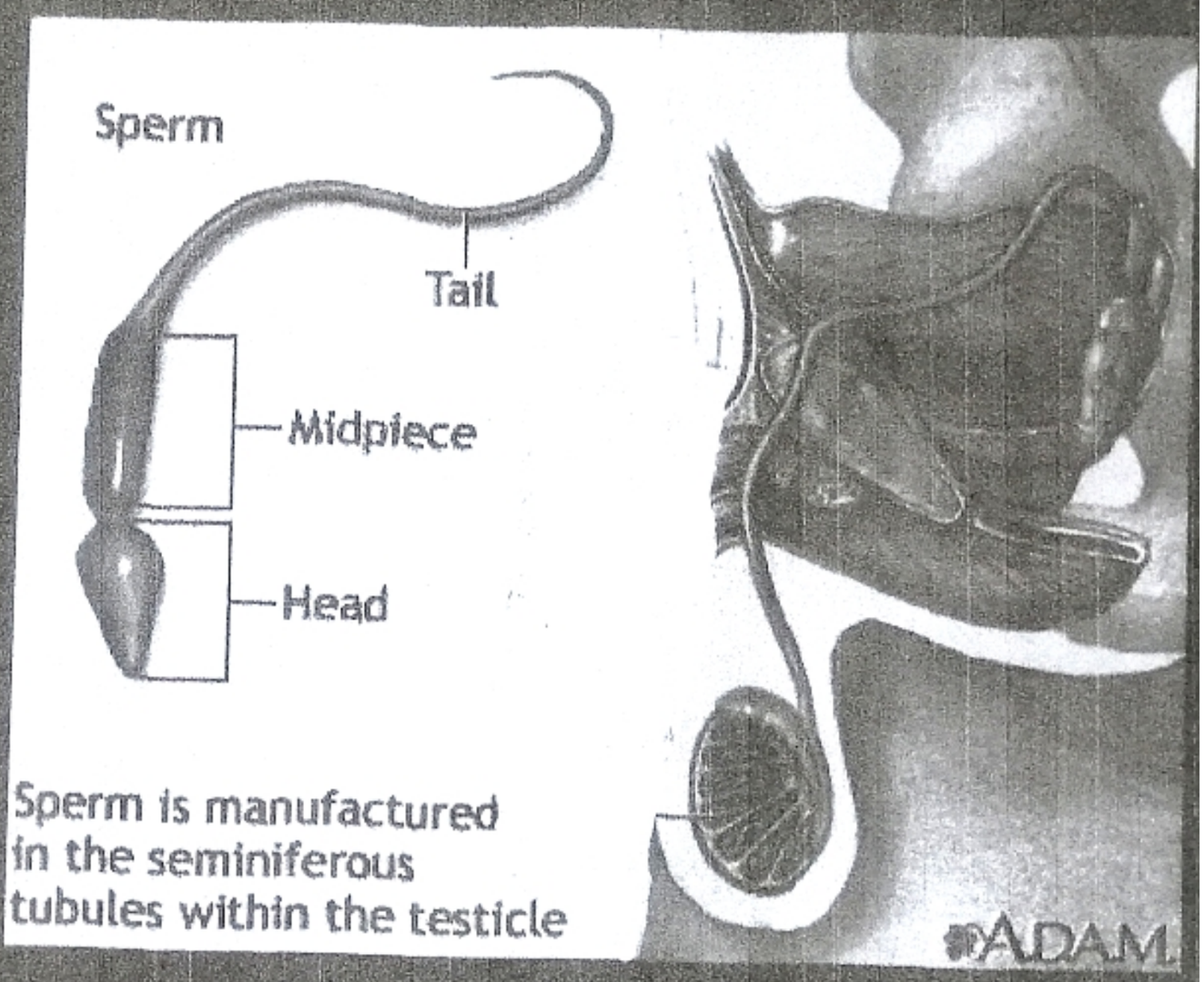
Spermatozoon

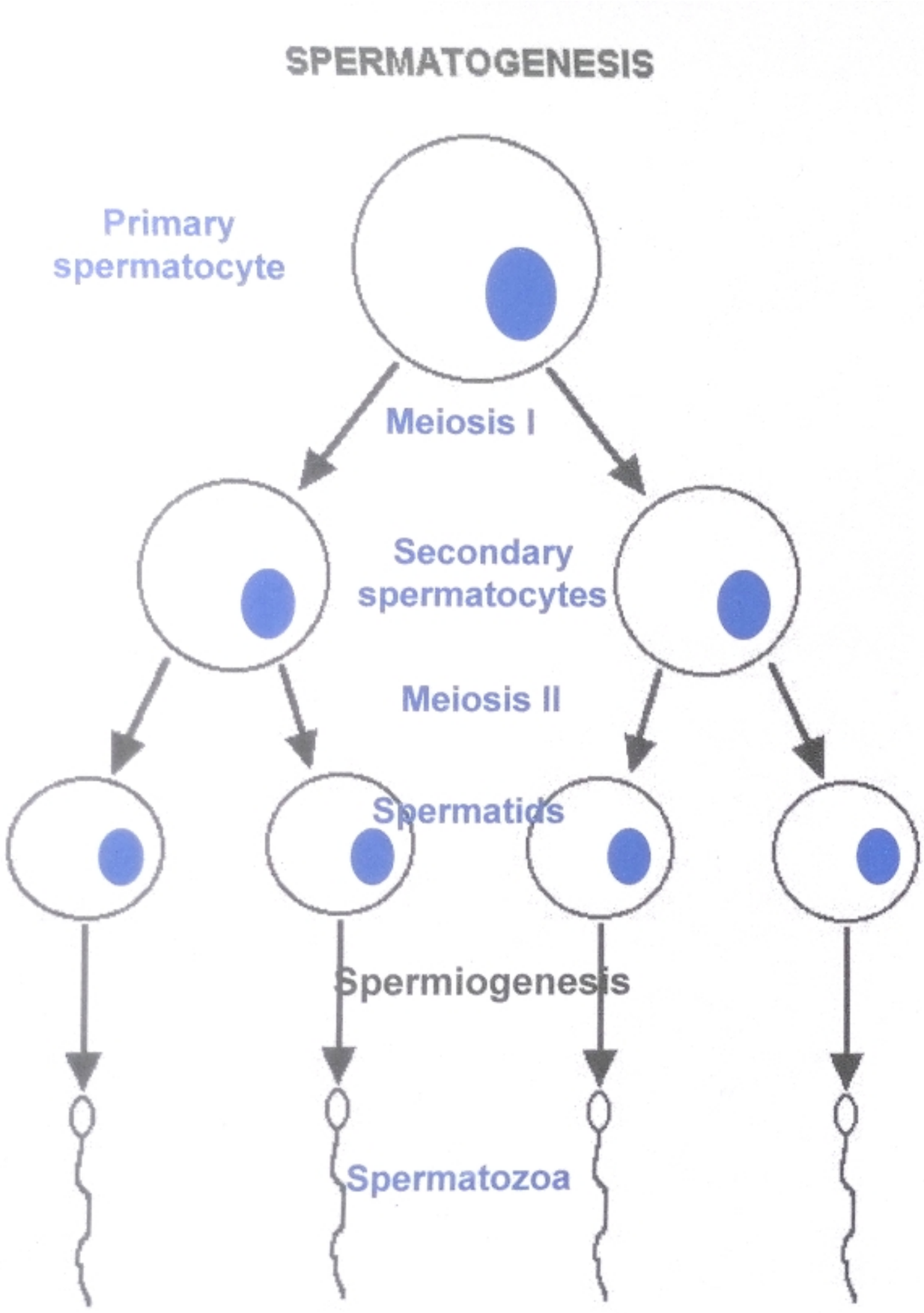
- An actively motile, free swimming cell.
- Consists of a head, neck and a tail (flagellum).

Head: ovoid, consists of nucleus. The anterior 2/3rd of nucleus is covered by acrosomal cap.

Tail has 3 segments:

middle piece, principal piece and end piece.



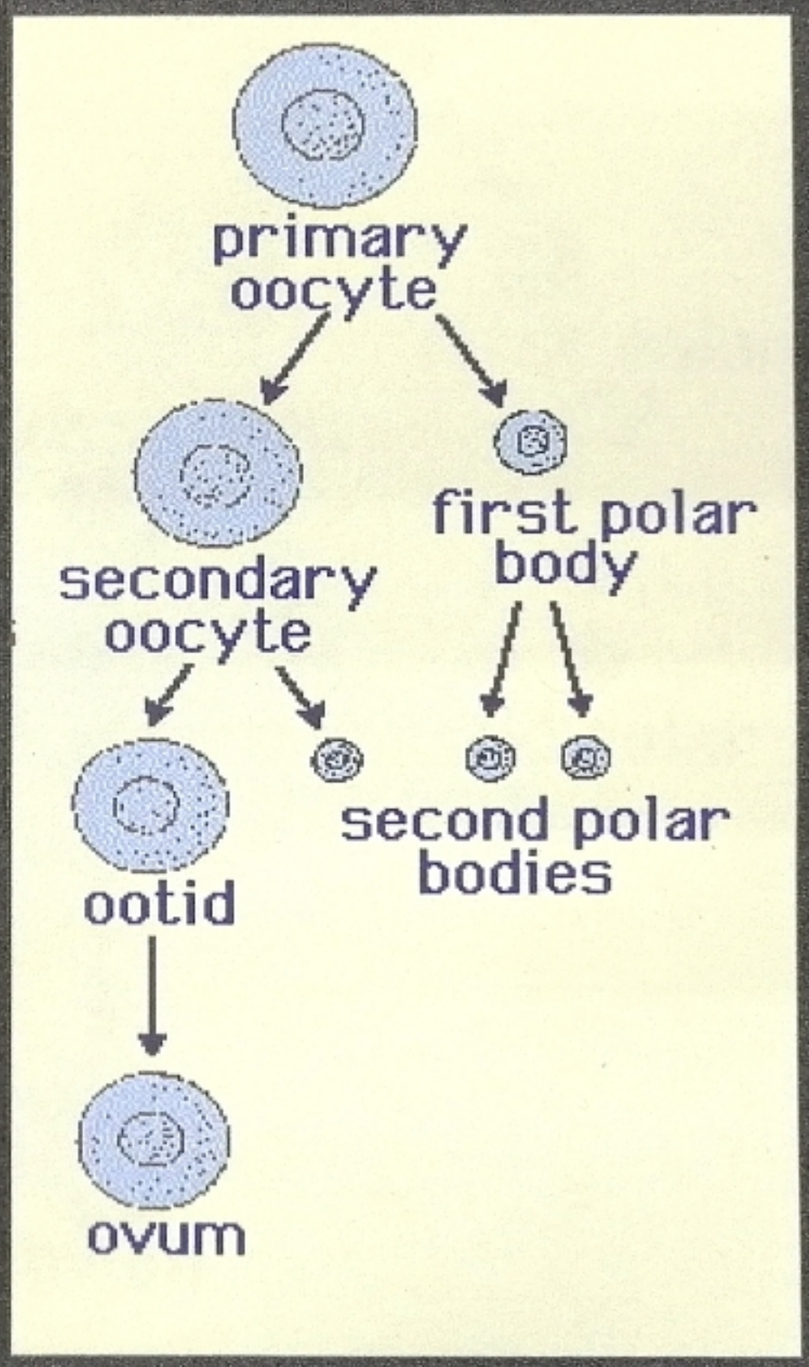


Spermiogenesis

- The process of transformation of a circular spermatid to a spermatozoon is called spermiogenesis.
- Golgi phase
- Cap phase
- Acrosomal phase
- Maturation phase

Oogenesis

- After Telophase I and II, the cytoplasm is not equally divided.
- One of the new cells gets the majority and it survives, while the other one, a polar body, gets broken down.

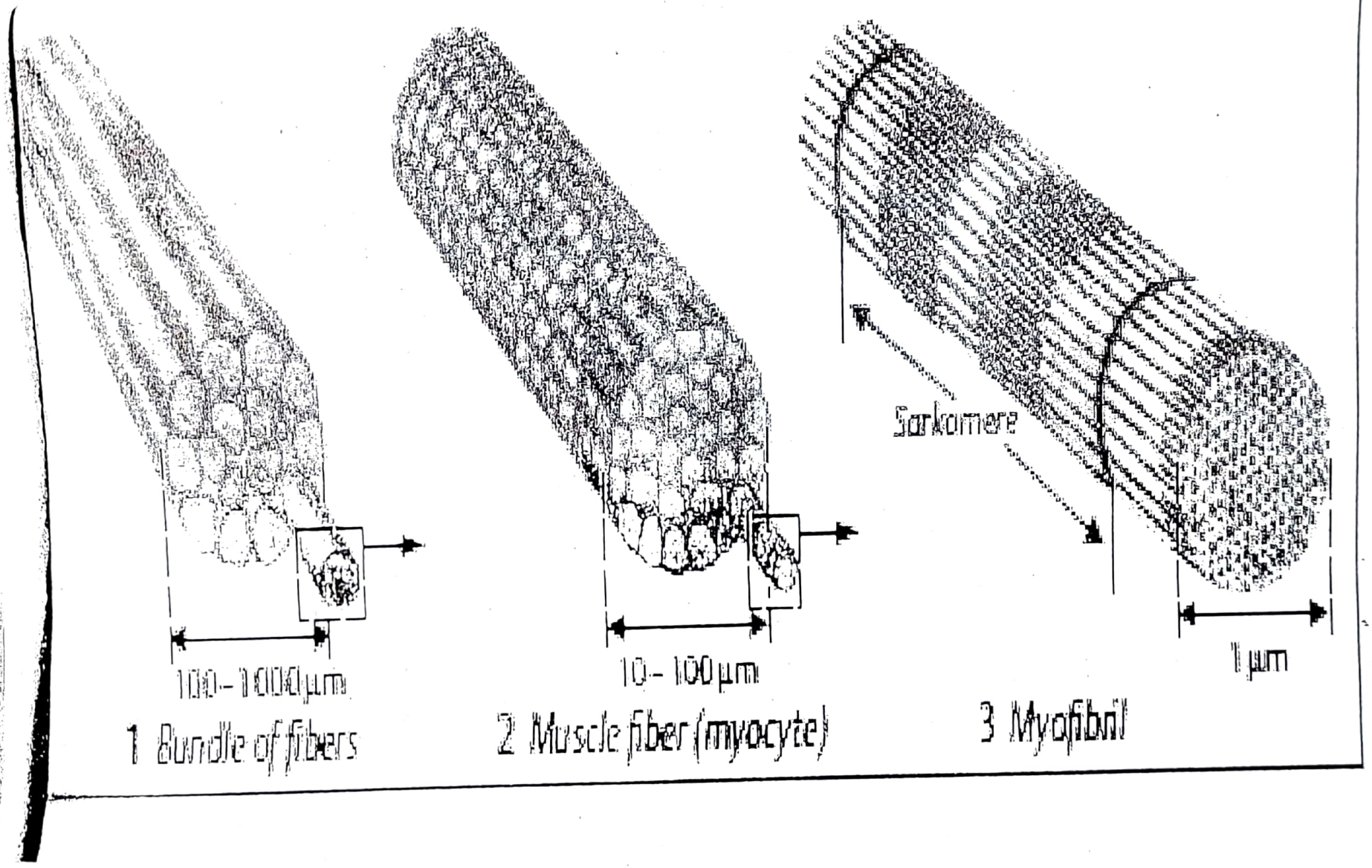


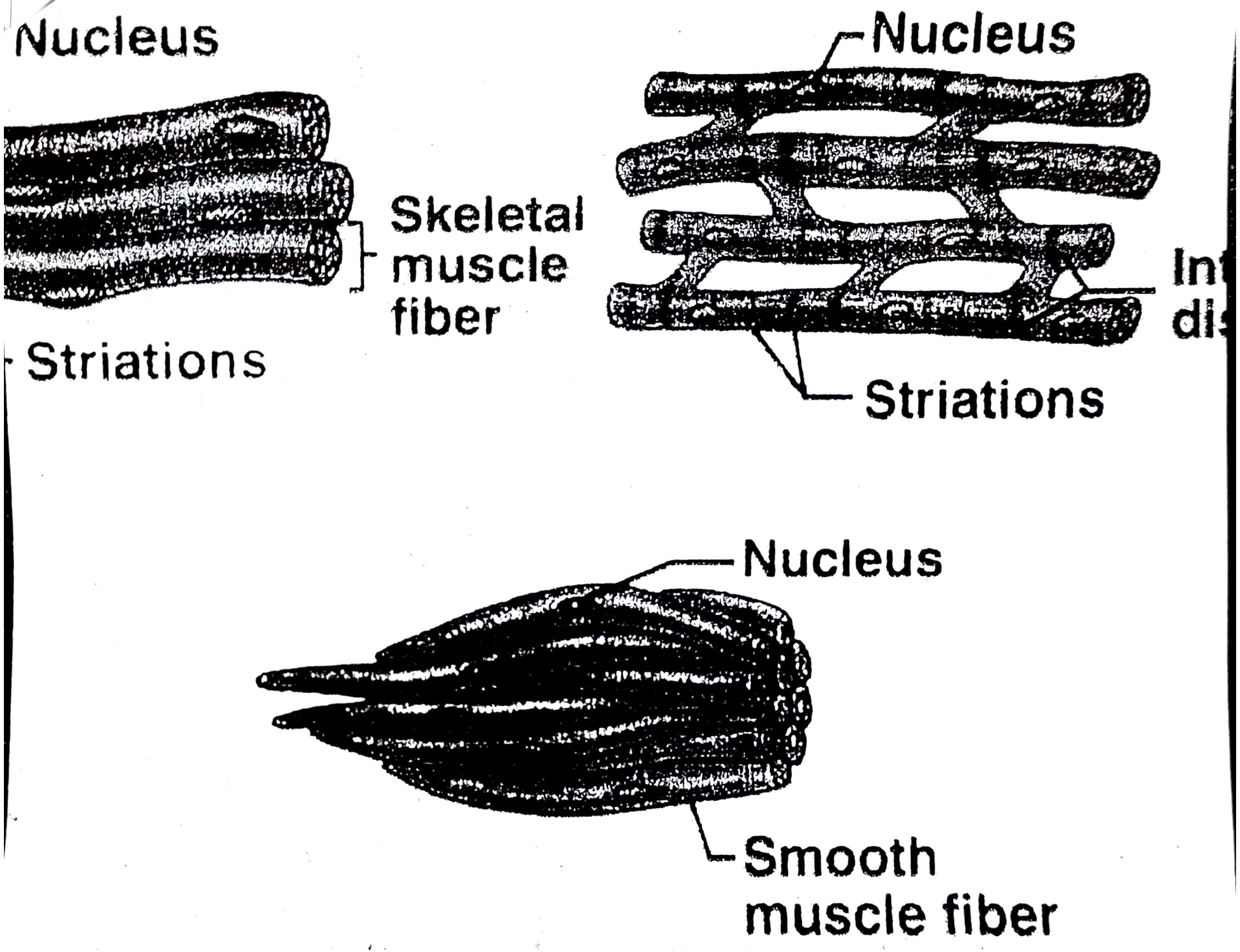
SPERMATOGENESIS
OOGENESIS
primary spermatocyte
primary oocyte
Meiotic division I
secondary spermatocytes
secondary oocyte
first polar body
Meiotic division II
spermatids
ootid
second polar bodies
Differentiation
ovum
spermatozoa

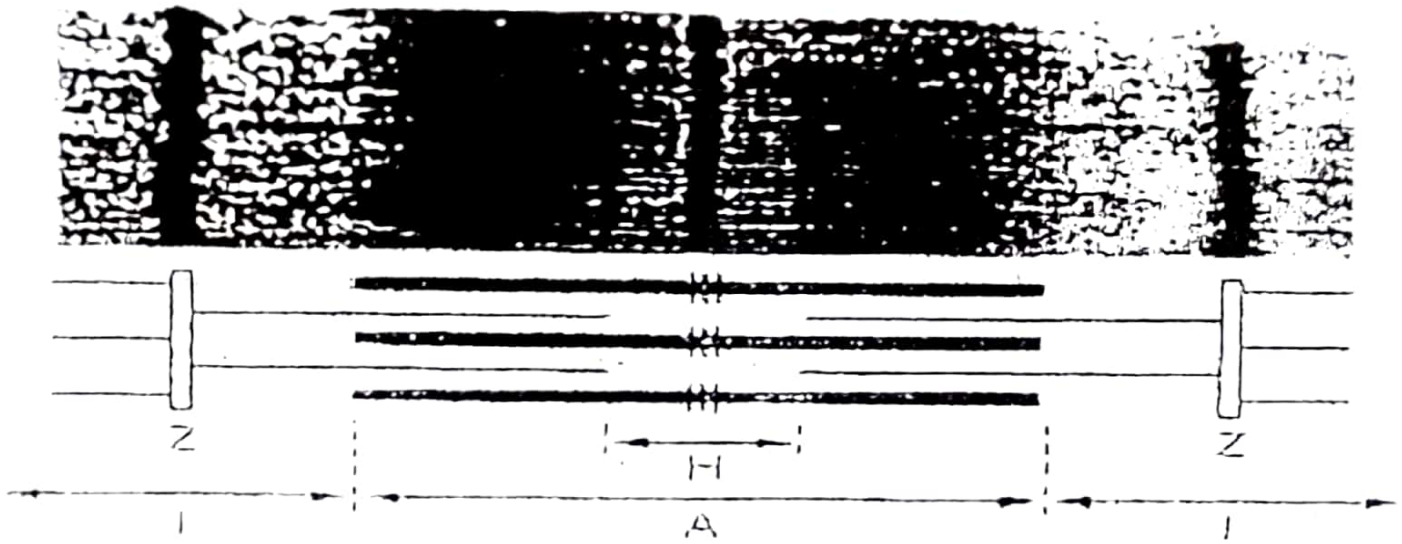
الفسلجة النظري / محاضرة ٤

Muscle physiology

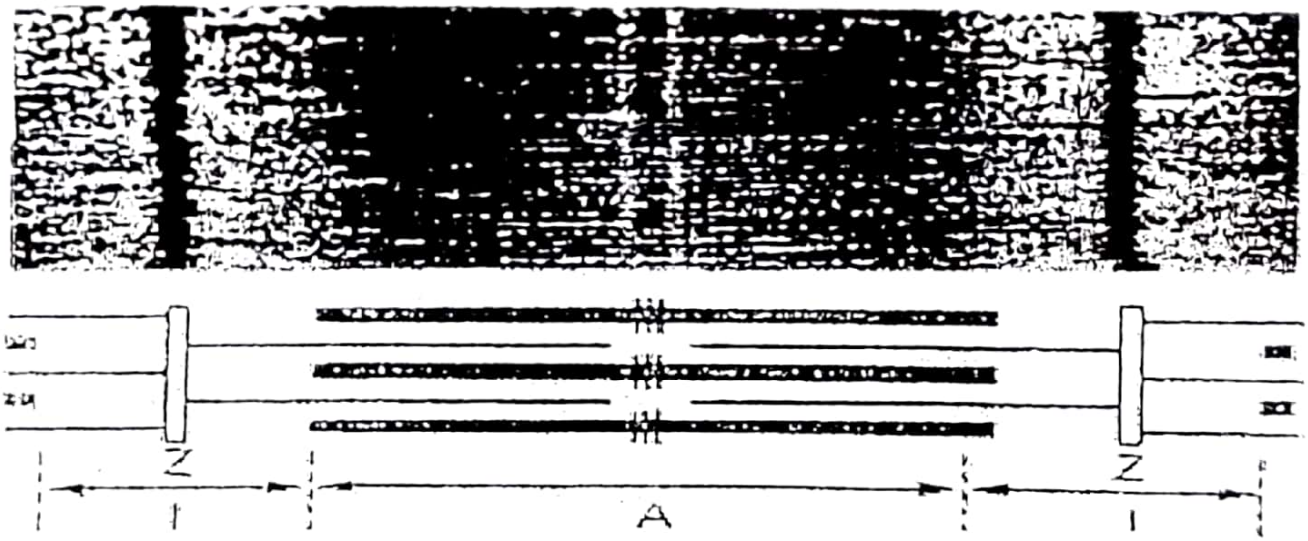
Ultrastructure of striated muscle fibers




Nucleus
Skeletal muscle fiber
Striations
Nucleus
Striations
Nucleus
Smooth muscle fiber



1



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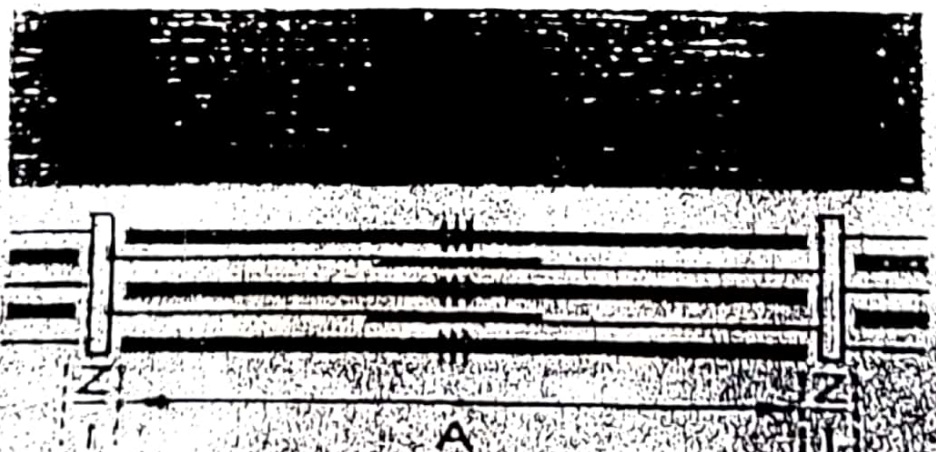


3

A AND I BANDS

Viewed with an electron microscope, a myofibril displays alternating dark bands (the A bands) and light bands (the I bands)

An A band is made up of a stacked set of thick filaments along with the portions of the thin filaments that overlap on both ends of the thick filaments.

The thick filaments lie only within the A band and extend its entire width; that is, the two ends of the thick filaments within a stack define the outer limits of a given A band.

The lighter area within the middle of the A band, where the thin filaments do not reach, is the H zone.

Only the central portions of the thick filaments are found in this region.

A system of supporting proteins holds the thick filaments together vertically within each stack.

These proteins can be seen as the M line, which extends vertically down the middle of the A band within the center of the H zone.

An **I band** consists of the remaining portion of the thin filaments that do not project into the A band.

Visible in the middle of each I band is a dense, vertical **Z line**.

The area between two Z lines is called a **sarcomere**, which is the functional unit of skeletal muscle.

Red blood cells

- Red cell a rise in bone morrow and remind for 120 days , after that it removed by phagocytic cell of reticuloendothelial system ,take it and broken down some of its constituent reutilized for formation of new red cells
  - Function
    - Transport oxygen from lungs to tissues and carbon dioxide from tissues to lungs

- Structure
  - Biconcave, a nucleate ,when stain by
  - (roman owsaky)(Lishman's stain) it appear as pinkish in color
  - Thickness of the red cell is (1.7-2,4) mm average 2 mm
  - Diameter is (6.7-7.2)mm
  - The total number 5 million in each cubic millimeter.

  This is depended on sex and age .
  - In Male (4.5-6.5) in female (3.9-5.6) million

Abnormality red cell for many causes

- Abnormal erythropoiesis
- In adequat hemoglobin .
- Damage of cell
- Attempte bone marrow to copensate in case anemia by increase production blood cell

Abnormalities in blood cell shape and size

- 1- Anisocytosis.. variation in size
- 2-Poikilocytosis .... variation in shape
- 3-Anis chromasia ..... Unequall hemoglobin
- 4- poly chromasia .... Sign is immaturity
- 5-spherocytosis ....irregular contracture or fregmentatation

Erythropoietin hormone

- It is glycoprotein , regulation red cell production derived from mitochondria of the kidney.

- Function :

1. Regulate red cell production .
2. Red cell maturation
3. Hemoglobin synthesis
4. Release of red cell from bone marrow to the circulation .

Causes of increase erythropoietin

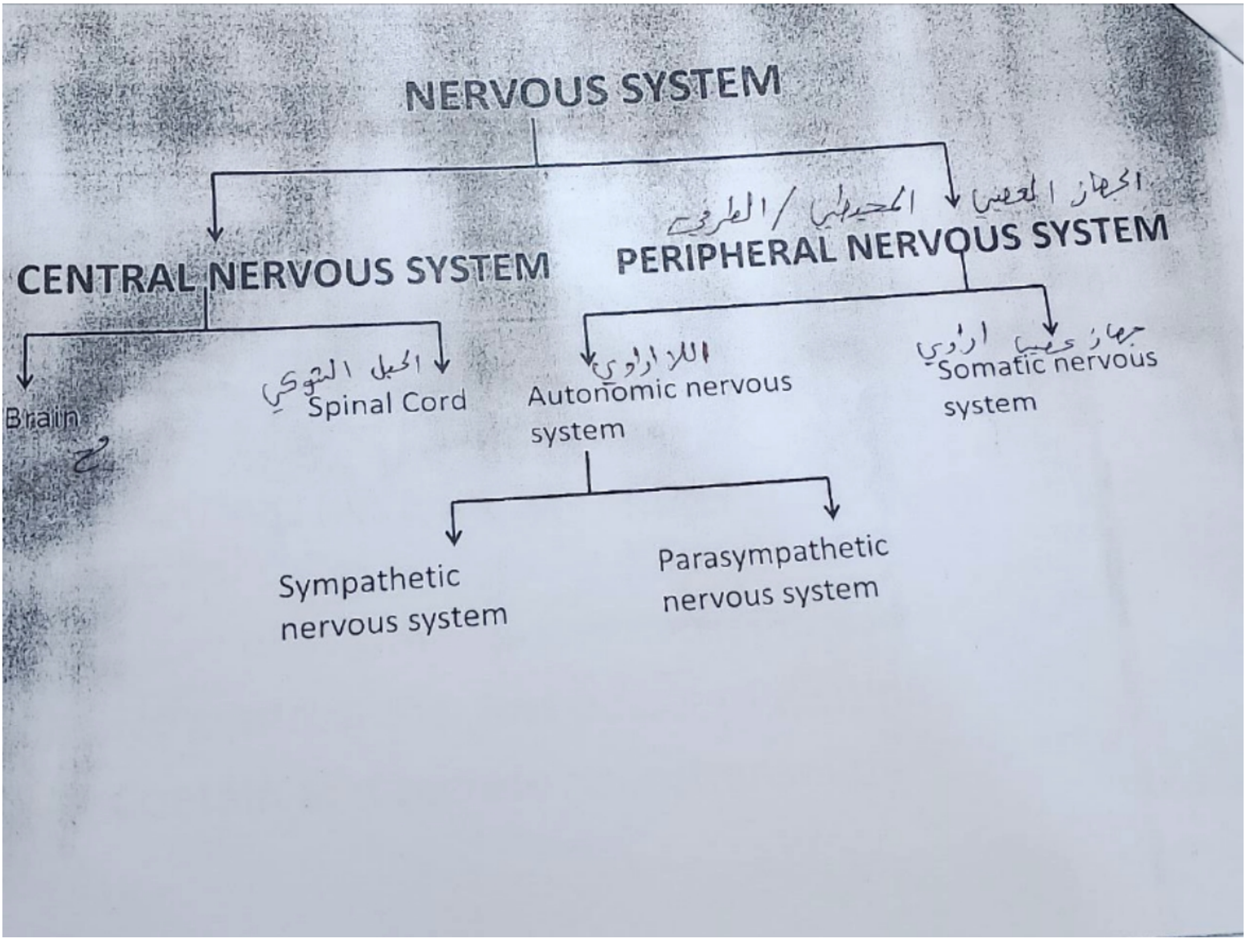
- 1-Hypoxia
- 2- Anemia for example ⟶
  - A-hemolytic anemia
  - B- hemorrhage anemia
  - C- iron deficiency anemia
  - D- aplastic anemia
- 3-Renal disease ⟶
  - 1-cysts
  - 2-hydronephrosis
  - 3-Renal transplantation
- 4-Tumor's ⟶
  - hepatic tumor
  - Ovarian tumor
  - Renal tumor
- 5-Endocrine disease ⟶ adrenal hyperplasia

Causes of decrease erythropoietin

- Renal failure
- Secondary anemia of chronic disease .

Introduction

- Human CNS contain >100 billion neurons
- 50-100 times this number glial cells
- About 40% human genes participating its formation
- Specialized function of muscle – contraction
- Specialized function of neurons – integration & transmission of nerve impulse
- Along with endocrine, nervous system forms the major control system for body functions


NERVOUS SYSTEM
CENTRAL NERVOUS SYSTEM
PERIPHERAL NERVOUS SYSTEM
الجهاز العصبي المحيطي / الطرفي
Brain
الحبل الشوكي
Spinal Cord
اللا ارادي
Autonomic nervous system
جهاز عصبي ارادي
Somatic nervous system
Sympathetic nervous system
Parasympathetic nervous system

NEURON

- Structural and functional unit of nervous system
- Similar to other cell in body having nucleus and most organelles in cytoplasm
- **Different from other cells:**

I. Neurons has branches or processes- dendrites and Axon

II. Have nissl granules and neurofibrillae

III. No centrosome- loss power of division

IV. Contain and secrete neurotransmitter

Classification of Neuron

1. Depending upon the number of poles

2. Depending upon the function

3. Depending upon the length of axon

1. Depending upon the number of poles

* فقط العناوين بدون شرح

a. **Unipolar:**

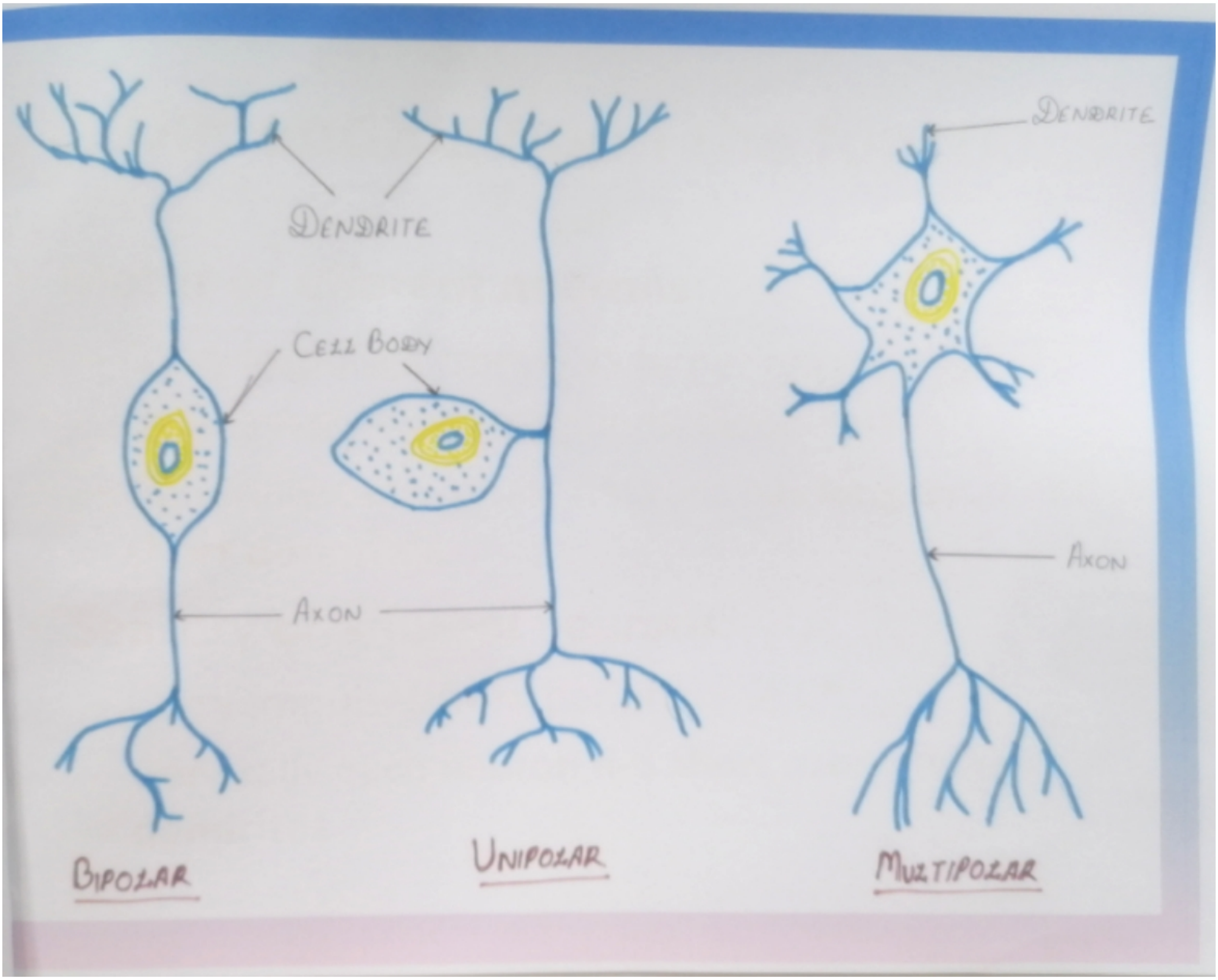
- Having only one pole
- From single pole both axon and dendrites arise
- Present in embryonic stage in human being

b. **Bipolar:**

- Having two poles
- Axon arises one pole and dendrites other pole

c. **Multipolar:**

- Nucleus having multipoles
- Axon arise one pole & all other pole give rise dendrites


DENDRITE
CELL BODY
AXON
BIPOLAR
UNIPOLAR
DENDRITE
AXON
MULTIPOLAR