UNIVERSITY OF JOHANNESBURG

PROGRAM : *BIOMEDICAL TECHNOLOGY*

MODULE : **Haematology III**

CODE : **GTH3112**

DATE : **MAIN EXAMINATION**
25 MAY 2019

DURATION : 180 MINUTES

WEIGHT : 50 : 50

TOTAL MARKS : 180

EXAMINER : MRS J PIENAAR

MODERATOR : MRS B XHAKAZA

NUMBER OF PAGES : 20 PAGES

INSTRUCTIONS : QUESTION PAPER MUST BE HANDED IN

REQUIREMENTS : EXAM SCRIPT/S AND 1 MCQ CARD

1. Do section A on the MCQ card.
2. Do section B and C in the exam script.

INSTRUCTIONS TO CANDIDATES:

1. THIS PAPER CONSISTS OF 3 SECTIONS.
2. EVERY SECTION MUST BE ANSWERED IN THE EXAMINATION ANSWER SCRIPT/S OR MCQ CARD PROVIDED.
3. THIS QUESTION PAPER MUST BE RETURNED WITH YOUR EXAMINATION ANSWER SCRIPT.
4. YOU MAY USE A CALCULATOR.

SECTION A: MCQ

INSTRUCTION: CHOOSE ONLY ONE CORRECT ANSWER AND MARK ON THE MULTIPLE CHOICE (MCQ) ANSWER CARD:
(1 mark per question).

1. All are true in regard to the basophil *except*:

    a. Only occasionally seen in P.B.
    b. Phagocytose bacteria.
    c. Dark cytoplasmic granules, overlie the nucleus and contain heparin and histamine.
    d. Have IgE attachment sites-----degranulation -----histamine release.
    e. In the tissues they become mast cells.

2. Which of the following leukocytes is the largest and partially degrades antigens to present the fragments on MHC II for helper CD4 T-cell recognition?

    a. Neutrophils
    b. Lymphocytes
    c. Monocytes
    d. Eosinophils
    e. Basophils

3. The characteristic surface markers on the T-cell are all of the following *except*:

    a. CD3
    b. CD4
    c. CD5
    d. CD8
    e. CD19

4. Which of the following leukocytes is azurophilic (lysosomes) and is associated with allergic reactions, parasitic infections, and chronic inflammation?

    a. Neutrophils
    b. Lymphocytes
    c. Monocytes
    d. Eosinophils
    e. Basophils

5. In postnatal life the primary lymphoid organs in which lymphocytes develop are:

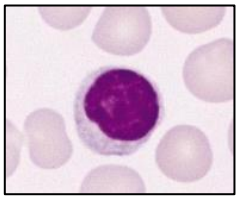
    a. Lymph nodes
    b. Spleen
    c. Respiratory tract
    d. Bone marrow and thymus
    e. None of the above

6. Which ONE of these statements is TRUE about B-lymphocytes?

    a. When plasma cells they secrete surface immunoglobulin
    b. They are divided into helper and killer cells
    c. They are all short-lived
    d. They are the atypical lymphocytes in infectious mononucleosis
    e. They are CD3+

7. What type of cell is shown here?

    a. Neutrophil
    b. Lymphocyte
    c. Monocyte
    d. Eosinophil
    e. Basophil

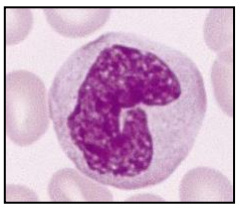


8. All are true regarding T-helper cells except:

    a. They have the CD4 molecule
    b. Recognise MHC II
    c. Can activate APC's
    d. Recognise MHC I
    e. Can be broadly subdivided into two types

9. What type of cell is shown here?

    a. Neutrophil
    b. Lymphocyte
    c. Monocyte
    d. Eosinophil
    e. Basophil



10. All of the following coagulation factors are serine proteases *apart from*:

    a. Factor II
    b. Factor XI
    c. Factor X
    d. Factor XIII
    e. Factor VII

11. Which of the following mechanisms does Heparin utilise to inhibit coagulation?

    a. Cleaves phospholipids to generate coagulase
    b. Binds with heparin ·cofactor to produce heparin cofactor II
    c. Cleaves oligosaccharides into o-glucosamine.
    d. Binds with antithrombin III to inhibit thrombin.
    e. None of the above.

12. Specific α-granules in the platelet contain all of the following *except*:

    a. Fibrinogen
    b. Platelet derived growth factor (PDGF)
    c. β-thrombomodulin
    d. ADP
    e. Platelet factor 4

13. Inactivation of factors Va and VIIIa is caused by:

    a. Antithrombin
    b. VWF
    c. Heparin Cofactor II
    d. Activated protein C
    e. Tissue factor pathway inhibitor (TFPI)

14. Prothrombin is converted to thrombin by:

    a. A complex of activated factors IX, VII and calcium ions.
    b. A complex of activated factors X and V, platelet factor 3 and calcium ions.
    c. Calcium ions only.
    d. A complex of phospholipids, factor VII and calcium ions.
    e. A complex of phospholipids factor VIII, platelet factor 3 and calcium ions.

15. Warfarin acts by:

    a. Interfering with the synthesis of vitamin K-dependent factors
    b. Neutralising the effects of thrombin
    c. Interfering with fibrin monomer formation
    d. Inducing hypercoagulation
    e. Inhibiting fibrin formation

16. Which of the following are classified as contact group proteins?

    a. Factors II, VII, IX, X
    b. Factors I, II, V, X
    c. Factors I, V, VIII, XIII
    d. Factors XII, XI, PK, HMWK
    e. Factors VII, TF

17. Which ONE of the following infections can often cause lymphocytosis?

    a. Haemophilus influenza
    b. Salmonella species
    c. Tuberculosis
    d. Bordetella pertussis
    e. Typhoid

18. Which ONE of the following is NOT a cause of neutrophil leucocytosis?

    a. Myocardial infarct
    b. Trauma
    c. Asthma
    d. Corticosteroid therapy
    e. Acute haemorrhage or haemolysis

19. Which ONE of these is NOT TRUE concerning infectious mononucleosis secondary to EBV infection?

    a. Corticosteroids should be given in all cases
    b. It only follows primary (acute) infection with EBV
    c. Patients treated with ampicillin often develop a rash
    d. The monospot test detects the presence of IgM antibodies that agglutinate horse red cells
    e. Onset is usually seen in young adults

20. Which ONE of these is NOT a common genetic abnormality in the aetiology of haemopoietic malignancy?

    a. Chromosomal translocation
    b. Amplification of tumour suppressor genes
    c. Mutation in oncogenes
    d. Duplication of oncogene
    e. Deletion of oncogenes

21. Which ONE of these statements is NOT correct concerning cytogenetics?

    a. Karyotype is the term used to describe the chromosomes derived from a mitotic cell that have been set out in numerical order
    b. A somatic cell with more or less than 46 chromosomes is termed hyperdiploid
    c. The normal somatic cell has 46 chromosomes and is called diploid
    d. An isochromosome, denoted by i, describes a chromosome with identical chromosome arms at each end
    e. A somatic cell with less than 46 chromosomes is termed hypodiploid

22. Which ONE of the following is TRUE about acute myeloid leukaemia?

    a. It is most common in children
    b. It is never caused by chemotherapy
    c. It is associated with more than 20% blast cells in the bone marrow
    d. Disseminated intravascular coagulation is not a presenting feature
    e. It has a typical immunophenotype of CD19+ and CD22+

23. Which ONE of the following is a common feature of all leukaemias?

    a. Low platelet count
    b. Anaemia
    c. Excess white cells in the bone marrow
    d. Enlarged spleen
    e. A DIC

24. Which ONE of these is NOT TRUE concerning the epidemiology of chronic myeloid leukaemia (CML)?

    a. It is more common in Caucasian rather than black individuals
    b. Incidence of CML was increased in survivors of atomic bomb exposure in Japan
    c. It can occur at any age
    d. The sex incidence is approximately equal
    e. The peak age of onset is 40-60 years

25. Which ONE of the following is NOT a cause of polycythaemia?

    a. Mutation of JAK-2
    b. Renal disease
    c. Congenital heart disease
    d. Haemoglobin abnormality
    e. Iron overload

26. What is the approximate frequency of the Val617Phe mutation in JAK2 in myeloproliferative neoplasms?

    a. 95% in polycythaemia vera (PV), 50% in essential thrombocythaemia (ET) and 56% in primary myelofibrosis (PM)
    b. Approximately 50% in PV, ET and PM
    c. 50% in PV and 25% in ET and PM
    d. 90% in PV, rare in ET and PM
    e. 85% in PV, 60% in ET and 56% in PM

27. Which ONE of these clinical features is often seen in patients with polycythaemia vera?

    a. Nocturnal cough
    b. Increased incidence of gallstones
    c. Pruritus (itch) after a bath
    d. Lymphadenopathy
    e. Patients are often asymptomatic

28. Which ONE of these is the most powerful predictive factor in patients with myelodysplastic syndrome?

    a. Serum β2-microglobulin
    b. Gender
    c. The number of blasts in the bone marrow
    d. The level of anaemia
    e. The level of neutropenia

29. Which ONE of these is least likely to be considered in the differential diagnosis of acute lymphoblastic leukaemia (ALL) in a child?

    a. Aplastic anaemia
    b. Haemolytic anaemia
    c. Chronic lymphocytic leukaemia
    d. Neuroblastoma
    e. Acute myeloid leukaemia

30. Which of the following statements is NOT TRUE about immune thrombocytopenia?

    a. Platelet lifespan is reduced to a few hours
    b. It is usually chronic in children
    c. It is associated with systemic lupus erythematosus
    d. It is more common in women than men
    e. It may be treated by gammaglobulin infusions

31. Which of the following is associated with a rise in platelet counts?

    a. Systemic lupus erythematosus
    b. Dabigatran
    c. Corticosteroid
    d. Polycythaemia vera
    e. Evans' syndrome

32. What factor is deficient in hemophilia B, which presents clinically almost identically to hemophilia A?

    a. Factor XII
    b. Factor XI
    c. Factor IX
    d. Factor X
    e. Factor VIII

33. Which ONE of these statements is TRUE concerning von Willebrand factor?

    a. It cross-links platelets to each other
    b. It carries factor IX
    c. After release it forms large aggregates that are needed for its function
    d. Plasma vWF is derived from endothelial cells
    e. It does not carry factor VIII

34. Severe haemophilia is typically associated with what percentage of factor VIII in the plasma?

    a. Less than 1%
    b. 2-5%
    c. 6-10%
    d. 50%
    e. 20%

35. Which ONE of these following statements is TRUE in haemophilia?

    a. The prothrombin time is prolonged
    b. The activated partial thromboplastin time (APTT) time is prolonged
    c. Thrombin time is prolonged
    d. The bleeding time is prolonged
    e. The level of von Willebrand factor (vWF) in plasma is reduced

36. Which ONE disease is most accurately described by this statement: ‘There is bleeding into mucous membranes, the platelet count is normal, factor VIII level may be moderately reduced and the partial thromboplastin time (PTT) may be normal or prolonged.’

    a. Haemophilia A
    b. Haemophilia B
    c. Von Willebrand disease
    d. Immune thrombocytopenic purpura
    e. DIC

37. Which ONE of these is NOT a typical feature of disseminated intravascular coagulation?

    a. Reduced platelet count
    b. Fibrinogen concentration is increased
    c. High levels of fibrin degradation products (d-dimers)
    d. PT and APTT are often prolonged
    e. The thrombin time is prolonged

38. Which ONE of these is TRUE concerning the factor V Leiden gene mutation?

    a. It leads to failure of activated protein S to prolong the APTT clotting test
    b. It occurs in approximately 5% of Caucasian factor V alleles
    c. Individuals carry an increased risk of bleeding disorder
    d. Homozygous inheritance carries the same coagulation risk as heterozygous inheritance
    e. It is the least most common inherited cause of an increased risk of thrombosis

39. Which ONE of the following is a major risk factor for venous thrombosis?

    a. Smoking
    b. Raised low density lipoprotein (LDL) cholesterol
    c. Cancer
    d. Hypertension
    e. Alcoholism

40. Which ONE of these is NOT used in the investigation of thrombophilia?

    a. Serum cholesterol
    b. Anticardiolipin and anti-β2-GPI antibodies
    c. PT (prothrombin) and APTT tests
    d. Protein C and protein S assays
    e. Serum iron

[40]

STATE WHETHER THE FOLLOWING STATEMENTS ARE “TRUE” OR “FALSE”.

For the following questions (41-50), choose either True (**a** on the MCQ card) or False (**b** on the MCQ card).

41. *True or False:* One of the essential constituents contained in the granules of eosinophils is Major Basic Protein (MBP).

    a) True
    b) False

42. *True or False:* In tissues, basophils become mast cells.

    a) True
    b) False

43. *True or False:* Platelet adhesion requires the presence of von Willebrand factor.

    a) True
    b) False

44. *True or False:* The t(15;17)(q22;q1) cytogenetic translocation is specific for AML M2.

    a) True
    b) False

45. *True or False:* A monocytosis is often seen in Hairy Cell Leukaemia.

    a) True
    b) False

46. *True or False:* AML M3 is often associated with a DIC.

    a) True
    b) False

47. *True or False:* Von Willebrands disease is inherited as a sex-linked disorder.

    a) True
    b) False

48. *True or False:* Oncogenes are genes whose protein products cause neoplastic transformation.

    a) True
    b) False

49. *True or False:* CML presents with immune paresis.

    a) True
    b) False

50. *True or False:* A patient with a severe decrease in factor VII activity would demonstrate an abnormal APTT.

    a) True
    b) False

[10]

SECTION A SUBTOTAL: 50

SECTION B: SHORT AND LONG QUESTIONS

INSTRUCTION: ANSWER THE QUESTIONS FOR SECTIONS B AND C IN AN EXAM BOOK (PLEASE MARK EACH SECTION).

QUESTION 1

1.1. Describe the morphology, transit time, granule components, and function of eosinophils**.** (7)

1.2 Discuss normal neutrophil and monocyte function under the following heading:
Killing and digestion (9)

[16]

QUESTION 2

Describe the origin, function and morphology of plasma cells. **[4]**

QUESTION 3

3.1. Describe the following benign abnormality of neutrophils:
Chédiak-Higashi syndrome (4)

3.2. Describe the **defects** of phagocytic cell function under the following heading:
Chemotaxis (3)

[7]

QUESTION 4

Match column A with the correct answer in column B. **[5]**

A	B
4.1. Myeloma	a) Association with DIC
4.2. Chronic myeloid leukaemia	b) Myelomonocytic acute leukaemia
4.3. AML M3	c) Smudge cells
4.4. CLL	d) Philadelphia chromosome
4.5. Hodgkin's Lymphoma	e) Bluish background staining
	f) Reed-Sternberg cells
	g) Refractory anaemia

QUESTION 5

Diagnose the following patients based on their lab results (be specific): **[4]**

	Patient A	Patient B	Patient C	Patient D
Sex	Female	Female	Male	Male
Age (years)	48	39	6	72
Hb (g/dl)	7.4	10.2	11.0	11.3
WCC (x 10^9/l)	108	11	7.9	87
Platelets (x 10^9/l)	56	84	340	103
MCV (fl)	85.2	83.8	85.8	90.7
MCH (pg)	27.3	28.3	29.5	28.9
MCHC (g/dl)	30.0	31.6	32.5	31.1
Bone marrow smear	Hypercellular Many binucleate hypergranular promyelocytes with auer rods	Not done	Not done	Hypercellular 81% lymphocyte line 2% blasts
Peripheral blood smear	Leucocytosis, with many abnormal promyelocytes. Schistocytes. Thrombo-cytopaenia.	Schistocytes. Thrombo-cytopaenia. NRBCs.	NNA	72% lymphocytes Smudge cells
Cytochemistry	Sudan black: negative	Not done	Not done	Not done
Immuno-phenotyping	CD13 positive CD 3 negative CD 10, CD19 negative	Not done	Not done	CD10, CD19 positive CD13 negative
Chromosomal analysis	t(15;17)	Not done	Not done	Trisomy 12
Other investigations	PT: prolonged. aPTT: prolonged. Fibrinogen: decreased. D-dimer: increased.	PT: normal aPTT: prolonged ADAMTS13 assay: decreased Anti-ADAMTS: positive Factor VIII assay: normal Factor IX assay: normal	PT: normal aPTT: prolonged Factor VIII assay: decreased Factor IX assay: normal	LDH: increased

QUESTION 6

Describe three (3) laboratory findings in chronic myeloid leukaemia. **[3]**

QUESTION 7

Complete the following table of the FAB classification for myelodysplastic syndromes. **[4]**

DESCRIPTION	PERIPHERAL BLOOD	BONE MARROW	MEDIAN SURVIVAL (MONTHS)
Refractory Anaemia (RA)*	Blasts < 1%	Blasts < 5%	50
7.1.	Blasts < 1%	Blasts < 5% Ring sideroblasts > 15% of total erythroblasts	50
RA with excess blasts (RAEB)	**7.2.**	Blasts 5 - 20%	11
7.3.	As any of the above with > 1.0×10^{9}l-1	As any of the above with promonocytes	11
RAEB in transformation (RAEBt)†	Blasts > 5%	**7.4.**	5

QUESTION 8

8.1. Describe the pathogenesis of multiple myeloma under the following heading:
Proliferation of abnormal plasma cells (myeloma cells) in the bone marrow: (1)

8.2. Describe two (2) of the clinical features seen in essential thrombocythaemia. (2)

[3]

QUESTION 9

9.1. Describe platelet release reaction and amplification (exclude inhibition of release). (7)

9.2. List the three types of storage granules found in platelets. (3)

[10]

QUESTION 10

Diagrammatically illustrate the coagulation cascade. (½ mark each) **[14]**

QUESTION 11

What is the major function of the fibrinolytic system and list three (3) of the major components needed to achieve this function. **[4]**

QUESTION 12

12.1. A patient presented with symptoms of abnormal bleeding. Her laboratory results are given in the table below. Supply the diagnosis of this patient. (1)

	Plt count	**Bleeding time**	**PT**	**aPTT**	**Factor VIII**	**Factor IX**	**vWF**	**Plt aggregation with ristocetin**
Patient results	Normal	Prolonged	Normal	Prolonged	Low	Normal	Low	Abnormal

12.2. List three (3) laboratory features of DIC. (3)

[4]

QUESTION 13

Answer the following questions on platelet disorders:

13.1. Concerning inherited disorders of platelet function, name the primary defect in the following conditions:

13.1.1. *Glanzmann's thrombasthenia* (1)

13.1.2. *Storage pool diseases* (2)

13.2. Defective haemostasis with abnormal bleeding may be caused by four general conditions. Name them. (4)

[7]

QUESTION 14

Virchow's triad suggests that there are three components important in thrombus formation. Name them. **[3]**

QUESTION 15

Describe the pathogenesis of TTP. **[6]**

SECTION B SUBTOTAL: 94

SECTION C: CASE STUDIES

INSTRUCTION: ANSWER THE QUESTIONS FOR SECTIONS B AND C IN AN EXAM BOOK (PLEASE MARK EACH SECTION).

CASE STUDY 1

History

A 62-year-old man presented with increasing shortness of breath on exercise and loss of weight. He had suffered five chest infections during the previous winter, despite being a non-smoker.

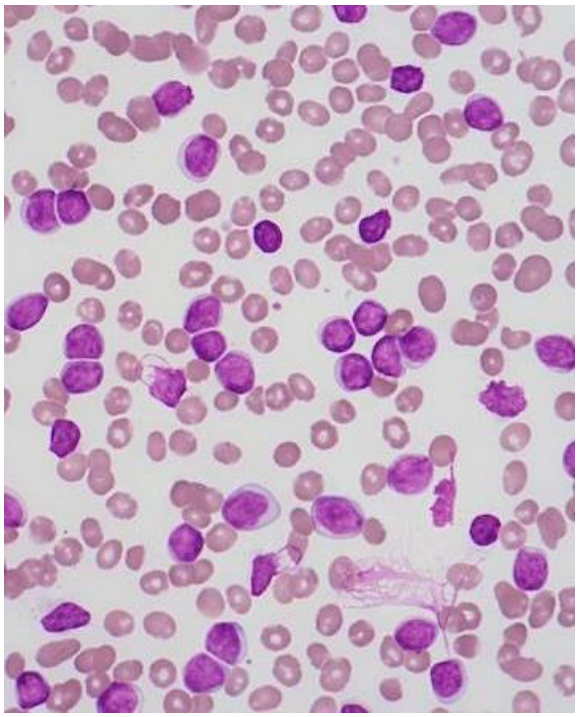
Physical examination

On examination, there was moderate, bilateral cervical lymphadenopathy and left inguinal lymph node enlargement. The spleen and liver were enlarged 5cm below the costal margins. There was no bone tenderness and there were no lesions in the skin.

FBC
(with microscopic differential)

RBC	3.21 x 10^{12}/l
HGB	10.1 g/dl
HCT	34.0%
MCV	89.9 fl
MCH	29.2 pg
MCHC	2.1 g/dl
RDW	14.3%

WBC	123 x 10^9/l
N	5 %
L	87
M	2
E	2
B	0
PLT	136 x 10^9/l



1.1. What morphologic alterations are seen in this blood smear field? (4)

After seeing the FBC results and peripheral slide, the doctor ordered the following tests:

Bone marrow biopsy:

Aspirate:

- The differential showed 90.1% lymphocytes, similar to those in the blood.

Sections:

- Markedly hypercellular.

Immunophenotyping:

- CD19 positive
- CD21 positive
- CD2 negative

Serum protein electrophoresis:

Immunoglobulins, quantitative:

- IgA 60 mg/dl (RI 85-450)
- IgG 256 mg/dl (RI 800-1700)
- IgM 38 mg/dl (RI 60-370)

1.2. What is the most likely diagnosis? (1)

1.3. How did you come to this conclusion? List six (6) reasons. Please explain, in detail, for each point that you list, the relevance/significance to this particular disease. (6)

1.4. Tabulate the Binet (international party) classification for this disease (½ mark per fact). (7)

1.5. Supply possible aetiologies (causes) for this disease. (2)

[20]

CASE STUDY 2

History:

A 19 year old male college student hailing from Malawi admitted himself into hospital with complaints of pain and restricted movement of left hip joint for 10 days, recurrent swelling and pain in multiple joint for last 17 years and prolonged bleeding following minor trauma since childhood.

Physical Exam:

On examination patient is mildly anaemic, non-icteric, pulse-92/min, BP- 110/70 mm of Hg, no oedema or lymphadenopathy. On examination of musculoskeletal system, there was wasting of thigh and calf muscles, tone was normal, power was 4/5, movement was reduced in both knee and elbow joints, as well as left hip joint. Nervous system and other system examination revealed nothing abnormal.

Laboratory Test Results:

	Patient	Normal Range
Platelet Count	330 x 10^9/l	150 - 400 x 10^9/l
Bleeding Time	2 min, 32 sec	1-9 min
PT	11.5 sec	10-12 sec
APTT	82.8 sec	28-35 sec

2.1. Interpret the laboratory results: *briefly describe the principle of each test, whether the patient's results are within the normal range or not, and if not what the status is, and describe the significance of the patient's results*. (5)

Based on the coagulation study results, the doctor ordered factor assays on factors VIII, IX, and XI and XII.

Factor Assay Results

Plasma Factor VIII Assay	Patient: 121%	Normal Range: 50-150%
Plasma Factor IX Assay	Patient: 26%	Normal Range: 50-150%
Plasma Factor XI Assay	Patient: 95%	Normal Range: 50-150%
Plasma Factor XII Assay	Patient: 93%	Normal Range: 50-150%

2.2. From the testing results, what is your final diagnosis for this patient?(1)

2.3. How did you come to this conclusion? List six (6) reasons. Please explain, in detail, for each point that you list, the relevance/significance to this particular disease. (6)

2.4. What is the inheritance pattern of this disease? Who is affected (symptomatic) in this type of genetic inheritance – males, females or both equally? (2)

2.5. Describe two (2) possible treatment modalities for this patient. (2)

[16]

SECTION C SUBTOTAL: 36

TOTAL MARKS: 180