UNIVERSITY of NICOSIA | MEDICAL SCHOOL

Course Code	Course Title	ECTS Credits
MED-401	**Haematology**	6
School	**Semester**	**Prerequisites**
Medical School	Fall (Semester 7)	MED-304 General Pathology MED-309 Systematic Pathology
Type of Course	**Field**	**Language of Instruction**
Required	Medicine	English
Level of Course	**Year of Study**	**Course Lead**
Undergraduate	4th	Dr Niki Vyrides **Other contributors:** Dr George Marcoullis Dr Maria Michael
Mode of Delivery	**Work Placement**	**Co-requisites**
Face-to-face	N/A	None

Objectives of the Course:

The haematology course aims to help the students understand and recognise the pathologies behind benign and malignant disorders of erythrocytes, leucocytes, thrombocytes and the bone marrow. This course was specially designed with the future doctor in mind and its main goals are:

- To provide in depth knowledge about the pathology and pathophysiology of haematological disorders.
- To help the students, read and evaluate laboratory values from routine blood examination and be able to differentiate between pathologies.
- To enhance the student's ability to produce a differential diagnosis based on clinical examination and laboratory values.
- To provide a basic understanding of the treatment protocols which are in place for haematology.

Learning Outcomes:

After completion of the course students are expected to be able to:

Week 1

Lobs covered during lectures and tutorial:

1. Describe the stages in red blood cell maturation from stem cell to maturity.
2. Recall the structure and function of the red blood cell, the synthesis of haemoglobin and the normal breakdown and recycling of components.
3. Define anaemia and give the classification of anaemia based on the size of the red blood cells and the etiology.

4. Describe the signs and symptoms of anaemia and the compensatory mechanisms to it.
5. Describe the investigative approach and management of a patient with anaemia.
6. Outline the nutritional and metabolic aspects of iron metabolism, including dietary iron, iron absorption, body iron distribution and transport.
7. Describe the absorption of iron at the level of enterocyte and the importance of Hepcidin.
8. Outline the common causes of iron deficiency anaemia.
9. Identify questions which, on history-taking, help elucidate likely causes of iron deficiency anaemia.
10. Describe the signs and symptoms of iron deficiency anaemia and diseases associated it.
11. Outline the investigations and management of a patient with iron deficiency anaemia.
12. Differentiate, by laboratory tests, anaemia due to iron deficiency from other causes of microcytic anaemia.
13. Recognize the appearance of red blood cells as defined by microcytosis, hypochromia, macrocytosis, spherocytosis, anisocytosis, reticulocytosis, and polychromasia.
14. Describe the common causes of macrocytic anaemia and macrocytosis without anaemia.
15. Outline the nutritional and metabolic aspects of vitamin B12 and folate metabolism including dietary aspects, absorption, body distribution and transport.
16. Describe the concept of megaloblastic anaemia and the effect of vitamin B12 and folate deficiency on inhibition of DNA synthesis. Compare megaloblastic to non-megaloblastic anaemia.
17. Describe the difference between B12 and folate deficiency with respect to underlying causes, time of development of clinical deficiency state and clinical manifestations.
18. Identify questions which, on history-taking, help elucidate likely causes of macrocytic anaemia.
19. Describe the signs and symptoms and laboratory diagnosis of macrocytic anaemia.
20. Outline the investigation and management of vitamin B12 and folate deficiency.

Week 2

Lobs covered during lectures and tutorial:

21. Define bone marrow failure and describe its clinical consequences.
22. Describe the etiology of acquired and inherited aplastic anaemias.
23. Discuss the pathophysiological mechanisms of acquired and inherited aplastic anaemias.
24. Describe the characteristic peripheral blood and bone marrow features in aplastic anaemia.
25. Classify aplastic anaemia as nonsevere, severe or very severe based on laboratory tests.
26. Discuss treatment modalities for acquired and inherited aplastic anaemia and the patients for whom each treatment is most appropriate.
27. Define pure cell aplasia and describe the most common causes.
28. Outline the genetics of alpha and beta Thalassaemia.
29. Discuss how genetic alterations affect the normal physiology of Haemoglobin and the red blood cell. Describe the clinical consequences of these genetic alterations with respect to

alpha and beta Thalassaemia.

30. Outline the laboratory diagnosis of alpha and beta Thalassaemia and compare the findings.
31. Describe the complications of beta Thalassaemia.
32. Describe the treatment of alpha and beta Thalassaemia and compare the severity of each disease.
33. Define sickle cell disease and sickle cell trait.
34. Outline the genetics of sickle cell disease.
35. Describe how genetic alterations affect the normal physiology of Haemoglobin and the red blood cell and the clinical consequences of these alterations with respect to Sickle cell disease.
36. Outline the laboratory diagnosis of sickle cell disease and compare the findings with those of beta thalassaemia and microdrepanocytic disease.
37. Outline the management of sickle cell disease and compare it with that of beta thalassaemia.
38. Recognise the signs and symptoms of the different types of sickle cell crises.
39. Define and recognize the Howell Jolly bodies and discuss the mechanism of production and their significance.
40. Describe the vulnerability to infection that affects people with sickle cell disease and describe what action is required.

Week 3

Lobs covered during lectures and tutorial:

41. Provide a differential diagnosis for normocytic anaemia.
42. Discuss investigation and management of normocytic anaemia.
43. Outline the concept of anaemia of chronic disease/inflammation and describe the pathogenesis.
44. Discuss which chronic diseases can cause anaemia and which mechanisms and types of anaemias are involved.
45. Outline a simplified classification for the haemolytic anaemias.
46. Describe additional clinical signs in a patient with haemolytic anaemia and explain how these may differ from those caused by anaemia due to other causes.
47. Describe the mechanism involved in the development of anaemia in congenital spherocytosis and in G6PD.
48. Describe the mechanism involved in anaemia in PNH and give the three different forms of the disease (haemolytic anaemia, Thrombosis, aplastic anaemia).
49. Outline the clinical consequences of Haemolysis.
50. Outline the laboratory diagnosis of a haemolytic process and discuss the concept of extravascular and intravascular haemolysis.
51. Describe the investigations and management of a patient with haemolytic anaemia.
52. Describe the pathological mechanism that leads to autoimmune haemolytic anemia and discuss warm and cold haemolytic anaemia.

53. Explain the allo-immune haemolytic anaemia (haemolytic anaemia of fetus and newborn).
54. Describe the mechanism of TTP and explain how it differs when compared to immune haemolytic anaemia.
55. Describe the main causes of HUS and discuss its predominance in children.
56. List common drugs which may induce haemolytic anaemia.
57. Discuss haematological manifestations of infections (Malaria, HIV).
58. Discuss haematological changes in cancer.
59. Discuss haematological changes in chronic renal failure and chronic liver disease.
60. Discuss haematological changes in rheumatic disease.

Week 4

Lobs covered during lectures and tutorial:

61. Describe the stages in lymphoid cell maturation from stem cells to maturity and describe the specific membrane markers for each stage.
62. Name the primary and secondary lymphoid organs and differentiate between their role.
63. Outline the mechanisms involved in B and T cell activation.
64. Describe normal lymph node morphology and discuss the function of its various compartments and constituent cells.
65. Outline the most common causes of reactive lymphadenopathy.
66. Describe the clinical signs and symptoms, diagnosis, differential diagnosis and treatment of Infectious Mononucleosis (IM).
67. Describe the late complications of IM.
68. Define the term lymphoma.
69. Outline the clinical manifestations and investigation of a patient with lymphoma.
70. Construct a simplified classification of Non-Hodgkin's lymphoma based on the cell size, cell type, pattern of growth and grade of malignancy.
71. Name the characteristic chromosomal translocation for each type of Non-Hodgkin's lymphoma and explain its mechanism of action.
72. Give the classification of Hodgkin's lymphoma.
73. Describe the staging of lymphoma and list the criteria used for staging.
74. Discuss the pathology of lymphoma including Hodgkin's and the most common types of non-Hodgkin's lymphoma.
75. Describe the differences between lymphoma and chronic leukaemia.
76. Describe the peripheral blood findings in Chronic Lymphocytic Leukaemia (CLL) and hairy cell leukaemia.
77. Describe the approach to the diagnosis of lymphomas as outlined by the World Health Organization classification.
78. Explain the importance of PET scan in the diagnosis and treatment of Hodgkin's and non-Hodgkin's lymphomas.
79. Discuss the most commonly occurring B cell lymphoma, including epidemiology, clinical

presentation, pathophysiology, lymph node histologic features, peripheral blood or bone marrow findings, and diagnostic test results.

80. Describe the approach followed for the management and treatment of lymphoma.

Week 5

Lobs covered during lectures and tutorials:

81. Describe the function of T cells.
82. Describe the clinical features and prognosis of peripheral T cell lymphoma.
83. Describe the likely clinical symptoms and signs, of cutaneous T cell lymphomas, Mycosis, Fungoides and Sezary Syndrome.
84. Outline the most frequent causes of splenomegaly.
85. Define hypersplenism.
86. Describe indications of splenectomy and explain the correct management before and after operation (antibiotics and vaccinations).
87. Describe the structure and function of immunoglobulins.
88. Define the term paraproteinaemia.
89. Explain the pathology and clinical manifestations of myeloma
90. Describe the biochemical and haematological abnormalities common in myeloma and their significance.
91. Outline the investigation and staging for myeloma.
92. Outline the diagnosis of multiple myeloma based on guidelines for myeloma.
93. Distinguish myeloma from benign paraproteinaemia.
94. Define MGUS and smoldering Multiple Myeloma.
95. Outline the complications of myelomas.
96. Discuss the management of myelomas.
97. Define solitary plasmacytoma.
98. Define Lymphoplasmacytic lymphoma (Macrogolulinaemia waldenstrom) and describe its clinical manifestation.

Week 6

Lobs covered during lectures and tutorials:

99. Describe the ABO and Rh blood groups.
100. Recognise the importance of the Blood Transfusion Service and describe the blood donor screening criteria.
101. Describe the precautions and testing that takes place to donated blood.
102. Identify the various blood components available for transfusion and their clinical indications.
103. Discuss the ward procedures required for safe blood transfusion practice.
104. Discuss the risks associated with transfusion and how these may be minimised.
105. Describe the principles of cross-matching including antiglobulin test.
106. List the indications and contraindications for transfusion of blood and blood components.

107. Describe the genetic and pathological basis of transfusion reactions.
108. Describe and compare TRALI (Transfusion Related Acute Lung Injury) and TACO (Transfusion Associated Circulatory Overload).
109. Develop a plan to investigate and manage a patient suspected of receiving an incompatible transfusion.
110. Describe the most important blood groups and their associated antibodies and antigens and their clinical importance.
111. Describe and explain the risks, adverse effects, interactions and monitoring when using: whole blood; packed red cells; platelet concentrate; fresh frozen plasma; cryoprecipitate; human albumin solution; clotting factor concentrates; immunoglobulins.
112. Describe sign, symptoms and management of Bruton disease x-linked Agammaglobulinamia (B cell deficiency).
113. Describe signs, symptoms and management of Di George syndrome (T-cell deficiency).
114. Describe signs and symptoms of severe combined immunodeficiency (B and T cell deficiency).
115. Describe granulomatous disease (Neutrophil defect).
116. Define bone marrow transplantation, peripheral stem cell transplantation and transplantation from cord blood.
117. Define autologous and allogeneic bone marrow transplantation.
118. Describe the indications for allogeneic bone marrow transplantation.
119. Describe the complications of bone marrow transplantation. Explain the concept of the graft versus leukaemia/lymphoma (GVL) and graft versus host disease (GVHD).
120. Outline the most frequent diseases that can be treated with autologous bone marrow transplantation.

Week 7

Lobs covered during lectures and tutorials:

121. Describe the basic structure and function of the circulating leucocytes.
122. Outline the proliferation and differentiation pathways of the different white blood cell types.
123. Explain the common causes of increases and decreases in the number of the different leucocytes.
124. Define neutropenia and describe its causes (congenital and secondary) and the consequences of this condition.
125. Describe the algorithm for the evaluation and management of neutropenia. Describe the management of a patient with neutropenia on the ward.
126. Define leucocytosis and leukemoid reaction and compare leukemoid reaction with leukaemia.
127. Describe the nature of the malignant process and the concept of clonality; relate this to haematological malignancy – abnormal growth, differentiation and apoptosis.
128. Define leukaemia and classify leukaemia into acute (AML and ALL) and chronic (CML and CLL) based on clinical and laboratory findings.

129. Compare and contrast the main differences between acute and chronic leukaemia.
130. Describe the classification of Acute Myeloblastic Leukaemia based on FAB and WHO classifications.
131. Describe the most important and common chromosomal abnormalities occurring in each type of leukaemia and explain how each chromosomal abnormality gives rise to pathology.
132. Compare and contrast the main differences between AML and ALL.
133. Explain the clinical features of leukaemia.
134. Describe the diagnostic pathway required to confirm the diagnosis of leukaemia and describe the prognostic factors that influence the treatment pathway.
135. Describe the clinical features and the prognostic factors of ALL.
136. Outline the basic principles of the management and treatment of leukaemia.
137. Describe the adverse effects of the most important drugs used for the treatment of leukaemia.
138. Describe the pathophysiology and management of tumour lysis syndrome.
139. Describe the pathophysiology and management of ATRA syndrome.

Week 8

Lobs covered during lectures and tutorials:

140. Compare and contrast the concept of myelodysplasia and myeloproliferative disorder.
141. Define myelodysplasia and describe its etiology, pathogenesis and clinical signs and symptoms.
142. Describe the morphological disturbances in the red blood cells, white blood cells and platelets of Myelodysplastic Syndrome and compare them to normal red blood cells, white blood cells and platelets respectively.
143. Classify Myelodysplastic syndromes based on the severity of the disease and explain their course.
144. Describe the treatment of Myelodysplastic syndromes.
145. Name the 4 myeloproliferative disorders and explain the relationship between them.
146. Explain the pathophysiology of Chronic Myeloid Leukaemia (CML) and the mechanism of action of BCR–ABL fusion.
147. Describe the clinical manifestation of CML.
148. Describe the treatment, the evaluation of the response to treatment and the course of the CML disease.
149. Outline the basic mechanisms leading to the development of erythrocytosis (polycythaemia).
150. Define polycythaemia, provide the differential diagnosis for this disorder (real/absolute and pseudo/apparent erythrocytosis) and outline its management.
151. Make a diagnosis of polycytaemia from history and investigations.
152. Define essential thrombocytaemia and describe its clinical manifestations and treatment.
153. Outline the causes of secondary thrombocytaemia.
154. Define myelofibrosis and explain the pathophysiology of the production of fibrosis.
155. Describe the treatment in myelofibrosis.

Week 9

Lobs covered during lectures and tutorials:

156. Describe the normal platelet structure and function (granules, surface membrane glycoproteins).
157. Explain the common causes of thrombocytopenia.
158. Describe the signs and symptoms of a patient with thrombocytopenia.
159. Outline the investigation and management of immune thrombocytopenia.
160. Give examples of drugs that inhibit platelet function, explain their mechanism of action and explain their indications.
161. Define the process of haemostasis.
162. Describe the key elements of the haemostatic mechanism (primary and secondary haemostasis). Outline the cascade of coagulation and explain the function of each coagulation factor.
163. Describe the relationships among platelet function, von Willebrand factor, fibrinogen and explain their impact on haemostasis.
164. Describe the origin and function of each of the tissue and plasma factors necessary for normal coagulation.
165. Explain the role of vitamin K in the production and function of the prothrombin group plasma clotting factors.
166. Explain the role of the liver in the synthesis of clotting factors.
167. Describe six roles of thrombin in haemostasis.
168. Explain how a balance is maintained between the opposing mechanisms of coagulation (coagulation and fibrinolysis)
169. Outline how the natural inhibitors, tissue factor pathway, Antithrombin III, protein C and S regulate the coagulation and prevent thrombosis.
170. Describe the fibrinolytic pathway, its regulators and its products.
171. Distinguish between signs and symptoms of primary haemostasis defects and secondary haemostasis (plasma coagulation defect).
172. Describe the screening test of haemostasis and list principal causes of an abnormal result.
173. Describe the clinical features and laboratory investigation for Von Willebrand disease.
174. Describe signs and symptoms in congenital diseases with platelet dysfunction (Bernard Soulier and Thrombasthenia Glanzmann).
175. Describe the causes of hypofibrinogenaemia and explain the mechanism of action.
176. Describe the clinical features and laboratory investigations and management of Haemophilia.
177. Describe the coagulation disturbances in liver disease.

Week 10

Lobs covered during lectures and tutorials:

178. Define Virchow's triad and explain its significance in thrombosis.
179. Compare arterial and venous thrombus and distinguish between venous and arterial thrombosis.
180. Outline the non-disease risk factors for arterial and venous thrombosis.
181. Outline the diseases with thrombotic risk components.
182. Describe the mechanisms leading to Venous Thrombo-Embolism (VTE).
183. Define pulmonary embolism and describe its signs, symptoms investigation and management.
184. Define thrombophilia and describe different factors of genetic and acquired thrombophilia.
185. Describe the circumstances during which thrombophilia might lead to thrombosis.
186. Describe antiphospholipid syndrome.
187. Describe heparin induced thrombocytopenia (HIT).
188. Describe the treatment of HIT.
189. Describe Disseminated Intravascular Coagulation (DIC) and explain its pathophysiology and clinical manifestation.
190. Outline the most frequent causes of DIC and describe treatment pathways.
191. Describe the value of quantitative D-Dimer assay and explain the difference between FDPs and D-Dimer.
192. Describe fibrinolytic treatment and its indications.

Week 11

Lobs covered during lectures and tutorials:

193. Compare the mechanism of action, half-life and indications of heparin to those of low molecular weight heparin (LMWH).
194. Describe the mechanism of action and the indications of warfarin.
195. Explain how warfarin treatment is influenced from diet and different drugs.
196. Explain post warfarin treatment skin necrosis.
197. Explain how the dosage of warfarin can be monitored in relation to other medications and describe possible cross-reacting drugs.
198. Compare the treatment with heparin to that of warfarin.
199. Describe the management of a bleeding due to anticoagulation therapy with warfarin and a high INR.
200. Explain how the anticoagulant effect of heparin can be monitored.
201. Name the most important Novel Anti-Coagulants (NOACs) and describe their mechanism of action, indications and contraindications.
202. Compare the mechanisms of action, metabolism and elimination of different NOACs.
203. Describe anticoagulant related bleedings and describe their management.

Week 12

Lobs covered during lectures and tutorials:

204. Describe the correct sequence by which haematopoiesis occurs embryonically in different organs.
205. Describe the physiological changes of the RBC, the MCV and haemoglobin and explain the switch from fetal to adult haemoglobin.
206. Describe the physiological changes of WBCs from fetal to adult.
207. Describe the physiological changes of coagulation factors from fetal to adult.
208. Describe the haemorrhagic disease of new born (Vitamin K deficiency at birth) and explain its management.
209. Describe the different pathological causes of anaemia in the newborn.
210. Describe the "Haemolytic disease of the new born"(HDN)and outline the recommendations for administration of Anti D.
211. Describe haemolytic anaemias in the newborn.
212. Outline the indications and explain the exchange transfusion in the neonate.
213. Outline the diseases that cause anaemia due to decreased production of RBC, inherited and acquired.
214. Describe Fanconi Anaemia. Outline the difference between Fanconi anaemia and Fanconi syndrome
215. Describe the acute ITP in children and its management.
216. Describe normal physiological changes of the blood count in pregnancy.
217. Define the conditions associated with thrombocytopenia in pregnancy.
218. Describe how pregnancy changes the haemostatic system.
219. Identify the risk factors of thromboembolic disease in pregnancy.
220. Describe the issues associated with pregnancy in sickle cell disease.

Course Contents:

- Production of erythrocytes and haemoglobin synthesis.
- Microcytic and macrocytic anaemia.
- Bone marrow failure and haemoglobinopathies.
- Normocytic anaemia, anaemia of chronic disease and haemolytic anaemia
- Lymph node morphology.
- Reactive lymphadenopathies.
- Hodgkin's and Non-Hodgkin's Lymphoma, CLL, Hairy cell Leukaemia.
- Mature T-cell lymphoma, Primary Infections of lymphoid tissue, Splenomegaly Lymphoplasmacytic Lymphoma, MGUS and Myeloma.
- Primary Immunodeficiencies, Bone Marrow transplantation, Blood transfusions.
- Leucopoiesis, Leucocytosis and Neutropenia, Leukaemia, chemotherapeutic agents.
- Myelodysplastic syndromes, Myeloproliferative disorders, Secondar Polycytaemia and Thrombocytaemia.
- Production and function of Platelets. Normal hemostasis (Coagulation and

fibrinolysis).

- Congenital and acquired Hypocoagulable conditions
- Arterial and venous Thrombosis, Thromboembolism, Thrombophilia.
- Antiphospholipid syndrome.
- Heparin induced thrombocytopenia, DIC, TTP.
- Heparin, LMWH, Warfarin, NOACS Anticoagulant treatment guidelines, Anticoagulant treatment related bleedings, management.
- Embryonic development, perinatal changes, paediatric haematology, haematological aspects of pregnancy, Patient with haematology disease.

Learning Activities and Teaching Methods:

Lectures, Tutorials.

Assessment Methods:

Midterm Exam (35%) and Final Exam (65%). Assessment is by Single Best Answer MCQs (SBAs) and Short Answer Questions (SAQs).

Required Textbooks/Reading:

Authors	Title	Publisher	Year	ISBN
Hoffbrand, A. V	Essential haematology	Wiley-Blackwell	2015	9781118408674

Recommended Textbooks/Reading:

Authors	Title	Publisher	Year	ISBN
Chris R.S. Hatton et al.	Lecture notes on haematology	Wiley-Blackwell	2013	9780470673591
Mehta, Atul B.	Haematology at a glance	Wiley-Blackwell	2014	9781119969228