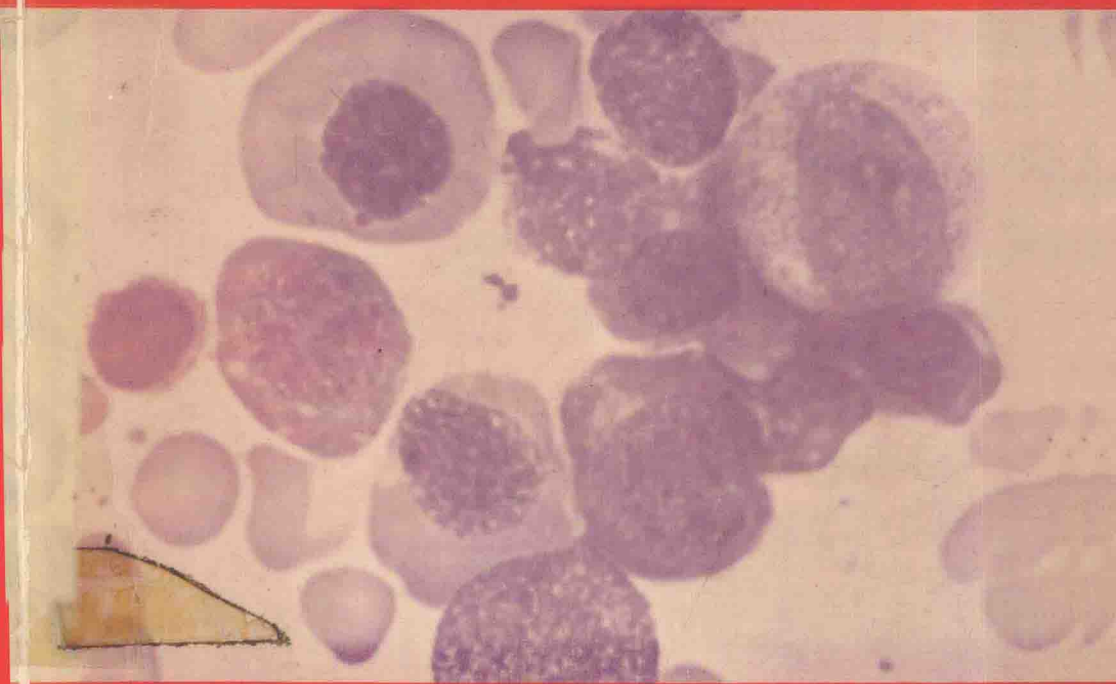
A. H. GOLDSTONE

EXAMINATION HAEMATOLOGY



Examination Haematology

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BLOOD COAGULATION

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Examination Haematology

for my family

Preface

This little book is intended for those preparing to sit the examinations for Membership of the Royal College of Physicians of the United Kingdom. In addition, I hope it will be of use to candidates for the Primary and Final Examinations of the Royal College of Pathologists, for the American Boards Examinations and ECFMG. It should also be of interest to those working towards HNC in Medical Laboratory Subjects, the Special Examination in Haematology for the FIMLS and not least the final year undergraduate medical examinations.

The book is presented in five separate parts. The first part provides multiple choice questions in which the answers are explained rather than simply stated. The second and third parts are presented as questions for the candidate on the interpretation of haematological data and photographs, and I hope these will be particularly suitable in preparing for the Part II MRCP.

For Part 4, Dr B. A. McVerry has prepared case histories in blood coagulation which provide a spectrum of all the common disorders, described and explained in the light of the laboratory and clinical findings. Lastly, I have included a series of review articles on haematological topics based on 'Haematology Seminars' which I wrote originally for *Hospital Update* (Update Publications Ltd). I hope that these will be helpful in preparing for essay type questions and vivas.

I would like to thank Dr J. D. M. Richards for helpful suggestions. *Hospital Update* and my co-authors have kindly granted permission to use material from the 'Haematology Seminars'.

Undoubtedly there are omissions from the text but it makes no claim to comprehensiveness, only to be a useful aid for those faced with examinations. For the structure and character of the book I am myself entirely responsible.

A. H. Goldstone

Contents

PART 1

Multiple Choice Questions

Questions

1. A huge spleen may be found in all of the following except:

   (a) kala-azar (b) Gaucher's disease (c) ITP (idiopathic thrombocytopenic purpura) (d) CLL (chronic lymphocytic leukaemia).

2. An increase in basophils may be seen in all of the following except:

   (a) CML (chronic myeloid leukaemia) (b) myelofibrosis (c) urticaria pigmentosa (d) ulcerative colitis (e) secondary polycythaemia.

3. All of the following are X-linked disorders except:

   (a) hereditary haemorrhagic telangiectasia (b) haemophilia (c) Christmas disease (d) Swiss-type agammaglobulinaemia (e) G6PD (glucose-6-phosphate dehydrogenase) deficiency.

4. Myeloid cells capable of mitotic division include:

   (a) myeloblasts (b) promyelocytes (c) myelocytes (d) metamyelocytes.

5. Administration of steroids causes:

   (a) eosinophilia (b) eosinopenia (c) neutropenia (d) neutrophilia.

6. Female carrier of haemophilia marries normal male:

   (a) all daughters are carriers (b) a daughter with Turner's syndrome could be haemophiliac (c) all sons are haemophiliac (d) half the daughters are carriers (e) half the sons are haemophiliacs.

7. Normal female marries haemophiliac:

   (a) all daughters are carriers (b) half the daughters are carriers (c) half the sons are haemophiliacs (d) all sons are haemophiliacs (e) all sons are normal.

8. All of the following are inherited as autosomal recessive except:

   (a) pyruvate kinase deficiency (b) hexokinase deficiency (c) triose phosphate isomerase deficiency (d) phosphoglycerate kinase deficiency (e) glucose phosphate isomerase deficiency.

9. The following cause secondary polycythaemia:

   (a) uterine leiomyoma (b) hydronephrosis (c) carboxyhaemoglobinaemia (d) renal cyst (e) hepatoma (f) Leishmania.

10. Howell—Jolly bodies in the blood film:

(a) appear after splenectomy (b) are seen in sickle cell disease (c) are eosinophilic (d) are often multiple (e) require supravital staining for recognition.

11. The following commonly cause hypochromic anaemia with or without microcytosis:

(a) rheumatoid arthritis (b) β-thalassaemia major (c) β-thalassaemia minor (d) hereditary sex-linked sideroblastic anaemia (e) sickle cell disease.

12. Macrocytic non-megaloblastic anaemia may be found in:

(a) liver disease (b) hypothyroidism (c) aplastic anaemia (d) a strict vegetarian (e) hypopituitarism.

13. The following infections can cause haemolysis:

(a) malaria (b) *Bartonella* (c) *Aspergillus* (d) *Clostridium welchii* (e) *Mycoplasma pneumoniae.*

14. The following are complications of PNH (paroxysmal nocturnal haemoglobinuria):

(a) pancytopenia (b) hypoplasia (c) sideroblastic change (d) iron deficiency anaemia.

15. Pyruvate kinase deficiency:

(a) is inherited as an autosomal dominant (b) splenectomy often helps the anaemia (c) the reticulocyte count can reach 70 per cent after splenectomy (d) patients are usually Northern European (e) penicillamine helps the anaemia.

16. In autoimmune haemolytic anaemia:

(a) Rhesus-negative blood should always be used for transfusion (b) splenectomy may not help (c) immunosuppressives are the treatment of choice (d) splenomegaly is always present (e) the red cells are always coated with complement (f) the red cells are never coated with complement (g) patients cannot be transfused because all blood will be incompatible.

17. Match the following antibodies with disease states:

(a) anti-P	(1) antibody seen in *Mycoplasma pneumoniae* infection
(b) anti-I	(2) Donath—Landsteiner antibody in PCH (paroxysmal cold haemoglobinuria)
(c) anti-i	
(d) ante-ē	(3) methyldopa haemolytic anaemia
	(4) antibody in infectious mononucleosis

18. During pregnancy:

(a) red cell mass increases (b) vitamin B_{12} deficiency is common in Britain (c) the commonest form of anaemia is folate-deficient megaloblastic anaemia (d) the fetus invariably becomes iron deficient if the mother does.

19. In the anaemia of liver disease:

(a) macrocytosis is usually due to B_{12} deficiency (b) macrocytosis is often seen without B_{12} or folate deficiency (c) pancytopenia may occur (d) acanthocytosis may be reversible (e) haemolysis often contributes.

20. The following are implicated in the anaemia associated with renal failure:

(a) haemolysis (b) sideroblastic change (c) blood loss (d) ineffective erythropoiesis (e) microangiopathy.

21. In polycythaemia vera:

(a) the red cell mass is normal (b) leucocytosis is unusual (c) the spleen is usually palpable (d) thrombocytosis is a rare finding (e) duodenal ulcer occurs quite commonly (f) the haemoglobin can be normal if iron deficiency is also present.

22. Complications of polycythaemia vera include:

(a) acute myeloid leukaemia (b) acute monocytic leukaemia (c) thrombosis (d) haemorrhage (e) lymphoma (f) myelofibrosis.

23. Thrombocytopenia is seen in:

(a) severe iron deficiency (b) untreated polycythaemia vera (c) severe untreated PA (pernicious anaemia) (d) PNH (e) Glanzmann's disease (f) von Willebrand's disease.

24. Circulating anticoagulants:

(a) usually occur in haemophiliacs without treatment (b) occur in pregnancy (c) occur with penicillin (d) occur after barbiturates (e) may develop in otherwise normal people.

25. In von Willebrand's disease:

(a) the bleeding time is usually normal (b) the bleeding time is short (c) factor VIII clotting levels are often low (d) women are affected more severely than men (e) platelet aggregation is often abnormal.

26. In von Willebrand's disease:

(a) transfusion of haemophiliac plasma can raise the factor VIII level (b) transfusion of von Willebrand's plasma to a haemophiliac can produce new factor VIII synthesis (c) haemarthrosis is commoner than in haemophilia (d) bleeding time can be corrected by plasma infusion.

27. Splenectomy in ITP:

(a) is indicated if a trial of steroids has failed (b) is almost always successful in producing a remission (c) may fail due to very high antibody levels on the platelets (d) may fail because of hepatic sequestration of platelets.

28. In Henoch—Schönlein disease:

(a) Hess's test may be positive (b) thrombocytopenia is frequently seen (c) fulminating glomerulonephritis is common (d) cirrhosis is a common complication.

29. Neonatal thrombocytopenia:

(a) occurs in the majority of cases if mother has ITP (b) can occur from isoimmunisation in normal mothers (c) steroids are usually indicated (d) should be treated always by splenectomy.

30. In haemarthrosis in haemophilia:

(a) bed rest, ice bags and compression bandages are the most important aspects of therapy (b) joint aspiration should be avoided if possible (c) fresh frozen plasma is of no benefit (d) it is always necessary to give factor VIII twice daily (e) aspirin is a useful analgesic.

31. In DIC (disseminated intravascular coagulation):

(a) thrombocytopenia is rare (b) factors V and VIII are among the first to be consumed (c) FDPs (fibrin degradation products) are almost always elevated (d) the FDPs have a coagulant effect.

32. Match the following:

(a) thrombasthenia	(1) abnormal ADP-induced platelet aggregation
(b) Bernard—Soulier disease	(2) abnormal platelet glycolysis
(c) Wiskott—Aldrich syndrome	(3) giant platelets

33. True or false? In haemophilia:

(a) the factor IX assay is often abnormal (b) the PTT (partial thromboplastin time) can be normal (c) the PT (prothrombin time) is usually abnormal (d) the bleeding time is usually prolonged (e) inhibitors are usually seen after 20 years treatment with cryoprecipitate.

34. In deficiency of vitamin K-dependent factors, indicate whether the following is true or false:

(a) i.v. vitamin K_1 is useful in an emergency (b) 100 mg or more is the usual dose of vitamin K_1 i.v. (c) fresh, frozen plasma is no use for treatment of vitamin K deficiency (d) vitamin K_1 is water soluble (e) vitamin K_1 is recommended for treatment but not prophylaxis of haemorrhagic disease of the newborn.

35. True or false?

(a) bleeding in haemophilia is usually more severe than that of Christmas disease (b) factor IX is concerned with the intrinsic pathway of coagulation (c) the prothrombin time is a good screening test for Christmas disease (d) factor V is depressed by oral anticoagulants.

36. True or false?

(a) aspirin is a common cause of thrombocytopenic purpura (b) aspirin blocks the secondary wave of platelet aggregation in vitro (c) aspirin prolongs the bleeding time in patients with von Willebrand's disease (d) ingestion of one tablet of aspirin can cause abnormal laboratory tests of platelet function for several days.

37. Hereditary haemorrhagic telangiectasia:

(a) is inherited as an autosomal dominant (b) is inherited as an autosomal recessive (c) blood vessels have inadequate smooth muscle and elastic tissue (d) arterioles are primarily involved (e) pulmonary arteriovenous fistulas occur.

38. Match the following:

(a) Swiss-type lymphopenic agammaglobulinaemia	(1) defective development of thymus and parathyroid
(b) intestinal lymphangiectasia	(2) low IgA and reduced thymic function
(c) DiGeorge syndrome	(3) loss of thymic lymphocytes and immunoglobulins in gut
(d) ataxia telangiectasia	(4) defective thymic and bursal function

39. In CLL:

(a) immunoglobulins are usually elevated (b) many patients die of chest infection (c) cell-mediated immunity is preserved better than in stage IV Hodgkin's disease (d) platelet factor III function is usually impaired (e) haemolytic disease is usually due to development of cold-type antibodies.

40. Antibodies capable of fixing complement are:

(a) IgG_1 (b) IgG_2 (c) IgG_3 (d) IgG_4.

41. Prophylactic anti-D should be given:

(a) to all Rhesus-negative mothers after delivery (b) within 72 hours of delivery (c) to all unimmunised Rhesus-negative mothers who have Rhesus-positive children (d) to all unimmunised Rhesus-negative mothers who have abortions (e) to immunised Rhesus-negative mothers at delivery (f) by i.m. injection only at all times.

42. Advantages of using frozen red cells for transfusion are:

(a) ready availability (b) virtual absence of white cells (c) decreased risk of hepatitis (d) much lower concentration of free potassium than bank blood (e) cheapness of cost.

43. Products which will significantly raise the factor VIII levels of severe haemophiliacs include:

(a) bank blood (b) cryoprecipitate (c) plasma protein fraction (d) porcine factor VIII.

44. A positive direct Coombs' test is almost always found in the following:

(a) cold agglutinin disease (b) Rhesus haemolytic disease of the newborn (c) PNH (d) G6PD deficiency (e) ABO haemolytic disease of the newborn.

45. Rules of inheritance demand:

(a) a blood group A or B father cannot have an O child (b) no blood group antigens not present in one or both parents can appear in normal circumstances in the child (c) X-linked characters possessed by the father will be present in the sons (d) there is a 1 in 4 chance of having an identical HLA type to sibling.

46. Anticoagulants which can be used safely for transfusion include:

(a) oxalates (b) heparin (c) acid citrate dextrose (ACD) (d) sequestrene (e) citrate phosphate dextrose (CPD).

47. Patients with hereditary angioneurotic oedema have:

(a) reduced C1 inhibitor (b) raised C4 and C2 during attacks (c) autosomal dominant disease (d) autosomal recessive disease (e) beneficial clinical response to ε-amino-caproic acid (EACA).

48. The following drugs cause autoimmune haemolytic anaemia (AIHA):

(a) chlorpromazine (b) mefenamic acid (c) Septrin (d) L-dopa.

49. G6PD deficiency:

(a) is more common in men than women (b) may lead to haemolysis after taking oxidant drugs (c) may be a cause of neonatal jaundice (d) produces characteristically a spherocytic haemolytic anaemia (e) occurs amongst Sephardic Jews.

50. The following agents can be useful in the treatment of aplastic anaemia:

(a) marrow transplantation (b) androgenic steroids (c) daunorubicin (d) cyclophosphamide.

51. Which is the least likely primary cause of iron deficiency anaemia in British adults:

(a) menorrhagia (b) multiple pregnancies (c) low dietary iron in a patient under 50 years of age (d) hiatus hernia (e) carcinoma of colon.

52. In untreated pernicious anaemia (PA) the following occur:

(a) increased serum iron (b) decreased LDH (lactate dehydrogenase) (c) raised bilirubin (d) decreased urinary methylmalonic acid (e) constipation.

53. Match the following:

(a) cyclophosphamide	(1) hyperpigmentation
(b) vincristine	(2) haemorrhagic cystitis
(c) methotrexate	(3) neuropathy
(d) busulphan	(4) oral ulceration

54. Burkitt's lymphoma:

(a) occurs only in malarial areas of Africa (b) is characterised by a 'starry sky' histological appearance (c) is derived from 'T'-lymphocytes (d) is not responsive to cyclophosphamide (e) is characterised by vacuolated cells.

55. Monoclonal gammopathy occurs in the following:

(a) CLL (b) CML (c) ALL (acute lymphoblastic leukaemia) (d) CHAD (cold haemagglutinin disease) (e) AML (acute myeloid leukaemia).

56. In hairy-cell disease:

(a) males are affected much more commonly than females (b) the cells have surface immunoglobulin (c) widespread lymphadenopathy is characteristic (d) steroids are contraindicated.

57. Thrombotic thrombocytopenic purpura (TTP) is usually characterised by:

(a) microangiopathic haemolytic anaemia (b) jaundice (c) changing neurological signs (d) positive Coombs' test (e) excellent response to heparin in virtually all cases.

Answers

1. Except ITP.

   It is a commonly held misconception that the spleen is quite large in chronic ITP. This is not so. It is normally impalpable but may sometimes be just palpable on deep inspiration. Profound splenomegaly argues against ITP as the primary diagnosis of thrombocytopenia; with splenic sequestration of platelets, SLE, lymphoma, and sarcoidosis should be excluded.

   Marked splenomegaly is common in kala-azar and the parasite *Leishmania donovani* can be demonstrated in the spleen by splenic puncture. In Gaucher's disease massive splenomegaly may be a prime clinical feature and the spleen is packed full of storage histocytes containing various glycolipids of the sphingolipid category, principally glucocerebrosides. The fundamental biochemical defect is a genetically determined profound reduction of the glucocerebroside-clearing enzyme. In CLL a huge spleen due to infiltration by the lymphoid cells of the disease is not uncommon.

2. Except secondary polycythaemia and urticaria pigmentosa.

   Basophilia is commonly seen in the myeloproliferative disorders such as chronic myeloid leukaemia and myelofibrosis. Basophil numbers often rise when chronic myeloid leukaemia transforms to a more accelerated or 'blastic' phase. In CML at presentation basophilia in excess of 15 or 20 per cent is generally regarded as a poor prognostic sign. Although basophilia (i.e. count $>0.15 \times 10^9$ cells/l) occurs in polycythaemia vera it does not occur in secondary polycythaemia. Basophils may also be increased in chronic ulcerative colitis but the circulating mast cells seen in the blood in urticaria pigmentosa can be readily differentiated from basophils.

3. Except hereditary haemorrhagic telangiectasia.

   This condition is inherited as an autosomal dominant trait and in its homozygous state may be lethal. The sexes are affected equally and the telangiectases appear throughout life and are quite florid in the fourth and fifth decade. All the other disorders: haemophilia, Christmas disease, Swiss-type agammaglobulinaemia and G6PD deficiency are inherited as X-linked disorders.

4. (a) YES (b) YES (c) YES (d) NO

   Myeloblasts are capable of mitotic division. This cell represents the earliest identifiable precursor of the mature granulocyte and has a large nucleus with two to five nucleoli and scanty basophilic cytoplasm.