Content Specifications are intended to guide diplomates in selecting their MOC Part II and Part IV activities. They are not intended to be study guides for the MOC Part III exam, although the exams may include some questions on topics and references included in the Content Specifications. Please refer to the MOC Study Guides for exam preparation.

New Validated Practical Knowledge

These content specifications provide a list of all the areas covered in hematology pathology. A listing of selected areas of newer validated knowledge and some older critical areas and associated references follows. The references are not complete, some contain more detailed information than is required for this examination and it is not our intention that candidates necessarily read every one. A good general reference for neoplastic hematopathology remains the WHO monograph on tumours of haematopoietic and lymphoid tissues, although it must be supplemented by some of the newer references.¹

Basic Methodology and Test Armamentarium

- Flow cytometric analysis, exclusion of “doublets”²
- Newer analysis technologies with expanding number of fluorochromes being used in flow cytometry (identification and definition of composite phenotype of abnormal populations)²
- Importance of using broad set of IGH and Kappa gene primers (eg, BIOMED-2) in assessment of B- cell clonality by PCR³,⁴
- Advantages and disadvantages of breakapart versus dual fusion cytogenetic FISH probes³
- General knowledge about array comparative genomic hybridization (CGH)/single nucleotide polymorphism(SNP) arrays (identification of copy number abnormalities and with SNP, loss of heterozygosity)⁵,⁷
- General knowledge about next generation sequencing and its utility⁸,⁹

I. Hemostasis and Thrombosis

Coagulation Testing
- D-dimer and diagnosis of venous thromboembolism
- Verifying correct INR and INR calibration
- Viscoelastometry
Qualitative Factor XIII assays
Platelet Disorders
  Platelet function instrumentation
    PFA-100
    Lumiaggregation
Coagulation Disorders
  Von Willebrand classification
  New assays for von Willebrand disease
    Collagen binding assay
    VWF functional immunoassays
Platelet Disorders
  Thrombotic thrombocytopenic purpura and ADAMTS13 assays
Thrombophilic Disorders
  Heparin induced thrombocytopenia diagnosis
  ISTH guidelines for lupus anticoagulant testing
  Laboratory diagnosis of antiphospholipid antibodies
Anti-thrombotic Drugs
  Direct thrombin inhibitor drugs
    Argatroban
    Bivalirudin
  Laboratory testing and pharmacogenomics of clopidogrel resistance
    CYP2C19
  The laboratory and the new oral anticoagulants
    Rivaroxaban
    Apixaban
    Dabigatran
  Indirect Xa inhibitors
    Fondaparinux

II. Leukocyte Disorders, B-lymphoid
Newer mutational abnormalities in B-cell neoplasms
  MYD88 – lymphoplasmacytic lymphoma
  BRAF V600E – hairy cell leukemia (and Langerhans cell histiocytosis)
  NOTCH1, SF3B1 – varied B-cell neoplasms including CLL/SLL, MCL
  NOTCH2 – splenic marginal zone lymphoma
  IDH3 & TCF3 – Burkitt lymphoma
Newer cytogenetic abnormalities in B-cell neoplasms
  IRF4 translocations in subset of pediatric follicular/other B-cell lymphomas
Newer immunohistochemical stains or newer recognized patterns of reactivity of stains
used in the assessment of B-cell neoplasms
  LEF1 – utility in diagnosing CLL/SLL
  MYC – utility in Burkitt lymphoma and other large B-cell lymphomas
SOX11 – utility in diagnosis of mantle cell lymphoma and in identification of MCL subsets
BRAF V600E – utility in hairy cell leukemia
CD5 – presence on normal mantle zone cells
IgD – use of mantle zone B-cell staining as a tool to assess architectural features in selected B-cell proliferations

Newer antibodies being used with flow cytometry
CD49d – prognostication in CLL/SLL
CD123 – (blastoid plasmacytoid dendritic cells, basophils), hairy cell leukemia

B-cell lymphomas that are considered very indolent or of uncertain/undetermined clinical significance
Clinical monoclonal B-cell lymphocytosis
Follicular lymphoma/neoplasia, in situ; FL-like B-cells of uncertain/undetermined significance
Mantle cell lymphoma neoplasia, in situ; MCL-like B-cells of uncertain/undetermined significance and non-nodal type of “indolent” MCL
Pediatric-type follicular lymphoma and subtypes

Concept of histologically aggressive CLL/SLL
Follicular lymphomas with unusual phenotype/cytogenetic findings (eg, CD10-, no BCL2 translocation)

B-cell lymphomas that are considered extra aggressive
Importance of MYC translocations, especially with BCL2 or BCL6 translocations (“double hit” lymphomas)
B-cell lymphomas with MYC and BCL2 protein expression (“double expressor” large B-cell lymphomas)
Recognition of “blastoid” diffuse large B-cell lymphomas

Current approach to cutaneous B-cell lymphomas
Unique features of cutaneous marginal zone lymphoma
Importance of/methods to distinguish germinal center from non-germinal/ABC type DLBCL
Prognostic and therapeutic implications
Immunohistochemical algorithms, gene expression arrays
EBV+ B-cell proliferations that may mimic an aggressive lymphoma such as EBV+ DLBCL of the elderly
Gray zones between classical Hodgkin lymphoma and non-Hodgkin lymphomas
Concept of lineage plasticity (eg, development of histiocytic/dendritic neoplasms clonally related to B-cell neoplasms)

III. Plasma Cell Neoplasms, Paraprotein Disorders and Amyloidosis
Current criteria for plasma cell myeloma
Utility of mass spectrometry to characterize types of amyloid

IV. Myeloid Neoplasms

Myeloid
- Myeloproliferative Neoplasms (MPN)
- Chronic myelogenous leukemia (CML)
- Primary myelofibrosis
- Essential thrombocytemia
- Polycythemia vera
- Genetics of MPN (JAK2, MPL, Calreticulin, KIT)
- Morphologic features of non-CML MPNs

MPN variants
- Chronic neutrophilic leukemia
- Atypical CML
- Chronic eosinophilic leukemia
- Mastocytosis
- Chronic neutrophilic leukemia and CSF3R mutations
- Mastocytosis and KIT mutations
- Mast cells in mastocytosis and myeloid/lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB, FGFR1

Myeloid and Lymphoid Neoplasms with Eosinophilia and Abnormalities of PDGFRA, PDGFRB or FGFR1

Myelodysplastic/Myeloproliferative Neoplasms
- Genetics (JAK2, calreticulin)
- Refractory anemia with ring sideroblasts and marked thrombocytosis

Myelodysplastic Syndromes
- Revised IPSS
- Refractory cytopenia with unilineage dysplasia
- Childhood myelodysplastic syndromes

Acute Myeloid Leukemia (AML) and Related Precursor Neoplasms
- Myeloid proliferations related to Down syndrome
- Blastic plasmacytoid dendritic cell neoplasms
- Criteria (expanded) for AML with myelodysplasia-related changes
- Categories with new balanced translocations, inversions, or mutations
- NPM1, CEBPA, FLT-3 and other mutations as prognostic markers

V. Leukocyte Disorders, T-lymphoid

Newer Mutational Abnormalities in T-cell Neoplasms
- ITK/SYK in nodular/follicular T-cell lymphoma, NOS
- DUSP22 (6p25) translocations in systemic ALK negative ALCL, C-ALCL, LyP
- IDH2 and TET2 mutations in AITL
- STAT3 mutations in large granular lymphocyte leukemias
Gene Expression Profiling in TCL
Clustering of distinct TCL and segregation from PTCL, NOS 90
GATA3 and Tbet as prognostic markers in PTCL-NOS90,91

Immunologic classification of TCL
Innate versus adaptive immune response92
The subset differentiation and the classification of helper (CD4+) TCL 93-97
FOXP3 expression in ATLL 98,99

Flow cytometric differentiation of thymocytes vs. T-lymphoblastic leukemia/lymphoma100,101

Newer immunohistochemical stains/ patterns of reactivity/pitfalls in routine stains used in the assessment of T-cell neoplasms
MATK/LSK in type II enteropathy associated TCL 102
Follicular helper T-cell antigens: BCL6, CD279/PD-1, CXCL13, ICOS in diagnosing AITL and primary cutaneous CD4+ small/medium T-cell lymphoma103-105
CD279/PD-1 expression in reactive conditions, MF, and other NK/TCL106-108
Correlation of ALK expression pattern with cytogenetic abnormalities109
ALK expression in non-lymphoid tumors110
Clusterin expression in ALCL, transformed mycosis fungoides, and FDC sarcoma111-113
Gamma-delta T-cell protein expression in extranodal/nodal lymphomas108,114-116

CD20 expression in TCL117
T-cell antigen expression in HL118
CD15 expression in TCL119
Presence of clonal plasma cells in T-cell neoplasms120
TCL-1A expression in T-cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, and B-cell tumors121-123

Early T-cell precursor leukemia124
Anaplastic large cell lymphoma
ALK+ ALCL
Good prognosis is age-related125,126
Variant histology associated with poor prognosis127
CD99 expression in ALCL128
Myeloid antigen expression in ALCL129

ALK- ALCL
ALK- ALCL associated with breast implants130
Newer cytogenetic abnormalities and significance (also see above)131

Follicular helper T-cell lymphoma132
Early lesion of AITL
Enteropathy associated T-cell lymphoma
Importance of separating type I from type II133-135

Mycosis fungoides
Updated diagnostic/staging criteria136
Hypopigmented variant 137,138
Transformation of MF and overlap with C-ALCL137,139
Cutaneous CD30+ lymphoproliferative disorders
Histologic variants of primary cutaneous ALCL
Treatment/prognosis
Rare occurrence of ALK+ primary cutaneous ALCL
ALKL with extensive leg disease
Lymphomatoid papulosis type C vs. primary cutaneous ALCL
Lymphomatoid papulosis, type D vs. CD8+ aggressive epidermotropic TCL
Lymphomatoid papulosis, type E vs. cutaneous NK/TCL nasal type
Benign lymphoid infiltrates with CD30+ large cells
Reactive/indolent clonal processes in the differential diagnosis of cutaneous TCL
Kikuchi-Fujimoto disease
Lupus profundus and subcutaneous panniculitis like T-cell lymphoma
Annular lichenoid dermatitis of youth and hypopigmented MF
Indolent CD8+ proliferation of the ear and other sites
Lymphocytic variant of hypereosinophilic syndrome
Mucocutaneous ulcer vs. cutaneous NK/TCL nasal type
T-cell lymphoma with MALT features
Extranodal non-cutaneous clonal proliferations that are considered indolent or of uncertain/undetermined clinical significance
Indolent cytotoxic T-cell and NK-cell proliferations, gastrointestinal tract

VI. Instrumentation/Methodology
CBC Analyzers
Basic Principles
Instrument Flags
Interferences
Cold agglutinins
EDTA-induced thrombocytopenia
W-G Stain
Trouble-shooting
Heparin effect
Other artifacts
EMA Test by Flow Cytometry
Appropriateness/Limitations of Hemoglobin Testing

VII. Morphology-Appropriate Recognition and Recommendation
Peripheral Blood
Spherocytes
Schistocytes
Hyposplenism
Target cells
Bite cells
Rouleaux
Cold agglutinin
Sickle cells
Hemoglobin C crystals
Hemoglobin S/C disease
Infectious disease
  Malaria
  Babesios
Elliptocytes
Bone Marrow
  Parvovirus
  Megaloblastic anemia

VIII. Anemia
Microcytic Anemia
  Interpretation of tests of iron metabolism
    Iron deficiency anemia
    Anemia of chronic disease
  Thalassemia/Hemoglobinopathies
    Recommendations of appropriate testing
Macrocytic Anemia
  Appropriate work-up and test recommendations
  B12/Folate deficiency – intrinsic factor, homocysteine, MMA
  Liver disease
Hemolytic Anemia
  Interpretation of tests to establish hemolysis
  Recommendations for further testing
  RBC enzymes
    G-G-PD deficiency
    PK deficiency
  RBC membrane disorders – appropriate testing
    Hereditary spherocytosis
    Hereditary elliptocytosis
    Hereditary pyropoikilocytosis
    Autoimmune hemolytic anemia
    Unstable hemoglobins

IX. Hemoglobinopathies/Thalassemias
Recommendation for Appropriate Testing
Clinical Significance/Diagnosis of:
  Alpha thalassemia trait
  Beta thalassemia trait
  Hemoglobin S trait
  Homozygous hemoglobin S
  Hemoglobin C trait
  Homozygous hemoglobin C
Hemoglobin E trait
Homozygous hemoglobin E
Hemoglobin E/Beta zero thalassemia

X. Miscellaneous
Paroxysmal nocturnal hemoglobinuria – appropriate testing/when to order
Erythrocytosis – only appropriate indications for JAK2
Methemoglobinemia – testing to order

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