BUKU PANDUAN

BLOK HEMATOIMUNOLOGI

PENANGGUNG JAWAB BLOK:

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FAKULTAS KEDOKTERAN

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PENDAHULUAN

1. GAMBARAN UMUM BLOK

Blok Hemato-imunologi akan dilaksanakan pada tahun ke-2 semester 4. Waktu pelaksanaan blok ini adalah 6 minggu, yang terdiri atas 5 minggu aktif dan 1 minggu terakhir yang diisi dengan ujian, meliputi ujian praktikum dan ujian akhir blok (UAB), pertengahan blok pada akhir minggu ketiga akan dilaksanakan quiz.

Blok ini terdiri dari 5 modul. Modul pertama akan mendiskusikan tentang sel darah merah. Modul kedua akan mendiskusikan tentang sistem hemostasis, plasma darah dan platelet. Modul ketiga akan mendiskusikan masalah keganasan hematologi, leukosit dan limfoid. Modul ke empat akan membahas tentang hipersensitifitas dan autoimune serta modul terakhir akan membahas tentang imunodefisiensi. Beberapa topik akan ditampikan sebagai skenario untuk meningkatkan pemahaman dalam pemecahan kasus. Dengan memahami blok ini, diharapkan mahasiswa dapat meningkatkan pengetahuannya tentang masalah hemato-imunologi.

Blok ini akan dipelajari dengan menggunakan strategi *Problem Based Learning* (PBL) yang bertujuan memenuhi standar kompetensi dokter Indonesia dengan metode diskusi tutorial menggunakan metode *seven*

jump, kuliah, praktikum, belajar mandiri dan keterampilan klinik (*skills laboratory*).

Kompetensi Blok diambil dari 7 area Kompetensi Konsil Kedokteran Indonesia :

1. Komunikasi efektif
2. Keterampilan klinik dasar
3. Penerapan ilmu biomedis dalam praktek kedokteran
4. Pengelolaan masalah kesehatan secara individu, keluarga dan masyarakat
5. Penggunaan teknologi informasi
6. Mawas diri dan belajar sepanjang hayat
7. Penerapan etik, moral dan profesionalisme serta keselamatan pasien

2. CAPAIAN PEMBELAJARAN BLOK

Capaian pembelajaran blok ini adalah mahasiswa diharapkan mampu menjelaskan patobiologi dan penatalaksanaan kelainan hematoimunologi serta mampu menjelaskan epidemiologi kelainan-kelainan ini pada masyarakat.

Sasaran Pembelajaran

Pada akhir blok ini, mahasiswa diharapkan mampu :

1. Menjelaskan tentang hematopoesis, fungsi komponen darah (plasma dan sel darah) dan faktor koagulasi.
2. Menjelaskan mengenai kelainan eritrosit (morfologi eritrosit, anemia dan hemoglobinopati).
3. Menjelaskan klasifikasi anemia dan morfologi eritrosit.
4. Menjelaskan penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana anemia normositik normokrom (anemia disebabkan perdarahan, anemia hemolitik, anemia aplastik, anemia autoimun hemolitik/ AIHA, dan Hemolytic anemia newborn/ HDN).
5. Menjelaskan penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana anemia mikrositik hipokrom (anemia defisiensi besi, anemia akibat penyakit kronik dan anemia akibat talasemia).
6. Menjelaskan penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana anemia makrositik (anemia asam folat dan anemia defisiensi vit B12).
7. Menjelaskan penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana hemoglobinopati (talasemia dan varian Hb).

8. Mengidentifikasi pemeriksaan apusan darah tepi (menggunakan pewarnaan Wright's, pemeriksaan morfologi darah tepi dan hasil interpetasi).
9. Mengidentifikasi yang normal dan kelainan apuasan darah tepi serta sumsum tulang.
10. Menjelaskan tentang nutrisi pada anemia, keganasan hematologi, autoimun, hipersensitifitas dan penyakit imunodefisiensi.
11. Menjelaskan kelainan pada platelet (morfologi platelet dan jumlah platelet, trombositopenia dan trombositosis) dan penyakit yang mendasari.
12. Menjelaskan kelainan pada hemostasis (deficiency faktor koagulasi, disfungsi faktor koagulasi, dan defek fibrinolisis) dan penyakit dengan manifestasi kelainan hemostasis seperti hemophilia, DIC.
13. Menjelaskan dan mengidentifikasi hasil pemeriksaan laboratorium untuk membantu menegakkan diagnosis, memonitoring dan follow up untuk tatalaksana terapi penyakit hemostasis.
14. Dapat menginterpretasikan hasil pemeriksaan hemostasis
15. Mengidentifikasikan kelaianan variasi lekosit (defek morfologi lekosit, dan kelainan jumlah lekosit, seperti lekopenia dan lekositosis) dan penyakit yang mendasarinya.
16. Menjelaskan dan menganalisis etiologi, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium, dan tatalaksana keganasan hematologi myeloproliferative (AML dan CML), limfoproliferative

(ALL dan CLL), myeloma, myelodysplastic, MDS, non-hodgkins lymphoma dan hodgkins lymphoma.

17. Mengetahui tentang stem cell dan aspek etika.
18. Mengetahui tentang efek radiasi dan radioterapi terhadap kanker.
19. Menjelaskan macam-macam reaksi hipersensitivitas (juvenil arthritis kronik, *Henoch-schonlein* purpura, Steven Johnson syndrome).
20. Menjelaskan tentang macam-macam penyakit autoimun.
21. Menjelaskan etiologi, patofisiologi, gejala klinis, diagnosis, pemeriksaaan laboratorium, dan tatalaksana SLE (sindrome lupus eritomatous), rematoid arthritis, dan polymialgia rematik.
22. Mengetahui komplikasi SLE, scleroderma, polyarthritis nodusa, vasculitis lupus.
23. Menjelaskan tentang etiologi, patofisiologi, diagnosis, pemeriksaan laboratorium, rencana pengobatan, dan pencegahan HIV.
24. Menjelaskan tentang pemeriksaan immunoglobulin (total konsentrasi Ig, specific konsentrasi Ig, dan imunoelektroforesis) dan pemeriksaan imunologi dari penyakit autoimun (Anti Nuclear Antibody/ANA, Anti Cardiolipin Antibody/ACA, beta 2 glikoprotein, dan rheumathoid faktor/RF), immunodeficiency (alur pemeriksaan HIV serta interpretasi), dan pemeriksaan spesifik laboarorium untuk keganasan hematologi (flowcytometri).

25. Menjelaskan Farmakokinetik, farmakodinamik obat-obat anemia, obat anti koagulan, obat anti alergi, obat autoimmune dan obat kemoterapi.

3. BIDANG ILMU TERKAIT

a. Patologi Klinik

b. Ilmu Penyakit Dalam

c. Ilmu Kesehatan Anak

d. Ilmu Gizi

e. Radiologi

f. Patologi anatomi

g. Mikrobiologi

h. Farmakologi

i. Etika Kedokteran

Kegiatan Praktikum:

1. Patologi Klinik
   a. Mengidentifikasi macam-macam sel darah serta menghitung jumlah sel pada apusan darah tepi dan menginterpretasi hasil.
   b. Mengidentifikasi pemeriksaan gambaran darah tepi dengan anemia serta interpretasi hasil.
   c. Mengidentifikasi morfologi sel-sel leukemia pada gambaran apusan sumsum tulang.

d. Melakukan pemeriksaan golongan darah dan resus serta menginterpretasikan hasil.
e. Melakukan pemeriksaan hemostasis (CT, BT, dan jumlah trombosit) serta interpretasi hasil.

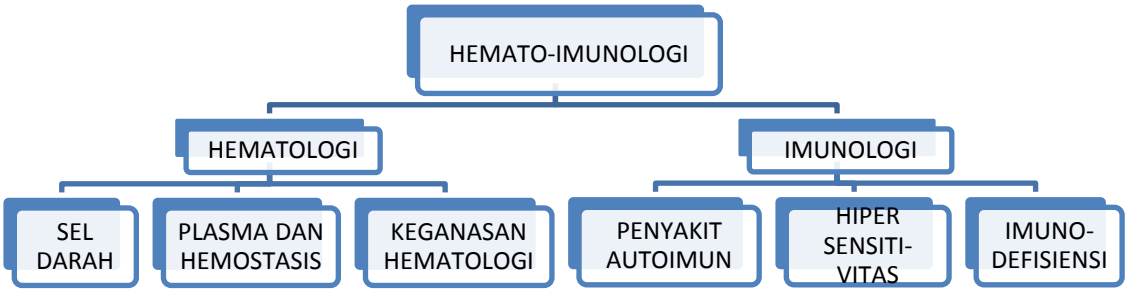
2. Patologi Anatomi:

Mengidentifikasi morfologi berbagai keganasan limfoid

4. HUBUNGAN DENGAN BLOK LAIN

1. Blok Medical Basic Science 3 (MBS3): faktor koagulasi, pemeriksaan hematologi secara umum, pemeriksaan hematologi secara spesifik, hemostasis, imunologi, dan tranfusi darah.
2. Blok Sensory System (SS): Rinitis alergi dan epistaxis.
3. Blok Dermato Musculo Skeletal (DMS): kegawatdaruratan dermatologi, dermatitis, atopi, dan eritema multiforme.
4. Blok Cardio Vascular System: rheumatic heart diseases.
5. Blok Tropical infection: DHF, malaria, dan HIV.
6. Blok Respirasi: asma, HIV dengan TB infeksi.
7. Blok Gastrointestinal: alergi makanan.
8. Blok Genitourinaria: glomerulonephritis acute, dan nephrotic syndrome.
9. Blok Emergency: hemorrhagic dan anaphylactic shock.

POHON TOPIK


HEMATO-IMUNOLOGI
HEMATOLOGI
IMUNOLOGI
SEL DARAH
PLASMA DAN HEMOSTASIS
KEGANASAN HEMATOLOGI
PENYAKIT AUTOIMUN
HIPER SENSITI-VITAS
IMUNO-DEFISIENSI

10

SISTEM HEMATOLOGI DAN IMUNOLOGI

No	Daftar Penyakit	Tingkat Kemampuan
1	Anemia aplastik	2
2	Anemia defisiensi besi	4A
3	Anemia hemolitik	3A
4	Anemia makrositik	3A
5	Anemia megaloblastik	2
6	Hemoglobinopati	2
7	Polisitemia	2
8	Gangguan pembekuan darah (trombositopenia, hemofilia, *Von Willebrand's disease*)	2
9	DIC	2
10	Agranulositosis	2
11	Inkompatibilitas golongan darah	2
Timus		
12	Timoma	1
Kelenjar Limfe dan Darah		
13	Limfoma non-Hodgkin's, Hodgkin's	1
14	Leukemia akut, kronik	2
15	Mieloma multipel	1
16	Limfadenopati	3A
17	Limfadenitis	4A
Infeksi		
18	Bakteremia	3B
19	Demam dengue, DHF	4A
20	*Dengue shock syndrome*	3B
21	Malaria	4A
22	Leishmaniasis dan tripanosomiasis	2
23	Toksoplasmosis	3A
24	Leptospirosis (tanpa komplikasi)	4A
25	Sepsis	3B
Penyakit Autoimun		
26	Lupus eritematosus sistemik	3A
27	Poliarteritis nodosa	1
28	Polimialgia reumatik	3A
29	Reaksi anafilaktik	4A
30	Demam reumatik	3A
31	Artritis reumatoid	3A
32	*Juvenile chronic arthritis*	2
33	*Henoch-schoenlein purpura*	2
34	Eritema multiformis	2
35	Imunodefisiensi	2

KEGIATAN PEMBELAJARAN

A. Tutorial

Terdapat 5 skenario selama 5 minggu. Setiap skenario terdiri dari 2 kali pertemuan, step 1-5 dan step 7. Step 6 belajar mandiri menelusuri literatur. Skenario adalah kasus yang banyak terjadi dalam praktek umum atau di rumah sakit.

B. Kuliah

Kuliah dilaksanakan dalam kelas besar. Pemberi kuliah adalah dosen ahli atau pakar. Kuliah yang diberikan akan disesuaikan dengan modul masing-masing tiap minggunya.

C. Praktikum

Praktikum merupakan penunjang teori-teori yang didapat mahasiswa. Topik praktikum menyesuaikan dengan tema pembelajaran yang diberikan. Peraturan mengenai pelaksanaan praktikum laboratorium diserahkan ke bagian masing-masing cabang ilmu. Kehadiran praktikum harus 100%.

D. Pleno

Pleno diadakan setiap minggu setelah setiap modul berakhir. Pleno bertujuan untuk menyamakan persepsi mahasiswa tentang *Learning*

Objektive pada skenario. Dihadiri oleh pengampu mata kuliah/pakar. Mahasiswa dapat langsung bertanya kepada pakarnya mengenai hal yang diragukan atau yang belum dimengerti.

E. Laporan Belajar Mandiri

Pada step 6 mahasiswa membuat laporan dengan tulisan tangan dan dilaporkan pada pertemuan ke 2. Mahasiswa melaporkan laporan tersebut di pertemuan ke 2. Kemudian setelah pertemuan ke 2 berakhir mahasiswa diminta untuk membuat refleksi diri tentang laporan yang telah dibuat. Kemudian hasil refleksi tersebut dikumpulkan kepada tutor tersebut. Penilaian berdasarkan kesesuaian laporan dengan LO yang ditentukan, kedalaman pembahasan materi, dan kesahihan sumber yang telah dipelajari.

F. Quiz

Quiz adalah penilaian sumatif yang dilakukan ditengah blok dengan ujian tertulis. Quiz akan dilakukan pada akhir minggu ke-3 dengan materi menyesuaikan dengan materi kuliah dan tutorial.

KERANGKA PENILAIAN

Nilai akhir blok Hemato-imunologi totalnya 100%, antara nilai satu dan lainnya tidak saling kompensasi, adapun perincian nilai adalah sebagai berikut:

1. Tugas (Laporan Belajar Mandiri 15%, Quiz 10%) : 25%
2. Praktikum : 15%
3. SOCA : 20%
4. Ujian Akhir Blok : 40%

A. Tutorial

Penilaian tutorial terdiri dari interaksi verbal mahasiswa selama tutorial. Dinilai menurut keaktifannya (sharing, argumentasi, dominasi, perilaku/ kesopanan, disiplin). Mahasiswa wajib mengikuti tutorial 100%.

B. Nilai Praktikum

Hasil penilaian praktikum berupa lulus atau tidak lulus didasarkan pada standar yang dibuat oleh masing-masing cabang ilmu. Evaluasi pratikum akan menilai afektif, kognitif dan keterampilan psikomotor di laboratorium.

C. SOCA

Dilaksanakan pada akhir semester. Syarat mengikuti ujian SOCA, kehadiran kuliah minimal 80%, Tutorial 100% , pleno 100% dan praktikum

100%. Ujian SOCA akan menilai *Clinical Reasoning* (Analisis) dengan diberikannya suatu kasus.

D. Ujian Akhir Blok

Dilaksanakan pada minggu ke 6 akhir blok. Syarat mengikuti ujian blok, kehadiran kuliah minimal 80%, tutorial 100%, pleno 100% dan praktikum 100%.

E. Quiz

Quiz adalah penilaian sumatif yang dilakukan ditengah blok dengan ujian tertulis. Quiz akan dilakukan pada akhir minggu ke-3 dengan materi menyesuaikan dengan materi kuliah dan tutorial.

F. **Laporan Belajar Mandiri**

Pada step 6 mahasiswa membuat laporan dengan tulisan tangan dan dilaporkan pada pertemuan ke 2. Mahasiswa melaporkan laporan tersebut di pertemuan ke 2. Kemudian setelah pertemuan ke 2 berakhir mahasiswa diminta untuk membuat refleksi diri tentang laporan yang telah dibuat. Kemudian hasil refleksi tersebut dikumpulkan kepada tutor tersebut. Penilaian berdasarkan kesesuaian laporan dengan LO yang ditentukan, kedalaman pembahasan materi, dan kesahihan sumber yang telah dipelajari.

CETAK BIRU

No	Tujuan	DM	LV	BB	JML	MTD	BGN
1	Mampu menjelaskan hematopoeisis, fungsi komponen darah (plasma dan sel darah) dan faktor koagulasi	Kognitif	C2,3	4%	7	MCQ, Quiz	PK
2	Mampu menjelaskan variasi kelainan eritrosit (morfologi eritrosit pada anemia dan hemoglobinopati)	Kognitif	C2,3	4%	7	MCQ	IKA IPD
3	Mampu menjelaskan macam-macam anemia serta morfologi eritrosit	Kognitif	C3	6%	8	MCQ Quiz SOCA	IKA
4	Menjelaskan tentang anemia normositik normokrom (anemia hemoragik, anemia hemolitik, anemi aplastik, AIHA dan HDN): • etiologi, diagnosis, dan tatalaksana • patogenesis, patofisiologi, dan pemeriksaan laboratorium	Kognitif	C3	5%	8	MCQ Quiz	IPD IKA PK
5	Menjelaskan tentang anemia mikrositik hipokrom (anemia defisiensi besi, anemia akibat penyakit kronik dan anemia akibat talasemia): • etiologi, diagnosis dan tatalaksana • patogenesis, patofisiologi, pemeriksaan laboratorium.	Kognitif	C3,5	5%	8	MCQ Quiz SOCA	IPD IKA PK

6	Mampu menjelaska n anemia makrositik (anemia def folat dan anemia def vit B12): • etiologi,diagnosis dan tatalaksana • patogenesis, patofisiologi, pemeriksaan laboratorium	Kognitif	C3	5%	8	MCQ SOCA	IKA IPD PK
7	Menjelaskan tentang hemoglobinopathy (thalasemia dan Hb Variant): • etiologi, diagnosis dan tatalaksana • patogenesis, patofisiologi, pemeriksaan laboratorium.	Kognitif	C3,5	2%	4	MCQ Quiz SOCA	IPD IKA PK
8	Dapat menunjukkan pemeriksaan apusan darah tepi (menggunakan pengecatan Wright's, morfologi sel darah serta menginterpretasi hasil.	Kognitif	C3	2%	4	MCQ	PK
9	Mampu menunjukkan yang normal serta kelainan pada apusan darah sumsum tulang	Kognitif	C3	4%	6	MCQ	PK
10	Menjelaskan tentang aspek nutrisi pada anemia, keganasan hematologi, autoimun, hipersensitivitas, dan penyakit imunodefisiensi	Kognitif	C3	4%	6	MCQ	Ilmu Gizi
11	• Menjelaskan kelainan hemostasis (defisiensi faktor koagulasi, disfungsi faktor koagulasi, dan defek fibrinolisis) dan penyakit dengan manifestasi hemostasis yang tidak normal (hemofilia, DIC)	Kognitif	C3	5%	8	MCQ	IPD PK IKA

	• Menjelaskan pemeriksaan laboratorium , follow up dan monitoring penyakit hemostasis dan follow up terapi penanganan penyakit hemostasis						
12	Menjelaskan kelainan pada platelet (morfologi platelet, dan jumlah abnormal dari platelet, seperti trombositopenia, trombositosis) dan penyakit dasarnya.	Kognitif	C3	4%	7	MCQ Quiz SOCA	IPD IKA PK
13	Mengidentifikasikan kelaianan variasi lekosit (defek morfologi lekosit, dan kelainan jumlah lekosit, seperti lekopenia dan lekositosis) dan penyakit yang mendasarinya.	Kognitif	C3	4%	7	MCQ Quiz SOCA	IPD
14	Menjelaskan dan menganalisis etiologi, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium, dan tatalaksana keganasan hematologi myeloproliferative (AML dan CML), limfoproliferative (ALL dan CLL), myeloma, myelodysplastic, MDS, non-hodgkins lymphoma dan hodgkins lymphoma.	Kognitif	C3	4%	7	MCQ SOCA	IPD IKA PK
15	Mengetahui tentang *stem cell* dan aspek etika	Kognitif Afektif	C3,5	3%	3	MCQ	Etika Kedokteran
16	Menjelaskan tentang pemeriksaan immunoglobulin (total konsentrasi Ig, specific konsentrasi Ig, dan	Kognitif	C3,5	2%	3	MCQ	PK

	imunoelektroforesis) dan pemeriksaan imunologi dari penyakit autoimun (Anti Nuclear Antibody/ANA, Anti Cardiolipin Antibody/ACA, beta 2 glikoprotein, dan rheumathoid faktor/RF), immunodeficiency (alur pemeriksaan HIV serta interpretasi), dan pemeriksaan spesifik laboarorium untuk keganasan hematologi (*flowcytometri*).						
17	Menjelaskan macam-macam reaksi hipersensitivitas (juvenil arthritis kronik, *Henoch-schonlein* purpura, Steven Johnson syndrome).	Kognitif	C3	4%	6	MCQ	IPD IKA Kulit Mikro
18	Menjelaskan macam-macam penyakit autoimun	Kognitif	C3	2%	3	MCQ SOCA	IPD IKA
19	Menjelaskan etiologi, patofisiologi, diagnosis, pemeriksaan laboratorium, dan tatalaksana SLE, Rematoid Artritis, dan Polimyalgia Rematik	Kognitif	C3	4%	6	MCQ SOCA	IPD IKA
20	Mengetahui komplikasi SLE, scleroderma, polyarthritis nodusa, vasculitis lupus.	Kognitif	C3	4%	6	MCQ	IKA IPD
21	Menjelaskan tentang etiologi, patofisiologi, diagnosis, pemeriksaan laboratorium, rencana pengobatan, dan pencegahan HIV.	Kognitif	C3	4%	6	MCQ SOCA	IKA IPD
22	Mengetahui tentang efek radiasi dan radioterapi terhadap kanker	Kognitif	C3	4%	6	MCQ	Radiologi

23	Menjelaskan Farmakokinetik, farmakodinamik obat-obat anemia, obat anti koagulan, obat anti alergi, obat autoimmune dan obat kemoterapi.	Kognitif	C3	4%	6	MCQ Quiz SOCA	IKA IPD

Ket : Menurut taksonomi Bloom, kompetensi yang harus dicapai :

- C1 = hanya sebatas tahu, mengingat/menghafal
- C2 = pemahaman, terjemah dan menyimpulkan
- C3 = aplikasi, penerapan, menggunakan konsep, prinsip, prosedur untuk memecahkan masalah
- C4 = analisa, memecah konsep menjadi bagian-bagian, mencari hubungan antara bagian
- C5 = sintesis, diagnosis, menggabungkan bagian-bagian menjadi satu
- C6 = evaluasi, membandingkan nilai-nilai, ide-ide, metode dengan standar SOP

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MODUL PEMBELAJARAN

MODUL 1: Sel darah merah

Tujuan Pembelajaran :

1. Mampu menjelaskan tentang hematopoeisis, fungsi komponen darah (plasma dan sel darah) dan faktor koagulasi.
2. Mampu menjelaskan mengenai kelainan eritrosit (morfologi eritrosit, anemia dan hemoglobinopati) serta penyakit yang mendasarinya.
3. Mampu membedakan berbagai jenis anemia serta morfologi eritrosit.
   a) Penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana anemia normositik normokrom (anemia disebabkan perdarahan, anemia hemolitik, anemia aplastik, anemia autoimun hemolitik/ AIHA, dan Hemolytic anemia newborn/ HDN).
   b) Penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana anemia mikrositik hipokrom (anemia defisiensi besi, anemia akibat penyakit kronik dan anemia akibat talasemia).
   c) Penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana anemia makrositik (anemia asam folat dan anemia defisiensi vit B12).
4. Menjelaskan penyebab, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium dan tatalaksana hemoglobinopati (talasemia dan varian Hb).
5. Membuat dan menginterpretasi apusan darah tepi (menggunakan pewarnaan Wright's, pemeriksaan morfologi darah tepi).
6. Mengidentifikasi morfologi darah tepi yang normal dan abnormal pada apuasan darah tepi serta sumsum tulang.
7. Menjelaskan tentang nutrisi pada anemia, keganasan hematologi, autoimun, hipersensitifitas dan penyakit imunodefisiensi.

Kuliah Pakar :

1. **Patologi Klinik**

a. Hematopoesis dan faktor koagulasi.
b. Anemia normositik normokrom.
c. Anemia mikrositik hipokrom.
d. Anemia makrositik.
e. Hemoglobinopati.

2. Ilmu Penyakit Dalam

a. Anemia normositik normokrom.
b. Anemia mikrositik hipokrom
c. Anemia makrositik
d. Hemoglobinopati (talasemia dan varian Hb).

3. Ilmu Kesehatan Anak

a. Hemoglobinopati (talasemia dan varian Hb).
b. Juvenile anemia defisiensi besi, juvenile AIHA, dan HDN.

4. Farmakologi

Tatalaksana anemia dan terapi pada *depresses hematopoeiesis*

5. Ilmu Gizi

Diet pada anemia

Praktikum

Patologi Klinik:

- Gambaran apusan darah tepi dan differential count.
- Gambaran apusan darah tepi pada anemia dan menginterpretasi hasil.

Belajar Mandiri

***Clinical Skill Laboratory* (CSL)**

MODUL 2: Platelet, Plasma darah, dan Sistem hemostasis

Tujuan Pembelajaran :

1. Menjelaskan kelainan pada platelet (morfologi dan jumlah platelet) dan penyakit yang mendasari.
2. Menjelaskan kelainan hemostasis (defisiensi faktor koagulasi, disfungsi faktor koagulasi, dan defek fibrinolisis) dan penyakit dengan manifestasi kelainan hemostasis seperti hemophilia, DIC.
3. Menjelaskan dan mengidentifikasi hasil pemeriksaan laboratorium untuk membantu menegakkan diagnosis, memonitoring dan follow up untuk tatalaksana terapi penyakit hemostasis.
4. Menginterpretasikan hasil pemeriksaan hemostasis.
5. Menjelaskan farmakokinetik, farmakodinamik obat anti koagulan, dan pengobatan pada efek hemostasis.

Kuliah Pakar :

1. **Patologi Klinik**
   Hemostasis
2. **Ilmu Penyakit Dalam**
   a. Abnormal platelet
   b. Abnormal hemostasis
3. **Ilmu Kesehatan Anak**
   a. Abnormal platelet
   b. Abnormal hemostasis
4. **Farmakologi**
   Farmakokinetik dan farmakodinamik obat antikoagulan dan pengobatan pada efek hemostasis.

Praktikum
Patologi Klinik: hemostasis

Clinical Skill Laboratory **(CSL)**

Belajar Mandiri

Pleno

MODUL 3. Leukosit, Keganasan hematologi dan Lympoid

Tujuan Pembelajaran :

1. Membedakan kelainan leukosit (morfologi dan jumlah) serta penyakit yang mendasari.
2. Menjelaskan etiologi, patogenesis, patofisiologi, diagnosis, pemeriksaan laboratorium, dan tatalaksana keganasan hematologi myeloproliferative (AML dan CML), limfoproliferative (ALL dan CLL), myeloma, myelodysplastic syndrome (MDS), non-hodgkins lymphoma dan hodgkins lymphoma.
3. Mengidentifikasi morfologi keganasan sel darah pada apusan darah tepi
4. Mampu mengenal pemeriksaan yang lebih spesifik terhadap dignosis keganasan (flowcytometri)
5. Menjelaskan aspek etika pada penggunaan stem cell.
6. Menjelaskan peranan radioterapi pada kanker.
7. Menjelaskan farmakodinamik dan farmakokinetik obat kemoterapi.

Kuliah Pakar :

1. **Patologi Klinik**
   a. Keganasan hematologi (AML, CML, ALL, CLL, MDS)
   b. Menjelaskan pemeriksaan yang lebih spesifik terhadap dignosis keganasan (flowcytometri).
2. **Ilmu Penyakit Dalam**

   Keganasan hematologi (AML, CML, MDS)
3. **Ilmu Kesehatan Anak**

   Keganasan hematologi (ALL dan CLL)
4. **Farmakologi**

Farmakokinetik dan farmakodinamik obat kemoterapi pada keganasan sel darah.

5. **Ilmu Gizi**

   Diet pada keganasan

6. **Patologi Anatomi**

   Histopatologi pada kegansan lympoid (non-hodgkins lymphoma dan hodgkins lymphoma)

7. **Radiologi**

   Efek radiasi dan radioterapi pada kanker.

8. **Etik Kedokteran**

   Aspek etik pada stem cell

Praktikum:

1. **Patologi Klinik**

   Mengidentifikasi pemeriksaan apusan darah tepi dan sumsum tulang pada keganasan hematologi.

2. **Patologi Anatomi**

   Mengidentifikasi pemeriksaan histopatologi morfologi pada keganasan limfoid.

Clinical Skill Laboratory **(CSL)**

Pleno

Belajar Mandiri

Quiz

MODUL 4: Hipersensitivitas dan autoimun

Tujuan Pembelajaran :

1. Membedakan macam-macam reaksi hipersensitivitas dan contoh penyakitnya.
2. Menjelaskan tentang macam-macam penyakit autoimun.
3. Menjelaskan etiologi, patofisiologi, gejala klinis, diagnosis, pemeriksaaan laboratorium, dan tatalaksana SLE, rematoid arthritis, dan polymialgia rematik.
4. Menjelaskan komplikasi SLE, scleroderma, polyarthritis nodusa, vasculitis lupus.
5. Menjelaskan pemeriksaan immunoglobulin (total konsentrasi Ig, specific konsentrasi Ig, dan imunoelektroforesis) dan pemeriksaan imunologi dari penyakit autoimun (Anti Nuclear Antibody/ ANA, Anti Cardiolipin Antibody/ ACA, beta 2 glikoprotein, dan rheumathoid faktor/ RF).

Kuliah Pakar:

1. **Patologi Klinik**
   a. SLE, rematoid arthritis, dan polymialgia rematik.
   b. Pemeriksaan imunoglobulin
2. **Ilmu Penyakit Dalam**
   a. Reaksi hipersensitivitas
   b. Penyakit autoimun.
3. **Farmakologi**
   Farmakokinetik dan farmakodinamik obat autoimun dan hipersensitivitas.
4. **Ilmu Kesehatan Anak**
   Penyakit autoimun pada anak
5. **Mikrobiologi**
   Reaksi hipersensitivitas.

Clinical Skill Laboratory **(CSL)**
Pleno
Belajar Mandiri

MODUL 5: Imunodefisiensi

Tujuan Pembelajaran :

1. Mampu menjelaskan etiologi, patofisiologi, diagnosis, pemeriksaan penunjang, rencana penatalaksanaan dan pencegahan HIV.
2. Menjelaskan farmakokinetik dan farmakodinamik obat antiretroviral.

Kuliah Pakar :

1. **Patologi Klinik**

   HIV-AIDS dan interpretasi hasil pemeriksaan laboratorium
2. **Mikrobiologi**

   Etiologi, patofisiologi, dan patogenesis HIV-AIDS.
3. **Ilmu Penyakit Dalam**

   Diagnosis dan tatalaksana HIV-AIDS.
4. **Ilmu Kesehatan Anak**

   Diagnosis dan tatalaksana HIV pada anak.
5. **Farmakologi**

   Obat anti retroviral.
6. **Etik Kedokteran**

   Cara pandang dari sudut sosial HIV-AIDS.

***Clinical Laboratory Skill* (CSL)**

Pleno

Belajar Mandiri

JADWAL KEGIATAN BLOK HEMATOIMUNOLOGI
(1 Maret- 8 April 2016)

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<tr><td>08.40 – 09.30</td><td></td><td rowspan="2">Ilmu Gizi</td><td rowspan="2">Ilmu Penyakit Dalam 2</td><td rowspan="2">Ilmu Kesehatan Anak 1</td></tr>
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<tr><td>10.20 – 11.10</td><td rowspan="2">CSL</td><td rowspan="2">Tutorial</td><td rowspan="2">CSL</td><td rowspan="2">Farmako</td></tr>
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<tr><td>08.40 – 09.30</td><td rowspan="2">Patologi Anatomi</td><td rowspan="2">Ilmu Penyakit Dalam</td><td rowspan="2">Patologi Klinik 2</td><td rowspan="2">Ilmu Kesehatan Anak</td></tr>
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LITERATURE REVIEW

1. MODULE 1 : RED BLOOD CELLS

Anemia

Anemia is functionally defines as an insufficient red blood cell (RBC) mass to adequately deliver oxygen to peripheral tissues. The laboratory test to establish the presence of anemia is hematology examination. For practical purpose, we can evaluate the three concentration measurement such as haemoglobin (Hb) level (g/dL), haematocrit (%), dan RBC number (10^{12}/L). Index of erythrocyte can be established by calculate that parameter. Erythrocyte index are mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCV) and mean corpuscular haemoglobin concentration (MCHC). They are used to determine the type of anemia based on erythrocyte morphology. (Glader, 2003, Adamson and Longo, 2008)

Based on erythrocyte morphology, anemia is divided into 3 types :(Glader, 2003)

1. Normocytic normochromic anemia (i.e blood loss, hemolytic anemia, aplastic anemia)
2. Microcytic hypochromic anemia (i.e iron deficiency anemia, anemia of chronic disease, thalassaemia)
3. Macrocytic anemia (i.e megaloblastic anemia caused by deficiency of folat or vitamin B12)

Based on the cause of anemia, it is divided into:(Adamson and Longo, 2008)

1. Anemia caused by decrease red survival (i.e blood loss, or hemolytic disease)

2. Anemia caused by defects of bone marrow production (hypoproliferative) i.e marrow damage, iron deficiency, decrease of stimulation in inflammation, metabolic defect, or renal disease.
3. Anemia caused by defects of red blood cell maturation (ineffective erythropoiesis) i.e cytoplasmic defects in iron deficiency, thalassaemia, sideroblastic anemia, or nuclear defects in folate deficiency, vitamin B12 deficiency, drug toxicity, and refractory anemia

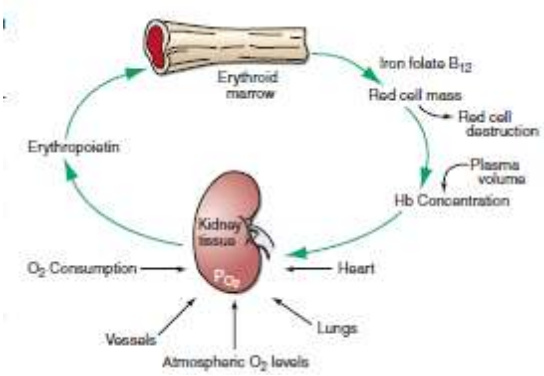

Figure 1. The physiologic regulation of red blood cell production by tissue oxygen tension (Adamson and Longo, 2008)

A. Iron deficiency anemia

Iron deficiency anemia is the condition in which there is anemia and clear evidence of iron lack. It is the most prevalent forms of malnutrition anemia. The causes of iron deficiency are :(Andrews, 2003, Adamson, 2008)

1. Increased demand for iron and or hematopoiesis i.e in infancy or adolescence, pregnancy, and erythropoietin therapy.

2. Increased of iron loss in chronic blood loss, menometrorhagia,or acute blood loss

3. Decrease iron intake or absorption i.e inadequate diet, malabsorpsi disease (sprue or Crohn's disease), surgery (post gastrectomy), or inflammation

The progression of iron deficiency are divided into three stages.There are: (Adamson, 2008)

1. The first stage is *negative iron balance*. In this stages, the iron demand is higher than the ability of iron absorption. Iron stores (serum ferritine) decrease, Total Iron Binding Capacity (TIBC) increases, but serum iron is normal. This stage can be found in several number of physiologic mechanisms such as pregnancy, rapid growth in children and adolescent.

2. The second stage is *iron deficient erythropoiesis*. In this stage, iron stores become depleted, serum iron begins to fall and TIBC increases. Haemoglobin synthesis become impaired and it causes of anemia. The morphology of erythrocyte in this stage is normocytic normochrome.

3. The third stage is *iron deficiency anemia*. The characteristic of this stage are anemia moderate (Hb value 10-13 g/dL), morphology of erythrocyte is microcytic hypochrome, serum iron, transferrin saturation and ferritin is low and TIBC is high.

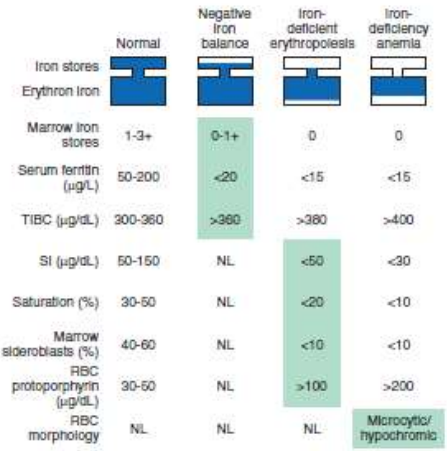

Figure 2. Laboratory studies in the evolution of iron deficiency (Adamson, 2008)

Signs and symptoms of iron deficiency anemia:

1. Impairs growth in infancy
2. Fatigue
3. Headache
4. Irritability and palpitation
5. Dizziness and breathlessness
6. Disorder of neuromuscular system

Laboratory findings of IDA:(Adamson, 2008, Andrews, 2003)

1. Hematology
   - Microcytic hypochrom anemia (MCV <80 fL, MCH and MCHC are low)
   - Blood smear : morphology of erythrocyte are microcytic hypochrom, anisopoikilositosis, pencil cell (+), and or sel target (+). Morphology of

leucocyte can be found granulocytopenia in longterm iron deficiency. Thrombocyte increases (thrombocytosis)

2. Iron status
    - serum iron is low
    - TIBC increases
    - Serum ferritin is low. Ferritin is acute phase reactan and its value will increase in inflammatory stage. In order to eliminate inflammation stage it is suggested to check C reactive protein (CRP). The marker of iron store that has better specifity than serum ferritin is soluble transferrin receptor (sTfR).

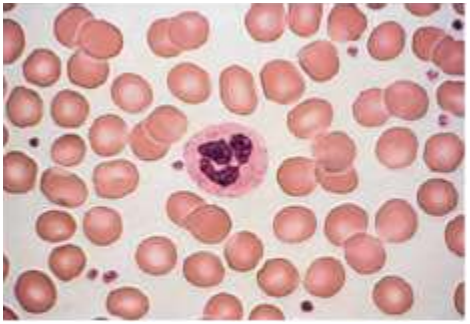

Figure 3. Normal blood smear (Wright's stain)(Adamson, 2008)

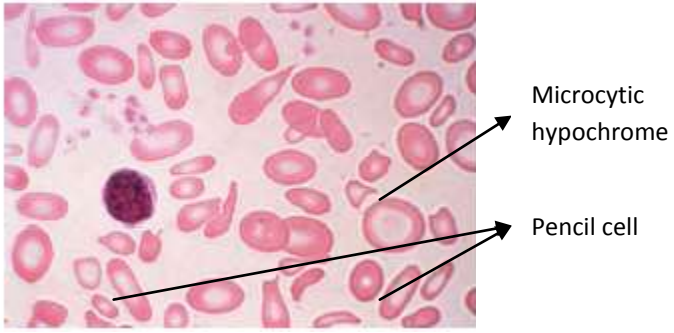

Figure 4. Iron deficiency anemia blood smear(Adamson, 2008)

Terapi IDA (Adamson, 2008)

1. Ferrous tablet
2. Ferrous injection
3. Blood transfusion

B. Anemia of Chronic Disease (ACD)

Anemia of chronic disease is anemia that is often observed in patients with infectious, inflammatory, or neoplastic disease that persist for more than 1-2 months. The syndrome does not include anemia caused by marrow replacement, blood loss, hemolysis, renal insufficiency, hepatic disease, or endocrinopathy. The characteristic of anemia of chronic disease are hypoferremia (serum iron is low) and normal or high of serum ferritin.

Conditions associated with anemia of chronic disease are chronic infectious (i.e pulmonary infections, pelvic inflammatory disease, osteomyelitis etc), chronic noninfectious disease (i.e rheumatoid arthritis, rheumatoid fever, SLE), malignancy (i.e carcinoma, leukemia, multiple myeloma etc), and miscellaneous (i.e alcoholic liver disease, congestive heart failure, thrombophlebitis, Ischemic Heart Disease etc)

Laboratory findings in ACD are:

1. Hematology :
   - Mild-moderate anemia (hemoglobin value is 1-2 lower than normal hemoglobin value, it is rare lower than 9 g/dl)
   - Microcytic hypochrom anemia (MCV 77-82 fl)
   - Haematocrit is more than 27%
2. Iron status :

- Serum iron is low (10-70 ug/dL)
- TIBC decreases (100-300 ug/dL)
- Transferrin saturation is low (10-25%)
- Serum ferritin value is normal or high. Its examination can be used to determine iron deficiency anemia from anemia of chronic disease

The specific of signs and symptoms in ACD are associated with the underlying disease.

Therapy of ACD depent on the underlying disease.

Thalassaemia

Thalassaemia is genetic disorders that characterized by reduced rate or lack of production on one or more of the globin chain. The reduced supply of globin diminishes production of haemoglobin. Based on genetic, thalassaemia is classified into αthalassaemia, βthalassaemia, γthalassaemia, δβthalassaemia, δthalassaemia, εζγβthalassaemia, and hereditary persistence of fetal haemoglobin (HPFH).(Weatherall, 2001)

- αThalassaemia

α Thalassaemia is inherited disorder in α globin chain synthesis. It causes an excess of β globin chain.

This thalassaemia is classified based on the number of gen deletion. It is divided into one gen deletion, two genes deletion, three genes deletion (HbH disease), and four genes deletion (Hb Bart/hydrops foetalis).

- β Thalassaemia

β Thalassaemia is genetic disorders in β globin synthesis. Clinically, it divided into three groups, that are β Thalassaemia major (need a routine transfusion, it is also called Cooley's anaemia), β Thalassaemia intermediate (need transfusion in a certain condition), and β Thalassaemia minor/trait/silent/asymptomatic (only diagnosed by laboratory examination).(Weatherall, 2001, Hoffbrand et al., 2005, Pignatti and Galanello, 2003)

2. MODULE 2 : PLATELET, BLOOD PLASMA, AND HEMOSTASIS SYSTEM

A. Disorder of Platelet's Number

Disorders of platelet's number can be determined into thrombocytopeni and thrombocytosis. Trombocytopeni is condition in which the number of thrombocyte is low. It is the most common cause of abnormal bleeding. The diseases that cause thrombocytopeni can be determined into:

a. Decreased platelet production (aplasy/hypoplasy of megakaryocytes, ineffective thrombopoiesis, hereditary thrombocytopenia)
b. Increased platelet destruction (immunologic thrombocytopenia purpura, infectious, drugs, thrombotic microangiopathies, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome)
c. Abnormal platelet distribution or pooling (hypersplenisme)
d. Miscellaneous (infectious disease such as dengue haemorrhagic fever)(Parker and Levine, 2003a)

Thrombocytosis is a condition in which the number of thrombocyte is high. It may result from physiologic or pathologic process. The physiologic processes of thrombocytosis are exercise, parturation, or ephinephrine. The pathologic processes are divided into primary (i.e myeloproliferative syndrome, essential

thrombocythemia, polycythemia vera, chronic myelocytic leukemia, or myelofibrosis), and secondary (infectious disease, inflammatory diseases, neoplasms, rebound after recovery thrombocytopenia, asplenia) (Parker and Levine, 2003b)

B. Disorders of Coagulation

Disorders of coagulation is caused by deficiency of coagulation factors or present inhibitor of coagulation factor activity. It is X-link disease. This disease is characterized by recurrent bleeding episodes into joint, muscles, and closed space, either spontaneously or following an injury. The most common of inherited factor deficiency are the hemophilias. The disease is caused by deficiency of Factor VIII (hemophilia A) or Factor IX (hemophilia B). The other causes, although it is rare, are deficiency of Factor II (prothrombin), Factor V, Factor VII, Factor X, Factor XIII and fibrinogen. They are usually inherited in autosomal recessive manner.

Clinical manifestations of hemophilia are bleeding episodes into joints (hemarthrosis), soft tissue and muscles after minor injury or even spontaneously.(Arruda and High, 2008)

Laboratory examinations to diagnoseof hemophilia are aPTT (activated Partial Thrombin Time), PT (Prothrombin Time), assay of activity and value of coagulation factor, and assay of inhibitor coagulation factor. Laboratory findings is isolated prolonged of aPTT, platelet count is normal, and normal bleeding time. In hemophilia A, there is a deficiency of FVIII or present FVIII inhibitor. In hemophilia B, there is a deficiency of FIX (Arruda and High, 2008)

3. MODULE 3 : Leukocyte and Malignancy of Hematologic andLymphoid

A. Leucocyte Disorders

The various forms of leucocyte are neutrophil, eosinophil, basophil, lymphocyte, and monocyte. They are derived from a common stem cell in the bone marrow. Their function is in inflammatory and immune responses. The schema event in granulocytes production and their function in inflammation can be saw in figure below.(Holland and Gallin, 2008)

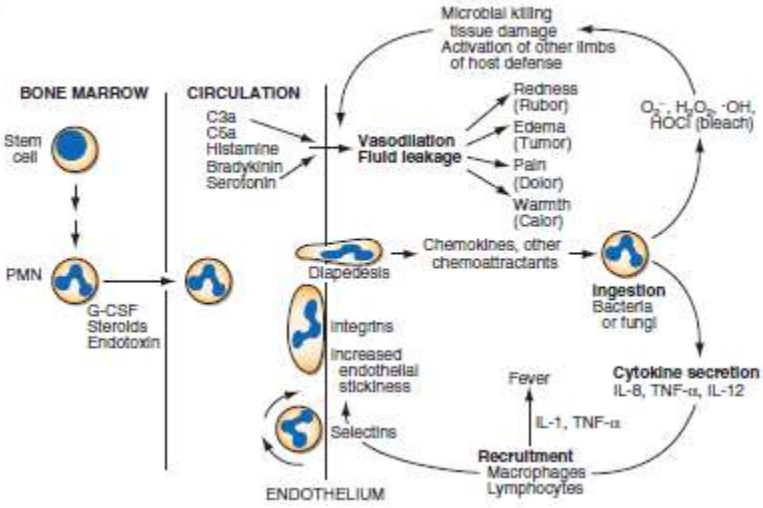

Figure 5. Schematic events in granulocytes production, recruitment, and inflammation (Holland and Gallin, 2008)

Leucocyte disorders are determined into morphological disorders and leucocyte number disorders. The morphological disorders is an abnormality of leucocyte form (i.e toxic granulation, hypersegmentation, Pelger-Huet anomaly, Dohle body, etc). The leucocyte number disorders are leucopenia and leucocytosis. The kind of leucopenia or leucocytosis depends on the form of leucocyte that has number alteration. (Holland and Gallin, 2008, Hoffbrand et al., 2005)

Neutropenia is a condition in which the absolute neutrophil number is low. The causes of neutropenia are decreased production (i.e drug induced, hematologic disease such as aplastic anemia, myelofibrosis, tumor invasion etc), peripheral destruction (antineutrophil antibody, autoimmune disorders, drugs), and peripheral pooling (i.e overwhelming bacterial infection, hemodialysis).(Holland and Gallin, 2008)

Neutrophilia is a condition in which the absolute neutrophil number is high. The causes of neutrophilia are increased production (idiopathic, drug induced, infection bacterial, fungal, or sometimes viral, inflammation, myeloproliferative disease), increased marrow release (glucocorticoids, acute infection, inflammatory such as thermal injury), decreased or defective margination (drugs induced such as ephinephrin, stress, or leucocyte adhesion deficiency), and miscellaneous (metabolic disorder, metastatic carcinoma, acute haemorrhagic, or haemolysis)(Holland and Gallin, 2008)

B. Hematology Malignancy

The hematology malignancy is determined based on the kind of hematology cell in which has abnormal proliferation. Abnormal proliferation in myeloid cell is called myeloid leukemia. It is divided into acute myeloid leukemia and chronic myelocytic leukemia based on the maturation stage of myeloid cell. Myeloid leukemias is characterized by infiltration of blood, bone marrow, and other tissue by neoplastic cells of the hematopoietic system. The malignancies of lymphoid cells arise from cells of the immune system at different stages of differentiation, resulting in wide range of morphologic, immunologic, and clinical findings. The form of lymphoid cell malignancies are leukemia and lymphomas (solid tumor of

the immune system). Lymphoid leukemia is determined into acute lymphoblastic leukemia and chronic lymphocytic leukemia.

B. 1 Acute Myeloblastic Leukemia

Incidence of AML is 3,7 per 100.000 people per year, the age adjusted incidence is higher in men than women, the incidence of AML increase with age. Etiologies of AML are radiation or chemical exposure, drugs, or heredity. There are 2 systems of AML classification. That are The World Health Organization (WHO) classification and French-American British (FAB) classification.(Wetzler et al., 2008)

The WHO classification includes different biologically distict group based on immunophenotype, clinical feature, and cytogenetic and molecular abnormalities in addition to morphology. But the FAB system classifies AML based of morphological features. The major difference between the WHO and the FAB systems is the blast cutoff for AML diagnosis to determine with myelodysplastic syndrome (MDS). The blast cutoff in WHO system is 20%, in other side the blast cutoff in FAB is 30%. The Classification Systems of AML can be saw table-1. (Wetzler et al., 2008)

Symptoms of AML are often nonspecific. They are the consequence of anemia, leucocytosis, leukopenia or leucocyte dysfunction, or thrombocytopenia. The symptoms was usually present ≤ 3 months before leukemia was diagnosed. They are fatigue, weakness, anorexia, weight loss, or fever. Signs are bleeding, easy bruising, bone pain, lymphadenopathy, non specific cough, or headache. The physical findings are fever, splenomegaly, hepatomegaly, lymphadenopathy, sternal tenderness, and evidence of infection and haemorrhagic.

Hematology findings are anemia (mild-severe), normocytic normochromic, the leucocyte count increase up to more than 100.000/µL, the morphology of the malignant cell varies in difference subsets, Auer Roads can be found, platelet count is sometime lower than 100.000/µL. Chemistry test can be foud the increased of uric acid, LDH, ureum, and hepatic enzymes.(Wetzler et al., 2008). The diagnosis is established based on blood smear, bone marrow punction (BMP), cytochemistry, and gene analyze.

Table 1. Classification AML(Wetzler et al., 2008)

World Health Organization Classification[a]
I. AML with recurrent genetic abnormalities
AML with t(8;21)(q22;q22);*RUNX1/RUNX1T1*[b]
AML with abnormal bone marrow eosinophils [Inv(16)(p13q22) or t(16;16)(p13;q22);*CBFB/MYH11*][b]
Acute promyelocytic leukemia [AML with t(15;17)(q22;q12) (*PML/RARA*) and variants][b]
AML with 11q23 (*MLL*) abnormalities
II. AML with multilineage dysplasia
Following a myelodysplastic syndrome or myelodysplastic syndrome/myeloproliferative disorder
Without antecedent myelodysplastic syndrome
III. AML and myelodysplastic syndromes, therapy-related
Alkylating agent–related
Topoisomerase type II inhibitor–related
Other types
IV. AML not otherwise categorized
AML minimally differentiated
AML without maturation
AML with maturation
Acute myelomonocytic leukemia
Acute monoblastic and monocytic leukemia
Acute erythroid leukemia
Acute megakaryoblastic leukemia
Acute basophilic leukemia
Acute panmyelosis with myelofibrosis
Myeloid sarcoma

French-American-British (FAB) Classification[c]	Incidence
M0: Minimally differentiated leukemia	5%
M1: Myeloblastic leukemia without maturation	20%
M2: Myeloblastic leukemia with maturation	30%
M3: Hypergranular promyelocytic leukemia	10%
M4: Myelomonocytic leukemia	20%
M4Eo: Variant: Increase in abnormal marrow eosinophils	
M5: Monocytic leukemia	10%
M6: Erythroleukemia (DiGuglielmo's disease)	4%
M7: Megakaryoblastic leukemia	1%

[a]ES Jaffe et al: *World Health Organization Classification of Tumours*. Lyon, IARC Press, 2001.
[b]Diagnosis is AML regardless of blast count.
[c]JM Bennett et al: Ann Intern Med 103:620, 1985.

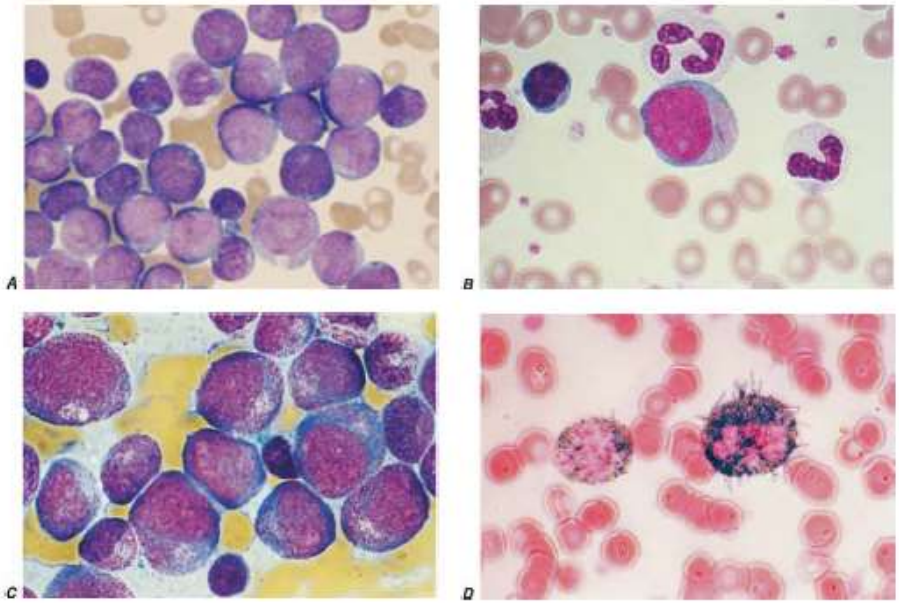

Figure 6. Blood film of AML (Wetzler et al., 2008)

B. 2 Chronic Myelocytic Leukemia

Chronic Myelocytic Leukemia (CML) is diagnose by identifying a clonal expansion of a hematopoietic stem cell possessing a reciprocal translocation between chromosomes 9 and 22. This translocation results in head to tail fusion of the breakpoint cluster region (BCR) gene on chromosome 22q11 with ABL gene located on chromosome 9q34. It is called BRC ABL gene.

Symtomps of CML are fatigue, malaise, weight loss, infectious, thrombosis, or bleeding. The physical findings are hepatomegaly and or splenomegaly. Hematologic findings are anemia normocytic normochromic, elevated of WBC's count with increases both immature and mature granulocyte. The majority cells are myelocyte and neutrophil (two peaks form). The diagnosis is established by blood smear and BMP.(Wetzler et al., 2008)

B. 3 Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia have been divided based on immunologic and cytogenetic abnormalities. The FAB classification is divided ALL into three types based on morphologic character. There are L1 (small uniform blast), L2 (Larger cell and more variable size cell), and L3 (uniform cells with basophilic and sometimes vacuolated cytoplasms, we are called Burkitt's lymphoma cells). ALL is most common found in childhood.(Longo, 2008). Diagnosis is established base on blood smear, BMP, and cytogenetic analyze.

Table 2. Classification of ALL based on FAB System(Longo, 2008)

Immunologic Subtype	% of Cases	FAB Subtype	Cytogenetic Abnormalities
Pre-B ALL	75	L1, L2	t(9;22), t(4;11), t(1;19)
T cell ALL	20	L1, L2	14q11 or 7q34
B cell ALL	5	L3	t(8;14), t(8;22), t(2;8)

Note: FAB, French-American-British classification.

B.4 Chronic Myelocytic Leukemia

Chronic Myelocytic Leukemia (CML) is the most common lymphoid leukemia. This leukemia has the similar clinical findings with other kind of leukemia. Hematology findings are anemia normocytic normochromic, increased of lymphocyte number in peripheral blood (the count is up to $>10^9/\mu L$), and the peripheral blood smear shows smudge cell/basket cell (it is nuclear remnant of cells damaged by the physical shear stress of making the blood smear).(Longo, 2008)

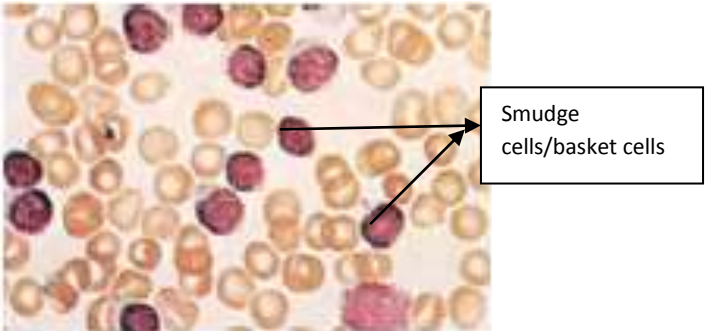

Figure 7. Chronic Lymphocytic Leukemia(Longo, 2008)

4. MODULE 4 : HYPERSENSITIVITY AND AUTOIMMUNE DISEASE

Disease caused by Immune Responses

Hypersensitivity disease is disorders caused by immune responses. There are 4 types of hypersensitivity that are classified according to the type of immune response and the effector mechanism responsible for cell and tissue injury. Type 1 hypersensitivity is called Immediate hypersensitivity. It is caused by IgE antibody and mast cells and the most prevalent type of hypersensitivity disease. The diseases caused by this hypersensitivity are brochial asthma, anafilactic shock, and allergic.

Type 2 hypersensitivity is called antibody mediated hypersensitivity. In this type, IgM or IgG against cell surface or extracellular matrix antigen. The disease caused by type 2 hypersensitivity are transfusion reaction, haemolytic anemia, and haemolytic in Newborne Disease.

Type 3 hypersensitivity is called immune complex mediated hypersensitivity. It is caused by present of immune complexes of circulating antigens and IgM or IgG

antibody. The disease are rheumatoid fever, nephrotic syndrome, Rheumatoid Heart Disease.

Type 4 hypersensitivity is called T cell mediated hypersensitivity. It is determined into CD4+ T cells (delayed type hypersensitivity) and CD8+ CTLs (T cell mediated cytolysis).(Abbas et al., 2007)

5. MODULE 5 : IMMUNODEFICIENCY

Immunodeficiencies

Immunodeficiencies is defects in one or more component of immune system. It is divided into primary or secondary immunodeficiencies. Immunodeficiency diseases increase susceptibility to infection.

The secondary immunodeficiencies develop as consequence of malnutrition, disseminated cancer, immunosuppresive agents, or infection (such as HIV infection that causes AIDS). HIV attack the T lymphocyte CD4 and make destruction in lymphoid tissue. It causes depletion of CD4 number. The depletion of T lymphocyte CD4 increases susceptibility to infection.(Abbas et al., 2007)

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