(5)

ONCOLOGY

PG-NOTES

2017

JAIN STATIONERY

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→ GENERAL ONCOLOGY ←

NEOPLASM : Abn, excessive, uncontrolled, uncordinated and unregulated growth → continues to presut in the same exces pattren → given of the the initial stimulus is withdrawn

all together K/A : "Autonomous growth"

Benign Malignant

MCQ ① Most reliable creteria : Metastasis

② 2nd reliable in absence of metastasis : Invasiveness

3rd most reliablity : a) ↑ N/c ratio
b) loss of polarity
c) Hyperchromatosis
d) ↑ cd mitotic activity

There is no 3rd creteria

Only 2 criteria

Sarcomas shows : a) Epithelial lining Creteria
b) connective tissue in

Benign > Encapsulated

Capsule

True Benign — False Pseudo Malignant

Locally Invasive

Ideal 1 cm ..... Minimum 0.5 cm

Chemotherapy → M/c for Haemotological malig

* Induction chemotherapy (high dose chemotherapy)

C out significant side effects (or)

Dose limiting side effect

M/c S/E = Bone marrow suppression (Nutropenia)

Induct^{n} chemotherapy

↓

Single drug / Multiple drug regimen

↓

High dose to achevie remission

(Remission does not mean cure)

clinical remission: pt free from clenical symptoms of the cancer

* Consolidation: (Repitation of induction chemotherapy) → Haemotological malig

traget is to prolong remission

* Intensification: change the → general malig

higher dose chemotherapy:

↓

Same (or) alternate drugs

↓

Further prolong remission

* Maintenance: defined as low dose CT i.e given over long periods i.e drug free intervals.
  ↳ General malig

  ↓

  traget is to prevent Recurrance

  , maintanance (or) cycles

* Adjuvent Chemotherapy: Sx and after that CT

  Eg: Epithelial Cancer

  ↓

  ♀ Serous cancer in ovary

  ↓

  Sx +/b CT

  Debulking Sx → IP/CT → systemic (or) IV CT

  ↓

  (Intraperitoneum)

* Chemosensitive

  Growth fraction of tumours

  proliferative pool / Replicative pool

  Definition: % of tumour cell that are actively multiplied (or) % of tumour cell that lie in the cell cycle.

⇒ chemosensitive phase in cell cycle: S phase

Growth fraction : CONSTANT

↓

Benign / Malignant = 15 to 20%

* Debulking sx : Excission of the tumour that is surgically amenable

100 cell (tumour) → Debulking → 70 cell (removed)

↓

30 cell (remaining)

⇓

↑Growth fraction

↓

Induction chemotherapy ⇒ (27/30) ← ↑90%

↓

Acheive remision

↓

3 cells remaining

↓

to remove these 3 cell Do Maintanance CT

↓

* After debulking → IP CT / HIPEC

↓

① Hyperthermic IP CT : (3/6/10 days)

[on OT table itself]

② Interval for 4-6 wk

↓

③ Systemic CT

* Neoadjuvant Chemotherapy

- Mostly for Breast Ca (Neo and adjuvant CT)
- T_4 lesion → LABC (locally advanced Breast Ca)

T_{4a} T_{4b}

T_0 No tumour

T_{is} DCIS

T_1 ≤ 2 cms

T_2 2-5 cms

T_3 > 5 cms

T_4 { T_{4a} Skin ulcer; T_{4b} Infiltration into chest wall } LABC

- Neoadjuvant CT = CT +/b Sx +/b CT

LABC = CT → Sx → CT → (RT) *

Neoadjuvant CT = Shinkage of Tumour (or)
Downstaging of Tumour

* Radiotherapy

External RT — Internal RT

Eg: LINAc — (*) Eg: Brachy therapy

Brachytherapy

Intracavitary (Body cavity)
eg: Ca Cx
Uterine Ca
Ca Colon

Interstitial Brachytherapy (Implant C in tumour/close to tumour)
↓
Permanent Implants

* Implants of Brachytherapy:
  - Short $t_{1/2}$ and Low energy
  - High dose in a close range
  - Low normal dose for the purpose of conformal treatment

→ METAPLASIA ←

Change of one type of epithelium into another type of epithelium (or)

Replacement of one type of mature epithelium by another type of mature epithelium

Eg: squamous, metaplasia lung & Cx
Scc

Q Cancer tumour: are adeno carcinoma of lung

Barrett's metaplasia : Goblet cells → AB-PAS (stain)

- for TB / Histoplasm : ZN stain
  (or)
  Lepra

- Lepra → Fite

- Melanin → Masson fontana and
  Melanin bleech

* DYSPLASIA " Disordered growth"

1. Loss of polarity:

Architectural disorientation of cell w respect to each other.

Q: Loss of polarity is the 1st change in the indicates the ongoing neoplastic process.

2. ↑ N/C ratio :

Q: Normal range : 1:6 - 1:4

Cancer cell : 1:2 - 1:1

But anaplastic → Seen in Highgrade anaplastic cancers

3. pleomorphism

4. Hyperchromasia / Course chromatin

5. ↑ed Mitosis / ↑ed mitotic activity / ↑ed mitotic Index

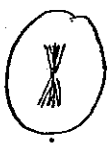
(N) tissues showing ↑ed mitosis = Skin
GIT
Highest Mitotic Index ← Bone marrow
} Normal process

* ANAPLASIA

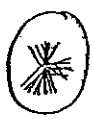
(1) All features of dysplasia are present in anaplasia

(1) Mitotic Index: ~~no~~ no of mitotic figure per 10 HPF

Q $\frac{15 \text{ MF}}{\text{"50" Hpf}}$ = used in GIST



(N) Bipolar Mitotic figure



Tripolar / Quadripolar / Multipolar Mitotic figures

(2) Atypical mitotic figure

↓

Anaplastic

* Metaplasia is always a reversable change
* Dysplasia in initial stage

D- Low grade = LSIL (reversable change)

↓

D- High grade = HSIL

(or)

A/k/A Carcinoma insitu

↓

Invasion

↓

Converted to malignancy → May / may not go into stage of anaplasia

(Scc)

High grade and Anaplasia = Irreversible

≠ All anaplastic tumours

- Clinically malignant
- All malignant tumour may / may not anaplastic

Definition of anaplasia: loss of differentiation

[Undifferentiation / poorly differentiation]

Q Desmoplasia:

1. Definition 2. Major factor 3. Mechanism 4. example

- Definition:

Excessive host stromal fibroplastic proliferation

Stony hard carcinoma = Scirrhous

Major factor: Vascular endothelial growth factor

Mechanism: Tumour cell (Tumour on host reaction)

↓

VEGF

↓

acts on host stromal fibroblasts

↓

PDGF & FGF

↓

trigger the cascading reaction

↓

excessive fibroblastic proliferation

⇒ Host on Tumour Reaction

Be host try to minimize tumour ☆ help

of capsule

Example:
- Ca Breast
- Ca colon
- Linitis plastica
- Fibrolamellar Ca Liver
- Anaplastic ca thyroid ↓ extremely Hard
- Ca Gall Bladder
- Cholangio carcinoma

- Perrampullary ca
- Desmoplastic variant, Ca pancreas

* DIFFERENTIATION

"the morphological and functional resemblance of tumour cells to the cell of origin".

Well diff	Mod. diff	Poorly diff
Carry Both, morphological & functional	M + No Func	No Morph + No Func

Q Adenocarcinoma:

Well diff adenocarcinoma: M+F present

Intact glands → Altered size/shaped
+
presence of Mucin
(or called as)
⇒ Musin secreting adenocarcinoma

Moderately diff adenocarcinoma: M + No funct
Broken / fragmented gland
+
No mucin

Poorly diff: No morp + No function

Single cell pattern

+

No mucin.

Exception: Poorly dif adenocarcinoma which has ↓ retained function

↓

Mucin is present + Single cell pattern

- Signet Ring cell Adenocarcinoma

↓

clinically called as Diffused Carcinoma Stomach

↓

Linitis Plastica

↓

M/c site : GIT

M/c site in GIT : Stomach > colon

↓ ↓

(Colorectal Carcinoma) CRC

M/c extra GIT site: Krukenburg's tumour

→ IMMINOHISTOCHEMISTRY ←

(IHC)

Epithelial: CK, EMA ↳ u better

Cytokeratin, epithelial memb Ag

Pan CK

Soft tissue tumour : Vimentin

(Vimentin is +ve also in epithelial cancer)

Q: * Carcinoma ⊖ Vimentin +ve = CarcinoSarcoma

(or)

always of grade 4 ← Sarcomatoid carcinoma cancer

Carcinosarcoma of uterus : MMMT

(malignant mixed mullerian tumour)

* Connective tissue / Sarcomas = ⊖ +ve CK

↓

*** Example: Synovial Sarcoma

- Monophagic
- * Biphasic
  - ↓
  - epithelium is well formed gland
  - ↓
  - Show +ve CK

* Examples of Biphasic :

Carcinosarcoma

Synovial Sarcoma

Wilms tumour

Mesothelioma
- Epithelioid mesothelioma (m/c type)
- Sarcomatoid (spindle shaped cells)

iphasic tumour

ilms tumour

nective tissue tumour

L are commonly = Vimentin +ve

Tumour of Fibroblast origin

Fibroma / Fibrosarcoma → Vimentin

umours of smooth muscle origin:

Uomgoma, Uomyosarcoma → SMA + Desmin

umours of skeletal muscle origin:

Rhadomyoma, Rhadomyosarcoma → Desmin + Myogenin + Myo D1 = Most specific And Sensitive

Blood vessel origin

Hemangroma, Angiosarcoma, Kaposi's Sarcoma → CD34, CD31, VWF, Factor XIIIa

↓

Most sand

Kaposi's Sarcoma ⇒ Must be +ve for HHV 8

5. Peripheral Nerve sheath origin

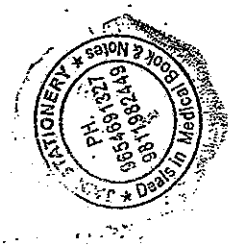
Schwannoma / Neurilemmoma } S 100
Neurofibroma

→ MOLECULAR ONCOLOGY ← (3 Sep 2017)

1st Rule : All cancer by virtue of their origin they are MONOCLONAL.

4 Classes of genes :

1. Oncogenes
2. Tumour supressor genes } Cancer
3. Anti apoptotic genes
4. DNA Repair genes

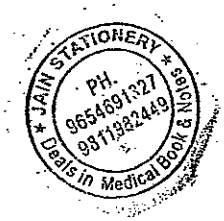


Que) Which one is not directly as a tumour formation

Ans) DNA repair gene

↓

- Maintain the integrety of the DNA molecule and repair any kind of damage
- Repair the damage in the remaining 3 classes



7 Commandments :

1. Self succient : Grocoth factor (oncogenes)
2. Insensitivity : Grocoth inhibitory signal (~~VEGF~~)
3. Evade apoptosis
4. Limitless replicative potential

   activation of enzyme (telomerase) ~~RACQ~~ (TSCS)
5. Ability for sustained Angrogenesis (VEGF)
6. Ability to Invade and metastasis APC, β-cadherin, E cadherin
7. Defective DNA Repair = Robbin 8th edition (aerobic glycolysis)

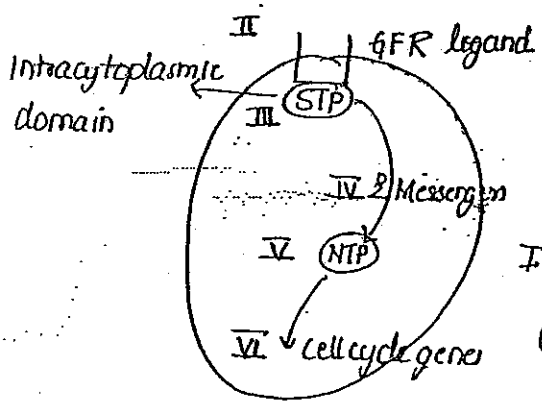
   WARBURG'S EFFECT = concept of tumour metabolism ↓ Robbin 9th edition

ONCOGENES

Proto oncogenes → (Mutation) → converted into oncogene

Proto oncogenes — Regulatory elements
↓
minus

promote growth / proliferations



STP: Signal transduct^{n} protein

NTP: Nuclear Transcriptn. protein

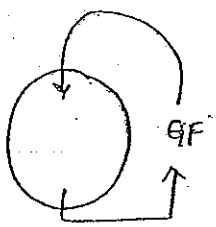
I Growth factor

Normal cell follow

↳ Paracrine / Endocrine / Synaptic

Cancer cells

Autocrine group



Mcq: which is the most common GF in human cancers TGFα

which is the following is m/c GF Inhibitor: TGFβ

II Growth factor / Receptors

Normal cells: GF + GFR → Dimerization

↓

Activation

↓

Reverse dimerizatn

↓

deactivation

ncer cells : GF + GFR → Permanent / Constitutive dimerization

Autonomy

↓

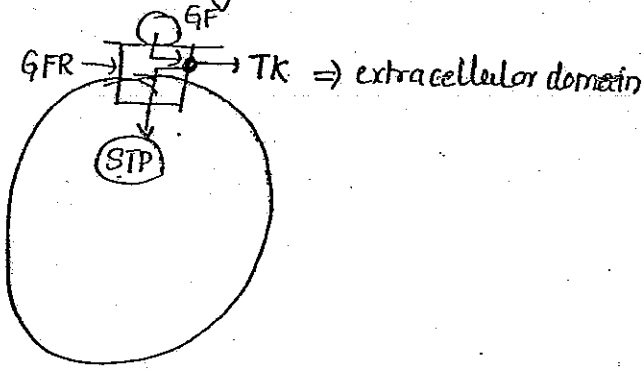
Preminantly Activated

GFR { G protein coupled receptor (Seven transmemb receptors)
Tyrosine kinase as receptor

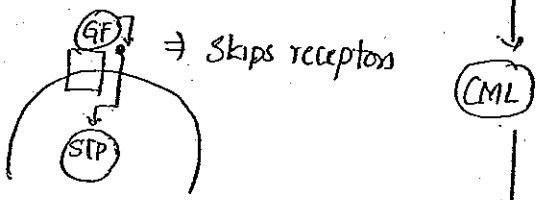
↓

Q M/c GFR-ligand in human cancer

eptor as Tk activity :



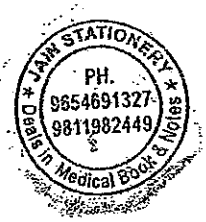
Non receptor as Tk activity :



Q Doc: Imatinib

Q ~~MOA~~ mechanism of action : Tk inhibition

* Imatinib, blocks the ATP supply to Tk



~~Normal~~ :

III Signal transduction protein

M/c STP : RAS

M/c oncogene : RAS

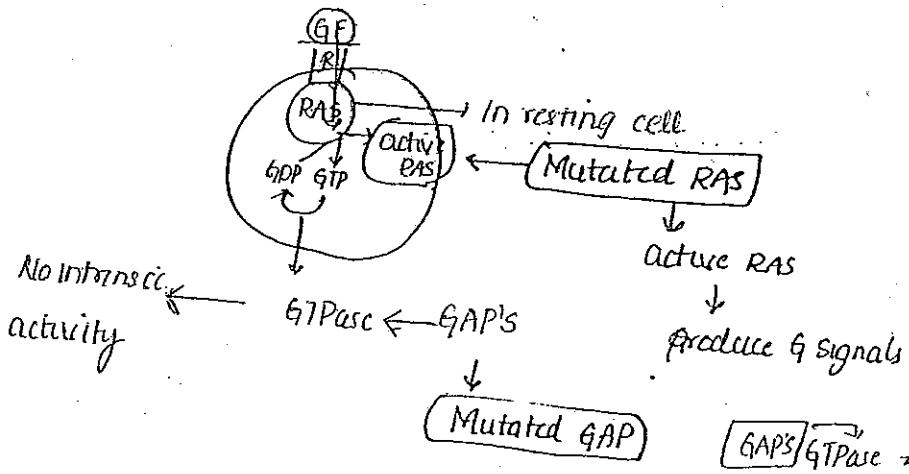
M/c gene : P53

Major mechanism of RAS :

Retino " " " " :

type of ass cancer :

Major mechanism of RAS



NF 1 = Molecule that controls RAS

(Neurofibromatosis)

(NF1 is m/c mutated RAS)

Minor Mechanism

RAS → RAF → MAP kinase pathway
↓ → Mitogen activated protein
RAS activated factor

type of Cancer

RAS
- KRAS — Colon ; Pancreas + Non small cell lung cancers (NSCLC) + Type I Ca endometriosis
- HRAS — Bladder & kidney + soft tissue sarcomas (STS)
- ** N RAS → Malignant melanoma + Leukaemia/lymphomas

IV 2° Messengers :

cAMP = M/c

V Nuclear Transcription protein

MYC JUN FOS β Catenin
↓
m/c mutated in NTP

MYC
- C MYC → Burkett's + Follicular lymphoma + DLB cell lymphoma (Diffused large B cell) + Ca Colon
- L MYC → Small cell lung cancers
- N MYC → Neuroblastoma

K RAS : NSCLC → Adenocarcinoma

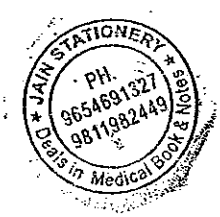
Mcq: EGFR (epidermal GF receptor)
↓
over expression of EGFR
↓
Aggresive behaviour cell
↓
① Poor response to Rx
② Poor prognosis

Mcq: A pt adenoca of lung = EGFR Mutation
Alk-1 positivity
Ros-1 mutation
} Good prognosis
↑
Trageted Rx

→ Cell Cycle Genes ←

VI Cell cycle genes
- cyclins
- CDK's
  - oncogenes
- Cell cycle Inhibitors
  - ↓
  - Tumour suppressor genes

Phase



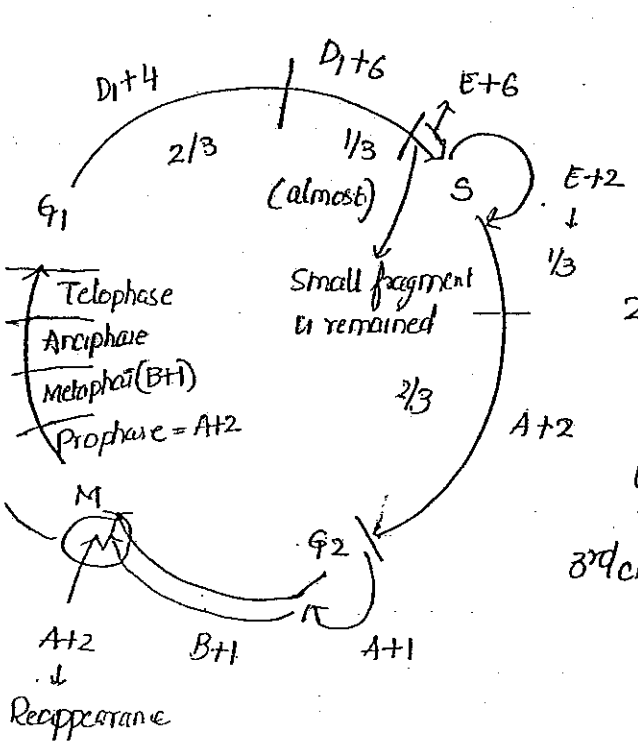
ase sequence : $G_0 - G_1 - S - G_2 - M$

equencial appearance of cyclin D-E-A-B

equencial appearance of CDKs 4-6-2-1

CDk are present, in the preactivated stage they depend on cyclins to push the cell into cell cycle

clins need to be activated



D $\begin{cases} D_1 \\ D_2 \end{cases}$ m/c

2 Check points: ① G_1 to S

② G_2 to M

↓

Controlled by p53 gene

3rd check point: Metaphase to Anaphase transition

⇒ Chemotherapy damage the S phase : so there is 2nd check point

→ once the cell enter the M phase it is not inhibited

→ The role of cell cycle inhibitor is at G2 to M

⇒ No -ve (or) inhibition of cell cycle in M phase

→ 3rd check pnt : check the alignment of chromatids

↓

Regulated by levels of cyclin B

2 check pnt regulated by : p53

* We can control 2 check pnts by external component

* 3rd check pnt is controlled by cell itself

* cyclin B touches the Basic line

↓

Anaphase open

↓

chromatin separated

↓

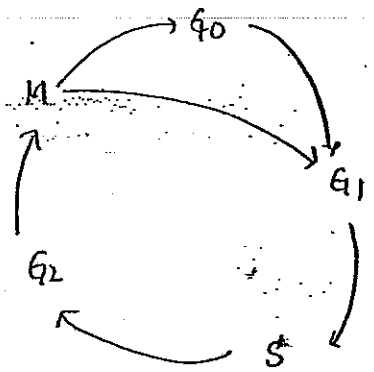
Telophase open

↓

cell seperated

* After M phase ⇒ if stimulus continues = G1 phase

if stimulus ceased = G0 phase



* Colchisine is mitotic inhibitor (3rd check point Regulator)

→ TUMOUR SUPPRESSOR GENE ←

key Role: Regulate the (N) cell proleferation

↳ Deletion/Inhibition: Unregulated growth

(Activation of oncogenes + Inhibition of T.S. genes } cancer)

1. cell cycle Inhibitors
2. P53 3. Rb 4. PTEN

Cell cycle Inhibitor

Non specific ← (G1 phase) → specific

Inhibit entire cell cycle — dual Inhibition — Restricted to G1 phase

(G1 - G2)

Cip/Kip family

- p 21 CDkN 1a
- P27 CDkN 1b
- p57 CDkN 1c

INK 4a family

- p16 CDkN 2a
- p15 CDkN 2b
- p18 CDkN 2c
- p19 CDkN 2d

MCQ: M/strongest & M/specific = p16/2a

G1 phase = p16 + p27

Entire cell cycle = (G1-G2) = p27 (universal cell cycle ⊖)

specific action at only checkpnts = p21

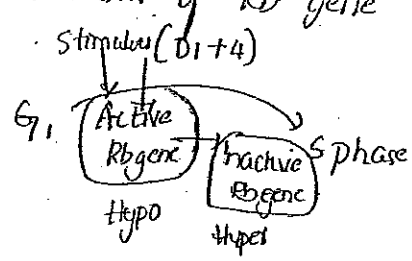
No independent role = p57

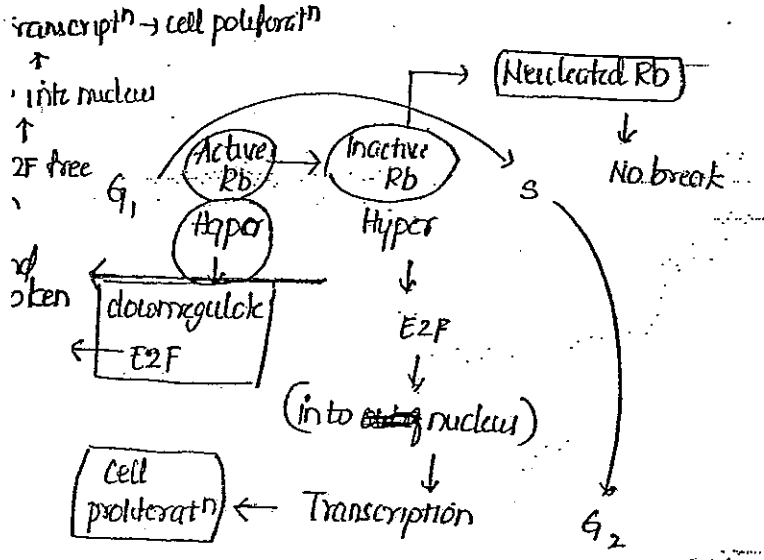
↓

acts ē synchronic ē p27

⟶ Rb Gene ⟵

Mechanism of Rb gene

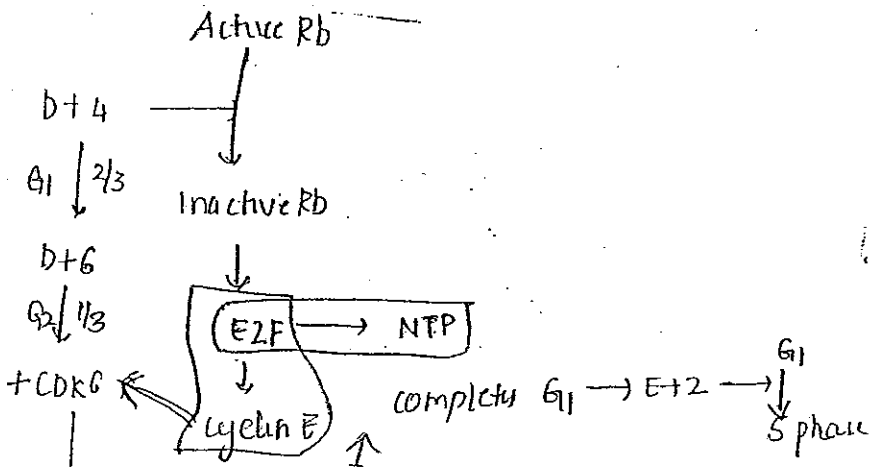




recruits hop enzymes (Histon deacetylase
Histon Methyl transferase

Chromatin remodeling - chromatin remodelam

Deacetylation
Hyper methylation
MCQ
Epigenetics



→ P53 GENE ←

Mechanism for cancer growth

1. Cell proliferation : clinically they are called

Fast growing cancers

↓

Markers : Ki 67 / MiB-1 *

↓

Ki 67 Index

other marker of cell prolif : Cyclin D1

* Cyclin D1 : diagnostic Marker for Mantle cell tumour

2. Anti apoptosis : clinically they are called

Slow growing cancer

↓

Marker : BCL-2 (follicular lymphoma)

3. Cell proliferation + Anti apoptosis : clinically called as

Explosive growing pattern

↓

Marker : Ki 67 ; BCL-2 → Diffused Large B cell lymphoma

Cyclin D1 + BCL 6 → Diffused Large B cell lymphoma

① P53 — Inhibitor Growth promoting oncogenes

Inhibit antiapoptotic factor Eg: BCL-2

noncoding RNA's

3 → Micro RNA's → MI RNA → Inhibits GP factor
⊖ Anti apoptotic factors

② → P-TEN ←

It for: phosphotase and tensin Analouge / Homologue

M/c malignancy ↓ PTEN mutation: Carcinoma
Endometrium / Type I
↓
PTEN + K-RAS

Second m/c malignancy: Ca breast

Second m/c lesion: Complex atypical endometrial hyperplasia
// (CAEH)
most specific answer than Ca breast

→ Ca colon

Ca prostate: only exclusive ♂ cancer carrying PTEN gene mutation

Ca thyroid

Ca pancreas

Gliomas

Cowden's synd (Last & least)

→ Anti apoptotic Genes ←

Apoptosis

Extrinsic

FAS / CD95

+

FAS L / CD95 L (L = Ligand)

↓

FADD (death domain)

↓

activate

procaspase 8 to caspase 8

↓

activate caspase 3

↓

Apoptosis

Intrinsic

Damage to the inner mitochondria memb

↓

Leakage of cytochrome C3

MCg

Bcl2 ⊖ →

⊖ → Cyt C3 + APAF-1

↓ (Apoptosis activating factor 1)

IAP's ⊖

procaspase 9 → caspase 9

↓

further actival caspase 6

↓

Caspase 3

↓

Apoptosis

Inhibitors of apoptotic protein (IAP's)

→ DNA REPAIR GENES ←

p53 ATM

↓

DNA damage sensors

↓

Not repaired

BRCA-1 BRCA-2

↓

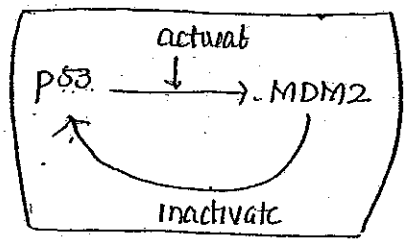
Independent DNA repair agents

DNA damage sensed → 1. Cell cycle arrest
→ 2. DNA repair
→ 3. Apoptosis

P53 : . Mech of action: remains the same at both checkpnts

P53 → cell cycle arrest (p21)
→ DNA repair : GADD 45
→ Apoptosis : BAX

GADD
Growth arrest and
DNA damage

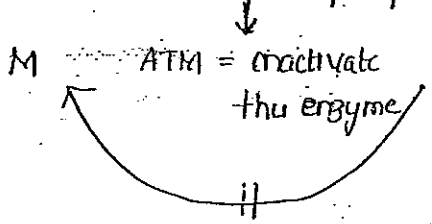


P53 lies in a -ve feedback Loop ~ MDM2

ATM : Mech of action changes ~ checkpnts

ATM: → G_1S checkpnt
P53 activation
ATM → P53
G_2 M checkpnt
↓
P53 Independent

activated CDC 25 phosphatase = complex integrity of B and 1



checkpnt

↓

By B+1

↓

break in B+1 ⇒ cell cycle arrest

1. Cell cycle arrest : Inactivation of enzyme
2. DNA repair : ATM combines with { BRCA-1, BRCA-2 }
3. Apoptosis : BAX

↓

depend on CDC 25 phosphatase

↓

So does not occur in G1–S

→

~~Lon~~ ATM/gene " p53 independent mechanism of ATM gene is targeted against ionizing radiation induced DNA damage!

⇒ If there is no radiation injury : p53 dependent DNA repair occurs.

taxia Telangectasia : ⊠ an ex g. radiatn Induced
concanogencee.

lismatch Repair dfect

Example: HNPCC

MSI / MMR gene (microsatellat Inbibitn
micro mismatch repair gen)

↓

MSH 1, MSH-2, MSH-3, MSH-6

Nucleotide excision repair defect

Pyramidine dimers

Eg: XP → dD/D :- Solar keratosis

↓

Xero pigmentosa

Recombinatn repair defect

AT, Bloom's synd, Fanconi's anemia

mptom of Ataxia Telangectasia

1. Cerebral ataxia
2. Telangectasia
3. Growth retradatio + Mental retradath
4. Strong predisposition to cancers
5. Immune deficiency

Bloom's synd: Multiple CNS cancers

Fanconi's anemia: ↓ + Aplastic anemia ⊂ predisposing to cancer

→ ANGIOGENESIS ←

Neovasculisation	Vasculogenesis
Sprouting of new capillaries from pre-existing vessels	Formation of blood vessels "denova"

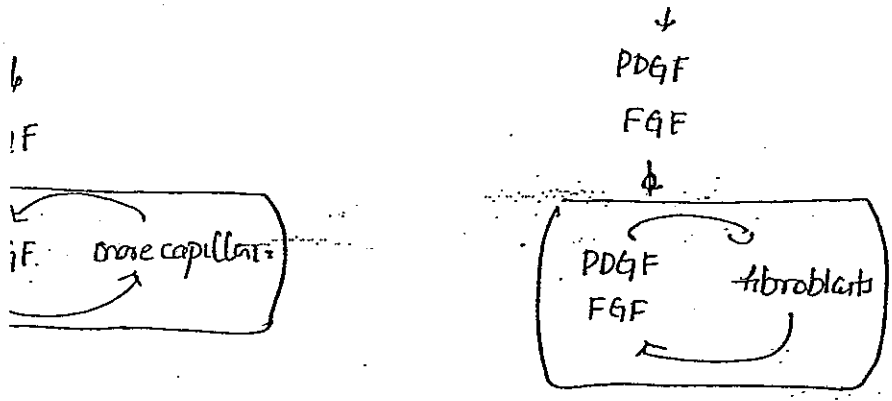
- Major angiogenic factor: VEGF
- Anti angiogenic agents from Host:
  1. Angiostatin
  2. Endostatin
  3. Vasculostatin
  4. Thrombospondin = major ⊖ to VEGF

Mechanism of angiogenesis

tumour cell
↓
VEGF

Tumour on Host reaction

- Acts on Host capillary endothelial cells
- Host cell fibroblasts



→ Tumour Metabolism ←

whenever cell enter hypoxia condition

↓

HIF-1α (Hypoxia Induced factor)

↓

Has a long $t_{1/2}$ to HIF-1α

↓

Inhibits thrombospondin → Promotes VEGF

Promotes enzymes involved in ~~angiogenesis~~ glycolysis → (or) Inhibit enzymes involved oxidative phosphorylation

↓

ever under aerobic condition

↓

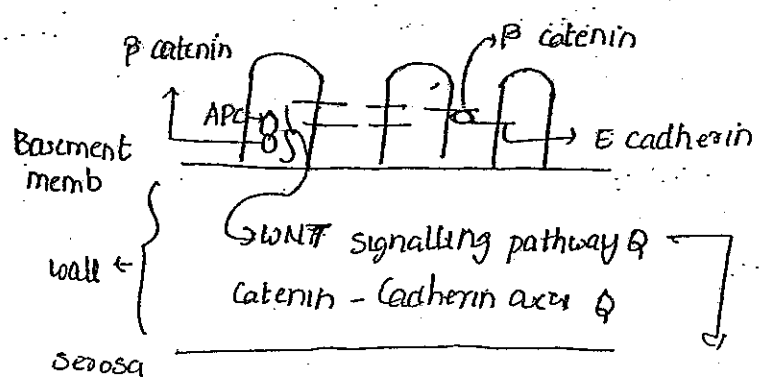
tumour cell follows aerobic glycolysis

↓

WARBURG'S effects

INVASION

Definition : Breech in the . Basement membrane



Maintains cell cell polarity

Mutated Gene	Molecular Effect	Clinical presentation
APC gene	→ cell proliferation	Pre malign Ex: polyps
β Catenin	→ cell proliferation Invasion	Malignant Ca colon Ca Breast
E cadherin	→ Invasion cell proliferation	2° > 1° 2° ♂ unknown Ca oesophagus

Eg: Ca colon
Ca Breast
Papillar ca thyroid

Breech of Basement Membrane

Basement membrane = Type IV collagen

Tumour = collagenase

Transmigration through extracellular matrix (ECM)

Pro invasive agents :

1. Collagenases
2. Elastases
3. MMPs (2, 4, 9 = major 9)
4. Urokinases
5. TPA's (tissue plasminogen activators)
6. Cathepsin - D

→ TUMOUR - IMMUNITY ←

T cell mediated immunity

always MHC I restricted

NK cells and macrophages are effective against Tumour cells

Tumour Antigens = ① products of oncogenic viruses

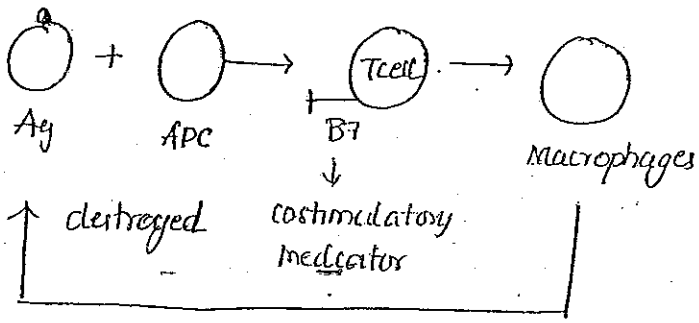
② Products of mutated genes

③ Abn expression of the cytoskeletal proteins such as Actin and myosin

④ Aberrent expression of cell surface Lipoproteins & Glycolipids

⑤ Oncofetal Ag : reexpression of fetal Ag in the adult life due to tumour

→ Mechanism of tumour Immunity

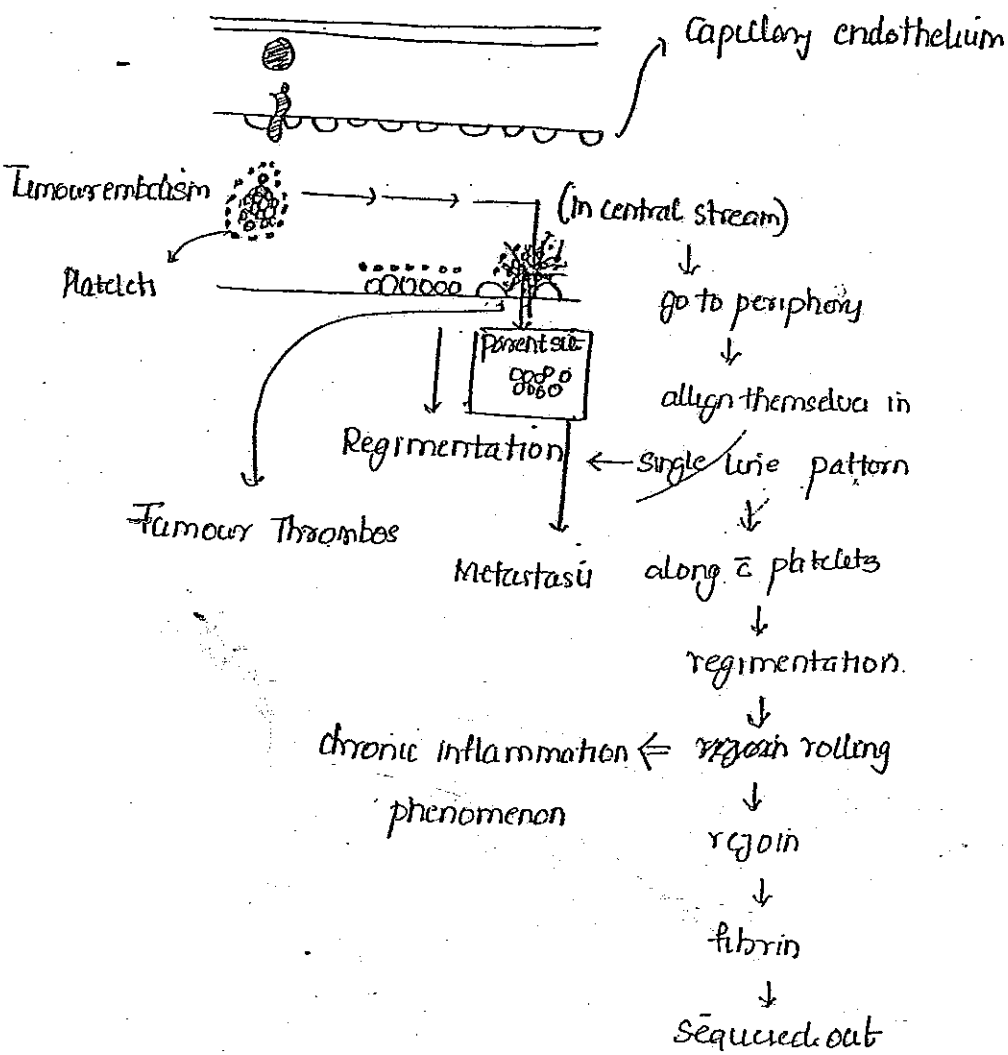


→ Mechanism to escape Immunity

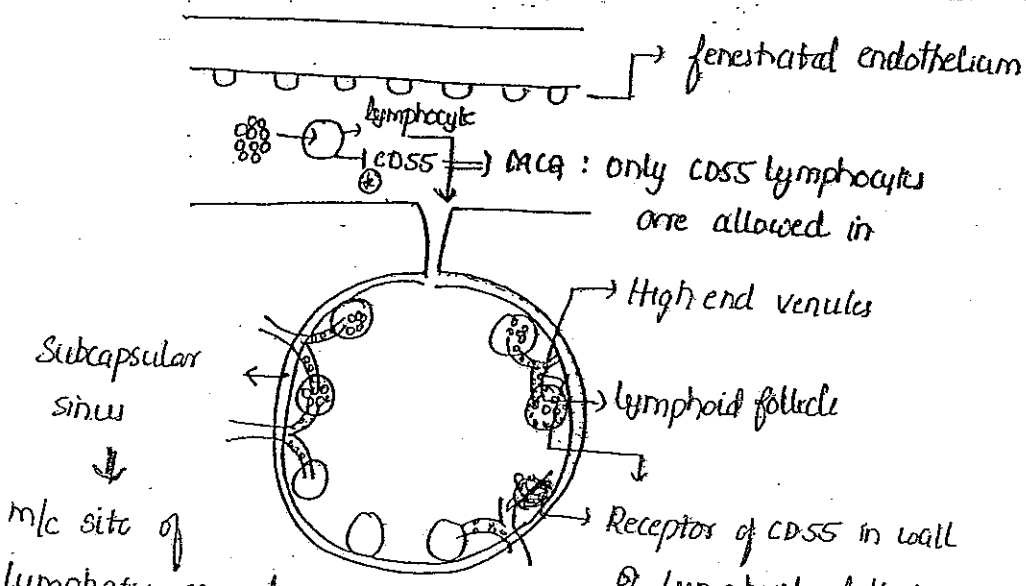
1. Selective outgrowth of Ag -ve variants
2. Loss of APC
3. Cytotoxic effect against Host T cells
4. Loss of co-stimulation
5. Cytotoxic effect against Host macrophages
6. Ag Masking
7. Ag sequestration

→ METASTASIS ←

I Blood Borne metastasis



→ Lymphatic spread ←



→ HAEMATO ONCOLOGY ←

gin of Haematopoietic cells

pluripotent stem cell PPSC

↓

Stem cell

↓

Colony forming units (CFU)

myeloid lymphoid Erythroid Megakaryocytes

CFU - Myeloid → Granulocytes (N/E/B)

→ Monocytes

Any change in myeloid cell (⇒) granulocyte ⊂

pective to quality / quantity (⇒) both

↓ ↓

Dysplasia proleferat

quantity

ecompained by the change in the no of / monocytes

↓

Never show dysplasia

Abn cell ⇒ Blast

Blast = Peripheral Blood / Bone marrow aspiration counts

Blast = BMA > PB

$$\text{Blast} \propto \frac{1}{\text{Platelet count}}$$

↑ Blasts = ↓ platelet count

→ MYELOID NEOPLASMS ←

CMPD	MPD / MDS	MDS	AML
Chr myeloid proliferative	↓ proliferath	↓ Dysplasia	Acute myeloid leukaemia
↑ed quantity	Dysplasia	Abn quality	Abn cell / blasts
	↑ quantity	+	
	+	↑ed quantity	
	Abn quality		

pt response ↓ lesser to Rx

- poor prognosis

Chronic Myeloproliferative disorders / Neoplasms

CMPD / CMPN

CML PV ET PMF CNL CEL / HES

↓

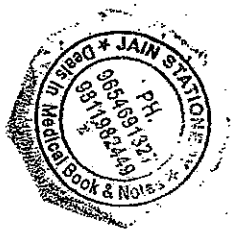
Hypereosinophilic Syn.

→ CML — Chronic phase
Accelerated phase
Blast phase

— CML, Chronic phase —

↓

D/D = leukaemoid Reaction



- It's a incidental findings
- Major cell = 1. Myelocyte MCQ

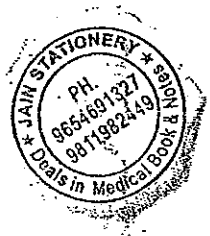
↓

2. Next m/c cell = Mature neutrophil

3. Basophilia (<10%)

4. platets (mild ↑)

Blast — PB <2%
BMA 2-5%



* pt's in chronic phase more responsive to drug
* pt's in chronic phase never present c Thrombocytopenia.

⇒ Thrombocytopenia related Rx

→ Accelerated phase ←

1. Basophils >20%
2. Thrombocytopenia ; unrelated to Rx
3. Monocyte ~~<20%~~ <20%
4. Blast — P. Blood, BMA

→ CML Blast phase ←

1. Blast PB/BMA ⇒ ≥20%

Blast crisis = CML blast phase ≅ Erythroblastic crisis

* Spleen & liver enlarged

PPSC

Myeloblast — Erythroblast

↓

↑ RBC

↓

↑ viscosity

↓

↓ flow

↓

MI symptoms

→ POLYCYTHEMIA VERA ←

1. Panmyelosis

↓

Major cells are: RBC

↓

2) Hb = ♂ = 18.5 gm

♀ = 16.5 gm

3) Rule out reactive erythrocytosis = Serum erythropoietin

↑

Hypoxia

- → High altitude
- ↑ chronic smoker
- ← COPD

4) Sr. Erythropoietin = ↓ / (N)

5) JAK 2 Mutation = Sensitive / but not specific

- ET
- 1° myelofibrosis

Essential thrombocythemia (ET)

1. Panmyelosis = major cell = platelets ↑↑↑
2. PB count >4.5 lakhs/mm^3 ⇒ current accepted criteria

>6 lakh/mm^3 = was the older WHO criteria

3 Rule out Reactive thrombocytosis

- Iron def Anemia
- Solid Tumours
- AIHA

4. JAK2 mutation

Primary myelofibrosis:

A/k/A : ~~Chr~~ CIMF

1. Pancytopenia

Q 2. Dry tap: dld = Hairy cell leukaemia
AML M7

3. JAK2 mutation

Q 4. Rule out 2° myelofibrosis

↓

CML

Essential thrombocythemia } ↑ platelets

PV

↓

↑ nos megakaryocyte in Bone marrow

↓

PDGF

FGF

↓

myelofibrosis

Chr Neutrophilic leukemia Chr Esinophilic leukaemia / HES

Dxn of exclusion

1. R/o Reactive neutrophilia
2. MN ~~and~~ and bands >80% of total
3. Blast <10% in BM

No blast in PB

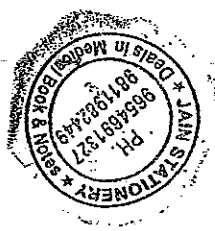
4. Established clonality
   ↓
   polyclonal
   ↓
   reactive

1. R/o reactive esinophilia
2. C/H of 6 months + ↑* Esino counts + Non remitting symptoms } HES

   HES + ↑Blast } CEL
3. Blast <10% BM

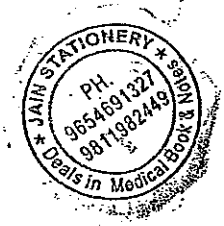
No blast in PB

4. Established clonality



→ MPD / MDS ←

Myeloid proleferatn = Granulocytes
+
Myeloid dysplasia
+
↑ no of monocytes
+
BCR ABL -Ve



I Chr myelomonocytic / ~~Lymph~~ leukaemia

CMML 50-60 yrs

1. Absolute monocyte count $> 1 \times 10^9/L$
   ↓ ↓
   N = 0·2 to 0·4 5 time ↑ed monocyte count
2. % of monocytes $\leq 20\%$
3. Dysplasia in one (or) more myeloid lineages
   i·e granulocyte + erythrocyte
4. BCR - ABL (-Ve)

II Juvenile myelomonocytic leukaemia

JMML 10-12 yrs

CMML - JMML
↳ No dysplasia

Above 4 + (5) ↑ HbF for age

(6) pt present c Hypergammaglobulinemia
↓
(↑ Lymphoid cell)

(7) Mimics EBV and CMV infections

D/D's = JCML (Juvinile CML)
↓
always BCR ABL (-Ve)

V Atypical CML

(Chronic phase CML + Dysplasia and − BCR ABL)

VI Myelo Dysplastic Synd = Granulo + Erythrocytic

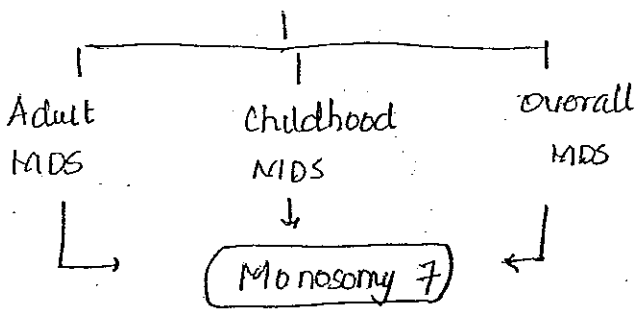
3 basic Rules

1. MDS pts : Male (++)
2. Thrombocytopenia presentation
3. Poor prognosis

VII MDS ± Isolated deletion 5q

1. Females ++
2. Thromobocytosis
3. Better prognosis

Genetic abnormalities in MDS



MDS => present as cytopenia

- Unicytopenia
  - presented as Anemia
- Bicytopenia
  - Anemia + Thrombocytopenia
- Pancytopenia
  - Cohore granulocyte also ↓ed

I Refractory Anemia (RA)

1. Anemia (↓ed Hb)
2. (N) Lab Investigations
3. Non responsiveness ~~for~~ to ~~Rx~~
   - ↓
   - cause ↓ erythroid dysplasia
   - Ineffective erythropoiesis

II RA ± ringed Sideroblasts

RA +

RS >15% of erythroid precursor

III RCUD = (Refractory cytopenia ± unilineage dysplasia)

- Bicytopenia = ① A+T (Anemia + Thrombocytopenia)
  - ② Dysplasia in one myeloid lineage
    - ↓ Mostly neutrophils

3. Blast ⟨ PB : <2%
BMA 2-5%

IV RCMD : / Refractory Cytopenia ⊂ multi dysplacia

RCUD + dysplasia in ≥2 lereages

V RAEB : Refractory anemia ⊂ excess blasts

RAEB ⟨ I
II

RAEB I : RCMD + Blasts ⟨ PB 2-5%
BM 5-9%

Aeur Rods -ve

RAEB II : RAEB I + Blasts ⟨ PB 5-9%
BM 10-19%

↓ Aeur Rods (±)

D/D : CML, Accelerated Phase

→ ACUTE / MYELOID LEUKAEMIA ←

WHO classification :

I AML c recurrent genetic Abn

No blast criteria

① translocation t(8:21) NOW IS AIIMS

② t(9:11)

③ t(15:17) ⇒ M3

④ Inversion Inv(16a) ⇒ M4 (AML c eosinophiles)

II AML c myelodysplasia

AML c myelodysplacia c MDS — RAEB2

~~c (or) t out M~~ — c out MDS

III AML therapy related

3A Alkylating agents related AML

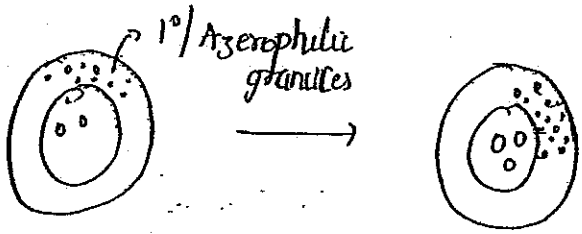
3B Toporsomerase inhibitor " "

IV AML - ~~NOS~~ NFS

M0 ⟶ M8

Ex: AML ⊼ Down's synd

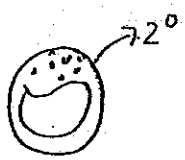
→ Maturation series of granulocytes ←



Myeloblast → Immature ← promyelocyte

↓

Apperance 2° granules indicate maturity



Myelocytes (1st Mature)

↓

Neutrophil ↖

Eosinophil ←

Basophil ↙

Band ← Metamyelocyte

• Most Immature blast: Megakaryoblast > Erythroblast
↑ old ↑

Myeloblast >, Monoblast

→

↑ing maturity

M0 = AML ~~c~~ out / minimal difference

① Stem cells ++

② MPO (Best Marker)

MPO ≤ 3% blasts (Negative)

③ CD34 ++

④ ↓ dedifferentiation / No maturation

M_1 AML ~~c~~ out maturation

① Stem cells + M·B + P·M

② MPO ≥ 3% blasts

③ Monocytes <20%

④ CD34 + (CD13 & CD33) Immature myeloid markers

↓ Maturation

M_2 AML ~~c~~ maturation

① M·B + PM + myelocytes

② Monocytes <20%

③ CD13 & CD33 +Ve ⊛ mature myeloid markers

(CD15 & CD65)

↓ Ted monocytes

ase ⇐ (M2 + >20% monocytes)

↓

A. myelo monocytes M4

CD 15 & CD 65 + (CD14 & 64) ← marker for monocyte

↓ Monocyte Immature

5

marker = CD14 & CD64

→ Acute monocytic leukemia

5a - 5b -

Acute monoblastic monocyte — Monoblastic/monocytic leukemia promonocyte

: acute erythroid leukaemia

6a — Erythro leukaemias (Erythroid / myeloid)

M.B + E.B + other Immature erythroid

0% ↓ 40%

marker: CD13 & 33 + HBA + Glycophorin A

6b — Pure erythroid leukemia

EB > 80%

marker:

HBA + glycophorin A

6a 6b

D/D ① M = CML blast phase D/D : M7
C. EB crisis

② clinically
polycethemia Vera

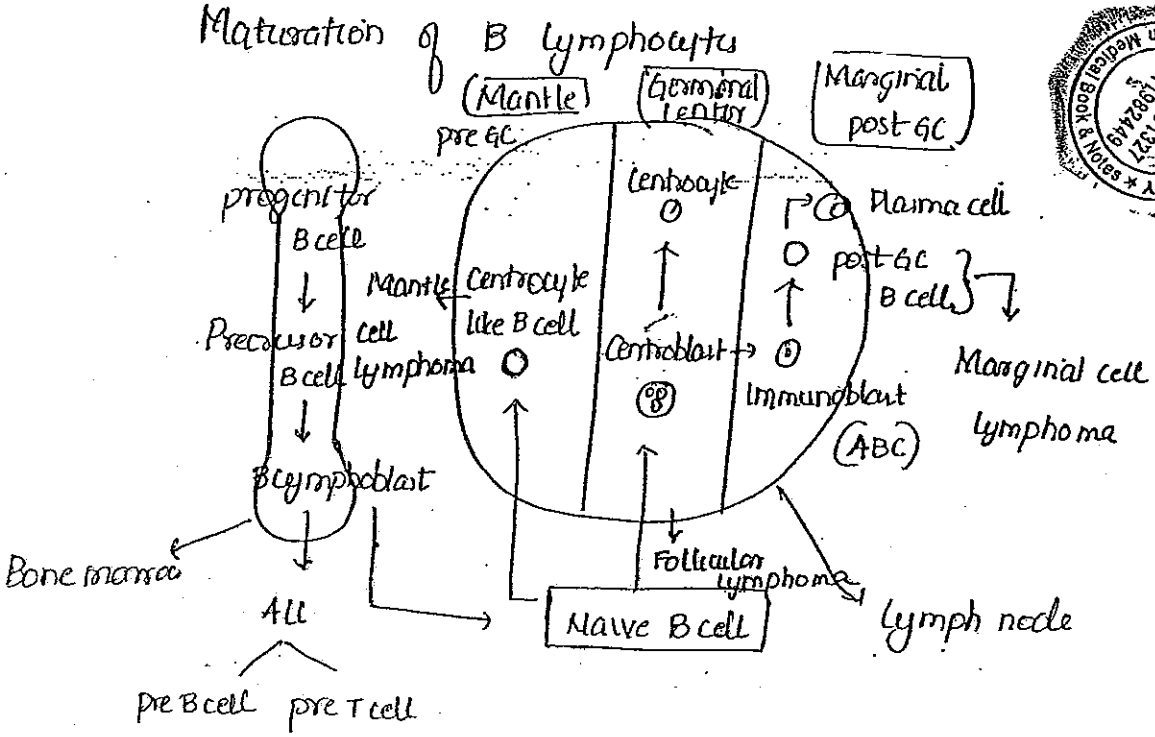
. AML - M7 Acute megakaryoblastic leukaemic
M.B + Mega blast + promega karyocytes
→ predominant
CD41 + CD42 + CD64

6a :

20	40 50%	40
M.B	E.B	other

CD41 + CD42 + CD61
↓ ↓ ↓
GP Ib GP IIb/IIIa GP IIIa
↓ ↓
B.S G.T

D/D = ① M6b ⇒ morphologically
② PMF ⇒ clinically



Cell of origin in Multiple myeloma is Post GC B cell →

① DLBCL : Diffused large B cell lymphoma

cell of origin = Centroblast

Immunoblast

Post GC Bcell

Variants : Centroblastic → CD 10

Immunoblastic → MUM

Plasmoblastic → CD 138

Tcell rich → CD3 & CD7

Anaplastic → ALK 1

3) Markers: CD19, CD20, CD79D

BCF-2, BCL6, Ki67

Follicular lymphoma

cell of origin: centrocyte

morphological pattern: equal sized follicles

DD: follicular hyperplasia

↓

unequal sized follicles

Markers: CD19, CD20, CD10

↓

GC B cell marker

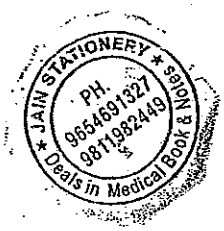
CD79a, BCL-2

→ Grading of Follicular lymphoma

Grade 1: 0-5 centroblasts / hpf

Grade 2: 6-15 centroblasts / hpf

Grade 3: >15 centroblasts / hpf



3a → Centrocyte present

3b → behaves like DLBCL → centrocytes absent

Mantle cell lymphoma

Cell q. origin: centrocyte like cell / Pre GC B cell.

Morphology: Mantle zone
- Diffuse small cell pattern

MCQ M/c DD ⇒ Small lymphocytic lymphoma (SLL)

Markers: CD19 and 20

↓

Morphology

↓

Diffuse small cell pattern

↓

MCL ← CD5 → SLL

↓

MCL −ve ← CD23 → +ve SLL

↓

CD5 negative

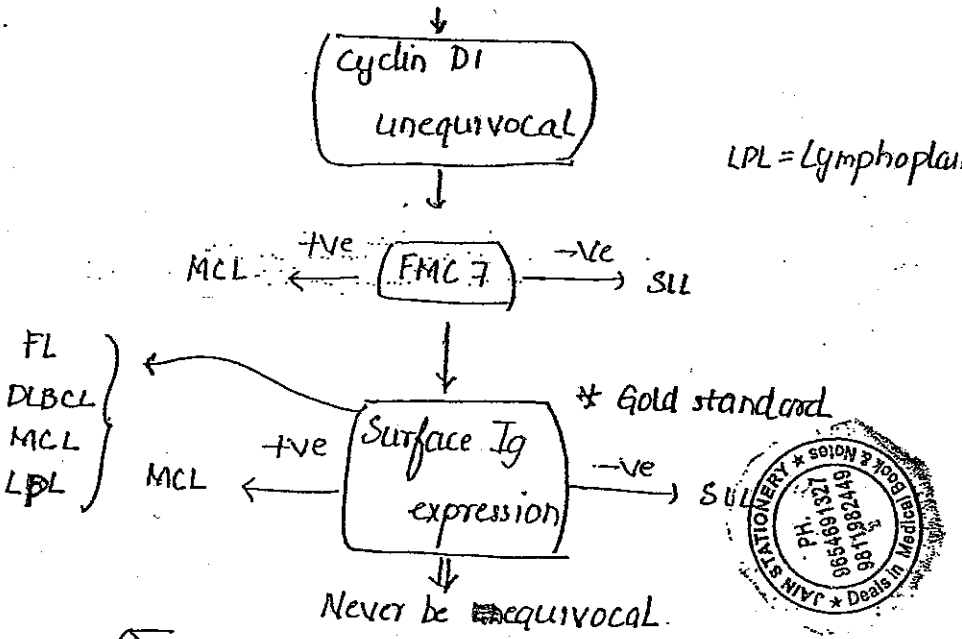
↓

MCL +ve ← Cyclin D1 → −ve SLL

MCL ← −ve

↓

"Sox 11"



LPL = Lymphoplasmacytic

Normal condition = Surface Ig expression shown by plasma cell

= Ig expression (in cytoplasm) by every immature cell

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