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Name : __________________________________________

Subject : Medicine
CVS

RHEUMATOLOGY

RESPIRATORY

ACID-BASE BALANCE
Examination

Non Auscultatory
- Pulse
- JVP
- Apex

Auscultatory: S₁, S₂
- clicks
- opening snap
- murmurs

CVS

Specific Disease:
Endocardial Disorders
- ARF, Valvular Heart Ds.
- Infective Endocarditis
Myocardial Ds
- Cardiomyopathy
  - CHF
- Pericardial Ds
  - Acute pericarditis
  - Tamponade
  - Constrictive Pericarditis
Vascular Disorders
- HTN,
- IHD,
- Aortie Dissec
PULSE

1. Pulse Rate
   a. 60 - 100/min
   Ab
   1) Bradycardia < 60/min

Causes

Physiological

1) Elderly
   (age-related SA node degeneration)
2) Sleep
   (1 in sympathetic activity)
3) Athletes
   (Baseline ↑ in vagal D/c)

Pathological

1) Cardiovascular Cause
   a) Bradycardias (AV Block)
   b) MI [inf. wall]

   SA node due to stimulation also supplied by vagal n/v nearby

   coronary artery

2) Non-CVS Causes
   1) Hypothyroidism
   2) Hypothermia
      (directly affects SA node)
   3) Drugs
      a) β blocker
      b) non DHP CCB [cause AV Block]
      c) Digoxin, Digitalis effect
   4) ↑ ICP
      Cushing's reflex = BP↑, HR↓, irregular EKG

To perfuse brain system
BP↑ → stimulate baro receptors in carotid
release vagal D/c
1. Tachycardia
   - 1) Infants (↑ SA node activity)
   - 2) Anxiety (↑ sympathetic activity)
   - 3) Exercise (↑ demand)

   Sympathetic system < Thoracic nts [Thoracolumbar] 

2. Pathological: CVS Causes
   - 1) Tachyarrhythmias, arrhythmias
      - a) PSVT
      - b) AF
   - 2) MI (ant. wall)

3. Non-CVS causes:
   - 1) Hyperthyroidism
   - 2) Fever
   - 3) Benz: -Benz
   - 4) Drugs
      - a) β agonist
      - b) Short-acting DHPs [reflex tachycardia due to compensation]
   - c) Digoxin toxicity
   - d) Thyrophyl
   - e) Thyroxin
Relative Bradycardia / FAGET'S SIGN

HR doesn't ↑ in proportion to body temperature.

For every 1°C from 37°C ↓

HR ↑ by 15-20/min from baseline

For every 1°F from 98.6°F → HR ↑ by 10/min.

E.g. if Body Temp is 90°C

\[ HR = \frac{112}{min} \quad \text{(baseline = 80/min)} \]

min expected HR = 80 + 45 = 125.

Causes

Infectious
(also θSA node)
1) Typhoid fever
2) Brucella
3) Legionella (sputum AFB +ve)
4) Viral

Non-Infectious

1) Drug induced fever
2) Self induced fever or Factitious Fever Q.
3) Fraudulent Fever (thermometer only)
Rhythm:
- Regular: Fixed interval b/w any 2 consecutive pulses

![Diagram showing heart rhythm with sinus arrhythmia and changes in HR during inspiration and expiration.]

Physiological:
- Sinus arrhythmia
- HR changes in inspiration and expiration

During Inspiratory Phase:
- Ve Intra-thoracic Pressure
  - Blood flow into R side of heart
  - Pulmonary venous dilatation
    - Blood pooling
  - Blood flow into L side of heart
  - CO will ↓
  - SBP will ↓
  - Baroreceptor stimulation ↑
  - Vagal release ↑
  - HR ↑
During Expiratory Phase:

- Intrathoracic Pressure
  - Blood flow into right side of heart
  - Pulmonary vessels are squeezed
  - Blood flow into left side of heart
  - CO will increase
  - SBP will increase
  - Baroreceptor will increase
  - Vagal will decrease
  - HR will decrease

Pathological:

1) Regularly irregular rhythm
   - Predictable variable
   - Cause:
     - Bigeminy rhythm
     - Digoxin toxicity
     - Every alternate ventricle contracts, depolarization is due to premature ventricular ectopic

EKG:

Pulse:

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Premature ventricular ectopic

Pulse: Bigeminus

Due to ectopic

Amplitude due to ventricle filling time hence + stroke volume

II. Irregularly Irregular Rhythm

No predictable variation in interval.

Cause = Atrial fibrillation. Variable HR

III. Pulse Pressure

How well a pulse felt.

N = SBP - DBP [30-60mmHg].

A/N

↓ PP. Thready Pulse.

Mech. If SBP ↓ & DBP ↑:

↓ CO

Stimulate sympathetic activity

Anterior constriction → PVR ↑
CAUSE = Shock [Hypovolemic, shock].
not found in septic or neurogenic shock.

II) ↑ PP /Bounding Pulse:
Mech: if SBP ↑ or DBP ↓
occurs if cot ↓
to ↓ LV strain → PVR ↓

CO is inversely related to PVR

CAUSE: 1) ↑ CO state

CVS
1) AR
2) MR.
3) PDA

Non-CVS
Physiological →
when plasma vol ↑

Pathological →
1) Hyperthyroidism
   β1 rec +
   ionotropic
   chronotropic

\[ \text{CO} = \text{TSV} \times \text{HR} \uparrow \]

[ Vit B₁ ≠ NO synthase

\[ \text{Def of Vit B₁} \rightarrow \text{Vasodilatation} \]
\[ \text{PVR ↓ → CO↑} \]

2) Anaemia
3) Bere-Bere
PVR is an arteriole, and bypassed

4) A-V fistula

5) Paget's Disease

Q: In a low CO state will cause bounding Pulse?

Ams. Severe bradycardia = complete AV Block

SV ↑ x HR ↓ → CO ↓

AV Block → depolarization of pacemaker fibres

Rate ↓ [slower speed in AVN]

But EDV ↑

SV ↑

W CHARACTER

Rate Rhythm best assessed in Radial artery

Character / contour "..." Carotid artery

N Waveforms of carotid.
S1 is due to closure of AV valve

Pressure changes in carotid

Due to closure of AV valve

Pericardial wave

Tidal wave

Diastolic notch

Diastolic wave (too small to detect clinically)

CO

(PVR)

S1

Mid systole

S2

Due to AV valve opening

Isovolumetric contraction

Ejection phase

WAVE

1. Pericardial wave
   It is due to pressure transmission by isovolumetric LV contraction onto carotids

2. Tidal wave
   Blood ejection into carotids ring its pressure further

3. Diastolic wave
   Due to back pressure reflection from small vessels

Diastolic notch represents closure of aorta + pulmonary valve (S2)
LV blood → → ← →
        \^
        systole
diastole

Recoil of small vessel lead to rise pressure impulse

Ab (N)
1. Hyperkinetic Pulse
   => ↑ amplitude

2. Hypokinetie Pulse
   though dicrotic wave in 1 but still not felt not felt clinically.
   => ↓ amplitude

3. ↓ amplitude: Parvus late peak: \( \text{et tardus} \)

Diagro

Cause
↑ CO state

most specific pulse of severe AS.
4. **Dicrotic Pulse**

- 2 peaks
  - One in systole
  - Other in diastole

5. **Bifurcated Pulse**

- 2 peaks
- In systole

Best assessed in peripheral artery

- Brisk, diovolumetric
  - Ventricular contraction
  - (? LV vol. + stretching)
  - Perfusion wave will shift to C
    - (as duration & len)
    - Gets separated from tidal wave

- Shock
  - (Hypovolemic Cardiogenic)

- Host specific pulse
  - Severe AR
  - Severe AR + AS

- HOCM
V MISCELLANEOUS POINTS IN PULSE.

1. PULSUS ALTERNANS - Best assessed in Radial. Regular alteration of pulse amplitude.

   ![Heartbeat Diagram]
   
   only amplitude changes, intervals remain same

   CAUSE → LV (systolic) Dysfunction

2. PULSE DEFICIT:

   a) HR - PR → due to adequate SV = 0
      ↓
      due to ventricle contract

   Ab if HR - PR = +ve → Pulse Deficit

   CAUSES
   1. AF & variable heart rate
      
      ![Heartbeat Diagram]
      
      inadequate ventricular filling → No pulse

      Pulse adequate
      ventricle filling

      Here 5 HR but 3 PR

   2. Premature Ventricular Ectopics
      
      less filling time → pulse not felt
If pulse deficit > +10/mmHg ⇒ AF only

37. Pulsus Paradoxuses:

- SBP_{exp} > SBP_{insp} = 0 to 10 mmHg.
- If this difference is > +10 ⇒ True Pulsus Paradoxus.
- Exaggeration of normal phenomenon; hence paradoxical word is wrong.
- Mech. ↓ in SBP_{insp} more than physio limits.

CAUSES

- CVS: H/o CVS cause = Cardiac Tamponade.
  "Compression" of heart due to pericardial effusion.

- During Inspiration:
  Blood flow is more in RV ventricle.
  RV wall dilates to accommodate extra blood.

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In Tamponade:

Inspiration

blood.

+ →

RV → septal bulge → LV filling further

↓

CO

↓

SBP during inspiration

less than physiological limits.

2) Constrictive Pericarditis

Failure of relaxation of heart due to stiff pericardium

Failure of relaxation of heart due to stiff endomyocardium.

Septum should be spared from stiffness to cause this sign.

3) Restrictive cardiomyopathy

Non CVS Cause

H/c overall cause → Acute Exacerbation of Asthma or COPD,

2) Pulmonary embolism

3) Kussmaul breathing [due to met-acidosis]

4) Obesity

5) SVC Obstruct [reason not known].
Deep Inspiratory efforts

\[ \text{Large } \rightarrow \text{ve intrathoracic pressure} \]

\[ \text{Venous return to the right side} \]

\[ \text{Septal bulge} \]

\[ \text{Pulvin Paradoxus} \]

**JVP**

1. Measure of **R** atrial pressure seen in **I** J V
2. Height -> 0-3 cm from sternal angle
   \[ \text{5 cm below} \]
   \[ \text{RA activity} \]
   \[ = 5-8 \text{ cm from RV activity} \]
Q. e wave: (b) systolic
⇒ \( V \) wave

Q. \( e \) wave will be more prominent?
⇒ \( a \) wave.

Q. \( e \) descent will be more prominent?
⇒ \( x \) descent.
Ab(+) JVP

1. **a wave** = due to right atrial contract

   1. Absent a wave = if ineffective atrial contract

   2. Large a wave = if right atria contracting against more resistance

Diastolic Wave

If right atria is contracting → Tricuspid valve give resistance

RV also gives resistance

cause:

a) **Tricuspid stenosis**

b) RV pressure ↑

"Compression of RV"

RVH (concentric)

↑

due to PS

PAH

RV failure (systolic)

RV blood retention.

↑

Pulmonary embolism

1) RV MI

2)

Cardiac Tamponade
Cannon A wave: if RA contracting against closed T. valve → cause TV closure if RA & RV are contracting simultaneously
Causa: 3 Functional Rhythm.
SA node → AV node becomes pacemaker → impulse reach B atria → ventricle simultaneously
Rate of Cannon a Wave = 50/min, Regular

2 Complete AV Block:
SA node will depolarize atria. →
Purkinje fiber will depolarize ventricle independently
So occasionally atria → ventricle can depolarize simultaneously
Cannon a waves → Intermittent

II X Descent:
N: due to tricuspid ring pulled down by RV contract: during eje: phase.
R: atria is free of significant blood (during this phase)
Abs X Descent
1. Absent X Descent
   if R atrial pressure doesn't fall as it contains significant Blood or Clot
Significant blood $\uparrow$ clot $\uparrow$

$\text{TR}'$

24

2. Deep \( \times \) Descent
   occur if tricuspid ring pulled more downward due to
   $\uparrow$
   \[\text{Increased RV contract}\]

? 1) Cardiac tamponade
2) Constrictive pericarditis

\[\text{V Wave}\]

[$\oplus$] due to venous filling of $\oplus$ atria

Ab[$\oplus$]

1) Absent or Low V wave $\Rightarrow$
   occur if venous filling of RA $\downarrow$
   cause - a obstruct s &

2) Large V wave $\Rightarrow$
   If RA pressure $\uparrow$ during venous filling

$\downarrow$ venous filling $\uparrow$

or $\downarrow$ compliance of $\oplus$ atria

[&]
   \[\text{failure of relaxation}\]

1) Constrictive pericarditis
2) Restrictive cardiomyopathy
IV. Y Descent

Due to passive blood flow from R atria to R ventricle.

1) Rapid Y Descent: FREIDRICH's sign.
   - Will occur if R atrial blood moves very fast into R ventricle as soon as Tricuspid valve opens.
   - All causes of large a = Rapidly

2) Slow Y Descent:
   - If R atrial blood moves into R ventricle slowly.
   - Causes:
     1) Tricuspid stenosis
     2) ↑ RV pressure

Causes of Large a = Slowly

Y descent absent if RA blood doesn't move into RV during papillary filling phase.

→ Occurs if R ventricle is fully "compressed."

Cardiac Tamponade
Signs of JVP

1. Abdomino-Jugular Reflex
   - Abdomen compressed for 30 sec

2. Kussmaul's Sign
   - In JVP during inspiratory phase
   - JVP is during inspiration

Description

- If JVP remain elevated by more than 3 cm even after release of compression for >15 sec

Causes

- Latent RVF
  - No RVF in basal state
  - RVF is manifested if RV workload ↑

- Kussmaul's Sign
  - RA relaxes further
  - Diaphragm goes down
  - Atrial goes down
  - JVP falls

Kussmaul's sign is absent in tamponade...

Q. Δ of etiology:

N
(1) a) TS  b) Constrictive Pericarditis

(2) a)  

\[ y \text{ is absent} \]

a2) Tamponade  d) TR

\[ \Delta = \text{slow } y \text{ descent} \]

\[ \text{ans} \rightarrow \text{TS} \]

(3) \[ a \]

\[ \Delta = \text{large } a \]  

\[ \text{TS} \]

Options

(1) TS

(2) Junctional rhythm

\[ \text{Here } a \text{ is systole} \]

\[ \Delta = \text{canon A-wave} \]

Junctional Rhythm
A P E X  B E A T

① due to iso-volumetric ② ventricular contract.

LV apex displaced superiorly

Nature → Tapping.

Site → ② 5 th ICS; just medial to mid-clavicular line

Area → <2.5 cm² [localized].

Ab ① of Apex

Ab ①

Hypercystic

Description
Palpable for upto 2/3rd of systole

Cause
① ventricular volume overload.
[↑ CO state]

② ventricle pressure overload.
e.g., As.

Dilated cardiomyopathy

③ Diffuse

area > 2.5 cm²

④ Double

2 impulses palpable in systole

LV aneurysm (complication of MI)
Asymmetrical septal hypertrophy

RV \rightarrow LV \rightarrow HOCM
Subvalvular
Hypertrophy
Aortic
a anterior, then stenosis palpable
as it obstructs LV outflow

3. Triple: 3 impulses palpable in systole

6. Absent: non-palpable

Pericardial effusion
Empysema
Obesity
Dextrocardia Q
L apex goes posteriorly, hence not palpable

Q. Double Apex seen in
1. AS [HOCM & subvalvular AS]
2. TS
3. HS
4. AR.
**AUSCULTATORY FINDINGS**

* S₁.
  due to closure of AV valve.
  \( \text{+) = M₃ T₁} \) [mainly contributed by mitral valve].
  Split < 20 msec.
  Site: Apex
  * Pitch: moderate

\( \text{AbN} \)

Factors affecting the intensity:
- Soft S₁
- Loud S₁
- Force of isovolumetric ventricle contraction
  - Force of weak force ↑
  - eg. Dilated CMP
  - LVF,
  - RVF
  - VSD
  
27 Cond. of A-V leaflets
  - if fail to strike each other
  - eg. MR
  - TR
  - Calcification of leaflet

Any mitral valve sound/murmur.
Best area = Apex
3) The presence of fluid, mls are fat between AV leaflet & stethoscope.

If ventricle blood thin, lean.

AR
PR

If ventricle wall thickness ↑
LVH ← AS
RVH ← Ps

LMR

All valvular lesions cause soft S, except MS. TS

4) Most imp factor
Position of AV leaflet at onset of ventricular contract.

If impulse reaches ventricle late, ventricular blood filling fully complete ↓

AV leaflets pushed to close position.

- Bradycardia
- PR interval ↑

If impulse reaches ventricle fast + ventricular blood filling incomplete ↓

AV leaflets fully open.

Tachycardia
Short PR interval
Q. In Hypothyroidism, S1 is soft.

Q. In Digoxin effect, S1 is soft and AV Block - PR↑ interval.

Q. Condition causing variable S1 intensity is -

If variable HR = AF

If variable PR interval = 2° AV Block

\[ \text{Mobitz-1, PP} \]

Progressively PR interval ↑ till atrial impulse fails to conduct to ventricle = Wenkebach's phenomenon.

\([\star] S_2\]

It is due to closure of Semilunar Valves

\(\text{aortic valve closes earlier than pulmonary valve}\)

\(A_2 \rightarrow P_2\)

LV ejection time is less than RV

Site = For \(A_2\), aortic area

For \(P_2\), Pulmonary area

2nd ICT

Best for \(S_2\) → Pulmonary area. [as both sounds heard]
Split = 30-60 msec.

During Inspiration → split Increase

\[ \frac{1}{A_2} \longrightarrow \frac{1}{P_2} \]

LV blood vol↓
LV ejection time↓
A\_2 early

During Expiration → split Decrease or Expired

\[ \frac{1}{A_2} \longrightarrow \frac{1}{P_2} \]

LV blood vol↑
RV ejection time↑
P\_2 early

\[ (*) \] Abnormality of S\_2 split

1. Wide Split

**CAUSES**

1. Early A\_2. (earlier than physio limit)

\[ \frac{1}{A_2} \longrightarrow \frac{1}{P_2} \]

If LV ejection time↓
VSD
MR

or

If LV early depolarisation:

WPW syndrome
H\_1 ≤ SCL < E Q
Accessory pathway from LA to LV will depolarise LV early.
Q (Bundle G\_Kent)
WPW SYNDROME

1) $a > 0$

2) (L) side more common

3) short PR interval

4) S, will be short Q.

III) $P_2 \text{ Late}$ [Later than physio limit]

\[ \Downarrow \]

RV eje" time ↑ or RV late depolarisation

eg. PS

RVF

(2) REVERSE SPLIT or

PARADOXICAL SPLIT

CAUSES

(1) $P_2$ is early (earlier than $A_2$)

\[ \Downarrow \]

RV eje" time ↓ or RV early depolarisation. WPW type B

- TR
- VSD $\to$ RtoL shunt
  (Eisenmenger Syndrome)
II. A₂ is Late (later than P₂)

LV ejec. time ↑
LV Late depolarisation
LBBB

AS
LVF

Q. How to differentiate both Split & Reverse Split.

During Inspiration:
Reverse split will decrease RV vol ↑

During Expiration:
Reverse split will increase

Q. In Pulmonary artery HTN, S₂ Split

@ (1)

b) ↑

c) No Change

P₂ comes early →

Hint - Pulmonary hang out interval
Wide + Fixed Split doesn't vary in Heart phase.

Cause → ASD.

RV blood ↑ → P2 late Wide
LV blood ↓ → A2 early

Split is fixed
Ventricular blood vol remain constant during Insp. → Exp.

RV blood → Insp. = ↑ + ↓
Exp. = ↓ + ↑ ⇒ Fixed.

Intensity of S2

Factors

1) Pressure of acute/Pulmonary to close SL valves.
2) Cond of SL valves leaflets: calcified

* Single S2 seen in

AR [A2 is absent]
PR [P2 absent]
AS/PS [Valves get severely calcified]

Soft

Hypotension

Loud

Systemic HTN

→ A2

P. HTN → P2
**S₃ / Ventricle Gallop**

It is due to ↑ in ventricle blood volume during early filling phase.

**Causes:**
- Systolic dysfunction
- Reduced systolic volume
- LV hypertrophy
- RVF
- RVF
- DCM
- MI
- LV aneurysm

Site → LV → S₃ → Apex

RV S₃ → Triangular area [↓ Lower parasternal]

**Pitch** → Low pitch.

**Q. In atrial septal defect L side S₃ → RV S₃ / LV S₃ ?**

**Ans → RV S₃.**

**Q. In VSD, L side o.S₃ = LV S₃**

**P. A.**

Pulmonary valve is open in systole

So. Blood from VSD goes into

P. A. → P. vein → L. Atrium
MV is closed in systole, blood is collected in it 1st chamber to enlarge is atria.

\[ S_3 \]  
\[ Atrial \ Gallop \]

It is due to atria contracting against stiff ventricles, ventricle vibrate

Causes-
1) Restrictive CMP
2) HOCM
3) LVH due to AS
4) RVH due to PS
5) Acute MI.

In acute MI both \[ S_3 \] \& \[ S_4 \].

↓ Relaxation  
↑↓ ATP due to ischemia.

Site - \[ LVS_q \] \rightarrow Apex  
\[ RVS_q \] \rightarrow Triumipid area

Pitch - Low pitch.

Q. \[ S_3 \] can be physiological \( \text{[True|False]} \).  
ans → False. young children, athletes
Q. S₄ can be physical (False)

Q. S₃ represents systolic failure

Q. S₄ represents diastolic failure

Q. S₄ seen in all except

a) AS (LVH)

b) Constrictive Pericarditis [ventricles are trapped can't vibrate]

c) AR → extreme (Ventriole dilatation → making it stiff)

d) Amyloidosis [RCP]

Constrictive Pericarditis doesn't produce S₃ & S₄.

**ADDITIONAL HEART SOUNDS**

<table>
<thead>
<tr>
<th>Name</th>
<th>Cause</th>
<th>Timing</th>
<th>Pitch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection click</td>
<td>due to sudden cessation of opening of SL valve as it open &amp; high pressure</td>
<td>s₁, s₂</td>
<td>High</td>
</tr>
</tbody>
</table>

LV 'P' = AS

max opening

Acute 'P' = acute aneurysm

RV 'P' = Ps

Pul. artery 'P' = P. artery aneurysm

Ejection click ↓ in coarcted lesions
2. Opening Snap

- Sudden cessation of opening of AV valve at it opens to high pressure.

| LA presssure ↑ = MS, LA myxoma |
| RA pressure ↑ = TS |

- Early diastole phase

- Early filling phase

- Late diastole

- Mid-diastole

3. Tumour Polyp

4. Pericardial Knock

- Blood ventricle wall strike [knock] on stiff pericardium

- Host specific sign of Constrictive Pericarditis

5. Non-ejection Click

- MVP prolapse ≥ mid systole
Summary

EC

Non
WEC

Opening
Snap

Pericardial
Knock

S1

A2

Tumour
Polyt

S3

S4

S1

Early filling

ate lethal

In AF:

JVP = a wave absent

Hs = S4 O [if previously present]

MURMURS

Due to turbulence of blood flow in the heart

If abS pressure gradient during normal direct of blood flow

due to stenotic lesions

If abS direct of blood flow

due to Regurgitant lesions or VSD

Types

I. Systolic Murmurs

Name

Hic murmur, overall harsh

Diagnosis

Ejection systolic murmur due to turbulence of blood flow due to ejection phase

Mid-systolic murmur

AS, PS

Crescendo-Decrescendo

TCD states: — [?] —

Diagram

S1

Mid systole

S2

SL valve opening

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2. Pansystolic Murmur

No peak.

VSD
[LV pressure remain > RVP throughout systole]
ch. MR
[LV 'p' remain > LA 'p' throughout systole]
ch. TR.

3. Early systolic murmur

A1 defect closer before mid-systole
A2 Small muscular VSD

A1 pressure gradient become zero (≤ mid-systole)
A2 Acute MR. ↓
[H1 or IE]. LA is not dilated unlike ch. MR.

During early systole, ① Ventricle blood enters LA

LA 'p' will rise rapidly

during mid systole ② Atretic 'p' = ③ Ventricle 'p'

murmur will stop

4. Late systolic murmur

④ Acute TR.

MV Prolapse
II. DIASTOLIC MURMURS

Name

1) Early Diastolic murmur
   or
   Decrescendo Murmur

2) Mid-Diastolic murmur
   Turbulence of blood flow from aorta to ventricle
   MS, TS

Q. Early Systolic murmur seen in all except
   a) TR (acute)
   b) VSD (small murmur)
   c) papillary muscle necrosis (MI → acute HR)

   a) Ms
   b) Ts
   c) Ps
   d) Ps

Q. Identify the valvular lesion
   a) Ms
   b) Ts
   c) Ps
   d) Ps
**CONTINUOUS MURMUR**

- Starts in systole
- Peak around $s_2$
- Ends in diastole
- Origin: single site

**Mechanisms:**
- If AB pressure gradient is maintained throughout systole & diastole
- If defect remains open throughout systole & diastole

**Continuous murmurs are never due to valvular lesions**

**Causes:**
1) AB communication b/w artery to vein
   - e.g. A-V fistula
   - Ruptured sinus of valsalva
   - Aorta to Batavia connection

2) AB communication b/w systemic to Pulm
   - e.g. PDA
5. Blood flow into blood vessels
   mammary artery souffle (lactation)  
   uterine artery souffle. (♀)

4. Severe arterial stenosis [70% narrowing of diameter]
   Renal artery stenoisis → bruit

Q. Continuous murmur can be physiological (True/False)
   ☑ True, lactation.

Q. All causes continuous murmur except:
   a) Pt. of CKD on hemodialysis [A-v fistula]
   b) Severe atherosclerosis [Carotid or renal artery stenosis]
   c) AR + AS
   d) Lactation.

D/D of Continuous Murmur.

<table>
<thead>
<tr>
<th>Continuous murmur</th>
<th>To d Feco</th>
<th>Systolic - diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systole +</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Diastrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Origin single</td>
<td>single</td>
<td>single</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td>Site</td>
</tr>
<tr>
<td>Peak around s2</td>
<td>✔</td>
<td>X</td>
</tr>
<tr>
<td>eq.</td>
<td>AS + AR</td>
<td>AS + MS</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Name</th>
<th>Cause</th>
<th>Type</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Gibbons's murmur</td>
<td>PDA</td>
<td>continuous</td>
<td>2nd ICS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>parasternal</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>area</td>
<td></td>
</tr>
<tr>
<td>2) Key Hodgkin's murmur</td>
<td>AR</td>
<td>early diastolic</td>
<td>3rd ICS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>= Ektro's area</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>= Neo-aortic</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>area</td>
<td></td>
</tr>
<tr>
<td>3) Graham-Steel's murmur</td>
<td>PR</td>
<td>early diastolic</td>
<td>2nd ICS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pulmonary area</td>
<td></td>
</tr>
<tr>
<td>4) Austin Flint murmur</td>
<td>AR</td>
<td>mid-diastolic</td>
<td>Apex</td>
</tr>
<tr>
<td></td>
<td></td>
<td>to late</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Regurgitant jet of AR striking mitral valve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5) Carey Coombs murmur</td>
<td>ARF</td>
<td>mid-diastolic</td>
<td>Apex</td>
</tr>
<tr>
<td></td>
<td>Turbulence of blood flow over inflamed rough mitral valve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6) Dock's murmur</td>
<td>ARF</td>
<td>continuous</td>
<td>3rd ICS</td>
</tr>
<tr>
<td></td>
<td>Severe stenosis of LAD artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>of LAD artery</td>
<td>Sternal margin</td>
</tr>
</tbody>
</table>
Factors Affecting Murmurs:

- If blood flow ↑ → all murmurs will ↑ except:
  - MVP
  - HOCM

Blood flow

1. Respiratory variation.
   a) Inspiration
   b)Expiration
   c) Valsalva effect

Pulmonary ejection click ↓ in inspiration

1. Ts, TR, PS, PR
2. MS, HR, As, AR
3. Persistent expiratory ↓ blood on R side
   Followed by L side

All murmurs will ↓

Except HOCM, MVP.
II Postural Variation

a) Standing  ↓ blood flow into R+L side
b) Squatting  ↑ blood flow into R+L side
   (Immediate effect)

III Effects of Afterload Change:

Lesion

[Diagram showing blood flow changes]

AS
Pressure gradient
= LV → aorta

AR
Pressure gradient
= aorta → LV

MR

Regurgitant lesions behave similarly
MVP

Cause: Deficiency of type III collagen in MV leaflets (posterior)

↑ Leaflet flexibility
↓ Surface area of MV leaflet
↓ too big for LV cavity

C/F:

Symptoms:
1) Chest pain
   - M/c symptom
   - Due to papillary M/c stretching

2) Palpitations
   - Ventricular fibres stretching
   - Produce ventricular ectopic
   - M/c sign → Non-ejected click

   → M/c sign → Due to doming of MV
   - It occurs when LV cavity size is significantly

2) Late systolic murmur (MR)
   - Occurs when post. leaflet looses contact → ant. leaflet

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If LV cavity blood vol ↓ → Prolapse will occur laterly
[ standing position]
[ inspiratory phase]

Non-Ejcc Click earlier

Diastolic will start earlier

D2D Echo

If prolapse is > 2mm into LA

T/t

1) Reassurance. (mostly benign)

2) β blockers (if palpitations) DOC

3) Sx Repair ← NYHA symp ≥ II

Severe MR on Echo.
**HOCM**

**Cause:** AD mutation of β-myosin heavy chain. 

["Private mutations"]

\[\downarrow\]

Asymmetrical proliferation of septum near the LV outflow tract.

\[\downarrow\]

Free wall hypertrophy

**Diastolic function ↓ as filling is impaired**

**c/F**

**Symptoms:**

1. **Earliest** → Dyspnoea ↔ LA \( \uparrow \) \( \downarrow \) LV \( \downarrow \) ↑

2. **Angina** ↔ LV workload + Coronary vessels compressed by hypertrophied myocytes

3. **Syncope**

4. **Sudden cardiac death**

- Irreversible loss of cardiac function
- c in 1 hour of symptoms
- HOCM ± Hicc.

- SCD is due to ventricular arrhythmias due to ischaemia
  - Na^+ K^+ ATPase
Signs:

1) Pulse = Bifid
   Pointed finger pulse

2) JVP:
   If hypertrophied septum bludge
   into right atrium
   Bernheim's effect  systolefunc → Brisk impulse. → Percussion
   concave be early
   Tidal wave due to obstruction of blood flow

3) Apex = Double / Triple

4) S1 = Intensity Soft
   S2 = Split Reverse
   S3 = Noe
   S4 = LV systole
   LV ejection time ↑
   (due to obstruction)

5) Most characteristic sign:
   Type → Ejection systole
   Site → 2nd ICS Ekb's area
2 most imp factors affecting obstruction:

1. Contractility
   - If ↑ → SAM → obstruction↑

2. Blood in LV if ↓ → obstruction↑
   (preload)
   (Blood acts as physical barrier separating MV & septum)

Ant
1) CXR → cardiac size
2) ECG →
   - (N)

HOCM
QRS amplitude↑

Depth >10mm
Giant Inverted T wave

3) Echo
   septum thickness
   ------------------
   LV free wall thickness

(SAH)
systolic ant movement of mitral valve toward septum
further fmging the obstruction.

Drug
Digoxin. Cl in HOCM.
Diuretics
Veno Dilators
Rx

1) β-blocker → Initial DOC
   - If CI → Non DHP ccb.
   - Doesn't prevent sudden cardiac death.

2) **Amiodarone**
   - Given if post MI ventricular arrhythmia

3) Implantable defibrillator. Device (intracardiac)
   - Prevent SCD

4) Septal artery sclerosis [ethanol]
   - Causes regression of septum.
**ARF**

**Cause:**
- Hypersensitivity reaction to Group A β-haemolytic Streptococci [Pharyngitis]
- Type II HSN reaction

**O/F & Inv:**
- Modified Jones Criteria
  - Major: (5)
    - Arthritis
      - Unique feature: M/c major manifestation Large joints asymmetrical migratory non-erosive (non-deformity) Polyarthritis
      - Duration ≤ 4 wks
    - Exception: Jaccoud's arthropathy (deformity +)
  - Carditis
    - M/c Valvular Lesion in RHD = MS
    - M/c of Death = CHF
      - M/c larger = Endocarditis
      - M/c Valve = Mitral
      - M/c Lesion = MR
      - L/c Valve = Pulmonary
      - Hypocarditis = no necrosis
        - Troponin - (−)
      - Pericarditis → Tamponade 
        - C/very Value

**Rx**
- Doc: Aspirin 75mg 11g/day

**Dae**
- Diuretic
  - no response
- Steroid
  - no response
- Valve Replacement
3. Sydenham's Chorea

[Ab against basal ganglia, cerebral cortex]

Motor = Tongue fibrillation +

Ext. Rotation of hand

"Scooping"

"Milkling action"

Disappear in sleep

$Q > 0$

Late manifestation

>1-7 months

Neuro-psychiatric disorder

4. Subcutaneous Nodule

Site: Extensor surface

Non-tender

Size: 0.5-2 cm

5. Erythema Marginatum

Site: Extremities, trunk

(never on face)

Serpentine edge

progress fast

Minor Manifestation

Clinical

Fever (Mild symptom)

Arthralgias

Lab

1) ↑ ESR

2) ↑ CRP

3) ↑ PR interval on ECG

4) [due to AV node inflammation]
Essential Criteria
1) Evidence of recent streptococcal infection (<45 days)
   Any one of 3 criteria -
   a) Throat culture +ve
   b) Ab +ve for [ASO I/II or AntidNAse]
   c) Rapid streptococcal Ag test

Minimum criteria needed to make A of
Clinical Major Minor Minor Essential

1) 1st ARF 2 major - 1 or - +
    1

2) Recurrent ARF 3 - +

3) Recurrent ARF
   On established RHD - 2 +

4) Sydenham’s chorea - - -

5) Indolent Carditis - - -
   (2 out any 4 causes)
Changes in Jones Criteria.

Low Prevalence
ARF < 2/1 lakh school going children

Major
Joint Involvement
= Polyarthritis

Minor
Fever > 38.5°C
Arthralgia - Polyarthralgia
ESR > 60 mm/hour

Polyarthritis
Polyarthralgia

High Prevalence
72/1 lakh [India]

Polyarthritis
Monoarthralgia

Polyarthralgia

Fever > 38°C
Monoarthralgia

ESR > 30 mm/hour

Prophylaxis:

1st Prophylaxis: Streptococcus → ARF pharyngitis

Antibiotic of choice = Benzathine Penicillin

1.2 MU if > 27 kg

0.6 MU if < 27 kg.

Should be started less than 10 days of Pharyngitis

If penicillin allergy:

Macrolide (Erythromycin or Azithromycin)
27 2° Prophylaxis  ARF → Recurrent ARF

Ab of choice = Benzathine Penicillin

(1.2 or 0.6 mU)

↓ if allergy to penicillin

Suladiazine Q

↓ if allergy

Macrolide

Clinical ±

ARF out carditis

ARF & carditis

ARF & RHD established

Duration of 2° prophylaxis:

1) 5 years or till pt's age 21 yr
   [even is longer]

2) 10 yrs or till pt's age 21 yr.
   [even is longer]

3) India - Lifelong ideally
   10 years till pt's age 40 yrs
   [even longer]

D/D of ARF:

1) Post-Streptococcal Reactive arthritis (PSRA)?
   • Small joints
   • Symmetrical
   • Duration > 1 month.
   • Poor response to aspirin.
(2) P - paediatric
A - autoimmune
N - neurovascular → NO other ARF manifestations
D - Disorder
A - associated
S - streptoc.

Complications of ARF: VALVULAR HEART DISEASE.

MS
Cause: H/c - RHD
H/c non-rheumatic
= congenital

Pathophysiology:
↑ LA 'P' (diastole
early
symptom)
↑ Pulm. Vein
Hts.
followed by
↑ Pulm. artery 'P'
↓
RV pressure overload
↓ remodelling
RV [concentric hypertrophy]
↓ later
RV systolic failure
↓
RV blood retention occur
↓ RA 'P' ↑ → systemic ven
↑
2nd site of stenosis → Pulmonary artery.

MR
H/c - RHD
H/c non-rheumatic
= MVP

↓ CO
Gradual LA dilatation.
↓ during diastole
↑ Blood will move from
LA to LV
↓
LV volume overload.
↓ Remodelling
LV eccentric hypertrophy
↓ later
LV systolic failure
↓
LA 'P' ↑
Symptoms
1. Dyspnoea ← LA 'P' ↑
2. Haemoptysis ← M/c source = Bronchial vein
3. Anaesthesia ← Systemic vein; hydrate; 'P' ↑
4. Recurrent laryngeal n/v

Hoarseness of voice

[Ortner's Syndrome]

Signs
- Pulse - irregularly irregular rhythm
- Pulse Defect

JVP -
Reversal occur
Absent → Prominent

Apex - LV N
Site - N
Nature - Tapping

Due to AF
Pulse +

LV - Dilated + vol. overload
Site - shifted laterally
Nature - hyperdynamic
Auscultatory Signs

$s_1 = \text{Soft}$

$s_2 = \text{Split} \ - \ \text{Wide}$

LV ejection time $\frac{1}{f} = A_2$ early

$s_3 = \text{LVS}_3 \ + \ +$

LV ejection time $\frac{1}{f} = A_2$ early

$s_4 = \frac{1}{f} = \text{Late} \ MR \ due \ to \ extreme \ LV$

$dilatation \ making \ + \ \text{Soft}$

Opening $= +\ve$

Snap $\rightarrow$ becomes $\ominus$ if calcified valve

Murmur

$1^{\circ}$

Type $= \text{mid-diastolic}$

Site: Apex

Pitch: Low pitch

if pressure gradient < 40 mmHg $= \text{Low pitch murmur}$

Radiation: Nil

Best pt's position $= \text{Lateral Decubitus}$

Phase: Expiratory

Opening $= -\ve$

Snap $\rightarrow$ becomes $\ominus$ if calcified valve

Murmur

$1^{\circ}$

Type $= \text{pan-systolic}$

Acute MR $= \text{early systolic}$

Mitral valve induced $= \text{late systolic}$

Site: Apex

Pitch: High pitch

Stenotic lesions are low pitch

Regurgitant $= \text{are high pitch}$

Radiation $= \text{Interscapular area Axille}$

Best pt's position $= \text{Lateral Decubitus}$

Phase: Expiratory

Opening $= +\ve$

Snap $\rightarrow$ becomes $\ominus$ if calcified valve

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Opening $= -\ve$

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Pitch: High pitch

Stenotic lesions are low pitch

Regurgitant $= \text{are high pitch}$

Radiation $= \text{Interscapular area Axille}$

Best pt's position $= \text{Lateral Decubitus}$

Phase: Expiratory
Clinical criteria for severity

1. Opening snap
   S2 - OS gap inversely related to severity

2. Length of murmur is directly related to severity

Ix
ECG sequence

1. Atrial enlargement
   ▼
2. RVH signs
   ▼
3. RA enlargement

Biventricular enlargement
= due to MS

CXR
1. 
   "\[\text{atrial enlargement} \]
   = due to MS

2° murmur

↑ blood flow across MV during diastole due to ↑ blood.
= mid-diastolic murmur
= Functional MS → severe MR

1) Apex = shifted laterally
2) S2 = wide split
3) S3 = thce of LV S3
4) murmur = mid-diastolic

Loudness or intensity is never a criteria for severity in Valvular Heart Disease

Ix
ECG
7) LAE
▼
2) RVH sign: LVH sign.

CXR

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② Double atrial shadow

RX

Severe MS [area < 1.5 cm²]

NYHA symp

[> II]

[symptomatic] [asymptomatic]

S_x

Af

Consider S_x

Observation

Severe MR

NYHA symp

[> II]

[symptomatic] [asymptomatic]

S_x

Af or

LVEF < 60%

S_x

Observation

Preferred S_x = MV Repair

If not possible

MV Replacement

S_x

Preferred S_x / Initial process of choice / S_x in 0

Balloon valvotomy

IVC

Done under Lung-Heart Bypass machine.
Criteria:

1. Isolated Ms
2. No calcification
3. No LA Thrombus

If not fulfilled

MV Replacement

- Metallic
- Bioprosthetic

Duration: 25 yrs
5-10 yrs

Anticoagulation: X
- Lifelong

Age Preference:
- Young
- Elderly

Q. 26yr old, unmarried female, K/o/o RHD & Ms
K/o/o dyspnea on 1st step. Echo = MVA 0.8cm.2

Next line Rx:

a) Observation
b) Balloon valvotomy
c) Bioprost, MV replacement
d) Metallic MV

Q. Same history, O/E: opening snap (+ve)

Ans - (b)

Q. Same history, O/E: Pulse Deficit, +20, opening snap (-nv)

Ans - (d)
Q. Same history. \[ marcel \] \[ OE - opening snap \ O, \]

ans \[ \text{a} \]

\[ \text{Give heparin in 1st Trimester} \]
\[ \text{anticoag in 2nd Trimester} \]
\[ \text{heparin in} \text{ 3rd} \]
\[ \text{delivery.} \]
\[ 2 \text{wk pre op to.} \]

\[ \text{AS} \]
Cause: H/c age related calcification

Pathophysiology:
LV pressure overload \[ \rightarrow \] remodelling

\[ \text{LV (concentric) Hypertrophy} \]
\[ \rightarrow \] later
\[ \text{LV systolic failure} \]
\[ \rightarrow \] LA 'P' ↑

Symptoms:

\[ \text{Decon to} \]
\[ \text{Anxiety} \rightarrow \] ↑ LV workload
\[ \text{Palpitations} \rightarrow \] LV force of contraction ↑
2) **Syncope** ← **Fixed CO**

- **Dyspnea** ← **LA 'P'↑**
  - [Worst Prognosis]
  - Mortality in 1½ yr even w medical Ht

**Signs:**
- Pulse - Most specific
  - Parvus et tardus

2) **Apex - LV 'P' overload**

  - **Site** = N
  - **Nature** = Sustained

3) **S₁ = Soft**

  - **S₂ = Split = Reverse**
  - LVEJ time ↑ → Late A₂
  - in early stages → narrow split
  - S₃ = + if LVF occur
  - S₄ = ++

  - Ejection Click = +

2) **Angina [Nocturnal]**

  - ↓ in Diastolic BP ↓ lead to less perfusion

  - This occurs more during night as sympathetic activity ↓ further ↓ vascular tone.

3) **Dyspnea** ← **LA 'P'↑**

**Most specific**
- Bisferiens

LV Dilated + vol. overload

Site = Shifted Laterally

Nature = Hyperdynamic

S₁ = Soft

S₂ = Single P₂.

Aortic valve leaflets fail to strike.

S₃ = +

S₄ = + Late AR.

∞
47° Murmur
Type: Ejection Systolic murmur
Site: ② 2nd ICS [Aortic area - 1st]

68° Murmur
Type: Early diastolic
Site: ③ 3rd ICS [Emb's Area]
2nd Aortic Area
or
Neo-aortic area

Pitch: Low
Radiation: Common carotid [or neck]
After striking arch of aorta
Radiation to apex
= Gallavardin Phenomena

Best Pt's Position: Leaning forward

Phae: Inspiration

2° Murmur
Not seen in AS

Pitch: High
Radiation: Toward apex
If radiation to axilla
= Cole-Cecil Murmur

1° Austin-Flint murmur
mid-late diastole

2° Functional AS
1. Blood flow across aortic valve
[Eviction Systole]
Clinical Criteria for Severe AS

1. S₁ = Soft
2. S₂ = Reverse Split
3. S₃ = +
4. S₄ = +

Severe Silent AS

1. Associated MS
2. LVF

Iₓ

ECG:
1. LVH Signs
2. LA Enlargement

ST Depression
T Inversion

CXR
Cardiac Size = +

Rx

Similar Severe AR

Area <1 cm²

NYHA Symptoms

I (Asymptomatic)

II (Symptomatic)
\[ S_x \]  
\[ \downarrow \]  
\[ \text{LVEF} \]  
\[ \downarrow \]  
\[ < 50\% \]  
\[ \downarrow \]  
\[ S_x \]  
\[ \downarrow \]  
\[ > 50\% \]  
\[ \downarrow \]  
observation.

Preferred \( S_x \) = Aortic Valve Replacement

Q. 60yr old o\^, Aortic valve pressure gradient of 60 mmHg \( k/\alpha \) AS, c/o \text{equivocal dyspnoea} symptoms.  
Next step?

\[ \text{Ans.} \]  
a) observation  
b) Tread mill test  
c) Aortic valve Replacement  
d) Diuretics.

Q. Same pt. underwent treadmill mill test \[ \text{Bruce Protocol}\]  
c/o Dyspnoea & Fatigue at 11 min of exercise  
Next step

\[ \text{Ans.} \]  
TMT  
\[ \downarrow \]  
Symptomatic  
\[ \downarrow \]  
Valve Replacement  
\[ \downarrow \]  
Asymptomatic  
\[ \downarrow \]  
observation.
### Bruce Protocol

**Bruce Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0 - 2:59 min</td>
</tr>
<tr>
<td>II</td>
<td>3 - 5:59 &quot;</td>
</tr>
<tr>
<td>III</td>
<td>6 - 8:59 &quot;</td>
</tr>
<tr>
<td>IV</td>
<td>9 - 11:59 &quot;</td>
</tr>
</tbody>
</table>

Pt. considered symptomatic if ≥ dyspnoea/ fatigue

Asymptomatic if < dyspnoea/ fatigue

### Severe AS + NYHA-I + underlying = Aortic valve replacement

### Sided Valvular Lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>M/c Cause</th>
<th>Other Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>TS</td>
<td>RHD</td>
<td></td>
</tr>
<tr>
<td>TR</td>
<td>RV dilatation. [eg. Pulmonary embolism] cor. pulmonale</td>
<td>M/c Valvular lesion due to CARCINOID</td>
</tr>
<tr>
<td>PS</td>
<td>Congenital</td>
<td>Carcinoid, Rubella</td>
</tr>
<tr>
<td>PR</td>
<td>PAH</td>
<td>Carcinoid</td>
</tr>
</tbody>
</table>

Valve fibrosis → Regurgitation
Ring fibrosis → Stenosis
INFECTIVE ENDOCARDITIS

CAUSE:

Predisposing Cause

17 Mitral Valvular lesion = HR > AR.
27 Mitral congenital HD = VSD [QC ventricle has vegetation]
37 Mitral cyanotic long. HD = TOF [QC ventricle has vegetation] → Systemic embolism.

47 Least common HD leading to IE = ASD
57 MC non-cv risk = " " " = IV Drug Abuse

Micro-organisms

* According to nature of valve affected.

\[
\begin{array}{c}
\text{NATIVE} \\
\text{PROSTHETIC}
\end{array}
\]

\[
\begin{array}{c}
\text{Community acquired} \\
\text{Hospital acquired}
\end{array}
\]

\[
\begin{array}{c}
\text{MC - Strepto.} \\
\text{VC - Staph. aureus}
\end{array}
\]

< 12 months after sx

\[
\begin{array}{c}
\text{MC - Coagulase neg. Staph} \\
\text{VC - Strepto viridians}
\end{array}
\]

> 12 months of sx

\[
\begin{array}{c}
\text{Overall MC = Staph. aureus} \\
\text{Overall VC = Coagulase neg}
\end{array}
\]

Max incidence = 6-12 months

HIV is the only virus to cause IE.
According to Onset of

**Acute**
- H/e: Staph aureus
  - Other
  - Strepto β-haemolyte
  - Fungi

**Subacute**
- H/e: Strepto, Viridians
  - Other
  - Staph coagulase neg.
  - Fungi

*Typical Bacteria of IE*
1. Strepto Viridians
2. " Bovis [Gallolyticus]" ass/é Colonie Cancer Poly
3. Staph aureus → H/e in IV Drug Abuse → (R) sided
4. Enterococci → H/e in IV Drug Abuse → (L) sided
5. HACEK group

**CF + Ix**

*Major Criteria*

1. Evidence of micro-organism consistent with IE.

2. >2 Blood culture + of typical bacteria

3. Persistent bacteremia of micro-organism consistent with IE.

>2 Blood culture +

[separated by 12 hours]

>3 Blood culture +

out of >4 samples

[1st & last sample separated by 1hr]

Modified Duke's Criteria

2 MAJOR

5 MINOR

3 EXCLUSION

http://mbbshelp.com

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Evidence of Endocarditis [Echo]

1. Oscillating Mass lesion or valve or its structure
2. Intra-cardiac abscess
3. New Valvular Regurgitant lesion \( \rightarrow \) H/c CVS complication of IE.
4. Partial Dehiscence of Prosthetic Valve

*Minor Criteria*

6. Fever >38°C \( \rightarrow \) H/c Symptom
7. Immune phenomenon = RRO4G
   
   R \rightarrow \text{Roth's Spots} \rightarrow \text{Immune complex vasculitis in Retina}
   
   \( \bigcirc \) Pale centre, \( \& \) haemorrhagic margin

Other causes:

- a. SLE
- b. CLL
- e. Osler's Node \( \rightarrow \) Immune complex deposit in finger tips, Palms, Soles.
  
  Tender
  Palpable
47 Vascular Events

* Major Arterial Embolisation
  
  [C sided] M1c Site → Brain [HCA territory → Parietal]
  
  M1c Organism → Staph Aureus
  
  M1c Valvular IE → Mitral Valve

* Septic Pulmonary Infarcts
  
  [B sided].

* Mycotic aneurysm

* Haemorrhagic stroke [if mycotic aneurysm rupture in Brain]

* Conjunctiva petechiae
  
  M1c Peripheral Sign of IE.

* Janeway Lesion = Palms
  
  Macular [non-palpable]
  
  Non-tender

57 Blood Culture Positive of micro-organism consistent + IE (not satisfying major criteria)

  Serology +ve
Definitive \( \Delta \) of IE = 2 Major

\[ \text{or} \]

1 Major + 3 Minor

\[ \text{or} \]

All 5 minor

* **Exclusion Criteria**

17 Firm alternate \( \Delta \) of Fever established.

27 If fever subsided \( \leq 4 \) days of Antibiotic Use.

37 If there is no histopathological evidence of IE \( < 4 \) days of Antibiotic Use.

\( R_x + \\text{Prophylaxis of IE} = \text{given in supplement} \)
CARDIOMYOPATHY

Definition:

Diseases of **endomyocardium**
Not due to valvular Heart disease.

27 Cong. Heart disease
37 HTN
47 Ischaemia
57 Pericardial Disease

Types:

- Dilated CMP (M/c pattern)
  - "Defect:
    - ↓ contract.
    - ↓ in systolic func
  - Preserved diastolic func till late stages

- Restrictive CMP (Least common)
  - Failure of relaxation
    - ↓ in diastolic func
    - ↑ in systolic func
    - Preserved systolic func
    - ↑ cavity space
    - ↑ diastolic func

DILATED CMP

- CAUSE I: Ischemic (M/c cause)
  - Rx - supportive. [chr. HF = low EF]

- Me 2° cause - alcohol
  - Mech: a) Direct ethanol effect
  b) Becoz of cobalt [cardiotoxic agent]
    - Foam stabilizing agent
Risk: Mutation of alcohol dehydrogenase
- Mutation of ACE (?)

Dose of alcohol: > 120 gm/day for 5-10 years

Rx = Reversible e in 3-6 months of cessation

Other CVS manifestation of alcohol (> 30 gm/day)

1) Dyslipidemia
   a) H/c = ↑ TG
   b) ↑ HDL Q.
   c) ↑ LDL

2) Effect on BP
   a) Acute - vasodilatation = ↓ BP
   b) Chronic - ↑ sympathetic system = ↑ BP

3) CVS events
   a) CAD → ↓ risk by ↑ HDL [French paradox]
   b) Stroke → ↑ risk due to ↑ BP

4) Atrhhythmia
   alcohol binge → AF [Holiday Heart Syndrome]

III) Genetic Cause
MOI
17 AD

27 AR

A gene/protein
TTN/Titin

sarcomere protein
N helps in "contrac" Desmosome protein
N helps in "contrac"

DSP/Desmoplakin

NAXOS Disease

Unique feature
M/c genetic cause of DCMP

Arrhythmogenic RV Dysplasia. (ARVD)

Sudden cardiac death
in young population.

- Waxy hair +
  thick palmar skin +
  ARVD

ECG. epsilon wave.

LV non compaction.

LV thrombus since birth.

TAZ/Mafazzin

N helps in compaction of ventricle cavity during embryonic development

Embryonic
IV Post Myocarditis

**Causes:**

1. **Infectious**
   - Viral - Coxsackie B
   - Other viral infect
   - Parvovirus B19
   - HIV
   - Hepatitis C

2. **Bacterial**
   - M/c - Diphtheria [death is by myocarditis]
     - Rx - anti-toxin

3. **Protozoa**
   - M/c - Trypanosoma Cruzi [Chagas Disease]
     - Rx - Benznidazole

4. **Parasite**
   - M/c - Trichinella
     - Rx - Albendazole

5. **Non-infectious**
   - M/c - Sarcoidosis [lung involvement]
     - M/c site - LV free wall
     - M/c pattern - DCM > RCM
     - Rx = steroids

6. Giant cell Myocarditis
   - No lung involvement
   - Rx = steroids

7. Hypersensitivity Myocarditis
   - Cause - Thiazide
     - Indomethacin
     - Methyldopa

8. Rx - cessation of drug ± steroid
Tako-Tsubo CMP / BROKEN HEART SYNDROME /
APICAL BALOONING SYNDROME

C/F - T + ↑ catecholamine release
↓
vasoconstrictor of LV apex
↓
LV apex non-contractile
↓
During systole RV apex bulge out in systole like balloon.

I/X - ECG - STR

Troponin = ↑ or N
coronary angiography → no thrombus
ECHO - LV apex bulging out in systole.

Rx - reversible, so supportive therapy
+ α-blocker followed by β-blocker [like phenoxybenzamine]
VI. Peri-Partum CMP

Mech: 1) Autoimmune damage to myocyte by portal Ag.
2) Prolactin fragments → myocyte damage

C/F: occur in 3rd trimester - 6 months post delivery

Risk ↑ → Twin Delivery
multipara
age > 30 yr.

Rx → Diuretics
2) [by ⊕ Prolactin]
   [Bucomisteine] → also used in Type 2 DM.
RESTRICTIVE CMP

Pathology: Infiltration → Fibrosis

1. Infiltration
   A: In between myocytes
   e.g., Amyloidosis
   H/c of RCMP

2. Types
   1° Amyloidosis

   Protein/causes
   AL/multiple myeloma
   Waldenström macroglobulinemia
   NHL

   Factor Xa adsorbs on
   AL protein leading to 1
   in blood → blood def. of Xa
   [lethymose]

2° Familial
   Trans thyroid [liver]
   ↑ genetic

   Age > 20 yrs
   H/c = CVS organism
   H/c of CVS death

   Liver Transplant
   only curable whole liver
   Transplantation is done out
   Liver failure

   Unique = ascending neuropathy

3°
37. Senile Cardiac amyloidosis

3. Transthyretin 

Age > 70yrs Transthyretin

H/c organ
dcs of death

# 2° amyloidosis doesn't cause lethal CHF
# ECG will show low voltage QRS as amyloid is poor conductor
# Echo = 1 ventricle wall QRS

B) Infiltration inside Myocyte.

1. Haemochromatosis

H/c pattern → DCMP > RCMP

H/c of death in untreated pt → CVS

H/c of death in treated pt → HCC

Rx - Phlebotomy → [CMP is reversible]

2. Fabry's Disease

Cause - Def of α-galactosidase

Glycosphingolipids accumulate
CF.
1) CVS → RCMF
2) Kidney → (GBM damage)
   3rd H/c systemic cause of Nephrotic Syndrome
3) Abdomen - Angiokeratoma Q

Tx.
- Kidney Biopsy = GBM 
  (electron microscopy)

Rx.
- Recombinant Galactosidase. [stop the progression of Ds]

II. Fibrosis
1) Radiation [ca breast/lung] support Rx.
2) Systemic sclerosis
3) Loeffler's Endocarditis
   Eosinophilia
   Release of Basic Protein
   Fibrosis

Rx.
- Steroids (by 1 eosinophile)
CHF

\[ \text{Acute HF} \uparrow \quad \quad \text{Chronic HF} \downarrow \]

\begin{align*}
\text{Acute MI} \\
\text{HT} \\
\text{Arrhythmia} \\
\text{IE} \\
\text{Low EF} \ [\text{<40\%}] \\
\text{CO will reduce} \\
\text{Systolic failure} / \uparrow \\
\text{eg. DCM} \\
\text{Late AS, AR, MR} \\
\text{Preserved EF} \ [\text{>40-50\%}] \\
\text{Diastolic failure} / \uparrow \\
\text{eg. HOCM} \\
\text{RCMP} \\
\text{Aging process}
\end{align*}

\text{Rx of Acute HF: } \quad \quad \text{Acute HF = Acute Cardiogenic Pulm. Edema}

\text{O}_2 \text{ can't enter}

\text{Alveolar capillary} \uparrow \\
\text{Hydrostatic Pressure} \uparrow \\
\text{LVF}

\text{AIM OF Rx - Shift alveolar fluid into capillaries} \\
\text{by ↓ capillary hydrostatic pressure} \\
\text{Achieved by ↓ B Sided Preload}
17 Diuretic [Furosemide] ← Initial Rx
27 Morphine [vasodilator] +
37 O₂ inhalation

↓ Systolic BP

<90
90-100
>110.

Cardiogenic Shock

Cardiac index <2.2 L/min/m² + SBP <90 for >30 min

Add - Dobutamine

Add - Nor-Epinephrine

Rx of CHF, Heart Failure  ± ↓ EF

Fluid Overload

17 ACE Inhibitors

a7 Metoprolol
b7 Carvedilol
c7 Bisoprolol

↓ → Standard t/t

27 β blocker

By ↓ workload + ↑ sympathetic activity

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if no response

↓ Add

↓ by ↑ contractility (↑) ↓ remodelling (↑)

ACE | ARB

↓ aldosterone effect

Spironolactone

chr. ↓ CO → chr. ↑ aldosterone (by ↑RAAS)

↓ Fibrosis

Heart Blood vessel

Rx of chr. HF if Preserved Ejection Fraction

Rx ppt. cause
cause.

thyrotoxicosis

↑ Anaemia

Rx underlying cause

HOCM

RIMP

Aging

↓ calorie intake

↑ Sirtuin protein (99)

(Anti-oxidant)
PERICARDIAL DISEASES

Acute Pericarditis

- Recovery
  - or Pericardial effusion
    - if rapid
      - Cardiac Tamponade

Acute Pericarditis

- Cause: Idiopathic

- Symptoms:
  - Acute Pericarditis
    - Site: Retrosternum
    - Nature: Sharp pain
    - Radiation: Trapezius
    - Aggravating factors: Supine, contact with pleura
    - Releasing factors: Leaning forward

- Ischaemic Pain
  - Retrosternum
  - Dull/constricting
  - Never sharp
  - On arm, forearm
  - Never radiate to Trapezius
  - Exertion
  - Cold Temp
  - Rest
  - Sublingual nitrate
Sign - Most Specific = Pericardial Rub.

- Crackling sound due to rubbing of 2 inflamed pericardial layers
- Diastolic Phase

I

ECG:

PR segment depression +
ST concave upward, ST elevation
[Smiling phase ST elevation]

Stage of Ac Pericarditis

I

II

ST & PR segment return

III

T wave inversion

IV

ST ECG [Recovery phase]
ECG

Ac. Pericarditis

1. ST↑ concave upward

2. ST↑ in all leads, almost except AVR, V1

3. ST↓ followed by T inversion

4. Trace of reciprocal ST depression in opp. wall lead

5. Pathological q wave, [indicate myocardial necrosis]

Ac. MI

1. Convex upward, specific lead

T inversion occurs before T normalizes

Rx - 1) Underlying cause

2) Holosystolic, DOC → NSAIDS

↓ no response

Colchicine

Anti-inflammatory +

Anti-fibrinolytic

no response → steroid
TAMPONADE

Cause - H/c (Aowards) - Idiopathic
H/c in India - TB

Pathophysio - Acute
"Compression" of heart + venous return + Aortic root
↓ ↓
↓ venous return ↓ CO
(40-50mL)

Compensatory vigorous ventricle contract to maintain CO.

Obstructive or shock
Compensive

Symptoms -
H/c → Dyspnoea due to ↓ in Htp. H/c perfusion
* Not due to Pulmonary congestion.
Lungs - Oligemia

Signs -
Place - Pulm Paradoxus ↑ in 90% cases
C in Tamponade

CONstrictive
PERICARDITIS

Idiopathic
TB

Chonic
"Failure of relaxation" of heart due to stiff pericardium + CO is preserved
↓ venous return (100mL)

Compensatory vigorous ventricle contract to maintain CO

H/c → Swelling due to ↑ in venous return.
↓
Hydrostatic 'p' ↑ in systemic Veins

≤ 1/3rd cases
Absent Pulmonary Paradoxus in Tamponade

17 AR Tamponade
27 CHF

JVP Deep

Vigorous RV constriction & Thrombosed ring pulled downward

Y = Absent

A = Prominent

Kussmaul = 

Sign of venous return doesn't increase significantly in Tamponade

Apex - Non-localised

S1/S2 Soft

S3/S4 

LAX

1. CXR - ↑ cardiac shadow (Not true cardiomegaly)

- Margins smooth
- Lung fields oligemic

CXR - cardiac size normal + calcified pericardium
ECG
QRS amplitude ↓
[Non specific ST ↓ or T ↓]
12 ECG lead.

Rx
Emergency Pericardiocentesis
Routine - Pericardectomy

Needle [Subxiphoid area]

<table>
<thead>
<tr>
<th>Signs</th>
<th>Description</th>
<th>Bert Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allenbaugger's</td>
<td>Epigastric Bellsign</td>
<td>Massive pericardial effusion</td>
</tr>
<tr>
<td>Beck's Triad</td>
<td>↓ BP + ↑ JVP + soft HS</td>
<td>Tamponade</td>
</tr>
<tr>
<td>Ewart's Sign.</td>
<td>compress ⊗ side airway</td>
<td>Massive Pericardial effusion</td>
</tr>
<tr>
<td></td>
<td>↓ collapse of distal lungs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bronchial Breath Sound</td>
<td></td>
</tr>
<tr>
<td></td>
<td>⊗ infracapular area</td>
<td></td>
</tr>
</tbody>
</table>
4) **Broadbent's sign**

Systolic Retraction of apex due to fibrous pulling

"Square root " sign $\rightarrow$ Constrictive Pericarditis

[Pressure change in RV]

![Diagram of RV pressure with phases labeled: isovol. early, late, S1, S2]
**Systemic HTN**

**Classification [AHA guideline Nov 2013]**

<table>
<thead>
<tr>
<th>SBP</th>
<th>AND</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120</td>
<td>AND</td>
<td>&lt;80</td>
</tr>
<tr>
<td>120-129</td>
<td>AND</td>
<td>&lt;80</td>
</tr>
<tr>
<td>130-139</td>
<td>(OK)</td>
<td>80-89</td>
</tr>
<tr>
<td>&gt;140</td>
<td>(OK)</td>
<td>&gt;90</td>
</tr>
</tbody>
</table>

**Causes**

I. Essential / 1° HTN (no identifiable cause)  
H/c cause

II. 2° HTN (identifiable cause)

1) H/c 2° cause - Reno - Parenchymal  
[cIN, chr KD].  
H/c Mech → vol. overload

2) 2° H/c of Reno - Vascular  
[Renal artery stenosis]

Mech - + RAAS  
DOC - ACE-I  
V/L Stenosis

3) Activating Mutation of Sodium channel of tubule  

DCT - Na⁺ channel  
Δ GORDEN’S SYNDROME  
CD = e Na⁺ channel  
Δ Liddle’s Syndrome
47. Endocrine causes.

- Hypothyroid

- Conn's Syndrome
  - by chr. ↑ aldosterone
  - L. venel. jectura

- Hyperthyroidism

- Phaeochromocytoma

57. Miscellaneous causes

- Hlsc cong. cv cause of HTN \( \Rightarrow \) Coarctation of Aorta

- Systeme. HTN \( \Leftarrow \) sympathet.↑ \( \Rightarrow \) Obstructive sleep Apnoea

- Pulm. HTN \( \Leftarrow \) hypoxia

- PCOD = Insulin resistance [acanthosis nigricans]

- Drug
  - NSAIDs by ↓ GFR
  - Corticosteroids
  - Estrogen
Symptoms
1) H/c Dyspnoea [due to CHF]
   H/c of CHF = HTN
2) H/c symp due to HTN → Occipital Headache
3) Sign : LVS₄⁺ (due to LVH)

Iₓ -
ECG Changes:
1) LVH signs
2) LA enlargement
3) LAD

Rₓ - Stable
>2 Reading on >2 occasions
should be ↑ to Δ HTN

Rx

Normotensive
not required

Elevated BP
Life style modification only
Meas 3-6 month.

Stage I
Atherosclerotic
vasc. disease
Lifestyle modification

Stage II
LSTM + Drug
Reass 1 month
Lifestyle Modification
1. Weight Reduction
2. Na < 1.5 g/day
3. IK 3.5-5g/day cause smooth H/s relaxation
4. DASH DIET
   Dietary Action To Stop HTN
   ↓ Na⁺, ↓ Fat dairy product,
   ↑ Fruits + Veg, ↓ saturated fat
5. brisk walk/exercise ≥ 150 min/wk
6. Alcohol 0 < 30 g/d 0 < 15 g/d

Other Terms
pResistant HTN
   If BP > 140/90 despite > 3 drug (one of ≤ ii diabetic)
   or
   If BP < 140/90 ≥ > 4 drug
   H/c/compliance

2. White Coat HTN
   In clinic If SBP > 20 /or DBP > 10 from non clinical readings

3. HTN Emergency = If BP > 180/120 ≥ Target Organ Damage
   ↓
   IV. Labetalol ← 1. Haemorrhagic Stroke
   IV. Nitro NTG or Nicardipine ← 2. Ac. Cardiogenie Palm. Edema
   IV. NTG
   IV. Esmolol ← 3. Ac. MI
   Nitro NTG ← 4. Aortic Dissect
   Nimesulide ← 5. SAH
* Mean BP reduction - 25% from presentation value
\[
\left[\text{DBP} + \frac{1}{3} \text{PP}\right] \ < \ 1-2 \text{ hrs.}
\]

* Doc for HT Emergency = IV. Nicardipine

* 4> HTN Urgency = BP > \frac{180}{120} + no target organ damage

\[\text{Rx = combination of oral drugs.} \ [\text{OPD}]\]

5> Orthostatic Hypotension
\[
\begin{align*}
\text{If DBP} & \ \downarrow \ \text{by } \geq 20 \ \text{in 3 min of standing} \\
\text{DBP} & \ \downarrow \ \text{by } \geq 10
\end{align*}
\]

H/l cause - Hypovolemia

2° HTN associated w/ orthostatic HTN = Phaeochromocytoma

chr. vol. depleted
\[
\uparrow \text{ due to chr. vaso constrictor}
\]
IHD

- Stable Angina
- Unstable Angina
- Non-ST ↑ MI (Subendocardial)
- ST ↑ MI [Transmural]

- Duration
  - 2-10 min

- Pain at rest
  - ()

- ECG at rest
  - ST depression
  - [except Prinzmetal Angina]

- Troponins
  - (N)

- Symptoms
  - M/c → chest pain
  - Painless MI → Autonomic Dysfunction [DM, elderly]
  - 'Angina' equivalent symptoms
    - Unexplained sweating
    - Dyspnoea
    - Sense of impending doom

- Signs
  - M/c → Levin Sign [Holding palm or fist against sternalum]
  - Pulse: if tachycardia = ant. wall
  - Bradycardia = Inf. wall
  - JVP: if Kussmaul sign = RV MI.
\[ S_2 = \begin{cases} \text{if split is wide} & \text{RVMI [late P}_2] \\ \text{if split is revolved} & \text{LVMI [late A}_2] \end{cases} \]

poor prognosis \( S_3 \) - if \( + \) - indicate systolic failure 
[Infarct >40%]

\( S_4 - + \)
[more common than \( S_3 \)]

Murmurs -

\[ \downarrow \]

Papillary MIs Necrosis

\[ \downarrow \]

Acute MR

\[ \downarrow \]

Early Systole

\[ I \]

ECG

Sequence of changes

1) Tall T Wave

\( (>50\% \text{ of R wave height}) \)

2) ST T(convex)

Paupees Sign

3) \[ T \downarrow \]

Mech

Leakage of \( K^+ \)

[Similar to hyperkalemia]

Early Repolarisation of infarcted mIs

Non-Specific
4) Pathological Q

Q wave

No use of thrombolytic therapy.

Localization:

- I, AVL
- Circumflex
- LAD
- Right marginal
- I, III, AVF

Site

1) Ant. Septum
2) Ant. wall [LV]
3) Lateral wall
4) Post. wall
5) RV H1

Artery

- LAD
- Circumflex

Lead

- \( V_2 \) (\( V_1 \) or \( V_3 \))
- \( V_3, V_4 \) \( (V_\text{circ}) \)
- \( V_5, V_6, I, AVL \)

- \( V_7 - V_9 \rightarrow ST \uparrow \)
- \( V_1 - V_4 \rightarrow \text{reciprocal} \ ST \downarrow \)
6. Inf wall

2. Coronary vix post descending

7. Antero-lateral MI

6. Main coronary

\[ V_1 - V_6, I, aVL \]

\[ R^6 = \text{CABG (not PCI)} \]

not possible

11. Cardiac F Markers

Time to F in blood (after symptoms)

24 hrs

Heart Type FA
Binding Protein

2 hrs

27. Myoglobin

3 hrs

24 hrs

37. Troponin I [Best]

6 hrs

10-14 days

40. CPK-MB

6 hrs

72 hrs

Preferred over Troponin if re-infarct

3-10 days

Troponin can be used in re-infarct:

if >20%↑ from previous
**RX**

1. **IST 🌹 MI**

**Initial Rx**

17. **Aspirin** [non-enteric coated]
   Dose - 325mg chewed

27. **O₂ inhalation** → if O₂ saturation ↓

37. **I.V. Morphine** → Analgesic + Ac. cardiogenic Pulmonary edema
   C/I in **RVMI**
   [↓ preload → further Lt CO]

47. **Nitrates** → coronary vaso-dilatation.
   + if BP ↑
   C/I - **RVMI**
   ↓ workload
   CI - Asthma
   PR interval > 0.25 sec

57. **β blocker**
   metoprolol

67. **ACEI**

77. **High Dose Statins**
   Atorvastatin 80mg/d.

87. **Clopidogrel**
   300mg loading Dose

**Role**

Essential in all

if O₂ saturation ↓

Analgesic + Ac. cardiogenic Pulmonary edema

C/I in **RVMI**
[↓ preload → further Lt CO]

coronary vaso-dilatation.

+ if BP ↑

C/I - **RVMI**

↓ workload

CI - Asthma

PR interval > 0.25 sec

All pts. for initial 48 hours

continue if HT (↑)

Ante-inflammatory +

Plaque stabilizing Property.

if pt undergoing procedure PCI.
Definitive Rx: PCI > Thrombolysis

If ST ↑ MI Presented to

↓ after initial t/t

PCI - center
↓
do PCI

Ideal Door to

Balloon Time ≤ 90 min

↓

< 120 min
↓
Shift the pt

> 120 min
↓
do Thrombolysis

Ideal Door to Needle
Time ≤ 30 min

If symptom < 12 hours duration.

ST ↑

If ST ↑ MI + ↓ BP

RVMI (Causing RVF)
Lung no crepts

Immediate Rx

I.V. fluids to ↑ preload

Definitive Rx

PCI is done when pt is haemodynamically stable

LVMI/ Ant. wall MI
(Causing LVF)
Lung crepts +

Intra-aortic Balloon Pulsation (IABP)

PCI
Non-ST ↑ MI / Unstable Angina

**Std. Rx**

1. Anti-platelets = **Aspirin** + **Dipidogrel**
2. Anti-thrombotic agents = **LMWH** or **Thrombin**

**Nitrates**

**β blocker**

If there is no relief

Add **CCB**

If no relief

PCI

Stable Angina

- Aspirin Life Long
- Sublingual dinitrate
- Rx risk factors

**Prinzmetal Angina**

Cause - Idiopathic vasospasm of at epicardial coronary artery. [non-atherosclerotic]

The artery affected → **R** coronary

C/F:

- Smoker + young age
- Associated symptoms = Raynaud's phenomenon
- Pain = 2AM to 8AM.
\[ I_x \] - ECG - \( ST^f \)

Thrombin = \( \Box \)

\[ R_x \] -
1) Acute \( \rightarrow \) Vasodilators \( \rightarrow \) Nitrate \( \rightarrow \) [CCB \& Blocker]
2) Maintenance \( \rightarrow \) [CCB]
3) C/I \( \rightarrow \) Alpimarin \( \rightarrow \) C/ Lower vasodilator PG

\( \beta \) blocker \( \rightarrow \) \( \beta \)/pt. Vasospasm

Q. In intraoperative MI is drug not used.

@ Heparin

\( \beta \) Blocker Lead \( V_5 \) or \( V_4 \)

@ Atropinin if AV Block

@ CCB

@ Nitro.
AORTIC DISSECTION

Causes -
1) M/c → HTN
   M/c site → ascending aorta
   Lateral wall

2) Large vessel vasculitis
   Takayasu
   Giant cell arteritis

3) Atherosclerosis [M/c of aortic aneurysm]

4) Drug - cocaine

5) 

Types
A/c to site of origin [Stanford classification]

- A
  Ascending aorta
  more common
  more fatal

- B
  Descending aorta

A/c to extension [DeBakey classification]

- I
  to descending aorta also
- II
  Limited to ascending aorta
- III
  Above diaphragm
  IIIA: Above diaphragm
  IIIB: Below diaphragm
Symptom
H/c - Chest pain
Retrosternal + Clearing Pain + Radiation to intercostal area

Sign
Asymmetrical Pulses
Acute Aortic Regurgitation [due to type A dissec]

Ix
1. CXR → Wide mediastinum
2. Sided Pleural effusion (20%)
   ↓
3. D/D of Oesophageal Rupture
   ↓
4. H/O vomiting

27 Unstable pt. → Trans oesophageal echo

37 If pt is stable → CT

47 Gold Std. Ix → MR angiography

Rx
Initial Rx → BP
↓
High or N
(Target SBP 100-120 mmHg)
Iv. Esmolol
Definitive Rx

Low
Iv. fluids
Urgent Surgical Repair

Type

A

B

Conservative

do surgery if

* impending rupture

* limb/visceral ischaemia
RHEUMATOLOGY
**IMMUNE SYSTEM**

**INNATE**
- **Anatomical Barrier**
- **PRR's** (Pattern Recognizing Receptors)
  - Inflammasome Proteins (Sensors)
- **Antimicrobial Peptide (AMPs)**
  - Lysozymes - Tears/saliva
- **NK Cell (Bouncers)**
  - Largest WBC
  - Regulated by T cells (IL-2)
  - Immune & Tumour surveillance
  - Non-immune mediated action
  - Only immune cell - non-MHC restricted action.
  - (Virus injected/mutated cells are also checked by these cells)

**ADAPTIVE**
- **B cells** (Humoral)
  - Express CD19,20 on surface
  - When activated
    - **Plasma Cells**
      - Immunoglobulins (antibodies)
- **T cells** (Cell mediated)
  - CD4, CD8
  - (Helper, Cytotoxic)
  - Most Potent Level of Immunity

**MONOCYTE - MACROPHAGE SYSTEM**
- (Police)

**Dendritic Cells**
- (Most Potent APC's)

**Granulocyte Series (N, B, E)**

**Complement Cascade**
- Regulator of immune response

**Cytokine**
**IMMUNE EXCESS DISORDERS**

**INNATE (AUTOINFLAMMATORY)**

**FAMILIAL MEDITERRANEAN FEVER (FMF)**
(Recurrent Polyserositis)
**EPID** - 10-20 yrs, of
**ETIOPATH** - Inherited defect of MEFV gene
**Overexpression of the PRR's**
**INNATE EXCESS IMMUNE STATE**

**C/F** - Recurrent Febrile Illness
(each last for 6-8 weeks)
- Constitutional symp: Anorexia
- wt loss myalgia

**HLA**
- Pleuritis
  - D/D - TB
- Peritonitis
  - D/D - Appendicitis
- Arthritis
  - D/D - Juvenile RA
- Pericarditis
  - D/D - Rheumatoid fever

**A** - Clinical suspicion - C's (Genetic testing MEFV gene)

**Rx** - COLCHICIN - Favourable Response & long term remission

**Dreaded complication** - 2° Amyloidosis - Nephrotic Syndrome - High Mortality

**Recurrent Febrile Illness & Unconfirmed Infection**
- Rheumatology
ANTIBODY TESTING

INDEX

LUPUS group
(Skin rash)
"Wolf-Bite"

1) SLE
2) Systemic sclerosis
3) Sjogren's (Sicca)
4) M.C.T.D.
5) Rheus

ARTHRITIS
Approach

1) RA
2) Spondylo arthritis
3) Crystal induced
4) Charcot's joint (neuropathic)

VASCULITIS

1) Misc. Pain syndrome
   - Fibromyalgia
   - Chronic fatigue
   - Syndrome
### Clinical Significance

M/c Ig found in autoimmune disorders (98% of cases)

**Most Sensitive Ig**

### ELISA

Methods → IF (preferred)

1. Quantitative (Result in titer)
   - $<1:160 = \square$ in 20% Healthy population
   - $>1:160 = \text{Significant (more specific)}$

2. IF Pattern (due to the $\Delta$

<table>
<thead>
<tr>
<th>IF Pattern</th>
<th>Antibody</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/C-Speckled</td>
<td>Anti-Ro/La [SSA/SSB]</td>
<td>SICCA SYNDROME.</td>
</tr>
<tr>
<td>Homogenous</td>
<td>Anti-dsDNA - M/C in SLE</td>
<td>SLE</td>
</tr>
<tr>
<td>Rim Pattern</td>
<td>Anti-Smith - Most specific for SLE</td>
<td></td>
</tr>
<tr>
<td>Centromere</td>
<td>Anti-centromere (specific)</td>
<td>Localised Systemic Sclerosis</td>
</tr>
<tr>
<td>Nucleolar Pattern</td>
<td>Anti-topoisomerase-1</td>
<td>Systemic Sclerosis</td>
</tr>
<tr>
<td></td>
<td>(SCL-70 commercial)</td>
<td></td>
</tr>
<tr>
<td><strong>ANTIBODY</strong></td>
<td><strong>CLINICAL SIGNIFICANCE (Astix Role in SLE)</strong></td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Anti-Sm</td>
<td>Most specific for SLE</td>
<td></td>
</tr>
<tr>
<td>(not preferred)</td>
<td>Only in 10% (lack sensitivity)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No correlation to disease activity</td>
<td></td>
</tr>
<tr>
<td>Anti-ds DNA</td>
<td>Sensitive, specific</td>
<td></td>
</tr>
<tr>
<td>(preferred)</td>
<td>Correlates to disease severity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Associated to risk nephritis/CNS involvement</td>
<td></td>
</tr>
<tr>
<td>APLA</td>
<td>Present in 60-70% cases of SLE</td>
<td></td>
</tr>
<tr>
<td>(phospholipid)</td>
<td>Associated to vascular thrombosis/fetal loss</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Most recent to be included in criteria of SLE</td>
<td></td>
</tr>
<tr>
<td>Anti-Histone</td>
<td>CVS: ACEI, β blockers, Thiazides, Statins</td>
<td></td>
</tr>
<tr>
<td>(specific for drug-induced SLE)</td>
<td>Metyldopa, Hydralazine, Procolaminide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anti-microbial: INH, Dapsone, Sulfonamides</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CNS: Phenytoin, carbamazepine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GIT: Sulfon Sulfasalazine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Endo: Propylthiouracil</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Misc: d-penicillamine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>New: Interferons</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anti-TNFα</td>
<td></td>
</tr>
<tr>
<td>Antibody</td>
<td>Clinical Significance</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Anti-Ro/La</td>
<td>↑ Risk of congenital Lupus, ↓ risk of maternal Nephritis, SSA/SSB, Asthma Role in SjS</td>
<td></td>
</tr>
<tr>
<td>↓ Crosse pl.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-Ribosomal P</td>
<td>↑ Neuro-psychiatric convulsion + Psychosis</td>
<td></td>
</tr>
<tr>
<td>Anti-Neuronal Ab</td>
<td>↑ Neuropathy, Painless, Axonal</td>
<td></td>
</tr>
<tr>
<td>Anti-Erythrocyte</td>
<td>Hemolytic anaemia</td>
<td></td>
</tr>
<tr>
<td>Anti-Platelet</td>
<td>↑ Risk of hematological involvement</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Centromere</td>
<td>Localised Scleroderma (CREST Syndrome)</td>
</tr>
<tr>
<td>Anti-Scl70</td>
<td>Diffuse SSc</td>
</tr>
<tr>
<td>Anti-U3 RNP</td>
<td>↑ Risk of PAH + RPAN, Prognostic Role in SSC</td>
</tr>
<tr>
<td>Anti-U1 RNP</td>
<td>Specific for Mixed Connective Tissue Disorder</td>
</tr>
<tr>
<td>Rheumatoid factor (RAF)</td>
<td>Best Screening Test for RA (PROGNOSIS) Correlates - Risk Bone erosions (PROGNOSIS) Non-Specific for ∆</td>
</tr>
</tbody>
</table>

IgM Ig against Fc portion of Ig G
<table>
<thead>
<tr>
<th>ACPA/Anti-ccp (host specific for R.A.)</th>
<th>Anti-cyclic citrullinated protein Ab. (Active role in RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCA (anti-neutrophil cytoplasmic Ag)</td>
<td>Vasculitis (Active role)</td>
</tr>
<tr>
<td></td>
<td>CANCA</td>
</tr>
<tr>
<td></td>
<td>Anti-PR3</td>
</tr>
<tr>
<td></td>
<td>(proteinase-3)</td>
</tr>
<tr>
<td></td>
<td>PANCA</td>
</tr>
<tr>
<td></td>
<td>Anti-Mpo</td>
</tr>
<tr>
<td></td>
<td>(myeloperoxidase)</td>
</tr>
</tbody>
</table>

**SLE**

M/c autoimmune disorder

Epid: 20-40 yr, $P > 0$

Cause: Idiopathic M/c

Risk factors -
1. Genetic - TREX-1 gene defect
2. Chromosomal - Kleinfelter's syn.
3. Infections - EBV
4. Toxins - UV rays, silica

**Manifestation**

- **Cutaneous**
  - Acute: Malar rash
  - Chronic: Discoid rash

- **Oral ulcers**
  - Considered as SLE

- **Alopecia**
  - Considered as SLE

- **Synovitis**
  - Non erosive arthritis
  - Symmetrical polyarthritis

- **Excluding**
  - a) Nutritional (Iron, Zn)
  - b) Endocrine - thyroiditis (Hypo)
  - c) Drug induced

Clinical Description:

- Excluding - a) Nutritional (Iron, Zn)
- b) Infective
- c) Behcet's disease

**Clinical Description**

NEVER DEFORMITY / Bone Disease
5) RENAL
Proteinuria >3+, Granular / RBC cast

6) CNS
Neuropathy

7) ANAEMIA
Hemolytic - Hb ≤ 10g/dL

8) LEUCOPENIA
WBC ≤ 4000 or Lympho ≤ 1000

9) Thrombocytopenia
Platelet ≤ 1,000,000

8) SLICC Criteria (Systemic Lupus International Collaborative Clinics)

9) Clinical
Above manifestations

6) Immunological
≥ 4 confirms SLE
(at least 1 of each)

1) ANCA
2) Antism

3) Anti Ds DNA

Rx

ACUTE SLE FLARE

Life-threatening features / cause of
ACUTE MORTALITY IN SLE

1) Lupus Nephritis (Type 3,4)
2) Neuropsychiatric manifestations
3) Coagulopathy / Pancytopenia

Autoimmune Crisis

Rx: IV Methyl Prednisolone
PULSE 1gm/day × 3-5 days

Oral Prednisolone
1-2 mg/kg/day

Add steroid sparing
Mycophenolate Mofetil
(Lifelong)

http://mbbshelp.com
WhatsApp: +1 (402) 235-1397
# Approved Alternatives to Methylprednisolone

<table>
<thead>
<tr>
<th><strong>RITUXIMAB</strong> (MAB ⊗ CD20)</th>
<th><strong>BELIMUMAB</strong> (MAB ⊗ BAF)</th>
</tr>
</thead>
</table>

## Poor Prognosis

<table>
<thead>
<tr>
<th>Affects Productive age group</th>
<th>Unpredictable course of the disease</th>
<th>High Cost of therapy</th>
<th>Long Term Adverse drug Rxn of immune suppression</th>
<th>No Cure (Lifelong therapy)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>ACUTE</strong></th>
<th><strong>MORTALITY IN SLE</strong></th>
<th><strong>CHRONIC/ Long-term</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Thrombotic events - Cardiac failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) Opportunistic Disease</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SCLERODERMA → SYSTEMIC SCLEROSIS

Sclerosis | skin

>98% have systemic involvement.

epidemic 30-50yr, f ≤ 6

cause: H/c - idiopathic

Risk factors → 1) INFECTION → CMV, Parvo B19

2) TOXIN EXPOSURE - Scleroses, "Toxic Oil Syndrome"

OF H/c

1) RAYNAUD'S → can precede skin changes >10 yrs

2) SKIN CHANGES: Hands & face

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>BASED on Extent of Skin Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONLY SKIN (&lt;2% CASES)</td>
<td>Restricted to face Dural to elbow Localised SSC</td>
</tr>
<tr>
<td>MORPHIA En-coup-de-sabre</td>
<td>Localised</td>
</tr>
<tr>
<td>only organ. SCLERODERMA SINE SYNDROME (leuc.-comm.)</td>
<td>SSC</td>
</tr>
<tr>
<td>Suspected</td>
<td>SSC</td>
</tr>
<tr>
<td>-----------</td>
<td>-----</td>
</tr>
<tr>
<td>Face ≤ Distal to elbow</td>
<td>Proximal to elbow</td>
</tr>
<tr>
<td>LOCALISED</td>
<td>DIFFUSE</td>
</tr>
<tr>
<td></td>
<td>125</td>
</tr>
<tr>
<td>Anti- Centromere</td>
<td>SCL - 70 / Topoisomerase - 1 Ab</td>
</tr>
<tr>
<td>Also called CREST</td>
<td>↓</td>
</tr>
<tr>
<td>Calcinosis</td>
<td>More risk of organ involvement</td>
</tr>
<tr>
<td>Raynaud’s (DO = CCB)</td>
<td>Lung: Mlc type of ILD in autoimmune disorders</td>
</tr>
<tr>
<td>Eso. dysmotility (GERD)</td>
<td>NSIP (non-specific interstitial pneumonia)</td>
</tr>
<tr>
<td>Sclerodactyly</td>
<td>Doc = Steroids (Pneumonia)</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>Iso Pulmonary artery HTN</td>
</tr>
<tr>
<td>Above features are Mlc E</td>
<td></td>
</tr>
<tr>
<td>localised &gt; Diffuse</td>
<td>RPGN</td>
</tr>
<tr>
<td></td>
<td>Renal urtic (Doc - Captopril)</td>
</tr>
<tr>
<td>Rx = only palliative</td>
<td>, NO CURE</td>
</tr>
<tr>
<td>, unfavourable prognosis</td>
<td></td>
</tr>
</tbody>
</table>
SICCA SYNDROME (Sjögren’s Syndrome)

M/c manifestation - Dryness of eyes + Mouth
Lymphocytic infiltration of exocrine glands

CAUSES

1° SICCA (Idiopathic) Rate
[SICCA - is the Disease]
- High Risk - Systemic (extraglandular manifestations)
  - High titres - SSA/SSB Ab
- High Risk - LYMPHOMA (M/c of death in SICCA)
  - Majority - Immunosuppressants
  - POOR PROGNOSIS

M/c 2° SICCA
[Underlying disease]
- SLE, SSc, MCTD, RA, Vasculitis
- 1° Biliary Cirrhosis
- chr. autoimmune Hepatitis

- only glandular symptoms
- Low titre - SSA/SSB
- No risk of Lymphoma
- Rx - only palliative
  FAVOURABLE PROGNOSIS

<table>
<thead>
<tr>
<th>Involved</th>
<th>c/f</th>
<th>TEST</th>
<th>Rx</th>
<th>Laboratory Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacrimal Gland</td>
<td>Dry-</td>
<td>Schirmer</td>
<td>Artificial tears</td>
<td>LUNG:* - M/c - NSIP</td>
</tr>
<tr>
<td></td>
<td>eye</td>
<td></td>
<td></td>
<td>Isolated PAH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Renal - (M)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Distal RTA</td>
</tr>
<tr>
<td>Salivary</td>
<td>Dry -</td>
<td>Jonto pho-</td>
<td>Protective</td>
<td>Interstitial nephritis</td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td>met</td>
<td>glasses</td>
<td>Liver - Cirrhosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CNS - neuropathy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LYMPHOMA - most dreaded</td>
</tr>
</tbody>
</table>
Rx  
2° SICCA → only palliative  
1° SICCA → depend on organ involvement  
**GOOD PROGNOSIS** (majority are 2°)

**POOR PROGNOSTIC FACTORS**

1. Elderly onset (>40) ⊣
2. Bl/I parotid enlarged
3. Systemic ⊗
4. High titres of SSA/SSB

**OVERLAP SYNDROMES**

\[\text{Epid} = 10-20\% \quad \text{♀} \gg \text{♂}\]
\[\text{C/F} = (\text{SLE} / \text{SSc} / \text{SICCA}) + (\text{R.A.})\]

\[\text{Screening} = \text{ANA}^+ \quad \text{RFA}^+\]

\[\text{Specific Ab}^+ \quad \text{U1RNP}^+ \quad \text{ACPA/Anti-CCP}^+ \quad \text{RA + Lupus} \quad \text{OVERLAP SYNDROME}\]

\[\text{Rx} \quad \text{SLE Dominant} \quad \text{RA Dominant}\]

<table>
<thead>
<tr>
<th>Immune suppression</th>
<th>DMARDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non erosive arthritis</td>
<td>Erosive arthritis</td>
</tr>
</tbody>
</table>

**Prognosis** - Better than individual disease  
Better response to therapy
**Approach to Joint Disorders**

- **True Articular**
  - Active
  - Passive

- **Pain**
  - Movement

- **Peri-Articular**
  - Active

**Approach to Inflammatory Arthritis**

- **Mono** (1 joint)
  - N/E Trauma
  - Septic

- **Oligo** (2-4 joints)
  - Pseudogout
  - Crystal

- **Polyarthritis** (≥5 joints)
  - Axial
  - Ankylosing Spondylitis

- **Approach to Inflammatory Arthritis**
  - Symmetrical (small)
    - Rheumatoid Arthritis
    - Psoriatic Arthropathy (Early DIP +)
  - Asymmetrical (large)
    - Enteropathic Arthropathy
    - Reactive Arthritis
      - Predominantly wt-bearing jt.

Spondylo Arthritis = GS + above 3
M/C Pattern of Joint Involvement in Diseases

Most Imp parameter for Diagnosis of arthritis

RHEUMATOID ARTHRITIS

Epid. 30,50 yr, $\geq 70$

M/C - Idiopathic

Risk Factors - 1> Genetic - HLA-DR4 (Most cases - Sporadic)
2> Infection - Mycobacteria, EBV

C/F

ARTICULAR (Predominant)

- Inflammatory Poly-arthritis
- Appendicular Dominant
- Spine involvement - Rare
  - M/C - Atlanto-axial Jt
- Symmetrical, small Jts. of hand
  - WRist, MCP Jt, PIP Jt

EXTRA-ARTICULAR

EPISCLERITIS

LUNG
- M/C Usual Interstitial Pneumonia (UIP)
  - M/C $\rightarrow$ O

PERICARDITIS
- Valvular M/C $\rightarrow$ MR

MUSCULO-SKELETAL
- Myopathy
- Osteopenia
- Fast progress - OA

FELTY'S (RA + SPLEEN)

- Anaemia / Neutropenia
- Risk of Lymphoma
- Least common
- $\leq 1\%$ - Advanced RA
- Early DMARD Rx
Δ: EULAR (European League Against Rheumatism) Guideline - A scoring system

A. PATTERN of joint involvement (Max: 5)
   • 1 joint (Predis. Large) → 0
   • 2-10 joints → 1
   • 1-3 joints → 2
   • 4-10 joints (Predis. Small) → 3
   • >10 joints → 5

B. SEROLOGY (Both RAF & ACPA) [Max: 3]
   NEGATIVE → 0
   MILD + [<3 × upper normal limit] → 2
   STRONG + [>3 × upper limit] → 3

C. DURATION
   <6 wks - 0
   ≥6 wks - 1

D. ACUTE PHASE REACTANT
   NEGATIVE → 0
   ELEVATED → 1

Δ = ≥6 confirms RA.
RADIOLOGY X → NOT Recommended for ASC.
OLD CRITERIA: X-Ray Hand \\
X-Ray - Least Sensitive test \\
MRI - MOST SENSITIVE test \\
impractical

Bone Erosions \\
Late, irreversible stage \\
Earliest feature of RA \\
Juxta-articular osteopenia \\
NON-SPECIFIC.

Rx Most preferred method → STAGE the severity
CDAI (Clinical Disease Activity Index)

<table>
<thead>
<tr>
<th>2.8 - 10</th>
<th>10 - 22</th>
<th>&gt;22</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILD RA</td>
<td>MODERATE RA</td>
<td>SEVERE RA</td>
</tr>
<tr>
<td>Single DMARD</td>
<td>COMBINATION DMARD</td>
<td>Early use of Biologicals</td>
</tr>
</tbody>
</table>

Prognosis: Favourable → REMISSION → can be achieved in 60-85% cases

POOR PROGNOSTIC FACTORS:
1. Elderly (>40)
2. ??
3. >10 yrs @ onset
4. High titer of RAF
5. Delay in initiation of DMARD > 3 months
<table>
<thead>
<tr>
<th><strong>DMARDs</strong></th>
<th><strong>Ind</strong></th>
<th><strong>ADR</strong></th>
<th><strong>Follow-up</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate (MTX)</td>
<td>1st choice (single or combination)</td>
<td>BM1, Hepatotoxicity (Dose dependent S/E)</td>
<td>CBC, LFT - 3 monthly</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Safest in 6, 2nd choice</td>
<td>Bull's macula pathy (rare occurrence)</td>
<td>Fundus, exam, Perimetry Baseline &amp; annually SOS</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>Safe in 6, 3rd choice</td>
<td>Gastritis, Hepatotoxicity</td>
<td>LFT - Baseline +3 monthly</td>
</tr>
<tr>
<td>Leflunamide</td>
<td>Approved at Mono Rx, completed Family MODEST efficacy (limited use)</td>
<td>No synergy to other DMARDs 6×↑ Hepatotoxicity Teratogenicity</td>
<td>Stop ≥ 2 ovulatory cycle before conception</td>
</tr>
</tbody>
</table>
**BIOLOGICALS** - Pathophysiology of R.A.

↑ ↑ ↑ Pro-inflammatory Cytokines

- TNFα most potent + IL-1
  - (Most preferred)
  - Anti-TNFα agents
    - ANAKINRA
    - TOCILIZUMAB

Stimulates T cell
- MODULATOR = ABATERCEPT

Stimulates B cell
- RITUXIMAB

Intracellular Signalling Pathways of Inflammation
- e.g. JAK- Janus associated Kinases
  - TOFACITINIB - Tyrosine Kinase Θ of JAK - 1st Oral Biological

- ANTI-TNFα AGENTS
  - ADA LIMUMAB, GOLIMUMAB
    - S/C every 2-3wk

ETARER
- ETARNACEPT
  - Chimeric form Mab against TNFα receptor
  - Limited efficacy
  - Copanion

INFLIXIMAB
  - Chimeric Mab against INFα itself
  - Excellent efficacy
  - Anaphylaxis

PEGYLATED CERTOZUMAB
  - Fully Humanised Mab against INFα itself
  - Equal efficacy
  - Safety

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Common ADR ⇒ Reactivation of TB.

Hence, screening for active/dormant TB is mandatory before Anti-TNF α agents.

<table>
<thead>
<tr>
<th>Tuberculin (MANToux)</th>
<th>WHO → In countaee (BCG) vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ HOST SENSITIVE.</td>
<td>Best screening test is</td>
</tr>
<tr>
<td>→ BCG vaccination.</td>
<td>Interferon γ assay</td>
</tr>
<tr>
<td>(fale truly)</td>
<td>(TB-GOLD) quantification</td>
</tr>
<tr>
<td></td>
<td>quantiferon</td>
</tr>
</tbody>
</table>

**Spondyloarthritis**

Group of Disorders Characterized by

**COMMON FEATURES**

1. Seronegative     RAF-ve
2. HLA B27 +ve     Strong family History
3. 1° Site "Gnethesis"  Junc Btw Bone & Tendon.
4. Axial Involvement is not Uncommon.
5. Extraarticular manifestations predominate
6. Excellent response to NSAIDS → 1st Line of Rx

SPA are D/D Inflammatory Polyarthritises
ANKYLOSING SPONDYLITIS / BECHET'S / HARRIE-STRUMPELL DISEASE

Epid: 10-20 years, > 90%, 90% - HLA B27

C/F ARTICULAR (Axial Dominant)

<table>
<thead>
<tr>
<th>Joint</th>
<th>LBP (non-specific)</th>
<th>Restricted movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacro-iliac Joint - H/L C</td>
<td>always B/L but asymmetrical</td>
<td>toward bending</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>Restricted</td>
<td>Thrust movement</td>
</tr>
<tr>
<td>Thoracic spine</td>
<td>Restricted</td>
<td>Heel movement</td>
</tr>
<tr>
<td>Cervical spine</td>
<td>Highest Heel of # in lower part of Cx spine</td>
<td></td>
</tr>
</tbody>
</table>

EXTR-ARTICULAR (Predominant)
70% - Recurrent U/L ANT. UVEITIES

A

BEFORE

Spine Involvement

HLA - B27 $\rightarrow$ TVE

- TVE

$\rightarrow$ 2 common features of SPA

(MRI proven sacroilitis)

CONFORMS A.S.

AFTER

$\rightarrow$ 1 common feature of SPA

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### NORMAL
- Vertebral Body
- Tendon of Paraspinal Muscle

### STAGES

<table>
<thead>
<tr>
<th>Stages</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENTHESIS</td>
<td>NSAIDS 136</td>
</tr>
<tr>
<td>MARROW EDEMA</td>
<td>BEST TIME for Biologicals</td>
</tr>
<tr>
<td>MARGINAL SYN DESMOPHYTES (unique feature)</td>
<td>DMARDs Biologicals (All TNF α agents)</td>
</tr>
<tr>
<td>FUSION (ANKYLOSIS)</td>
<td></td>
</tr>
</tbody>
</table>

**MRA is mandatory**
Only Test - Detect the stage of A.S.

**Rx - UNFAVOURABLE**
Unlike RA only 10-15% active complete Remission

### PSORIATIC

- M/C - Guttate/
- Pustular type of psoriasis

### ENTEROPATHIC

<table>
<thead>
<tr>
<th>M/C - U.C. /Crohn’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Pathology</td>
</tr>
<tr>
<td>Bowel Severity</td>
</tr>
<tr>
<td>Disease &amp; of activity arthritis</td>
</tr>
</tbody>
</table>

### Reactive

**Post-infective**

<table>
<thead>
<tr>
<th>M/C - Diarrhoea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most-specific =</td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
</tr>
<tr>
<td>(Unique in U.C.)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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</tr>
<tr>
<td>(Unique in U.C.)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M/C - Febrile illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratoderma Blenorragia (Keratotic, Painless plaques - sole + Palm)</td>
</tr>
<tr>
<td>Asymmetrical polyarthropathy (Predom. - foot-bearing joints)</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th></th>
<th>GOUT</th>
<th>PSEUDO GOUT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal</td>
<td>Monosodium urate (M.S.U.)</td>
<td>Ca$^{2+}$ pyrophosphate dehydrate (L.P.P.D)</td>
</tr>
<tr>
<td>Epsid</td>
<td>30-50 yrs 0° &gt; 9</td>
<td>&gt;50 yrs 0° &gt; 9</td>
</tr>
<tr>
<td>Etiopathy</td>
<td>90% - Renal defect in urate excretion</td>
<td>90% - Jt. Degeneration</td>
</tr>
<tr>
<td></td>
<td>10% - Diet/Drgue (Pyrazinamide/Thiazide)</td>
<td>10% - Hypercalcemia = Severe</td>
</tr>
<tr>
<td>C/F</td>
<td>Acute - Inflammatory Mono-Arthritis (M/C-1st MTP, ankle Jt)</td>
<td>Acute, inflammatory oligo (M/C Knee, Heps, Shoulder)</td>
</tr>
<tr>
<td>Screening</td>
<td>Serum Uric Acid</td>
<td>S. Ca$^{2+}$</td>
</tr>
<tr>
<td></td>
<td>Non-Specific NORMAL VALUE doesn't Exclude</td>
<td></td>
</tr>
<tr>
<td>Synovial fluid</td>
<td>NEEDLE SHAPED</td>
<td>RHOMBOD SHAPED</td>
</tr>
<tr>
<td>Analysis</td>
<td>STRONG -ve Birefringence</td>
<td>MILD +ve Hfrangence</td>
</tr>
<tr>
<td>Polarising microscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate crystals</td>
<td>Gold Std.</td>
<td></td>
</tr>
</tbody>
</table>

CHICKENGUNYA ARTHRITIS

Hydroxychloroquine (additional anti-inflammatory action)
<table>
<thead>
<tr>
<th>Rx</th>
<th>NSAIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Attack</td>
<td>Colchicine MAB</td>
</tr>
<tr>
<td></td>
<td>Canakinumab IL-1β</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>FEBUXOSTAT (X-O-1)</td>
</tr>
<tr>
<td></td>
<td>Hepatic excretion</td>
</tr>
<tr>
<td></td>
<td>Additional anti-inflammatory</td>
</tr>
<tr>
<td>Chronic Prevention</td>
<td>TARGET uric acid &lt;6mg/dL</td>
</tr>
<tr>
<td></td>
<td>1st Line: X-O-Inhibitor (Allopurinol, Febuxostat)</td>
</tr>
<tr>
<td></td>
<td>Refractory case</td>
</tr>
<tr>
<td></td>
<td>PEGLOTICASE</td>
</tr>
<tr>
<td></td>
<td>Regulated uricase</td>
</tr>
<tr>
<td>Prog</td>
<td>Favourable</td>
</tr>
<tr>
<td></td>
<td>Unfavourable</td>
</tr>
</tbody>
</table>

Intra-articular Steroids

Encourage Physical therapy

Avoid unnecessary Ca²⁺/vit D supplements

In elderly

Majority require Jt. Replacement Sx.
CHARCOT'S

1st described - Taber (Neurosyphilis)

Associations: DM, Leprosy, Amyloidosis

Pathophysiology

**NEUROVASCULAR**
- Autonomic neuropathy
  - Disrupts microcirculation
  - Recurrent microtrauma
  - Degeneration
  - Loss of pain sensation (Neuropathic joint)

**NEURO-TRAUMA**
- Sensory neuropathy

M/C: Forefoot joint → Hindfoot joint → Ankle joint

Assessment: XR → 'Loose Bodies' in joint cavity

Only Rx: Strict immobilization → Total rest
  - Facilitate recovery of joint
  - Only palliative → Unfavourable prog.
VASCULITIS

(A) Based - Pathological Mechanisms

- Antibody (ANCA) Mediated
  - Wegener's (W.G.)
  - Churg Strauss (C.S.S.)
  - M.P.A. Microscopic Polyangiitis

- Immune-complex Mediated
  - Hep. B - PAN
  - Hep C - Cryoglobulinemia
  - H.S.P. Henoch-Schönlein Purpura

- T. cell mediated
  - Giant cell arteritis
  - Takayasu's
  - W.G.
  - C.S.S.

(B) Based - Size of vessel affected (Preferred)

- LARGE
  - Giant cell arteritis
  - Takayasu

- MEDIUM
  - Polyarteritis nodosa
  - Kawasaki

- SMALL

- ANCA +ve
  - Anti-PR3 W.G.
  - Anti-MPO M.P.A.

- ANCA -ve
  - H.S.P. vs Hypersensitivity
  - Cryoglobulinemia
  - BECHET'S Disease
**G.C.A.**

> 50 yr, f > 0°

<table>
<thead>
<tr>
<th>C/F</th>
<th>Artery Involved (Carotid)</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Poly myalgia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rheumatism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Myalgia, fever, Anorexia,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wt loss &gt; 3 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Br. of External Carotid</th>
<th>Br. of Int. Carotid</th>
<th>1st Br. Ophthalmic A.</th>
</tr>
</thead>
<tbody>
<tr>
<td>H/Ic - Sup. Temporal</td>
<td>End artery -</td>
<td>No Collaterals</td>
</tr>
<tr>
<td>Headache (Worke-Supine)</td>
<td>End artery -</td>
<td>Permanently</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BLINDNESS</td>
</tr>
<tr>
<td>± Diplopia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>± Jaw Claudication Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>± Parasthesia over Jaw</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ESR (Screening) > 60 (Significant)**

**Cold Std →**

- **L Temporal A. Biopsy** → Minimum > 2 cm Length
- HPE - Granulomatous Vasculitis

**Rx - Steroids → Relief of Symptoms**

*Only Drug to Prevent Dreaded Complication → BLINDNESS*

*Early Rx = Good & Prognosis*

![Diagram](image)

- Lymphocytes
- Macrophages
- Giant cell
- Intimal Hyperplasia
- Fragmentation of Intimal Elastic lamina
TAKAYASUS / AORTIC ARCH SYNDROME

Epid - 10-20yr, $q > 0$

C/F - Depend on artery Involved = All direct Br. of AORTA

<table>
<thead>
<tr>
<th>SUBCLAVIAN (HIC)</th>
<th>CAROTID VERTEBRAL</th>
<th>COELIAC</th>
<th>RENAL</th>
<th>CORONARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIL Claudication</td>
<td>Recurrent TIA/Stroke</td>
<td>chr. mesenteric Insufficiency</td>
<td>Refractory HTN (RAS)</td>
<td>&lt;1% Acute Coronary Syndrome</td>
</tr>
<tr>
<td>Unequal/ABSENT</td>
<td>PULSELESS DISEASE</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Δ - CT- AORTOGRAPHY Gold Std

Rx - Immunosuppression + Angioplasty (Specific) (Palliation)

POOR PROGNOSIS

KAWSASAKI’S / Muco-cutaneous L.N-Syndrome

HIC vasculitis; <5yr, $0 > q$

Replaced R.H.D. → HIC cause of Cardiac death in children. due to Acquired heart Disease

AHA Guidelines

HIC manifestation → Febrile episode

Any Fever - on/after 4th Day (min. dur 5 days)

4/5 of following features are +

1) 90% B/L non-exudative conjunctivitis
2) Erythema over extremities
3) Peri-anal Rash
4) Strawberry Tongue
5) non-suppurative Single, cervical L.N.
**Rx - IVIG +**  Long-term Aspirin prophylaxis

- Relieve symptoms
- Reduces risk of coronary involvement to 4-6%
- Cannot reverse coronary aneurysm

**Dreaded:** Coronary Aneurysm complication

- Rupture (4-6% case)
- Thrombosis 95% of case
- Elective angioplasty prevents.

**Prognosis - FAVOURABLE**

**ULINASTATIN:** Neutrophil elastase inhibitor

(NeW, approved) only IVig refractory case

**Pathology** Immune complex mediated

- Fibrinoid necrosis
- Bi-furcation of medium vessel
- Micro aneurysm formation

**H/F** HIC 90% arthralgia

**Hematuria** - CONUT ON
  (rupture of micro aneurysm)

**CNS:** Mononeuropathy - multiplex (neuropathy) - asymmetrical

**Skin:** Raynaud's phenomenon

**PAN / Systemic Necrotising Vasculitis | MPA (PART of PAN prior to 1999)**

Epid 30-50 yr, O > F

**Etiology** Classical HIC - Idiopathic

30% Chronic Hepatitis B infection

**ANCA** - mediated vasculities

- Small vessel predominant
- 70% Anti-MPO +ve.

Always due to AN
<table>
<thead>
<tr>
<th>Digital gangrene, LIVEDO</th>
<th>Purpura Rash</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital arteries</td>
<td>Pulmonary</td>
</tr>
<tr>
<td>Menses torsion</td>
<td>Spaced</td>
</tr>
<tr>
<td></td>
<td>But bronchick may be involved</td>
</tr>
<tr>
<td></td>
<td>Alveolar H()ge</td>
</tr>
<tr>
<td></td>
<td>(ANCA +ve ⇒ DLB - Good Paster's Syndrome)</td>
</tr>
</tbody>
</table>

Asia - Exception

Biopsy - Gold std

Renal angio - muros aneurysm @ bifurcation of vessel.

Rx Immunosupressants → Favourable Prognosis

---

**WEGENER’S GRANULOMATOSIS**

or **chronic Granulomatous angiitis**

30-50 yrs, 0\(^\circ\)♀

Closest D/D → Good Paster's.

<table>
<thead>
<tr>
<th>C/F Pulmonary</th>
<th>Renal</th>
<th>Eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>H/c Lungs</td>
<td>URT() specific</td>
<td>H/c - Pan-uveitis</td>
</tr>
<tr>
<td>B/L abscess</td>
<td>H/c - chr. sinusitis</td>
<td>SKIN</td>
</tr>
<tr>
<td>Multiple thin walled cavity</td>
<td>Nasal bridge deformity</td>
<td>Purpuric Rash over L.L</td>
</tr>
<tr>
<td>Alveolar H()ge</td>
<td>Serous otitis media (GLUE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subglotticstenosis (change in timbre of voice)</td>
<td></td>
</tr>
</tbody>
</table>

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SEROLOGY: 70% Anti PR3 +ve (Wegener's Antigen) (SCREENING) 30% Anti MPO +ve

Absence cannot exclude W-G.

BEST TEST → LUNG BIOPSY

Rx cyclophosphamide → favourable response

Good & PROGNOSIS

GTH

CHURG STRAUSS (eosinophilia & granulomatous angiitis)

30-50yrs. 6-9%

OF

PULMONARY

RENAL

SKIN involvement

LUNG

LATE ONSET asthma

URTI

allergic rhinitis

RPN

Purpuric/urticarial rash

W-G. can be differentiated by ocular involvement

Asu: Short course of steroids

Lung Biopsy/skin bx = eosinophilic vasculitis

Rx: Short course of steroids

favourable prognosis, long term remission

Good & PROGNOSIS
**H.S.P. (ANAPHYLACTOID PURPURA)**

- >90% cases - occur <10yrs, age M > F.

**ADULT H.S.P.**

**HYPERSENSITIVITY VASCUITIS**

**EPID - 20-40yrs, O > F**

**Etiopath** Post Infective H/C - preceded by URTI

<table>
<thead>
<tr>
<th>C/F</th>
<th>PALPABLE PURPURA</th>
</tr>
</thead>
<tbody>
<tr>
<td>LL &amp; Buttocks</td>
<td>Distribution</td>
</tr>
<tr>
<td>Common Abd. pain, Malaena</td>
<td>Mucus memb. involvement</td>
</tr>
<tr>
<td>3-5% - IgA deposits on GBM - Gross Hematuria</td>
<td>Renal involvement</td>
</tr>
<tr>
<td>Capillaries</td>
<td>Site: Biopsy (Gold std)</td>
</tr>
</tbody>
</table>

**Rx - Reassurance/Self limiting Disease.**
ESSENTIAL MIXED CRYOGLOBULINEMIA (EMC)

Usually indicate Idiopathic cause

Majority = 90% = 2° cause

- Multiple myeloma
- chr. Hep. C., Hep B
- Lymphoproliferative states

Pathophy.: Exposure to cold → Cryoglobulins ppt.
(T < 37°C)
(Ig ≤ ppt.)

H/L - Skin capillaries
98% - multiple areas of skin
Necrosis

Renal tubulus
A.T.N. (Direct toxicity)

△ Ser. Incubate plasma in cold bath - ppt. +

Rx - Prog - underlying cause (unfavorable)
**Bechet's Disease**

- **Epidemiology**: 30-50yrs, <90° (worse in 0°)

<table>
<thead>
<tr>
<th>MAJOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent, painful, oral aphthous ulcers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MINOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>17. Recurrent superficial thrombophlebitis</td>
</tr>
<tr>
<td>20. Bul Hypepsoyon</td>
</tr>
<tr>
<td>37. Erythema Nodosum</td>
</tr>
<tr>
<td>47. Painful genital ulcers</td>
</tr>
<tr>
<td>57. Pathergy Test +ve</td>
</tr>
<tr>
<td>Skin Prick &gt; 5mm deep</td>
</tr>
<tr>
<td>Induration +</td>
</tr>
</tbody>
</table>

Δ65 - MAJOR + 2 MINOR - confirm.

Rx - Steroids - excellent response

Favourable Prognosis
FIBROMYALGIA (Pain Sensitivity Syndrome)

- Epid: 30-50yrs, $f > 0$
- Risk: Stress
- Pathway: ↓ Blood flow to thalamus
  (Minor) ↓ Cortisol Response to stress

C/F: Multiple aches & pains (Somatic complaint)
  ≥ 3 months

- Associated w/ Defect of NREM Sleep

Assessment - 18 point pain testing (Screening)
  (>11/18 +ve tenderness → significant)

MR spectroscopy - gold std

Rx - Pregabalin
  Gabapentin
  TCA
  SSRI

Unfavourable Prognosis → Prone to analgesic abuse
  Poor QoLI
CHRONIC FATIGUE SYNDROME

20-40yrs, o > f
e/f - FATIGUE > 6 weeks

Asu- of exclusion

1) Obesity
2) Substance abuse
3) All medical causes

Nutritional

2) Endocrine
   Hypothy., DM.

2) Chronic Infection

4) Autoimmune

5) Neoplasm

Rx = Lifestyle Modification
RESPIRATORY
LUNG DEVELOPMENT

1) Embryonic stage - lung buds
2) Pseudoglandular stage - up to terminal bronchiole
3) Canalicular - Alveolar ducts
4) Sacular - Primitve alveoli
5) Alveolar - Mature alveoli

BRONCHOPULMONARY SEQUESTRATION

Def: Separation of part of lung during development from tracheobronchial tree in separate blood supply.

Types:
- Extrapulmonary
  - Separated & having separate covering
- Intralobar
  - Separated part in adjacent lung covered by lung's pleura

Mc:
- Location: Lower lobe post basal segment
- Blood: Thoracic aorta supply
- IOC: CT Angiography or HR angiography
- Rx: Resection if pt is symptomatic
**SURFACTANT**

1. Dipalmitoyl Phosphatidyl Choline (lecithin).
2. Produced by Type II pneumocyte.
3. Also by Clara cells.
4. Removed by Alveolar macrophage.
5. Functions:
   a. Surface tension
   b. Maintain alveolar stability / FRC
   c. Compliance

6. Surfactant inducer starts at **20 wk**
   Peak at **35 wk**

So, if < **35 wk** → Respiratory distress syndrome or Hyaline membrane disease.

---

**Pathophysiology → RDS**

**HYALINE MEMBRANE DISEASE**

- Surfactant deficiency → collapsed alveoli → To open collapsed alveoli → Respiratory Distress
- Energy resource
- Hyaline layer causes Damage to Alveolar cell → Hypoxemia → Met. acidosis
- Cyanosis ← R-L shunt
  Patent foramen ovale → Pul. vasomotoric
X-ray Findings:
1. Reticulo granular granular pattern
2. Ground glassing
3. White out lungs
4. ↓ Lung volume (↓ FRC)

Inv:

Lecithin > 2 → MATURE LUNG
Sphingomyelin

Rx:
mild to moderate → O₂ + CPAP
Severe → Invasive Mech. ventilation + Surfactant Deficient Replacement

Surfactant [Hyaline appears pink on biopsy]

PULMONARY ALVEOLAR PROTEINOSIS

Surfactant clearance is impaired

Etiology:
1° form (H/L) → Auto Ab against Gmese
2° form → Acute Silicosis
Haematopoetic malignancy
Immunodeficiency

Silica particles are toxic to alveolar macrophage
Chronic silicosis pt are prone to TB.

In malignancy, macrophages are not matured enough to carry out func.
In immunodeficiency, macrophage ↓
Pathophysiology

Diffusion from O₂ → Hypoxemia

Δ:
1) Broncho-pulmonary Lavage → milky white
2) BAL → PAS +ve
3) CT Chest → CRAZY PAVING PATTERN

Rx - Whole Lung Lavage

**WIEBELS LUNG MODEL**

- Trachea → Alveoli

  **Functional / ventilatory unit / Acinus = Distal to terminal Bronchiole**

  Radiological unit / 2° Pulmonary Lobule = Roof of a Group of acinus (5-7) involved in EMPHYSEMA

  Alveolar duct & Sac

  **Upto terminal Bronchiole - Conducing Pathway**

  ② Main Bronchus

  "Aspiration is more common on this side as it is short, stout, straight"

  "Bronchiectasis more common in lower part - narrow, angulated, & drainage"

  ⑥ Main Bronchus
BP Segments + ASPIRATION PNEUMONIA

M/C segment involved in Asp. Pneumonia:
- Lower Lobe Superior
- Upper Lobe Inferior

M/C segment involved in Asp. Pneumonia in Supine Lobe Post

Asp. Pneumonia in Sitting/Standing
- Lower Lobe Posterior Basal

Asp. Pneumonia in Bending forward
- Middle Lobe

Best Inv.: Bronchoscopy

HEMOPTYSIS

Lung
- High P. Systemic Circulation → Bronchial Artery
- Low P. Pulmonary Artery → Pulmonary Artery

M/C Source of hemoptyis → Bronchial Artery

M/C Source of massive hemoptyis

M/C of hemoptyis in India → TB

M/C of worldwide → TB

M/C of Death in hemoptyis → Asphyxiation & Blood clot
**Approach to Hemoptysis**

**Massive (≥200 - 600 mL/d)**
- **Stable**
  - CT Scan
  - Low Risk
  - Fiberoptic Bronchoscopy
  - Rigid Bronchoscopy
    - [Diagnostically Therapeutic]
      - [Dual t bleed better]
- **Unstable**
  - Stabilize
  - Fiberoptic Bronchoscopy

**Non-Massive**
- **CXR (N)**
- **CXR Ab (N)**

- **High Risk**
  - Old age + heavy smoker
  - CT Scan
  - Bronchoscopy

- **Low Risk**
  - CT Scan
  - Young + less smoker

- **Single**
  - Reassure + Antibiotic
  - CT Scan

- **Multiple**
  - Fiberoptic Bronchoscopy

**Persistent Cases**
- Bilateral embolisation
- Resection of affected lobe

**Sources of Hemoptysis**

- **Mitral Stenosis**
  - Rupture of Pulmonary Bronchial Vascular "connex" - Br. veins

- **Pulmonary Embolism**
  - Pulmonary artery

- **TB**
  - Bilateral artery

- **Rasmussen's aneurysm**
  - Pulmonary artery

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organism that cause pseudohemopysis
\[ \text{Serratia marcescens} \]

**INTRAPELVIC**

Lung always try to collapse to centre

Chest wall always try to move outward

There is a **Balancing Force between the 2**

-ve Intrapleural Pressure (IPP)

\[ \text{Usually -ve during \textbf{N} Inspiration} \]

\[ \text{Maintains equilibrium Lung volume \Rightarrow \textbf{FR} (Relaxing volume)} \]

\[ \text{\textbf{N} Value: -2 to -6 cm H}_2\text{O} \]

\[ \begin{array}{c}
-6 \\
-2 \text{ cm H}_2\text{O}
\end{array} \]

More -ve IPP

Deep Inspiration

- Pulley
- Collapse
- Fibrosis

Less -ve IPP / +ve IPP

1) Forced Expiration

* Cough, valsalva maneuver

2) Pushing lesions

3) * Tension Pneumothorax

* Haemoe. **
**COMPLIANCE**

- Stretchibility of Lung.
- Change in unit volume per unit change in pressure
  \[ c = \frac{\Delta v}{\Delta p} \]

**Static Compliance** = air flow & resistance not considered

**Dynamic**, air flow & resistance considered

---

**EMPHYSEMA PATHOPHYSIOLOGY**

- Insp: Exp. 2:3 early closure
- End expiration
- If elastic fibers damaged

**CXR**

1. Bil Hypertranslucency
2. Flat Diaphragm
3. Tubular Heart
4. Barrel shaped chest wall

**Emphysema**
- RV ↑
- PRC ↑
- TLC ↓

**Dynamic Hyperinflation**
- ↓ diameter of airway
- ↓ Airway resistance
- ↓ Dynamic compliance in emphysema

**Loss of elastic fibers**
- ↑ static compliance
1. Surfactant Deficiency
2. ARDS
3. Pulmonary Edema
4. Fibrosis (ILD)
5. 100% O₂ damage

HOOVER'S SIGN - Paradoxical inward movement of lower ribcage during inspiration

Since diaphragm is not there, that's why.
HISTOLOGY OF ALVEOLI

TYPE I
- Pavement epithelium
- Vulnerable to damage
- More surface area

TYPE II
- Secretes surfactant
- Can divide and reconstitute Type I cells

ZONES OF LUNG

Vertical regions based on hydrostatic pressure

\[ P_A = \text{alveolar pressure} \]
\[ P_a = \text{arterial pressure} \]
\[ P_v = \text{venous pressure} \]

Zone 1: \[ P_A > P_a > P_v \]
Zone 2: \[ P_e > P_A > P_v \]
Zone 3: \[ P_e > P_v > P_A \]

\( \text{Lung} = \text{combination of Zone II + III.} \)

DEAD SPACE:

Area ventilated but no sufficient gas exchange (blood flow)

Anatomical D.S.
- Ext. nares to Terminal Bronchial
- Measured by Fowler's method
- \( N_2 \) used

Physiologic D.S.
- \( P_d = P_{\text{Anat D.S.}} + P_{\text{Alveolar D.S.}} \)
- \( P_d = P_{\text{Total D.S.}} \)
- \( P_{\text{Anat D.S.}} = 0 \)
- \( P_{\text{Alveolar D.S.}} = P_{\text{F.O. D.S.}} \)

* Bonus Equations
Anat D.S.

1. Neck Extension
2. Bronchodiilation
3. Old age

Anat D.S.

1. Neck Flexion
2. Broncho constriction
3. Bronchomachial intubation

Tracheostomy

Bypass oral
Bypass nasal

Laryngectomy

COPD

Wasted ventilation

P Embolism

Wasted ventilation

In P embolism, predominant defect is in perfusion

Mechanisms of hypoxemia

1. V/P mismatch (H/c)
2. Shunt
3. Diffusion defect
4. Hypoventilation
SHUNT -
Bypass of blood to out oxygenation.

\[ \text{INTRACARDIAC} \]
\[ \text{INTRAPULMONARY} \]

\[ \text{Rx} \rightarrow \text{sev. Pneumonia} \]
\[ \text{Rx} \rightarrow \text{ARDS} \]

bad \( O_2 \) \( \rightarrow \) good \( O_2 \)

Mixed \( \rightarrow \) Hypoxemia

Less responsive to supplemental \( O_2 \).

\[ \text{Rx} = \text{Mechanical Ventilation.} \]
\[ \text{Rx} = \text{Infection.} \]

Cure pathology.

\[ \frac{V}{P} \text{ Ratio} \]

Max. Ventilation
Max. Perfusion
Min. \( V/P \) ratio

\[ \text{BASE} \]

\[ \text{APEX} \]

\[ \text{MIDZONE} \]

\[ \text{BASE} \]

<table>
<thead>
<tr>
<th></th>
<th>( V )</th>
<th>( P )</th>
<th>( \frac{V}{P} )</th>
<th>( P_{A0_2} )</th>
<th>( P_{Aco_2} )</th>
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</thead>
<tbody>
<tr>
<td>APEX</td>
<td>2 L</td>
<td>0.5 L</td>
<td>4.</td>
<td>130</td>
<td>28</td>
</tr>
<tr>
<td>MIDZONE</td>
<td>4 L</td>
<td>5 L</td>
<td>0.8</td>
<td>104</td>
<td>35</td>
</tr>
<tr>
<td>BASE</td>
<td>6 L</td>
<td>10 L</td>
<td>0.8</td>
<td>92</td>
<td>42</td>
</tr>
</tbody>
</table>
1st TB ⇒ Mid & Lower Lobe
2nd TB ⇒ Apex.

- active disease due to 
  proliferation of Bacilli
  
Reason

↑ O₂ tension  ➔ ↑ V/P ratio

**DIFFUSION CAPACITY OF LUNG** \( DCO \)

↓ \( DCO \)

1) Fibrosis ⇒ ILD
2) Severe emphysema
3) Pneumonia
4) ARDS
5) Sarcoidosis
6) P. embolism
7) Anaemia
8) Pul. HTN

No blood for exchange

↑ \( DCO \)

- Polycythemia
- Exercise (↑ blood flow)
- Alveolar Hoge
  - good patiens
  - Wegener
4) Acute Asthma

↑ eosinophil inflammation

↓ NO produc

↓

P. vasodilation

↑ \( DCO \)

New

FeNO = Test for Acute Asthma
SPIROMETRY

Tidal Volume = Normally in/out = 500 mL

IRV = air accommodated & effort after Tidal Inhalation = 3000 mL

ERV = air expelled & effort after Tidal expiration = 1100 mL

RV = Air that remains after flex forcible expiration = 1200 mL

TV + IRV + ERV

IC = TV + IRV

FRC = ERV + RV

TLC = \[
\frac{TV + IRV + ERV + RV}{VC + FRC}
\]

IC

VC

FRC

TV

ERV

IRV
Conventional Spirometer: can't measure

- RV
- FRC
- TLC

Method: (for RV, FRC, TLC) 
He Dilution Method
N₂ washout
Body Plethysmography. (Best)

**DYNAMIC LUNG VOL**

1. Forced Vital Capacity = Rapid & forcible VE

   - FeV₁ = FVC @ end of 1st sec = 80%
   - FeV₂ = FVC @ end of 2nd sec = 90%
   - FeV₃ = FVC @ end of 3rd sec = 98%

2. PEFR = Peak expiratory Flow Rate
   - Peak of FVE
   - Indicates Large airflow flow
   - 400-500 mL/min

3. MEFR = Avg. velocity during mid portion of exhalation
   - Sensitive indication of small airway function
   - 300 mL/min

<table>
<thead>
<tr>
<th>N</th>
<th>OBSTRUCTIVE</th>
<th>RESTRICTIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC N</td>
<td>FeV₁ II</td>
<td>FeV₁ ↑/↓</td>
</tr>
<tr>
<td>FeV₁ N</td>
<td>FVC N</td>
<td>Fvc lll</td>
</tr>
<tr>
<td>FeV₃ N</td>
<td>FVC ↓</td>
<td>FeV₁ = ↑/↓</td>
</tr>
<tr>
<td>FeV₁/FVC</td>
<td></td>
<td>FeV₁ = ↑/↓</td>
</tr>
</tbody>
</table>
OBSTRUCTIVE

1) Asthma
2) Bronchiectasis
3) COPD → Chv. Bronchitis, Emphysema

RESTRICTIVE

Infralesion RLD
Pul. parenchyma involved

Extensio RLD
Pul. parenchyma uninvolved.

1) Fibrosis
2) Pneumonia
3) Sarcoidosis
4) Occupational lung disease
5) Kyphoscoliosis
6) Neuromuscular Disease
   a) CFS
   b) Polymyelitis
   c) Myasthenia Gravis
   d) Amy. Lat. Sclerosis
7) Diaphragmatic Dysfunction
EMPHYSEMA

1) Obstructive

2) \( \frac{\text{FEV}_1}{\text{FVC}} \)

3) RV↑, FRC↑, TLC↑

4) Compliance
   - Static
   - Dynamic
   - DLCO↑

INTERPRETATION OF SPIROMETRY

LOW < 0.7

\( \frac{\text{FEV}_1}{\text{FVC}} \) \( \rightarrow \) N/↑

FVC < 80%

OBSTRUCTIVE

RESTRICTIVE

INTRINSIC

\( \frac{\text{RV}}{\text{TLC}} \)

EXTRINSIC

\( \frac{\text{RV}}{\text{TLC}} \) N

FLOW VOLUME LOOPS

OBSTRUCTION
Restrictive

FeV1, FVC

SPO2 on exercise

DLCO (young girl)

Pulmonary HTN

Breathing Patterns

Kussmaul's breathing - rapid, deep breathing
2) CHEYNE STOKES BREATHING.
   → Periodic Breathing → Cyclic Pattern.
   
   
   → altered response to CO₂
   → CHF, narcotic overdose, Head injury

3) BIOTS BREATHING
   → Irregular Respiration → Apnoea
   
   → Meningitis
   
   ↑ ICP

4) ATAXIC BREATHING
   Irregularly irregular rate → ↑ Apnoea
   
   till pt. goes into resp. arrest
   
   eg. Brainstem injury.
BREATHE SOUNDS

- Vesicular Breathing
  - Similar to sounds of rustling of leaves
  - Low pitch, soft
  - I:E 3:1
  - No pause

- Bronchial Breathing
  - Similar to tracheal sound
  - High pitch, Harsh
  - I:E = 1:1
  - Pause

1. Tubular Breathing
   - Consolidation
2. Cavernous
   - Cavity
3. Amphonie
   - Metallic quality
   - e.g., Broncho-Pleural fistula

ADVENTITIOUS BREATH SOUNDS:

- WHEEZE (musical)
  - Produced when air flows past an obstruction due to vibration of airways
  - Monophonic Polyphonic
    - Local involvement
    - Diffuse involvement
  - e.g., Bronchial Tumour
  - e.g., Asthma, COPD

- Rhonchi: Low pitch wheeze

CREPES/CRACKLES/RALES

- Non-musical sounds
  - 1. When air flows into secretions
    - Bubbling noise
    - Cause crepts
    - Bronchiectasis
  - 2. When alveoli suddenly pop open during inspiration
    - Velcro crepts
    - Fine crepts
Fine & Course Crepts

1) P. Edema (fine >7 course)
2) Pneumonia
3) TB

STRIDORE - Loud, audible inspiratory & expiratory wheeze due to Laryngospasm.
F.B.
Laryngeal Edema
Subglottic stenosis

LEES -

PULLING
Collapse
Fibrosis

PUSHING
Lesion
Pleural effusion
Pneumothorax

Percussion = Dull in collapse
Impaired in fibrosis

Auscultation
Bs Θ in collapse
Bs ++ in fibrosis

CXR
Collapse - Homogenous white
Fibrosis - Heterogeneous white

Dull note
Bronchial breathing +

Air Broncho gram

Pl. eff = white meniscoid fluid level
Pneumothorax
Z Black 🅗
Compressed lung margin

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PLEURAL EFFUSION

- Straight line of dullness
- Shifting dullness
- Suction splash
- Sound of coin

HYDROPNEUMOTHORAX

RESPIRATORY FAILURE

Low \( P_{O_2} < 60 \text{mmHg} \), High \( P_{aCO_2} > 45 \text{mmHg} \)

(HYPOXIA) (HYPERCAPNIA)

Type I RF - Hypoxemic RF

Type II RF - Hypercapnic RF

Type III RF - Perioperative RF due to lung atelectasis associated with general anaesthesia

Type IV RF - due to hypoperfusion of respiratory muscle due to shock.

TYPE I

Diffusion defect

\[ \text{Transfer of } O_2 \]

\[
\begin{array}{ccc}
\text{Pao}_2 = 100 & \text{PaO}_2 = 90 & \text{Paco}_2 = 50 \\
\text{A}-\text{a} = 50 & \text{P}_{a-a}O_2 = 10 \text{mmHg}
\end{array}
\]

\[
\text{Pao}_2 = \downarrow,
\]

\[
\text{Paco}_2 = \downarrow
\]

\[
\text{P}_{a-a}O_2 = \uparrow
\]

TYPE II

Hypoventilation

\[ \downarrow \text{Resp. Effort} \]

\[
\text{Pao}_2 = \downarrow,
\]

\[
\text{Paco}_2 = \uparrow
\]

\[
\text{P}_{a-a}O_2 = \uparrow
\]

\[
\text{pH} \downarrow \downarrow \text{(Resp. Acidosis)}
\]
CAUSES
Pneumonia
ARDS
ILD
Pulmonary edema
P. thromboembolism

Rx \ O_2 + Rx of underlying disease
If pt. not improving
Pneumonia
ARDS

Invasive +ve pressure ventilation preferred

CENTRAL CAUSE
Narcotic use
Head injury

OBSTRUCTION
P: B.
Severe COPD

PERIPHERAL
Neuromuscular Disorder

DIAPHRAGM CAUSE
Palsy
\[ \Rightarrow \text{COPD - pneumothorax} \]
O_2 + Rx underlying cause

If pt. not improving
[COPD / NMD]

Non-invasive +ve pressure ventilation is 1st choice
NI PIPV \[ \Rightarrow \text{BiPAP (NIV commonly used)} \]
CPAP

If no response \[ \Rightarrow \text{IPPV} \]

c/1 of non-invasive ventilation
1) Altered sensorium
2) ↑ chance of aspiration
3) Cardiac arrest
4) Hemodynamically unstable
5) Uncooperative pts.
ARDS

Definition: Acute shortness of breath + Hypoxemia + Diffuse Pulmonary infiltrate

Causes:
- DIRECT
  1) Pneumonia
  2) Aspiration of gastric content
  3) Lung contusion
  4) Near drowning
  5) Toxin inhalation

- INDIRECT
  1) Sepsis (M/C)
  2) Severe Trauma
  3) Multiple Blood Transfusions
  4) Severe Burns
  5) Pancreatitis

Other Names:
- Noncardiogenic Pul. Edema
- "P" permeability Pul. Edema
- Low pressure Pul. Edema
- Diffuse Alveolar Damage (most characteristic)
- Shock Lung
- Wet Lung

Pathogenesis:
- Cardiogenic Pul. Edema
- Non-cardiogenic Pul. Edema

6) Claustrophobic
7) Active GI Bleed
8) Recent Facial Trauma or Sx
CARDIOGENIC P. Edema

NON-CARDIOGENIC

Damage to capillary endothelium & alveolar epithelium.

↑ Neutrophil entry = inflammation.

↓ Damage = ↑ inflammatory exudate.

SHOCK LUNG.

PCWP = ↑ in CPE.

PCWP / Pulmonary Arterial Occlusion Pressure

Swanzganz Catheter used

Indirect measure of LAP

In CPE PCWP > 18 mmHg

In NCPE PCWP < 16 mmHg

As of Berlin 2012 Definition

1) Acute Onset < 7 days

2) Origin of edema = non-cardiogenic &
   PCWP < 18 mmHg

3) Bil. diffuse infiltrate in CXR - PA

4) \[
   \frac{P_{O2}}{FIO2} < 300 \]

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\[
\frac{P_{aO_2}}{F_iO_2} \quad \text{200 - 300} = \text{Mild ARDS}
\]

\[
\frac{P_{aO_2}}{F_iO_2} \quad 100 - 200 = \text{Mod. ARDS}
\]

\[
\frac{P_{aO_2}}{F_iO_2} \quad < 100 = \text{Severe ARDS}
\]

**Rx**

- **Most Recommended Strategy / Beneficial**

- **Low Tidal Volume Mechanical Ventilation** (4-6 mL/kg body wt.)
  - Assist control mode to avoid ventilation associated lung injury
  - Adequate +ve end expiratory pressure
  - Gluco-corticoioid may be helpful
  - Newer Ventilation Mode

- **Extra corporeal Membrane Oxygenation.**

  ![Diagram](Diagram.png)

  **Mech:** Blood is pumped into membrane oxygenator, oxygenate blood & sent back into body.

  *Beneficial in Severe ARDS.*
2) Prone Ventilation.

**MECH.:** In prone ventilation, diaphragmatic pressure on lower alveoli ↓ = ↑ed alveoli for oxygenation at wt. of abdomen.

For Benefit: Done for 16 consecutive hours.
- Helpful in improving oxygenation in pts. with severe hypoxemia.
- Not helpful in pt. with pre-existing chest wall deformity/severe fibrosis.

37 High Frequency Oscillator Ventilation
- Low tidal volume are given at more frequency.
- Beneficial in few studies.

**TRALI**
(Transfusion Related Acute Lung Injury)
- Occurs in or during 6hr of transfusion.
- Donor Plasma antibodies vs Recipient leukocyte
  → Mediator release

- Features of ARDS
  - **Rx:** supportive
  - 1/1c of Transfusion Related fatalities
P. THROMBOEMBOLISM (M/c of cor. Pulmonale)

Migration of thrombus into Pulmonary arteries

CAUSES

1°

1) Protein C, S deficiency
2) Factor V Leiden mutation
3) Lupus anticoagulant
4) Antiphospholipid antibody syndrome
5) Hyper homocysteinuria

2°

1) Prolonged immobilization
2) Recent Trauma. Sx
3) High estrogen state
4) Malignancy
5) Nephrotic syndrome

PATHOPHYSIOLOGY

LUNG

1) Pulmonary arterial Pressure
2) Rupture of vessel
3) Hemostasis
4) Alveolar Dead space = Hypoxemia
5) Shortness of Breath

37) Serotonin by platelets

RA

LA

RV

LV

P.A.

R.V. Pressure
RV Dilatation
RV Hypokinesia
Movement of septum into LV
LV Ventricular Interdependence
SHOCK [Cor Pulmonale]
47 Lung ischaemia → ↑ infl. mediators

5) Pleuritis → chest pain

6) Pleural effusion → Exudate >> Transudate

**TRIAD**

1) Chest pain
2) SOB (H/c symptom)
3) Hypotension

*OR PULMONALE*: alteration in function of right ventricle due to 1st disorder of Resp. system excluding diseases of left heart

H/c of chr. cor pulmonale → COPD
H/c of Acute " → Massive PTE

**DIAGNOSIS**

7) ABG → Type I Resp. Failure

8) ECG → H/c → Tachycardia, T wave inversion V1-4

7) Most specific → S1 Q3 T3 pattern, Massive PTE

23) CXR → N MLc

Focal oligemia (Westermark sign)
2) Wedge shaped deformity above diaphragm
   Hampton's hump

3) Pallad's sign - dilatation of right descending pul. artery

D-Dimer:
- fibrin degradation product
- elevated in PTE
- sensitive not specific
- poor predictive value but good neg. predictive value

5) Ioc > CT Pulm. Angio

6) Gold Std > Invasive Pul angiography

7) V/Q scan - outdated used in contrast intolerance.

RX

**Massive PE**
- Shock + RV Dysfunc
- Thrombolysis
- Surgical embolectomy

**Submassive PE**
- Low BP + RV dysfunc
- Individual Rx
- Thrombolysis / Anticoagulation

**Minimal PE**
- Low BP + Low RV function
- Anti-coagulation
PULMONARY HTN

MPAP > 25 mmHg @ rest
MPAP > 30 mmHg @ exercise

MECH. WHO CLASSIFICATION

Group 1 - Direct involvement of Pul. artery
a) Heritable cause/ 1st Pul HTN - mutation in BMPR
   - Smooth m/s proliferation
   - Young F.

   Biopsy - Plexiform lesion,

b) Connective Tissue Disorder
   - M/c cause is scleroderma, SLE.

c) Drugs/Toxin - Fenfluramine
   - Tox in rapeseed oil

Group 2 - Due to 2 Heart Disease

Group 3 - Due to Resp. Diseases:
   - COPD/ ILD/ Bronchectasai/ OSA

   Hypoxemia -> Pulm. vasoconstrictor -> P. HTN - con
   Pulmonale

Group 4 - Due to chronic thromboembolic events in Pulm. circulation.
**Group 5 - Miscellaneous / Unclear Cause**

Sarcoidosis

Sickle cell Disease

Langerhans cell histiocytosis / Langerhans histiocyte granuloma

Lymphangiomatosis

Lymphangioleiomyomatosis

---

**Diagram:**

Pul. artery → Pul. vein → Post-capillary Pul. HTN → Group 2

**Group 1, 3, 4**

Pre-cap Pul. HTN

MPAP > 25 mm Hg

PCWP < 15 mm Hg

**Rx**

**Group 1** Refractory cases from other groups

Other groups Rx underlying disease

1) CCB - Nifedipine (now not used frequently)

2) PDE 5 Inhibitors
   - Sildenafil
   - Tadalafil

3) Endothelin Receptor Antagonist
   - Bosentan
   - Ambrisentan
4) Prostacyclin - 
   Epoprostenol (IV) 
   Fluprost (Inhaled)

5) Guanyl cyclase activator
   Riocugat

Doc for Low Risk Cases: Initial monotherapy of
Less symptoms or ETRA
followed by combination Rx.

Doc for High Risk/Emergency - Prostacyclins
(Symptoms at Rest)

PNEUMONIA

AcuteHelp illness characterised by Radiological
Pulmonary shadowing.

CLASSIFICATION-

COMMUNITY - ACQUIRED P.
- Occurs in ambulatory individual.
- <48 hrs of hospitalisation
  M/c CAP - Strept. Pneumonia
  M/c CAP - Hospitalisation
  ILV Admin

HOSPITAL ACQUIRED P.
- Occurs after 48-72hrs of hospital stay.
  M/c HAP
  Gram -ve Bacilli
  > Staph. aureus

VENTILATOR ASSOCIATED R.
- Occurs 48-72hrs after endotracheal intubation & Mech.
  Ventilation
CLINICAL CLASSIFICATION

**TYPICAL**
- Fever + Productive cough
- Predominant neutrophilic leukocytosis
- Gram staining → reveal organisms
- CXR → Alveolar exudates
- H/c - Strept: Pneumoniae
  - Staph. aureus
  - Klebsiella
  - Pseudomona

**ATYPICAL**
- Intestinal Inflammation
- Fever + cough → scanty sputum
- Mild Leucocytes
- Gram staining → no organism
- CXR - No alveolar oxidation
  - Intestinal pattern
- H/c - Mycoplasma
  - Legionella
  - Clostridium
  - Chlamydia
  - Viral Pneumonia
Typical Pneumonia

I. Strept
- Risk Factors
  - History of smoking
  - Alcoholics
  - DM
- Red, rusty, sputum
- CXR
  - Localised involvement of lobe/segment
  - Pattern in CAP
- Rx - Beta-lactams

II. Staph
- IV drug users
- Pneumonia
- Fatal pneumonia post viral illness
- Mucopurulent sputum
- CXR
  - Bronchopneumonia
  - Bilateral patchy involvement
III. Klebsella
- Alcoholics
- DM, malnourished
- Red, current
- Jelly sputum
- CXR
  - Bulging fissure sign
  - Cavities
  - Dense consolidation
  - Lower lobe involvement
  - Seen if hematogenous spread
- Rx - Beta-lactam + Aminoglycoside

IV. Pseudomonas
- Frequently occurs as VAP
- Occurs as recurrent pneumonia in
- Fever, mucopurulent secretion
  - Leucocytosis

Structural Lung disease
- Emphysema
- Bronchiectasis

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- B/L infiltration of CXR

Rx: Two Antipseudomonal 
Abs of 2 different cl. 

Antipseudomonal Abs + a lactam + FQ (or) Aminoglycocide

**ATYPICAL PNEUMONIA**

MYCOPLASMA / Walking P.

M/c atypical pneumonia

Eaton agent pneumonia

Man → Man Transmission

Extrapulmonary features

1) CNS - GBS

   Peripheral neuropathy

2) Ear - Bullous myringitis

3) Blood - I cold agglutinins

   Hemolytic anaemia

4) CVS - Myocarditis

   Pericarditis

5) Skin - erythema nodosum

   No cell wall

Rx - Macrolide / FQ / Tetracycline

LEGIONELLA

M/c mode of transmission -

Micro aspiration > Alveolitis

Spread through contaminated water

Limited man to man transmission

Special Features:

> Associated GI features: diarrhoea

> " CNS features: 

   Confusion, headache, high grade fever

3) Altered LFTs

4) S. Na⁺ < 130 meq

Usual staining - no organism

Poor response to β lactam

Old age, Immuno compromised

Occur in 10 days discharge from hospital

Rx - "FQs / Macrolide / Tetracycline

Resp FQs - Levo / Moxi
PNEUMOCYSTIS PNEUMONIA (PCP)

HIV opportunistic infection in HIV = TB
HIV pneumonia in HIV = TB
HIV pleural effusion in HIV = TB
HIV fungal pneumonia in HIV = PCP

R/F:-
1) CD4 < 200 /μL in HIV
2) Long Term Immunosuppressive Rx
3) Organ Transplant
4) In Immuno compromised

C/F:-
Subacute onset
Fever
Shortness of Breath
Hypoxemia

CXR:-
Perihilar infiltrates
Diffuse interstitial infiltrate

In few - pneumatocele
Complicate as Pneumothorax

Δ:- Visualize the cyst ✧ Wright - Giemsa
Hematoxylin - methamine stain
Broncho-alveolar lavage (Best sample)
Rx - COTRIMOXAZOLE (Septan)

If sulpha allergy -
1) Clindamycin + Primaquine
2) Trimethoprim + Dapsone
3) Pentamidine
4) Atovaquone

DOC for Prophylaxis - COTRIMOXAZOLE

DOC for NECARDIOSIS.

VIRAL PNEUMONIA

BIRD FLU (H5N1)
- Avian Influenza
- Less M → M transmission
  Epidemic not Pandemic

DOC - Oseltamivir

SWINE FLU (H1N1)
- M → M transmission
  Epidemic + Pandemic

DOC - Oseltamivir
75mg BD for 5 days
(Neuraminidase Inhibitor)

DOC prophyaxis - Oseltamivir
75mg OD for 10 days

Other drugs - Zanamivir
Peramivir
ASSESSMENT of SEVERITY

Confusion

Urea > 7 mmol/L or UO > 20 mg.

RR > 30/min

BP - SBP < 90 mmHg DBP < 60 mmHg

65 Age age > 65

0-1 ⇒ Home Rx ± antibiotics

2 ⇒ Hospitalisation + Rx

3-5 ⇒ Consider as severe pneumonia, may require ICU admittance

EMPIRICAL REGIMEN FOR HOSPITALISED PT OF PNEUMONIA

Typical + Atypical

β Lactam + Macrolide
LUNG ABSCESS

1° ABS. FORM

H/c type

Due to aspiration

H/c oropharynx - oral anaerobes

Rx - IV. clindamycin.

2° FORM

Occurs due to pre-existing disease process in lung

Bronchial obstruction

Immune deficiency

Staph, Klebsiella

Rx - Broad spectrum ABs

STRATEGIES TO PREVENT VAP:

1. Elevation of Head of Bed 30°-45°

2. Oral decontamination with chlorhexidine

3. Sedation vacation (rapid sedation)

4. Assessment of readiness to extubate daily

5. Use of NIV whenever feasible

X Frequent change of Tubex

ORAL ANAEROBES:

- Peptostreptococci
- Fusobacterium
- Bacteroides
PLEURAL EFFUSION

TRANSUDATE

LIGHT's CRITERIA

EXUDATE

Ple. fluid Protein < 0.5
S. protein

Ple. fluid LDH < 0.6
S. LDH

Caue-
1. CHF (Hi cc overall)
2. Hepatic Hydrothorax
3. Nephrotic Sx

70.5, 0.6.
cytology = ?malignant cell
cell count
Gram staining = ? infection
TB marker = ADA,
Interferon y

Special Features
17. Low glucose ple. fluid (<60mg/dl)
   a. Empyema
   b. Malignancy
   c. RA
   d. TB (Here)

2. High Amylase
   a. Pancreatitis
   b. Oesophageal rupture
   c. Malignancy

3. High Lipid Ple. Eff / white colour

Chylothorax

Accumulation of
Pl. TGA >110mg/g Chyle due to develop of thoracic duct
Hsc = Surgical trauma
Malignancy

Pseudochylothorax

Accumulation of cholesterol crystals in long standing eff.
TB, RA, eh. empyema
Malignancy
cholester >200 mg/dl.
Parapneumonic Eff

HiCe of exudative pleural Eff

Eff associated to Pneumonia
Bronchiectasis
Lung abscess

Indications of ICD insertion in parapneumonic Eff:

1. Pus in pleural cavity
2. pH < 7.2 (pleural fluid)
3. Ple f. glucose < 60mg%
4. Loculated pleural effusion
5. Gram staining reveals organisms

TB Effusion

- HiCe exudative effusion in India
- Occurs due to hypersensitivity response to TB bacilli in pleural tissue

- Exudative - Lymphocyte predominant
  ADA > 40 IU
  INF Y > 140 pg/ml
  ↓ mesothelial cells

- Pleural fluid for AFB only positive in 20-50% cases.

Gold Std - Thoracoscopic pleural biopsy + culture for M. tb.
PNEUMOTHORAX & PNEUMOMEDIASTINUM

Classification of Pneumothorax:

- **Spontaneous**
  - No underlying lung disease
  - Pre-existing lung disease
    - COPD
    - M/C of 2nd spon. pneumothorax
    - Bronchiectasis
    - ILD, TB

- **Traumatic**
  - Fatrogenic
    - Needle aspiration, RTA
    - M/C of 2nd spon. pneumothorax
  - Chest wall injuries
    - Mech. ventilation
    - Insertion of subclavian catheter

**Tension Pneumothorax**

1. Large air leak
2. Ball valve (or) one way valve mechanism
3. ↑↑ Positive intrapleural pressure
4. Compressing adj. lung + mediastinal vesse
5. LVR
6. Shock (medical emergency)
7. Rx: Next step/Best step- Insertion of wide bore needle @ 2nd I.C.S. anterolong mid clavicular line on affected side followed by ICD insertion.
High Inspiratory Pressure alarm on ventilator suggest Tension Pneumothorax.

**Pneumo Mediastinum**

Air in mediastinum

**C/F** - Shortness of Breath

Chest pain

**HAMMAN'S CRUNCH** → Crunching sound synchronous to heart beat.

**CXR** - Continuous Diaphragm Sign.

Subcutaneous Emphysema

**ASTHMA**

Characterized by recurrent symptoms due to variable, reversible bronchoconstriction caused due to airway hyper-responsiveness to variety of stimuli.

**COPD** - Characterized by persistent symptoms & airflow limitation due to airway and alveolar abcess caused by significant exposure to noxious stimuli.

<table>
<thead>
<tr>
<th><strong>ASTHMA</strong></th>
<th><strong>COPD</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergen Related</td>
<td>Smoking Related</td>
</tr>
<tr>
<td>Reversible airflow limitation</td>
<td>Persistant airflow limitation</td>
</tr>
<tr>
<td>Early Presentation</td>
<td>Delayed presentation</td>
</tr>
<tr>
<td>Relief = Bronchodilators</td>
<td>only partial response</td>
</tr>
</tbody>
</table>
**Types**

**Pathogenesis**

**Extrinsic / Atopic / Allergic**

- Allergen related
- S. IgE
- Skin test +ve for allergen
- Mild form
- Young onset

**Intrinsic / Non-atopic / Idiopathic**

- Oral injection → Trigger
- S. IgE
- Skin test -ve
- Severe forms
- Late onset

**H/c allergen world**

- House Dust Mite / Dermatophagoides

Pollen → Cause Thunderstorm Asthma

\[ \Delta \]

**Spirometry**

- Obstructive
- Broncho dilator: reversibility = \( \text{FeV}_{1} > 12\% \) (or) 200cc after SABA

\[ \text{FeV}_{1} 65\% \text{ SABA 15 min} \rightarrow \text{FeV}_{1} 80\% \]

**PEFR Variability**

- > 20% diurnal variation

**Meth. Choline Challenge Test / Broncho Provocation Testing**

- Fall in \( \text{FeV}_{1} > 20\% \) after meth. choline
- For airway hyper-responsiveness

**FeNO > 50 Ppb** & Eosinophilic inflammation
ACUTE SEVERE ASTHMA

1) Pt. speaks in words
2) Can't recline
3) RR > 30/min
4) HR > 120/min
5) RL Wheeze
6) Accessory muscle use
7) Pulm Paradoxus \[ \text{Rapid change in intrapleural pr.} \]

Functional Parameters: -

1) PEFR < 50% predictive value
2) SpO₂ < 95%
3) PaO₂ < 60mmHg

Ifêt Type 2 RF can occur in severe cases due to fatigue of resp. muscles

Life Threatening Asthma:
1) Patient - altered sensation
2) Silent chest
3) Respiratory effort
4) PaO₂ < 60mmHg
5) Paco₂ ↑

Rx - 1) O₂ +
2) SABA + (Salbutamol) + Inhaled corticosteroid
3) SAMA (Albuterol)
4) I.V. Steroid \[ \text{Sensitivity of} \ β₂ \text{ receptor to broncho dilator} \]
37 Theophylline now not used routinely

47 In few cases IV MgSO_4 given

57 In deteriorating /life threatening cases = Invasive Mech. ventilation

Step Wise Therapy & Classification Persistent
Intermittent  Mild  Mod  Sev

Day Time S_x  < 2/week  > 2/week  daily  through-out day
Night time awakening  < 2/month  > 2/month  > 2/week  daily

Anti IgE omalizumab

Relievers

β agonist
Bronchodilators

Controller

Omal Steun

L Ics

Antileukotrom

LDIcs = low dose Ics

HDIcs = High dose Ics
Most imp. in asthma management is pt. self education & active self Mx.

**EXERCISE INDUCED ASTHMA**

- In susceptible individuals, exercise can induce asthma more frequent during cold, dry climate, hot humid conditions.
- Doc for short term prophylaxis: SABA > Anti-leukotrienes / Mast cell stabilizers.
- Doc for long term prophylaxis: Corticosteroids
- Overall control of disease

**ASPIRIN INDUCED ASTHMA**

```
COX  \[\text{Arachidonic Acid} \rightarrow \text{Lox} \]
     \[\text{PGs} \rightarrow \text{LTs} \]
```

**Samter’s TRIAD**

- Nasal polyposis + Aspirin sensitivity + Asthma

In susceptible individuals, aspirin blocks COX pathway → Shifts balance toward LOX pathway $\uparrow$ LTs → Bronchoconstriction

- Rx = ICS + Aspirin BABA + Anti-leukotrienes + Aspirin desensitization.

**BRITTLE ASTHMA**

Unstable Disease & frequent exacerbations.
Lung Function

Type 1 Brittle
Persistent fluctuation in lung functions

Type 2 Brittle
Near normal lung function → Rapid fall → Death

Difficult to Rx asthma
* Oral corticosteroids
  + Continuous infusion = β₂ agonist

Localized anaphylaxis
  + Laryngospasm
  Doc.: Subcutaneous Adrenaline + Epinephrine

Corticosteroid Resistant Asthma

Poor response to Rx after 2 weeks of oral corticosteroids (40mg/day) Rx
Steroid sparing drugs can be used.

Anti-IgE = Omalizumab
Anti-IL5 = Mepolizumab
COPD

CHR. BRONCHITIS:
- Cough & sputum for >3 months in 2 consecutive years

EMPHYSEMA:
- "Destrue" distal to terminal bronchide.

R/F:
1) Smoking
2) α₁ AT Deficiency
3) Indoor & outdoor pollution
4) Coal exposure

Types of Emphysema

CENTRICOINAR
- Occurrence: Smokers
- M/C overall upper lobes
- Pathology:
  RB involved
  Alveolar duct & Sac spared

PANACINAR
- α₁ AT Def
- More severe in LL
- Pathology:
  Resp. Bronchiole + Alveolar duct + Sac involved

DISTAL ACINAR
- Adjacent to peripheral POC
- Upper 2/3 of Lung
- Pathology:
  Resp. Bronchiole spared
  Alveolar duct & Sac involved
Spirometry

\[
\frac{FEV_1}{FVC} < 0.7 \Rightarrow \text{Obstructive}
\]

No significant bronchodilator reversibility

GOLD Staging (Global Initiative for Obstructive Lung Disease)

I Mild \( FEV_1 / FVC < 0.7 \) \( FEV_1 \geq 80\% \text{ Pred. FEV}_1 \)

II Moderate \( \quad \) \( FEV_1 \text{ 50.74}\% \quad \)

III Severe \( \quad \) \( FEV_1 \text{ 30.49}\% \quad \)

IV Very Severe \( \quad \) \( FEV_1 < 30\% \quad \) Pred. value

Prognosis Index

BMI

Obstruction (FEV₁)

Dyspnoea (MRC scale)

Exercise Capacity \( \Rightarrow \) Distance covered in 6-minute walk test

Low score \( \Rightarrow \) Good Prog.

High score \( \Rightarrow \) Poor Prog., ↑ mortality

Character

Pathology

Symptom

Appearance + Posture

Breath Sounds

CXR

PET

Blue Bloaters

Chronic Bronchitis

Cough + expectoration

Obese, uncomfortable at rest

Rhonchi - Noisy

↑ Interstitial Marking - Obstructive

Pink Puffers

Emphysema

Shortness of breath

Lean, tachypnoeic at rest

Less noisy

Hyperinflated Lung - Obstructive
Rx:

1. Smoking cessation. → most imp. intervention.
2. Bronchodilators
   a) LABA
      Ultra LABA → O.D. dose
      IndacEtrol
      Vilanterol
      Oladetrol
   b) LAMA
      Tiotropium
      Umclidinium
      Glycopyronium.

3. Steroid:
   a) Inhaled
      ↓ freq. of exacerbation
   b) Systemic
      During exacerbation.

4. Selective PDE4 inhibitor:
   Roflumilast

5. Ant biotics:
   During exacerbation (H. influenza)

6. Mucolytics:
   N Acetyl cysteine

7. If Hypoxemia → Long Term O₂ therapy (15 hours a day)

8. Lung volume reduction surgery

9. Lung transplantation (H/e indication for lung transplantation in COPD)

10. During exacerbation, 1st choice - non-invasive ventilation.
    > Invasive.
**Bronchiectasis**

Abnormal permanent dilatation of bronchi due to loss of muscle and elastic tissue.

Initiating event

↓

Altered mucociliary clearance

\[ \text{Vicious Cycle Theory} \]

Obstruction

→

→ Recurrent infection

→ Inflammation

\[ \text{Destruction} \rightarrow \text{Dilatation} \]

**CF:**

- Cough
- Sputum
- Wheeze
- Crepts

**Etiology & Mechanism:**

I) Bronchial Obstruction

a) Anatomical

\[ \text{Tumours} - \text{Carcinoid} \]

- Sq. cell carcinoma
- Small cell carcinoma

Enlarged TB hilus can compress middle lobe.

Bronchus of middle lobe collapses, bronchiectasis

↓

Boss's Syndrome
II) BRONCHIAL INJURY

A) Infection
   - TB, adenovirus

B) Altered Immune Response
   - Connective Tissue Disorder
   - Allergic Broncho Pulmonary Aspergillosis (ABPA)

III) TRACTION BRONCHIECTASIS in ILDs

II) GENETIC CAUSES

A) 1° Ciliary dyskinesia
B) Cystic fibrosis
C) Cartilage Defect
   - William Campbell's, Mounier Kuhn Syndrome

D) Yellow Nail Syndrome
   - Long Lymphedema + Yellow nail + Pleural Effusion + Bronchietasis

CYSTIC FIBROSIS

Inheritance - AR
   - Chromosome 7q
   - Gene - CFTR
   - Channel - Cl-
   - Mutations - Class I-Ⅲ
     - N/c class II, ΔF508
     - "Thick secretions"
PATHOPHYSIOLOGY

Resp. Tract

CIR

Reproductive Tract

ENaC → Responsible for pathophysiologic process

ENaC

Sweat Gland

Other Invrs.-

1) DNA analysis for mutations
2) ↑ Nasal Pot Difference
3) CFTR Gene Sequencing → Gold Std.

SYSTEMIC MANIFESTATIONS-

1) Respiratory Tract

URT

Recurrent Infections
Sinusitis

Recr. pneumonia
(M. pseudomonal), staph
Bronchiectasis, Lung abscess
Emphyema, P. Thrombosis,
Resp. failure, Hypoxemia,
P. HTN, Cor Pulmonale

2) Gastro-intestinal
neonate Melonium ileus
Liver → Biliary Cirrhosis,
GB - Gall stone
Pancreas
- Enzyme insufficiency - early manifestations
- DM, + occur later.

3) Reproductive Tract -

- In utero occlusion of vas deferens
- Thick cervical secretions
- By thick secretion → Azoospermia.

	infertile

Rx:
17 CFTR Modulators -
- Ivacaftor - G551D mutation class III
- Lumacaftor + Ivacaftor - titled in class II

Types of Bronchiectasis -

H/C-cylindrical Varicose Sacculare

Sites of B'xis -
> Upper Lobe
> Cystic fibrosis
> TB
> Post radiation Bxis
2. Lower Lobe

3. Middle Lobe - non-tubercular mycobacteria. Mycobacterium avium complex (MAC)

Rx of Bx:

1. Airway clearance.
   Mucolytics → Chest Physiotherapy.

2. Antibiotics
   During exacerbation
   Prophylaxis
   Long-term
   Azithromycin (6 months)
   Tobramycin (1 month on-off)
   Inhaled

3. Bronchodilators - ICS beneficial in some

4. If hypoxemia → O₂.

5. Localised Disease → Sx

High flow O₂ not recommended. Y?

1. Abolition of Hypoxemic Hct drive
2. High O₂ given can cause release of CO₂ from RBC
   - Haldane effect.

 IOC: - HRCT chest

**EOSINOPHILIC LUNG DISEASES**

[Peripheral eosinophilia + Lung infiltrate]

**CLASSIFICATION**

- Unknown cause
- Known cause
  1. Parasitic infestation (nematode)
  2. Loeffler's Pneumonia
  3. ABPA
  3. Drugs:
     - Nitrofurantoin
     - Sulfonamide
     - Isoniazid
     - Pencillamine

**Hypereosinophilic Syndrome**

- Persistent eosinophilia > 1500/mm³
- End organ infiltration.

**CHARACTER**

- Smoking Ht/o
- Asthma Ht/o
- C/F - Radiology
- Peripheral eosinophilia

**Ac. EP**

+++ , new onset smokers

- -

Acute shortness of breath + Hypoxemia +
Bll diffuse infiltrate

Initially not seen but seen
during later course of disease

**Chy. E.P.**

±

+++ cough + wheeze

Peripheral opacities

Usually seen
BAL eosinophilia  |  AEP  |  CEP  
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>BAL &gt; 25% eosinophil</td>
<td>steroid</td>
<td>BAL &gt; 40% eosinophil</td>
</tr>
</tbody>
</table>

**ASPERGILLUS & LUNG**

**HYPERSENSITIVITY RxN. → doc + steroid**

- **Type I**
  - Asthma

- **Type I, III, IV**
  - ABPA

**PNEUMONIA IN IMMUNOD COMPROMISED → DOC + VORICONAZOLE.**

- Invasive Aspergillosis
- Transbronchial angio invasion → may develop hemoptysis
  - Fever + SOB

DOC for **I + II → STEROID.**

DOC for **I → VORICONAZOLE**

**COLONISATION IN PREEXISTING LUNG CAVITY**

Aspergilloma / Fungall BALL

CXR → Air crescent sign
  
→ Ball changing its position = deumbitus.

Rx - Resection of pt. is symptomatic
CRITERIA FOR ABPA

1) Preceding Cond = Asthma
   Cystic Fibrosis
2) Peripheral \textbf{Eosinophilia}
3) S.IgE $> 1000$ IU
4) Aspergillus specific IgE + IgG will be +ve
5) Skin test +ve \textbf{Aspergillus fumigatus}
6) CXR \text{fleeting opacities} \rightarrow \text{upper zone}
7) Central (or) Proximal \textbf{B'xis}

Dox: Systemic Steroids

CT chest
- Finger in glove
- Toothpaste

\underline{HYPERSENSITIVITY} \hspace{1cm} \underline{PNEUMONITIS}
\hspace{3cm} \text{or} \hspace{1cm} \textbf{Extrinsic Allergic Alveolitis}

Type III + IV HSN
S.IgE $\rightarrow$ (B
No. peripheral eosinophilia
\textbf{Biopsy} $\rightarrow$ non caseating granuloma + cellular bronchiolitis +
Interstitial inflammation.

\textit{Egs.}
<table>
<thead>
<tr>
<th>DISEASE</th>
<th>EXPOSURE</th>
<th>ANTIGEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer's Lung</td>
<td>Moldy hay</td>
<td>Microsporobacter fermentis</td>
</tr>
<tr>
<td>Bagassosis</td>
<td>Sugar cane dust</td>
<td>Thermactinomyces flavus</td>
</tr>
<tr>
<td>Bird fancier Lung</td>
<td>Pigeon excrete</td>
<td>Saccharomyces cerevis</td>
</tr>
<tr>
<td>Malt worker Lung</td>
<td>Mouldy barley</td>
<td>Avian protein</td>
</tr>
<tr>
<td>Hot tub Lung</td>
<td>Contaminated water</td>
<td>Non-Tubercular mycobacterium</td>
</tr>
</tbody>
</table>

**Asitic Criteria:**
1. Exposure to known antigen.
2. Presence of serum precipitins against offending Ag.
3. Occurrence of symptoms in 4-6 hrs of exposure.
4. Recurrence of symptoms on exposure.
5. Inspiratory crepitation.

**Types**
- **Acute** - hours to days
  - CT. Chest: Ground glass opacities
- **Subacute** - week
  - Centrilobular nodules
- **Chronic** - month
  - Fibrosis (upper zone)

Rx - Most Important → Avoidance of allergen
  - Systemic steroids
ILD

Defn.: Group of Disorders characterized by predominant involvement of interstitium progressing to fibrosis & vary in mechanism & magnitude

ETIOLOGY:

I. Inhalational ILD
   - Organic Dust
     - Hypersensitivity
     - Pneumonitis
   - Inorganic Dust
     - Silica
     - Asbestos

II. Drugs/Radiotherapy
   - Amiodarone
   - Methotrexate
   - Busulfan

III. Connective Tissue Disorder
   - Scleroderma
   - RA
   - SLE

IV. IBDs

V. Infection - TB

VI. Malignancy

VII. Sarcoidosis

VIII. Idiopathic

PATHOLOGICAL PATTERNS:

I. Usual Interstitial Pneumonia (UIP)

2. Non-specific " " (NSIP)

3. Acute Interstitial Pneumonia (AIP)
Cryptogenic Organising Pneumonia (COP)

Respiratory Bronchiolitis (RBILD)

Desquamative Interstitial Pneumonia (DIP)

Lymphocytic " " (LIP)

Ioc :: HRCT chest

Confirmatory Test :: Surgical Lung Biopsy

Radiologic Patterns

Reticular Pattern

CT Chest

Mild opacity = Ground Glass opacity

Fibrosis

Fibrosis + fibrosis + traction + lung volume = Honeycombing

Subpleural involvement (near to pleura)
NIC form
Usual Interstitial Pneumonia or Idiopathic Pul. Fibrosis

CLF. 50-60yrs 0 > Q, Smoker
insidious,
Accumulation - inspiratory crepts
Exem - clubbing

Biopsy Heterogeneous involvement
Fibroblastic foci

Radiology - B/L Lower Zone d
- Subpleural involvement
- Minimal Ground glass opacity
- Significant Traction B/L
- Honey coombing

Rx: Prognosis Poor Response
00 Pulmonary
Nintedanib

NSAIP (M/c form of connective tissue disorder associated ILD)
40-50yrs 0 > Q
Non-smoker, subacute onset

No fibroblastic foci
Lymphocytic inflammation
B/L ground glass opacities
Minimal Traction Bronchiectasis
Rare honey coombing

Good response 0 0 steroid

ACUTE INTERSTITIAL PNEUMONIA / HAMMAR RICH SYNDROME
PT: present 0 acute SOB + Hypoxemia + Diffuse infiltrate
Idiopathic ARDS
Rx: Supportive, High mortality

CRYPTOGENIC ORGANISING PNEUMONIA / BRONCHIOLITIS
OBLITERANS ORGANISING PNEUMONIA (BOOP)
0 Pneumonia like illness
0 Proliferation of granulation tissue in airway =>
MAISON BODIES
2) Presence of Intestinal infiltrate.

CXR: Bilateral Peripheral Consolidation.

Rx: STEROID.

SMOKING AND ILDs

Resp. Bronchiolitis Associated ILD
Desquamative Intertitial Pneumonia
Adult Pulmonary Langerhans cell histiocytosis
Acute eosinophilic pneumonia
Pulmonary hemorrhage syndromes
Idiopathic pulmonary fibrosis

ILDs less prevalent in smokers:

1) Sarcoidosis
2) Hypersensitivity pneumonitis

SARCOIDOSIS

Multisystem disorder characterized by non-caseating granuloma.

Etiology:
1) Autoimmune
2) Propionibacterium
3) Mycobacterium
4) Unknown.
5) Genetic susceptibility - HLA DRB1*1101

H/c ↔ Pul. Involvement.
Scadding Staging I - Hilar adenopathy

II - LN ↑ + Lung infiltrates

III - Lung infiltrates alone

III - Fibrosis

Upper zone predominant Disease

PHENOTYPES

LUPUS PERINIO-
Cutaneous involvement → Bridge of nose area beneath eyes + cheeks

LOFGREN SYNDROME-
ERYTHEMA NODOSUM, Hilar LN ↑
UVEITIS (MC - Anterior), Arthritis

UVEO-PAROTID FEVER
Uveitis + Parotiditis + Fever + CN 7th Palsy

Release ACE + 1,25(OH)2 VITD

Hypercalcemia

Blood: Peripheral lymphopenia - Sequestration of lymphocyte into lung

Bronchoscopy:
BAL - Lymphocytes

Biopsy - non-caseating granuloma

TOC → Incompatible clinical scenario → Biopsy of involved organ showing non-caseating granuloma is 5/0 sarcoidosis
57 CT chest → Lung infiltrates
LN ↑.

In TB LN → Caseating → Central hypodensity + peripheral rim enhancement

Sarcoidosis → uniform density

67 Gallium Scan

↑ uptake by Parotid, Lacrimal gland, → ↑ uptake by mediastinal LN

"PANDA SIGN"

"LAMBA SIGN"

Rx Steroid + Immunosuppresson.

†. LEVELS OF ACE

1. Sarcoidosis
2. Leprosy
3. Gaucher's Disease
4. Hyperthyroidism
5. Disseminated granulomatous infections such as
6. Pulmonary TB

Pneumonia [Sarc Le Ga DM Hyper- thyrotoxic]
CONNECTIVE TISSUE DISORDER

RA
- H/c pulmonary manifestation
- Pleuritis
- Low glucose Pleural Effusion
- ILD → NSIP, B’xix
- Rheumatoid Arthritis Nodule
- Scleroderma Nodule
- Kaplan’s Syndrome
- DPL → NSIP, B’xix
- Pneumocytis
- [Silica expo, coal expo]

SLE
- H/c pul. manifestation = Pleuritis
- Acute lupus pneumonitis
- Pulmonary capillaritis
- Pulmonary alveolar H’ge
- ILD → NSIP
- Shrinking Lung Syndrome
- Diaphragmatic involvement in SLE

SCLERODERMA
- Diffuse bound chest
- ILD NSIP → UIP, Pul. HTN
- H’ge of death in scleroderma → Pulmonary Cause

POLYMYOSITIS
- ↑ Anti Jo1 Abs
- Anti Synthetase Sx
- C/F → Fever
  1) Myositis
  2) ILD
  3) Arthritis
  4) Mechanic Hands
DIFFUSE ALVEOLAR HEPATOID PUL HEMOSIDEROSIS

IDIOPATHIC PUL HEMOSIDEROSIS
1) Intra alveolar bleed
2) Fe accumulation as hemosiderin in alveolar macrophages
3) Fe deficiency anaemia

PUL. RENAL SYNDROME
1) SLE
2) Good Patau Syndrome
3) Small vessel vasculitis
   
   WEGENER'S GRANULOMATOSIS
   
   1) Necrotising granulomatous vasculitis
   
   2) RPUN
   
   3) Necrotising involvement of
      
      URT → Epithaxis Sinusitis
      LRT → Cavities, Diff. Alveolitis

OCCUPATIONAL LUNG DISEASES

SILICOSIS
HC occupational lung disease worldwide

<2.5μ = Dangerous particle

ASBESTOSIS
occupation: ship building, construction workers

Particles ~ curly serpentinite

> straight amphibole (cancerogenic)

FEATURES
1) Pleural Plaques
   Most specific for asbestososis
2) Fibrosis
   - duration of exposure

SILICOSIS
sand blasting, quarrying

CRISTALLINE SILICA

AMORPHOUS SILICA

1) Silicotic Nodules

COAL WORKERS
PNEUMOCONIOSIS
Coal miners

Anthracite Bituminous

> Anthracosis

1) Anthracite

2) Bituminous

1) Anthracosis

2) Merging of nodules with macrophages

3) Progressive massive fibrosis

4) COPD
3) Silico-TB: - Chronic exposure
4) Alveolar proteinosis - acute exposure
5) Malignancy.

Lung Cancer
Smoking + Asbestos
⇒ Synergistic

Most specific
⇒ Mesothelioma

Lower zone Disease

Round Atelectasis

Organised Pleii around segment

Localised atelectasis
Comet tail appearance

Upper zone Disease

SLEEP APNOEA

Apnoea: Cessation of airflow for at least 10 sec.
Hypopnoea: > 30% reduction in airflow associated with > 3% fall in SpO2.
SLEEP APNOEA

CENTRAL
Resp. effort Θ
Apnoea Θ
Resp. drive Θ

Obstructive
Apnoea Θ
Persisting Resp. effort
1) collapsibility of airway
   at neck.

eg. CHF
Narcotic Abuse

RF

RIF for obstructive Sleep Apnoea:
1) Obesity
2) O2
3) Craniofacial Abnormalities
4) Hypothyroidism
5) Alcoholism

PATHOPHYSIOLOGY:
Hic Symptom → Snoring.

APNOEA → HYPOXEMIA → Pul. HTN, COT
            Pulmonale

↑ Daytime loss of quality
Sleepiness of sleep
Loss of interest
Depression, Personality
change, Uncontrolled
RTA
Poor glycemic control

↓ Alarm

↑ Catecholamine surge
CAD, MI,
Arrhythmia,
Sudden Cardiac death,
CVA
Gold Std Δ: - Polysomnography

- EEG
- EOG
- ECG
- EMG
- SpO2
- Oxymenal flow
- Snore mic
- Yorax, Abd. movement sensor
- Body position / limb movement

Other scales for assessment:
1. Epiworth Sleepiness Scale
2. STOP Bang Questionnaire

Severity of OSA ⇒ Apnoea Hypopnea Index (AHI)

No. of Apnoea + Hypopnoea

Hour

< 5/hr ⇒ B
5-14/hr ⇒ Mild OSA → Behavioural Rx
15-29/hr ⇒ Mod. OSA → Medical Rx of choice
> 30/hr ⇒ Severe OSA → CPAP – mild OSA +
Commercial

In few cases → Uvulo-palatopharyngosplasty.
MALIGNANCY

1° LUNG MALIGNANCY -

Non-Small Cell Lung Cancer (NSCLC)

Small cell lung cancer (SCLC)

1) Small cell ca /

Oat cell tumour.

2) Adeno Ca H/c worldwide

3) Sq. cell Carcinoma H/c in India

3) Large cell "

LOCATION & ASSOCIATION OF TUMOURS -

1) Central Location
   Cigarette smoking

   => Sq. cell

   Small cell (Strongest association)

   Endobronchial location.

2) Peripheral Location
   Less m/c smoking

   Adeno Ca (q, young q, less smoker)

   Large cell

3) Cavitation

   Squamous

   Large.
**ADENO**
- Oncogene: KRAS/EGFR/ALK
- Biopsy: Glandular differentiation
- Features: Lepidic pattern
- Lung: Lung metastasis
  - Scar Ca → Adeno Ca
  - (H/c Ca in asbestosis)
- Clubbing → Hypertrophic osteoarthropathy
- Paraneoplastic → Hematologic

**SQUAMOUS**
- FGFR, P13K
- Keratinisation → intercellular keratin bridges
- Central cavity
- Calciemia
  - Pneumonia → Life threatening
- Parathormone related peptide

**SMALL CELL**
- MYC, BCL2
- Small round cell → hyperchromatic nuclei
- Chemoradio sensitive
- Rapid recurrence
- Metastasis
- SVC obstructions
- Poor prognosis
- Clubbing is rare
- Paraneoplastic syndromes

---

**Paraneoplastic associated with SCLC**

1. Hyponatremia - SIADH
2. Hypokalemia - Ectopic ACTH
3. Hypocalcemia - Calcitonin
4. Lambert Eaton Syndrome

**Clinical Manifestations of SCLC**

- Irritation → Cough (H/c Symptom)
- Hemoptysis → Tumour infiltrate, venel
- Size & cause → Bronchial obstruction (Fever, SOB)
- Pleural involvement → Pleuritis
  - Chest pain, Pleural effusion → SOB
57 Skin & Intercostal n/vs. → chest pain
67 Pericarditis / Pericardial effusion.
7) Esophagus → dysphagia
8) Recurrent Laryngeal n/v → Hoarseness of voice
9) SVC obstruction.
10) Stellate Ganglion → HORNER's Syndrome
    (sympathetic ganglion)

Migratory thrombophlebitis
= Thrombophlebitis
+ clubbing = Adeno ca

Anhydrosis
Miosis
Ptosis
Loss of ciliospinal reflex
Enophthalmos

11) Distant Metastasis
    . H/c Site → Brain
    . Host Specific → Adrenal

INVESTIGATIONS ?

17 CYTOLOGY
    → Sputum
    → Pleural fluid

malignant cells

27 CXR - PA - Solitary Pulm. Nodule
    Collapse
    LN ↑
    Pleural Eff

37 CT - Chest - Precise Anatomical Location.

4) Cold Std → BIOPSY < CT guided
    Bronchoscopy

http://mbbshelp.com
WhatsApp: +1 (402) 235-1397
PET SCAN - Staging
Bone Scan

Rx

NSCLC

SCLC

Resectable

Unresectable

Stage I, II, IIIa

IIIb, IV

Surgery

Medical Rx

Chemo Rx + Radio Rx.

Cisplatin + etoposide

Medical Rx

Squamous

Adeno

Cisplatin +

Targeted Rx

+ Gemcitabine/Paclitaxel

Pembrexed

EGFR Antagonist -
Erlotinib, Gefitinib

ALK Antagonist -
Crizotinib

Adeno Cal / n / non-smoker / Asian ⇒ EGFR mutation.

Pancoast Tx - usually occur in Sq cell

Located at apex

May involve stellate ganglion.

PANCOAST SYNDROME = 1) Tumour in Lung Apex

2) Involve → 1st 2 ribs

↓ Stellate ganglion

C8 T1 T2 ⇒ pain-weakness in Ulnar distribution
TUBERCULOSIS

Tabes NOMENCLATURE

Tabes Pulmonale - Pul. TB (H/L)
Tabes mesentrica - Abd. TB
Carrie Sicca - Shoulder TB
Potts Disease - Spinal TB
Spina ventosa - TB Dactylitis
Scoliose - LN TB (H/c Extrapulmonary)
Lupus vulgaris - Skin TB
Poncet Disease - TB Rheumatism

ORGANISM & LAB DIAGNOSIS

1) Direct Microscopy → ZN staining / LED FM
Under ZN staining to visualize each ml of sputum should contain 10,000 bacilli

2) Solid culture → LJ media 6-8 week.

3) Liquid → BACTEC
   HAIN
   Sept. check

4) Rapid Molecular Method
   q) CBNAAT -/ Liene expert → TB Bacilli + Ref. Sensitivity 2 hours

   b) Line probe assay / LPA - TB Bacilli + Drug Sensitivity (1st line, 2nd line drug) = 48-72 hour
Most Rapid method to identify of TB → Direct microscopy

Most Rapid method for rifampicin sensitivity = Gene expert

PRESumptive TB

Any one of the following:
- Cough > 2 wks
- Fever > 2 weeks
- Hemoptysis
- wt. loss

Abnormalities on CXR-PA view

ALGORITHM FOR Δ of TB

Pt. is HIV → PRESumptive TB

Pt. Sputum → CXR-PA

Sputum +ve
- CXR ±
  - Start ATT

Sputum -ve
- CXR +TB
  - C-BNAAT

IGRA/Quantiferon Gold

Advantages:
1. TB specific Ag → CFP, ESAT used
2. Less cross-reactivity to BCG, Non-Tubercular mycobacterium
3. Blood Test
4. Serial Testing can be done out boosting phenomena
5. Single visit to hospital

http://mbbshelp.com
WhatsApp: +1 (402) 235-1397
Disadvantage
- Can't differentiate infection vs. active disease

**Pathology**

1° TB → unsensitised individual

2° TB or Post 1° TB → sensitised individual → Reinfection
  → Reactivation

1° TB
- TB bacilli → mid + lower zone
- Area of 1st contact
  - 1° focus / Ghon's focus
- Alveolar macrophage engulf TB bacilli
  - Phagolysosome fusion
  - Survival of M.tub

- For immunity macrophages reach hilux LN → LN ↑
  Ghon's complex → Ghon's focus + LN↑.

In LN ↑
- T helper response
  - ↑ IFN-γ, TNFα
  - ↑ Killing capacity of macrophage
  - Limit TB
  - Memory cells are formed
2° TB

- TB bacilli reach apex & actively grow
- Body's immune response will try to wall off infection.
- After few weeks, Delayed Type MHC Response TB produced & destroys TB bacilli & lung parenchyma
- 2°TB is more infectious & it is active disease.
- Calcified Ghon's Complex → Reinke's Complex.

TB/HIV

- If ART is started 1st → Risk of immune reconstitution. Inflammatory syndrome (IRIS)

Start ATT 1st & merge ART 3 in 2 weeks to 2 months.

ATT = Always The Treatment

* If pt. is on TLE regimen. → Rifampicin can be given
  If pt. is on Neviparone / Protease Inhibitor
  Rifampicin can't be given
  Rifabutin is given.

DISSET
### Disseminated TB

<table>
<thead>
<tr>
<th>Classical Military TB</th>
<th>Cryptic Military TB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1st/2nd form</strong></td>
<td>Elderly, chronic symptom</td>
</tr>
<tr>
<td>Hematogenous/Lymphogenous spread</td>
<td>Fever, weight loss, anaemia</td>
</tr>
<tr>
<td>Pathognomonic (\rightarrow) choroidal Tubercles</td>
<td><strong>CXR</strong> (\rightarrow)</td>
</tr>
<tr>
<td>Sputum (\rightarrow) -ve</td>
<td>Sputum (\rightarrow) -ve</td>
</tr>
<tr>
<td><strong>CXR</strong> (\rightarrow) 1-2mm, Bil Symmetric Homogeneous, millet shaped shadowing</td>
<td>Pt. collapses (\rightarrow) death, autopsy reveals meningeal tubercles. This is also military TB, but hidden on CXR.</td>
</tr>
</tbody>
</table>

### Non-Reactive (54) Areactive TB

Rate form

Acute septicaemic form

Underlying hematological abnormality

Fatal form

Autopsy shows areas of necrosis \(\rightarrow\) cut granuloma formation

**Rx**

**New Case** = 2HRZE + 4HRE = 6 months = DAILY

**Previously Rx** = 2HRZES + 1HRZE + 5HRE = 8 months = DAILY

HDRTB = Resistance to both H & R = DAILY

- 6-9 months \(\rightarrow\) E + Z + Kanamycin + Levofox + Cycloserine + Ethionamide

- 18 months \(\rightarrow\) E + Levofox + Cycloserine + Ethionamide
XDR-TB: MDR-TB + Resistance to 2nd line aminoglycosidel + Resistance to 1 FQ

6-12 months: Capreomycin + Moxi + PAS + Clofazamine + High dose INH + Amoxiclav + Linezolid

18 months: Moxi + PAS + Clofazamine + High Dose INH + Amoxiclav + Linezolid

(24-30 months)

NEWER Anti-TB Drugs

**BEDAQUILINE/SITUXIDE**

2012

Diaryl quinolone

**MOA**: ATP synthase inhibition

**S/E**: QT Prolongation

DR TB

Conditional access in India

**Dose**: 400mg
**duration**: 24 weeks

**DElamANID**

2014

Nitroimidazole

**MOA**: Mycolic acid synthase inhibitor

**S/E**: QT Prolongation

DR TB

Soon available in India
ACID, BASE, BALANCE & ABG

I) NORMAL VALUES

\[ \text{pH} \quad 7.35 - 7.45 \quad \text{pH} \leq 7.35 \Rightarrow \text{Acidosis} \]
\[ \text{Paco}_2 \quad 35 - 40 \text{mmHg} \quad \text{pH} \geq 7.45 \Rightarrow \text{Alkalosis} \]
\[ \text{HCO}_3^- \quad 22 - 26 \text{meq} \]
\[ \text{Pao}_2 \quad 70 - 100 \text{mmHg} \]
\[ \text{HCO}_3^- = 26. \]

II) Relation Between pH, Paco₂, HCO₃⁻

- Henderson Hasselbach Equation

\[ \text{pH} = 6.1 + \log \left( \frac{[\text{HCO}_3^-]}{\text{Paco}_2 \times 0.03} \right) \Rightarrow \text{pH} \propto \frac{\text{HCO}_3^-}{\text{Paco}_2} \]

\[ \downarrow \text{pH} \uparrow \propto \frac{\text{HCO}_3^- \uparrow}{\text{Paco}_2 \uparrow} \Rightarrow \text{BASE} \]

\[ \frac{\text{Paco}_2 \downarrow}{\text{BASE} \downarrow} \Rightarrow \text{ACID} \]

III) REGULATION OF pH, Paco₂, HCO₃⁻

- Lungs: T ↓ CO₂ ⇒ Resp. process
- Kidneys: T ↑ HCO₃⁻ ⇒ Met. process

SIMPLE ACID BASE DISORDER

1° process + Adequate compensatory response

Respiratory Acidosis
\[ \text{pH} \downarrow \quad \text{Paco}_2 \uparrow \quad \text{HCO}_3^- \uparrow \]

Respiratory Alkalosis
\[ \text{pH} \uparrow \quad \text{Paco}_2 \downarrow \quad \text{HCO}_3^- \downarrow \]

Metabolic Acidosis
\[ \text{pH} \downarrow \quad \text{Paco}_2 \downarrow \quad \text{HCO}_3^+ \]

Metabolic Alkalosis
\[ \text{pH} \uparrow \quad \text{Paco}_2 \uparrow \quad \text{HCO}_3^- \]
In simple acid base disorder, always 1° change & compensation move together.

In 1° Resp. process \( \rightarrow \) change in pH w.r.t. Paco₂ \( \neq \) HCO₃⁻ in opposite direction.

In 1° met. process - change in pH with Paco₂ \( \neq \) HCO₃⁻ in same direction.

\[
\text{ROME}
\]

Resp. opp. met. same direction.

Q. pH: 7.33, Paco₂ 60, HCO₃⁻ 34

\[\text{↓ \hspace{1cm} ↑ \hspace{1cm} ↑} \rightarrow \text{Resp. Acidosis}\]

\[\text{酸} \hspace{1cm} \text{碱} \]

Q. pH: 7.48, Paco₂ 26, HCO₃⁻ 16

\[\text{↑ \hspace{1cm} ↓ \hspace{1cm} ↓} \rightarrow \text{Resp. Alkalosis}\]

\[\text{碱} \hspace{1cm} \text{碱} \]

Q. pH: 7.27, Paco₂ 25, HCO₃⁻ 10

\[\uparrow \downarrow \downarrow \rightarrow \text{Met. Acidosis}\]

Q. pH: 7.55, Paco₂ 50, HCO₃⁻ 40

\[\uparrow \uparrow \rightarrow \text{Met. Alkalosis}\]
COMPENSATION

Resp. Acidosis

Acute: For every 10 mmHg ↑ \( P_{\text{aco}_2} \), \( HCO_3^- \) ↑ by 1 meq.

Chronic: For every 10 mmHg ↑ \( P_{\text{aco}_2} \), \( HCO_3^- \) ↑ by 4 meq.

Resp. Alkalosis

Acute: For every 10 mmHg ↓ \( P_{\text{aco}_2} \), \( HCO_3^- \) ↓ by 2 meq.

Chronic: For every 10 mmHg ↓ \( P_{\text{aco}_2} \), \( HCO_3^- \) ↓ by 4 meq.

Q: Acidosis due to ingestion (pH = 7.32), \( P_{\text{aco}_2} \) = 70, \( HCO_3^- \) = 29.

Acidosis:

\[ 40 \to 70 \]

Resp. acidosis & compensatory met. alkalosis.

Q: Ch. neuromuscular disorder (pH = 7.34), \( P_{\text{aco}_2} \) = 60, \( HCO_3^- \) = 34.

Ch. Resp. acidosis:

\[ 40 \to 60 \]

Ch. compensated Resp. Acidosis.
Metabolic Acidosis
Acute expected $P_{aCO_2} = (1.5 \times HCO_3^-) + 8 \pm 2$. [Winter's formula]

Q. pH = 7.27, $HCO_3^- = 10$, $P_{aCO_2} =$?

$$(1.5 \times 10) \pm 8 \pm 2$$
$$15 \pm 8 \pm 2$$
$$21 - 25 = \text{compensated}$$

Q. pH = 7.26, $P_{aCO_2} = 18$, $HCO_3^- = 6$?

$$(1.5 \times 6) + 8 \pm 2$$
$$9 \pm 2$$
$$a + b \pm 2 = 17 \pm 2 = 15 - 19$$

Met. acidosis + compensatory alkalosis

Metabolic Alkalosis
Expected $P_{aCO_2} = [HCO_3^- + 15]$

\[ \begin{align*}
\text{pH} \quad & \quad \text{Acidosis} \quad \Downarrow \quad \text{Alkalosis} \\
& \quad \text{1st process} \quad \text{Heup} \quad \text{metabolic} \\
& \quad \text{Compensation} \quad \text{Calculate metabolic compensation} \quad \text{Calculate Heup compensation} \\
& \quad \text{Given value} = \text{Expected value} \quad \text{Given value} = \text{Expected Heup} \\
& \quad \text{Simple ABD} \quad \text{Mixed process} \quad \text{Simple ABD} \quad \text{Mixed process}
\end{align*} \]
METABOLIC ACIDOSIS & CONCEPT OF ANION GAP

\[
\text{(Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-) = \text{Anion Gap.}
\]

\[
\text{(Na}^+ + \text{K}^+) + \text{unmeasured} = (\text{Cl}^- + \text{HCO}_3^-) + \text{unmeasured anions}
\]

\[
\text{(Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-) = \text{unmeasured anions}
\]

\[
- \text{unmeasured cations}
\]

\[
[\text{Anion Gap}] = \text{unmeasured anions} - \text{unmeasured cations}
\]

Common value of 

in Anion Gap = 1 in unmeasured anions

New Formula for Anion Gap

\[
(\text{Na}^+) - (\text{Cl}^- + \text{HCO}_3^-) = \text{AG}
\]

8-12 mEq.

HIGH AG METABOLIC ACIDOSIS

unmeasured compartment

Addition of Acid

\[
\text{H}^+ + \text{Acid} \rightarrow
\]

Consumed for compensation

\[
\text{H}^+ + \text{Acid} \rightarrow
\]

\[
\text{H}^+ + \text{Acid} \rightarrow
\]
In pure High AG Metabolic Acidosis

Rise in AG = Fall in HCO₃⁻

AG - 10 = 25 - Given carbonate.

Δ AG = Δ HCO₃⁻

CAUSES:

I) Toxins / Drugs -
1) Methanol
2) Formaldehyde
3) Ethylene glycol / antifreeze
4) Oxalic acid
5) Salicylate

II) Ketosis / Acidosis - D DKA
1) Alcoholic Ketosis
2) Starvation

III) Renal Failure

IV) Lactic Acidosis
a) Type A Lactic Acidosis → [Hypoxemia] [↓ perfusion]
   - e.g. shock
   - Anaemia
   - CO poisoning
b) Type B Lactic Acidosis → [Perfusion ↓]
   - e.g. Renal failure
   - Hepatic failure
   - Drug - metformin
   - Zidovudine
AG METABOLIC ACIDOSIS

\[ \text{Loss of } \text{HCO}_3^- \]

Hyperchloric Acidic Metabolic Acidosis

**RENIN - ANGIOTENSIN - ALDOSTERONE SYSTEM IN ACID-BASE**

\[ \text{Urine: } \text{Body} \]

\[ \begin{align*} 
\text{Na}^+ & \rightarrow \text{Na}^+ \\
\text{Na}^+ & \rightarrow \text{Na}^+ \\
\text{Na}^+ & \rightarrow \text{K}^+ \\
\text{K}^+ & \rightarrow \text{K}^+ \\
\text{H}^+ & \rightarrow \text{H}^+ \\
\end{align*} \]

Hyponatremia

Hyperaldosteronism

↑ RAAS

Hypokalemia

Met. alkalosis

Hyperaldosteronism

Hyperkalemia + Met. acidosis

**CAUSES**

1. CRIT CAUSE

1) Diarrhea

2) Pancreatic fistula

3) Ureterosigmoidostomy

4) Enterocutaneous fistula

**II RENAL CAUSE**

1) RTA

2) Drugs

3) Carbonic Anhydrase Inhibitors

4) ACEI

5) ARB

6) Aldosterone antagonist
**RTA**

Type I RTA  
**Type II RTA**  
**Type IV RTA**

Met. acidosis + hypokalemia

**Causes**

- Hyporenemic state
- Aldosterone resistance
- "deficiency"
- Hyporenemic state
- Diabetic nephropathy
- Chronic tubulo-interstitial

**Type I RTA**

- Distal RTA
- H⁺ excretion lost at collecting duct

\[
\begin{align*}
Na^+ &\rightarrow Body \\
K^+ &\leftarrow Body \\
H^+ &\rightarrow Met. acidosis
\end{align*}
\]

Hypokalemia

**Type II RTA**

Proximal RTA

\[
\begin{align*}
\text{HCO}_3^- \text{ reabsorption lost in PCT} \\
\text{Bicarbonaturia can} \\
\text{induce kaliuresis} \\
\text{Met. acidosis +} \\
\text{Hypokalemia}
\end{align*}
\]
Urine anion gap

To differentiate anion gap Met. acidosis of diarrhea vs.

RTA

\[ \text{UAG} = (\text{Na}^+ + \text{K}^+) - \text{Cl}^- \]

\[ \text{N value} = 0.5 \]

\[ \text{---} \quad + + + \quad \text{---} \]

\[ \begin{array}{c}
\text{taking 0 as reference level} \\
\end{array} \]

Renal Handling of Acid

\begin{align*}
\text{Urine} & \\
\text{Body} & \\
\end{align*}

\[ \begin{array}{c}
\text{OH}^+ \\
500 \text{H}^+ \\
\text{NH}_3^- \\
500 \text{NH}_4^+ \\
500 \text{SO}_4^2- \\
\text{H}^+ \text{O} \\
250 \text{H}^+ \\
0 \text{H}^+ \\
125 \text{H}^+ \\
250 \text{H}^+ \\
\end{array} \]

\[ \begin{array}{c}
\text{NH}_4^+ \\
\text{Na}^+ \\
\text{K}^+ \\
\text{Cl}^- \\
\end{array} \]

\[ \text{RTA} = \text{UAG} + \text{ve.} \]

Diarrhea: Met. acidosis.

10,000 H+

Urinary NH$_4^+$ is increased.

RTA:+

UAG is indirect measure of urinary NH$_4^+$ excretion.

UAG is negative in G1T cause diarrhea.
**Metabolic Alkalosis**

**Initiating Event**
- ECFV contraction, hypotension
- 1st mineralocorticoid excess
- (3) initiating + persisting event
- Saline responsive/U^+^ response
  - U^cl^- < 20 meq

1) Vomiting
2) Ryle's Tube aspiration
3) Diuretic use
4) Post hypercapnic Met. Alkalosis

**Persisting Event**
- 2nd Hyperaldosteronism
- ECFV expansion & HTN
- Saline unresponsive/U^+^ unresponsive
  - U^cl^- > 20 meq

1) 1st Hyperaldsteronism
2) Cushing's Syndrome
3) Renin Seclreting Tumour
4) Renal artery stenosis
5) Liddle's Syndrome
6) Bartter Syndrome
7) Gitelman Syndrome

**Respiratory Acidosis**

Type 2 Resp. Failure

**Respiratory Alkalosis**

Chronic Resp. Alkalosis:
- M/acid base Ab in critically ill pt
  1) Pain, Panic, Psychogenic, Progestrone
  2) Hyperventilation

2) Aspirin
   a) Vomiting → met. acidosis alkalosis
3) High AG metabolic acidosis.
   → When aspirin goes to blood

37 Theophylline

47 Fever, sepsis (change in sensitivity of Resp. centre)
5) CHF → Pul. oedema → Stimulate of chemoreceptors
6) Cirrhosis of Liver → ↑ Glutamate
7) Severe Hypotension Hypoxemia → Hyperventilation

87 ↑ ICP
    ICU pts are also prone to Resp. alkalosis due to
    pain, panic, psychogenic

Q. \[ \text{pH} = 7.32, \quad \text{Paco}_2 = 60, \quad \text{HCO}_3^- : 32 \]
   \[ \downarrow \quad \uparrow \quad \uparrow \]
   \[ 90 \rightarrow 60 \quad 26 ightarrow 34 \]
   \[ \text{CHF, compensated} \quad \text{Resp. Acidosis} \]

Q. \[ \text{pH} = 7.35, \quad \text{Paco}_2 = 60 \quad \text{HCO}_3^- = 40 \]
   \[ \downarrow \uparrow \]
   \[ \text{Increased value} \quad \text{Expected} \]
   \[ \text{CHF, Resp. acidosis + Add. metabolic alkalosis} \]

Q. \[ \text{pH} = 7.28, \quad \text{Paco}_2 = 60 \quad \text{HCO}_3^- = 26 \]
   \[ \downarrow \uparrow \]
   \[ \text{Given value < Expected} \quad \text{CHF, Resp. acidosis + Add. metabolic acidosis} \]
AG

High AG or Normal AG.

In pure High AGMA

\[ \Delta AG = \Delta HCO_3^- \]

Rue in AG = fall in HCO_3^-

\[ \text{[Given AG-10]} = [25 - \text{[Given HCO_3^-]}] \]

Q: Pt. is having DKA.

Pt. AG = 20 \hspace{1cm} HCO_3^- = 15

\[ \Delta AG = 20 - 10 \hspace{1cm} \Delta HCO_3^- = 25 - 15 \]

\[ 10 \hspace{1cm} 10 \]

\[ \Rightarrow \text{Pure HACi Met. Acidosis.} \]

Q: Pt. w. DKA

Pt. AG = 20 \hspace{1cm} HCO_3^- = 20

\[ \Delta AG = 10 \hspace{1cm} \Delta HCO_3^- = 25 - 20 = 5 \]

\[ \Delta AG < \Delta HCO_3^- \rightarrow \text{Additional metabolic acidosis} \]


Q: DKA

AG = 20 \hspace{1cm} HCO_3^- = 10

\[ \Delta AG = 20 - 10 \hspace{1cm} \Delta HCO_3^- = 25 - 10 \]

\[ = 10 \hspace{1cm} = 15 \]

\[ \Rightarrow \text{High AGMA + NAGi metabolic acidosis} \]
Compare $\Delta AG \cdot \Delta HCO_3^-$ relation

$\Delta AG = \Delta HCO_3^- \Rightarrow$ pure HAGMA

$\Delta AG > \Delta HCO_3^- \Rightarrow$ HAGMA + additional met. alkalosis

$\Delta AG < \Delta HCO_3^- \Rightarrow$ HAGMA + additional met. acidosis

$\text{pH} = 7.2 \quad \text{Paco}_2 = 60 \quad \text{HCO}_3^- = 19$

Decrease acidosis (mixed disturbance)
NEPHROLOGY
PHYSIOLOGY

Kidney performs diverse functions:

1. Excretory: urine formation
2. Homeostasis: water & acid base balance
3. Hormonal: erythropoietin synthesis, Vit D activation.

4. RENAL BLOOD FLOW

Kidneys are highly vascular.

Received 25% of cardiac output.

Even in presence of adverse conditions to the renal blood flow.

1. Dehydration
2. Hypotension
3. Renal artery stenosis

↓

Auto-regulatory mechanisms activated.

↓

Maintain adequate GFR.

↑ Glomerular capillary pressure
Afferent arteriole

\[ \text{Myogenic Reflex} \rightarrow \text{Tubulo-glomerular feedback} \rightarrow \text{Angiotensin mediated} \rightarrow \text{Vasoconstriction of efferent arteriole} \]

\[ \uparrow \text{Pressure in capillary network} \rightarrow \uparrow \text{GFR.} \]

\[ \text{NO} \rightarrow \text{Vasodilation of afferent arteriole} \]

\[ \times \text{ACEI or ARB} \]

\[ \times \text{NSAIDS} \rightarrow \text{Cyclophosphamide} \]

Can disrupt autoregulation. If used in the presence of adverse conditions, these can precipitate hypoperfusion. \[ \downarrow \text{Pre-Renal AKI} \]

**RENAL ARTERY STENOSIS**

- **Cause**
  1. 90% - atherosclerotic arteriosclerosis
  2. 10% - FMD (fibromuscular dysplasia)

**Pathophysiology**

- Activate RAAS
Vasoconstriction

\[ \text{MLC (GFR) } \rightarrow \text{Sy. HTN} \]

[MLC cause - 2° HTN - Renovascular]

**ESG GUIDELINES** - Evaluation & Management

**When to suspect/screen for R.A.S.?**

1. Young HTN (onset < 50 yrs of age)
2. Severe HTN < 55 yrs of age ( > 160/110 mmHg)
3. HTN emergencies (sudden BP rise target organ damage)
4. Refractory HTN (uncontrolled > 3, I is a diuretic)
5. Decline in GFR > 10% after ACEI therapy (Disrupt autoregulation)
6. Asymmetrical Kidneys on USG (Diff. > 1.5cm)
7. Unexplained Renal failure

**Screening Tests**

<table>
<thead>
<tr>
<th>Specific</th>
<th>1. Conventional Renal Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality</td>
<td>GRADING</td>
</tr>
<tr>
<td>% of Stenosis</td>
<td>Severity &amp; Rx</td>
</tr>
<tr>
<td>&lt; 50%</td>
<td>No further testing</td>
</tr>
<tr>
<td>50-70%</td>
<td>Follow-up</td>
</tr>
<tr>
<td>&gt; 70%</td>
<td>Always hemodynamically significant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conventional Renal Angiography</th>
<th>Specific</th>
</tr>
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<tbody>
<tr>
<td>% of Stenosis</td>
<td>Severity &amp; Rx</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Functional assessment of Kidney</th>
<th>Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR ≤ 60 ml/min</td>
<td>No further testing</td>
</tr>
<tr>
<td>GFR ≤ 30 ml/min</td>
<td>Follow-up</td>
</tr>
</tbody>
</table>

1. Duplex Doppler (Best)
   > 98% sensitivity
   - Non-invasive, easy available

2. CT-Renal Angiography
   C/I - GFR ≤ 60 ml/min

3. MR-Renal angiography
   C/I - GFR ≤ 30 ml/min

4. DTPA Scan (Radio-isotope)
Rx 1st line → Medical
  U/L
ACEI
(only drug &
protects < kidney)

MOA of ACEI in U/L RAS.

AXIOMATIC N capillary
pressure
↓
\begin{align*}
\text{Renin} & \rightarrow \text{angiotensin} & \rightarrow \text{eff. autoreg.} \\
\text{ACEI} & \rightarrow \text{vasoconstrictor} & \rightarrow \text{Capillary HTN} \\
& \downarrow
\end{align*}

Predispose: glomerulosclerosis
(B) endothelial injury/GBM injury

Prognosis –
Favourable

URINE FORMATION

1st step → Ultrafiltration → Glomerulus
Intra-GBM ← Mesangium → outside GBM (extra-GBM)

- Podocytes (foot processes of GBM)
  -ve electrostatic charge
  - Repel Anions

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All Blood Components
- RBCs, WBCs, platelets

All plasma proteins (except albumin = 4.6 nm)

Glomerulonephritis
Predominantly affect GBM except minimal change disease
(only podocyte affected)

17 Dysmorphic Haematuria
(MF)

27 RBC cast - most specific

37 Non-selective proteinuria

47 Glomerular range proteinuria
(\geq 2.9 g/day /1.73 m²)

No Hematuria

Selective proteinuria (albuminuria)

Dyslipidaemia

Hypercoagulable state

Tubules
Reabsorption + secretion (concentrating ability)

Mechanisms: Tubular transport

A) Cellular transport (across the cell)

1) Active → ATPase pumps.

2) Passive → exchange/co-transporter

B) Paracellular
   (in bet' cells of tubule)

PCT
Leaky epithelia
Allow bulk transport

DCT
Tight junctions
Highly regulated

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**URINE**

- H⁺ secretion (most potent)

**Role: Water Balance**

- PCT
  - Max. H₂O reabsorption (≈70%)  

- ADH (Vasopressin)
  - V₂ receptors
  - Aquaporin channels
  - Facilitates H₂O reabsorption
  - Restores plasma volume

**Body**

- CHA. Acidemia
- Mild Hypokalemia
- Mild Hypomagnesemia
- Hypercalcemia
- Hyperuricemia
  - (Unknown mech.)

**ROLE: WATER BALANCE**

- Det & CD → always hypo-osmolar

**FINAL UOSM**

- (Based on fluid status)

**If Dehydrated**

- Aldosterone
  - Mineralocorticoid
  - Upregulates eNa⁺ channels
  - Na⁺ reabsorption
  - Sequesters H₂O
  - H⁺, K⁺, exchange
HYPOKALEMIC ALKALOSIS
Due to aldosterone excess state

Causes:
1. Endocrine
2. Chronic Drug Use
   - Loop Diuretics
   - Thiazides
   - Steroids
3. Inherited Channelopathies

INHERITED CHANNELOPATHIES

- Gitelman's Syndrome
  - AR inhibitory Na⁺Cl⁻ cotransport (Thiazide)

- Liddle's Syndrome
  - AD-stimulatory eNa⁺C
  - Pseudo-hyperaldosteronism
  - Steroid-mimic TH2

- Bartter's Syndrome
  - AR inhibitory
  - Na⁺K⁺2Cl⁻ ATPase Pump

<table>
<thead>
<tr>
<th>Bouteau's Syndrome (6 genetic mut*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Fluid → I.V.L. → Adolescence</td>
</tr>
<tr>
<td>2) Patho : Na⁺ - K⁺ -2Cl⁻ pump</td>
</tr>
<tr>
<td>××× - severe</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>×××× H₂O reabsorp</td>
</tr>
<tr>
<td>3) Plasma Volume</td>
</tr>
<tr>
<td>4) B.P.</td>
</tr>
<tr>
<td>5) Renin, Angiotensin, Aldosterone</td>
</tr>
<tr>
<td>6) Associated Defects (Unknown mechanism)</td>
</tr>
<tr>
<td>7) G/F → Polyhydramnios</td>
</tr>
<tr>
<td>2) Failure to thrive</td>
</tr>
<tr>
<td>3) Hypotension (syncope)</td>
</tr>
<tr>
<td>4) Renal calculi</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Liddle's Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30 yrs</td>
</tr>
<tr>
<td>Na⁺ - Cl⁻ cotransport</td>
</tr>
<tr>
<td>× Mild</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>× H₂O reabsorp</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pseudohyperaldosteronism</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30 yrs</td>
</tr>
<tr>
<td>eNa⁺ c</td>
</tr>
<tr>
<td>⊕ Mild</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>⊕ H₂O reabsorp</td>
</tr>
<tr>
<td>↑</td>
</tr>
<tr>
<td>Pseudohyper</td>
</tr>
<tr>
<td>aldosteronism</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Associated Defects (Unknown mechanism)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30% - BSNHL (Deaf)</td>
</tr>
<tr>
<td>↓ Paracellular (Ca) transport defect</td>
</tr>
<tr>
<td>(Hypercalciuria)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Paracellular Mg²⁺ transport Defect</th>
</tr>
</thead>
</table>

| Muscle cramps                         |
| Paralytic ileus                       |
| Cardiac arrhythmias                   |

| Asymptomatic Detection - HTN in young |

| Low                                   |
| Metabolic alkalosis.                  |

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ROLE OF KIDNEY IN ACID BASE BALANCE

Human Body → "Pro-alkaline" Acidic State
Every living cell requires energy (ATP)
During ATP Production → Acid is generated.
\[ \text{pH} = 7.35 - 7.45 \text{ (slightly basic)} \]

Mechanisms → ABB → Regulate pH Efficiently

1) Buffering
At tissue level
\[ \text{HCO}_3^- \text{ (extra-cellular)} \rightarrow \text{CO}_2 \text{ (intra-cellular)} \]
\[ \text{[H}^+] + \text{[HCO}_3^-] \rightarrow \text{CO}_2 + \text{H}_2\text{O} \]

Backup mechanism

Resp Mechanism
Excrete acid in form of CO₂

Renal Mechanism
Most Potent
Acidification of Urine
Most Imp. Form of H⁺ Secretion in Urine → NH₄⁺ Ion.
Combine Cl⁻ → NH₄Cl
ACIDEMIA

$U_{i}^{c} \text{ or } U_{e}^{c}$ levels

$U_{i}^{c}$

Blood $pH$ (259

$U_{i}^{c}$

Highly acidic

$U_{e}^{c} \uparrow$

kidneys are

Deficit in acidification of urine

$U_{i}^{c}$ $> 5.5$, $U_{e}^{c}$ low in disease

H$_2$O$_3$ - exhaustion

PO$_4$ - required

Bone resorption

Rickets

Osteomalacia

H$_2$O$_3$ - depletion (also nutrient depletion)

Type 2 RTA

(proximal RTA)

H$_2$O$_3$ regeneration

Action - carbonic anhydrase

Type 3 RTA

(Marble Bone Disease)

<100 cases (worldwide)

Majority - cerebral calcification.

also - marble bone disease

(Osteopetrosis)

Not included in routine classification

RTA

$H^{+}$ secretion

$H^{+}$-K$^{+}$ ATPase

Aldosterone

$H^{+}$/K$^{+}$ secretion

in exchange of

$Na^{+}$, $H_{2}O$

Type 4 RTA

(Hyper acidosis)

Minor role

$H^{+}$-K$^{+}$ ATPase

Type 1

(Distal RTA)
RTA

Type I
- Epidemiology: <10 yr, M>F
- (Most severe)
- M/C: Inherited RTA

Type II
- Inherited
- M/C: Sjogren Syndrome
- SLE
- HTN (Mif Tiwai)
- Mixed connective tissue disorder

Type IV
- M/C: RTA

Causes
- Inherited
- FANCONI's syndrome
- Glycosuria
- Aminoaciduria
- Syndactyly

Association
- Acquired
- ACEI/ARB
- K⁺ sparing diuretics
- Thiazide

C/F
- Short stature, Rickets
- • Hypercalciuria: ↓ stone
- ↑ Renal calculi
- Nephrocalcinosis
- Hypomagnesemia: ↓ M/C cramps

Mild acidemia
- Asymptomatic
- VIt D₃/P₃₂ def. (20 to loss in urine)
- Osteomalacia

Mild acidemia
- Asymptomatic
- Rarely
- Hyper K⁺ complications

Metabolic Acidosis

Anion Gap

(\(U_{Na^+} + U_{K^+}\) - \(U_{Cl^-}\) [High/Positive]

\(U_{An}\)

Always > 5.5

\(U_{PH}\)

Always < 5.5
**S. K+**

**Rx**

- Oral HCO₃⁻ supps.
- Oral K⁺
- Citrate supps.
- ↓ Renal calculi
- Bone disease

Prognosis:

- Worst: Stop offending drug, offer urea
- Favourable: **BEST**

---

**ANEMIA**

Deficit in Erythropoietin Synthesis

**ANEMIA → Mechanism in Nephropathy**

- Anorexia → Uraemia → BM suppression
  - Nutritional Deficiency: ↓ Iron, B₁₂, folate
  - Gastritis → Occult GI blood loss

↓ Blc → Nutritional Deficiency: ↓ Iron, B₁₂, folate

EPO Deficiency

↓ Normocytic anaemia: MCV

Rx = Recombinant EPO therapy

Monitor ↑ Hb every 2 weeks

- > 0.8 g/dL: Success
- < 0.8 g/dL: Failure
- Non-compliance
- Inadequate Dosage

Rx = Recombinant EPO therapy

- Monitor ↑ Hb every 2 weeks
- > 0.8 g/dL: Success
- < 0.8 g/dL: Failure
- Non-compliance
- Inadequate Dosage
Vitamin D — final step of activation into \( \text{Vit D}_3 \) and its reabsorption occurs in \( \text{PCT} \). If defective, bone disorders in nephropathy only CKI - Minimum (≥ 6 months) disease.

**Renal Osteodystrophy**

- **Osteomalacia**
  - \( \text{Vit D}_3 \) deficiency
  - Oral vit \( \text{D}_3 \)

- **Osteitis Cystica Cartilaginosa**
  - Secondary Hyper PTH.
  - Hypocalcemia
  - Most imp. Hyper Phosphate
  - Sevelamer (binding Resin)
  - Oral \( \text{Ca}^{2+} \)

- **Adynamic Bone Disease**
  - Remodelling Defect of Bone
  - Poor at Bearing
  - Encourage mobility

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ASSESSMENT METHODS IN NEPHROLOGY

S. CREATININE LEVELS (Best screening Test)

C. PRODUCED
   endogenously @ constant rate
   By protein breakdown.

Excreted
   freely filtered at glomerulus
   barely secreted/absorbed @ tubules

S. creatinine = GFR

↓ GFR

Renal Dysfunction

↑ S. creatinine level

Early, sensitive marker

Limitations of Test
- nonspecific for Δ of nephropathy.
- may not correlate immediate outcome of the disease
  (limited prognostic value)

FALSE tve ↑ S. creatinine

↑ Production
   ar High Protein Diet
   by strenuous exercise
   (athlete)

Δ Infection (sepsis)
   Δ Inflammation (A.I.D.)
   Δ Neoplasms (some)

Alternative Test To S. creat

S. CYSTATIN-C LEVELS

Produced endogenously
   by all nucleated cells
   @ constant rate

Freely filtered @ glomerulus

Excretion = GFR
Adv - not related to Diet or Exercise

**Novel Markers of AKI**
- Specific for Asu of Nephropathy
- NGAL (Neutrophil Gelatinase Associated Lipocalcin)
- KIM-1 (Kidney Injury Molecule)
- IL-18

Tests in spot urine sample
Are secreted by tubules in response to injury
Hence detectable only in Renal causes of AKI (nephropathy)

**Tests - Detect:** Site/Cause/Severity

- **Urinalysis**
  - **Usg-KUB (Structure)**
  - **GFR Estimation (Functional Status)**

  - Proteinuria
  - Albuminuria
  - Hematuria
  - Pyuria
  - Cast/Sediment

**Proteinuria**

- **Def:** >150 mg/24 hours.
- Detected using Dipstick Method
  (Very sensitive)

- Non-specific for Asu of Nephropathy
- Valuable in K/C/O - Nephropathy = Identify SITE.
  (Based on quantity)

- <2 g/day (Tubular Range)
  - Tubular interstitial Disorders

- ≥ 2 g/d/1.73 m² (Glomerular Range Proteinuria)
  - <3.5 g/d
    - Nephritic Range
  - ≥ 3.5 g/d
    - Nephrotic Range
<table>
<thead>
<tr>
<th>Albuminuria</th>
<th>(More Specific Marker)</th>
<th>Quantitative Tests</th>
<th>Micro-alb</th>
<th>Gross-alb</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30 mg/24 hrs</td>
<td></td>
<td>24 hr urinary Alb estimation (most reliable/gold std)</td>
<td>30 - 300 mg of Alb/24 hrs</td>
<td>&gt;300 mg</td>
</tr>
<tr>
<td>(Most Preferred)</td>
<td></td>
<td>Spot urinary ACR (Alb/creatinine ratio)</td>
<td>30 - 300 mg of Alb/gm of creat</td>
<td>&gt;300 mg</td>
</tr>
<tr>
<td>USE: Diagnostic</td>
<td>Early marker</td>
<td>Reversibility of stages</td>
<td>Late/Reversible stages</td>
<td></td>
</tr>
<tr>
<td>Staging of CKD</td>
<td>DOC = ACEI</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Approach - HEMATURIA (RBC in urine)**

Step 1 - Establish "SIGNIFICANT" (any 1) only observation.
- >3-100 RBC/hpf  > 3 occasions Repeat after 48hrs.
- >100 RBC/hpf single occasion.
- Gross HEMATURIA

↓

**Step 2 - Urine microscopy : RBC morphology in urine**

<table>
<thead>
<tr>
<th>EUMORPHIC</th>
<th>DYSMORPHIC (SOURCE → Renal)</th>
<th>DYSMORPHIC (DUE TO → GN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source: Below the Renal Pelvis</td>
<td>Gross H. Microscopic Hematuria</td>
<td>Gross H. Microscopic Hematuria</td>
</tr>
<tr>
<td>Renal calculus</td>
<td>IgA nephropathy</td>
<td>Lupus Nephritis (SLE)</td>
</tr>
<tr>
<td>Cystitis</td>
<td>Post-infective</td>
<td></td>
</tr>
<tr>
<td>Carcinoma bladder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>Post-streptococcal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GN (PSGN)</td>
<td></td>
</tr>
<tr>
<td>Radiological Testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X-ray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KUB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inconclusive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystoscopy ± Biopsy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Approach - PYURIA (Pus / WBC in urine)**

Step 1: "SIGNIFICANT" > 5 WBC/hpf in → observe/repeat.
- Centrifuged sample if not significant.
Step 2: Urine Culture.

H/c cause of significant pyuria = UTI.

STERILE PYURIA

CAUSES

Infective

M/c Partially Rx UTI.

(>72 hrs antibiotic)

FAScIDIOUS ORGANISMS

(special growth requirements)

Chlamydia Renal TB.

M/c of STD

Inflammatory

1) Renal Calculi

2) Papillary Neurosis

(Severe tubular neurosis)

Vascular Insufficiency - Mech.

DM - analgesic abuse

Sickle - Kawasaki Disease

3) Post-Radiotherapy

4) Post-Transplant Rejection

Approach: CASTS/SEDIMENTS

Common CASTS

But non-specific for Diagnosis

M/c cast in urine

HYALINE CAST

Most Benign Cast

No further Rx Tests

M/c found in AKI

M/c cast in nephropathy

GRANULAR/CELLULAR

Present in

Tubulo-interstitial GN

RARE CASTS

(10-15% cases)

DIAGNOSTIC

RBC Cast

GN* (Acute GN)

WBC Cast

Pyelonephritis

Muddy Brown Cast

Acute Tubular Neurosis

Eosinophilic Cast

Acute Interstitial Nephritis

Broad/Waxy Cast

C.K.I.*

Indicates total breakdown of tubule.

WORST CAST

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## USG - KUB

### Site:
- Anatomical

### Size:
- 7-11 cm
  - < 7 cm (shrunken)
  - CKI (exceptions)

### Symmetry:
- < 1.5 cm

### Echotexture:
- = N

### Cortex-Medullary Differentiation (CMD)

### Collecting System

<table>
<thead>
<tr>
<th>Ab Normal Interpretation</th>
<th>Ectopic</th>
<th>No relation to Junction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1 cm - Enlarged / Bulky</td>
<td>AKI -&gt; classical in acute interstitial nephritis</td>
<td></td>
</tr>
<tr>
<td>Early DM nephropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult PKD (APKD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV associated nephropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Amyloidosis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| > 1.5 cm - asymmetrical kidneys |
| Pathology = always in smaller kidneys |

### Increased Echogenicity
  - Active Disease in the Kidney

### Most Imp. Parameter
- AKI

<table>
<thead>
<tr>
<th>CRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preserved</td>
</tr>
<tr>
<td>Loss</td>
</tr>
</tbody>
</table>

| Obstructive nephropathy |
GFR ESTIMATION (Functional Status)

Most preferred = (Creat clearance) (Indirect/surrogate marker)
Easy, cheap, no radiation expo
Cockcroft Gault formulae (Estimated)

\[
\text{eGFR} = \frac{[140 - \text{Age}] \times \text{wt (kg)}}{72 \times \text{S.Creat}}
\]

- [ ] \times 0.85 \text{ F}

Most Reliable/Gold Std:
Radio-isotope scan.
(DTPA, MAG-3)

Direct method.
Accurate
Single Kidney GFR
Segmental GFR.
Total Kidney GFR.

---

Died

1) Inaccurate (esp in AKI)
2) Only - total kidney GFR

Uses - Medical
1) Staging of CKI
2) Follow-up - chronic medical Renal Disease
   - e.g. DM, HTN, HIV associated Nephropathy
3) Dose adjustment of Nephrotoxic drug

Uses - Pre-Transplant assessment of Donor
- Pre-op assessment of urea, creatinine, medico-legal
- Decision making
  - To operate on better kidney
    - never done B/L to H/K

Invasive
Expensive
Radiation exposure
INDEX: RENAL DISORDERS

AKI
Preserved

Parameters
USG1 = CMD

CKI
Lost

USG - size

N or ↓

Osmolarity

Isothenuria

Fluctuates - Posm

Hyaline Cast

Casts

Broad waxy Cast

N or ↓

Anemia

↑ common

Renal osteodystrophy

Pre-renal

Acquired

M/c - DM

Hypertensive

Post-Renal

Aldosteronism

Acute Interstitial Nephritis

RRT (Renal Replacement Therapy)
AKI

Definition: Abrupt decline in GFR over short period of time

KDIGO Guidelines (Kidney disease improving Global outcome - part of National Kidney Found)

Any 1

- ↓ U.O. ≤ 0.5 mL/kg/hr ≥ 6 hrs. [oliguria].
- ↑ S. Cr. ≥ 0.3 mg/dL from ≤ 48 hrs Baseline
- ↑ S. Cr. > 1.5x Baseline ≤ 7 days. (50% involve)

Causes of AKI

<table>
<thead>
<tr>
<th>Pre-renal</th>
<th>Renal</th>
<th>Post-Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-85% - HYPOPERFUSION</td>
<td>INTRINSIC</td>
<td>1.5% - OBSTRUCTIVE UROPATHY</td>
</tr>
</tbody>
</table>

1) Dehydration
- Diarrhea
- Hypoalbuminemia
- Massive Hoge Burns
- (Insensitive loses through skin)

2) Hypotension
- Cardiogenic
- Septic Shock.

3) Drugs - disrupt autoregulation.

<table>
<thead>
<tr>
<th>Renal</th>
<th>Post-Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>95%</td>
<td>5%</td>
</tr>
<tr>
<td>Tubulo Interstitial Disorders</td>
<td>UN</td>
</tr>
</tbody>
</table>
C/F | PR | Renal | Post-R
---|---|---|---
Classical 3 stages |
Oliguria <400mL/d
Anuria <100mL/d
Diuretic phase (Recovery) |
1) Non-Oliguric AKI
   eg. Sepsis
   (In Tubulo-Interstitial)
2) Hematuria - UN

Rarely - Serious Uremic Manifestations
(Causes - mortality in A.K.I.)

1) Encephalopathy / Convulsion
2) Pericarditis / Shock
3) Coagulopathy

Asia → KDIGO Guidelines

Approach - AKI

USG - Collecting System

Post - Renal AKI

Excludes Post - Renal AKI.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-Renal</th>
<th>Renal</th>
</tr>
</thead>
</table>
| Mechanisms | RAAS +
   ↓
   Na⁺/H₂O Reabsorption
   ↑ Urate Reabsorption |
| BUN : Creat |
| Uₙa |
| FNa⁺ |

> 20:1
< 20mEq
< 1%

Loss of concentrating ability
Nat lost in urine
Dilute urine

< 12:1
> 40mEq
> 2%
<table>
<thead>
<tr>
<th>Uosm</th>
<th>(7500 \frac{mOsm}{L})</th>
<th>&lt;350 \frac{mOsm}{L}</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASTS</td>
<td>Hyaline casts</td>
<td>Cylindrical/cellular</td>
</tr>
<tr>
<td>USG- Echotexture</td>
<td>(\text{N})</td>
<td>(\uparrow/\text{Bright Kidney})</td>
</tr>
</tbody>
</table>

**Single Best Novel markers of AKI**

| UNDETECTABLE | DETECTABLE |

---

**Rx PALLIATIVE**

**Indications of Dialysis**

1. \(\text{UREA} > 100\)
2. \(\text{CREAT} \geq 7\)
3. \(\text{SERIOUS UREMIC MANIFESTATIONS}\)
4. \(\text{Refractory Pulmonary Edema}\)
5. \(\text{Hyperkalemia} > 6.5 \text{mEq}\)
6. \(\text{Refractory pH} < 7.20\)

**Single most Imp. Indication for emergency Dialysis**

- \(\text{Ingested Dialyseable Toxin}\)
  - (commonly used: Accidental/Suicidal)
  - a7 Salicylates
  - b7 Methanol
  - c7 Lithium
  - d7 Polyethylene glycol (solvent)

---

**SPECIFIC**

- Depend on cause
  - **A Post-Renal AKI**
    - Early Sx relief
    - Excellent recovery
  - **B Pre-Renal AKI**
    - Fluid challenge (1st line)
    - Diuretics
    - Antibiotics
    - Stop offending drug
    - Excellent recovery
    - Delay in Rx, \(\rightarrow\) progress to ATN
  - **C Renal AKI**
    - \(\downarrow\)
    - Further evaluation.
### Approach - RENAL AKI

<table>
<thead>
<tr>
<th>Tubulo-Interstial</th>
<th>Parameters</th>
<th>GN</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2g/day</td>
<td>Proteinuria</td>
<td>&gt;2g/day</td>
</tr>
<tr>
<td>Granular</td>
<td>Hematuria</td>
<td>Common</td>
</tr>
<tr>
<td></td>
<td>CSte</td>
<td>RBC</td>
</tr>
</tbody>
</table>

#### T.I.

<table>
<thead>
<tr>
<th>ATN</th>
<th>Parameters</th>
<th>Acute Interstitial Nephritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4%</td>
<td>FeNa⁺</td>
<td>2-4%</td>
</tr>
<tr>
<td>CSte</td>
<td>USG - size</td>
<td>enlarged / Bulky</td>
</tr>
<tr>
<td></td>
<td>CSte</td>
<td>eosinophiluria</td>
</tr>
</tbody>
</table>

#### ATN (Tubule-Hc site)

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prone to vascular insufficiency</td>
<td>1) Unreaned Pre-Renal</td>
</tr>
<tr>
<td>Physiology</td>
<td>2) Sepsis</td>
</tr>
<tr>
<td>Site of conc.</td>
<td>3) Contrast Induced Nephropathy</td>
</tr>
<tr>
<td>Direct</td>
<td>4) Drugs - aminoglycosides</td>
</tr>
<tr>
<td>Luminal contents</td>
<td>5) Toxins - Heavy metal poison</td>
</tr>
</tbody>
</table>

#### AIN

1) Allergic Response to Drugs (Hc- 95% of case)

- NSAIDS
- Sulfonamides
- Penicillen
- Cephalosporin
- Rifampicin
- Fos
- Dapsone
- Nitrofurantoin

2) Viral Infe"  
3) Autoimmune  
4) Lympho- proliferative
Supportive therapy Rx
- Underlying cause
- 4-6 wk Avg. recovery
- 1-5% Risk of ESKD
- Favorable prognosis

Stop offending Drug Rx
- 1-2 wk
- <1%

Good

GLomerulonePhritis

Causes:

A. PATHOLOGICAL: Mesangial Involvement on Biopsy

1. Proliferative GN
   - Mesangio-proliferative GN
     - (IgA, PSGN)
   - Crescentic GN (Worst phase)
     - (RPGN)
   - Membrano-epithelial proliferative GN
     - MPGN - mesangio-capillary

2. Non-Proliferative GN
   - Minimal Change Disease
   - FSGN
   - Membranous nephropathy

B. CLINICAL Presentation of GN (More Preferred)

- Asymptomatic
- Proteinuria/microscopic hematuria
  - H/IC
- Nephritic
  - Hematuria
  - HTN
  - Rapid ↓ GFR
    - (HESK-RPGN)
  - Proteinuria <3.5g/day
- Nephrotic
  - Anasarca (Serous Cavity)
  - Hypercoagulable State
  - Preserved GFR
  - >3.5g/day
  - >1.73 m²

Reno-vascular HTN
- c.K.I
  - e.g. Alport's Syndrome

http://mbbshelp.com
WhatsApp: +1 (402) 235-1397
Nephritic
- PSGN
- Lupus nephritic
- RPGN

↓

Proliferative GN  Non-Proliferative

More likely nephritic  More likely nephrotic

MESANGIO-PROLIFERATIVE

IgA nephropathy
- Worldwide
- 20-30 yr, 90%
- Post-infective
- <1st week
- Syn-pharyngitic

PSGN
- India
- 5-15 yr, 9%
- Preceded by URTI
- 1-3 weeks
- 4-6 weeks

Microscopic hematuria
- Common
- [classical nephritic syndrome]

Recurrent Gross Hematuria
- 10-15% Persistent microscopic
- Uncommon
- Benign nature of the disease

Screening (Serology)
- S. IgA - I level ↑↑

Screen complement

HTN
LURF

HEMATURIA

Anti DNAase (70% Case +)
- Aso, anti-hyaluronidase
- Initially low
- Return to N in 6-8 wk

M/C Cause

Epidemi
Biopsy ↚ Mesangio-proliferative change →

Immunoflowescence

Grumular Pattern of Ig deposits →

Anti IgA staining

Anti IgG Staining

Rx

Reassurance
(Majority - Self limiting
Risk of RPN ≤ 1%
Plasmapheresis

Penicillin - no role in nephropathy
To eradicate residual infect:
Long Term prophylaxis

2nd Best (Risk of RPN 1-5%

Prognosis
BEST among GN

Poor Prognostic Factors
1) Elderly onset (> 40yrs)
2) Nephrotic
3) Progression to RPN - any GN requires RRT
   ≤ 1 month of onset

Lupus Nephritis

Kidney involvement - most dreaded.

Organ involvement in SLE - H/C of acute mortality
Deposition of Anti-dsDNA on GBM. (100% specific)

Type | Pathology
-----|------------------
I    | Minimal Mesangial proliferation.
II   | Definite mesangial proliferation.

CIF

Asympt - Proteinuria
Microscopic Hematuria
Presevered GFR

Rx

No active Rx

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http://mbbshelp.com
III  Focal nephritis
IV  Diffuse nephritis
V  MPGN/membranous
VI  Glomerulonephritis

Classical nephritic syndrome
High risk - RPGN (15-20%)

Nephrotic syndrome
CKI

I.V. methylprednisolone therapy
oral steroids

consider RRT

RPGN  ----> Crescentic GN
(clinical acu)
(biopsy pending)

APPROACH - RPGN

Anti-GBM Ab

Goodpasture's syndrome
Autoimmune
20-40yrs ♂ > ♀
α3 subunit - Type 4 collagen
Goodpasture's Ag

Alveolar BM  GBM
(Pulmonary + Renal syndrome)

Me among smokers

I.F. : Linear pattern of Ig deposits

PLASMAPHERESIS

Poor prognosis 70% acute mortality

ANCA

Vasculitis mimics GPS
So, D/D for
Pulmonary Renal Syndrome
- Wegner's
- Churg-Strauss

Low C3
Anti dsDNA
Lupus (SLE)

C3
IgA
Hemolytic
Schistocytosis

Serum Complement levels

PSN  HbsAg
PAN
HCV-Ab
Cryoglobulins

Plasma Pheresis
Poor Prog.
MPGN

Biopsy Based Diagnosis
30-50yrs.
0° > 9

90% cause = 2° cause

Causes

1. Infections - Leprosy
   Malaria
   Syphilis
   Hep. B
   Hep. C

2. Autoimmune - Type V MPGN Lupus nephritis

3. Solid Organ Tumours - [H/c Renal manifestation = MPGN]

4. Lymphoproliferative states

C/F

Majority → "NEPHROTIC SYNDROME"

As in Renal Biopsy - Double BM/
Thick track appearance of GBM.
[Only INTRA GBM HESANCHIAL involvement]

→ Causes splitting of GBM.

10% Idiopathic → Rx - Immunosuppressants
FSGS (Hc - adults)

1° (Idio)
Mlc Biopsy finding = sclerosing type of FSGS

2° Cause
End point of DM HTN
Reflex induced

Most Severe = HIV associated nephropathy

Collapsing type of FSGS

C/F - HTN
Early = severe feature

Rx underlying disease + strict HTN control

MEMBRANOUS NEPHROPATHY (Hc > 50 yrs)

85%

1° (Idio)
EM finding: gold stard spike dome appearance of GBM

2° Cause
Same as in MPGN

NPHROTIC WORST Hypercoagulable state

Hence, max. risk RV thrombosis

Anti-coagulation (all cases) + Immunosuppressants

Risk of ESRD
Common - slow 15-20 yrs

Acute mortality
No
 Favorable Prognosis

Present (vascular) WORST PROG.
C.K.I.

Gradual ↓ GFR ≥ 3 months duration.
Kidneys → Large Functional Reserve.

Clinical Disease 70% Loss of nephrons 25-40 ml/min eGFR

GFR-
17 UREMIA Symptoms (M/c) → M/c neurological feature (90%)
- Encephalopathy / convulsions
- Pericarditis / shock
- Gastritis / Anorexia
- Infertility / Loss of Libido
- Proximal myopathy
- Peripheral neuropathy
- Restless Leg Syndrome
- Generalized pruritus

27 FLUID OVERLOAD Symptoms
- periorbital edema
- peripheral "
- CHF

37 Metabolic Acidosis

47 ANAEMIA - CKI

57 Renal Osteodystrophy

Asu - Done
Rx STAGE of CKD

<table>
<thead>
<tr>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuminuria</td>
<td>eGFR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microalbuminuria (Reversible stage)</td>
<td>90-120 mL/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross (Irreversible stage)</td>
<td>60-89 mL/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross</td>
<td>30-59 mL/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross</td>
<td>15-29 mL/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross</td>
<td>&lt;15 mL/min (90% nephron loss)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rx 282

- ACEI + strict control of risk factors (DM, HTN)
- Counsel + Prepare for RRT
- RRT is mandatory

Specific Rx - Depend on Cause.

DIABETIC NEPHROPATHY

Microvascular complication of DM.

Pathophysio → Hyperglycemia

↓

GLYCOSURIA = ↑ urine osm

RAAS activation (absence of dehydration)

↓

Efferent arteriolar vasoconstriction

↑ Glomerular capillary pressure (already)

↑ GFR supra

Capillary HTN

GLOMERULOSCLEROSIS (P.S.G.S)

Gradual nephron loss

Return to N

ESKD (>90% loss)
- Stage Duration of DM Alh. eGFR.
  - O Hyperfunctioning 1-5 yrs @ Supra-\( \geq 120 \text{mL/min} \) \( \pm \) 1
  - II Silent stage 5-8 yrs B Returns to N
  - III Incipient 8-12 yrs Microalbuminuria I/II
    +ve

<table>
<thead>
<tr>
<th>Early-EM</th>
<th>Thickening of ABM non-specific to AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV Overt</td>
<td>12-18 yrs Gross Cki stage 3/4</td>
</tr>
<tr>
<td>V ESRD</td>
<td>18-25 yrs Gross Stage 5</td>
</tr>
<tr>
<td>Late/Advanced/EM</td>
<td>Nodular glomerulosclerosis irreversible (K-W - Kimmelettin - Wilson nodules)</td>
</tr>
</tbody>
</table>

Rx
283 Strict DM control
1 Adequate Hydration.
2 ACEI/ARB 3
# Alport’s Syndrome

**H/c - XL - X\(^{-}\) defect**

20-40 yr.

\(\sigma > 0\)

**\(\alpha_5\) subunit - Type IV collagen = ABSENT**

<table>
<thead>
<tr>
<th>H/c</th>
<th>GBM</th>
<th>Cochlear B/M.</th>
<th>Lens</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>GN</td>
<td>SNHL</td>
<td>H/c = 75%</td>
<td>Most Specific</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Recurrent Hematuria</td>
<td>Dot &amp; Fleak Retinopathy (Not Specific)</td>
<td>Anti-Leptinemia ((\approx 25%) cases)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Asy** - Renal Biopsy \(\Rightarrow\) "Basket-Weave" appearance of GBM.

**Only Rx** - Renal Transplant:

\(\Rightarrow\) Never recur in graft

Excellent survival

Post-Transplant Complication - Mimic Recurrence (Hematuria)

(Rare) \(\Rightarrow\) Already on Anti-GBM disease Immunosuppression (Ab against \(\alpha_5\) subunit).
POLYCYSTIC KIDNEY DISEASE

Group of inherited disorders characterized by

A) multiple cyst in multiple organs
   - Kidney
   - Liver
   - Pancreas
   - Spleen

B) Berry Anerysm
   - Risk of SAH

C) Colonic Diverticuloses
   - Recurrent Colita
   - ↑ Oxalate Reabsorption from gut
   - Hyperoxaluria
   - Oxalate Renal Calculi

Mode of Inheritance
- AD- PKD
- AR- PKD

Survive till adulthood
Called - adult - Polycystic KD

APKD-1
- POLYCYSTIN-1
- Chr. 16
- moderate form
- 20-30 yrs.

APKD-2
- POLYCYSTIN-2
- Chr. 4
- mildest form
- 30-50 yrs. of age

PKHD (Hepatice)
- Fibrous cyst
- Chr. 6
- most severe
- I.U. Life / Infancy
**CF AD**

Recurrent Loen Pain

H/Lc

+ Hematuria / fever (Infections, Renal cysts)

H/Lc - Extra-renal (Hepatic cysts)

- Mechanical compression - Bel. Headache
- Cholestasis / Cholangitis

| Asia | USG <30 yrs | 30-59 yrs | >60 yrs | >4 Renal cysts | >2 in each
|------|-------------|-----------|--------|----------------|-------------|

Rx - Renal Transplant
No Recurrence
Good Prognosis

**AR**

- Oligohydramnios (30% fetuses)
- Uremic symptoms in infancy
- ESKD < 10 yrs of age
- Cirrhosis < 10 yrs of age
(CAROLI's Disease = Defect of Intra-Hepatic Biliary Radicles)

Present in 30% cases

No cure
Groove Prognosis
RENEAL REPLACENT THERAPY

BEST FORM → TRANSPLANT
- Potential Cure
- Better Survival
- Better Quality of Life

Limited Donor Availability

DOMINO Tx
Kidney swapping
1st Pt. 2nd Pt. 3rd Pt.
1st D 2nd D 3rd D

HLA Registry
All Sx must be done on
Same Calendar
(Limits - chain size)

HAPLO - Identical
(MHC/HLA matching) - 6 Ag matching
Class I A B C
Class II DP DQ DR

>3 = good match.
≤3 = Poor match.
(Less than half match)
• Most imp. HLA match & HLA-DR
  Best Success

DIALYSIS

HEMODIALYSIS (H.D.)
• Vascular access
  (Cannula, AV fistula)
• High Complications Rates
  (Bleeding, sepsis, thrombosis)
• H.D. Centers
  (Limited availability)
• Biocompatible - methyl
  cellulose polymer (filter)
  (High cost)

PERITONEAL (P.D.)
• Intra peritoneal catheter
  placement → done in LA
• Low complication rates
  (≤1% HAK → Peritonitis)
• No problem
  only c/fi - P-rule, H/o recurrent
  GI sx
• Lower cost - omentum acts as
  filter
<table>
<thead>
<tr>
<th>Risk → Infectious transmissible (HIV, Hep B, Hep C, CMV)</th>
<th>No Risk → Installing sterile peritoneal dialyzer basket</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huge Hemodynamic/osmotic shift → poorly tolerated</td>
<td>Low shifts → Better Tolerated</td>
</tr>
<tr>
<td>H/O acute comp → Hypotension</td>
<td>Safe in cardiomyopathy</td>
</tr>
<tr>
<td>Muscle cramps /fatigue</td>
<td>Post cardiac sx</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
<td></td>
</tr>
<tr>
<td>In cardiomyopathy EF &lt;15%</td>
<td></td>
</tr>
<tr>
<td>L = 0.1</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk → Hypoglycemia</th>
<th>Risk → Hyperglycemia/</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred Form. Excellent filtration rate</td>
<td>Wt. 42 kg</td>
</tr>
<tr>
<td>800 - 1200 mL/min</td>
<td>Poor Filtration</td>
</tr>
<tr>
<td></td>
<td>15 - 25 mL/min.</td>
</tr>
<tr>
<td></td>
<td>only Back-up</td>
</tr>
</tbody>
</table>

Dialysis Associated Amyloidosis

- Accumulation of β₂-microglobulin (β₂-MG)
- In the musculoskeletal system
- M/C → entrapment neuropathy
- On dialysis → 3 - 7yr
- Neither form (HD/PD) can filter β₂-MG
- X-Ray Hand - Deposits in metacarpals
- Only Rx = Renal Transplant
PRE-TRANSPLANT - Indications

1) APLD
2) Horse-shoe Kid
3) Obstructive uropathy

↑ Risk of infections in the native kidney
↑ Post Transplant Immunosuppression

Septicaemia → stop Immunosuppressant
↓ Rejection of graft
CNS

achin_mehra<@yahoo.com

Re Priyachin mehra
SEIZURE DISORDER & EPILEPSY

SEIZURE
Paroxysmal event due to hypersynchronous CNS discharges

EPILEPSY
≥2 unprovoked seizures

EPILEPTOGENESIS

↑ GLUTAMATE
Excitatory

↓ GABA
Inhibitory

Pyramidal cell layer

Spinal cord

Motor cortex
CLASSIFICATION OF SEIZURES

- Discrete Lesion
- Diffuse Lesion

FOCAL
PARTIAL

Structural AbN

GENERALISED

DRUGS

Antibiotics - Quinolone
Antivirals - Acyclovir
Antimalarials - mefloquine, chloroquine

Analgesics - Tramadol

Toxins
Abuse
Cocaine
Alcohol
Amphetamine

Metabolic

↓ Na⁺ (Hlc Biochemical AbN ppt. seizure)
↓ due to cerebral oedema <100

2) ↑ K⁺, ↓ K⁺ doesn't cause seizure
**Focal Seizures**

**Loss of Consciousness**
- Contact
- Cognition
- ☩ = Dys cognitive (complex) → Partial
- ☩ = Non Dys cognitive (simple)

**Todd's Palsy**
- Post ictal Paralysis
- Self recoverable
  - Starts in 1st 24 hours of onset

**Focal Seizure**
- Distal → Proximal

**Jacksonian March**
- Focal seizure arising from in a limb.

**Generalised**

**Absence Seizure** / **Petit Mal Epilepsy**

- Loss of contact & environment
- Tone of body ☩
- Abrupt onset
- ≤30 sec
- Subtle Motor Signs ☩
  - (minor)
- Aura ☩
- No post ictal confusion

**Pyknolepsy**

[http://mbbshelp.com](http://mbbshelp.com)

WhatsApp: +1 (402) 235-1397
Starts - 4-8 yrs of age

Spontaneous Remission

in 60-70% by 18 years of age

**EEG:**

B/L 2-4 Hz spike + wave

Precipitated by Hyperventilation (1-3 min)

\[\text{1 sec} \quad \text{3 spikes + 3 waves}\]

\[\text{Spike + Dome pattern}\]

\[\text{Spike + wave}\]

---

**ATYPICAL ABSENCE SEIZURE**

- Loss of consciousness - Less abrupt
  
  ↑ Duration.

- Mental Retardation

- Structural Ab

- **EEG** - ≤ 2.5 Hz spike + wave
  
  (slow)

- Resistant to Anti-epileptic Drug

**MYOCLONIC SEIZURE**

- Jerky movement

**CAUSE:**

1. Hypoxia

2. Degenerative
H/o Hanging → Compress Carotid + cause hypoxia

Juvenile Myoclonic Epilepsy

- Early Adolescence
- Family H/o
- Chromosome No. 6
- Unknown cause. ⇒ x hypoxia
  ⇒ Degeneration.

- Bil Myoclonic jerks
  [on awakening]
  ppt by — Fatigue
  Alcohol

- IQ

- Loss of consciousness ⊗

- Subtle motor Signs ⊗ [eye Blinking]
  [Automatism]
  [fing Smarking]

Majority may turn into GTCS. pt

GENERALISED TONIC CLONIC SEIZURE

-grand mall epilepsy

PREMONITARY SYMPTOMS -
Nausea
Vomiting
Abdominal Pain
AURA  +  Focal
     \  Generalised
         ↓
Hallucinations

- Olfactory  MEDIAL TEMPORAL
- Gustatory
- Auditory  LATERAL TEMPORAL
- Visual  OCCIPITAL

[NOTE: Aura seen in Focal Lesions.]

↑ Tone
- Flexors of UL  DECORTICATE
- Extensors of LL  POSTURING
- Neck VERSIVE HEAD TURNING
- Intercostal  Ictal CRY
- Adductor (Larynx)  Cyanosis +
  ↓
  Clonic
  (Jerk)
  ↓
  Post Ictal Confusion
  (Urinary Incontinence)

JUVENILE MYOCLONIC EPILEPSY

- Myoclonus
- Majority  G.I.T.s
- 1/3rd  Absence Seizure
M/c Presentation of JME & Myoclonus (Alims)

Mesial Temporal Lobe Epilepsy

- Focal Seizure & Loss of Consciousness [Dysgognitive]
- Deja vu
- Febrile Seizure
- Enlarged Temporal Horn
  - Small Temporal Lobe
  - Hippocampal Sclerosis
- Resistant to Anti-epileptics

S: Prolactin
- 30 mins after True Seizure

Anti-Epileptic Drug

AED X 2 years Taper → 3rd year Stop

Seizure ppt. while withdrawal in 1st 3 months more commonly.

X Drug Provoked
- Febrile Seizure
- Alcohol withdrawal
  - BZD - Injectable

→ Status Epilepticus
→ Family H/o +
→ Ab® neurological exam
chlor Diazepoxide  
oral  
for gen. alcohol withdrawal  
not for seizures  

\[
\text{AbN} \xrightarrow{\text{Q-EEG}} \text{CT/MRI.} \\
\text{IOC} \xrightarrow{\text{Seizure} \Rightarrow \text{EEG}} \\
\]

DOC =  

↑ EFFECT  

↓ SIDE EFFECT  

**Focal**  

L - Lamotrigine \(\rightarrow\) STEVENS-JOHNSON SYNDROME (1%)  

D - Oxcarbamazepine \(\rightarrow\) ↓ Na⁺ (SIADH)  

C - Carbamazepine \(\rightarrow\) Aplastic anemia  

P - Phenytoin  

↓ L-Leviteracetam  

↓ irritability mood disorder  

↑ hypersensitivity  

↑ hyperglycemia  

↑ hyperplasia of gums  

↓ hydantoïn syndrome  

↓ irsutism  

↓ hepatitis  

↓ megaloblastic anemia  

↓ excretion of folate  

↓ osteomalacia  

**Fetal Hydantoin**  

Microcephaly  

Hypoxia of Limbs  

Cleft Lip  

Cleft Palate  

Valproate  

Phenytoin  

Carbamazepine
GTCs
Valproate
Lamotrigine
Topiramate

Absence
Ethosuximide → Doc
Valproate
Lamotrigine

Atypical absence
Seizure

Safest AED
Lamotrigine > Carbamazepine > Phenobarbitone
↓ teratogenicity
↑ sedative even for fetus

Doc → as per seizure type
Monotherapy
Lowest effective dose
GTCs → Valproate → Neural Tube → (Preg) 1-2%
Defect
→ AED = 10-20%

AED is not 100% Teratogenic
Do not change Rx during pregnancy changing
Rx can ppt. seizure [Break Through].
Seizure frequency during preg
50% → Unchanged
20% → ↓
30% → ↑

Sembis,
Y ↑ in 30% 

1) Emesis → laboured drug 

2) Hormones
   - Progesterone
   - Estrogen [Epileptogenic] 
   - ↑ seizure threshold

AED. Excreted In Breast Milk

MAXIMUM
Levetiracetam

MINIMUM
Valproate

Breast feeding is recommended
AED is also continued

JME

AED. x Lifelong

DOC = Valproate
Levetiracetam

⇒ DRUGS NOT USED IN JME
   - Carbamazepine
   - Phenytoin → ↑ myoclonus
   - Lamotrigine

⇒ PRE ↑ on valproate
   on change to Levetiracetam
STATUS EPILEPTICUS

↑ Interictal LOC ↑

Seizure ⩾ 5 mins

Convulsions ⩾ 30 min

EPILEPSIA PARTIALIS CONTINUA

⇒ Continuous partial seizure

⇒ Status epilepticus in focal seizure

1st Drug

\[
\text{LORAZEPAM or MIDAZOLAM} \quad \text{(0.1 mg/kg or 0.2 mg/kg)}
\]

IV. A.E.D.

\[
\frac{\text{PHENYTOIN}}{20 \text{ mg/kg}} \quad \text{or} \quad \frac{\text{VALPROATE}}{25 \text{ mg/kg}}
\]

\[
\text{or} \quad \frac{\text{LEVETIRACETAM}}{20-30 \text{ mg/kg}}
\]

\[
[\text{POST-TRAUMATIC EPILEPSY} \quad \text{⇒ LEVETIRACETAM}] + \text{Seizure}
\]

I.V. MIDAOLAM

\[
\frac{0.2 \text{ mg/kg}}{0.2 - 0.6 \text{ mg/kg/hr}}
\]

OR

I.V. PROPOFOL

+ Seizure
THIOPENTONE

CARBAZEPINE - not recommended in status as found in oral form

MOVEMENT DISORDERS

ATHETOSIS / CRAWLING
- Slow
- Sinuous
- Writhe
- Seen in lesions of GLOBUS PALLIDUS - G A P

CHOREA / DANCE LIKE MOVEMENT
Semi purposeful movement
Lesion - CAUDATE NUCLEUS

CAUSES -
C - Chorea Wernicke
H - Huntington's chorea
O - Ocp
R - Rheumatic / Sydenham's chorea
E - Endocrine / Thyrotoxicosis
A - Athero sclerotic / Senile
H/c/e - SLE
HEMIBALLISMUS ⇒ Exclusively on ONE SIDE

- Large Amplitude
- Flapping
- Proximal
- Limb
- Lesion ⇒ SUBTHALAMIC NUCLEUS (STN)
  ↓
  C/L

PARKINSONISM

Degeneration / Atrophy ⇒ SUBSTANTIA NIGRA
PARS COMPACTA (SNPC)

↑ LEWY BODY

- Intra- neuronal
- Intra- cytoplasmic
- Eosinophilic inclusion body
  Contains α Synuclein

↓ DA

Level: 100% → 70% → 30%

TREMORS

RIGIDITY

ETIOLOGY:

↓ DRUGS ⇒ DA

(Mitochondria of 2nd Parkinsonism)

TYPICAL ANTI PSYCHOTICS

- Haloperidol
- CPZ
- METOCLOPRAMIDE

DA Depleters ⇒ Methyl dopa
  Reserpine
27 Toxins → Co
   → Manganese
       MPTP - Heroin Addicts.

37 Trauma
   → Boxers

47 Familial / Genetic
   → Mutations
      → Genes → α Synuclein gene
             → PARKIN gene
             → LRRK-2 gene

     <40 yrs
     >40 yrs
     ↓
     Age of onset
     ↓
     Early Onset

57 Idiopathic -
     85-95% pts.
      ↓
      Parkinson Disease. (H/c type)
         ↓
         Paralysis Agitans

C/F:
UL > LL Spacing neck

Symmetrical
Tremors → 1st H/c Symptom
Resting → Pill Rolling Movement 4-6 Hz.
Rigidity
A Kinesia

Postural Instability - Last symptom or advanced.
TITUBATION → ☐ Parkinsonism

↓ ☐ Cerebellum

TREMOR

RESTING TREMOR ⇒ PARKINSONISM

INTESTINAL TREMOR ⇒ CEREBELLAR LESIONS

FLAPPING TREMOR ⇒ HEPATIC ENCEPHALOPATHY

"ASTERIXIS" ⇒ UREMIA → CO₂ NARCOSIS

FINE TREMORS ⇒ THYROTOTOXICOSIS

BENIGN ESSENTIAL TREMORS

→ 5-11 Hz
→ AD inheritance
→ UL > LL
→ ORIGIN = Cerebellum
→ ↑ anxiety
↓ on alcohol consumption

= Rx → Propranolol

RIGIDITY - BEST Jt to show Rigidity = WRIST

Resistance to passive movement

LEAD PIPE ⇒ EXTRA PYRAMIDAL SYNDROME

Superimposed tremors on COG WHEEL ⇒ PARKINSONISM

UL = COG WHEEL

LL = LED PIPE

COG WHEEL

CLASP KNIFE = UMNL
RIGIDITY
Tone ↑ Flexors = Extensors
Bidirectional

SPASTICITY
Flexors > Extensors
Unidirectional
Velocity Dependent

GAIT
FESTINATION GAIT - Parkinsonism
(ready to run)
Kinesia Paradox
↑ acceleration on running
wk. distal proximal

CIRCUMDUCTION GAIT - Hemiparesis - corticospinal

WADDLING GAIT - Myopathy (Proximal)

Lurching GAIT - Polio Lesion → Ant. Horn Cells

BROAD BASED - Cerebellum - Drunken Gait

HIGH STEPPING - Foot Drop] Deep Peroneal N/V

STAMPING - TABES DORSALIS
L lesion → post column
loss of vibration

POSTURAL INSTABILITY
Loss of Postural Reflexes → FALL

MICROGRAPHIA
Small handwriting

N I am a doctor
PD I am a doctor
MONOTONOUS SPEECH
Hypophonia
MASK LIKE & FACE

Depression
Dementia

PARKINSONISM + ATYPICAL PK → Levodopa [unresponsive to]

17 Progressive Supranuclear Palsy / STEEL RICHARDSON SYNDROME

→ Extended Posture
→ Defective Downward Gaze
→ H/0 fall → early in this type
→ Dementia

Q Tremors

27 LEWY BODY DEMENTIA. (LBD)

Parkinsonism + Visual Hallucination

37 MULTIPLE SYSTEM ATROPHY (MSA)

Parkinsonism + cerebellum + Autonomic
Symptom Instability

47 CORTICO BASILAR DEGENERATION (CBD)

Parkinsonism + myoclonus + Dystonia
     Sustained Posturing
**Rx**

1. ↓ DA
   - (Rigidity)
   - **PD**

2. **TACH**
   - (Tremor)

3. **LEVODOPA** → **DOC**
   - **DA**
   - (Decarb oxylose)

4. **LD → DA**
   - (PD)
   - Rigidity ↑ ↓
   - Akinesia ↑ ↓
   - Quit festa. N
   - off on

5. **ANTICHOLINERGICS**
   - TRIHEXYPHENYDYL

6. **PERIPHERAL DECARBOXYLASE INHIBITORS**
   - CARBIDOPA
   - BENSERAZIDE

7. **MAO B**
   - SELEUGLINE
   - RESAGULINE (neuro protective)

8. **COMT**
   - ENTACAPONE
   - TOLCAPONE

9. **AMANTADINE**
   - ↑ DA level

10. **DA + D₂**
    - PRAMIPRAZOLE
    - ROFINIRROLE
    - ROTIGOTIN
7) APO MORPHINE

1 sedative DA off Injectable on RESCUE THERAPY

CEREBROVASCULAR ACCIDENT (CVA) STROKE

- Focal neurological deficit due to vascular cause > 24 hrs
- TIA (Transient Ischaemic Attack) < 24 hrs
  - Most → for 1 hour

20 ml/100gm brain tissue/min = Ischaemia + Infarction ☠

16 ml/min × 1 hour = Infarction ☠

0 ml/min × 4-10 min → DEATH

CLASSIFICATION

- ☠

ISCHEMIC (85%)

EMBOLIC (75%)

THROMBOTIC (25%)

H/e/e
AF
- non-rheumatic
AF

Most epileptogenic stroke

Embolic > H/o/Ge > Thrombotic

Cerebral edema

HAEMORRHAGIC (15%)
Lacunar Infarcts - Subcortical
So no seizures

FRONTAL LOBE

17 Motor Area

Hand

Finer skills

L.L

Larger area

Face

DESTRUCTION → Paralysis

IRRITATIVE → Seizure

Paracentral lobule (Jacksonian March in L.L.)

27 Micturition Area

? Where

Social inhibition

Incontinence

Infant Bladder

37 Supplementary Motor Area

Primitive Reflexes

Sucking

Grasping

RESURGENCE OF PRIMITIVE REFLEXES

47 Broca's Area

Word area

Located in Inf. Temporal Gyrus
Pre Frontal Area

↑

Control

↑

Emotions

Formed → Limbic System

Civic Lobe = Frontal Lobe

Parietal Lobe

1st Sensory Area

Localization of stimulus

Perception → Thalamus

Spinothalamic Tract

Dermatome

LE

27 Stereognosis

Ability to identify on touch.

37 Taste

Lesion → Dysgusia

47 Optic Radiation

↓

Scotoma
5) **Angular Gyrus**
   - Stores images a/c to Reading
   - Calculation
   - Naming Fingers

- **Bombay**
  - **Bombay**
  - R to L Confusion

**Developmental**
- a) R to L confusion
- b) Dysgraphia (Reading)
- c) Dyslexia (Learning)
- d) Acalculia
- e) Finger Agraphia
  - Cannot Identify

**Gerstman Syndrome**
- Lesion = L Hemisphere

**Temporal Lobe**

1) **1st Auditory Area**
   - Hearing
   - Lesion → Cortical Deafness

2) **Wernicke's Area**
   - Sup. Temporal Gyrus
   - Comprehension

3) **Olfaction → Anosmia**

4) **Optic Radiation → Scotoma**

5) **Deep/Medial Temporal Lobe**
   - Memory
MEMORY

Immediate

\[\text{Short term} \rightarrow \text{MEDIAL TEMOPARAL}\]

\[\text{converted to} \rightarrow \text{Hippocampus}\]

\[\text{Long Term} \rightarrow \text{Stored} \rightarrow \text{NEOCORTEX}\]

NEOCORTEX

AMNESIA

\[\text{Retrograde} \rightarrow \text{Anterograde} \rightarrow \text{AMNESIA}\]

\[\text{Retrograde} \rightarrow \text{AUDITORY}\]

\[\text{Anterograde} \rightarrow \text{WR-WERNICKE}\]

\[\text{AMNESIA} \rightarrow \text{BR-BROCA}\]

\[\text{WR+ BR+ LEFT/ DOMINANT / CATEGORICAL} \rightarrow \text{AUDITORY}\]

\[\text{WR-, BR- RIGHT/ NON-DOMINANT / REPRESENTATIVE \rightarrow VISUAL}\]

\[\text{Inability to recognise faces (PHOSOPAGNOSIA)}\]

Handedness → Right → 90%

\[\text{Left → 60%} \rightarrow \text{Left hemisphere} \rightarrow \text{Dominant}\]
**APHASIA**

<table>
<thead>
<tr>
<th><strong>Temporal AUDITORY</strong></th>
<th><strong>Visual</strong></th>
<th><strong>Auditory</strong></th>
<th><strong>WERNICKE's</strong></th>
<th><strong>BROCA's</strong></th>
<th><strong>Speech</strong></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>APHASIA</strong></th>
<th><strong>COMPR.</strong></th>
<th><strong>NAMING</strong></th>
<th><strong>REPETITION</strong></th>
<th><strong>FLUENCY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>WR.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>- / ↑ EXPLOSIVE JARGON SPEECH</td>
</tr>
<tr>
<td>BROCA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↓ Insight ↓ Depression</td>
</tr>
<tr>
<td>CONDUCTION</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>- / ↑</td>
</tr>
<tr>
<td>ARICATE FIBRES DAMAGED</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>TRANS CORTICAL SENSORY (POST)</td>
<td>-</td>
<td>-</td>
<td>- / ↑</td>
<td></td>
</tr>
<tr>
<td>TRANS CORTICAL SENSORY MOTOR (ANTERIOR)</td>
<td>N</td>
<td>-</td>
<td>- / ↑</td>
<td></td>
</tr>
</tbody>
</table>

- Neologism
- Telegraphic speech
- Melodic circumlution speech
- Explosive jargon speech

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<table>
<thead>
<tr>
<th>Mixed Trans cortical (Isolation aphasia)</th>
<th>317</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure Word</td>
<td>N</td>
</tr>
<tr>
<td>Deafness Auditory Damage</td>
<td>N</td>
</tr>
<tr>
<td>Pure Word Blindness (Alexia)</td>
<td>N</td>
</tr>
<tr>
<td>Anomic Aphasia</td>
<td>N</td>
</tr>
</tbody>
</table>

**seen in**

- M1c type
- Angular gyrus

**Alzheimer**
- Head Trauma
- Metabolic Encephalopathy

**Scanning Speech**  
IAM A DOCTOR  
CEREBELLAR LESION.

⇒ Broca’s Lesion ⇒ Couldn’t write a Dictation
Ant Cerebral Artery

- Frontal
  - Paracentral lobule
  - Supplementary motor - Primitive reflexes
  - Prefrontal - Antisocial Behaviour

Hemiparesis

Wk. UL > LL = MCA Involved

Internal Capsule

MCA

ACo

Corticospinal Tract

Posterior Limb

MCA

APHASIA → MCA → Broca's

L

Wernicke's

AMNESIA → Posterior cerebral → Medial Temporal artery → Hippocampus

Gait Apraxia - Anterior cerebral artery

○ movement
Rx [ISCHEMIC]

1) THROMBOLYSIS

Recombinant tissue Plasminogen activator (tPA)
(I.V.) = 0.9 mg/kg \( \rightarrow \) 10% \( \rightarrow \) Loading Dose
MAX DOSE = 90 mg/kg
WINDOW PERIOD = 4.5 hours from onset

2) ANTIPLATELETS

ASPIRIN
NO clopidogrel

3) ANTI COAGULANTS \( \rightarrow \) AF

HEPARIN \( \rightarrow \) Prosthetic value

\[
\begin{array}{c}
\text{B POWER} \\
\text{GRADING (MRE SCALE)} \\
0 \rightarrow \text{no movement} \\
1 \rightarrow \text{thickening} \\
2 \rightarrow \text{with gravity eliminated} \\
3 \rightarrow \text{against gravity} \\
4 \rightarrow \text{against resistance} \\
5 \rightarrow \text{NORMAL}
\end{array}
\]

Power:
\( \uparrow \frac{1}{5} \rightarrow \frac{4}{5} \rightarrow \text{EMBOLIC} \\
\( 1 \left( \frac{4}{5} \rightarrow \frac{1}{5} \right) \rightarrow \text{THROMBOTIC} \)
HAEMORRHAGIC STROKE

M/c ICH

M/c/л ICH = HTN

SITES

1) Basal Ganglia (Putamen)  →  HEMI PARESIS

2) Thalamus  →  HEMI ANAESTHESIA

3) Cerebellum  →  ATAXIA VERTIGO  →  Decompression  diameter >3cm

Worst

Pontine

HR
RR
Temp
Swelating

PIN: POINT → OP Poisoning
PUPIL → morphine

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S A. space

CSF → Formed CHOROID PLEXUS

Absorbed ARACHNOID VILLI.

CIRCLE OF WILLIS

SACCULAR/BERRY ANEURYSM

ETIOLOGY

1. Trauma (Hc/c).
2. Rupture of Berry Aneurysm (Hc/c spontaneous SAH)
3. A-V malformations
4. Extension from ICH
5. Idiopathic

LOCATION = Perimesencephalic cistern
Angiography = N
Source = Venous
85% of aneurysm ⇒ ANT. CIRCULATION
15% of " ⇒ POST. CIRCULATION

Les Common
↑ Head of Rupture

M/c cranial n/v

- Berry Aneurysm ⇒ IIIrd
- ↑ ICT ⇒ VIth
- UBS ⇒ VIIth
- DM ⇒ IIIm
- HIV ⇒ VIIth
- Sarcoidosis ⇒ VIIth

ACA = anterior inter communicans junction

ICA

MCA

Post. Inter

Communicating artery

RETRO ORBITAL PAIN

Int. Carotid Artery

MCA not the part of circle of Willis

BROCA's

TEMPORAL PAIN

WERNICKE's

PCA

↑ Head of Rupture

Basilar Artery

LEAST COMMON

Vertebral-Basilar Junction
**C/F - Onset/Immediate**

- Peak
- Declined
  - THUNDER CLAP
    - Headache
    - Neck Rigidity
    - Loss of consciousness (transient)
    - No focal neurological deficit

**Delayed**

- Vasospasm
  - SAH
  - Infarct
  - SAH (compresses vessel from outside)

- Re-Hemorrhage
  - 4-14 days after SAH
  - Peaks in 1st 7 days of onset
  - M.C.C. (mortality morbidity)

- dome
- HEMORRHAGE
- neck
- Defect in Tunica media

- 30% re-hemorrhage in 1st month
- Peaks in 1st 7 days

- rupture
- clots
- May rebleed if undetected
3> Hydrocephalus

SAH → Blood

Blocks → CSF Absorption

Arachnoid villi: ↑ ICT

47 \( \text{Na}^+ \) Hypovolemia

↑ ICT → BNP

Cerebral salt wasting → DISEASE

\( \text{H}_2\text{O} \)

\( \downarrow \text{Na}^+ \)

INVESTIGATIONS

NEUROIMAGING

CT

Acute \( \text{H}^+\text{ge} \) (Clot)
Calified

MRI

Inflammation
Infarction
Ischaemic

CVA

\( \text{NCC} \) (Brain)

[To exclude acute \( \text{H}^+\text{ge} \)]

\( \uparrow \)

MRI (Brain)

[To exclude acute Infarct]
Acute SAH = NCT (Brain)

Aneurysm = ANGIOGRAPHY

\[ \xrightarrow{\text{Dye}} \text{MR angio} \]
\[ \xrightarrow{\text{4 vessel angio}} \quad \text{2ICA} \]
\[ \text{Injected} \quad \text{L 2ICA + L VA} \quad \text{via femoral vein} \]

Digital Subtraction Angiography (DSA)

Rx

SURGICAL

TITANIUM

\[ \xrightarrow{\text{Clipping}} \]

PLATINUM

\[ \xrightarrow{\text{Coiling (better)}} \]

Wide neck = Clipping

Narrow neck = Coiling
**MEDICAL**

- NIMODIPINE
  - \( \Theta \) Vasospasm
    - Intracerebral

\[ 3H \]

- HTN \([160/90]\)
- Hypervolemia
- Hemoconcentration
  - (I.V. fluid)

SAH

SDH
occurs due to rupture
of cortical bridging
veins

EDH
Rupture of middle
meningeal artery (MMA)

HEAD INJURY (Closed)

- Headache
- + neurological deficit

Progresses

\[ \text{Days - weeks - months} \]
slowly

SEMI LUNAR

\[ \text{Hours - minutes} \]
rapidly

LENTICULAR
SDH

CT MRI

- Acute = HYPER-DENSE
- Subacute = ISO-DENSE
- Chronic = HYPO-DENSE

MRI > CT

LUCID INTERVAL = EDH

H^gic CVA

ICH > ECH

HTN

- Putamen
- Thalamus
- Cerebellum
- Pons

AV malformation → CORTICAL / LOBAR

H^gic

Post-Traumatic

SAH → H/c

SDH → BOXERS

EDH

SUB CORTICAL

APHASIA

CORTICAL

ARThICATION

MEDULLA

DYSARTHRIA

DYSPHONIA

PHONATION

Tongue

LARYNX

Wernicke's

BROCA'S

CORTEX

INTERNAL CAPSULE
HEADACHE

TEMPORAL ARTERITIS

Elderly

Headache → Throbbing

Stabbing

Scalp Tenderness → Touching inflamed artery

Jaw Claudication [SPECIFIC]

Difficulty in chewing food

Blindness → Irreversible

↓ due to involvement of post cerebral artery

Inv-↑ESR

Biopsy → Temporal Artery Biopsy

Giant cell

Rx- DOC = STEROIDS
PSEUDO TUMOUR CEREBRI / BENIGN IDIOPATHIC

H/c - young obese, ♀

Headache

Projectile vomiting (nausea ☐)
Papilloedema
Ventricle size ☐

No focal neurological deficit
↓ CSF Absorption

ETIOLOGY

1) Hyper vitaminosis A
2) Expired Tetracycline
3) OCP
4) Steroid withdrawal (Abrupt)

Rx = ACETAZOLAMIDE
↓ CSF formation.

TENSION HEADACHE

♀ > ♂

H/c 1st Headache = Tension Headache
Associated ☐ DEPRESSION

Tension is not an etiology

Dull Aching Pain

Band like

EPISODIC → <15 day/month = ANALGESICS

RX

CHRONIC → >15 day/month = T.C.A.

Amytryptiline

H/c/c
↓

Idiopathic
MIGRAINE

D > 6°
† 4-72 hours

P → Pulsatile
U → U/L
M → Moderate to Severe in Intensity
A → Aggravation

+ any 1 → Nausea (M.C.)

Or any 1 → Photophobia

AURA = Visual > Sensory

CLASSICAL (20%)

COMMON (80%)

ACCEPTED THEORY

1. Cortical Spreading Dissociation

Main Trigger → vaso constriction → [scotoma]

↑

Intracranial (Occipital)

↓

FORTIFICATION SPECTRA

vasodilatation → flashes of light
Vasodilation

Headache → [Hypertension] → Pain → Brain

- Hyngeal
- Incitation

Calcitonin gene related peptide (CGRP)

II SEROTONINERGIC

\[ 5HT \Theta \] → Throbbing

\[ RX = 5HT \Theta \]

NON SELECTIVE → ergotamine
SELECTIVE → 1B/1D

Triptans]

DOC for acute attack

RIZA Triptan > SUMA Triptan

NSAID

TRIPTAN

III DOPAMINERGIC → DA \( \Theta \)

DA \( \Theta \) → Nausea

Metoclopramide

Prophylaxis x 5-6 months

- \( \beta \Theta \) → Propranolol (widely used)
- TCA → Amitryptiline
3. CCB → Flunarizine
4. A.E.D. → Valproate  Ethosuximide
   Topiramate  Not Recommended
   Gabapentin

**CLUSTER HEADACHE**

\[ \mathcal{Q} \Rightarrow \mathcal{Q} \]
peri/rhino orbital pain

- U/L
- 30 min - 2 hours
- In pt. by consumption of alcohol
- awakens from sleep.

Autonomic

+ hyperactivity

\[ \xrightarrow{\text{Lavation}} \]
\[ \xrightarrow{\text{Rhinorrhea}} \]

\[ R_x = O_2 \text{ inhalation (Ros) } \]
\[ \text{at } 10-12 \text{ L/min } \times 10-15 \text{ min} \]

Prophylaxis = Verapamil (Doc)
(lifelong)
PAIN

SENSITIVE
- Circle of Willis
- Meningeal arteries
- Dural sinuses/veins

INSENSITIVE
- Dura mater
- Arachnoid mater
- Choroid plexus
- Ventricular ependyma

D/D of MIGRAINE
> Glaucoma
Ascending/Sensory

Spinothalamic

Post./Dorsal Column

Lesion

Spinothalamic Tract

Spino-Cerebellar Tract

Stamping Gait

Romberg's Test

Sways w/ eyes closed
Descending Tract
Corticospinal Tract

Paralysis

UMN
- Tone ↑ (spasticity)
- DTR brisk
- Plantar extensor (Babinski +)

LMN
- ↓ (flaccidity)
- Dull/absent
- Wasting/atrophy
- Fasciculation
- Twitch visible
- Lesion palpable
- Ant. Horn cell
BROWN-SEQUARD SYNDROME

ST₁ ST₁ ST₁ T₁ T₁ T₁ T₁ ST₁

HEMISECTION

AH₁

ST₁

AH₁

corticospinal tract
HEMISECTION of T₃

At T₄ → S.L. Loss of spinothalamic → C/L
    Post. column → I/L
    Weakness → UMN
    I/L.

At T₄₃ = P. Loss of Post column → I/L
    Weakness → LMN, I/L

* * *

Spinothalamic → I/L.

AT THE LEVEL ⇒ Spinothalamic → Post. column → SAME
LMN
SIDE

Ab. BELOW the LEVEL ⇒

Spinothalamic → Opposite Side.

P.C. → Same Side
UMN
**SPINAL SHOCK**

*Transient* LMN weakness below the level of lesion

Most occurs at 48-72 hrs

- Flaccidity
- Areflexia
- Urinary retention
→ Sensory Loss

→ Wasting

Transient process internal nutrition is intact

Spinal Shock = LMN - Wasting


CREM A S T E R I C

FLEXOR WITHDRAWAL.

BEEVOR SIGN

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BEVOR SIGN  
Supine → Sitting position  
If umbilicus moves upward ⇒ Lesion @ T10 below.

PRONATOR DRIFT SIGN  
Weak Side  
Pronation + Drift  
Injury CS Tract  
CVA in Evolution.

INTRA MEDULLARY  
IV Disc Prolapse  
Root Radicular Pain  
Descending (S) Loss  
Burning Pain +

Extra MEDULLARY  
Early SACRAL LOSS  
Ascending (S) Loss  
ST CS
TRANVERSE MYELITIS \rightarrow extramedullary lead to transverse myelitis.

vertebral artery

Occlusion of 1 side ASA + PVA
\uparrow
BROWN SEQUARD
due to vasculitis

SYRINGOMYELIA

CAUSE:
1) congenital
2) 3T \rightarrow Trauma
Tumour
TB

AT THE LEVEL \Rightarrow LMN WEAKNESS
BELOW THE LEVEL \Rightarrow UMN WEAKNESS

Selective loss of
\begin{align*}
\text{Pain} \\
\text{Temp}
\end{align*}

Assymmetrical

Syrinx = cavity

M/l site

Lower cervical
upper thoracic

\text{CAPE LIKE DISTRIBUTION OF SENSORY LOSS}
CHIARI MALFORMATION > 50%
  (Type 1)
  ↓
Cerebellar tonsilla herniation into foramen Magnum
  ↓
compresses central canal containing CSF
  ↓
it starts enlarging due to compression
  ↓
always expands anteriorly

Rx = DECOMPRESSION LAMINECTOMY
  to relieve pressure on expanding
  spinal cord from vertebra

DISAD
  → doesn't relieve symptoms.

NOTES (CF of Syringomyelia)
  → Painless burning of hands occur easily
    ↓
    Neuropathic ulcers
  → absent deep tendon reflex (5, 6)
  → extensor plantar (+5, 5, 5)
URINARY BLADDER

FRONTAL

(Paracentral Lobule) where \( \text{ACA} \)

PONS

CENTRE

\[ + \leftarrow \text{contraction} \rightarrow \text{micturition} \rightarrow \text{PARA} \left[ S_2, S_3, S_4 \right] \]

\[ - \leftarrow \text{Relaxation} \rightarrow \text{storage} \rightarrow \text{SYPHATIC} \left[ T_{11-12} \right] \]

\[ \mathbf{[A]} \quad S_2, S_3, S_4 \quad \mathbf{-} \quad \text{AUTONOMOUS BLADDER} \]

\[ S_2, S_3, S_4 \quad \mathbf{-} \quad \text{Sensory} \]

\[ \mathbf{-} \quad \text{Para} \]

\[ T_{11-12} \quad \mathbf{+} \quad \text{SYPHATIC} \quad \mathbf{+} \quad \text{L SYMPATHETIC} \]

HYPOTONIC
FLACCID
LARGE CAPACITY
OVERFLOW
INCONTINENCE
T11 - L2 \( \Theta \) [AUTOMATIC BLADDER]

- HYPER TONIC
- SPASTIC
- LOW CAPACITY
- URGE INCONTINENCE

CONUS MEDULLARIS

S.C. ends opp to L1 L2.
S1-S5 segments
KNEE JERK
L3-L4 \( \Theta \) [N]

ANKLE-JERK
S1-S2 \( \Theta \)

BLADDER

AUTONOMOUS (early)
Intra /

MIXED (NEUROGENIC)
(Late)
\[ \uparrow \] Extra

Bladder

CTLS

Asymmetrical
Areflexic
LMN Paralysis

CAUDA EQUINA

nerve roots
L1-L5
S1-S5
LESION ABOVE T1, QUADRI PareSis

LESION BELOW T1, UL = N, LL = WEAKNESS, PARA PareSis

C1 C2

PHRENIC N/V

C3 C4 C5

HIGH

APNOEA

INTERCOSTAL N/V

C6 C7 C8

LOW

DIAPHRAGMATiC BREATHING

Rx = NIFEDiNE, CLONiDiNE

Rx = NIFEDiNE, CLONiDiNE

T1] UPPER Lesion Above T6

T6]

T7] LOWER Pain

T12]
TRIGEMINAL N/V

\[ V^{th} N/V \]

- SENSORY → Face
  - CORNEA
- MOTOR → MASTICATION

NUCLEUS

SUPRANUCLEAR → UMN

PONS

NUCLEAR → LMN

INFRANUCLEAR

SPINAL II SENSORY

Jaw Jerk

BRISK → UMN

\[ V^{th} \]

Loss of sensations over face

[Lesion above Pons]

\[ V^{th} \]

\[ VII^{th} \]

Teste
  - Chorda Tympani
  - Tongue Ant 2/3rd

PONS

\[ VII^{th} \]

SMILE

RESORIEUS

\[ V^{th} \]

HASTICATION
MEDULLA → X

**BEGLUTITION***

XII

**ARTICULATION***

**FACIAL N/V**

**TRIGEMINAL NEURALGIA**

Electric shock on face / Tic Dolo ESAUX

Rx → Injen of C2H5OH / glycerol in Gasserian ganglion

RHIZOTOMY - Radio Frequency Ablation

**FACIAL N/V (VII**

**PONS**

**sup. petrosal n/v**

Lacrimation

Wrinkling

Blinking

Stapedius

Acoustic Reflex

Styloglossus

Taste ant 2/3rd tongue

Salivation

Smiling

**styloglossal foramen**

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Upper 2/3rd of Face is having B/L cortical innervation

Lower 1/3rd of Face supplied by opposite cortex

A) Cortical lesion $\Rightarrow$ UMN paralysis
   (Supranuclear)

B) Pons lesion $\Rightarrow$ LMN paralysis
   U/L $\rightarrow$ Cause
   1) Trauma
   2) Herpes Zoster virus [Ramsay Hunt syndrome]
   3) Idiopathic [Bells palsy]

B/L Cause
   1) UBS
   2) HIV
   3) Sarcoidosis
RECOVERY

Abercrombie Reinnervation

1. Crocodile Tear Syndrome

2. Synkinesia (Smiling Blinking together)

H/O ⇒ S/O Cervical Cord Injury

1. Fall from height
2. Road Traffic accident
3. Hanging

Hermitte Symptom

1. Multiple on flexion of neck
2. Sclerosis
3. Pain/electric shock across spine
MYASTHENIA GRAVIS

Ach R Antibodies
Destroy Block

Ach E \( \rightarrow \) Ach Levels

Thymic AB

\( \downarrow \) 75% Myasthenia Gravis

\( \downarrow \) 65% Hyperplasia

\( \downarrow \) 10% Thymoma

LOCAL Compressive

PARANEOPLASTIC

Pure red cell Aplasia
Pernicious Anaemia
Hypoglobinemia
Dermatomyositis

MRI (Chest)

\( \frac{0}{0} = 2 \frac{2}{2} \)

20 30 50 60

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3-7% MG
↓
suffer from Hypothyroidism

C/F:

1) easy fatiguability
   • proximal
   • asymmetrical

2) ocular [1st m/l to involve]
   [m/l m/l to involve]

   Ptosis, ophthalmoplegia

2) Facial

   - snarling
   - can't maintain smile for long

   close eyes for some time then
   opens as if seeing through small
   aperture

3) Skeletal

   → DTR
   • sensory intact
   • bladder
   • cognition
**INV: -**

1. **EDROPHONIUM / TENSILON TEST**
   - Shorter acting
   - Peripheral action
   - **BEST SCREENING TEST**

2. **Ach \( \mathbb{R} \) Antibodies**
   - Most Specific Test
   - + in 85% of pts. c gen. MG.
   - 50% **Ocular MG.** → [Eye symptoms x 3 yrs]
   - -ve does not rule out MG.

3. **Muscle Specific Tyrosine Kinase (MUSK)**
   - MUSK Antibodies

---

**Diagram:**

- **Ach** → **Na\(^+\)** → **\( \alpha \)-subunit**
- **Ab** → **CLUSTERING**
- Lipoprotein Related Protein
- **Ab against** → +ve in 40% Ach \( \mathbb{R} \)
- **MUSK**
- **Ab** → +ve in BULBAR MG

**Adv.:** Ach can act on all \( \mathbb{R} \) at same time
RAPID/REPEATED NERVE STIMULATION (RNS)

ACH

Action Potential (A.P.)

DECREMENTAL RESPONSE

↓

MOST SENSITIVE TEST CONFIRMATORY
GOLD STD. TEST.

Difference in AP ⇒ JITTER ↑↑

EMG shows myopathic pattern
doesn't record Jitter well

BEST

SFEMG > EDROPHONIUM > RNS
Rx

17 AChE

PYRIDOSTIGMINE

DO

Ach ↑

ORAL

NEOSTIGMINE

Ach ↑↑↑

Cholinergic crisis
Injectable

27 IMMUNOSUPPRESSANTS

MYCOPHENolate MODIFIL (MMF) — Best

37 IVIg

[→ Refractory MG]

47 Plasmapheresis

[Myasthenic crisis
Resp m/s weakness
↑?
Injection.

57 THYMECTOMY

35% MG → Drug Free

85% MG → Symptom Remission

It is Recommended Inspite of medical control (15-55yrs) [MUSK Ab Θ]

MOST USEFUL → In Thymoma pts.

local effect

Paraneoplastic synd.

NOT USEFUL IN

<15 yrs

Immuno Def.

>55 yrs

Vestigial

http://mbbshelp.com

WhatsApp: +1 (402) 235-1397
- Ocular MG
- Risk surgery >> Disease
- Musk Ab + [1 Benefit]

LAMBERTEN EATON MYASTHENIC SYNDROME
[LEMS] [PARANEOPLASTIC SYNDROME]

P/Q Ca^{2+} CHANNELS
Voltage gated
\[\text{antigen}\rightarrow\text{sarcoplasmic}\]
Small cell Ca Lung
(SCLC)

↓ Ach Release
[PRE SYNAPTIC DEFECT]

C/F:
- Weakness skeletal > facial > ocular [MG opp. seq.]
- DTR ↓/⊕ [MG, DTR 0]
- Bladder Involved [MG, Bladder 0]

INV:
- Edrophonium +ve. (weakly +ve compared to MG)
- Rapid N/V stimulation Test

muscle
↑ A.P. by 10%

↑ A.P. by 10%
INCREMENTAL RESPONSE
Rx -

3. Diaminopyridine $\leftarrow$ Doc

3DAP [Tach Release]

MOTOR NEURON DISEASE

amyotrophic lateral sclerosis (M/L)

corticospinal tract weakness affects distally.

Amyotrophic $=>$ no trophic failure weakness occurs.
10 LATERAL SCLEROSIS (PLS)
Degeneration of CS Tract \(\Rightarrow\) UMN

SPINAL MUSCULAR ATROPHY
only LMN

ALS

O/F -
1) elderly
2) Fasciculations \(\rightarrow\) [PATHOGENOMIC]
3) SUPEROXIDE DISMUTASE (SOD1) Deficiency

\[ \begin{align*}
\text{BRAIN CELL} & \quad \text{EDARAVONE} \\
\text{SOD}_1 & \quad \text{Deficiency} \Rightarrow \text{APOPTOSIS} \\
\text{H}_2\text{O}_2 & \quad \text{O}_2 \\
\text{Ca}^{2+} & \quad \text{GLUTAMATE} \\
\text{RILUZOLE} & \quad \text{=} 
\end{align*} \]

4) [N] \(\Rightarrow\) eye m/s
- sensory
- Bladder
- Cognition.

5
Cortex

Frontal

IX

X

XI

XII

gag reflex

Bulbar palsy

Cortico

Medulla

Bulbar

Tract

×

Pseudo bulbar palsy

Dysarthria +

Dysphagia +

Labiopharyngeal effect +

Gag reflex + + +

Bulbar palsy

ALS

->

Palio

->

M.G. [Bulbar MG]
# ATAXIA

<table>
<thead>
<tr>
<th>TRACTS</th>
<th>TABES DORSALIS</th>
<th>SUBACUTE COMBINED DEGENERATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyr./c.s.</td>
<td>Post</td>
<td>Post</td>
</tr>
<tr>
<td>Spino cerebellar</td>
<td></td>
<td>Pyr./c.s.</td>
</tr>
<tr>
<td>PAIN TEMP</td>
<td></td>
<td>Peripheral plus</td>
</tr>
<tr>
<td>DTR</td>
<td></td>
<td>Early DRG involved</td>
</tr>
<tr>
<td>Babinski</td>
<td>+ve</td>
<td>+ve</td>
</tr>
<tr>
<td>ASSOCIATE B &amp; T</td>
<td>Cardiomyopathy</td>
<td>Syphilis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ARP +</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bladder disturbance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DM</td>
</tr>
</tbody>
</table>

**FREIDRICH ATAXIA**

- VIBRATION
- PROPRIOCEPTION
- **Early DRG involved**

**DRG = Dorsal Root Ganglion**

**1 Vit B12**

**Megaloblastic anemia**
FREIDRICH's

Trinucleotide Repeat sequence = GAA

AR
Ch. 9

TABES DORSALIS

Syphilis.

Agyll Robertson Pupil.
Bladder Disturbance

SACB

↓ Vct B12.

Megeloblasti
Anaemia

CEREBELLAR LESIONS

Dysmetria → Past Pointing
Titubation → persistent head nodding
Intentional Tremor:
Dysdiadochokinesia
Pendular Knee Jerk
Romberg's Test $\bigoplus$ → Lesion in Post. column
Broad Based Gait
Tendency to fall towards lesion.
ALZHEIMER DISEASE

AMYLOIDOSIS
↓
ATROPHY
↓
AMNESIA

Amyloid precursor protein (APP)

Encode

Chr. 21

[MUTATIONS]

GENETIC

β SECRETASE

Chr. 14

Chr. 1

AP$_{42}$ peptide

→ Neurotoxic
→ Resistant to Degeneration
→ Aggregates Rapidly

RISK

↑

Elderly

0

†

Chr. 19: Apo E$_4$ gene
Aluminium
Mercury
Family H/o
Low Education (poor maths)

↓

Post Menopausal. Estrogen
NSAID Use
Apo E$_2$ gene.
Smoking
↓ Risk
Parkinsonism
Ulcerative colitis
ATROPHY
Temporal
Parietal
+ Hippocampus

Earliest

C/F

TROPHY
Mnnesia (anterograde)
PHASIA (Anomic)
Nosognosia (unaware)
Praxia
Gnosia (can't identify)
Nosmia
Spiration pneumonia (cause of death)

↓ Ach

→ Acalculia
   not seen.
   [DSM CRITERIA]

→ Agnosia
   not seen in early onset
   Alzheimer's (age < 65y)
   [ICD CRITERIA]

→ Delusion → Doctor replaced by enemy
   (false belief)
   Capurias Syndrome
   (in 10% of pts)
**BIOPSY**

\[
\text{APP} \rightarrow \text{NFT} \\
\]

17 **NEUROFIBRILLARY TRIANGLES**

- Intracellular
- Correlate to severity

**TAU**

- Hyper p-tau - microtubular proteins
- Slow neurodegeneration

Also seen in **TAU Pathies**

1. **Fronto Temporal Dementia**
   - Behavioural Ab due to frontal lobe involvement → early
   - Memory loss → late
     - Mild
   - Age of onset < 65 yr
   - Insight ☐

2. **Progressive Supranuclear Palsy (PSP)**
   - Extended posture
   - Downward gaze ☐
   - Dementia

3. **Corticobasilar Degeneration** (PD + myoclonus + Dystonia)
27. **SENILE NEURITIC PLAQUES (SNP)**
   - extracellular
   - correlate to age

**CEREBRAL AMYLOID ANGIOPATHY (CAA)**

- Large vessel
- Small vessel

- Cortical
- Subcortical

**Alzheimer's Disease**

**DEMENTIA**

**Progressive Supranuclear Palsy**

37. **GRANULOVASCULAR DEGENERATION**
   - Best seen in **HIPPOCAMPUS**

**HUNTINGTON'S CHOREA**

- Huntington gene [chr 4 - short arm] Trinucleotide Repeat Sequence defect
  - CAG > 40 repeats

- **AD Inheritance**
  - 2 successive generations are affected
  - 1 Parent affected
    - [Chance 50%] 1:2
  - If both parents affected
    - [Chance 75%] (3:4)
ANTICIPATION

\( O^{	ext{3}} = \text{early onset 2nd Decade} \)

(11-50 yr)

\((\text{Father})\)

\( \text{Mother} = \text{late onset 4th Decade} \)

LENGTHENING

Larger Defect \( \rightarrow \) Severe

\( \rightarrow \) \text{early onset (from father)}

\[
\begin{array}{c|c}
\text{Father Repeats} & \text{Mother Repeats} \\
400 & 400 \\
\downarrow & \downarrow \\
40,000 & 400 \\
\end{array}
\]

Anticipation occurs due to lengthening.

C/F

AD inheritance

Seizure \( \rightarrow \) if inherited from father

\[
\text{Chorea} \quad \text{Ahetosis} \quad \text{Dementia} \quad \text{Personal changes}
\]

ATROPHY \( \text{in CAUDATE NUCLEUS.} \)

\( \downarrow \text{ACH} \quad \downarrow \text{GABA} \quad \downarrow \text{intra striatal} \)

\( \uparrow \text{DA} \)

\( R_5 \rightarrow \text{DA} \Theta \rightarrow \text{Haloperidol} \)

\( \text{DA Depleter} \rightarrow \text{Tetrabenzine} \rightarrow \text{DOC} \)
NORMAL PRESSURE HYDROCEPHALUS (NPH)

CSF PRESSURE → \( N = 50 - 150 \)

\[ \rightarrow \text{NPH} = 150 - 180 \]

↓ CSF Absorption ← SAH

↑ Meningitis

C/F

Gait Ataxia

MAJNETIC GAIT

→ external hip rotation

Dementia

→ shorter strides

→ low grad and clearance

UCINARY INCONTINENCE

SCISSORING GAIT → spastic CP

CHARLIE CHAPLIN GAIT → Tibeal Torsion

Rx

V-P shunt

↓

1st / Most responsive symptom to improve on VP shunt

ATAxia
**WERNICKE’S ENCEPHALOPATHY**

**PREDISPOSED—**

1. Hyperemesis
2. Alcohol Intake

\[ B_1^+ \text{ Deficiency} \]

\[ \text{CO-FACTOR} \]

\[ \alpha\text{-Keto glutarate dehydrogenase} \]

\[ \text{Pyruvate Dehydrogenase} \]

\[ \text{GLUCOSE ACCUMULATION} \]

\[ \text{Mitochondrial Damage} \]

\[ \text{NEUROTOXIC} \]

**C/F**

GLOBAL CONFUSION

\[ \text{GOA} \]

- Ophthalmoplegia
- Ataxia

**RX**

THIAMINE REPLACEMENT × 14 Days
(100 mg/day)

1st Improve = ophthalmoplegia

[Glucose infusion can precipitate it]
KORSAR KOFF'S PSYCHOSIS / ALCOHOL DEMENTIA

DEMENTIA ➔ CONFABULATION
False story to hide memory loss

SITES
- Periaqueductal Grey Matter
- Mamillary Bodies
- Thalamus ➔ [AMNESIC DEFECT]

CONFUSIONAL STATE
1) Seizure
2) T.I.A.
3) Metabolic - i glucose
   L. alcohol

TRANSIENT GLOBAL AMNESTIA
Both anterograde & retrograde amnesia
CNS INFECTIONS

BACTERIAL / PYOGENIC MENINGITIDES

H/c/c
Adolescent / Adult = N. MENINGITIDIS
Elderly = STEPTO. PNEUMONIA
(Community acquired)

CSF

Appearance

Transparent

Turbid

Cell count ≤ 5

Pleocytosis (N >75)

Protein 15-45 mg/dl

ηη

Glucose 40-70 mg/dl

↓↓↓

Cl- 116-126 meq/l

↓↓↓

Hypoglycorrhiza = ↓ CSF Glucose

Rx

N. MENINGITIDIES → Ceftriaxone × 7 Days

S. PNEUMONIAE → Ceftriaxone + Vancomycin × 14 Days

>60 yr pt ↓

LISTERIA → Ampicillin
C/F

FEVER

† HEADACHE.

NECK RIGIDITY

ALTERED SENSORIUM

Dexamethasone

10 mg IV stat

1st Dose of antibiotic

TBM ATT × 1 month

↓ Sensorium

1. ATT induced hepatitis
   ↓ hepat enceph pathy

2. ICT cerebral salt wasting

3. Infarct

4. Tuberculoma

5. Hydrocephalus

Endarteritis

Hydrocephalus

Tuberculoma

Reactivation

Basal exudates

Endarteritis

Infarct

TBM

M/C Meningitis in India

C SF

→ COB-WEB

→ Pleocytosis [L > N]

→ Protein ↑↑

→ Glucose ↓ Ca↓↓

COLD STD TEST = Culture of CSF

Rx

ATT × 12-18 months (↓ Reactivation)

Steroids × 2 mths [↑ Endarteritis]
VIRAL ENCEPHALITIES

M/CC → ENTEROVIRUS
    → Epidemic = ARBOVIRUS
    → Sporadic = HSV Type 1

HSV ENCEPHALITIS

CSF → Xanthochromia

Haemorrhage lesions

SAH → CT scan.

N CSF Xanthochromia

Traumatic LP

- Pleocytosis
- ↑ Protein
- ↓ Glucose
- ↓ Cl

Most sensitive test = PCR for HSV in CSF

MRI

Bitemporal hyperintensities.

T1 ↑, T2 ↑ = it's

Brain ↑ ↓

CSF ↓ ↑

Rx

Acyclovir 10mg/kg IV q8h x 14 days
Progressive Multifocal Leuкоencephalopathy (PML)

Jc virus → oligodendrocyte
Inclusion bodies

A/c -
- Immunocompromised host
  - HIV + (80%, M/L host)
  - Transplant recipient

VF - visual field defects (M/L)

Inv
  - MRI → hyperintensities
  - Demyelination
  - CSF (PCR for Jc virus)
  - Brain biopsy

Rx not available

Prognosis Death 3-6 months of onset
PRION DISEASE

CReutzfeld Jackob Disease (CJD)

DNA/RNA θ

Transmittable ↔ Dural Grafts
          corneal grafts

C/F-
    Dementia + myoclonus (H/c)

Inv
    EEG - Biphasic waves
    Brain biopsy - Spongiform degeneration

Rx - not available

NCC [Neurocysticercosis]

Agent = Taenia Solium

HOST - DEFINITIVE = Human
       INTERMEDIATE = PIG

via consumption of undercooked pork
  consumption of undercooked raw vegetables

C/F - Seizure (H/c)

Inv -

CE ↔ CT
MRI

Sclera ○ Ring enhancing lesions
STAGES
(viable) oedema
VESICULAR +
(dying) ++
COLLOIDAL +
(dead) -
CALCIFIED

Rx
ANTI-PARASITIC

DOC → ALBENDAZOLE ↓ 15 mg/kg/day × 8-28 days

+ Steroids + A.E.D. × 6 months ↓ CT scan

↓ calcified
Taper 2-3 months ↓ STOP

DOWN OTHER TYPES OF CUBS

<table>
<thead>
<tr>
<th>AIDP</th>
<th>&lt;4wk</th>
<th>AMAN</th>
<th>AMSAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor</td>
<td>Motor</td>
<td>M-S</td>
<td></td>
</tr>
<tr>
<td>Sensory</td>
<td>only</td>
<td>Mostly</td>
<td></td>
</tr>
<tr>
<td>&gt;90% children</td>
<td>children</td>
<td>adult</td>
<td></td>
</tr>
<tr>
<td>mostly</td>
<td>young adult</td>
<td>WORKS PROG.</td>
<td></td>
</tr>
<tr>
<td>GM1 Ab +ve</td>
<td>GD1a Ab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIDP</td>
<td>&gt;9wk</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
GUILLAIN BARRE SYNDROME

Ab
C. jejuni

Schwann cell

↓ schwann cell
↓ myelin
↓ conduction

→ Post Infection
→ Demyelinating
→ Polyneuropathy

VACCINES causing GBS %

RABIES (neural)

Influenza

C/F

ASHBURY CRITERIA

→ Ascending Paralysis
Distal → Proximal ≤ 4 weeks

< 4 weeks
Areflexia
Minor sensory
Bladder - spared

H/c cranial N/V Involved
= VIIth (Bl, LMN)

**Acute** = **Inflammatory** = **Demyelinating** = **Polyneuro**

**Pathy**

(AIDP)

**Variant of GBS**

**Miller Fischer Variant/Syndrome**

GQ1b
Antibodies

Ataxia
Areflexia
Ophthalmoplegia

**Miller Fischer Test**

Done in Normal Pressure Hydrocephalus

CSF Drained (30ml)

↓

Cognition

↓

Improved

Then go for

V-P - Shunting

INV for GBS

↓ Nerve Condu icon Study

↓ N/V Condu icon Velocity

↓ A-P.
CSF

↑ Albumin
No pleomorphism
[Albumeno cytological dissociation]

Rx

1) IVig
2gm/1kg over 5 days. Both are equally effective
2) Plasmapheresis

Best in 1st 14 days
Steroids is not recommended

Prognosis

Recovery occurs in 85%
Sequela → 10%
Death → 5%

Inflammatory

<table>
<thead>
<tr>
<th>Age</th>
<th>Muscle Invol.</th>
<th>Skin Changes</th>
<th>Ass. Malignancy</th>
<th>Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>Proximal</td>
<td>+</td>
<td>+ (15%)</td>
<td>+</td>
</tr>
</tbody>
</table>

Myopathy

<table>
<thead>
<tr>
<th>Dermato Myositis</th>
<th>Poly Myositis</th>
<th>Inclusion Body Myositis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20 yrs</td>
<td>Proximal</td>
<td>&gt;50 yrs</td>
</tr>
<tr>
<td>Distal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Phospho-Kinase ↑

http://mbbshelp.com
WhatsApp: +1 (402) 235-1397
MULTIPLE SCLEROSIS

Inflammation

Demyelination

Sclerosis

DISSEMINATED

Time

Space.

c/s

1) SENSORY

1st HR symptom
↑ Exposure to HEAT ⇒ UTHOFF SIGN

ICE PACK TEST

Cold = Ache ⇒ In Mgr pts. weakness ↓

2) OPTIC NEURITIS

3) SPASTICITY

TYPES

↑ Disability

Time

RELAPSING REMITTING

85%

[RRMS]
1° Progressive MS (PPMS)

2° Progressive MS (SPMS)

Progressive Relapsing MS (PRMS)

STAGING

MS = Extended Disability Scoring Scale (EDSS)

SAH = Hunt & Hess Scale

MG = Osserman Grading
**INV**

**MAC DONALD CRITERIA**

\[
\text{MRI} \xrightarrow{\text{Demyelination}} \text{Periventricular Plaque}
\]

**CSF**

\[
\text{Oligo Clonal} \rightarrow \text{IgG Bands}
\]

\[
\text{Liquid Chromatograph}
\]

**RX**

**ACUTE ATTACK**

**METHYL PREDNISOLONE (DOC)**

**DISEASE MODIFYING AGENTS**

1) IFN \( \beta \) \( \beta1a \) \( \beta1b \) DOC

2) Glatiramer

3) Fingolimoo [ORAL]

4) Natalizumab [BEST] \( \text{SLE = PMLE} \)
D/D of DESCENDING PARALYSIS

Botulism
Polio, Porphyria
Diphtheria
ENDOCRINE

- Dr. Achin
PROLACTIN

Secrete in Ant. Pituitary

Prolactin makes cells LACTOTROPH

**FUNCTIONS:**

1. Induce and maintain the process of lactation

2. Prolactin hormone $\rightarrow$ GnRH $\rightarrow$ LH $\rightarrow$

- ↓ Ovulation
- ↓ Sexual drive
- ↓ Testosterone $\rightarrow$ ↓ Menstruation
- ↓ Spermato genesis

Hypothalamus

Dopamine $\rightarrow$ Prolactin

HYPERPRLACTINEMIA

**ETIOLOGY:**

A) PHYSIOLOGICAL

1. Lactation

2. Female

   $\uparrow$ Estrogen $\rightarrow$ ↑ PL

3. Sleep [NREM sleep]

4. Chest wall stimulation

   - Nipple stimulation
   - Chest trauma or surgery
1) Hypothyroidism

\[ T_3, T_4 \downarrow \]

\[ +ve \rightarrow \uparrow TSH \rightarrow \uparrow TRH \rightarrow \uparrow Lactotroph \rightarrow \uparrow PL \]

\[ \text{Somatotroph} \rightarrow \uparrow GH \rightarrow \downarrow \text{Acromegaly} \]

Paradoxical response

2) CKD

\[ \rightarrow \downarrow \text{excretion of Proteins} \]

3) SEIZURE

Postictal (30 mins)

C) DRUGS (iatrogenic)

Dopamine \( \uparrow \)

- Typical Antipsychotics
  - Haloperidol
  - CPZ

- Atypical Antipsychotics
  - Risperidone
Metoclopramide

Dopamine Depleters

CH₃Dopa
Reserpine
CCB - verapamil

H₂ Antagonist
Ranitidine
Cimetidine

→ These drugs cause hyperprolactinemia due to blockage of Infundibular Pathway

Dy Pituitary Adenoma

Prolactinoma \( \rightarrow \) Mic type

\[ \begin{align*}
& < 10 \text{mm} \\
& \text{Micro (90\%)} \\
& \text{F:M = 20:1}
\end{align*} \]

\[ \begin{align*}
& > 10 \text{mm} \\
& \text{Macro (10\%)} \\
& \text{F:M = 1:1}
\end{align*} \]

C/F → ? → Galactorrhea \( \rightarrow \) 80%

\[ \text{Infertility (Mlc presentation)} \]

Amenorrhea

↓ PL \( \rightarrow \) ↓ LH

↓ Luteinogen

↓ Ovulation

↓ Osteoporosis
$\theta^+ \rightarrow \text{ Libido}$

Azoospermia
Infertility

Chiasma

$\Rightarrow$

Compressive
MACRO $\gg$ MICRO

**S. PROLACTIN**

$N = 5 - 25 \mu g/mL$

- PHYSIOLOGICAL $\rightarrow 25 - 40$
- IATROGENIC $\rightarrow 25 - 100$
- PRACTINOMA $\rightarrow >200$
- MACRO PRACTINOMA $\rightarrow >250$

Stop offending drug
Reasses PL after 72 hours

**MACRO PRACTINOMA**

Symptoms $\oplus$

Prolactinoma $\Theta$

$S. \text{ Prolactin} \uparrow \uparrow \uparrow$

**[FALSE HIGH]**

Prolactin = Peptide hormone (198 A: A)

75% monomeric

**HOOK EFFECT**

Symptoms $\oplus$

Prolactinoma $\Theta$

$S. \text{ Prolactin} \oplus$

**[FALSE $\ominus$]**
Polymeric
↓
Bio INACTIVE.

S. PROLACTIN

> 200

MRI

< 10 mm

MICRO

DA +

BROMOCRIPTINE

CABERGOLINE

1-2 mths

S. PROLACTIN

< 50

Continue
Same therapy
(CST)

> 50

STOP DA +

MRI @ 4 mths

> 10 mm

MACRO

DA +

MRI @ 4 mths

SIZE = l = CST x lifelong

unchanged.

Trans Sphenoidal Resection (TSR).

Always 1st Line = Medical Rx
Prolactinoma on DA → wants to conceive

1. Allow 3 cycles
2. Stop DA → Jaratogenic pregnancy?
3. Assessment
4. Rare: [Headache] DA → [Bromocriptine]
5. No response → SURGERY (TSR)

Prolactinoma is → are asymptomatic

Doc for Prolactoma = Cabergoline

- Long acting
- Convenient intake
- Less nausea
- Better effect

Fertile → Bromocriptine
GROWTH HORMONE

- Released from Ant. Pituitary
- By SOMATOTROPHS (Most abundant cells) 50%
  - Lactotrophs > Gonadotrophs
    (20-30%) (10-20%)

- GH
  - SOMATOSTATIN
    (S cells of Pancreas)
  - GHRH
  - GHRELIN
    - Gastric Peptide
    - ↑ motility
    - ↑ appetite
  - FASTING (most potent)
  - EXERCISE
  - SLEEP

- GH feedback
  - Liver
    "Somatomedin c"
  - IGFI
    - Bone
    - Soft tissue
**GH**

**Carbohydrate**
- Diabetogenic

**Protein**
- Anabolic

**Fat**
- Lipolytic

\[ \text{GH} \xrightarrow{+} \text{Lipase} \rightarrow \text{TFFA} \]

- Insulin Resistance
- Diabetogenic

\[ \text{TGH} \]

- Epiphyseal fusion
  - Before = Gigantism
  - After = Acromegaly

**Acromegaly**

**Etiology**
- \( \uparrow \text{TGH} \)

**Pituitary**
- Somatotrophic Adenoma (H/cells)
  - Loss of feedback

- Hamartomatous Somatotrophic Adenoma \( \rightarrow \uparrow \text{PL} \)
- \( \uparrow \text{TGH} \)

**Hypothalamus**

- Hamartoma

- Ectopic
  - Bronchial carcinoma

**IGF-1**

- Anti-diabetic

- Anabolic

- Anti-lipolytic
ECTOPIC

ISLET CELL CA OF PANCREAS

C/F

CVS → LVH
  Diastolic Dysfunction
  HTN
  CAD

Resp → Nasal turbinate hypertrophy
  Obstructive sleep apnoea (OSA)

GIT → T. Liver & spleen (Hepatosplenomegaly)
  [Colon polyps] ⊃ cancer
  Benign

ENDOCRINE → DM (Insulin resistance)
  Goitre

SKELETAL → Tall stature
  Large digits
  Prognathism
  Jaw malocclusion
  [↑ space bet. lower incisors]
  Fleshy nose.
INVESTIGATION

1> **GH ASSAY** → not useful test

2> **IGF-1 ASSAY**
   Best screening Test

3> **GH SUPPRESSION TEST** → confirmatory Test
   \[
   \text{[GH} \times \frac{1}{\text{glucose}}\]

   75 gm glucose (oral)

   \[\text{GH} \rightarrow \text{N} \rightarrow \downarrow\]

   ACRO → unchanged

Rx

TSR - ROC

F/B → ADJUVANT THERAPY

Somatostatin
Octreotide
Canreotide

Peqvisomant

INSULIN STIMULATION TEST

\[
\text{GH} \times \frac{1}{\text{glucose}} \rightarrow \text{on giving insulin}
\]

\[
\text{glucose} \downarrow \rightarrow \text{GH} \uparrow \text{(DM)}
\]

Dwaffum → GH unchanged
**ADH / VASOPRESSIN**

- **Blood vessels**
  - Vaso constriction

- **Smooth H/L**
  - (contraction)

- **Kidney**
  - 1, Vascular smooth endothelium
  - 2, Pituitary
  - 4, ACTH

- **Aquaporin 2**

**Lumen**

- **Cortical Collecting Duct**

- **Basolateral**

- **H$_2$O**

- **AQP$_1$**
  - ↓
  - PCT ← ADH

**Independent**

**N values**

- Serum osmolality = 275 - 295 mosm/L
- Urine osmolality = 300 - 1000 mosm/L
- Serum Na$^+$ = 135 - 145 meq/L
- Serum K$^+$ = 3.5 - 5 meq/L
POLYURIA
>50 ml/kg/day
>3 l/day

SOLUTE/OSMOTIC DIURESES
↓
Glucose
Mannitol
Ca²⁺
Urine osmolality >300

↑ Solute = ↑ Hp
Isosmolar

DILUTE
H₂O > Solute
Urine osm < 300

→ DI
→ Psychogenic Polydipsia (PP)
H₂O Deprivation Test

Urine osm. → ↑ = P.P.

Unchanged = D.I.

ADH Stimulation Test
Urine osm. → ↑ = ADH Def.

Unchanged = ADH Resistance
Nephrogenic DI
Phases

Psychogenic Polydipsia

Lumen

\[ H_2O \rightarrow H_2O \]

\[ \uparrow s. osm \rightarrow \text{Thirst} \rightarrow \text{No dehydration} \]

\[ \uparrow s. Na^+ \]

Polyuria

\[ \downarrow u. osm \rightarrow \text{N} \]

solute diuresis

26 Cerebral Salt Wasting Disease

\[ \uparrow ICT \rightarrow \text{BNP} \]

\[ \downarrow Na^+, H_2O \]

Hyponatremia  Hypovolemia

Solute diuresis

\[ \uparrow ICT \rightarrow \uparrow ADH \rightarrow \text{SIADH} \]

\[ \downarrow ADH \rightarrow \text{DI} \]

\[ \rightarrow H_2O \rightarrow \uparrow s. osm \]

\[ \rightarrow \uparrow s. Na^+ \]

High output due to diuresis
SIADH (Syndrome of Inappropriate ADH)

\[ \text{ADH} \uparrow \]

\[ \text{H}_2\text{O} \rightarrow \text{H}_2\text{O} \uparrow \]

\[ \text{H}_2\text{O} \rightarrow \text{H}_2\text{O} \uparrow \]

\[ \text{Low Osm} \]
\[ \text{Low Na}^+ \]

\[ \text{Dilutional} \]

\[ \text{Volume} \rightarrow \text{Renin} \]

\[ \downarrow \]

\[ \text{ANP} \]

\[ \text{Aldosterone} \]

\[ \text{Net Reabsorption} \]

\[ \text{Natriuresis} \]

\[ \text{K}^+, \text{HCO}_3^- \]

\[ \text{Euvolemic} \]

\[ \text{Hyponatremia} \]

\[ \text{Hyponatremia} \]

\[ \text{H}_2\text{O} \]

\[ \text{in urine} \]

Cerebral Salt Wasting Disease

Euvolemic

SIADH

\[ \text{H}_2\text{O Loading Test} \]

Pi. produce less urine than N pt

RX = H₂O Restriction

ADH \( \text{\textendash} \) DEMECLOCYCLINE

VAPTAN (Doc)
\[ \text{Na}^+ \]

\[
\begin{align*}
[\text{N}] &= 135 - 145 \text{ meq/L} \\
>120 &= \text{Asymptomatic} \\
110 - 120 &= \text{GI symptoms, nausea} \\
100 - 110 &= \text{mild CNS symptoms, giddiness, Ataxia} \\
\text{Seizures} &\rightarrow <100 \text{ cerebral oedema}
\end{align*}
\]

**Parathyroid Hormone**

\[- \text{Ca}^{2+} \rightarrow \uparrow \text{PTH} \]

\[- \text{Bone} = \text{Resorption} \\
\text{Intestine} = \text{Absorption} \\
\text{Kidney} = \text{Reabsorption} \]

\[ \uparrow \text{PTH} \]

\[- 20^\circ \rightarrow \text{CKD} \\
\text{Vit D deficiency} \\
\text{Malabsorption} \]

\[- \text{Parathyroid} \rightarrow \text{Hyperplasia} \]

\[ \text{Adenoma} [H/c/c] \]

\[- \text{H/c type} = \text{solitary} \\
\text{H/c site} = \text{Inf. Pth lobule} \]
3° = PTH hyperplasia → ADENOMA (3°)

2° → 1°

HYPERCALCEMIA

C/F:
- Nausea, vomiting
- Constipation
- Bony pains Ø
- Renal calculi
- Abdominal Pain
- Depression
- Psychosis

Rx:
1) Hydration.
2) Diuretics
   Calciuretic → Loop Diuretics
3) Bisphosphonates
   Ø osteoclastic activity
   Dronates.
   [Delayed onset of Action]
4) Gallium → Osteoclast Ø
5) Plicamycin
6) Calcitonin
7) Dialysis
PSEUDO HYPO PTH

↓ Sr. Ca²⁺
Sr. PTH ↑
PTH Resistance

ALBRIGHT HEREDITARY OSTEODYSTROPHY (AHO)

Short Stature

Round Face

Short 4th/15th metacarpal (Breachyclasty)

PSEUDO PSEUDO HYPO PTH

Sr. Ca²⁺ = (5)
Sr. PTH = (5)

AHO Phenotype (+)
**Thyroid**

- **Hypothyroid (Hypo)**
  - TSH (↑)
  - T4 (Free)
  - T3 (Free)
  - TRH (↑)

- **Central**
  - TSH (↑)

- **5' Deiodinase**
  - T4 → T3

- **Thyrotoxicosis Crisis**
  - DOC: PTU
  - Impending CCF

- **Hypothyroid**
  - STSH (↑)
  - FT3 (↓)
  - FT4 (↓)

- **Hyperthyroid**
  - STSH (↓)
  - FT3 (↑)
  - FT4 (↑)

- **2° Hypothyroid**
  - STSH (↓)
  - FT3 (↓)
  - FT4 (↓)

- **Subclinical Hypothyroid**
  - STSH (↑)
  - Low (N)
  - Low (N)
HYPOTHYROID
Weight Gain
Fatigue
Cold Intolerance
Constipation
Menorrhagia
Menopause
↓ H.R.
mild diastolic HTN
Delayed Relaxation of Veal
[Hung Up Reflex]

HYPERTHYROID
Weight Loss
Anxiety
Heat Intolerance
Diarrhoea
Amenorrhoea
↑ H.R.
↑ S.B.P. / ↑ D.B.P.
Fine Tremors
Exophthalmos

RX
HYPOTHYROIDISM
L-Thyroxine
[1.6 μg/1 μg/day]
↓ Dose = elderly
IHD
TSH after [6 weeks]
[N = 0.35 - 5]
[Target = 0.35 - 2.5] → L-Thyroxine X lifelong

TSH
L-Thyroxine
10
75 μg/d
↓ +25
8
100 μg/d
SUBCLINICAL HYPOTHYROID

↑ TSH, [FT₃, FT₄] low N

RX -
TSH > 10 \Rightarrow \text{Start L-thrye}

[5-10] L-thyroxine.

\Rightarrow \text{Infertility}

♀ → TSH ↑ → FT₃, FT₄↑

\Rightarrow \text{ve}

↑ TSH

♀ → TPO Antibodies
ADRENAL.

CUSHING SYNDROME

Loss of -ve feedback

ETIOLOGY

A) EXOGENOUS / IATROGENIC

B) ENDOGENOUS

ACTH

\[ \text{ACTH} \rightarrow \text{Cortisol} \uparrow \]

\[ \text{ACTH} \rightarrow \text{Dependent (90\%)} \]

\[ \text{ACTH} \rightarrow \text{Endogenous cause} \]

\[ \text{ACTH} \rightarrow \text{Ectopic ACTH} \]

M/e malignancy → small cell CA of lung

- medullary CA of thyroid
- Phaeochromocytoma
- CARCINOID → Bronchial
- Thymus
- Pancreatic

H/c/c → CUSHING DISEASE

Cushing Syndrome due to Pituitary Adenoma.
C/F:

↑ CORTISOL → ↑ Gluconeogenesis

17 PROTEIN → MYOPATHY (proximal)

→ s/c Tissue Tear = STRIAE Purple colour due to rupture of vessel.
→ THIN SKIN
→ EASY BRUISING.

27 FAT Redistribution of fat
CENTRIPETAL OBESITY

→ BUFFALO HUMP
→ MOON LIKE FACE

37 DM

47 HYPERNATREMIA

\[
\begin{array}{c}
\text{Cortisol} \\
\downarrow \text{activity}
\end{array} \xrightarrow{11\beta, \text{OH}} \text{Dihydrogenase} \xrightarrow{\downarrow \text{activity}} \text{Cortisone}
\]

\( \text{G.C.} \rightarrow \text{M.C.} \)

- ↑ Na\(^+\) Reabsorp'
  \downarrow \text{HTN}
- ↓ K\(^+\), alkalosis
  ectopic ACTH, pts.

57 ♀

oligomenorrhoea → Amenorrhoea
Hirsutism
6) CNS -
- ↑ appetite
- ↓ sleep
- Euphoria [Psychosis]

Peak 8:30 am
6:30 pm
Cushing Syndrome

S. Cortisol
A.M. - 7 P.M.

Pseudo - Cushing (mimic Cushing Syndrome)

Chronic add. alcoholics
Cocoholic pts
Pts. of Hyperthyroidism
Pt. of Depression

Clinical suspicion of C.S.

Weight Gain (80%)
Skin = thin skin > HTN (80%)
(75%)

1st M/C symptom
> Central obesity (50%)
> ↓ K⁺, alkaloses (15%)

Screening Test
**SCREENING TEST**

- 24 HR. URINARY CORTISOL ↑
- MIDNIGHT S. CORTISOL ↑
- ORAL DEXA CHALLENGE TEST [BEST]
  
  1 mg DEXAMETHASONE @ 11:00 PM
  (oral)
  ↓
  S. CORTISOL @ 9:00 AM
  → N = N
  ↓
  CS = + (due to loss of +ve feedback)

**CONFIRMATORY**

  2 mg 0.5 mg DEXA I/V 6 hourly x 2 days
  ↓
  SH. CORTISOL → N = C.S. & O
  ↓
  R. C.S O & O

  [LOW DOSE DEXA TEST]

**ETIOLOGY**

H/O - exogeneous

↑

DEPENDENT

↑

PITUITARY ADENOMA

ECTOPIC ACTH

MRI can't visualize pituitary
adenoma (2-5mm)

1) INF. PETROSAL SINUS SAMPLING (IPSS)

CRH

↑

ACTH

↓

Sample ← PETROSAL SINUS (PS)

Peripheral vein (PV)

ADRENAL ADENOMA

[CT Abdomen]
RATIO

\[
\frac{PS}{PV} \uparrow \rightarrow \text{Increased} \quad \frac{PS}{PV} \downarrow = \text{Decreased.}
\]

PITUITARY ADENOMA

ECTOPIC ACTH

2mg DEXA IV. q6h x 2 Days

↓

\[ \text{S.Cortisol} \quad \text{↓} = \text{Pituitary Adenoma} \]

UNCHANGED = Ectopic ACTH.

PITUITARY ADENOMA

ECTOPIC ACTH

C/F

ONSET → Insidious

PROGRESSION → Slow

HYPERPIGMENTATION → +

IPSS

\[ \frac{PS}{PV} \uparrow \]

HIGH DOSE DEXA +ve Test Response

\[ \text{Rx} \]

Ketoconazole

Metapyrone

Etomidate

Mitotane

\[ \text{โอ Cortisol Synthesis} \]
HYPER ALDOSTERONISM

↓ volume → ↑ Renin → ↑ Aldosterone

[EPITHELIAL]

Na⁺ channel

[ENAC]

↓

↑ Na⁺ → ↑ H₂O

↓ volume

10 ← Hicc.

↓ Bll Adiopathic Cortical Hyperplasia (60%)

27 Adrenal Adenoma (40%)

↑

M/c/c - CONN SYNDROME

↑ Aldosterone

(Transient) ↑ Na⁺

↓

↑ H₂O

↓

↑ volume (↓ Renin)

↓

↑ ANP

→ NATRIURESIS

[ESCAPE PHENOMENA]

Cardiac Remodelling

Diastolic Dysfuntion

↓ K⁺, alkalosis.

[No edema]

Polyuria

↑
CLINICAL SUSPICION

Diastolic HTN

↓

JK⁺

↓

ALKALOSIS

[SCREENING TEST]

ALDOSTERONE RENIN RATIO (ARR) > 20

↓

[CONFIRMATORY TEST]

2 Litres of Normal Saline x 4 Hours

↓

Volume → ↓ Renin → ↓ Ald. ⇒ (N)

↓

NO Suppression of Aldosterone

⇒

[SALINE INFUSION TEST]

↓

ETIOLOGY

↓

CT Abdomen

↓

ADENOMA

HYPERPLASIA

Age

<40 yrs

>40 yrs [Incidentaloma] ↓ heplenore

↓

ADRENELECTOMY

↓

Adrenal venous sampling

ALDOSTERONE

HIGH

⇒ (N) = watch

↓

Medical Therapy

Rx: Aldosterone C

↓ Spironolactone
17 Syndrome of apparent mineralocorticoid excess [SAME]

Cortisol → Deficiency of → Cortisone

↑ Na⁺

↓ K⁺, Alkalosis

Rx = Steroids → ↓ ACTH

↓ Cortisol

27 Glucocorticoid Remediable Aldosteronism [GRA]

Zona → Glomerulosa → Aldosterone

ACTH ↑

Fasciulata → Cortisol

Retinol

Rx - Steroids → ↓ ACTH → ↓ Aldosterone

37 Liddle's Syndrome

↑ Functioning of ENAC → ↑ Na⁺

↓ K⁺, Alkalosis

Rx - ENAC ⊥ → Triamterene

Amiloride
ADRENAL INSUFFICIENCY

- **ADDISON DISEASE**
  - **1°**
    - AUTOIMMUNE (HCG in WORLD)
    - TB (HCG in INDIA)
  - **2°**
    - PITUITARY
      - Surgery
      - Trauma
      - Radiation
      - Apoplexy

  ↓ CORTISOL
  ↓ DEFICIENCY

  ↓ Gl.C. ← Activity → M.C. ↑

  ↓ Glucose
  ↓ Protein Breakdown

  ↓ C. loss
  ↓ Thirst

  ASTHENIA
  M/C: 1st symptom

  Lethargy
  /Fatigue

  ↑ ACTH

  **Hyperpigmentation. (localised)**

  1. Oral mucosa
  2. Conjunctive
  3. Palmar crease
  4. Nipple, areola, Hilgson
  5. Moles, scars
ACTH administration

\[ L \overset{\text{N}}{\rightarrow} \text{CORTISOL} \uparrow \]

\[ \rightarrow \text{Addison's pt} \rightarrow \text{CORTISOL (unchanged)} \]

\[ \text{ACTH STIMULATION TEST / COSYNTRIPIN / SYNACTHEN TEST} \]

Dx = Diagnostic Test

Rx = STEROIDS

Hydrocortisone (DOC)
DIABETES MELLITUS (T2DM)

Food (glucose) → Intestine → Glucose → β cell (Pancreas)

ATP sensitive K⁺ channel

Glucose → Glu-6-Poi → Gluokinase

[Box: K⁺, ATP, ADP, Insulin, Insulin secretion, Deficiency, Resistance, Target cell, Insulin t1/2, 44]

1 Unit of Insulin

11 units

2.5 g/m of glucose

Deficiency = Type-I

Secretion → Type-II

Resistance
**TYPE-I**

- β cell Destruction (>90%)
- HLA Mediated
  - Aninkulinemia
- Age of Onset: <30 yrs
- Habitus: Thin
- Family H/o: +
- HTN: -
- Dystlipidemia: -

DKA

**TYPE-II**

- Secretory Defect
- Insulin Resistance
- Hyperinsulinemia
- >30 yrs
  - Obese
  - + + + +
  - + [↑TG - ↓HDL]

Hyperosmolar
Non-Ketotic Coma

---

20 yrs → 25 yrs
- RBS ↑↑
- K.B. +
- Obese
- Insulin ↓
- (OHA)
- (Type 2)

KETOSIS PRONE DIABETES (KPD)

---

30 yrs → 25 yrs
- RBS ↑↑
- K.B. -
- Obese
- Insulin
- (OHA)
- (Type 1)

LATENT AUTOIMMUNE DIABETES IN ADULTS (LADA)
Maturity Onset Diabetes in Adults (MODY)

Onset 5-15 yr of Age.

Thin
OHA Response
AD Inheritance
DKA ⊗
HTN ⊗

6 types of MODY

↓

TYPE 3 (H1c type)

↓

HNF -1α Deficiency

Type-3 Diabetes / Brain Diabetes / Alzheimer

Insulin Resistance / Deficiency

↓

Ppt the Cond.

Type-4

Elderly >60yrs

OHA Response (minimum dose)
DIAGNOSIS

Polyuria

Polydipsia

Wt. Loss

± Polyphagia

± non-healing wound.

+ RBS ≥ 200 mg/dL

or

Fasting <br> 8 hrs

Fasting BS ≥ 126 mg/dL

or

Oral GTT

75gm glucose (oral)

↓

2hr BS ≥ 200 mg/dL.

or

HbA1c > 6.5%

(glucose + globin)

ACUTE COMPLICATION of DIABETES

DIABETIC KETOACIDOSIS

Type-1

(1) RBS = 250 - 600 mg/dL  \( \text{(Reliable)} \)

(2) Ketone Bodies \( \rightarrow \) Blood \( \rightarrow \) KETONEMIA

Urine \( \rightarrow \) KETONURIA  \( \text{(Best Bed side)} \)

(3) \( \downarrow \) pH

C/F

1. Nausea, vomiting \( \text{(persistent)} \)

K.B. \( \rightarrow \) CTZ

2. Abdominal Pain ± Tenderness
3) \( \uparrow \text{HR} \)

4) TMR \[ \text{KUSMALL BREATTHING} \]

\[
\text{Metabolic acidosis} \quad \xrightarrow{\text{CO}_2} \quad \text{Respiratory alkalosis}
\]

\[
\text{\( \uparrow \text{CO}_2 \) acidosis} \quad \xrightarrow{\text{\( \uparrow \text{CO}_2 \) acidosis}} \quad \text{\( \uparrow \text{alkalosis} \)}
\]

5) Fruity odour → due to acetone

6) Dehydration (severe)

\( \text{H/h of mortality} \)

\[ \text{Rx} \]

1) I.V. fluids (4-6 L)

\[
\text{Host effective Rx:} \quad \text{4-6hR} \quad \text{to prevent hypoglycaemia}
\]

\[
\text{RBS < 200}
\]

2) Insulin

\[
\text{Regular} \quad \text{10 units IV Bolus} \quad \text{\( 0.1 \text{U/kg/hr} \)}
\]

3) KCl \( @ \) 20-40 meq/hr

4) NaHCO\(_3\)

\[
\text{pH < 7.}
\]
HYPEROSMOLAR NON- KETOTIC COMA

TYPE=2

\[ \text{RBS} = 600 - 1000 \text{ mg/dL} \]
\[ \uparrow \text{Skr. Osm.} \]
\[ \text{KB} \implies \text{Altered Sensorium} \]

\[ R_x = iv \text{ fluid (6-10L)} \]
2) Insulin

CHRONIC COMPLICATION

DIABETIC NEUROPATHY

A) POLYNEUROPATHY

Distal Symmetry Sensory
(H/Tc type)

\[ \text{Loss of Vibration [128 Hz Tuning Fork]} \]

PARAESTHESIA → ANAESTHESIA

\[ R_x \]

1) Improved Glycemic Control
2) Pain
   - AED: Prebagalin
   - TCA: Amitryptiline
(B) HONONEUROPATHY

H/c Truncal N/v

III > VII

(Pupillary sparing)

Honeoneuritis multiplex = Patchy involvement

L M/c/l - metabolic = DM [B in India, world]

Infective = LEPROSY

Vasulitis = POLYARTERITIS NODOSA

(C) AUTOMM AUTONOMIC NEUROPATHY

Hypoglycemic Unawareness

β- avoided in diabetic pts.

Intensive control is avoided ⇒ ↑ risk of hypoglycemia

HYPOGLYCEMIA

WHIPPLES TRIAD

< 55 mg/dl

S/s of HYPOGLYCEMIA

DOCUMENTED
HYPOGLYCEMIA

REVERSAL OF
SYMPTOMS ON
CORRECTION
1) ↓ Insulin
2) ↑ Glucagon
3) ↑ Cortisol
   | Epinephrine
   | GH

EXTENSIVE FASTING X 72 HOURS

↓

↓ Glucose

↑ Insulin

Hyper-Insulinemia

 ↑ Insulin ↑ C-Peptide

Endogenous

Hyperinsulinaemia → Radiological

Insulinoma, Sulphonylurea Induced

Only ↑ Insulin

Exogenous

SOMOGYI EFFECT

3-5 A.M. 8 A.M.

Hypoglycemia [↑ night Insulin] Hyperglycemia

Counte regulatory hormones

Rx = Long Acting Insulin
DAWN PHENOMENA

\[ 3-5\text{AM} \quad \text{Hyperglycemia} \]
\[ \substack{\text{Insulinopenia} \\ \text{Insulin Resistance}} \]

\[ 8\text{AM} \quad \text{Hyperglycemia} \]

\[ \text{Rx: } \uparrow \text{ night Insulin} + \downarrow \text{ Insulin sensitizer} \]

\[ \text{Rx of TYPE-2} \]

\[ \text{FBS} \]

\[ \begin{array}{c}
\downarrow \\
126 - 200 \\
\text{Diet} \\
\text{Exercise} \\
\text{Insulin} \\
\end{array} \quad \begin{array}{c}
\downarrow \\
200 - 300 \\
\text{Obese metformin} \\
\text{Non-obese} - \text{Sulfonylurea} \\
\text{GLICAZIDE} \\
10-14 \text{ Days} \\
\text{GLIPTIN} \\
\end{array} \]
STALK LESIONS

↑ Prolactin

Hypothyroidism (central)

↓ glucose

↓ BP

Central DI

PITUITARY APoplexy

↓ SHEEHAN SYNDROME

↑ Incidence = Sickle cell disease

Predisposing Factors

DM

HTN

↓ vision → progressive Decompression.

Haemorrhagic necrosis

GH → LH → TSH → ACTH → ↓ Cortisol → ↓ BP

STEROIDS
after few months

functioning pituitary

EMPTY SELLA SYNDROME (Incidental finding)
**MEDICINE (GIT)**

Liver → Intestine

- Disorder of Bilirubin metabolism
- Malabsorption syndrome
- Acute viral hepatitis + Diarrhoea
- Chronic hepatitis + GI infection
- Comp. of liver failure + IBD
- IBS

**BILIRUBIN METABOLISM**

\[\text{Heme} \xrightarrow{\text{UConj}} \text{Bilirubin} \xrightarrow{\text{UGT}} \text{Conjugated Bilirubin} \]

**DISORDERS OF BILIRUBIN METABOLISM**

1. Unconjugated Bilirubin

   a) Increased synthesis:
      a) Hemolytic anaemia → Premature destruction of RBC in periphery
      b) Ineffective erythropoiesis → Premature destruction of RBC in bone marrow

Causes:
- Thalassemia
- Megaloblastic anaemia
- Severe Fe def.
- Pb poisoning

OATP - Organic anion transport protein
Large haematoma

Lobar pneumonia (TRBC death + exudate)

↓ Uptake↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓↓→
CNZ  |  CNII  | Gilbert Syndrome
---|---|---
Inv | N | N  
Liver Bx |  
---|---|---
Liver |  
Enzyme | No T/t Needed  
Transplant |  
Inducer |  
---|---|---
Phenobarbital |  
---|---|---
25% | in S. Bil. |  
---|---|---
If no Response then  
go for Liver Transplant  

*Acquired cause :-

1) Drug  
- Gentamicin  
- Chloramphenicol  
- Prednisolone  

2) Breast Milk Jaundice (Self Limiting)  

FA → UGT of neonate  
No need to stop feeding  

3) Lucey Driscoll Syndrome :- (Self Limiting)  
Maternal Serum Ab → UGT of neonate
II. ↑ Conjugated Bilirubin (Isolated).

Liver enzyme (\( \text{N} \))

Dubin Johnson Syndrome

Rotor Syndrome

Heh (\( \text{O} \)) Mutation of MRP2

\( \text{O} \) Mutation of OATP

Mode of AR

Inheritance

S. Bil. < 4

Keratitis (\( \text{C} \))

Mortality not ↑

Inv.

Liver Biopsy

Black Pigmentation

(EPINEPHRINE metabolite (\( \text{N} \))

Excreted by MRP2)

BSP clearance

test

(Bron sulfadine)

IV. BSP → Liver

\( \text{(HRP2)} \times \)

GIT

IVBSP → BSP

\( \text{O} \) BSP clearance ≤ 90 min

Delayed clearance

*\( \text{HRP}_2 \text{ absent, hence no clearance of BSP} \)
RX not Req.  Not Req.

Q. 5 feature will suggest cause of I of unconjugated
Bil except -

a) GB pigmented stones (H. anaemia) True
b) Pls -> spheroocytes (H. anaemia) True

c) Acute hep c viral infection Enzyme ↑ + conglut.
d) H/o gout. True (Probemid)

ACUTE VIRAL HEPATITIS

called by hep A to E

Hep A. Hep B

B Mode of - H/o Feco-oral Feco-oral
Transmission.

Transmission to - common rare

Close contact community spread

New epidemic in community

Rare - Blood Transfusion Vertical

Viremia during late incubation period

Sexual

Not a mode Vertical BT

Transmission Sexual
Hep A

c/E M/C cause of Ac. Viral Hep in children

[H/c of Viral Hep - B]

Relapsing Hepatitis
2 clinical episodes by same virus in acute phase (<6 months)

Inv.

Serology IgM Anti - HAV = Acute Hep A infect
IgG Anti - HAV = Pt is immune

Possibilities
· Post vaccination ✓
· Remote recovered past infect ✓
· Chronic infection. x
   (Virus B > 6 months)

Complications
3) Fulminant hepatitis - 0.1%
   (Encephalopathy < 2 wk of jaundice)

Hep E

M/c of Ac. Viral Hep in adults

[H/c of Viral Hep in Q = B]

Cholestatic hepatitis
Swollen hepatocytes cause obstruction to intrahep bile flow
[ALP also P]
2) Chronic Hep 0% 0%
    (Viral +ve for >6mths
    + Liver damage (2))

3) Carcinex 0% 0%
    (Virus + >6mths
    Liver damage (3))

LMR Topic

Hep B

Mode of

Transmission

↓
Mother HbeAg+ AntHCe Ab
↓
Risk - 90% Risk - 10%
↓
Needle > BT

Hep C

Mode of

Transmission

↓
Needle BT

↓
6-30% Risk 1 in 2day of
viability of virus BU transfused
↓
M/C BT related virus (B)

↓
Needle IV drug 0.6%
↓
accidental 0.3%
↓
BT 1 in 22 day
Some donors have low levels of HBsAg and are NOT detected by routine lab methods.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical</td>
<td>5% Hk</td>
</tr>
<tr>
<td>Sexual</td>
<td>5% Hk</td>
</tr>
</tbody>
</table>

**Rare, MoJ**
- Secreted into saliva = Yes
- Human bite = Yes

**Not MoJ**
- Virus secreted into:
  - Stool = Yes
  - Feces - oral transmission (destroyed in stomach)

- Breast milk secreted = Yes

- Secreted:
  - All are transmitted by blood except:
    - Hep A
    - Hep B
    - Hep C
    - Hep E
    - HIV
    - G...
Q. All cause AVH, transmitted by blood except
   a) Hep A
   b) B
   c) C
   d) G. → never cause AVH.

Q. Mode of transmission of Hep B
   1) Vertical vs Horizontal
   2) Vertical vs Percutaneous vs Sexual vs Human Bite

Q. Hep B not transmitted by
   a) Saliva
   b) Semen
   c) Feco-oral
   d) Breast feeding

\[
\begin{array}{|c|c|c|}
\hline
\text{Hep B} & \text{Hep C} \\
\hline
\text{HCC of viral cause of HCC} & \text{HCC viral cause of cirrhosis} \\
\text{Express HBxAg} & \text{[HCC of cirrhosis = Alcohol]} \\
\text{p53} & \text{Viral replication} \\
\text{HCC viral cause of chr. Hep} & \text{HCC AVH leading to chr. Hep.} \\
(Prevalence wise) & \text{or}
\text{Max. Risk of chronicity} \\
\text{HCC of carrier} & \\
\hline
\end{array}
\]
Serum sickness like illness

Insulin Resistance by

Joint pain + rash

↑ Risk of T2DM

In children = LN + Hepatomegaly

+ Rash

Gianotti-Crosti Syndrome

*Serology of Hep B Infection*

1) If Hep B limited to Acute phase only.

![Diagram showing serology of Hep B infection with stages and lab detection](http://mbbshelp.com)
2) If hep B converted to chronic infection

![Graph showing HBsAg and IgG over time]

<table>
<thead>
<tr>
<th>Phase</th>
<th>Marker</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>HBsAg, HBeAg.</td>
</tr>
<tr>
<td>I.P.</td>
<td>Earliest marker of HBsAg.</td>
</tr>
</tbody>
</table>

2) Acute (symp)  
Hep B infection  
HBsAg, Ig M Anti HBe  
Most reliable marker of Ac Hep B infection.

3) Window period  
Ig M Anti HBe

4) Recovery period  
Ig M Anti HBe, Anti HBs  
of Ac Hep B

5) Remote past infection  
Ig G, Anti HBe, Anti HBs +  
(disappear after year?)

6) Chronic infection  
HBs Ag + Ig G Anti HBe.
Carrier 
Bx Liver Damage Liver Damage +  Fibrotic Nodules
Chronic Hepatitis 
Chronic Hepatitis Cirrhosis

HAI (Histological Activity Index) ≤ 3

≤ 3
Active
Replication +
DNA Copy ≥ 1000/ml

Replication markers:
1. Quantitative marker → DNA copies
2. Qualitative marker → HBe Ag.

Exception: Pre-core mutants of Hep B virus

Inability to make HBeAg but replication is +

DNA HBeAg
1. + 2. + 3. -

Replicative phase of Hep B virus
Pre-core mutants of Hep B
Non-replicative phase
Serology of Hep C Infection:

1) If Hep C limited to Acute phase only

2) If Hep C converted into Chronic infection
Complication

Hep B

Hep C

0.1 - 1%

0.1%

0.1 - 10%

85%

0.1 - 30%

1.5 - 3.2%

Hepatitis

Carrier

State

Mean - 15%

Mean - 2.5%

Hep D

Mode of transmission -

1. Percutaneous (Non-endemic zones)

2. Close contact (Endemic zones)

QF-

1. N/c AVH leading to fulminant Hepatitis D

or max risk

2. Always associated with Hep B

Serology

1. Co-infection: Acute hep D + Acute hep B

IgM Anti-HDV IgM Anti-HBC

2. Superinfection: Acute hep D + Chronic hep B

IgM Anti-HDV IgG Anti-HBC

3. Comb

0. Fulminant Hep. 5% in co-infection.

20% in superinfection.
1. Chn. Hep: Depend on Hep B.
2. Carrier:

T/T
3. AVH

- Supportive care (mostly self-limiting).
  - IV fluid of choice = Dextrose at hypoglycemia rate.
  - Hct. Dextrose Req. = 150 g/day.

If 5% D$_x$ = 3000 mL/day
(5g/100mL)

If 10% D$_x$ = 1.5L/day, → Fluid of choice

If 25% D$_x$ = 600 mL/day, → May cause thrombophlebitis.
  - Not used for maintenance.
  - Reserved for emergency.

2. Antivirals for Acute Hep C

- Interferon α, 12-24 Wks

III Chronic Viral Hepatitis

- Approach to Chn. Hep B infection
Non-cirrhosis

SAPT

Compensated

Liver failure

Sign

<2 times upper normal

HIV DNA

Anti-viral

DNA > 2000

LT

Liver biopsy

Observation

Anti-viral

HAI

HBeAg

DNA +

Anti-viral if > 20,000 IU/ml in HBeAg

if > 2000 IU/ml in HBeAg

(Pre-core mutants)
Anti-viral for Hep B

1. Initiate with Monotherapy from 1st Line agents

2. Interferon α -
   - Oldest
   - Less effective in Cirrhosis

3. Entecavir -
   - Most potent
   - More effective in lamivudine resistant cases

4. Tenofovir → DOC
   - Safest & effective even in Lamivudine R cases
   - Duration > 1 yr

II. Chronic Hep. C Infection

Non-Cirrhosis

Start Anti-viral if

1) HCV-RNA detectable

2) Bx - mod-sev hepatitis compensated → Decompensated
   \[ HA1 > 3 \]
   \[ Anti-viral \]
   \[ LT \]

Anti-viral for Hep C

Initiate with Dual therapy (oral combination therapy)

INFα → outdated nowadays
Sofosbuvir + Velpatasvir → effective in all 6 genotypes

Sofosbuvir + Daclatasvir

Duration - 12 wks. for all genotypes

FATTY LIVER

↓

Alcoholic Liver Disease

Patho
- Dose → 40-80 g/d = fatty liver
- 80-160 g/d = cirrhosis
- Duration 10-20 yr.

Dose ↓ 1/2 half

Stages
1. Fatty Liver
   Mechanism
   - Ethanol
   - FA metabolism
   - Transaminase

2. Hepatitis
   - TNFα
   - IL + enzymes

Non-Alcoholic Liver Disease

Patho
- Dose of → 0-20g/d.
- Alcohol

Cause - Insulin Resistance

Stage
1. Fatty Liver
   - TG deposit
   - Insulin Resistance
   - Lipolysis → free FA

2. Hepatitis
   - Oxidative injury
3. Cushing's

Stellate cell

Chc. Hepatitis

C/FE

1) Peripheral Neuropathy
   i. Pure sensory
   ii. Direct alcohol
   iii. Effect of alcohol induced by alcohol

2. Zieve's Syndrome
   Deep jaundice due to additional effect of haemolysis induced by alcohol

RBC: Irregular Acanthocytes

Q. C/FE suggest alcohol as a cause of Cushing's
   a. Spider angiomata due to catabolism in liver
   b. Gynaecomastia
   c. Loss of deep tendon reflex
   d. Ascites

I/X

1. SGOT > 2 Highly specific
   SGPT for ALB

2. SGOT ≤ 1
   SGPT
   (SGPT synthesis needs pyridoxine)
2) \( \gamma GT \rightarrow \uparrow \)
   Site = Bile duct + (ER)
   Fat squeeze ER to release \( \gamma GT \).

3) Peripheral Neutrophilia +
   TNF\( \alpha \) Recruits
   if neutrophilia > 5500/mm\(^3\)
   Poor Prognosis

Rx

0) Fatty Liver = Reversible after cessation

2) Hepatitis: Doc. Steroid
   act on TNF\( \alpha \)
   Indication if MADDREY's
   alcoholic duodenum function >32
   \[ = 4.6 \times \left( \frac{PT \ of \ pt \ - \ PT \ of \ control}{12 \ sec} \right) + S. \ Bil \]

B) Cirrhosis
   Best Rx = Liver Transplant
   Liver Transplant

Recurrence of 1st disease
after LT = Nil if underlying cause remains treated
AUTOIMMUNE

Autoimmune

1° Biliary Cirrhosis

Hepatitis

Patho

- Direct Ab damage to hepatocytes
- Autoimmune process of interhepatic bile ducts
  (Type II, MCT)
- Bile duct damage
- Bile accumulation
- Damage hepatocytes

C/F
♀

Age
20-30 yrs
40-60 yrs

Recurrent
(Heur over years)

Pruritus

(Cholestasis)

Inv Ab depend on type of

ATH
MCT

MC/Host sensitive/Host specific

Assess
(1)
MCT
(ANA) Host sensitive

Ab ➔ Anti mitochondrial Ab

Ab ➔ Smooth ms cell

P-ANCA

(II)
Anti LKM (Liver Kidney)
Microsome
(also +ve in Hep C Infection)

(III)
Least common, most severe
Ab ➔ Liver soluble antigen

Most specific
### Wilson's Disease vs. Hemochromatosis

<table>
<thead>
<tr>
<th>Wilson's Disease</th>
<th>Hemochromatosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patho</strong> AR mut(^n) of ATP7B</td>
<td>AR mut(^n) of HFE</td>
</tr>
<tr>
<td></td>
<td>↓</td>
</tr>
<tr>
<td>↓ Cu excretory protein in liver</td>
<td>↓ Hepcidin([\text{up regulating} Fe absorption})</td>
</tr>
<tr>
<td></td>
<td>↓ Fe absorption</td>
</tr>
<tr>
<td>Cu overload in the body</td>
<td>Fe overload</td>
</tr>
<tr>
<td><strong>QF</strong> Liver</td>
<td>Most common site Liver</td>
</tr>
<tr>
<td>age &lt;20yr</td>
<td>&gt;40yr</td>
</tr>
<tr>
<td>Choreatic Hepatitis</td>
<td>+</td>
</tr>
<tr>
<td>Eunodonal Macronodular</td>
<td>Mixed or Macronodular</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>+ HEC</td>
<td>+ (M/c cause of death even in old pt.)</td>
</tr>
<tr>
<td>2° Mayan CNS</td>
<td>CNS</td>
</tr>
<tr>
<td>affected Basal Ganglia</td>
<td>Hypothalamic pituitary astra</td>
</tr>
<tr>
<td>M/c CNS Tremor</td>
<td>Hypogonadism</td>
</tr>
<tr>
<td>manifestation</td>
<td></td>
</tr>
</tbody>
</table>

- Frontal lobe
  "neuropsychiatric abnormality."

- Cr. NV → XII (M/c Cr. NV affected) (Dysarthria) |
- Autoimmune dysfunction |
- 2° Postural Hypotension |

- Not affected -1. Sensory system |
  2. Motor power (Pyramidal pathway) |

- 3° Colour Change |
  - Eye |
  - 1. Daytime vision = sunflower cataract |

- Kayser-Fleischer Ring (0) |
- (Viron N) |

- Skin |
  - due to Fe + melanin deposits |
  - Bronze Pigmentation |

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4. Functional Effect
   - Kidney
     - Proximal Tubular Dysfunction
     - RTA - 2
     - Fanconi Syndrome
     - Pancreas
       - β cells affected
       - BronyDM
         - * Reversible after 1/4 of haemochromatosis under other

5. Structural Damage
   - RBC Membrane
     - Haemolytic Anaemia
     - Joints (3rd MCP j)
     - Fe in joints (P) Pyrophosphate
       - Ca Pyrophosphate
         - Pseudogout

6. ×
   - CVS - Fe infiltrate inside myocyte
     - Hypo myocyte relaxation
       - Contraction ↓
     - DCM P > ICMP
       - M/c cause of death → CVS
       - in untreated pt.

Inv
   - Free Cu + Apoceruloplasmin
   - Ceruloplasmin (Bound Cu)
<table>
<thead>
<tr>
<th>Binding of free Cu</th>
<th>1. S. Fe → ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>apo ceruloplasmin</td>
<td>2. % Transferrin → ↑</td>
</tr>
<tr>
<td>1. S. Free Cu → ↑</td>
<td>Saturation</td>
</tr>
<tr>
<td>2. S. ceruloplasmin → ↓</td>
<td></td>
</tr>
<tr>
<td>3. S. Total Cu = ↓</td>
<td></td>
</tr>
<tr>
<td>(mainly in bound form)</td>
<td></td>
</tr>
<tr>
<td>4. Urinary free Cu levels → ↑</td>
<td></td>
</tr>
<tr>
<td>5. Bx - Liver Cu &gt; 200 μg/g</td>
<td></td>
</tr>
<tr>
<td>dry liver wt</td>
<td></td>
</tr>
<tr>
<td>6. Bx → ↑ Fe.</td>
<td></td>
</tr>
<tr>
<td>Prussian Blue Stain</td>
<td></td>
</tr>
</tbody>
</table>

**Rx**

- Hepatitc → Zn (Doc) [5mg tid]

**Cu absorption**

- 1ml Blood will remove → 0.5mg Fe
- Single phlebotomy → 500ml Blood (250mg Fe removed)
- Fe overload >20g
- 80 phlebotomy Req.

**2) Cirrhosis**

- According to NAZER SCORE
  - SGOT
  - S. Bil
  - PT.
  - <7 7-9 >9

- Zinc +
- Thiamine
  - PT will be lifelong
- Recurrence after LT → rare <10%

- LT
  - Recurrence after LT → NIL
  - Heavy
Q. S cause ↑ Cu in Liver → KF rings -
(a) autoimmune cholangitis
(b) 1st Biliary cirrhosis → CHF. Cholestatic condition
(c) 1st sclerosing cholangitis
(d) All

Q. After phlebotomy manipulation of haemochromatosis ?

- Reversible
  - Hepatomegaly
  - Skin pigmentation
  - Diabetes
  - CHF
- Irreversible
  - Cirrhosis
  - Arthritis
  - Hypogonadism

Q. HFE mutation ↑ risk of C cancer = Breast, colon cancer

Complications of liver failure

17. Hepatic Encephalopathy

Mech. ↓ Urea cycle
↑ NH₃
Astrocyte Damage

CF - West HAVEN's grading
Restlessness I  Early symptom = altered sleep cycle
     " sign = altered handwriting (constitutational apraxia)

Drowsiness II

Stupor III  Join to ① to ⑵ numbered circle

Coma IV

Deep coma V

Inv

EEG → ① most characteristic
     " = suppression, large amplitude waves
     (Grade II IV)

② S Wave – Grade V
     (1-4 Hz)

Rx

① Rx ①ppt cause
     Mech.
     Rx

② GI injection ① bacterial proliferation ① Ab of Choice
     Azithromycin
     (500 mg BD)

③ Upper GI Bleed ① blood protein ① Vital signs → Ryle’s tube
     (Ruptured perforated
     volvulus) ① Mech.
     (gut bacteria ① ↑ NH₃

Rc → Endoscopic Band Ligation of Varices
Doc → Octreotide
2° prophylaxis = β blocker
(never in acute bleed)

3. S. K⁺↓
   1. Peristalsis
      2. P. E. KCl Infusion
      10-20 mEq/hr
   → Bacterial Propagation

4. Metabolic
   NH₃ + H⁺ → NH₄⁺
   Alkalosis
   (toxic) (non-toxic)
   → if pH↓ → eq. shift to B
   (H⁺ loss)
   if pH↑ → eq. shift to C

5. Constipation
   Bacterial Propagation
   → Laxative of choice 2
   Lactulose
   Cause acid pH.
   → Target 2-3 stools/day
   Otherwise may cause diarrhea.

6. Hypovolemia
   ↑ Renal → Aldosterone
   CI → RL
   Lactate
   S. K⁺↓ + → Liver
   Met. alkalosis
   HCO₃⁻
   Met. alkalosis
   So, IV fluid → NS
ASCITES

Mech. → sinusoidal pressure (compression by nodules)

Na & H₂O retention →

↓ NO synthesize (↓ degraded in liver)

↓ NO

Systemic vasodilation
(Blood pooling in systemic circulation)

Pulmonary vasodilation

↓ Hepato-Pulmonary syndrome

Hepato-Renal Syndrome

* C/F. Sign

↓ Min fluid needed

Mint PUDDLE ← 120 mL

Shifting dulleness ← 500 mL

Fluid thrill ← 1500 mL

* Inv. Ascite fluid

- Preferred site → L lower quadrant

- Needle size = Diagnostic 20-22G
  Therapeutic 15G
Step 1: Albumin - Ascitic Albumin (SAACh)

- < 1.1
  - Sinusoidal Pressure
    - Nephrotic Syndrome
  - Ascitic Albumin ↓
  - Peritoneal Venel Permeability
    - TB Peritonitis
    - Cancer
    - Acute Pancreatitis

- > 1.1
  - Sinusoidal Pressure
  - Ascitic Albumin ↑
  - Portal Vén.

Diagram:
- Hep. Vein
- Vénules
- Sinusoids
- NCPF
- EHPVD
- Heart
Step 2 - Ascites Total Protein ≤ if SAAG > 1.1.

- Cirrhosis
- Non-cirrhosis
  - Post-hepatic obstruction
  - > 2.5
  - Ovarian disease
  - Budd-Chiari
  - IVC obstruction
  - CHF/constrictive pericarditis

Fibrosis

- H₂O/Alb small
- Sinusoidal
- H₂O/Alb small protein
- Peritonitis

Rx Grade

I = Mild Ascites
- No clinical signs
- Salt restriction

II = Moderate
- Clinical signs +ve
- Add diuretics
- Respiratory distress - spironolactone (max = 400 mg/day)

- Furosemide (max = 160 mg/d)

III. Severe
- Resp. Distress +
- Large vol. paracentesis (5-6 L removed)

IV. Severe
- Resp. Distress +
- Large vol. paracentesis (5-6 L removed)
- I.V. albumin (to replace serum fluid)
<table>
<thead>
<tr>
<th>TV Refractory</th>
<th>No Response</th>
<th>Sans A Grade III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 7 days</td>
<td>Max dose of 1</td>
<td>Both diuretics</td>
</tr>
</tbody>
</table>

5) Non-Cirrhotic Portal Fibrosis

<table>
<thead>
<tr>
<th>Event</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&gt; 20 yr</td>
</tr>
<tr>
<td>J/U</td>
<td>U I bleed +</td>
</tr>
<tr>
<td>Portal HTN</td>
<td>+</td>
</tr>
<tr>
<td>Spleen</td>
<td>+</td>
</tr>
<tr>
<td>&gt; 7 cm below</td>
<td>Costal margin</td>
</tr>
<tr>
<td>Jaundice</td>
<td>+</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>+</td>
</tr>
<tr>
<td>Ascites</td>
<td>+</td>
</tr>
</tbody>
</table>

6) Extra-hepatic Portal Venous Occlusion

<table>
<thead>
<tr>
<th>Event</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt; 20 yr</td>
</tr>
<tr>
<td>J/U</td>
<td>U I bleed +</td>
</tr>
<tr>
<td>Portal HTN</td>
<td>+</td>
</tr>
<tr>
<td>Spleen</td>
<td>+</td>
</tr>
<tr>
<td>&gt; 7 cm below</td>
<td>Costal margin</td>
</tr>
</tbody>
</table>

Rx: Endoscopic band ligation +
HEPATO - PULMONARY SYNDROME

Mech. Pulmonary vasodilatation

Blood → →

O₂

Pulmonary artery dilation

If vasodilatation occurs in the pulmonary artery, mixing of deoxygenated blood on one side with oxygenated blood on the other side leads to a right-to-left shunt.

CF:

Platypnea - dyspnea ↑ on standing, dizziness, more common with shunt open

Hypoxia ↑

Inv

O₂ in O₂ saturation by 3% on standing from hypoxia

Orthodeoxia

Rx:

1) Sclerosis of dilated vessel

2) R/c = Liver Transplant
## Intestinal

### Malabsorption Diseases

Due to SI disease

- **Proximal**
  - Fe, FA, Ca, Mg

- **Distal**
  - Bile, Vit B_{12}

- Fat, Chol.
- Protein

### Tests for Malabsorption

1. **For Fat**
   - Gold std → 72-hour stool fat estimation
     - if fat excretion > 70% → Steatorrhea

   - H/C abnormality seen in Malabsorption Syndrome

2. **Spot Ix → Sudan III stain**
   - +ve if stool fat > 10%

### For Carbohydrate

1. **Host Specific Ix → Dxylose Test**

   - Cause of <4.5gms excretion
     1. Pyloric stenosis
     2. Proximal SI disease
     3. Coeliac disease
     4. Bacterial overgrowth syndrome

   - 3rd phase: Co2 absorption

   - 2.5gms Oral.

---

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5. Renal failure

(III) Vit B_{12} malabsorption

**SCHILLING'S TEST**

1. Oral radiolabelled cobalamin

2. I.M. Vit B_{12} (1 mg)

3. 24-hour urine collection

- If excretion <10% AND becomes >10% after adding.

4. I.F. → Pernicious Anaemia

5. Pancreatic enzyme → Chv. Pancreatitis

6. At x 5 days → Bacterial overgrowth syndrome

- If remains <10% → Ileum disease

7. In dietary deficiency of Bix, Schilling test (N)
Q. Mut' q cubulin  → IMERSLUND GRIEBECK'S SYNDROME

IV. Intestinal Biopsy
- Gold Std. Ix or Host Specific Ix for Malabsorption

Etiologies of Malabsorption:

<table>
<thead>
<tr>
<th>Celiac Sprue</th>
<th>Tropical Sprue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cause: GLIADIN Hypersensitivity</td>
<td>Bacterial Toxin +</td>
</tr>
<tr>
<td>(+ve in gluten)</td>
<td>Folic acid deficiency (impaired repair)</td>
</tr>
<tr>
<td>Local contact HS</td>
<td></td>
</tr>
<tr>
<td>Prox SI &gt; Distal SI</td>
<td>Distal SI &gt; Prox SI</td>
</tr>
</tbody>
</table>

YE: Age - Typical 6-12 months
- Adults

- Can occur at any age
- Spontaneous remission - 2nd decade

- Steatorrhea (large, foul smelling) → Chronic >4 weeks

- Non-inflammatory
  (No blood or pus in stool)

- Extra-intestinal manifestations:
  - Diabetic Keratopathy
  - Other - TIDM, Ig A deficiency
Invasive Sprue

1. Serology
   - Most specific Ab = Anti-endomysial Ab.
   - Most sensitive Ab = Anti-tissue Transglutaminase (TTG)
   - Most sensitive + Specific Ab/He/o But = Anti TTG

2. Biopsy
   - Loss of villi + + repairable after
   - Flat mucosa + gluten free diet
   - Lymphocyte infiltration

3. HLA DQ2 (+) in 100% case
   - HLA DQ8 but non-specific

Rx
- Gluten free diet
- Antibiotics → Doxycycline or Rifaximin

2. Steroids: Indications
   1. Refractory sprue
   2. (No response up to 12 months) of gluten free diet
   3. Celiac shock (↑ gluten load)
   4. SI lymphoma
   5. Possible cause of death
WHIPPLE'S DISEASE

1. Cause: Tropheryma Whippelii

2. 
   - Acute
   - Chronic (H8 reaction)

   1) Acute GE
      a) Me presentation = migratory
   2) Pneumonia
      Poly/oligo arthritis

3. CNS
   H/c = Dementia
   Host characteristic CNS manifestation
   Oculo-Masticatory Myorithmie
   (conv./dysng.)
   (hypnagraphe)

   Other CNS manifestation:
   - Cerbellar ataxia
   - Myoclonic seizure
   - Encephalopathy
   - P. Neuropathy

4. CVS - Pancarditis
   H/c - Pericarditis

5. Eye - Uveitis

6. Polyserositis = Ascites
   Pleuritis
Intrabiliary positive macrophage containing

D/D → TB

Bacilli
AFB -
AFB +

Rx 0 GST → Ceftriaxone (2wk) → Cotrimoxazole (1yr)

Rx 0 CNS/CVS
↑ Risk of recurrence
→ Ceftriaxone (2wk) → Doxycycline
+ Chloroquine
or
Hydroxychloroquine

Bacterial Overgrowth Syndrome
Proliferation of colonic bacteria in prox SI

Causes:

↓ Communication by

Anatomical Stenosis
Functional Stenosis
LI → SI of SI of SI
↑ Fistula Structure ↑ Intussusception
DM → Peristalsis

CF

1) Steatocholecystosis Bile is deconjugated by bacteria in SI.
Inr

1) 72 hour stool test > 6%

2) D-xylene test  
   excretion < 4.5 gm

3) Scillings test ab (0)

4) S. Folic acid level (Synthesis by bacteria is inhibited by Proc. SI mutant)

5) Lactulose Breath test or H₂ Breath test  
   +ve in Breath 2-8 hour after giving lactulose  
   at Bacteria in SI metabolite

6) Endoscopic Jejunal aspirate culture  
   +ve organism E.coli > 10⁵/ml

Rx

1) Treat underlying cause

2) Cyclic antibiotics [Co-amoxyclov]  
   Ab x 1 week
   ↓
   gap 3 wk.
   ↓
   Ab 1 wk
**Approach to Diarrhoea**

**Essential Criteria for Diarrhoea**
- Stool Vol. > 200 ml/d
- Stool wt. > 200 mg/d

**Duration**

- Acute
- Persistent
- Chronic

**Type**

- <2wk
- 2-4wk
- >4wk

90% Due to Infection > 90% due to non-infectious

**If Inflammatory Diarrhoea**

- Toxin induced
  - Inflammation induced
  - (Electrolyte + H2O secretion)
  - Exudative

- Fever
- Pus in stool
- Blood in stool

**If Toxin induced**

- Preformed
- Enterotoxin
  - I.P. 5 in hours
  - 1-2 days

1) Bacillus cereus
   - (Chinese Restaurant diarrhoea)
     - ↑ Hemo in stool - Yellow stool
   - Watery stool

1) Vibrio cholerae
2) Staph. aureus  
2) Enterotoxig E.coli
H/c of Traveler's diarrhea

3) Clostridium Perfringens

If inflammation induced

I. Mild = mucosa limited. (blood in stool G)

II. H/c Viral diarrhea in adults = Noro virus
    " " " Children = Rota virus

III. Mod. = submucosa
1) Salmonella → involve ileum
   ↓
   Bile Nekrosis
   ↓
   Bile in stools.

IV. Severe
2) Yersinia → severe ileum inflammation
   Pseudo appendicitis

E) Campylobacter J. H/c infection cause of GBS

III. Severe = Deep layer
1) Shigella → Toxic encephalopathy
   Eiki Syndrome

2) E. histolytica → flat shaped ulcer
Rx - acute/persistent diarrhea

1. Essential - Rehydration
   IV fluid of choice → RL contains mmol/l
   \[\begin{align*}
   K^+ & : 4 \\
   Na^+ & : 130 \\
   Ca^{2+} & : 2 \\
   Cl^- & : 109 \\
   HCO_3^- & : 26 \\
   \text{Osmolarity} & : 273
   \end{align*}\]

2. Antibiotics
   Indication - Mild to severe inflammatory infectious diarrhea
   If > 1 of 3 criteria:
   a) Fever > 101°F
   b) Blood in stool
   c) Pus in stool

   Empirical = Fluoroquinolone.

Chronic Diarrhea

\[\text{Non-inflammatory} \quad \begin{array}{c}
\text{eg. Malabsorption syndrome} \\
\text{Irritable Bowel Syndrome (IBS)}
\end{array}\]

\[\text{Inflammatory} \quad \begin{array}{c}
\text{LHR} \quad \text{Ulcerative Colitis} \\
\text{Topic} \quad \text{Crohn's Disease}
\end{array}\]
UC

CD

*Risk/Associated
1. Smoking ↓
2. Appendectomy ↓
3. Drugs
   OCP ↔
   Methyl dopa ↑
   Ab use 2 in 1 year ↑
4. Infections ↔
5. Turner's ↑

5. Hc = Mycobacterium
   Para TB.
   Infection & Role of CD
   H. Pylori

6. IL-10 Receptor ↑
   Deficiency

7. Anti-inflammatory
   Early onset IBD.

Cl. Intestinal
H/c site → Rectum +
   Sigmoid
   > Rectum only
H/c Isolated site – Ileum
H/c isolated site – Rectum
   Rectum is usually spared
   Site not involved → SI.
1. Malabsorption Synd. (−)

2. Bleeding PR (Teneurin) (+)

3. Fistula formation (−)

4. Toxic Megacolon. (+)
   (Dilation of colon >6 cm)

   Ulcer -> Collar Button

   ⊗ (non-erosing)

   Cobblestone Ulcer

   ⊹ (erosing)

5. Inv

6. stool exam
   Lactoferrin (+)
   correlates to disease activity

   Calprotectin (+)
   predicts/prophylactically relapse

7. Serology
   He Anti
   ANCA

   He Anti
   Sacromyelie cereverence
   Ab

   Role - ↑ risk of early complication

8. Conform Bx
Rx of Ulcerative Colitis

I. Mild to mod. severity (Stool freq. < 6/day)
   ↓
   Distal DU → Pancolitis
Doc. - Per Rectal ASA → Oral ASA
Mesalamine → Mesalamine + Sulfasalazine

If no response in 4 weeks:
   Oral steroid therapy

II. Severe IBD (Stool frequency > 6/day or shock).
   Doc. - I.V. Steroid
   ↓
   Steroid responsive → Taper & Stop steroid
   Steroid resistant
   Steroid dependent (No response in 5 days)
   → Taper & Stop
   ↓ Steroid sparing agent
   TNF α Ab or Cyclosporine
   Agathistidine
   ↓ if unresponsive
   only for CD - Anti-Integrin
Only in Crohn’s Disease (Resistant)

Integrin (β) helps in vascular adhesion

Lymphocyte

Ab against β₃ & β₇ = NATALIZUMAB.

(Less in Multiple Sclerosis)

S/E → Reactivate TC Vom

Progressive multifocal leukoencephalopathy

Ab against β₇ = VEDOLIZUMAB

Rx of Crohn’s Disease

I. Mild to Mod. IBD

Disease limited

Doc: 5-ASA, Laxatives

Budesonide

Small intestine

Doc: Prednisolone

no response → 4 weeks

Methotrexate

* Miscellaneous Points

1. The cause of death → Cancer

2. Colon cancer risk → Ulcerative Colitis → Crohn’s Disease
3) Colon & Rectum (C & R) → Folic acid, A & A agents

4) Extraintestinal Manifestation of IBD (usually more in CD)

- Correlated to Bowel activity
- Independent of Bowel activity

Skin:
- Erythema Nodosum (red, hot, tender, nodules on shin)
- N - Neutrophil Infiltration
- N - Non-infective
- N - Necrosis of skin
- Pyoderma Gangrenosum

Joints - Migratory Polyarthritis, Ankylosing Spondylitis (Peripheral joints)

Eye - Episcleritis, Uveitis

Liver - Non-alcoholic fatty liver disease (Fatty liver, Dilate Liver, Sclerosing Cholangitis, Risk factor for Cholangio carcinoma)

Q. H/C extra-intestinal organ affected in IBD - Joints

Q. H/C " " manifestation → Erythema Nodosum

Q. C " " " more in UC → Pyoderma

1° Sclerosing cholangitis
Addison Harrison selected.

Part I → Involuntary ur. loss → Dehydration → Inv (Table)

Ascites

Table of cause of diarrhea

Part II - Table of I/II of Hepatitis C
(exclude dose or regimen)

Table of Intestinal biopsy findings:

Protein losing enteropathy
(1st 2 para - causes)

Inv