LUNG MECHANICS

Airways Resistance

- ***Measurement at 30 l/min***

a.	awake		~ 0.6-3.2	$cmH_2O/l/s$	
b.	paralysed		~ 6.0	$cmH_2O/l/s$	
c.	partially paralysed + ETT		**~ 10-15**	$cmH_2O/l/s$	(AB says 5-10 $cmH_2O/l/s$)
d.	PEFR	males	~ 450-700	l/min	
		females	~ 300-500	l/min	
e.	FEV_1		~ 50-70	ml/kg	
			≥ 70%	of FVC	

- ***Factors***

a.	airway narrowing		- oedema, congestion - inflammation, FB, etc.
b.	lung volume		- expiration > inspiration - closing volume
c.	posture		- supine FRC ≤ CC
d.	neural factors		
	i.	constriction	- smoke, dust, chemicals - hypoxia, hypercarbia, hypothermia - pulmonary emboli - ↑ PNS activity
	ii.	dilatation	- systemic hypertension - inspiration - ↑ SNS activity
e.	hormonal factors		- catechols, histamine, PG's, leukotrienes
f.	drugs		
	i.	constriction	- histamine, methacholine - alveolar hypocarbia - ACh-esterase inhibitors - anaphylactoid reactions
	ii.	dilatation	- catechols (β_2-agonists) - PDE inhibitors, aminophylline - anticholinergics - steroids - volatile anaesthetic agents - nitric oxide

- ***Anatomical Site***

a. nasal passages ~ 50%
b. larynx ~ 25%
c. large airways ~ 15%

NB: airways resistance is maximal at ***segmental bronchioles***,

→ ≥ 5th generation / ≤ 2mm

Lung Compliance

Def'n: the change in ***lung volume*** per unit change in ***transpulmonary pressure***

	Static		Dynamic	
Posture	Lung	Respiratory	Lung	Respiratory
Upright	200	100	180	100
Supine	150			
GA & NMB'd	100-150	**75**	80	55
* all values in ml/cmH_2O				

- ***Factors Affecting Static Lung Compliance***

1. ↑ FRC → ↑ C_L
   i. age
   ii. body size
   iii. posture
   - *see below factors affecting FRC
2. ↓ lung volume → ↓ C_L
   i. lobar, lung resection
   ii. collapse or consolidation
   iii. diffuse atelectasis
3. changes in lung ***elasticity***
   i. ↑ lung elasticity - emphysema
   ii. ↓ lung elasticity - pulmonary oedema, congestion, fibrosis

- ***Nunn: Lung Compliance***

1. lung volume - absolute and relative
2. posture
3. pulmonary blood volume
4. age
5. restriction of chest expansion ? this is chest wall C, not lung
6. recent ventilatory history * ***monotonous ventilation***
7. pulmonary disease

- ***Factors Affecting Dynamic Lung Compliance***

1. airways resistance
2. respiratory rate
3. peak flow rate & inspiratory time for ventilated patients
4. autoPEEP

- actually should refer to ***time constant***, $\tau = R \times C$
- the concept of dynamic compliance is flawed, as it is ***resistance & flow rate dependent***
- resistance includes in its definition the time frame ($cmH_2O/l/s$), compliance ***does not***
- ergo, compliance should be ***time independent***, but dynamic compliance is not

- ***Factors Affecting Chest Wall Compliance***

1. muscle tone and phase of respiration
2. diaphragmatic movement
   i. neural input
   ii. muscle performance, fatigue
   iii. abdominal hypertension - pregnancy, ascites, obesity
3. chest wall diseases
   i. spine & costo-vertebral joints
   ii. obesity
   iii. pleural disease, space occupying lesion
   iv. skin & overlying tissues

- ***Factors Affecting FRC***

1. body size - FRC ∝ height (~ 32-51 ml/inch)
2. sex - females ~ 90% of male FRC (≡ height)
3. age - Nunn → ***no correlation*** !
   - others have shown small increase
4. diaphragmatic muscle tone
   - originally, FRC believed to represent equilibrium for lung/chest wall system
   - diaphragmatic tone maintains FRC **~ 400 ml *above*** true relaxed state

   → ↓ FRC with anaesthesia / ventilation
5. posture → ↓ FRC in the supine position ~ 0.5-1.0 l
6. lung disease
   - consolidation, collapse, atelectasis → ↓ FRC
   - ↑ blood volume, alveolar oedema → ↓ FRC
   - loss of lung ER with emphysema → ↑ FRC
   - increased expiratory resistance → ↑ FRC
7. chest wall
   - increased abdominal contents → ↓ FRC
   - pleural space occupying lesion → ↓ FRC
8. alveolar-ambient pressure gradient
   - PEEP increases the FRC

Closing Volume

Def'n: lung volume in which closure of dependent airways begins, or more precisely, lung volume in which dependent lung units cease to contribute to expired gas,
ie., the beginning of ***phase IV*** of the washout curve to RV
normal values ~ 15-20% of VC, ie. a part of the VC manoeuvre
~ 10% of the FRC in a young adult
~ 40% of FRC at 40 years of age

this is distinct from ***closing capacity***, which is the difference between the onset of ***phase IV*** and zero lung volume = CV + RV, expressed at a % of TLC

- measured by either a ***bolus*** or ***resident gas*** technique,

1. ***bolus technique***
   - originally xenon or argon, usually now ***helium***
   - inspiration from RV to TLC creating differential tracer gas composition
   - apical areas contain most of the gas cf. bases
2. resident gas technique
   - also dependent upon a pre-expiration concentration gradient, but
   i. N_2 already present, and
   ii. normally little difference in [N_2] between apex & base at TLC
   - therefore, inspiration of O_2 is used to dilute the already present N_2
   - this results in an apical to base concentration difference of ~ 2x
   - may result in smaller values cf. bolus technique in the presence of asthma or bronchoconstriction, probably due to air trapping (??)

NB: → single breath (100% O_2) ***nitrogen washout***

→ ***4 phases*** I dead space
II transitional zone
III alveolar plateau (~ 1.5% rise)
IV closing volume

- as CV represents a portion of the VC manoeuvre, it is usually expressed as a percentage of such
- expiration must be performed ***slowly*** to prevent ***dynamic*** airways collapse ~ 0.5 l/sec
- changes in CV may represent small airways disease, or loss of elastic recoil and parenchymal supportive tissue
- loss of elastic recoil results in the gradual increase in CV with age, such that at 65 yrs CC > FRC
- young children similarly have decreased elastic recoil & relatively increased CC's
- minimal values for CV/CC are seen in late the late second decade
- sensitive marker of early dysfunction, but difficulty defining normal limits

NB: ***closing capacity*** ~ FRC in the supine position at 6 & 44 years

- ***Factors***

• CV is increased by,

1. age
2. smoking
3. lung disease

• ***tidal volume*** encroaches upon CV in,

1. children < 6 years of age
2. adults progressively over the age of 45
3. where FRC is decreased
   - obesity
   - pregnancy
   - postoperatively
   - paralysed/ventilated without PEEP
   - ascites
4. most lung diseases

Pulmonary Dead Space

Def'n: ***Anatomical:*** that fraction of the inspired gas volume which,
is contained in the ***conducting airways***,
is ineffective in arterialising mixed venous blood, and
is exhaled unchanged at the beginning of expiration

Alveolar: that fraction of the inspired gas volume which,
enters the ***alveoli***, but
is ineffective in arterialising mixed venous blood

Physiological: alveolar + anatomical dead space

- ***Factors Affecting Anatomical Dead Space***

1. body size
2. age
3. lung volume
4. posture
5. drugs - bronchodilators / bronchoconstrictors
   - anaesthetic agents
6. lung disease - emphysema, asthma, CAL
7. IPPV
8. flow pattern - high flows and turbulence increase V_D

- ***Additional Factors Affecting Alveolar Dead Space***

1. blood volume
2. pulmonary artery pressure
3. lung disease
4. IPPV including waveform and PEEP
5. anaesthesia
6. respiratory rate and minute volume
7. oxygen - rise in P_{AO2} vasodilatation & increased V_D

Bohr Equation (1891)

$$\frac{V_D}{V_T} = \frac{F_{ACO_2} - F_{\bar{E}CO_2}}{F_{ACO_2}}$$

- originally used to measure F_{ACO2}, using estimates of V_D^{Anat} from autopsy cast specimens
- not used to estimate V_D^{Anat} until the ***constancy of alveolar air*** was established by Haldane and Priestly (1905)
- following this,

1. F_{ACO2} is estimated from $ETCO_2$ with a rapid gas analyser
2. the mean expired concentration from a Douglas bag

- this estimated anatomical V_D as $ETCO_2$ estimates mean, not "ideal" alveolar CO_2
- subsequently modified by Enghoff to estimate total, or ***physiological*** $\mathbf{V_D}$, viz.

Enghoff Modification (1938)

$$\frac{V_D^{Phys}}{V_T} = \frac{P_{aCO_2} - P_{\bar{E}CO_2}}{P_{aCO_2}}$$

Ventilation/Perfusion Relationships

Causes of Non-Uniformity		
	Perfusion	Ventilation
Physiological	• gravity • PA pressures • posture • exercise	• airway closure (FRC < CC) • V vs. Q mismatch • posture
Pathological	• hypovolaemia • hypervolaemia, LVF • embolism • regional ↑ PVR • PEEP • drugs	• exaggeration of above • regional compliance differences • regional airway resistance change • collapse, consolidation • mucosal oedema, plugging • diffusion block

Assessment	
Perfusion	Ventilation
• CXR • lung scan • spiral CT + contrast • pulmonary angiography • Xe^{133} washout • calculation of V_D/V_T • $P_{a\text{-}ET}CO_2$ difference	• clinical assessment • CXR • single breath N_2 test • N_2 washout • Xe^{133} • venous admixture • $P_{A\text{-}a}O_2$ difference • pulmonary function tests

■ ***The Shunt Equation***

$$\frac{\dot{Q}_S}{\dot{Q}_T} = \frac{C_{c'O_2} - C_{aO_2}}{C_{c'O_2} - C_{\bar{v}O_2}}$$

Alveolar-Arterial Oxygen Tension Gradient

Def'n: normal $P_{A\text{-}aO2}$ £ **20 mmHg**

• where the P_{AO2} is given by the alveolar air equation, simplest form,

$$P_{AO_2} = P_{iO_2} - \frac{P_{aCO_2}}{R}$$

• rearranging the shunt equation,

$$Q_S/Q_T = (C_{cO2} - C_{aO2}) / (C_{cO2} - C_{mvO2})$$

$$C_{aO2} = C_{cO2} - (C_{a\text{-}mvO2} \times Q_S / [Q_T - Q_S])$$

also, $C_{aO2} \sim ([Hb] \times 1.34 \times S_{aO2}) + (0.003 \times P_{aO2})$

- therefore, the $\mathbf{P_{A\text{-}aO2}}$ is dependent upon,
    1. $_{FI}O_2$ and P_{AO2} - hyperbolic relationship
    2. mixed venous P_{mvO2}
    3. cardiac output - inverse relationship
    4. DO_2 & VO_2 - linear relationship
    5. pulmonary shunt - linear relationship
    6. minor factors
        i. [Hb] & position of dissociation curve
        ii. respiratory quotient
        iii. hypovolaemia

Pulmonary Gas Exchange

- O_2 diffusion is dependent upon,
    a. F_IO_2
    b. alveolar ventilation
    c. effective alveolar/capillary exchange area
    d. effective diffusion distance
    e. pulmonary capillary blood flow
    f. mixed venous Hb saturation
    g. position of Hb-O_2 dissociation curve

- normal Hb "fully" saturated in **0.3 sec**, with a normal transit time of 0.75 s
- factors affecting diffusing capacity,
    a. increased diffusion path length
    b. decreased area - definition of emphysematous lung disease
    c. posture - increased in supine position
    d. exercise

CO_2 Transport

- ***Content***

a.	arterial	~ **49**	ml/100ml	
b.	mixed venous	~ **53**	ml/100ml	
c.	added to capillary blood	~ 3.75	ml/100ml	
	• by where,			
	i. plasma	~ 2.35	ml/100ml	**65%**
	ii. rbc	~ 1.4	ml/100ml	35%
	• by form,			
	i. CO_2 as HCO_3^-	~ 2.43	ml/100ml	**65%**
	ii. carbamino Hb	~ 1.0	ml/100ml	26%
	iii. dissolved CO_2	~ 0.3	ml/100ml	8%
	iv. carbamino plasma protein			< 1%

- ***Haldane Effect***

Def'n: the shift of the Hb-**C**O_2 dissociation curve with variations in the SaO_2

- effectively reduces the rise in P_{aCO2} in venous blood, thereby limiting the fall in mixed venous pH

	Arterial	Mixed Venous
$\mathbf{P_{CO2}}$	40 mmHg	46 mmHg
$\mathbf{C_{CO2}}$	49 ml/100ml 22 mmol/l	53 ml/100ml 24 mmol/l
pH	7.4	7.37
$\mathbf{P_{O2}}$	100 mmHg	40 mmHg
$\mathbf{S_{O2}}$	97.5%	74 %

- ***Effects of Hypocapnia***

1. ↑ TPR
2. cerebral vasoconstriction
3. placental vasoconstriction
4. ↓ cardiac output
5. ↓ ICP
6. ↑ pain threshold
7. hypoventilation
8. respiratory alkalosis
9. ***left*** shift of the HbO_2 dissociation curve
10. hypokalaemia → ICF shift
11. ↓ HCO_3^- reabsorption by the kidney
12. ↓ plasma ionized Ca^{++} → tetany

- ***Effects of Hypercapnia***

1. cerebral vasodilatation
2. ↑ ICP
3. ↑ CNS sympathetic outflow
4. ↑ cardiac output & BP - indirect effect
5. direct depressant effect upon the CVS
6. cardiac arrhythmias
7. hyperventilation
8. respiratory acidosis
9. ***right*** shift of the HbO_2 dissociation curve
10. hyperkalaemia
11. ↑ HCO_3^- reabsorption by the kidney

CONTROL OF VENTILATION

- ***Feedback Mechanism***

1. sensory mechanisms - central / peripheral
2. central integration
3. effector systems

- ***Brainstem Influences***

a. carotid and aortic chemoreceptors - P_{aO2} / P_{aCO2} / pH

b. central CSA
- P_{aCO2}
- CSF pH

c. cerebral blood flow

d. lung reflexes
   i. Hering-Breuer reflex - ***inhibito***-inspiratory reflex
   ii. paradoxical reflex of Head - inspiratory triggering
   iii. chest wall/parenchymal reflexes

e. muscle spindles
- respiratory muscles
- ***not*** diaphragm

f. carotid and aortic baroreceptors

g. thoracic chemoreceptors

h. peripheral receptors
- pain
- temperature
- mechanoreceptors

i. cerebral cortex
- emotion
- voluntary control
- speech

j. reticular activating system
- SNS
- olfactory sense
- speech

k. hormones - progesterone

l. drugs - almitrine, ? aminophylline

- ***Peripheral Chemoreceptor Stimulation - Factors***

a.	ischaemia	
b.	***hypoxia***	- rectangular hyperbola - inflexion at ~ 60 mmHg & maximal ↑ V_M ~ 32 mmHg
c.	increase P_{aCO2}	~ 10 mmHg
d.	decrease in pH	~ 0.1-0.2
e.	drugs	- cyanide, nicotine - lobeline, doxapram
NB:	***not*** by	- anaemia - carbon monoxide - methaemoglobinaemia *ie. responds to P_{aO2} ***not*** C_{aO2}

- ***Chemoreceptor Stimulation - Effects***

a.	↑ V_T, frequency & V_M	
b.	bradycardia	- carotid body
c.	tachycardia	- aortic body
d.	hypertension	- systemic & pulmonary vasoconstriction
e.	bronchoconstriction	

- ***Effects of Apnoea***

NB: **P_{aCO2}** → initial rise ~ 6 mmHg in first minute → lung "washin"
→ subsequent rise **~ 1-3 mmHg/min**

P_{aO2} → falls dependent upon F_IO_2, FRC and VO_2

• body stores of O_2 are small, being **~ 1550 ml** on air, which corresponds to only 6 mins consumption at a basal VO_2
• thus, with changes in V_A the P_{aO2} rapidly assumes its new value, the ***half time*** of change being only 30s
• in contrast the body stores of CO_2 are large, being ~ **120 l**, or 600 mins of the basal output
• the time course of change for P_{aCO2} is slower for a reduction of V_A than for an increase
• the half time of rise for P_{aCO2} ~ 16 mins

• thus, during the ***acute phase*** of hypoventilation, the P_{aO2} may be low while the P_{aCO2} is still within the normal range

NB: ∴during acute hypoventilation, the ***respiratory exchange ratio*** may fall far below the ***respiratory quotient***, which it equals at steady state, as CO_2 production is partly diverted to the body stores

CO_2 & Ventilation

NB: $\uparrow V_M \sim 2.0$ l/min/mmHg $\propto$ $\uparrow PaCO_2$

the predominant effects are upon the ***central chemosensitive area*** CSA
large interpatient variation in slope of the V_M/P_{aCO2} line

Factors Shifting the V_M-CO_2 Curve	
Left	Right
• hypoxia • acidosis • hyperthermia • catecholamine release	• sleep • ↑ work of breathing • ↑ resistance • ↓ compliance • drugs - narcotics - barbiturates, etc.

OXYGEN THERAPY

- ***Isobaric***

a. ***fixed*** performance
- high flow - venturi masks
- low flow - anaesthetic machine

b. ***variable*** performance
- small capacity - nasal specs, Hudson
- large capacity - O_2 tent, cribs

Device	**FGF (l/min)**	**F_IO_2%**
Nasal Canulae[1]	2-6	28-44
Hudson Mask	4 6 8 **10** 12	35 50 55 **60** 65
O_2 Tent	7-10	60-80
Incubator	3-8	20-40
Head Hood	4-8	30-50

[1] increase $F_IO_2 \sim 4\%$ / litre flow of O_2 up to 44%

■ ***Venturi***

• delivered F_IO_2 is estimated as follows,

1. 6-8 l/min FGF + entrainment gas ~ 40-60 l/min total flow
2. 8 l/min O_2 + 21% of (40-8) l/min ~ 30% F_IO_2
3. 10 l/min O_2 + 21% of (60-10) l/min ~ 35% F_IO_2

• the actual delivered F_IO_2 is determined by,

1. O_2% of FGF and variability of flow
2. maximal FGF
3. entrainment ratio
4. size of O_2 reservoir
5. patient peak inspiratory flow rate and minute ventilation

Oxygen	
MW	• 32
BP	• -182.5°C
H_2O solubility 37°C[1]	• 2.4 vol%
H_2O solubility 0°C	• 4.9 vol%
Critical temperature	• **-118.4°C**
Critical pressure	• 50.14 atm.
Liquid:gas volume ratio	• **1:840**
Specific gravity (gas)	• 1105 (air = 1000)
Cylinders	• pressure 132 atm. • vol. at STP 682 l C • colour code black/white

[1] Ostwald solubility coefficient for O_2 in blood at 37°C
= 0.0034 ml/100ml blood/mmHg

∴ at 760 mmHg = **2.58 ml** / 100 ml

■ ***Methods of Preparation***

1. fractional distillation of air by pressure / cooling
2. electrolysis of H_2O
3. Brin process using BaO_2

Oxygen Toxicity

1. ***hyperoxic*** syndromes
   - i. optic - neonatal retrolental fibroplasia
   - ii. neural - hyperbaric O_2 seizures
   - iii. pulmonary - tracheobronchitis, ARDS
     ? bronchopulmonary dysplasia
2. ***normoxic*** syndromes
   - presence of factors enhancing formation of free radicals at normal O_2 tension
   - i. excessive phagocytic activity
   - ii. ***reperfusion*** following ischaemia
   - iii. drugs / toxins - paraquat, bleomycin

- ***Mechanisms***

a. free oxygen radicals
b. oxidation of glutathione
c. lipid peroxidation
d. glycolytic GPDH inhibition
e. altered glutamate & GABA metabolism

- species generated,

a.	***superoxide***	O_2^-	+	***superoxide dismutase***	→	hydrogen peroxide
b.	hydrogen peroxide	H_2O_2	+	***catalase***	→	water
c.	***hydroxyl radical***	$OH^\bullet$	+	catalase, or		
			+	***glutathione peroxidase***	→	water

- factors influencing O_2 toxicity,

a. increased tolerance with increased levels of,
   - i. SOD
   - ii. catalase
   - iii. glutathione peroxidase
   - pulmonary levels are increased with ***endotoxin***
   - may reduce O_2 lung injury in sepsis

b. decreased tolerance with,
   - i. nutritional deficiency - vit. E, C, selenium, glutathione & SH-compounds
   - ii. hyperthyroidism
   - iii. hypercortisolism
   - iv. drugs / toxins

■ ***Pulmonary Oxygen Toxicity***

- first described by J.L. Smith in 1899
- difficult to distinguish from the effects of hypoxia in critically ill patients
- CXR changes are non-pathognomonic
- ***inspired oxygen tension*** is more important than F_IO_2
- tracheobronchitis & ↓ VC may occur after 12-24 hours breathing 100% O_2 at 1 Atm.
- the pulmonary ***endothelial cell*** is most sensitive, progressing to

  → type I alveolar cells showing damage at ≥ 48 hrs

- there is considerable patient variation
- an absolute "safe level" of O_2 has not been established, but ≤ 50% tolerated for prolonged periods
- two phases,

  1. ***acute exudative phase***
     - endothelial oedema, capillary damage & haemorrhage
     - cellular infiltrate
     - reduced compliance & VC
     - ? type I alveolar damage
  2. ***late proliferative***
     - type II alveolar proliferation with type I cell destruction
     - leukocyte infiltrate, interstitial fibrosis and septal thickening

- pulmonary oxygen toxicity is hastened by,

  1. higher F_IO_2
  2. inhalation of CO_2
  3. radiation
  4. paraquat, bleomycin
  5. chemotherapy

- pulmonary oxygen toxicity is delayed by,

  1. brief intermittent exposure to F_IO_2 = 21%
  2. a high $P_{A\text{-}aO2}$ gradient

- secondary cardiovascular changes,

  1. ↑ SVR & PVR
  2. ↓ cardiac output

- ***Pulmonary Changes in Early Oxygen Toxicity***

1. ↓ VC *most useful
2. ↓ FRC
3. ↓ compliance
4. ↓ CO-diffusing capacity
5. ↑ respiratory rate

• the following factors are ***not altered*** in early oxygen toxicity,

1. RV
2. airways resistance
3. $P_{A\text{-}aO2}$ gradient

- ***Complications***

1. chemical toxicity - tracheobronchial tree, alveolar & endothelial cells
   - pulmonary damage, atelectasis
   - hypoxia, acidosis
2. retinal damage
3. erythrocytic damage, haemolysis
4. hepatic effects
5. myocardial damage
6. endocrine effects
7. renal damage
8. CNS enzyme / cell toxicity - twitching, convulsions, cell necrosis

- ***Organ Systems Susceptible to Oxygen Damage***

a. blood-brain barrier, cognition, neuromuscular function
b. glomerular function
c. endocrine function, reproduction
d. vision, auditory-vestibular function
e. hepatic function
f. respiratory function
g. myocardial function
h. haemopoietic function
i. temperature regulation

- ***Oxygen Limits in Normal Man***

1. $F_IO_2 \leq 55\%$ - safe for indefinite periods
2. 1 Atm. / 24 hours ~ 10% fall in VC
3. ≥ 2 Atm. / 24 hours - CNS toxicity

- ***Other Factors: Animal Studies***

a. ***factors hastening toxicity***
   i. corticosteroids, ACTH
   ii. CO_2
   iii. convulsions
   iv. drugs - paraquat
   - dextroamphetamine
   - adrenaline, noradrenaline, insulin
   v. hyperthermia
   vi. thyroid hormones
   vii. vitamin E deficiency

b. ***factors delaying toxicity***
   i. acclimitization to hypoxia
   ii. adrenergic blocking agents, ganglionic blocking agents, reserpine
   iii. antioxidants
   iv. general anaesthesia
   v. chlorpromazine
   vi. GABA, glutathione
   vii. hypothermia, hypothyroidism
   viii. starvation
   ix. vitamin E
   x. immaturity

Oxygen Cost of Breathing

Def'n: normal ~ 0.5-1.0 ml.O_2 / litre of ventilation
~ 2-4 ml.O_2 / min

- this is increased by,
  1. exercise
  2. asthma, CAL
  3. cardiac failure
  4. obesity

  NB: lung disease (↓ compliance / ↑ resistance) increases both the ***baseline*** O_2 consumption and the ***slope*** of the graph

SIMV Work of Breathing

- demand flow SIMV systems → ↑ VO_2 ~ 6-46% (***mean* ~ 16%**)
- factors in this increase are,
  a. work during IMV
  b. ***triggering*** of the demand valve
  c. circuit/ETT resistance
  d. isometric contraction prior to reduction of airway pressure
  e. ***auto-PEEP***
  f. inefficient action of the diaphragm with ***hyperinflation*** states
  g. low ***compliance*** disease states of the lung
  h. insufficient ***peak flow*** rates during inspiration

Hyperbaric Oxygen

- ***Clinical Uses***

a. decompression sickness *not really hyperbaric O_2

b. gas gangrene

c. other severe anaerobic infections

d. severe carbon monoxide poisoning
   i. COHb **> 40%**
   ii. associated cardiorespiratory limitation

e. cerebral air embolism

f. research

g. with DXRT as cancer chemotherapy

h. surgery - to prolong cardiac arrest time
- superseded by hypothermia

Dissolved Plasma Oxygen			
sea level	21 %	~ 0.3	ml
sea level	100 %	~ 2.1	ml
2 atm.	100 %	~ 4.2	ml
3 atm.	100 %	~ 6.3	ml (~ total VO_2)
α_{O2} ~ 0.003 ml / 100ml / mmHg			

- ***Other Effects***

a. ***hypercarbia***
   - $P_{vO2} \geq 50$ mmHg → ~ no CO_2 bound to Hb ***Haldane effect***
   - ↓ buffering capacity → ↑ minute ventilation

b. ***left*** shift of HbO_2 dissociation curve

c. ↑ work of breathing - ↑ gas density

d. pulmonary vasodilatation - ↑ Q_s/Q_t ∝ loss of HPV

e. systemic vasoconstriction - ↑ diastolic BP

f. cerebral vasoconstriction

g. ↓ HR - reflex baroreceptor

h. ↓ cardiac output ? reflex / direct

- ***Other Effects 100% O_2***

a. absorption atelectasis - lung
- middle ear
- pneumothorax

b. ↑ P_{A-aO2} gradient

c. reduces the effect of low V/Q areas but ***increased shunt fraction***

d. ↑ O_2 stores, apnoea time ~ FRC/VO_2

e. O_2 toxicity

- ***Hazards***

a. fire, explosion

b. pulmonary O_2 toxicity

c. cerebral O_2 toxicity - convulsions, coma

d. avascular bone necrosis head of femur

e. barotrauma - middle ear
- lung

f. "bends" if removed rapidly

g. retrolental fibroplasia

h. CO_2 narcosis - CAL
- high altitude dwellers
* loss of hypoxic drive

HYPOXIA			
Cause	P_{aCO2}	δP_{A-aO2}	δP_{aO2} 100%
low F_IO_2	low	low	large increase
hypoventilation	high	normal	large increase
V/Q mismatch	normal	high	large increase
low D_{O2}	normal	high	increase
R→L shunt	normal	very high	small increase

Humidification

- ***Complications***

1. bulk, complexity
2. condensation
   - "rain-out", drowning
   - ↑ resistance
   - scalding
   - circuit valve malfunction
   - decrement in filter function
3. over-spill of water - scalding
   - pulmonary oedema
4. bacterial contamination
5. high compliance
6. high resistance
7. overheating
8. electrocution
9. disconnection sites

- ***Consequences of Dry Gases***

1. heat loss ≤ 1-3°C/hr
2. water loss
   - impaired mucociliary escalator
   - mucociliary damage
   - mucosal desquamation, ulceration
   - drying of secretions, sputum retention
3. altered lung mechanics
   - ↓ FRC
   - ↓ compliance
   - ↑ shunt fraction
   - ↓ P_{aO2}
   - bronchoconstriction
4. increased incidence of ***respiratory infections***

Heat & Moisture Exchangers

- ***Advantages***

  a. cheap, simple, lightweight, silent, reliable
  b. disposable, no energy source
  c. bacterial filtration, low dead space & resistance
  d. useful for,
     i. children and adults
     ii. transport, retrievals
     iii. tracheostomy, spontaneous ventilation via ETT

- ***Disadvantages***

  a. inefficient with high minute volumes & gas flows
  b. inefficient after 1-2 hours
  c. airways resistance / dead space significant for small children
  d. potential for disconnection or obstruction

INTUBATION

- ***CVS Response***

a.	hypertension	- ↑ MAP ~ 20-40 mmHg * may have up to 60% ↑ MAP
b.	tachycardia	- ↑ HR ~ 50%
c.	arrhythmias	
d.	↑ ICP	- up to 100%
e.	↓ uterine blood flow	

NB: potential for,

i. myocardial ischaemia / infarction
ii. LVF
iii. intracranial hypertension / haemorrhage
iv. foetal hypoxia
v. eclampsia

• methods for minimising CVS changes,

a.	rapid laryngoscopy		≤ 45 secs
b.	avoid vasoconstrictors		- ketamine - cocaine - adrenaline, POR8
c.	adjuvant dose of STP		
d.	deep volatile anaesthesia		
e.	fentanyl	~ 5-10 µg/kg	5-7 min pre-ETT
f.	lignocaine	~ 1.5-3.0 mg/kg	2-3 min pre-ETT
g.	nitroprusside	~ 0.5 µg/kg	30 secs pre-ETT
h.	hydrallazine	~ 5-10 mg	5-10 min pre-ETT
i.	GTN		
	i.	paste 5cm (30 mg)	15 mins
	ii.	infusion 0.1%	20 mins
	iii.	IV bolus 50-250 µg	30 secs
j.	α / β-blockade		- phentolamine 1-5 mg - propranolol 1-4 mg - esmolol 2-4 mg bolus or infusion
k.	trimethaphan		- 0.7 mg/kg bolus - then 0.1-0.4 mg/kg over 10 mins

- ***Indications***

1. upper airway obstruction
2. airway protection
   - gastrointestinal contents
   - blood or secretions
3. application of mechanical ventilation
4. inability to clear secretions
5. to enable specific therapy
   i. induced hypocapnia
   ii. high F_IO_2 / PEEP
   iii. pulmonary toilet / lavage
   iv. BAL

- ***Complications***

a. ***immediate***

i.	laryngoscopy	- trauma - aspiration - autonomic reflexes
ii.	ETT	- misplacement - obstruction / kinking / disconnection
iii.	cuff	- herniation - overinflation - perforation, leakage

b. ***short-term*** (hours-days)

i.	obstruction	- endobronchial misplacement - obstruction / kinking - overinflation, herniation
ii.	dislodgement / disconnection	
iii.	colonization	- sinusitis, tracheitis - nosocomial pneumonia
iv.	dry gases	- dehydration - hypothermia - thickened secretions, inspissation

c. ***long term*** (days-weeks)

i.	laryngeal trauma	
ii.	tracheal trauma	
iii.	infections	- sinusitis, otitis - tracheitis, nosocomial pneumonia - microaspiration, lung abscess - septicaemia

Difficult Intubation

- ***Physiological***

  a. short muscular neck
  b. receding mandible
  c. prominent upper teeth
  d. narrow mouth with high arched palate
  e. limited jaw opening
  f. large breasts
  g. anterior larynx
  h. effective mandibular length - thyromental distance
  i. receding lower jaw / maxillary protrusion
  j. short occipito-atlantis distance
  k. short C_1-C_3 distance

- ***Pathological***

a.	TM joint disease	- RA - trismus - fracture
b.	limited cervical extension	- trauma, fracture - spondylitis - RA
c.	oropharyngeal masses	- tumours - oedema - abscess, cysts
d.	contractures of face/neck	- burns, scars - tumours
e.	trauma	- mandibular, facial bones - cervical spine - larynx - airway bleeding
f.	congenital	- craniofacial disorders - macroglossia, Down's - encephalocele - cleft palate
g.	endocrine	- obesity - acromegaly - goitre

Assessment of Airway

1. ***history***
   - i. letters etc. re previous difficult intubation
   - ii. previous anaesthetic records
2. ***examination*** → **"MOUTHS"**
   - i. **M**andible
     - thyromental distance > 6 cm, or > 3 "finger-breadths"
     - alveolar-mental distance < 2 cm
     - "receeding", length
     - subluxation
     - obtuse mandibular angles
   - ii. **O**pening
     - incisor gap > 4 cm
   - iii. **U**vula
     - Mallampati grades I-IV - as per Samsoon & Young
   - iv. **T**eeth
     - prominent upper incisors, "buck" teeth
     - solitary incisors, "nuisance" teeth
     - loose teeth
     - crowns, caps, plates & dentures
   - v. **H**ead & Neck
     - flexion, extension, lateral flexion & rotation
     - tracheal position, neck masses, upper mediastinal masses
   - vi. **S**ilhouette
     - obesity
     - Dowager's hump
     - "no neck"
     - craniofacial anomalies
3. ***investigations***
   - i. awake laryngoscopy - direct or indirect
   - ii. fluoroscopy
   - iii. XRays (Bellhouse)
     - mediastinal masses & tracheal position / diameter
     - effective mandibular length
     - atlanto-occipital distance & C_1-C_2 interspace
     - anterior-posterior thickness of the tongue
   - iv. CT scan
     - tracheal deviation, luminal diameter
     - intrathoracic trachea, mediastinal masses

VENTILATION

- ***claimed advantages*** of IMV over CMV,
    a. minimises respiratory alkalosis
    b. minimise sedative/relaxant requirements
    c. lower mean airway pressures
    d. more uniform gas distribution
    e. expedite weaning process
    f. reduce muscle atrophy & dis-coordination
    g. reduce cardiac decompensation with weaning

- possible ***disadvantages***,
    a. risk of hypercarbia, cf. with AMV
    b. increased work of breathing
    c. respiratory muscle fatigue
    d. prolonged ventilation if rate reduced too slowly
    e. cardiac decompensation in patients with compromised cardiac function

- Groeger (CCM, 1989), SIMV vs. assist control → advantages of SIMV
    1. lower P_{IP}
    2. improved
        - CO & MAP
        - DO_2
        - LVSWI
    3. less alkalosis

    NB: SIMV was associated with a ***higher*** respiratory rate, despite similar minute volumes and oxygen consumption

IPPV and Muscle Relaxants

- ***Short Term***

1. masking of clinical signs
   i. level of consciousness
   ii. epilepsy, neurological change
   iii. acute abdomen, etc.
2. inadequate analgesia and sedation
3. impaired secretion clearance - loss of cough reflex
4. histamine release, anaphylaxis / anaphylactoid reactions
5. asphyxia from circuit malfunction

- ***Long Term***

1. muscle wasting & atrophy
   - ↑ negative nitrogen balance
   - difficulty in weaning
   - ? ***myopathy*** associated with steroid use, especially in status asthmaticus
   - ?? predisposition to CIP, but EMG changes are ***dissimilar***
2. DVT & pulmonary emboli - need for prophylaxis/anticoagulation
3. pressure sores
4. drug metabolite accumulation - laudanosine
   - M_6G

- ***Advantages***

1. tolerance of mechanical ventilation - particularly PCIRV
2. tolerance of hypercarbia
3. avoidance of - breath stacking
   - high peak P_{AW} ? theoretically may not matter
   - inadequate ventilation
4. reduction in VO_2
5. in infants - improved oxygenation
   - reduced inspiratory time
   ? reduced barotrauma
6. R_X in patients with raised ICP
7. less baro/volutrauma ? evidence for this
8. ? neurophysiological studies

- ***Special Indications***

a. infant respiratory distress syndrome,
   - decreased pneumothorax rate
   - ***no change*** in intraventricular haemorrhage rate
   - ***no change*** in mortality

b. cerebral disorders
   - less rise in ICP with various stimuli
   - ***no change*** in ICP rise with ***pain***
   - less sedation required therefore aiding CNS assessment
   - less indication now propofol allows adequate sedation & periodic assessment
   - recent article in ?J.Trauma showing ↑mortality in NMJ paralysis group for management of severe head injury

c. tetanus

d. severe acute asthma

e. severe restrictive respiratory deficits, ARDS

f. ? cardiogenic shock to reduce VO_2

IPPV Adverse Effects

a. ***respiratory***

i. ***barotrauma*** - alveolar rupture, PIE
- pneumomediastinum / pneumothorax

• alveolar overdistension - hyaline casts, ? fibrosis

ii. ***surfactant*** loss / inactivation

• ↓ FRC and encroachment of CC on FRC

iii. ↑ lung water ∝ ? ↓ lymphatic drainage
? ↑ LAP

• disproportionate effect on PV & PA pressures → ↑ $\mathbf{P_{PC}}$

iv. ↑ V/Q mismatch - ↑ $\mathbf{Q_S}$, $\mathbf{V_D}$ & regional alkalosis
- low flow areas & regional ischaemia

v. frequently associated with potentially toxic F_IO_2

b. ***cardiovascular***

i. RV effects ↓ venous return
↑ PVR & RV afterload
↑ RVEDV
↓ RV perfusion pressure

ii. LV effects ↓ LV afterload
↓ LVEDV
* ventricular interdependence

iii. dual effects - global cardiac compression
? ↓ coronary blood flow (most studies → no change)

iv. ↓ VO_2

v. ↓ inspiratory muscle blood flow

c. ***renal***

i. ↑ ADH / ↓ ANF secretion → ↓ urine output and Na^+ excretion

ii. redistribution of intrarenal blood flow

iii. ↑ IVC & renal vein pressure

d. ***CNS***

i. ↑ ICP

• unpredictable, but clinically insignificant at levels of PEEP ≤ 10 cmH_2O

ii. ↓ cerebral blood flow ∝ induced hypocapnia

e. ***hormonal***

i. ↑ plasma adrenaline and noradrenaline

ii. ↑ ADH / ↓ ANF

iii. ↑ renin & aldosterone

• most of these effects are reversed with ***volume replacement***

Assessment of Respiratory Function During IPPV

1. ***clinical***
   - i. signs of hypoxia - tachycardia, hypertension, cyanosis
   - ii. signs of hypercarbia - bounding pulse, tachycardia
2. ***shunt fraction*** - $AaDO_2$, PaO_2:F_IO_2 ratio
   - shunt equation
3. ***dead space*** $\propto P_{aCO2} :: V_M$
4. ***lung volumes*** * VC ≥ 15 ml/kg
5. ***respiratory rate*** ≤ 30 bpm
6. ***compliance*** ~ $\delta V_L/(P_{MAW} - [PEEP + autoPEEP])$
   - [3] **75** ml/cmH_2O

   intrinsic PEEP present in most ventilated patients,
   - i. ARDS ≥ 8 cmH_2O
   - ii. ARF ~ 4 cmH_2O

   → ***underestimation*** of compliance by ~ 20-30%
7. ***resistance*** ~ $(P_{max} - P_{p1})$/flow
   - ~ 2-6 cmH_2O/l/s ≤ 10-15 cmH_2O (NMJB/ETT)
8. ***MMV*** ~ 2 x V_M
9. maximal inspiratory occlusion pressure $MIP_{0.1} \geq -20$ cmH_2O
10. **$f / V_T > 100$** → not ready to wean (V_T in litres)

Pressure Support

- optimal pressure support is influenced by,

a. ***ventilator factors***
   - i. size of ETT
   - ii. ventilator circuit - demand valves
     - tubing resistance / compliance
     - ± humidifier
   - iii. ventilation mode - CMV, IMV, CPAP
   - iv. trigger method & sensitivity

b. ***patient factors***
   - i. airways resistance
   - ii. respiratory compliance
   - iii. respiratory rate
   - iv. minute volume
   - v. muscle strength

CPAP Circuits

- ***Benefits***

  a. ↑ FRC → ***alveolar recruitment***

  b. improved V/Q match

  c. improved oxygenation

  d. ↓ work of breathing
     i. ↑ compliance
     ii. ↓ inspiratory muscle work
     iii. ↓ autoPEEP * some, not all patients

  e. "open lung" theory

- ***Other Effects***

  a. ↓ LV afterload

  b. ↓ venous return in CCF, acute LVF

  c. redistribution of lung water out of alveoli
     - however, total lung water ***increases***

- ***Clinical Uses***

  1. low FRC states
     i. ARDS
     ii. IRDS
     iii. acute pulmonary oedema
     iv. diffuse interstitial lung disease
     v. pneumonitis
     vi. bronchiolitis
  2. high autoPEEP states
     i. asthma
     ii. CAL

- ***CPAP Potential Disadvantages***

a. excessive ↑ FRC

b. ↑ work of breathing

c. ↓ venous return

d. patient discomfort

e. gastric distension / aspiration

f. skin / nasal bridge necrosis

NB: the work of breathing is proportional to the δP_{AW}, where,

$$\delta P_{AW} \propto \textbf{resistance \& reactance}$$

resistance = pressure / flow
reactance = (inertia x acceleration) - (volume / compliance)

• therefore, the work of breathing through a CPAP circuit is affected by,

1. flow < PIFR → ↑ W_{BR}
   > PIFR → ↑ turbulence
2. ↑ resistance - narrow tubing
   - demand valves
   - flow resistors
3. gas inertia & circuit geometry
4. gas acceleration
5. bag compliance

Inverse I:E Ratio

- claimed advantages,
    a. adequate ventilation without high peak inspiratory pressures
    b. less barotrauma
        - not substantiated in RCTs where ***mean*** P_{AW} has been equal
    c. use of a lower F_IO_2

    NB: assumption, peak $P_{AW} > 60$ cmH_2O and a $F_IO_2 > 0.6$,
    → probably cause damage unless very brief

- Lachmann, ***lung lesion index***,

$$LLI = P_{aO2} / (F_IO_2 \times P_{AW})$$

£ **4** suggests high probability of lung damage

- main aims of ventilation during ARDS are,
    a. restoration/maintenance of FRC
    b. maximise ***recruitment*** of functional gas exchange units
    c. minimise ***barotrauma***

- the respiratory pressure/volume curve changes throughout the disease process, therefore one ventilator setting may not be the best
- the justifications for reversing the I:E ratio include,
    a. overcome the critical opening pressure during inspiration
    b. sustain opening pressure
    c. expiratory time short enough to prevent closure of lung units

- additional PEEP is usually required but is low, ~ 4-8 cmH_2O

    NB: the ***autoPEEP*** produced may be profound, ~ 8-16 cmH_2O

- Lessard *et al.* (Anaesthesiology 1994) review of PCIRV versus conventional ventilation, controlling for mean airway pressures & PEEP, showed ***no advantage*** for the former with respect to,
    1. oxygenation
    2. barotrauma

Positive End-Expiratory Pressure

NB: the important therapeutic change is an ***increase in FRC***

- ***Possible Beneficial Effects***

NB: dependent upon the level of PEEP

a. respiratory
- ↑ transpulmonary pressure → ↑ end-expiratory lung volume / FRC
- ↑ lung compliance
- ↓ V/Q mismatch / ↓ shunt → ↑ P_{aO2}/C_{aO2} ??DO_2
- conflicting information on V_D/V_T
- reduced ***apnoeic periods*** in infants and sleep apnoea patients

b. CVS
- ↑ stroke volume / ↓ LVESV
- ?? reversal of LVF

- ***Adverse Effects***

NB: especially if excessive PEEP

a. respiratory
- adverse redistribution of blood flow → diseased lung
  → ↑ V/Q mismatch / ↑ shunt
- ↓ lung compliance
- ↑ in total lung water
- barotrauma, alveolar rupture/pneumothorax
- inactivation of surfactant

b. CVS
- ↑ pulmonary capillary pressure
  - P_C = LAP + 0.4(P_{mPA} - LAP)
  - PEEP increases LAP & P_{mPA}
  - P_C increases ~ 0.5 x PEEP, assuming $C_L \sim C_{CW}$
- ↑ RV afterload
- ↓ cardiac output / ↓ venous return
- ventricular interdependence
- humoral factors → ↓ ANF / ↑ ADH
- global cardiac compression
- ? decreased coronary blood flow - disproved in most studies

c. renal
- ↓ urine output / Na^+ excretion
- ↑ ADH, ↓ ANP
- ↑ IVC, renal vein pressure
- redistribution of intrarenal blood flow

d. CNS
- ↑ ICP - unpredictable
- ? decrease in CBF

e. hormonal
- ↑ adrenaline, noradrenaline ~ 3x after 5 min of 20 cmH_2O
- ↑ renin, aldosterone
- ↑ ADH (conflicting data)
- ↓ ANP

NB: most of these effects are ***reversible*** with volume replacement

Optimal PEEP

Def'n: "that level of PEEP which provides the maximal increase in **O_2-*flux***"

first coined by **Suter** *et al.*, NEJM 1975

• schools of thought actually vary as to the ***end-point***,

1. **Suter** (NEJM, 1975)
   - maximum DO_2
   - also happened to equate with best compliance
   * however, this was not substantiated by later studies
2. **Gallager, Civetta** (CCM, 1978)
   - pulmonary shunt fraction ≤ 15%
   - used fluid loading and inotropes to maintain cardiac output
   - PEEP required ranged from 15-65 cmH_2O !!!
3. **Carroll**[§] (Chest, 1988)
   - minimal PEEP with $P_{aO2} > 60mmHg$ / $F_IO_2 \leq 0.5$
   - aimed at avoidance of hypoxia and barotrauma
   - claimed "maximal" PEEP of no benefit and increases the risk of barotrauma
4. other terms
   i. ***best PEEP***
   ii. ***minimal effective PEEP***[§]

NB: 1. practically, where PEEP ≤ $10cmH_2O$, most patients benefit in terms of FRC and P_{aO2} without significant adverse effects

2. adverse effects are minimal if the patient has an adequate BP, peripheral perfusion and renal output (UO, Cr/Ur)

3. where PEEP > $10cmH_2O$, or the patient is critically-ill (sepsis, MODS, multiple trauma), O_2 flux and haemodynamic variables should be calculated to optimise PEEP

■ ***Consensus Statement ICM 1994***

• beneficial effects of PEEP,

1. lung recruitment
2. elevation of P_{mAW}
3. improved oxygenation

NB: assessment of "best" level of PEEP depends upon physiological response desired;

"most agree that in ARDS the ***lower limit*** should be set at, or slightly above the ***inflexion point*** of the pressure-volume curve"

AutoPEEP

• causes of ***dynamic hyperinflation***,

1. ↑ airways resistance
   - bronchospasm, asthma, CAL
   - bronchomalacia
   - dynamic airways collapse
   - foreign body
2. tachypnoea
3. inspiratory muscle activity during expiration (asthma)
4. glottic closure during expiration
5. mechanical ventilation
6. resistance of ETT, circuit

• present in most ventilated patients → ***underestimates*** of compliance by 20-30%

a. ARDS ~ 8 cmH_2O (AB says virtually zero in ARDS patients)

b. ARF ~ 4 cmH_2O

• ***static autoPEEP*** monitored by measurement of airways pressure after ***end-expiratory occlusion***
• ***dynamic autoPEEP*** monitored by oesophageal balloon or intrapleural catheter & δP_{IP} prior to the onset of gas flow
• dynamic autoPEEP generally 2-3 cmH_2O < static, and thought to be more clinically relevant
• effects of end-expiratory occlusion,

a. dynamic hyperinflation

b. decrease compliance & under-estimation of static compliance by ~ 50%,

Compliance = $\delta V_L/[P_2 - (PEEP + autoPEEP)]$
~ $\delta V_L/P_{AW}$
~ 75 ml/cmH_2O (N)

c. ↑ work of breathing

d. barotrauma

e. CVS and renal effects of conventional PEEP

■ ***Treatment***

1. treat bronchospasm & clear secretions
2. ↓ I:E ratio → long expiratory times
3. ↓ circuit resistance
4. CPAP
   - maintain airways open
   - ↓ inspiratory activity & ↓ inspiratory threshold load
   - ↓ LV afterload
   - facilitate weaning

High Frequency Ventilation

IPPV	< 60	bpm	< 1.0	Hz
HFPPV	60 - 110	bpm	1.0 - 1.8	Hz
HFJV	110 - 400	bpm	1.8 - 6.7	Hz
HFO	400 - 2400	bpm	6.7 - 40	Hz

- ***Advantages***

a. less movement of the operating field

b. adequate O_2 & CO_2 exchange

c. adequate gas exchange where IPPV complicated or impossible,
   i. bronchopleural fistula
   ii. communicating lung cyst
   iii. tracheal surgery

d. lower peak airway pressures
   i. less barotrauma
   ii. ***no studies*** showing more beneficial than IPPV/PEEP in ARDS

e. surfactant not damaged

f. less effect upon cardiac function

g. volume and ? clearance of secretions increased

- ***Disadvantages***

a. requires expensive equipment and trained personnel

b. the increased volume of ***secretions*** may be detrimental

c. ***humidification*** difficult

d. **CO_2** ***exchange*** dependent upon resistance to mass flow and diffusion,
   → limited at high frequencies, ? > 20Hz

e. **O_2** ***exchange*** proportional to mean lung volume, ie. maintenance of FRC important
   → ***mean*** intrathoracic pressure similar to IPPV/PEEP

f. resonant frequency may be reached in some alveoli,
   → ? resulting in increased barotrauma

NB: high frequency ventilation appears very effective at removal of CO_2 over a wide range of frequencies, however ***oxygenation*** appears more dependent upon lung volume and therefore mean airway pressure

- ***Mechanisms of Gas Movement***

1. convection - simple in large airways
   - complex at bifurcations & in expiration
2. diffusion
3. pendelluft

Extracorporeal Membrane Oxygenation ECMO

- the overall average mortality from ARDS ~ 50-70%
- hypoxia is rarely the cause, usually due to ***MODS*** or ***septicaemia***
- this implies that current ventilation modes either,

1. are adequate and other factors need to be addressed
2. prevent more rapid lung recovery and allowing more time for extrapulmonary complications to develop

- in ARDS to main problem is hypoxia due to increased ***shunting***
- the small areas of near normal lung have to do the "work" of the whole lung
- this requires therapy with a high F_IO_2, high PEEP, and high P_{IP}, with their iatrogenic complications

- ***Extracorporeal Lung Assist (ECLA) Terminology***

a. ECMO
b. EC-CO_2-R
c. PE-CO_2-R

- it is necessary to define,

1. the type of bypass - VV probably better than AV
2. bypass flow:CO ratio ~ 20-30% of CO adequate for EC-CO_2-R
3. lung ventilatory mode

- clinical studies of EC-CO_2-R include a total of 115 patients in 8 trials
- there were a total of 57, ~ 50% survivors
- improvement was usually rapid, within the first 48 hours
- the average duration of therapy was ~ 7 days
- when conventional ventilation → total static lung compliance £ **25 ml/cmH_2O**
  → ***survival*** ~ 0

- this may improve to ~ 50% with EC-CO_2-R
- subsequent studies have shown ***no improvement*** in survival cf. conventional ventilation

- ***Complications of ECMO***

1.	anti-coagulation and bleeding	~ 1000 ml/d
2.	complement activation	
3.	cost	- manpower & equipment

- ***Potential Advantages***

a.	avoids lung hypoxia, maintains a high lung O_2 supply	
b.	avoids high airway pressures	- ↓ barotrauma - ↓ surfactant loss
c.	reduction in PA pressure	- ↓ HPV - reduced effects of PEEP/IPPV
d.	correction of V/Q ratios	- all areas equally oxygenated - avoids regional alkalosis
e.	? anticoagulation reduction of intrapulmonary thrombosis	
f.	? reduced incidence of septicaemia	

TRACHEOSTOMY

- ***Indications***

1. prolonged intubation > 7-10 days
   > 2-3/24 in professional singer
2. early for condition where extended airway management highly likely
3. upper airway obstruction
   i. failed intubation
   ii. elective for threatened impossible intubation
   iii. transport of critically ill patient
   iv. postsurgical where re-intubation is likely impossible
      - laryngectomy, radical neck procedures
      - maxillofacial procedures with jaw wiring
   v. traumatic upper airway disruption
      - laryngeal fracture, tracheal disruption

- ***Advantages***

1. reduced dead space
2. improved patient tolerance → less sedation required
3. removal of secretions
4. reduced incidence of laryngeal injury

- ***Complications***

1. procedural
   - haemorrhage
   - misplacement
   - hypoxia
   - pneumothorax / pneumomediastinum
2. decannulation, disconnection
3. colonization, infection
4. with tube
   - cuff herniation
   - obstruction
   - displacement
5. long term
   - ulceration, erosion
   - fistula
   - tracheomalacia
   - granulomata, stenosis
   - haemorrhage

Clinical Studies

- ***El Naggar 1976***

- 56 patients with an early tracheostomy (day 3)
- showed an increase in ***colonisation*** rate but no increase in infections
- increased frequency of airway lesions but all resolved in time
- laryngeal trauma from ETT was progressive after day 11

→ therefore recommended tracheostomy at ***day 10***

- ***Stauffer 1981***

- large study with 150 patients suggested ETT safer than tracheostomy ≤ 3/52
- however, a non-randomised study with bias, as the tracheostomy group,

a. were sicker
b. were intubated longer
c. tracheostomised later
d. different surgeons
e. high complication rate
   i. infection 36%
   ii. haemorrhage 36%
   iii. wrong incision 8% !!
   iv. cardiac arrest 4%
f. ***stenosis*** criterion was too strict, only 10% narrowing, therefore,
   i. tracheostomy group ~ 65%
   ii. ETT group ~ 20%

- ***Dunham 1984***

- total of 74 trauma patients managed with either,

a. ETT for 14 days, or
b. tracheostomised on day 3

→ ***no difference*** in laryngotracheal trauma, sepsis, or morbidity

- ***Whited 1984***

• total of 200 patients with ETT,

a. duration < 5 days ~ 6% transient injury
b. 6-10 days ~ 5% reversible laryngeal stenosis
c. > 11 days ~ 12% extensive laryngeal stenosis

• conclusions,

1. tracheostomy has many potential therapeutic advantages
2. laryngeal injury after 6-10 days becomes significant
3. tracheal stenosis is more easily treated than laryngeal stenosis
4. the high incidence of infectious and laryngeal complications in part relates to the preceding prolonged ETT
5. maintain on ETT for 7-10 days then tracheostomy if not contraindicated

- ***Berlauk 1986***

• factors affecting laryngotracheal injury,

1. duration of intubation
2. cuff shape and pressure
3. tissue compatibility of tube & cuff

• areas of damage from ETT,

1. posteromedial portion of true cords
2. posteromedial surface of the arytenoid cartilages
3. posterolateral surface of cricoid cartilage
4. mucosa of 4-7th tracheal cartilages
5. anterior wall of the trachea

• pathology of injury,

a. ulceration, perforation
b. ischaemia necrosis
c. mucosal hypertrophy & granuloma formation
d. adhesions, fibrosis, stenosis

- ***Kopp 1987***

• intubation injuries related to,

1. duration
2. hypotension
3. severity of underlying disease

• no correlation found with hypoxia or steroids
• complications and overall incidence,

a.	glottic oedema	- 100%
b.	glottic granuloma	- 96%
c.	superficial ulceration of the arytenoids	- 81%
d.	mucosal ulceration of the cricoid	- 75%
e.	dilatation of the posterior commissure	- 60%
f.	deep mucosal ulceration of the arytenoids	- 37%
g.	cartilage ulceration of the arytenoids	- 24%
h.	cartilage ulceration of the cricoid	- 12%
i.	glottic maceration	- 6%
j.	glottic synechia	- 3%
k.	fracture of the arytenoids	- 3%

• higher incidence than previous studies
• severity of injury increased significantly after ***day 3***

NB: concluded, *"conversion to tracheostomy should be considered between day 4 & 7 of intubation"*

• incidence of ***hoarse voice***,

a.	on extubation	~ 100%
b.	at 1 week	~ 45%
c.	at 1 month	~ 16%
d.	permanent	~ 1.5%

- ***Tracheostomy: Haemorrhage***

• tracheo-arterial fistula usually involves the,

a. ***innominate artery*** ~ 70%

b. common carotid artery ~ 4%

• most common site is at the cuff, ∴***may*** be decreased by high volume/low pressure cuffs
• fistulas related to the stoma are more common if performed below the 4 th tracheal cartilage
• not yet reported as a complication of percutaneous tracheostomy
• ***overinflation*** of the balloon will tamponade bleeding in 80% of cases, ∴first step

- ***Stenosis Summary***

a. tracheostomy
   i. strict criteria ~ 98%
   ii. ≥ 30% stenosis ~ 36% ("30% in 30%")
   iii. ≥ 70% stenosis ~ 11% (symptomatic)

b. ETT ≥ 3 weeks ~ 19%
   ≤ 0.5% symptomatic

NB: ***but:*** less tracheal, more laryngeal injury, which is more difficult to treat

- ***Jones et al. Ann-Surg. 1989***

• 5-year burn center experience with tracheostomies → 99 tracheostomies (n=3246)
• indications of prolonged respiratory failure or acute loss of airway
• sputum ***colonization*** was universal, however rates of ***pulmonary sepsis*** & ***mortality*** were ***not*** significantly increased
• 28 patients developed late upper airway sequelae,

a. tracheal stenosis - TS

b. tracheoesophageal fistula - TEF

c. tracheoarterial fistula - TAF

• ***duration*** of intubation correlated only with development of TAF
• TEF patients were significantly older and more likely to have evidence of tracheal necrosis at the time of tracheostomy
• the pathogenesis of upper airway sequelae in these patients

→ divergent responses to inhalation injury, infection, and intubation

NB: use of tracheostomies in burned patients with inhalation injuries is now reserved for ***specific indications***, rather than as prophylactic airway management

- ***Mortality***

a. tracheostomy
   i. elective ~ 0.4-3%
   ii. emergency ~ 6-15%

b. ETT > 3 weeks < 1%

Tube Characteristics		
Type	Red Rubber	PVC, Silastic
Tracheal Loading Force[1]	1000 g	200-500 g 100-250 g after 24 hrs (moulding)
Cuff Pressure	~ 120 mmHg	≤ 20 cmH_2O

[1] force exerted in deformation of the tube to the anatomy of the upper airway

PULMONARY BAROTRAUMA

Def'n: the side effects of high airway pressures during IPPV

→ air outside the alveolar space

now probably inappropriate, trend toward ***"volutrauma"***

• traditional risk factors during IPPV,

1. large tidal volume
2. high mean and peak inspiratory pressures > 50 cmH_2O
3. high levels of PEEP
4. volume cycled ventilators
5. short expiratory time - especially with increased resistance
6. low lung compliance *CAL, ARDS, ?asthma

- ***Clinical Features***

a. interstitial emphysema
   - small parenchymal cysts
   - linear air streaks radiating toward the hilum
   - perivascular haloes
   - intraseptal air
   - pneumatoceles
   - subpleural air

b. pneumothorax
   i. simple
   ii. loculated - anterior, subpulmonic
   iii. tension

c. mediastinal emphysema

d. subcutaneous emphysema

e. pneumatoperitoneum

f. deterioration in lung function 2° surfactant inhibition

Peak Airways Pressure and *Ventilator Associated Lung Injury*

▪ ***Manning Chest 1994***

- 2 forms of VALI,
    1. barotrauma
        i. pulmonary interstitial emphysema
        ii. pneumothroax
        iii. pneumomediastinum
        iv. subcutaneous emphysema
    2. acute lung injury
        - less well described, acute injury associated with IPPV

    NB: growing evidence that ***lung volume***, or more accurately ***lung overdistension***, is the primary determinant of VALI

▪ ***Airway Pressure vs Lung Volume***

- P_{aw} usually measured as ventilator generated pressure
- pressure acting to distend alveoli $\rightarrow$ ***transmural pressure*** $P_{alv} - P_{pl}$
- therefore, 2 factors influence difference between P_{aw} and P_{tm},
    1. non-zeroflow states $\rightarrow$ $\delta(P_{aw} - P_{alv}) \propto \boldsymbol{Q.R_{aw}}$
    2. alteration of P_{pl} with P_{aw} / lung volume
        i. pulmonary compliance
        ii. inspiratory / expiratory muscle activity
        iii. thoracic cage / abdominal compliance

▪ ***Barotrauma***

- multiple studies document correlation between peak P_{aw} and barotrauma
- Petersen & Baier, CCM 1983, prospective study of 171 patients,
    1. $P_{pAW} > 70$ $\rightarrow$ 10/23 43%
    2. $P_{pAW} \sim 60\text{-}70$ $\rightarrow$ 4/53 8%
    3. $P_{pAW} < 60$ $\rightarrow$ 0/95 0%

- however, conclusion that P_{pAW} ***causes*** barotrauma is tenuous,

1. correlation of P_{pAW} & barotrauma not always this strong
   - Leatherman, ARRD '89, 42 asthmatic patients, no barotrauma despite,
     - P_{pAW}'s as high as **110 cmH_2O**
     - mean P_{AW} ~ 68 cmH_2O
2. barotrauma well documented at low levels of P_{pAW}
   - Rohlfing, Rad. '76, 6/38 patients with BT had $P_{pAW} < 25$
3. ventilatory methods aimed at reducing P_{pAW} of little benefit
   - Mathru, CCM '83, CMV vs IMV
     → lower incidence with IMV despite higher P_{pAW}
   - Clevenger, Arc. Surg. '90, converted IPPV to HFJV for "Salvage"
     → ↓ mean P_{AW} from 92 to 41 cmH_2O,
     ↑ BT from 0/15 to 7/15 within 21 hrs of conversion
   - Tharratt, Chest '88, converted 31 pts with ARDS to PCIRV
     → ↓ mean P_{AW} by 20 cmH_2O,
     ↑ BT from 0/31 to 8/31
4. incidence of BT also associated with V_L
   - Bone, ARRD '75 / '76, 2 studies looking at BT and V_T in ARDS

   i. 50 patients → mean V_T ~ 22 ml/kg with BT (40%)
   mean V_T ~ 17 ml/kg without BT

   ii. 106 pts → mean V_T ~ 11 ml/kg with BT (3.8%)
5. "large increases in P_{pAW} are often associated with large increases in V_L, but in most studies to date, no assessment of V_L changes was made which would allow one to distinguish between the effects of high P_{pAW} and those of lung overdistension", *Manning*
   - Williams, ARRD '92, prospective study
     22 asthmatics → risk factors for BT & CVS instability,
     "only variable predictive of BT was ***end-inspiratory lung volume***,
     a measure of dynamic pulmonary hyperinflation"
   - two animal studies looking at BT with / without thoracoabdominal binding :

     unbound group → lower mean tracheal pressure
     higher incidence of BT

- ***Acute Lung Injury***

• studies looking at ventilator induced ALI limited to animals (obviously)
• various study end-points,

1. macroscopic lung appearance
2. histologic lung appearance
3. alveolar permeability
4. microvascular permeability

NB: studies separating P_{pAW} and V_L, ie bound versus unbound animals, support the concept that V_L and ***not*** P_{pAW} is associated with ALI

Patient Management

- ***Low Thoraco-Abdominal Compliance***

• P_{pl} should increase in proportion to mean P_{AW}, \ minimal increased risk of BT
• however, situations of predominately thoracic or abdominal compliance changes may result in ***regional overdistension***

- ***High Airways Resistance***

• potential problem, as P_{pAW} may not correlate with hyperinflation
• Tuxen & Lane, ARRD '87, in severe asthmatics requiring mechanical ventilation,

1. $\downarrow V_T$ $\rightarrow$ $\downarrow$ both P_{pAW} and hyperinflation
2. $\downarrow$ PIFR (V_T const) $\rightarrow$ $\downarrow P_{pAW}$ but $\uparrow$ hyperinflation

NB: "management .... should focus on providing the minimum V_T and V_M consistent with acceptable (but not necessarily normal) gas exchange, and on using a sufficiently ***high inspiratory flow rate*** to allow adequate time for exhalation"

ARDS

• Maunder, JAMA '86, ARDS affects the lung in a "patchy" fashion,

→ areas of diseased and areas of ***near-normal*** lung

• thus, V_T will tend to be preferentially distributed to the areas of "normal" lung
• no specific ventilatory guidelines to ensure the absence of regional hyperinflation
• on the basis that static ***transpulmonary pressure*** ~ 35-40 cmH_2O inflates normal lung to VC, suggested peak $\mathbf{P_{alv}}$ < 35-40 cmH_2O
• however,

1. Marini, CCM '92 → P_{pAW} may not correlate with peak P_{alv}
2. Egan, J.App.Phys → "normal" P_{pAW} tolerated by whole lung inflation may result in BT with regional inflation

• theoretical approach would be to scale V_T in proportion to lung compliance

1. ↓ normal lung → ↓ compliance → ↓ V_T requirement
2. monitor P_{plat} & adjust V_T, but ?? at what level

Questions

1. what influence does PIFR, or more accurately $\mathbf{dV_L.dt}$, have upon BT?
2. is patient-ventilator asynchrony a risk factor for BT?
3. what are the relative roles of mean versus peak V_L on VALI?
4. what is the best approach for ventilation of ARDS patients?
5. is there a difference between PCV and SIMV, providing both focus on avoidance of lung overdistension, with respect to VALI?
6. does repetitive opening/closing of units result in higher BT?
   - ie. should we ensure V_T occurs above inflexion point

- ***Amato, Et Al AJRCCM 1995***

• overdistention and cyclic reopening of collapsed alveoli implicated in the lung damage found in animals submitted to artificial ventilation
• 28 patients with early ARDS were randomly assigned to

1. new approach (15) - end-expiratory pressures > lower inflection point of the PV curve
   - V_T < 6 ml/kg, P_{pAW} < 40 cm H_2O, permissive hypercapnia
2. conventional (13) - volume-cycled ventilation, V_T ~ 12 ml/kg
   - minimum PEEP guided by F_IO_2 and hemodynamics
   - 'normal' PaCO2 levels

• NA exhibiting better,

1. evolution of the PaO_2/F_IO_2 ratio ($p < 0.0001$)
2. compliance ($p = 0.0018$)
3. shorter periods under $F_IO_2 > 50\%$ ($p = 0.001$)
4. lower F_IO_2 at the day of death ($p = 0.0002$)

NB: but ***no significant*** improvement in survival (5/15 vs 7/13, p = 0.45)

concluded that "the NA ventilatory strategy can markedly improve the lung function in patients with ARDS, increasing the chances of early weaning and lung recovery during mechanical ventilation"

ACUTE RESPIRATORY DISTRESS SYNDROME

▪ *Definition*

• Ashbaugh *et al*. (Lancet 1967) described a condition in adults which was similar to the respiratory distress syndrome of infants (1 of the 12 patients was 11 yrs old)
• the term ***ARDS*** was coined by Petty & Ashbaugh in 1971
• previously no agreed diagnostic criteria, therefore difficulty in comparing studies of incidence, mortality and treatment efficacy
• actually represents a subset of ***acute lung injury***
• the essential features include,

a. ***acute*** respiratory failure, usually requiring mechanical ventilation

b. ***severe hypoxaemia*** with a high $P_{A\text{-}aO2}$ gradient

c. ***bilateral*** diffuse infiltration on CXR

d. stiff lungs with $C_T \leq 50$ ml/cmH_2O

e. pulmonary oedema should ***not*** be cardiogenic in origin,
the PAOP should not be elevated, definitions PAOP ≤ 12-18 mmHg

f. presence of a known ***predisposing condition*** - sepsis, trauma
- aspiration

NB: Lloyd, Newman and Brigham (1984) objected to this as it precluded the diagnosis in patients with pre-existing conditions which raised LAP

▪ *American-European Consensus Conference*

Def'n: ***acute lung injury*** is a ***syndrome*** of inflammation and increased permeability that is associated with a constellation of clinical, radiologic, and physiologic abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension:

1. timing → ***acute*** onset
2. oxygenation → $PaO_2 / F_IO_2 \leq$ **300** mmHg
irrespective of PEEP
3. CXR → ***bilateral*** infiltrates on frontal CXR
4. PAOP → £ **18 mmHg**

Def'n: ***acute respiratory distress syndrome***, is a subset of ALI, meeting the above criteria, where,

1. oxygenation → $PaO_2 / F_IO_2 \leq$ **200** mmHg

NB: ALI/ARDS are a ***continuum*** and are not specific disease entities,
therefore, any cut-off limit for definition purposes is strictly ***arbitrary***

• studies of ARDS subgroups show that of those with $PaO_2/F_IO_2 \leq 200$, **98%** progress within 1 to 7 days to a ratio < 150 mmHg
• thus, the higher figure allows earlier 'diagnosis' for study purposes, however care must be taken to exclude other causes
• mechanical ventilation was ***not*** considered a requirement for definition, as when this is instituted is very institution/clinician dependent
• chronic lung diseases such as interstitial pulmonary fibrosis, sarcoidosis etc. would meet the criteria except for ***chronicity***, and are thus excluded from the diagnosis

• CXR infiltrates should be ***bilateral***, consistent with pulmonary oedema and importantly may sometimes be very mild
• PAOP measurement is not considered essential for diagnosis, but is clearly useful
• diffuse pulmonary ***infection***, if meeting the above criterea, ***is*** included in the diagnosis
• however, this was not agreed upon by all members at the consensus

■ ***Diagnostic Criteria Petty***

NB: included for historical comparison

1. ***clinical setting***
   - i. catastrophic event - pulmonary or non-pulmonary
   - ii. exclusions - chronic respiratory disease
     - LV dysfunction
   - iii. respiratory distress - RR > 20 bpm
     - laboured breathing
2. ***CXR*** * diffuse / bilateral pulmonary infiltrates
   - i. interstitial - early
   - ii. alveolar - late
3. ***physiology***
   - i. $P_{aO2} \leq 50$ mmHg * with a $F_IO_2 \geq 0.6$
   - ii. $C_T \leq 50$ ml/cmH_2O * usually ~ 20-30 ml/cmH_2O
   - iii. Q_S/Q_T increased[§]
   - iv. V_D/V_T increased[§] [§] increased V/Q anomaly
4. ***pathology***
   - i. heavy lungs - usually ≥ 1000 g
   - ii. congestive atelectasis
   - iii. hyaline membranes & fibrosis

- ***Murray ARRD 1988***

Lung Injury Score			
• CXR Score:	**alveolar consolidation**	none	0
		1 quadrant	1
		2 quadrants	2
		3 quadrants	3
		4 quadrants	4
• Hypoxaemia Score:	**PaO_2/F_IO_2**	≥ 300	0
		225-299	1
		175-224	2
		100-174	3
		< **100**	4
• PEEP Score:	**PEEP**	≤ 5 cmH_2O	0
		6-8 cmH_2O	1
		9-11 cmH_2O	2
		12-14 cmH_2O	3
		≥ 15 cmH_2O	4
• Compliance Score:	**C_{RS}**	≥ 80 ml/cmH_2O	0
		60-79 ml/cmH_2O	1
		40-59 ml/cmH_2O	2
		20-39 ml/cmH_2O	3
		≤ 19 ml/cmH_2O	4
	No Lung Injury[1]		0
	Mild to Moderate Lung Injury		0.1-2.5
	Severe Lung Injury (ARDS)		**> 2.5**

[1] Final Score = aggregate sum / number of components used

Pathophysiology

- useful to consider 2 distinct pathways,
  1. ***direct*** insult to lung cells
  2. ***indirect*** effects of systemic inflammatory response

- despite effort, ***no consensus*** could be reached on the order of events leading to ALI
- many believe the pathogenesis is different for various precipitating causes

NB: *"current knowledge is neither sufficient to allow an intelligent conclusion about the precise **sequence** of events, nor sufficient to allow determination of which of these putative mechanisms are more **important**"* Consensus Report, ICM 1994

- ***Risk Factors***

Direct injury[1]	Indirect injury
1. apiration syndromes • acid aspiration • gastric aspiration • near-drowning 2. infections • bacterial, viral, PCP 3. pulmonary contusion 4. embolic syndromes • amniotic fluid • fat • rarely air 5. radiation pneumonitis 6. drug toxicity • bleomycin, salicylates, opioids • paraquat, O_2 7. toxic gas / vapour inhalation • NO_2, NH_3, SO_2, Cl_2 • industrial solvents	1. severe SIRS / sepsis 2. major non-thoracic trauma • ISS, APACHE II, TISS • clinical description 3. shock / prolonged hypotension • reperfusion injury 4. massive blood transfusion 5. transfusion reaction 6. anaphylaxis / anaphylactoid reactions 7. rarely associated with • pancreatitis • DIC • cardiopulmonary bypass • head injury • burns • diabetic coma • high altitude • uraemia

[1] modified from Nunn 3rd Ed., LIGW & Consensus Report, ICM 1994

• Pepe's group found the highest single risk factor was ***sepsis syndrome***, with 38% of patients in this group developing ARDS

1. risk factor → ~ 25%
2. risk factors → ~ 42%
3. risk factors → ~ 85% risk of developing ARDS

• Fowler's group found the highest incidence in ***aspiration*** (35.6%) followed by DIC (22.2%) and pneumonia (11.9%)
• the ***major*** predisposing factors are now agreed to be,

1. severe sepsis - particularly gram (-)'ve
2. aspiration of gastric contents
3. multiple trauma - particularly with pulmonary contusion
4. massive transfusion
5. DIC

NB: ICM 1994, highest incidence appears to be ***septic shock*** **~ 25-42%**

• it is extremely difficult, if not impossible to separate the toxic effects of a high F_IO_2 from the pathological conditions requiring their use
• however, it is ***unlikely*** that O_2 plays a significant role in pathogenesis

• there is considerable difference in the reported incidence, probably reflecting the different diagnostic criteria in different studies
• ***T.Oh:*** the true incidence is unknown and may only be ~ 7% of "at risk" patients
• there is, however, good agreement on the overall ***mortality***, which is as high as **50%**
• this tends to be higher in cases which follow ***septicaemia***, being reported as

a. Fein *et al*. (1983) ~ 81%
b. Fowler *et al*. (1983) ~ 78%

• multiple papers stating that mortality has remained relatively ***unchanged*** over the last 20 yrs

■ ***Milberg et al. JAMA 1995***

• 918 patients in 5 ICU's between 1983-1993, over 18 years age

1. outcome measure → 30 day hospital mortality
2. major causes
   i. ***sepsis syndrome*** ~ 37%
   ii. trauma ~ 25%
3. crude mortality rates, adjusted for age, ARDS risk, sex were ***unchanged***
4. however, significant decrease in mortality in,
   i. sepsis related ARDS * 67% → **40%**
   ii. patients < 60 years of age

▪ *Infiltrative Phase*

• earliest histological lesion is interstitial & alveolar ***oedema*** ~ 24-96 hrs post-injury
• this is characterized by damage to the integrity of the blood-gas barrier,
both endothelial cells and alveolar type I cells → ***not visible*** by light microscopy
• EM shows extensive damage to ***type I alveolar epithelial cells***, which may be totally destroyed
• the BM is usually preserved and the epithelial cells form a continuous layer, with cell junctions seemingly intact
• ***endothelial permeability*** is nevertheless increased
• interstitial oedema is found predominantly on the "service" side of the capillary, sparing the "active" side
• this pattern is similar to that observed with cardiogenic oedema
• pulmonary ***lymph drainage*** is capable of increasing **~ 8x** without formation of oedema
• protein containing fluid leaks into the alveoli, together with rbc's and leukocytes bound in an amorphous material containing fibrous strands → triggers replication of ***alveolar type II cells***
• this exudate may form sheets lining alveoli → ***hyaline membrane***
• impaired ***surfactant*** production results from either alveolar epithelial injury or secondarily from the effects of therapy (IPPV / O_2)
• ***intravascular coagulation*** is common at this stage
• in patients with septicaemia, capillaries may be completely plugged with leukocytes and the underlying endothelium damaged

▪ *Proliferation Phase*

• ***cellular proliferation*** starts within 3-7 days of injury
• there is thickening of the endothelium, epithelium and interstitial space
• there is less oedema, but the spaces are filled with rbc's and inflammatory cells
• type I epithelial cells are destroyed and replaced by ***type II epithelial cells*** which proliferate but ***do not*** differentiate immediately to type I cells
• they remain cuboidal and ~ 10 times the thickness of normal type I cells
• this appears to be a non-specific response, as it also occurs in ***oxygen toxicity***
• characterized clinically by worsening hypoxaemia and development of pulmonary hypertension
• ***pulmonary hypertension*** results from,

a. vascular microthrombi
b. platelet aggregation & release of vasoactive mediators
c. impaired endothelial synthesis of ***nitric oxide***

• ***fibrosis*** commences after 7-10 days and ultimately fibrocytes predominate
• extensive fibrosis is seen in resolving cases
• within the alveoli, the protein rich exudate may organise to produce the characteristic 'hyaline membrane', which effectively destroys alveoli

Mechanisms of Causation

• due to the diverse aetiology several mechanisms of causation, at least in the early stages
• in all cases, initiation seems to occur following damage to the ***alveolar/capillary membrane*** with transudation often increased by pulmonary venoconstriction
• thereafter, the condition is accelerated by a number of positive feedback mechanisms
• the initial insult may be either direct or indirect (see table above)
• much of the interest is in the ***indirect causes***, which may be mediated either by cellular or humoral elements
• ***cell types*** capable of damaging the membrane include,

a. neutrophils
b. basophils
c. macrophages
d. platelets - through arachidonic acid derivatives

• ***humoral agents*** include,

a. bacterial endotoxin
b. O_2 free radicals
c. proteases
d. thrombin, fibrin and FDP's
e. histamine, bradykinin, and serotonin
f. platelet activating factor (PAF)
g. arachidonic acid metabolites

• various chemotactic agents, especially C_{5a}, play a major role in the direction of formed elements onto the pulmonary endothelium
• Malik, Selig and Burhop (1985) drew attention to the fact that many of the humoral agents are capable of producing ***pulmonary venoconstriction***
• this facilitates transudation caused from increased permeability
• Seeger *et al*. noted that a number of proteins, including albumin but particularly ***fibrin monomer***, antagonize the effects of surfactant

• ***T.Oh:*** two possible mechanisms of causation,

1. C' activation
2. fibrinolysis and platelet activation

NB: however, both suffer from sparse clinical evidence,
C' has nopredictive value and is non-specific
FDP-D 'antigen' identified in patients with ARDS and may be a marker of mediator injury

Neutrophil Mediated Injury

• the postulated sequence begins with activation of C_{5a}, which results in ***margination*** of neutrophils on vascular endothelium
• this is known to be activated in ***sepsis*** and during ***cardiopulmonary bypass***
• significant margination is seen in many cases of ARDS
• however, margination can occur without significant lung injury, as occurs during haemodialysis with a cellophane membrane
• the postulate is that the neutrophils are somehow ***primed*** prior to margination
• this may occur with ***endotoxin***, which results in firm adherence of neutrophils to the endothelium
• C_{5a} results in temporary adherence but more importantly triggers inappropriate release of lysosomal contents to the cell exterior, cf. into phagocytic vesicles
• four groups of substances released in this way may potentially damage the endothelium;

1.	O_2 derived free radicals	→	lipid peroxidation inactivate α_1-antitrypsin
2.	proteolytic enzymes (esp. ***elastase***)	→	direct endothelial damage monocyte/macrophage chemotaxis (elastin fragments)
3.	arachidonic acid metabolites	→	vasoconstriction increased permeability neutrophil chemotaxis
4.	platelet activating factors	→	intravascular coagulation direct tissue damage

• the role of neutrophils has been studied in depleted animals with conflicting results
• ARDS does seem less severe in ***neutropaenic patients***, however it still may develop
• while they possess the capability for tissue damage, it seems unlikely they are the sole agent

Macrophages & Basophils

• these have been studied to a far lesser extent
• they contain a similar array of potentially tissue destructive factors and are already present within the alveoli
• there numbers are greatly increased in patients with ARDS

Platelets

• these are also present in large numbers in the capillaries of patients with ARDS
• aggregation at that site is associated with an increase in capillary hydrostatic pressure, possibly due to a release of arachidonic acid metabolites
• they may also play a role in the normal integrity of the capillary endothelium (Malik, Selig & Burhop, 1985)

- ***Mediators***

a. ***prostaglandins*** - TXA_2
- PGI_2

b. ***leukotrienes*** - chemotaxis
- vasoconstriction
- bronchoconstriction

c. ***lymphokines***

i. IL-1 & TNF - widespread immune stimulation
- activation of inflammatory response
- septic syndrome, fever
- vasodilatation
- hyperdynamic circulation
- systemic catabolism, hepatic anabolism
- acute phase response

ii. IL-1 & 2 - T-cell stimulation/activation

iii. IL-3 & CSF's - marrow & specific colony stimulation

iv. IL-4 & 6 - B-cell stimulation

v. interferons - antiviral activity
- T & NK cell stimulation

- IL-1, or ***endogenous pyrogen,*** acts on the pre-optic area of the hypothalamus with subsequent heat production

d. ***complement*** - chemotaxis
- vasodilatation
- increased capillary permeability

e. others

i. endotoxin

ii. kallikrien / kinin system

iii. histamine

iv. serotonin

v. FDP's

Lung Mechanics

• lung ***compliance*** C_L is reduced (< 40 ml/cmH_2O) and is adequately explained by histology
• there is impaired production of ***surfactant*** (Fein *et al*. 1982)
• Petty (1979) using BAL showed abnormally aggregated and inactive surfactant
• FRC is reduced below CC by collapse, tissue proliferation and increased elastic recoil
• alveolar/capillary permeability is increased as demonstrated by studies of transit times with inert tracer molecules
• the concept of "non-cardiogenic" capillary leak is oversimplified, possibilities being,

a. C' activation
b. fibrinolysis and platelet activation

• Dankzer *et al*. (1979) found a ***bimodal*** distribution of ***perfusion***
→ one range of near normal V/Q ratios, the other to areas of near zero V/Q
• this was sufficient to explain the $P_{A\text{-}aO2}$ gradient without the need to evoke changes in the diffusing capacity DC_{O2}
• physiological shunt Q_S is usually so large (~ 40%) that a near normal P_{aO2} cannot be achieved even with a $F_IO_2 = 1.0$
• the increase in V_D, which may exceed 70%, would require a large V_M to preserve normocapnia
• it may be argued that attempting normocapnia in these patients is inappropriate management
• gaseous exchange is further impaired, in that VO_2 is usually increased, despite the patient being paralysed and artificially ventilated (Sibbald & Dredger, 1983)

- ***Changes in Respiratory Mechanics (Start in Phase 1)***

a. ↓ total pulmonary compliance
b. ↓ FRC
c. ↑ airways resistance
d. ↑ work of breathing
e. ↑ respiratory rate & decreased V_T

- ***Changes in Haemodynamics (Sibbald, 1983)***

a. ↑ P_{pAW}
   - ↑ RV afterload
   - ↑ RVEDV & RVEDP
   - ↓ RVEF ∝ 1/(mean P_{AW})
   - ↓ RV contractility
b. normal LV function early
c. ↑ PAOP, ***without*** ↑ LVEDV
   → ? ventricular interdependence / ? ↓ LV compliance
d. LV dysfunction in later stages

Principals of Management

NB: → treatment of ***primary cause***,
other management is essentially supportive

• no specific therapeutic measure has been shown to significantly reduce the development / progression of the disease
• there are four main objectives of management (Nunn)

1. maintenance of an adequate P_{aO2}
2. minimize pulmonary transudation
3. maintenance of an adequate circulation
4. prevent complications, particularly ***sepsis***

- ***T.E. Oh***

1. ventilation
   - PEEP, CPAP, PCV, IRV
   - permissive hypercapnoea, "open-lung" models
2. fluid management
3. cardiac support
4. nutrition
5. physiotherapy
6. other therapies
   - i. antibiotics — * only by M,C&S, not prophylactic
   - ii. steroids — - late fibroproliferative phase, in absence of infection
   - iii. heparinisation — - not useful for ARDS
   - iv. ECMO
   - v. ultrafiltration — - patients unresponsive to diuretics with H_2O retention
     ? clearance of mediators of sepsis, medium MW

- ***Concensus Conference ICM 1994***

• several therapeutic methods are so universally accepted that, although not formally tested, may be considered as standard,

1. suplemental O_2
2. PEEP / CPAP
3. mechanical ventilation
4. avoidance of fluid overload
5. delivery of care in an ICU setting

■ ***Ventilation***

• ventilation should be adjusted to maintain adequacy of oxygenation and to reduce peak and mean airway pressure
• PEEP is almost universally required to maintain an adequate P_{aO2}
• it is of no prophylactic benefit but ***does*** improve survival
• benefits of PEEP are,

a. reduction in F_IO_2
b. improved DO_2
c. increased compliance
d. reduction in atelectasis

• hazards of PEEP include,

a. ***increase*** in total lung water
b. inactivation / destruction of surfactant
c. may produce a fall in CO and DO_2

• normocapnia becomes a lower priority as ***barotrauma*** becomes more likely
• HFJV & HFPPV provide no advantage over traditional ventilation
• they do result in a decrease in mean P_{IP}, but there is no improvement in mortality
• ECMO has shown ***no proven*** benefit, mortality remains the same
• Morris *et al.* (AJRCCM '94) "Salt Lake City Trial", comparing,

1. computer driven models of ventilation with SIMV
2. PCIRV & EC-CO_2R

NB: maintaining similar mean P_{AW} → ***no benefit*** in mortality

• Lessard *et al.* (Anaesth. '94) showed ***no benefit*** in terms of barotrauma, oxygenation, or survival with the use of PCIRV versus conventional ventilation when efforts to keep total PEEP and ***mean airway pressure*** the same were made

• the level of ***optimal PEEP*** is described using various end-points,

1. maximal DO_2
2. lowest Q_S < 15%
3. P_{aO2} > 60 mmHg * with lowest $F_IO_2 \geq 30\%$
4. maximal improvement in C_L
   i. dynamic V/P curves
      • maximal volume recuitment for given P_{AW} *above inflexion point
   ii. static V/P curves
      • inflexion point with recruitment

■ ***Pharmacotherapy***

• fluid balance should be adjusted to lessen the formation of oedema
• Fein *et al*. recommend values of **PAOP ~ 5-10 mmHg**
• administration of NSA-C / 5% ***does not*** reduce the formation of oedema
• some early work suggested the administration of massive doses of ***steroids*** may halt the development of the disease, Sibbald *et al*. 1981
• subsequent work has shown ***no benefit***, or an increased incidence of sepsis and a higher mortality, thus the administration of steroids is not recommended for routine cases
• Meduri *et al*. (Chest '94) showed steroids may be of benefit for the subgroup of ***late proliferative ARDS*** providing underlying infection was meticulously ruled-out,

1. blood cultures, CUD urine specimen
2. BAL + quantitative culture, or PSB
3. no other septic foci - lines, GIT

• other pharmacotherapy includes,

1. endotoxin Ab's - anti-LPS Ab
2. free radical scavengers - antioxidants, SOD, catalase, NAC
3. cyclo-oxygenase inhibitors - Indomethacin, Ibuprofen
4. thromboxane inhibition - ketoconazole
5. cytokine inhibition - anti-TNF
6. surfactant replacement
7. PGE_1

NB: these are only of prophylactic benefit in animal studies,
none has been shown to improve outcome in human studies,
Ibuprofen improves early ***haemodynamic stability*** but not mortality

■ ***Outcome***

a. mortality **~ 50-70%**
   - unchanged over last decade
   - ? small decrease depending upon criteria for diagnosis

b. poor prognosis
   - elderly
   - severe disease, uncontrolled 1° cause
   - high PVR, RV dysfunction
   - impaired DO_2

c. associated problems
   i. ***nosocomial pneumonia*** **~ 70%**
   ii. high incidence of sepsis syndrome
   iii. MODS

Fluid Management in ARDS / Pulmonary oedema

- ***Simmons et al., ARRD Apr-1987***

• effect of fluid balance on survival in ARDS
• 213 patients in a prospective data collection study → 113 met criteria for ARDS
• multiple variables up to 14 days after intubation → CO, PAOP, MAP, I-O, ΣI-O, δWt
• significant differences in ΣI-O and δWt between survivors and nonsurvivors on almost every day
→ survivors lost weight and significantly lower ΣI-O cf. nonsurvivors
• logistic regression to determine if δWt and ΣI-O could predict survival,
  • ↓ wt. ≥ 3 kg → 67% survival
  • ↑ wt. ≥ 3 kg → 0% survival day 14

• similar results obtained using comparably low and high values for ΣI-O

NB: this ***does not*** establish a cause and effect relationship,
likely means only that "sicker" patients needed more fluid resuscitation & developed "leakier" capillaries

- ***Humphrey et al., Chest. May-1990***

• looked at survival and ICU length of stay of 40 ARDS patients
• analyzed to determine if a management strategy of lowering the PAOP was associated with an increased survival or a decreased ICU length of stay
• patients were divided into two groups:

1. group 1 - reduction of PAOP ≥ 25%
2. group 2 - reduction of PAOP ≤ 25%

• survival to hospital discharge

1. group 1 - 12/16 75%
2. group 2 - 7/24 29%

• difference remained statistically significant stratifying patients by age & APACHE II

NB: concluded that, *"analysis supported the notion that treatment of low pressure pulmonary edema with reduction of PAOP is associated with an increased survival"*

similarly, this ***does not*** imply a causal relationship for therapy,
patients in whom greater reductions in PAOP can be achieved are likely less severe and more likely to survive anyway

■ ***Eisenberg et al.*** ***ARRD Sep-1987***

• prospective evaluation of ***extravascular lung water*** (EVLW) instead of pulmonary artery wedge pressure measurements to guide the hemodynamic management of 48 critically ill patients

• randomized → protocol management, PM
→ routine management, RM groups

• RM group → EVLW measurements blinded
• groups similar for age, gender, and severity of illness
• of patients with initially high EVLW → EVLW decreased
→ PM ~ 18 ± 5%
→ RM ~ 4 ± 8% ($p < 0.05$)

• difference was ***greater*** in patients with CCF
• following the protocol, no adverse effects on - oxygenation
- renal function

• ***mortality*** →

1. not statistically different for entire groups
2. significantly better ($p < 0.05$) for PM patients with initially high EVLW and normal PAOP (predominantly sepsis or ARDS patients)

• mortality for both groups of patients,

1. initial EVLW > 14 ml/kg → 13/15 **87%**
2. initial EVLW < 14 ml/kg → 13/32 **41%** ($p < 0.05$)

NB: concluded that, *"management based on a protocol using EVLW measurements is safe, may hasten the resolution of pulmonary edema, and may lead to improved outcome in some critically ill patients"*

■ ***Mitchell, Schuller, et al. ARRD 1992***

• randomised prospective trial to assess effect of management emphasising diuresis & fluid restriction on,

1. development or resolution of EVLW
2. mechanical ventilation hours
3. ICU duration

• 101 patients requiring PAC insertion,

1. 52 patients → EVLW management
2. 49 patients → PAOP management

• 89 patients with pulmonary oedema = EVLW > 7 ml/kg (ideal BW)
• no significant differences in baseline disease status (APACHE II, OSF), minor age difference

	PAOP Group	EVLW Group
$EVLW_t : EVLW_{t=0}$ [1]	No change	↓ t > 24 hrs ($p < 0.05$)
Cumulative I-O[2]	2239 ± 3695 ml median = **1600** ml	142 ± 3632 ml median = **754** ml
Median ICU Days[3]	16 days	7 days ($p = 0.05$)
Median MV	22 days	9 days ($p = 0.047$)
↑Creatinine[4] ↑BUN	17.6 ± 79 µmol/l 2.1 ± 6.4 mmol/l	35 ± 88 µmol/l 4.6 ± 9.6 mmol/l
Mortality[5]	**47%**	**35% (p = 0.21)**

[1] only for the 89 patients with initial EVLW > 7 ml/kg

[2] ***No difference*** in - the number of patients requiring vasopressors/inotropes
- the duration of use of vasopressors/inotropes

[3] ***No difference*** in MV or ICU duration for the subset of patients with CCF / volume overload

[4] Small but statistically significant increase in plasma ***creatinine & BUN*** in EVLW group

[5] ICU plus within 48 hours of discharge if related to ICU admission pathology

■ ***Schuller, Mitchell et al. Chest 1991***

• aim to evaluate fluid balance and changes in ***extravascular lung water*** (EVLW) on survival in the ICU and short-term outcome in patients with pulmonary edema
• retrospective analysis of data, sorting by survival and "treatment received"
• taken from a randomized controlled trial of fluid restriction (Mitchell *et al*., ARRD 1991)
• 89 patients requiring PA catheterization with high EVLW > 7 ml/kg,

1. survival
   - survivors had no significant fluid gain or change in EVLW
     but decreased wedge pressure and body weight, cf. nonsurvivors
2. fluid balance
   - < 1000 ml fluid gain at 36 hrs → survival ~ 74 %
   - > 1000 ml fluid gain at 36 hrs → survival ~ 50 % ($p < 0.05$)
3. median ventilation days
   ICU days
   hospital days → ~ 50% for < 1000 ml fluid gain

NB: accounting for differences in the severity of illness,
fluid balance was an ***independent predictor*** of survival ($p < 0.05$)

NB: "These data support the concept that positive fluid balance *per se* is at least partially responsible for poor outcome in patients with pulmonary edema and defend the strategy of attempting to achieve a negative fluid balance if tolerated hemodynamically."

ASPIRATION SYNDROMES

- there is a spectrum of presentations,

a. ***acute massive aspiration***
   - i. acid aspiration pneumonitis - Mendelsonn's syndrome
   - ii. non-acid aspiration
     - particulate - food, FB, non-acid vomitus
     - non-particulate - blood, water, near drowning

b. ***sub-acute aspiration*** - microaspiration
   - nosocomial pneumonia

c. ***chronic aspiration*** - nosocomial pneumonia
   - bronchopneumonia
   - bronchiectasis
   - lung abscess
   - ch. interstitial fibrosis
   - atypical mycobacterial fibrosis
   - late onset "asthma"

■ ***Acute Acid Aspiration***

1. acute pulmonary oedema
2. ARDS
3. acute "asthma"
4. "atypical pneumonia"
5. acute bronchopneumonia

- often previously healthy person & rapid in onset, frequently preventable
- frequently ***non-infected*** acid aspirate
- antacids often useful

■ ***Chronic Micro-Aspiration***

1. nosocomial pneumonia
2. recurrent bronchopneumonia
3. chronic "asthma"

- frequently in hospitalised patients and insidious in onset
- multiple risk factors and difficult to prevent
- the aspirate is frequently infected
- ***antacids*** may actually predispose → GIT colonisation
- ?? recent studies would ***not*** support his concept

- ***Risk Factors***

a.	altered ***conscious state***	- trauma - coma - ETOH, drugs (CNS depressants) - CVA - epilepsy - hypotension
b.	impaired ***airway reflexes***	- drugs (CNS, NMJ) - intubation / extubation - tracheostomy - CVA - motor neurone disease, MS, GBS, CIP - elderly
c.	***regurgitation***	- pregnancy - hiatus hernia - obesity - bowel obstruction - NG tube - oesophageal disease - LOS dysfunction

- ***Nature of Aspirate***

1. gastric acid
2. particulate
3. infected fluid
4. blood
5. fresh vs. salt water

■ ***Infected Aspiration***

- differences for micro vs. macro-aspiration
- frequent colonization of the upper airways of hospitalized and critically-ill patients,

a. ***pre-hospitalized aspiration***

→	predominantly anaerobes	- Bacteroides m. & f. - Fusobacterium - Peptostreptococcus
&	some aerobes	- Pneumococcus - Micrococcus

R_X Penicillin & Metronidazole

b. ***hospitalized patient + antacids***

→	predominantly gram (-)'s	- E. coli - Klebsiella - Proteus - Pseudomonas
&	some gram (+)'s	- Staphlococcus
	some fungi	- Candida

R_X Flucloxacillin & Gentamicin, or
Cefotaxime + Flucloxacillin ± Metronidazole

Treatment

1.	prevention	- sucralfate, antacids - topical antibiotics - cricoid pressure
2.	protection of airway	- ETT
3.	tracheobronchial toilet	- suction, lavage - flexible/rigid bronchoscopy
4.	oxygen & ventilatory support	
5.	chest physiotherapy	
6.	bronchodilator therapy	
7.	antibiotics	- ***no*** proven benefit or harm - most would treat as above
8.	steroids	- no proven benefit or harm - may increase 2° infections
9.	systemic support for ARDS, sepsis syndrome etc.	

ACUTE ASTHMA

Def'n: a disease characterized by wheezing, dyspnoea and cough,
resulting from ***airways hyperreactivity,*** and
variable degrees of ***reversible airways obstruction*** (ATS, 1987)

• current emphasis is on airway ***inflammation*** in pathogenesis, in conjunction with smooth muscle mediated bronchoconstriction and intraluminal mucus
• a subgroup suffer sudden, unexpected increases in airflow obstruction, due mainly to bronchospasm, termed variously as,

a. ***sudden asphyxic asthma*** - Wasserfallen, ARRD 1990
b. hyperacute asthma - ? Tuxen

• characterized by,

1. minimal baseline airflow obstruction, but marked hyperreactivity
2. innocuous or unrecognized stimulus
3. very rapid severe onset, often fatal within 1 hr
4. relatively rapid resolution
5. comprise **~ 75%** of ventilated asthmatics

• this contrasts ***acute severe asthma***, characterized by,

1. persistent significant airflow obstruction → FEV_1 < 50% pred.
2. relatively asymptomatic, with ***underperception*** of disease
3. behaviour modification & denial
4. attacks result from small deteriorations in function
   → 'apparent' sudden severe symptoms
5. slow resolution, with large chronic component
6. comprise **~ 25%** of ventilated asthmatics

• studies of patients dying from SAA, cf. patients with chronic asthma, show,

a. ↑ ***neutrophils*** / ↓ eosinophils in airways submucosa
b. less intraluminal mucus

• Kikuchi, *et al.*, NEJM 1994, found patients with a history of ***near-fatal*** asthma have,

a. a blunted hypoxic ventilatory response, and
b. diminished dyspnoea during inspiratory resistive loading, cf. other asthmatics

NB: diminished ***patient perception*** increases the risk of future life-threatening or fatal asthma

Assessment of Severity

NB: no ***single*** clinical measurement has been shown to reliably predict outcome

Mild / Moderate[1]		Indications for IPPV
• loudness of wheeze[2]		• conscious state = ***most useful***
• forced expiratory time		• inability to speak
• respiratory rate	> 30	• pulsus paradoxus[3] > 15 mmHg
• HR	> 130 bpm	• respiratory fatigue
• use of accessory muscles[3]		• P_{aCO2} ≥ normal, or ***rising***[4]
• PEFR	**< 30%** pred.	• failure to respond to therapy
• $FEV_{1.0}$	**< 30%** pred.	

[1] generally ***not*** useful in severe failure

[2] poor correlation with degree of airflow limitation, Shim. *et al.*, Arch.Int.Med.1983

[3] may actually decrease with the onset of severe respiratory failure

[4] ***hypercapnoea*** usually only occurs with a FEV_1 < 25%, but alone doesn't mandate IPPV; ***absence*** of hypercapnoea ***does not*** exclude severe obstruction & impending arrest

- ***ICU Admission***

1. patients requiring IPPV
2. severe airflow obstruction
   i. accessory mm., exhaustion, diaphoresis
   ii. p.paradox > 12 mmHg
   iii. PEFR < 25%
3. poor response to initial therapy / deteriorate despite therapy
4. altered mental status
5. cardiac toxicity / complication

Assessment During Ventilation

a. expiratory time

b. pulsus paradoxus

c. autoPEEP
   i. static - end-expiratory occlusion pressure
   ii. dynamic - δP_{IP} prior to onset of airflow

d. alteration in P_{aCO2}

e. pressure differential
   i. end-inspiratory occlusion P - P_{IP}
   ii. peak-to-plateau gradient ~ 0.5-0.75s inspiratory pause
      - δP / PIFR → ***resistance***
      - but, with severe airflow obstruction 0.75s is inadequate for equilibration

f. end-expiratory trapped gas volume
   = volume expired after prolonged expiration ($\geq$ 1')

g. ECG - RAD, RVH & 'strain', acute TR

h. CXR - limited use, see over

Indications for CXR

1. any asthmatic post-intubation
2. signs / symptoms of ***barotrauma***
3. clinical findings suggestive of ***pneumonia***
   localizing signs on chest examination
4. when the diagnosis is uncertain → ***exclusion***

NB: Zieverink, Rad. 1982, 528 CXR's in 122 asthmatics

→ abnormalities in **~ 2.2%**

Factors to Exclude

a. pneumothorax

b. FB

c. upper airway obstruction

d. LVF & severe emphysema ± echocardiogram

e. pulmonary emboli ± lower limb doppler, lung perfusion scan

- ***Investigations***

a. FBE, MBA
b. serial AGA's
c. CXR
d. ECG
e. microbiology - tracheal aspirate for MC&S
   - blood cultures if febrile
f. paired serology - atypical pneumonia
g. PFT's during recovery - serial PEFR
   - FEV_1/FVC

- ***CVS Effects of Severe Asthma***

1. pulmonary hypertension- HPV, 2° mediator release
   - acute ↑ RV afterload
   ± ↓ LV preload ∝ interdependence
2. impaired venous return
3. ↑ LV afterload - SNS outflow
4. 2° effects from - hypoxia, hypercarbia & acidosis
5. 2° effects from drugs - β-agonists, aminophylline

- ***Mechanical Abnormality***

→ increased ***airways resistance***
a. all airways involved but to differing degrees
b. regional variation in ***time constants***
c. hyperinflation and obstruction
d. rapid shallow respiration
e. ↑ ***work*** of breathing

- ***Pathology***

a. smooth muscle contraction
b. inflammatory infiltrate & mucosal oedema
c. mucus plugging & inspissation of secretions
d. segmental/lobar obstruction or collapse
e. barotrauma

- ***Mediators***

a. histamine
b. leukotrienes * $LT\text{-}D_4$
c. cholinergic nervous system
d. neuropeptides from NANC nervous supply
e. PG's
f. IgE
g. PAF

- ***Complications***

a. hypoxia, hypotension - myocardial, cerebral hypoxic damage
b. respiratory
   i. barotrauma / volutrauma - pneumothorax, pneumomediastinum
      - pneumopericardium, subcutaneous emphysema
   ii. mucus plugging, airway obstruction, atelectasis
   iii. infection
   iv. respiratory arrest
c. biochemical disturbances
   i. hypokalaemia, hypophosphataemia, hypomagnesaemia
   ii. hyperglycaemia
   iii. lactic acidosis - hypoxia / hypotension
      * β-agonists, aminophylline
d. drug related
   i. theophylline toxicity
   ii. neuropathy / myopathy ? neuromuscular blockade & steroids

- ***Long-Term Beta-2-Agonists***

1. heavy use (> 1 cannister/month) is a marker of severe asthma
2. heavy or increased use warrants additional therapy with steroids
3. use may make asthma ***worse***
4. patients currently using β_2-agonists should slowly withdraw non-essential doses & use as rescue medication during "breakthrough" asthma

NB: position statement, American Academy of Allergy & Immunology, 1993

Treatment

- ***Medical Treatment***

a. O_2 therapy

b. inhaled β_2-agonists - continuous nebulized salbutamol
   - in non-intubated patients MDI's + spacing devices are equally effective as nebulizers
   - **~ 3%** of radioactive aerosol delivered by small volume nebulizer reaches the lungs in mechanically ventilated patients (MacIntyre, CCM 1985)

c. IV β_2-agonists
   - ***no*** proven advantage for - IV cf. inhaled route
     - selective agents cf. adrenaline
   - result in hypokalaemia & tachyarrhythmias
   - increase the VO_2, P_{aCO2} and lactic acidosis
   - $\therefore$ use in younger patients (preferrably < 40) not responding to inhaled R_X

d. aminophylline ~ 6 mg/kg/30 mins IV
   ~ 0.5 mg/kg/hr maintenance
   - inferior to β_2-agonists as monotherapy
   - various studies have demonstrated addition of theophylline ***does not*** confer therapeutic benfit and increases tremor, N&V, arrhythmias, etc.
   - other studies show opposite, AJRCCM '95
     *"inadequate evidence to **support** or **reject** the use of theophylline in this setting"*
   - $\therefore$ use in patients with poor or incomplete response to β_2-agonists/steroids
   - ***NB:*** $\downarrow$ clearance $\propto$ CCF, liver failure, macrolides, ciprofloxacin

e. ipratropium
   - conflicting evidence but probably an additive effect, not first line agent

f. ***steroids***
   - not useful via the nebulized route in the acute attack
   - early IV administration useful, significant difference at ***12 hours***
   - reduce the need/duration of hospitalisation & number of relapses
   - *"failure to treat with steroids contributes to asthma deaths"* AJRCCM '95

g. others
   i. $MgSO_4$ infusion
      - benefit has been described in patients with ***normal*** plasma Mg^{++} levels
      - ~ 50% of patients with SA have low plasma levels
      - the 2 largest PRCT's ***failed*** to show any benefit
      - *"available data **do not** support the use of magnesium in SA"* AJRCCM '95

   ii. nitric oxide

   iii. heliox

   iv. ECMO

- ***Effects of Steroids***

1. anti-inflammatory
2. potentiate the effects of β-agonists
3. receptor upgrading
4. stabilisation of lysosomal membranes
5. reduce capillary permeability
6. inhibit histamine release

- ***Indications for Antbiotics***

1. fever & sputum containing polymorphs/bacteria
2. clinical findings of pneumonia
3. signs & symptoms of acute sinusitis

NB: majority are ***viral*** & there is no role for routine use

- ***Bronchioalveolar Lavage***

- autopsy studies show marked mucus impaction of both large and small airways
- ***no benefit*** in SA has been demonstrated for chest physiotherapy, mucolytics or expectorants
- BAL using either saline or NAC may be useful in some patients
- in intubated patients, potential risk of an acute increase in V_{EI} due to increased resistance

NB: *"should **not** be considered a part of routine management of ventilated asthmatics"*

- ***CPAP Ventilation***

a. potential advantages
   i. ↓ work of breathing
   ii. ↓ inspiratory muscle load & ↑ muscle efficiency
   iii. ↓ need for sedation / anaesthesia / intubation
   iv. ? ↓ incidence of - nosocomial pneumonia
   - otitis & sinusitis

b. potential disadvantages
   i. gastric distension & risk of aspiration
   ii. less control over ventilatory pattern
   iii. exacerbation of gas-trapping & overexpansion
   iv. pressure necrosis

NB: *"further studies involving large numbers of patients are needed"*

Paralysis

1. potential advantages
   i. ↓ VO_2 & CO_2 production
   ii. ↓ lactate production
   iii. ***may*** decrease risks of barotrauma *theoretical, not proven
   iv. ↓ expiratory muscle activity may ↓ airways resistance
2. potential disadvantages
   i. difficulty assessing mental status / risks of awareness
   ii. ↑ risk of DVT
   iii. disuse muscle atrophy
   iv. ? causative role in ***myopathy*** in acute asthmatics with ***steroids***
      - other possible factors include hypokalaemia, hypophosphataemia & high dose beta-agonists
      - the contention that the steroid molecule of vecuronium/pancuronium would potentiate this effect is ***not supported*** Fleugel, AJRCCM 1994

NB: concensus view, *"until further data available, NMJ blockade should be reserved for patients unable to be ventilated with sedation alone"*

Ventilatory Parameters

→ low V_T ≤ 10 ml/kg
low rate ≤ 10 bpm
high flow rate ≥ 80 l/min
high F_IO_2 ≥ 0.5

a. $\mathbf{F_IO_2}$ → adequate to prevent hypoxia

b. $\mathbf{V_T}$ → limits peak P_{AW} ≤ 50 cmH_2O (*not necessarily)

c. ***rate*** → allows full expiration - ie. minimal auto-PEEP

d. pulse paradox ≤ 30 mmHg

e. end-expiratory P_{Occ} £ **10 mmHg**
   - measures of ***autoPEEP*** are only accurate in ***paralysed patients***
   - has ***not*** been shown to correlate with complications
   - may significantly ***underestimate*** hyperinflation due to noncommunicating gas

f. end-inspiratory volume **< 20 ml/kg**
   - V_{EI} > 20 ml/kg → ↑ barotrauma, hypotension (Tuxen *et al.*, ARRD'92)
   - however, not prospectively validated & doesn't measure all trapped gas

g. end-inspiratory P_{Plat} < 25 mmHg (30 cmH_2O)
   - more easily determined than V_{EI} but not a reliable predictor of complications
   - like V_{EI}, not prospectively validated, but complications rare at P_{Plat} < 30 cmH_2O
   - this equates to ~ 1.6 l increase above FRC

- ***Risks of Permissive Hypercapnia***

1. cerebral vasodilatation
2. cerebral oedema
3. decreased myocardial contactility
4. systemic vasodilation & hyperdynamic circulation
5. pulmonary vasoconstriction

NB: most of these are not significant for otherwise healthy patients, hypoventilation is well tolerated with $P_{aCO2} < 90$ mmHg (Darioli, ARRD 1984)

• virtually all studies of permissive hypercapnia in SA report near-zero mortality rates, significantly less than studies where 'normal' AGA values are achieved, though there is no large RCT

- ***Prevention of Further Episodes***

1. education - disease and drug administration
2. monitoring using a peak flow meter
3. regular anti-inflammatory therapy
   - use of a spacing device & mouth washing post-inhalation
4. rescue use of β-agonists
5. early presentation for medical assessment with deterioration

- ***Causes of Death***

NB: a history of near-fatal asthma requiring mechanical ventilation is the ***single best predictor*** of subsequent asthma death

1. cerebral hypoxia
2. barotrauma
3. tension pneumothorax

ATYPICAL PNEUMONIA SYNDROME

- ***Common Causes***

1. viral pneumonia - influenza A&B, parainfluenza
   - RSV, CMV, varicella
2. *Mycoplasma pneumoniae* ~ 5% community acquired
3. *Legionella pneumophilia* ~ 3% community acquired
   - probably underdiagnosed to a significant degree
4. *Chlamydia psittaci* pneumoniae
5. *Coxiella burnetti* * Q fever
6. atypical mycobacteria

- ***Other Causes***

1. infective
   i. atypical presentation of bacterial pneumonia
   ii. pulmonary TB
   iii. opportunistic infections in immunocompromised
2. non-infective
   i. thromboembolic disease
   ii. collagen vascular disorders
   iii. malignancies
3. aspiration pneumonitis

- ***Slowly Resolving Pneumonia***

a. ***organism*** causes - antibiotic resistance *ESBL producers
   - viral, fungal, parasitic
   - superinfection

b. ***therapeutic*** causes - inappropriate agent / dosage

c. ***host*** causes
   i. lung disease - bronchiectasis, empyema, lung abscess
   - bronchial obstruction
   - chronic aspiration
   - underlying malignancy
   - interstitial & other lung diseases
   ii. other host diseases - immunocompromised
   - LVF
   - malignancy, HIV

NOSOCOMIAL PNEUMONIA

- from McLaws, MJA 1988, looking at ***general hospital*** populations

  → nosocomial infections occur in **6-7%** of patients

- Chastre, , 15-35% of these are pneumonia with a ***mortality*** rate of 50-70%

- most are endogenous ***gram negative*** bacteria, many are ***polymicrobial***
- a high proportion occur in ICU patients

- Daschner, ICM 1982, ICU patients

  → the overall ***incidence*** of nosocomial infections in ICU patients ~ **12-20%**

  1. UTI ~ 40%
  2. septicaemia ~ 20%
  3. pneumonia ~ 16%

  NB: nosocomial infections in patients with ARDS **~ 70%**

- ***Aetiology***

a.	gram negative bacilli	**~ 70%**	- E. coli - Pseudomonas - Enterobacter - Klebsiella
b.	gram positive cocci	~ 15-25%	- Staphlococci - Enterococcus
c.	fungal	~ 5%	- Candida

- ***Mortality***

a.	gram negatives		~ 50-56% overall
	i.	Pseudomonas	~ 70%
	ii.	Klebsiella Serratia Enterobacter	~ 40%
	iii.	E. coli	~ 30%
b.	gram positives		~ 5-25%
c.	viruses		~ 7%

Risk Factors	
Host Factors	Therapeutic Factors
• age newborn elderly > 60 • multiple trauma • severe 1° disease • neutropaenia • immunosuppression	• ICU or SCN • systemic antibiotics • invasive catheters • large transfusion • need for haemodialysis • corticosteroids

- ***Meduri Chest 1990***

a. diagnosis of ***nosocomial pneumonia*** in an intubated patient is difficult

b. ***tracheal aspirate*** in ventilated patients is often inaccurate & misleading

c. ***colonisation*** rate **> 60%**

d. risk factors for colonisation and infection are similar

e. other conditions can simulate pneumonia and may go untreated

f. recognition of a specific pathogen is important for effective treatment

g. a large number of patients ***do not*** have pneumonia

h. inappropriate antibiotics
   i. ↑ colonisation risk → superinfection
   ii. ↑ resistant bacterial strains
   iii. potential side effects
   iv. cost

i. many diagnostic techniques - histology = "gold standard"

Technique	Sensitivity	Specificity
Clinical	**64%**	80%
Tracheal Aspirate	80-95%	40-60%
LRS	95+%	40%
Bronchio-Alveolar Lavage	75-100%	30-75%
Protected Sputum Brushings	40-100%	40-100%

* these figures are from different studies, animal and patient, with different diagnostic criteria for pneumonia

■ ***Andrews Chest 1981***

• histology at PM versus ***clinical findings*** → sensitivity **~ 64%**
specificity **~ 80%**

1. fever
2. leukocytosis
3. purulent tracheal aspirate
4. new pulmonary infiltrate on CXR

NB: ARDS patients with a new infiltrate frequently ***do*** have pneumonia,
non-ARDS patients with a new infiltrate frequently ***do not*** have pneumonia

■ ***Fagon & Chastre ARRD 1989***

• looking for rate of development of nosocomial pneumonia in intubated ICU patients
• diagnosed with PSB with semiquantitative culture → ***sequential incidence***,

a. day 10 ~ 6.5%
b. day 20 ~ 19%
c. day 30 ~ 28% → overall incidence **~ 9%**

• 40% of these were ***polymicrobial***
• for the NCP group mortality was 71% cf. 29% in the non-pneumonia group
• the use of antibiotics selects out resistant *Pseudomonas* and MRSA

■ ***Salata ARRD 1987***

• 51 intubated ICU patients
• effectiveness of ***tracheal aspirate*** to distinguish colonisation from infective pneumonia

	Nosocomial pneumonia	Colonisation
PMN's	> 1^+ > 10/hpf > 30,000/µl	< 2^+
Bacteria	> 1^+ > 1-10/oil field	< 2^+
CFU	> 100,000	< 100,000
ICF organisms	> 1-5% of PMNs	< 1%
Elastin Fibres	+'ve 52% gram(-)	+'ve 9%
Squamous cells	< 10/hpf	> 10/hpf

- ***Johanson ARRD 1982***

• ventilated animal study of diagnostic tools

Investigation	Sensitivity	Specificity
TA	80%	60%
BAL	74%	?30%
PSB	40%	?60%
needle Bx	50%	?50%

Investigation	Sensitivity	Specificity
LRS[1]	100%	40%
PSB[1]	80%	100%
PSB[2]	70%	100%
PSB[3]	100%	60%

[1] Richard, ICM 1988, suction samples (LRS) versus PSB (< 10^3 CFU)

[2] Higuchi, ARRD 1982, primate model of acute lung injury ± pneumonia

[3] Chastre, ARRD 1984, PSB versus immediate post-mortem histology

• Kirkpatrick, ARRD 1988, 8 "normal" subjects studied with BAL & PSB looking at the sterility of the samples, ie. contamination of the specimen

1. PSB = 7/8 but < 10^4 CFU
2. BAL = 1/8

• Gassorgues, ICM 1989, BAL vs PM in 13 intubated patients

→ BAL 100% sensitive but 75% specific

- ***Chastre & Fagon AJM 1988***

• BAL vs. PSB in 21 intubated ICU patients,

a. "both useful and complimentary" in diagnosis

b. BAL → +'ve gram stain with ***intracellular bacteria*** > 25% PMN's rapid and useful
   • WCC and semi-quantitative cultures (> 10^4 CFU) less useful

c. PSB → > 10^3 CFU useful in diagnosis but results delayed 48 hrs

d. PSB gives higher false negatives - ie. ***lower sensitivity***
   • supported by below

- ***Papazian AJRCCM 1995***

• prospective post-mortem study of diagnostic tool efficacy in diagnosis of VAP
• histology & culture performed within 30 min of death in 38 patients ventilated > 72 hrs

a. histology (+) - 18/38 patients ~ 47%

b. culture (+) - 12/18 patients **~ 32%** ***definite VAP***

	Threshold[1]	Sensitivity %	Specificity %
CPIS	> 6	72	85
mini-BAL	> 10^3 cfu/ml	67	80
BAL	> 10^4 cfu/ml	58	95
PSB	> 10^3 cfu/ml	**42**	95
BBS	> 10^4 cfu/ml	83	80

[1] Figures for ***definite VAP***, ie histology & culture positive

• conclusions,

1. as BBS is more sensitive & non-invasive, ∴ preferrable to PSB
2. due to ***low sensitivity***, results of a negative PSB should be viewed with caution
3. overall diagnostic ***accuracy*** was greatest for BBS/BAL at 81%

• CPIS, Pugin *et al.*, ARRD 1991 (Clinical Pulmonary Infection Score)

1. clinical - temp., quantity & character of tracheal asp.
2. biological - WCC, P_{aO2}/F_IO_2 ratio
3. radiographic - CXR
4. microbiological

■ ***Bonten et al. AJRCCM 1995***

• evidence for a causal relationship between ***gastric colonization*** and VAP based on studies relating colonisation to species causing pneumonia Torres *et al.*, ARRD 1993

1. VAP diagnosed by ***clinical criteria*** *poor sensitivity/specificity
2. no chronological relationship established
3. gastric pH values determined only ***once daily*** by indicator slide test
4. no studies used double-blind PRCT study

• PRCT of 141 patients, of whom **112** had continuous gastric pH monitoring

a. group 1 58 - antacids, (Al/Mg-OH), 30 ml q4h
b. group 2 54 - sucralfate 1g q4h

NB: no significant differences in ***median pH values***

• stratifying patients by colonization,

a. median pH values were higher in patients with ***gastric*** bacterial colonization
b. ***no difference*** seen for oropharyngeal or tracheal colonization

• ***ventilator associated pneumonia***,

a. diagnosed by BAL (> 10^4 CFU) / PSB (> 10^3 CFU)
b. occurred in ~ **22%** → same in both groups
c. polymicrobial in 19/31 episodes → 51 isolates
   i. prior tracheal isolation ~ 96%
   ii. prior oropharyngeal isolation ~ 75%
   iii. prior gastric isolation ~ 31%

NB: in ***one case*** the organism resulting in VAP initially colonized the stomach, in five cases, colonization occurred ***simultaneously***

• this is supported by Inglis *et al.*, Lancet 1993, who showed ***chronological*** colonization from stomach to trachea in only 6/100 ventilated patients

• ***enteral feeding***,

a. did not alter gastric acidity
b. ***increased*** gastric colonization with *Enterobacteriaceae*
c. no change in oropharyngeal or tracheal colonization
d. confounding factor of ↑ ***gastric volume*** controlled

NB: ***gastric acidity*** influenced gastric colonization, but ***not*** colonization of the upper respiratory tract or the incidence of VAP

ICU Pneumonias

1. early onset ≤ 4 days
2. nosocomial, or late onset

- the ***incidence*** of ICU acquired pneumonia **~ 21%**
- and ~ 54% of these occur within the first 4 days
- risk factors include,
    a. impaired airway reflexes
    b. severity of underlying pathology
    c. duration in ICU

- ***Early Onset Pneumonia***

    a. occurs within 4 days
    b. is very common
    c. is unrelated to
        - age
        - type of illness
        - immune suppression
    d. frequently oropharyngeal pathogens
    e. mainly in intubated patients
    f. little affected by antibiotic prophylaxis

- ***Late Onset Pneumonia***

    a. usually gram (-)'ve pathogen
    b. frequently impaired airway reflexes
    c. should (?) be influenced by antibiotic prophylaxis

Haemoptysis

a. ***airways*** - trauma
- tumour
- infection
- FB

b. ***lung*** - trauma
- tumour, 1° or 2°
- infection, inflammation/vasculitis, infarction

c. ***CVS*** - LVF, MS
- pulmonary emboli, infarction
- pulmonary AVM

d. ***coagulopathy***

Def'n: ***massive haemoptysis***, defined arbitrarily as blood loss,

1. between 200-600 ml expectorated per 24 hours, or
2. resulting in acute ***airway obstruction***, or
3. resulting in acute ***hypotension***

• more than 90% of cases are due to ***chronic infection***, as inflammation leads to profuse vascularisation of the high pressure bronchial circulation
• the most common causes are,

1. TB
2. bronchiectasis / pulmonary abscess
3. bronchial neoplasms

• resections for haemoptysis > 600 ml/24 hrs carry a high ***mortality rate*** **~ 15-20%**
• this is better than conservative management, which averages up to 75%
• surgery is probably ***indicated*** in those patients who,

a. require multiple transfusion
b. show progressive deterioration of pulmonary function
c. continue to bleed despite adequate medical management

• surgery is probably ***contra-indicated*** in those patients who,

a. have inoperable bronchial carcinoma
b. fail to have their bleeding site localised
c. have severe bilateral pulmonary disease
d. have severe debilitating systemic disease

• most patients should have a ***rigid bronchoscopy***, due to the greater ease of ventilation and suctioning
• upper lobe bleeding may require the use of a flexible scope
• moderate bleeding may be controlled through the bronchoscope
• prevention of soiling of the innocent lung may be achieved by the use of a bronchial blocker, such as a balloon-tipped Fogarty catheter, or DLT intubation
• if the patient is deemed inoperable, then bronchial ***embolisation*** may be attempted

- ***Anaesthesic Principals***

1. preoxygenation and ventilation with 100% O_2
2. several large bore IV canulae should be inserted
3. the patient should be cross-matched + baseline FBE
4. the patients coagulation profile should be checked
5. antibiotics should be commenced preoperatively
6. adequate suctioning should be available
7. ***on induction*** the bleeding lung should be ***dependent***, and anti-aspiration measures should be employed
8. alternatively, in the patient with massive haemoptysis, an awake, semi-upright intubation may be required
9. separation of the two lungs, - DLT
   - SLT + bronchial blocker
10. IPPV + PEEP - with regular intermittent suctioning

NB: after the airway is secured and the lungs ***separated***, the bleeding lung should be in the ***non-dependent*** position

• patients are frequently ***hypovolaemic***, therefore induction should follow adequate volume replacement and should be achieved with either a small dose of STP or ketamine, or alternatively use narcotics
• if a SLT is already in place, consideration should be given to,

a. replacing it with a DLT
b. the addition of a bronchial blocker
c. endobronchial intubation

DIFFUSE INFILTRATIVE LUNG DISEASE

- ***Aetiology***

  a. idiopathic
  b. infective
  c. circulatory
  d. inflammatory / autoimmune
  e. neoplastic
  f. industrial / occupational diseases
  g. iatrogenic - drug induced, radiation, O_2 toxicity
  h. metabolic
  i. congenital
  j. physical

- ***Differential Diagnosis***

  a. ***infective pneumonias***
     i. community acquired
        - typical - Streptococcal
          - Haemophilus
        - atypical - influenza, parainfluenza
          - mycoplasma, Legionella, Chlamydia
        - uncommon - other viruses
          - Coxiella
          - TB
          - fungi
          - Pneumocystis
          - Brucella
          - Leptospirosis
          - Syphilis
          - MRSA

     ii. hospital acquired - gram (-)'ves
          - staphylococcal, MRSA
          - anaerobes
          - fungi

  b. ***septicaemia*** ± DIC

c. ***occupational diseases***
   - i. pneumoconioses - asbestosis, silicosis, berylosis, coal workers disease
   - ii. zoonoses
   - iii. chemical pneumonitis

d. ***neoplasms*** - bronchogenic carcinoma
   - alveolar cell carcinoma
   - lymphomas, leukaemias
   - metastatic carcinomas, lymphangitic carcinomatosis

e. ***congenital*** - cystic fibrosis
   - α_1-antitrypsin deficiency

f. ***metabolic*** - uraemia
   - hypercalcaemia
   - haemosiderosis

g. ***physical*** - irradiation
   - heat, thermal
   - oxygen toxicity
   - blast injury

h. ***circulatory*** - LVF
   - mitral stenosis
   - thromboembolic disease
   - bacterial endocarditis

i. ***immunological***
   - i. hypersensitivity
     - allergic alveolitis - farmer's lung, bird fancier's lung
     - ***drugs***
   - ii. autoimmune - SLE, RA, scleroderma, polyarteritis nodosa
     - Wegener's granulomatosis
     - dermatomyositis/polymyositis
     - Goodpasture's synd.

j. ***drugs***
   - i. cytotoxic agents - adriamycin, bleomycin, busulphan, cyclophosphamide
     - hydroxyurea, methotrexate, mitomycin
   - ii. non-cytotoxics - amiodarone, acetylsalicylic acid, chlorpropamide
     - carbamazepine, hydralazine, penicillamine
     - phenytoin, lignocaine, methadone, heroine
   - iii. toxins - paraquat

k. ***idiopathic***
   - idiopathic pulmonary fibrosis
   - familial pulmonary fibrosis
   - sarcoidosis
   - alveolar proteinosis
   - amyloid

Causes of Infective Pneumonias

a. ***viruses*** - influenza A & B, parainfluenza
- CMV, RSV, varicella
- rhinoviruses, adenoviruses, enteroviruses

b. ***bacteria***

i. gram (+)'ve cocci
- Staphlococci* *aerobic
- Streptococci*
- Micrococci - anaerobic

ii. gram (-)'ve cocci
- Branhamella, Acinetobacter

iii. gram (+)'ve rods
- Bacillus, Lactobacillus
- Clostridia
- Nocardia

iv. gram (-)'ve rods
- Haemophilus
- Klebsiella
- Legionella
- E. coli
- Enterobacter, Proteus, Serratia
- Pasteurella, Yersinia, Citrobacter
- Salmonella, Shigella

• anaerobes
- Bacteroides
- Fusobacterium
- Pseudomonas

• obligate anaerobes
- Bordetella
- Brucella

v. acid fast bacilli
- Mycobacterium tuberculosis, M. kansii

c. ***cell wall deficient bacteria*** * obligate intracellular parasites
- Coxiella burnetti
- Mycoplasma pneumoniae
- Chlamydia psittaci

d. ***fungi***
- Aspergillus niger, Aspergillus fumigatus

yeasts
- Candida albicans, Cryptococcus

dimorphic
- Histoplasma
- Coccidioides
- Sporotrichium
- Blastomyces

e. ***protozoa***
- Pneumocystis (rRNA ? ***fungal phylogeny***)
- Toxoplasma
- Entamoeba
- Strongyloides, Ascaris lumbricoides
- Toxocara carnis (visceral larva migrans)
- Echinococcus (hydatid disease)
- Schistosomiasis (blood fluke)
- Paragonomiasis (lung fluke)

Environmental Factors

a.	***minerals***	- silicon, asbestos - beryllium - coal, bauxite - diatomaceous earth, talc - iron, barium, silver, tin - manganese, vanadium
b.	***fumes***	- nitrogen dioxide - chlorine, bromine - ammonia - phosgene, sulphur dioxide - acetylene, kerosene, carbon tetrachloride, hydrogen fluoride - hydrochloric, nitric, picric acids
c.	***antigens***	- Farmer's lung - pigeon fanciers lung - humidifiers, air-conditioners - maple bark, wood pulp, oak - mushroom, malt, sugar cane - furrier's - detergents, vineyard sprayers - fish, cheese, wheat weevil
d.	***drugs***	- hydrallazine - busulphan, bleomycin, methotrexate - nitrofurantoin, sulphas - methysergide - ***amiodarone***
e.	***poisons***	- paraquat - petroleum derivatives

- ***Investigation Stage 1***

a. ***history***
   i. age, family history
   ii. drugs, smoking, allergies
   iii. occupation, pets / animals, hobbies, environment
   iv. personal contacts, friends / relatives
   v. overseas travel
   vi. nature, severity and time course of symptoms
   vii. past medical history - esp. CVS / RS

b. ***examination***
   i. upper & lower respiratory tracts
      - amount & type of sputum
      - presence/severity of respiratory failure
   ii. cardiac bruits/failure
   iii. vital signs
   iv. liver/spleen size, lymph nodes
   v. fundi
   vi. skin manifestations - purpura, erythema

- ***Investigation Stage 2***

a. FBE, ESR
b. blood film
   i. RBC's: anaemia, haemolysis, agglutination
   ii. WBC's: left shift, eosinophilia, blasts
c. U,C&E's, LFTs
d. blood cultures
e. sputum
   - M, C & S
   - cytology
   - AFB micro and culture
f. urine
   - M, C & S
   - sediment examination for active changes
   - haematuria
g. CXR
h. ECG
i. Echo

- ***Investigation Specialized***

1. ***blood***
   - i. paired serology
     - viruses, Legionella, Q fever, Chlamydia, Mycoplasma and fungi/parasites
   - ii. cold agglutinins
   - iii. HTLVIII / HIV Ab titre
   - iv. autoantibodies - RF, SLE, cANCA, Goodpastures, ENA
   - v. coagulation profile - INR, APTT, FDP's, fibrinogen
   - vi. protein electrophoresis - immune complexes, myeloma
     - α_1-antitrypsin deficiency
2. ***sputum***
   - i. Ziehl-Neilson stain & culture for AFB's
   - ii. immunofluorescence microscopy - Legionella
     - Influenza
   - iii. silver stain - Pneumocystis
     - * 3% saline induced sputum
   - iv. wet preparation - parasites → ova, cysts, larvae
     - yeasts → hyphae
3. ***nasopharyngeal washings*** - viruses
4. ***mantoux skin test***
5. ***viral cultures*** - throat swabs
   - faecal and sputum samples
6. ***faecal specimens*** (x3-6) - micro → protozoan cysts, ova
   - culture → bacterial, viral
7. ***PA catheter*** - exclude / confirm LVF
8. ***echocardiogram*** - SBE → low sensitivity, ∴ use TOE
   - atrial myxoma
   - LV function, valvular competence
9. ***ultrasound*** - liver / spleen / kidneys
   - fluid collections, abscesses
   - tumours
10. ***CT chest & abdomen*** - abscess, tumour
    - lymphadenopathy, mediastinal masses
    - CT directed biopsy
    - ***fine-cut CT chest*** - moderate ability to differentiate pathology

11. ***bronchoscopy***

i.	brushings	- MC&S - cytology - differential WCC
ii.	washings	- as above
iii.	bronchiolar lavage	- MC&S - effector cell type & count
iv.	biopsy	- tumours - asthma - transbronchial lung biopsy

12. ***open lung biopsy***, if

i. diagnosis remains unclear after the above

ii. the condition deteriorates despite empirical treatment

iii. prior to a trial of immunosuppressives or steroids

iv. no other (more accessible) organ is involved in the disease

→
- MC&S
- M&C for AFB's
- histopathology & frozen section
- silver stain for Pneumocystis
- immunoflorescence for Legionella

13. ***pleural fluid***
- MC&S
- cytology
- biochemistry, pH, LDH, protein

14. ***renal biopsy***
- autoimmune diseases
- Goodpasture's

15. ***bone marrow biopsy***
- metastatic carcinoma
- myeloma leukaemia, lymphoma
- TB culture

Interstitial Pneumonitis

a. idiopathic interstitial pneumonitis

b. familial pulmonary fibrosis

c. autoimmune diseases
- rheumatoid arthritis, SLE
- Wegener's granulomatosis, Goodpastures syndrome
- scleroderma, polyarteritis nodosa, dermatomyositis

d. sarcoidosis

e. alveolar proteinosis

f. congenital
- cystic fibrosis
- α_1-antitrypsin deficiency

g. pneumoconioses
- silicon, asbestos
- beryllium, coal, bauxite
- diatomaceous earth, talc
- iron, tin, barium, silver, manganese, vanadium

h. chemical pneumonitis
- nitrogen dioxide, chlorine, bromine
- phosgene, ammonia, sulphur dioxide
- acetylene, kerosene, carbon tetrachloride, hydrogen fluoride
- hydrochloric acid, nitric, picric acids

i. extrinsic allergic alveolitis
- farmer's lung, bird fanciers lung
- maple bark, wood pulp, oak
- mushroom, malt, sugar-cane
- furrier's, detergents, vineyard sprayers
- humidifiers, airconditioners, etc.

j. drug-induced intrinsic allergic alveolitis
- hydrallazine, methotrexate
- busulphan, bleomycin, nitrofurantoin
- methysergide, amiodarone
- sulphur derivatives

k. amyloidosis

- ***Interstitial Pneumonitis*** ****Common Causes***

1. infective pneumonia
2. atypical pneumonia
3. malignancy
4. lymphangitis carcinomatosis
5. chronic LVF

- ***Upper Lobe ® SCHART***

1. S - silicosis (progressive massive fibrosis)
   - sarcoidosis
2. C - coal workers pneumoconiosis
3. H - histiocytosis X
4. A - ankylosing spondylitis, aspergillosis
5. R - radiation
6. T - TB

- ***Lower Lobe ® RASIO***

1. R - rheumatoid arthritis
2. A - asbestosis
3. S - scleroderma
4. I - idiopathic
5. O - other
   - busulphan, bleomycin, amiodarone, methotrexate

FAT EMBOLISM SYNDROME

Def'n: clinical syndrome of pulmonary & systemic embolic features, associated with a predisposing cause for bone marrow/fat emboli

- ***Aetiology***

a.	pelvic, or long bone fractures	~ 100% have emboli ~ **5%** develop FES (LIGW ~ 1-2%)
b.	orthopaedic surgical procedures	~ 60% have emboli - FES rare
c.	hyperlipidaemic states	- pancreatitis - diabetes mellitus - lipid infusions - hepatic failure or trauma - SLE ? nephrotic syndrome
d.	adipose trauma	- crush injury - bends - liposuction - lymphography
e.	others	- external cardiac massage - poisoning - sickle cell crisis - extracorporeal circulation

NB: for (c-e) the majority of these, the finding is usually a post-mortem one, they ***rarely*** result in clinicaly significant FES

- ***Massive Fat Embolism***

- distinct from FES, with the clinical picture being that for any massive embolic syndrome
- this may be exaggerated by ***platelet aggregation*** and granule release
- lethal dose of fat for an average adult estimated at ~ 50-70 ml
- cf. the volume of fat contained in the femur ~ 70-100 ml

- ***Clinical Features***

NB: ***1 major*** and ***3 minor*** criteria are as sensitive & specific as any laboratory test

a. ***major features***

i. petechial rash - chest, neck, palate, retina
~ 25-50%
- this is the only feature ***pathognomic*** of FES
- usually appears on 2nd-3rd days and lasts 2-3 days

ii. respiratory dysfunction
- arterial hypoxaemia & bilateral CXR infiltrates

iii. CNS dysfunction
- drowsiness, confusion, convulsions, coma
- * unrelated to head injury or other cause

b. ***minor features***

i. tachycardia

ii. pyrexia - 38°-39°C
~ 60%

iii. FBE - sudden fall in [Hb]
- sudden thrombocytopaenia
- high ESR

iv. fundi - fat emboli, petechial haemorrhages

v. urine - anuria, oliguria
- fat globules

vi. sputum - fat globules

- ***Laboratory Investigations***

1. arterial hypoxaemia
2. fat globules - blood, urine or sputum
* ***nonspecific*** and may occur in other conditions
3. haemolytic anaemia
4. thrombocytopaenia
5. hypocalcaemia
6. elevated serum lipase

- ***Management***

- heparin, aspirin, glucose, steroids & aprotinin ***do not*** alter incidence or mortality
- therapy is largely supportive once established
- ***all*** long bone fractures should be immobilized early

CHRONIC AIRFLOW LIMITATION

Def'n: ***Asthma:*** ≥ **15%** δFEV_1 with
- bronchodilators
- methacholine, histamine challenge

Chronic bronchitis:
morning cough with sputum production for > 3 months of the year for 2 successive years, in the absence of any underlying disease which may account for these symptoms

Emphysema: abnormal, permanent enlargement of the airways distal to the ***terminal bronchiole***, with destruction of their walls and without obvious fibrosis (ATS), or
diminished gas transfer interface (area), ↓ DL_{CO}

- ***Smoking***

1. produces both chronic bronchitis & emphysema, but little reversible airways disease
2. impaired ciliary function & sputum clearance
3. immunoparesis
4. ↑ frequency of upper & lower respiratory tract infections
5. ↑ COHb
   - chronic tissue hypoxia
   - polycythaemia
6. nicotine
   - hypertension, ↑ SAP & DAP, ↑ PVR
7. accelerated atherosclerosis
8. ↑ platelet adhesiveness
9. major risk factor for ischaemic heart disease
10. increased peripheral vascular disease
11. increased bronchogenic carcinoma > 10 pkt/years (1 pkt/yr = 20/d)

- ***Exacerbation of CAL***

a. ***respiratory***
   - infection - bacterial, viral, fungal
   - aspiration
   - bronchospasm
   - pneumothorax
   - trauma, surgery
   - neoplasm
   - air pollutants

b. ***cardiac***
   - AMI
   - LVF, pulmonary oedema
   - pulmonary emboli
   - arrhythmia

c. ***drugs***
   - sedatives, opioids
   - anaesthetics
   - muscle relaxants

d. ***metabolic***
   - fever
   - sepsis
   - pancreatitis
   - hyperthyroidism

e. ***electrolytes***
   - low K^{+}, Mg^{++}, $PO_4^{=}$
   - metabolic alkalosis

f. other
   - malnutrition
   - high CHO intake
   - depression of hypoxic drive

Acute Respiratory Failure Complications

a. hypoxaemia
   - organ ischaemia / infarction
   - mental confusion, agitation

b. pulmonary
   - infection
   - aspiration
   - barotrauma
   - fibrosis
   - pulmonary emboli

c. cardiovascular
   - hypertension, tachycardia, arrhythmias
   - late hypotension, bradycardia, QRS prolongation, EMD
   - altered organ perfusion

d. CNS
   - anxiety, distress
   - acute psychosis
   - obtundation, coma
   - ↑ ICP

e. renal
   - acute renal failure
   - salt & water retention

f. GIT
   - pneumoperitoneum
   - ileus, gastric dilatation
   - acalculous cholecystitis
   - mucosal atrophy (TPN)

g. nutritional
   - malnutrition
   - muscle wasting

h. microbiology
   - nosocomial pneumonia
   - bacteraemia, septicaemia

i. technical
   i. IV access
   ii. mask CPAP
   iii. intubation
   iv. mechanical ventilation
   v. PA catheter problems

j. drug side effects
   i. steroids
   ii. antibiotics
   iii. aminophylline
   iv. β-agonists

BRONCHIAL CARCINOMA

- ***Clinical Presentation***

1. ***pulmonary***
   - i. bronchial obstruction — collapse; pneumonia, abscess, empyema; emphysema
   - ii. pleural effusion
   - iii. bleeding / haemoptysis
   - iv. SVC obstruction
   - v. Horner's syndrome
   - vi. brachial plexus or T_1 lesion
   - vii. recurrent laryngeal nerve or phrenic nerve palsy
   - viii. incidental lesion on CXR
2. ***metastatic disease***
   - i. bone pain, pathological fracture, hypercalcaemia
   - ii. hilar and cervical lymphadenopathy
   - iii. cerebral
   - iv. adrenal
3. ***paraneoplastic***
   - i. cachexia
   - ii. anaemia of chronic disease
   - iii. hypertrophic osteoarthropathy — finger clubbing; arthritis, periosteal new bone
   - iv. neuropathy
   - v. myopathy — carcinomatous myopathies; Eaton-Lambert syndrome
   - vi. skin lesions — pigmentation, erythema; scleroderma, acanthosis nigrans; herpes zoster, herpes simplex
   - vii. endocrine
     - ectopic ADH → SIADH
     - ectopic PTH → hypercalcaemia
     - ectopic TSH → thyrotoxicosis
     - ectopic ACTH → Cushing's syndrome
     - carcinoid syndrome
     - gynaecomastia
   - viii. haematological — aplastic anaemia; thrombophlebitis; DVT's

- ***CXR***

a. changes usually antedate symptoms by ~ 7 months

b. ***symptoms*** → abnormal CXR ~ 98%

c. further, the changes are suggestive of tumor in ~ 80%

d. ~ 70% are centrally located

e. at presentation, average size is ~ 3-4 cm

f. other important diagnostic features include,

i. tracheal deviation/obstruction
ii. mediastinal mass - SCV, PA, main bronchi
iii. pleural effusions
iv. cardiac enlargement
v. bullous cyst - rupture, compression
vi. air-fluid levels ? abscess, soiling
vii. parenchymal changes - V/Q inequality

- ***Inoperability of Bronchial Carcinoma***

1. distant metastases - brain, liver, adrenals & bone
2. malignant pleural effusion
3. recurrent laryngeal nerve involvement
4. phrenic nerve involvement
5. regional lymph nodes within 2 cm of the hilum
6. high paratracheal, or contralateral hilar spread
7. SVC syndrome
8. PA involvement
9. cardiac tamponade
10. bilateral disease

NB: operability also depends upon ***cell type***,
unilateral or pleural spread may be operable with less invasive cell types

Pneumonectomy Assessment		
Test Type	PFT	Risk Limits for ***Pneumonectomy***
Whole-Lung Tests	AGB's	• ***hypercapnia*** on room air
	Spirometry	• FEV_1/FVC £ **50%** • FVC £ **2.0 l** • MBC ≤ 50%
	Lung volumes	• RV/TLC ≥ 50%
Single Lung Tests	Split function tests (R&L)	• predicted FEV_1 ≤ 0.85 l • PBF > 70% diseased lung
Simulated Pneumonectomy	Balloon occlusion R/L PA	• mean PAP ≥ 40 mmHg • $PaCO_2$ ≥ 60 mmHg • PaO_2 ≤ 45 mmHg

COR PULMONALE

Def'n: ***RV enlargement*** 2° to thoracic, lung or pulmonary vascular disease, in the ***absence*** of congenital, or left sided heart disease;
*RV failure ***is not*** required for the diagnosis

right heart failure is defined as a chronic increase in the RV end-diastolic transmural pressure gradient, that is not expected from an increase in pulmonary blood flow (HPIM, 12th Ed)

Aetiology

1. pulmonary ***vascular*** disease
   - primary pulmonary hypertension
   - chronic multiple emboli
   - pulmonary vasculitis
2. chronic ***parenchymal*** lung disease
   - CAL
   - diffuse interstitial lung diseases
3. lung ***pump*** failure
   - kyphoscoliosis
   - neuromuscular diseases
   - morbid obesity
4. ***central drive*** failure
   - obstructive sleep apnoea syndrome
   - chronic mountain sickness

Pathogenesis

NB: may be either - acute or chronic
- episodic or progressive

a. acute → RV dilatation

b. chronic → RV hypertrophy, later dilatation

- initially PAH occurs only during ***exercise*** or during stress
- this is accompanied by episodic RV dilatation with normal RVEDP and RV output
- later, persistent PAH leads to RV hypertrophy ± dilatation
- this is associated with sustained high RVEDP's and RVF, initially during exercise but later at rest

- ***Mechanisms***

a. loss of vascular bed

b. irreversible pulmonary vasoconstriction
   i. chronic ***hypoxia***
   ii. chronic acidosis pH < 7.2
   iii. chronic hypercapnia

- ***Exacerbating Factors***

1. progression of 1° lung disease
2. intercurrent respiratory infection
3. pulmonary emboli
4. cardiac decompensation
   - arrhythmias
   - RV ischaemia
5. sedative & analgesic drugs
6. ↑ work of breathing
   - resistance (bronchospasm)
   - compliance
7. hypercatabolic states
   - surgery, trauma
   - endocrine
8. surgery
   - pulmonary resection
   - upper abdominal/thoracic

- ***Signs***

a. stigmata of chronic lung disease
   - nicotine stains
   - dyspnoea, tachypnoea
   - central cyanosis
   - clubbing, skin changes
   - asterixis

b. RV hypertrophy
   - RV thrust ± palpable P_2
   - loud P_2 & wide split S_2
   - RV-S_4
   - TI
   - recurrent SVT, MAT

c. ***RV failure***
   - high JVP
   - peripheral oedema
   - ascites, hepatomegaly

- ***Symptoms***

a. those of chronic bronchitis / emphysema
b. dyspnoea
c. tiredness, fatigue, decreased exercise tolerance
d. peripheral oedema
e. palpitations - AF
f. daytime somnolence - OSAS

- ***Investigations***

a. FBE, ESR - polycythaemia, anaemia chronic disease
- ↑ WCC, left shift
b. EC&U, LFT's, AGA
c. ECG - P pulmonale
- RVH (qv), RAD, RBBB
- sinus tachycardia, AF, MAT
  - RVH on ECG is ***rare*** except in primary pulmonary hypertension
  - 'q'-waves in II, III, aVF may simulate AMI due to vertically placed heart
d. CXR - lung disease with large PA's
- peripheral field ***oligaemia***
- usually no LVF or cardiomegaly
e. PFT's - obstructive | restrictive components
± reversibility
f. Echo - dilated RV
± TI
g. V/Q Scan - to exclude chronic PE

- ***Complications***

1. acute respiratory failure
2. recurrent respiratory infections
3. chronic hypoxia
4. polycythaemia
5. right heart failure
6. arrhythmias
7. sudden death (1° PAH)
8. cirrhosis

- ***Treatment***

a. treat primary lung disease & cease ***smoking***

b. optimise remaining lung function
   i. lose weight
   ii. bronchodilators
   iii. steroids
   iv. diuretics
   v. antibiotics
   vi. physiotherapy

c. prompt treatment of chest infections

d. prevent pulmonary emboli

e. respiratory stimulants (aminophylline)

f. improve cardiac function
   i. digoxin
   ii. antiarrhythmics
   iii. diuretics

g. pulmonary vasodilators
   i. nitric oxide ~ 10-40 ppm
   ii. PGI_2 ~ 5-35 ng/kg/min
      - expensive pulmonary & systemic vasodilator
      - PA catheter required for monitoring
      - noradrenaline 1 µg/min can be used to overcome the systemic vasodilation
      - side effects include systemic vasodilatation, hypotension and nausea
      - some units are now using this via the ***inhaled*** route
   iii. adenosine ~ 50-500 µg/kg/min
   iv. GTN
   v. ACEI
   vi. β_2-agonists - isoprenaline
      ? dopexamine
   vii. Ca^{++} entry blockers

h. heart/lung ***transplantation***

OBESITY HYPOVENTILATION SYNDROME

- ***Clinical Features***

1. marked obesity
2. hypersomnolescence - especially daytime
3. periodic breathing
4. central ***and*** obstructive apnoea
5. pulmonary hypertension
6. cor pulmonale ± RF failure

- ***Diagnostic Investigations***

1. hypercapnoea
2. hypoxia - especially night-time / sleep studies
3. polycythaemia
4. depressed ventilatory response to CO_2 & O_2

- ***Rochester 1974***

• common mechanical and circulatory factors in ***morbid obesity***,

a. lung volumes ↓ FRC
↓ VC

b. lung function ↓ MBC (MVV)
↓ lung and chest wall compliance
↓ respiratory muscle efficiency ~ 30%

c. ↑ V/Q mismatch - V to apices
- Q to bases

d. ↑ cardiac output ~ 100-400%

e. ↑ pulmonary and systemic blood volume

f. pulmonary hypertension

NB: these changes are ***proportional*** to the degree of ***obesity***

- ***Leech 1987***

• multiple regression analysis of factors associated with ***hypercarbia*** and ***sleep apnoea***, ($p < 0.05$)

a. obesity - height/weight ratio
b. ↓ FVC & FEV_1 - absolute volume changes, cf. predicted
c. daytime hypoxia $P_{aO2} < 70$ mmHg
d. ***severity*** of desaturation during sleep apnoeic periods

• factors with poor, or ***no association***,

a. age
b. FEV_1/FVC ***ratio*** - ie. airflow obstruction
c. the number of sleep induced respiratory events
d. the $P_{A\text{-}aO2}$ gradient

• the syndrome is ***multifactorial***,

1. chronic hypoxia
2. ↑ work of breathing
3. altered O_2 / CO_2 drives

- ***Aetiology***

• suggested factors include,

a. ↑ weight → ↑ mechanical load
b. obstructive airways disease *not supported by Leech above
c. impaired respiratory mechanics & muscle function
d. central sleep-apnoea
e. ↑ V/Q mismatch, shunt and dead space
f. impaired respiratory control mechanisms, ie. O_2/CO_2 drive

Parameter	Simple Obesity	OHS
Total compliance	slight fall	30% fall
Lung compliance	25% fall	40% fall
V/Q, Shunt	increased mismatch	large mismatch < **40% *shunt***
Work of breathing	30% increase	**300%** increase
VO_2 cost of breathing	↑ VO_2 ~ ↑ work	↑↑ VO_2 >> ↑ work
Diaphragm response to ↑ P_{aCO2}	increases	300-400% ***decrease***
Effects of weight-loss on the following variables		
P_{aCO2}	no change	decreases
VC	increase	marked increase
MBC	increase	increase
Apnoeic periods	decrease	marked decrease
Level of desaturation	improved	markedly improved

- ***Sampson, Grassimo 1983***

• during quiet breathing there is little difference in the following parameters,

a. V_T, VC, TLC, FRC, RV, ERV, FEV_1/FVC, and RR
b. ABG's
c. mouth occlusion pressure
d. age, sex, weight

however, during ***hypercapnoeic rebreathing***,

Parameter	Normal	Obese	OHS
Rebreathing (l/min/mmHg-CO_2)	3.5	1.83	1.06
Mouth occlusion pressure (cmH_2O/mmHg-CO_2)	0.5-0.6	0.91	0.29
Diaphragmatic EMG (δ%/mmHg-CO_2)	25%	23.8%	13.9%
CO_2-Response	normal or increased		blunted

- ***Obesity Hypoventilation Syndrome***

• lung volumes are similar in OHS/SO, ∴it is unlikely that OHS relates solely to ***muscle weakness***
• the ***slope*** of the CO_2-ventilation curve is altered, not shifted in a parallel fashion
• muscle diseases show a different pattern, with the diaphragmatic EMG showing the same pressure gradient
• the disease therefore, in summary, is

a. multifactorial
b. related to
   i. mechanical load
   ii. sleep apnoea
   iii. chronic hypoxia
   iv. altered central respiratory drive
   v. ? enhanced buffering of metabolic alkalosis

NB: represent a sub-group of obese patients,
with probable pre-existing impaired central response to CO_2 and O_2,
in whom the added load of obesity results in chronic respiratory failure, ie.

"non-fighters, unable to prevent CO_2 retention"

PNEUMOTHORAX

NB: tension pneumothorax, from any cause but especially,

1. chest trauma
2. barotrauma during mechanical ventilation
3. obstructed pleural drains

- ***Aetiology***

a.	trauma	
b.	surgery	
c.	lung diseases	- asthma - infections - emphysema - pulmonary infarction - bullous disease
d.	iatrogenic	- CVC cannulation - tracheostomy - U-S/CT guided drainage/biopsy - bronchoscopy - thoracentesis
e.	barotrauma	- artificial ventilation - diving - aviation, training
f.	idiopathic	

PLEURAL EFFUSION

Def'n: an ***exudate*** is pleural fluid having ***one or more*** of the following

1. fluid:serum protein ratio **> 0.5** * protein > 30 g/l
2. fluid:serum LDH ratio **> 0.6**
3. absolute fluid LDH > 2/3 normal serum upper limit
   > 200 U/l

- ***Transudative***

1. CCF
2. cirrhosis, ascites
3. renal failure, nephrotic syndrome
4. hypoproteinaemia
5. peritoneal dialysis
6. myxoedema
7. Meig's syndrome + ascites & ovarian fibroma

- ***Exudative***

1. infectious
2. inflammatory - collagen vascular disorders
3. neoplastic
4. pulmonary infarction
5. traumatic - haemo/chylo-thorax
6. drugs - nitrofurantoin, methysergide
7. GIT - subphrenic abscess
   - oesophageal rupture
   - pancreatitis
8. uraemia
9. post-AMI
10. other - asbestosis, DXRT

- ***Management***

1. full history and examination
2. treat obvious cause
3. thoracentesis ± pleural biopsy if suspected exudate

	Transudate	Exudate
Appearance	clear	clear, cloudy, or bloody
LDH		
• absolute[1]	< 200 U/l	> 200 U/l
• fluid:plasma	< 0.6	**> 0.6**
Protein		
• absolute	< 30 g/l	> 30 g/l
• fluid:plasma	< 0.5	**> 0.5**
pH	> 7.2	< 7.2
Glucose	> 2.2 mmol/l	< 2.2 mmol/l
WCC (PMN's)	< 1,000 / ml	> 1,000 / ml

[1] LIGW states < or > 1000 IU ??

- ***Other Tests***

a. microbiology
- M,C&S
- stain & culture for AFB's

b. cytology
- malignancy

c. "blood picture"

i. eosinophilia → ? drug induced

ii. RBC's > 100,000
- traumatic tap, trauma
- malignancy
- pulmonary emboli, infarction

d. amylase > 50-60 IU →
- oesophageal rupture
- pancreatitis
- rarely in malignancy

e. chylous
- high TG / low cholesterol
± high amylase

f. ANA
+ low C' & low glucose
→ collagen vascular disorder

NB: despite full evaluation, no cause will be found in **~ 25%** of patients

CHYLOTHORAX

- the ***thoracic duct*** starts as an extension of the ***cysterna chyli*** in the upper abdomen
- enters through the aortic hiatus and ascends extrapleurally between the aorta and azygous vein
- at the level of T_5, crosses to the left border of the oesophagous, ascending behind the aortic arch and subclavian artery
- it enters the venous system at the junction of the internal jugular and subclavian veins
- between 40-60% have anomalies of the course

Aetiology

a. congenital
b. traumatic
c. surgical — - any thoracic procedure; - rarely dissection of the neck
d. infiltration or extrinsic compression — *especially lymphoma
e. thrombosis of the left subclavian vein

Biochemical Characteristics

a. sterile, "milky" fluid — - alkaline, pH ~ 7.4-7.8; - SG ~ 1012-1025
b. amylase (+)'ve — - pancreatic enzymes present
c. contents:

total fat	~	4-60 g/l
total protein	~	20-60 g/l
albumin	~	12-41 g/l
globulin	~	11-30 g/l
glucose	~	3-11 mmol/l
lymphocytes	~	400-6,000/µl
erythrocytes	~	50-600/µl
U&E's	~	plasma

Treatment

a. chest drain
b. low fat diet
c. TPN
d. indications for surgical correction,
   i. drainage ≥ 1500 ml/d
   ii. failed conservative R_X after 14 days
   iii. metabolic complications

PHRENIC NERVE PALSY

- ***Unilateral***

  a. idiopathic
  b. congenital
  c. mediastinal mass
     - tumour, lymph nodes
     - thyroid, thymus
     - aortic dissection
  d. trauma
     - cervical
     - surgical, post-CABG
  e. local anaesthetics
     - interpleural, interscalene
     - stellate ganglion
  f. features
     i. asymptomatic
     ii. small fall in VC
     iii. elevated hemidiaphragm on CXR
     iv. no movement on ***double-exposure CXR***

- ***Bilateral***

  a. cervical cord damage
  b. motor neurone disease
  c. polyneuropathies
  d. poliomyelitis
  e. mediastinal tumour
  f. congenital
  g. "cryoanaesthesia" of phrenic nerves during open-heart surgery
  h. features
     i. paradoxical respiration
     ii. respiratory failure
     iii. large decrease in VC
     iv. failure to wean from IPPV after CABG

Pulmonary Function Testing

• reasons for performing PFT's include,

1. identification of the ***type*** of lung disease - obstructive vs. restrictive
2. quantification of the ***extent*** of lung disease
3. determination of the ***response*** to therapy
4. monitoring the rate of ***progression***

• the value of PFT's is most clearly demonstrated in those undergoing ***pulmonary resection***
• for other surgery, there is little evidence of benefit as a routine screening technique, in the absence of clinical symptoms
• patients who may be considered for PFT's include,

1. patients with chronic pulmonary disease / symptoms
2. heavy smokers with a history of chronic productive cough
3. patients with chest wall or spinal deformities
4. morbidy obese patients
5. elderly > 70 years
6. patients for thoracic surgery
7. patients for major upper abdominal surgery

NB: the objective of testing is to predict the likelihood of postoperative complications, ***no single test*** is the best predictor of complications

• Hall *et al.* (Chest 1991) showed,

1. single best predictive factor was the ***ASA classification***
2. followed by ***site of incision*** - upper vs. lower abdominal
3. ***age, smoking & obesity*** also ranked highly

NB: ASA grading may have in part been based on PFT's, but ***clinical assessment*** remains the best predictor

• a single spirometric study can provide FVC, FEV_1/FVC, $FEF_{25-75\%}$, PEFR and VC
• "normal" limits are obtained from a sample population (***Morris 1971***) and the lower limit taken as 1.64 x SEE (SD of the regression line) below the same weight & height on the regression line
• this range should by definition include ~ 95% of the population
• the widely used practice of taking 80% of the predicted value should be ***avoided***
• abnormalities on spirometry correlate with the incidence of postoperative complications
• however, the incidence and severity of postoperative complications ***do not*** correlate with the severity of the preoperative lung dysfunction

- ***Clinical Spirometry***

1. ***vital capacity*** ***VC***
   - effort independent, performed without concern for rapidity of exhalation
   - decreases may be associated with restrictive lung disease, following excision, or from extrapulmonary factors, ie. chest wall disease
2. ***forced vital capacity*** ***FVC***
   - during forced exhalation FVC < VC with significant dynamic airways closure
   - principally disorders with increased airway resistance, or destruction of supporting architecture
3. ***forced expiratory volume, 1 second*** ***FEV_1***
   - usually expressed as a percentage of FVC, where $FEV_1/FVC > 80\%$
   - largest observed FEV_1 and FVC from 3 readings are used, even if different curves
   - reduced mainly by increased airways resistance, usually normal in restrictive defects
4. ***forced expiratory flow, 200-1200*** ***$FEF_{200-1200}$***
   maximal expiratory flow rate ***MEFR***
   - peak flow can be measured by drawing a tangent to the steepest part of the curve
   - more commonly the average flow over 1000 ml, after the initial 200 ml of exhalation is used
   - this is slightly lower than the true peak flow, normal values > 500 l/min
   - values < 200 l/min are associated with impaired cough & postoperative sputum retention, atelectasis and infection
   - markedly impaired by obstruction of larger airways & responsive to bronchodilator therapy
   - results are extremely effort dependent
5. ***forced midexpiratory flow, 25-75%*** ***$FEF_{25-75\%}$***
   maximal midexpiratory flow rate ***MMFR***
   - less effort dependent than PEFR, as avoids the initial highly effort dependent part of the expiratory curve
   - however, still affected by patient effort and submaximal inspiration
   - values in healthy young men ~ 4.5-5.0 l/s (300 l/min)
   - abnormal values < 2 l/sec (120 l/min)
   - initially thought to be more sensitive in detecting small airways disease cf. FEV_1, but this has ***not*** been supported

- ***Maximum Breathing Capacity*** ***MBC***

- patient is instructed to breath as hard & fast as possible for 12 seconds
- extrapolated to 1 minute, expressed as l/min, normal ~ 150-175 l/min
- predominantly affected by increased resistance & correlates well with FEV_1 (MBC ~ FEV_1 x 35)
- 80% of MBC can be maintained for ~ 15 minutes
- affected by patient cooperation & effort

Respiratory Muscle Strength

1. P_{Imax} ~ -125 cmH_2O
   < -25 cmH_2O reflects inability to take an adequate inspiration
2. P_{Emax} ~ 200 cmH_2O
   < 40 cmH_2O reflects inability to cough

Airway Resistance

• using a body plethysmograph, panting against a closed then open shutter,

1. shutter closed → Boyle's law & lung volume
2. shutter open → R_{AW} calculated from δV and flow
   → $G_{AW} = 1/R_{AW}$
3. ***specific*** airway resistance and conductance are calculated for the given lung volume

NB: a mouthpiece is used to remove the effects of the upper airway,
panting is used to keep the larynx dilated

• in ventilated patients, may use peak to plateau δP / instantaneous flow at P_{pAW}
• bi-exponential decay from P_{pAW} to plateau,

1. first phase due to airways resistance
2. second phase due to "stress relaxation"

Alveolar-Arterial Oxygen Gradient

• normal gradient on room air ~ 8 mmHg
→ increasing with age ~ 25 mmHg at 70 yrs
• increased commonly in smokers & mild early chronic bronchitis

Frequency Dependent Compliance

Def'n: abnormal where C_{Dyn} < 80% of C_{Stat}

• decreases early with small airways obstruction
• both measurements require insertion of an oesophageal balloon, with flow measured by a pneumotachograph,

1. $C_{Stat.}$ - inspiratory slope of a static pressure volume curve at tidal volume
2. C_{Dyn} - $\delta V/\delta P_{IP}$

■ ***Flow Volume Loops***

- differentiation of intrathoracic / extrathoracic obstruction
- the entire inspiratory, plus the immediate expiratory portions of the curve are highly ***effort dependent***
- ratio of expiratory flow:inspiratory flow at 50% TLC ~ 1.0
- upper airway obstruction inspiratory flow is reduced disproportionately & $EF:IF_{50\%} > 1.0$
- other patterns described on flow-volume loops,

1. ***fixed obstruction***
   - no significant change in airway diameter during inspiration/expiration
   - $EF:IF_{50\%} \sim 1.0$, with both curves showing a flattened plateau
2. ***variable obstruction***
   - i. extrathoracic
     - vocal cord paralysis
     - chronic neuromuscular disorders
     - marked pharyngeal muscle weakness
     - obstructive sleep apnoea syndrome
     - accompanied by inspiratory stridor & flow resistance
     - $EF:IF_{50\%} > 2.0$
   - ii. intrathoracic
     - tracheal & bronchial tumours
     - tracheomalacia
     - vascular rings, thoracic aortic aneurysm
     - accompanied by expiratory airway compression & ↑ flow resistance
     - inspiration may be normal, with $EF:IF_{50\%} < 1.0$

NB: differentiation is most accurate in the ***absence*** of diffuse airways disease

■ ***Multiple-Breath Nitrogen Washout***

- normal lung behaves as a single compartment, with a single exponential washout curve for N_2
- there is a direct correlation between abnormal N_2 washout and frequency dependent compliance
- uneven distribution of ***time constants*** is believed to be the basis of both
- curve analysis is tedious, requiring computer analysis

Single-Breath Nitrogen Washout

• originally described by Fowler in 1949, but adapted to,

1. full inspiration from RV to TLC with 100% O_2
2. expired N_2 concentration measured
3. line of best-fit drawn through the alveolar plateau
4. increase in $[N_2]$/l quantified → δN_2 % per litre
   i. normal ~ 2% / l
   ii. smokers ~ 10% / l
   iii. abnormal in ~ 50% of asymptomatic smokers,
      • therefore ***sensitive*** index of early lung dysfunction
      • ***poor specificity*** due to large number of asymptomatics who do not progress to CAL

• the original technique by Fowler involved only 1000 ml O_2 from FRC and due to preferential ventilation of the bases resulted in a steeper plateau

Forced Expiratory Flow Rates

• difficulty defining abnormal flows at low lung volumes
• during expiration early flow resistance is in the ***large airways***, where flow is predominantly turbulent
• comparative curves using He/O_2 show increased flow in the early expiratory phase
• as expiration continues, the site of resistance moves proximally toward the alveoli, where flow is predominanlty laminar, and unaffected by altered gas density (He)
• therefore, at some point, the ***volume of isoflow***, the two curves rejoin
• with small airways disease, flow becomes less density dependent and the difference between maximum flow rates decreases, and the V_{isoV} increases
• normal values for V_{isoV} ~ 10-15% of VC
• values > 25% are abnormal