Pathophysiology of Respiratory Compromise

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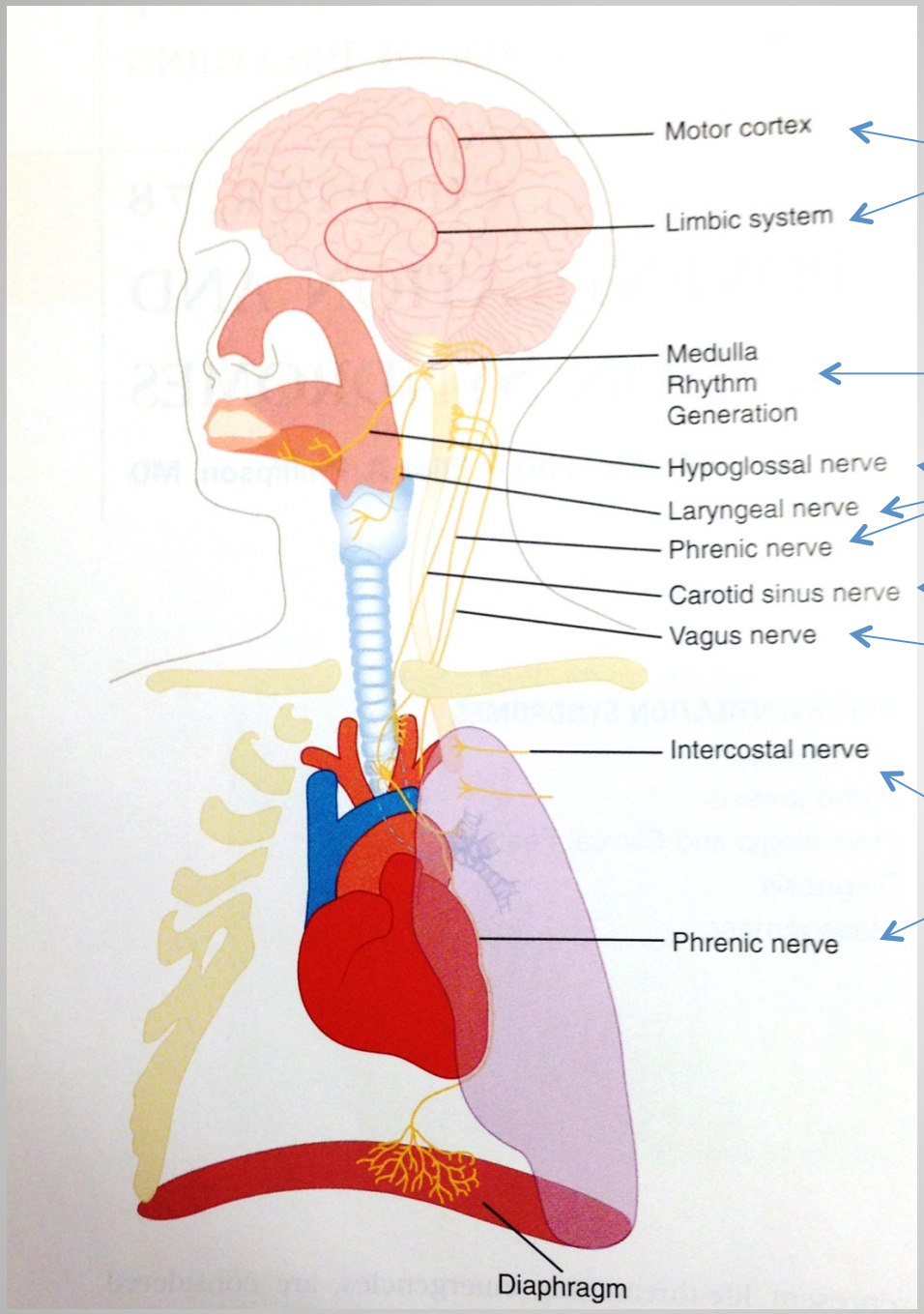
- Determinants of Respiratory Homeostasis
  - Ventilatory pattern
  - Lung resting size (FRC)
  - Gas exchange
  - Right heart function
- Mechanisms and Physiologic Consequences of Compromise
  - CNS injury/depressants (incl sleep disorders)
  - Compliance loading
  - Resistance loading
  - Vascular loading
- Systemic Manifestations

Ventilatory Pattern

- Inputs into brainstem pacer network
  - Neural (conciousness, stress response)
  - Mechanical (stretch [loads, volume], irritant)
  - Gas exchange (PO2, PCO2, pH)
- Outputs into phrenic (and other) nerves
  - Rate, tidal volume, I:E timing (flow)
- Overall "goal":
  - Maintain adequate PO2 and pH while minimizing loads and irritant activity



Cortical Inputs

Rhythm Generator

Outputs

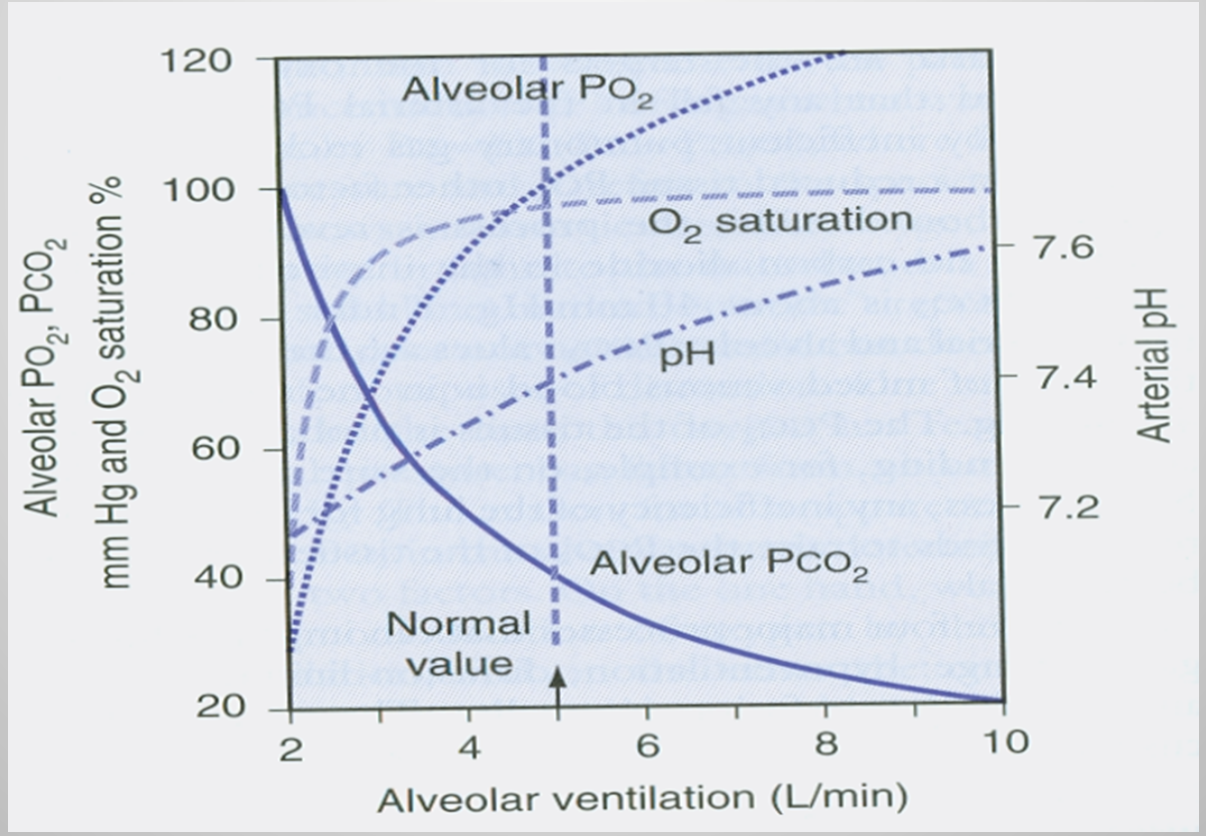
PO2, pH inputs

Stretch, irritant inputs

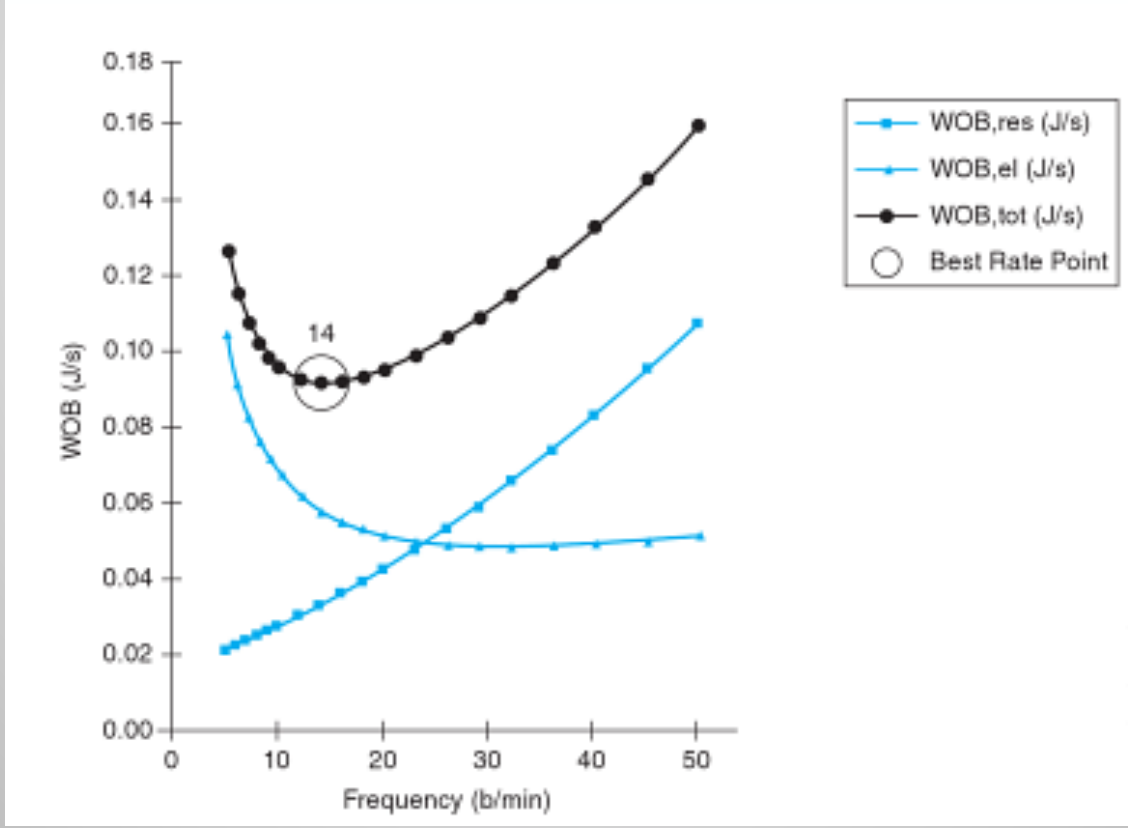
Outputs

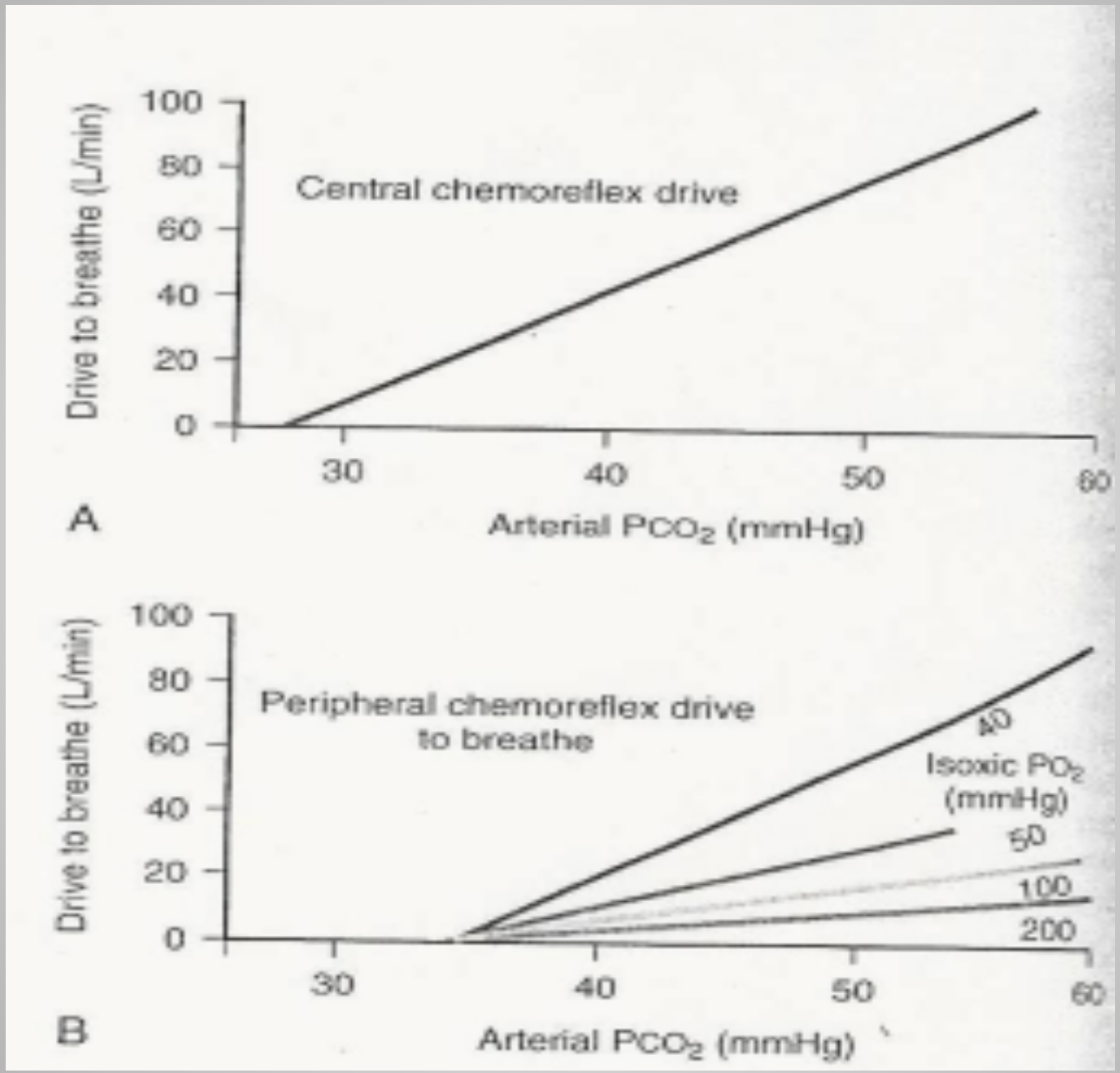
Ventilatory Pattern

- For PAO2 to fully saturate hemoglobin, must approach 100 mmHg



$$f = \frac{1 + 2a \times \mathrm{RC} \times \dfrac{\text{Min Vol} - (f \times V_d)}{V_d} - 1}{a \times \mathrm{RC}}$$




Drive to breathe (L/min)
100
80
60
40
20
0
Central chemoreflex drive
30
40
50
60
A
Arterial P_{CO_2} (mmHg)
Drive to breathe (L/min)
100
80
60
40
20
0
Peripheral chemoreflex drive to breathe
40
Isoxic P_{O_2} (mmHg)
50
100
200
30
40
50
60
B
Arterial P_{CO_2} (mmHg)

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  - True in both health and disease but goals may compete

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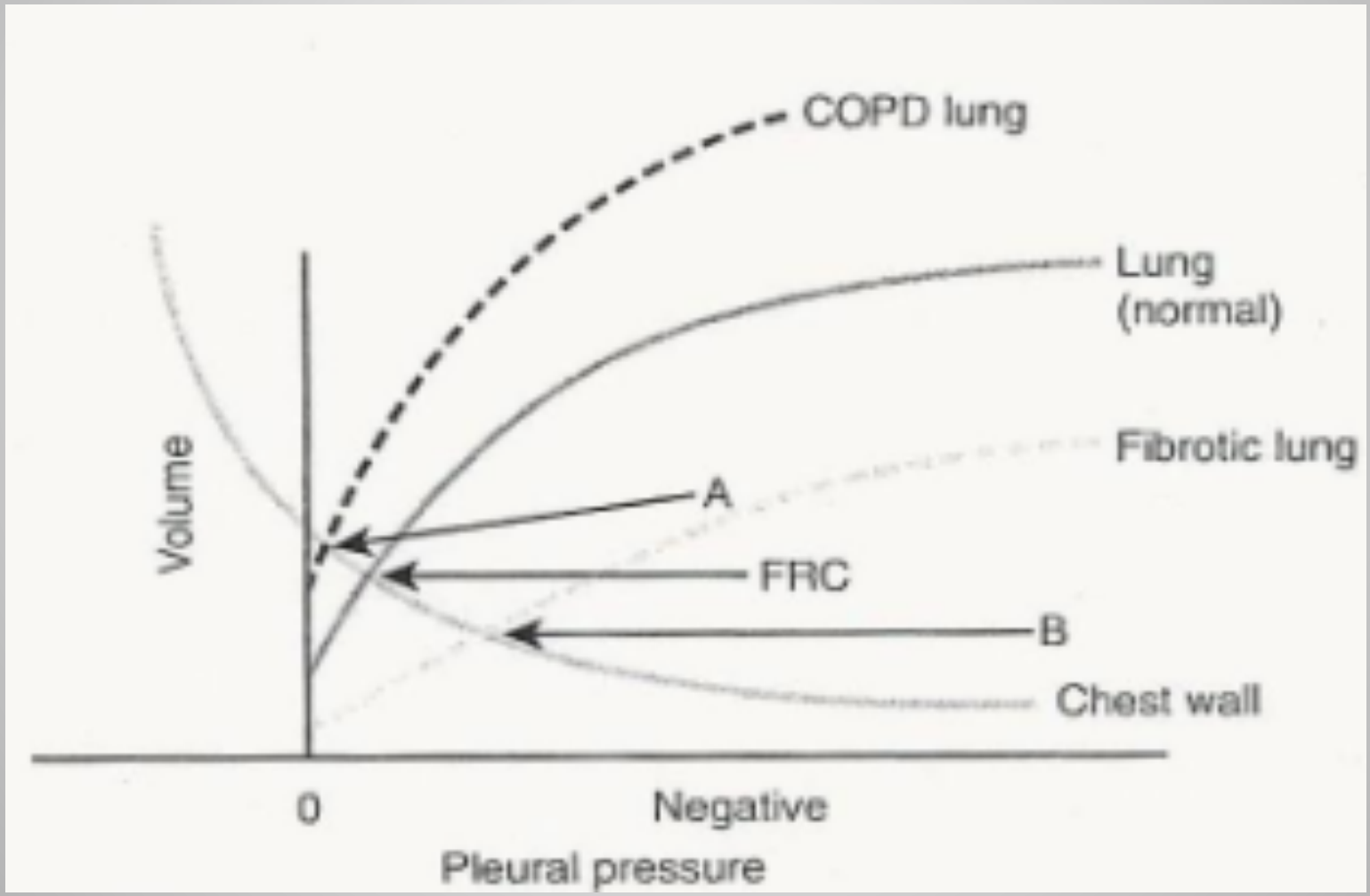
Lung Resting Size (FRC)

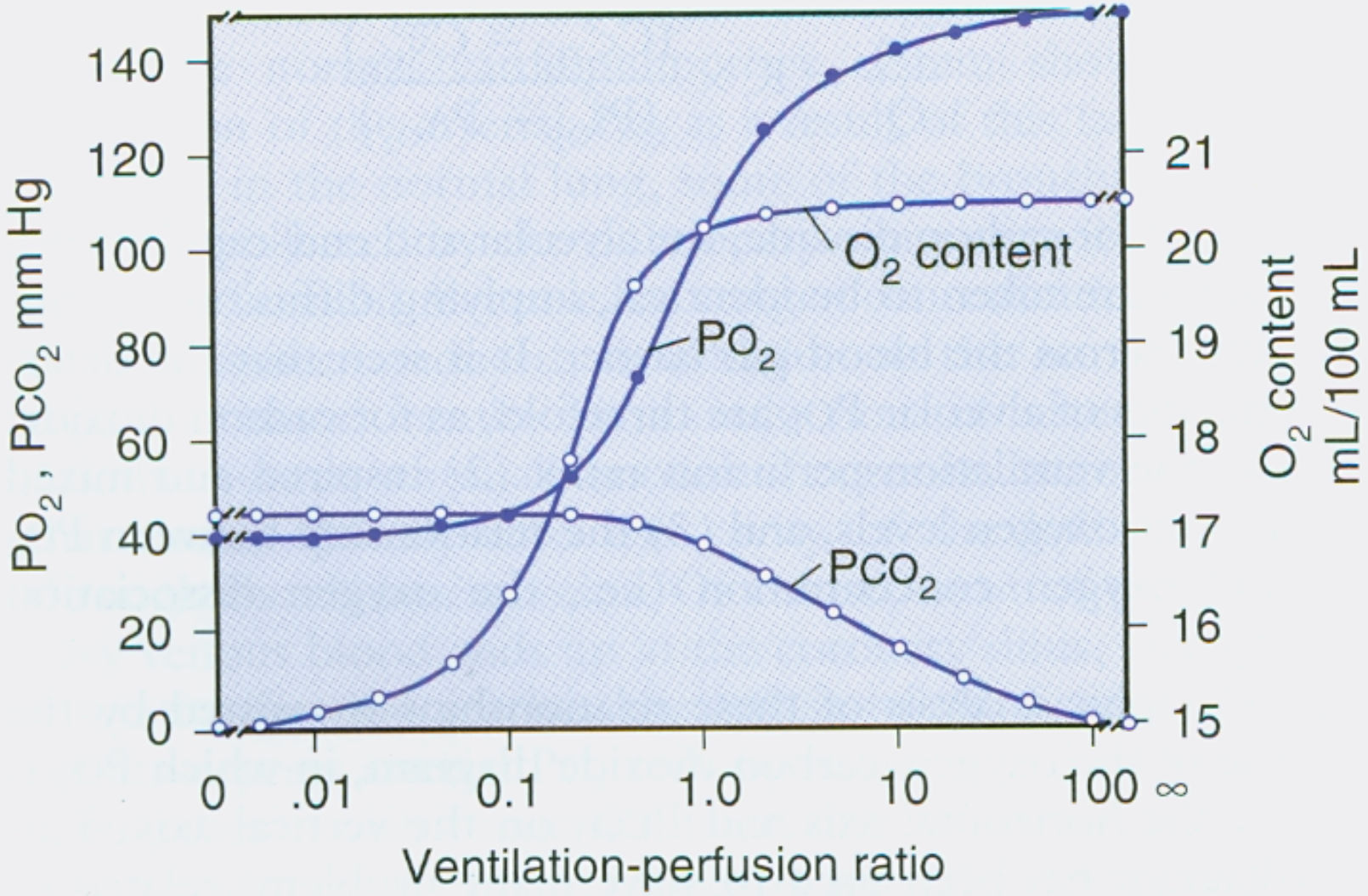


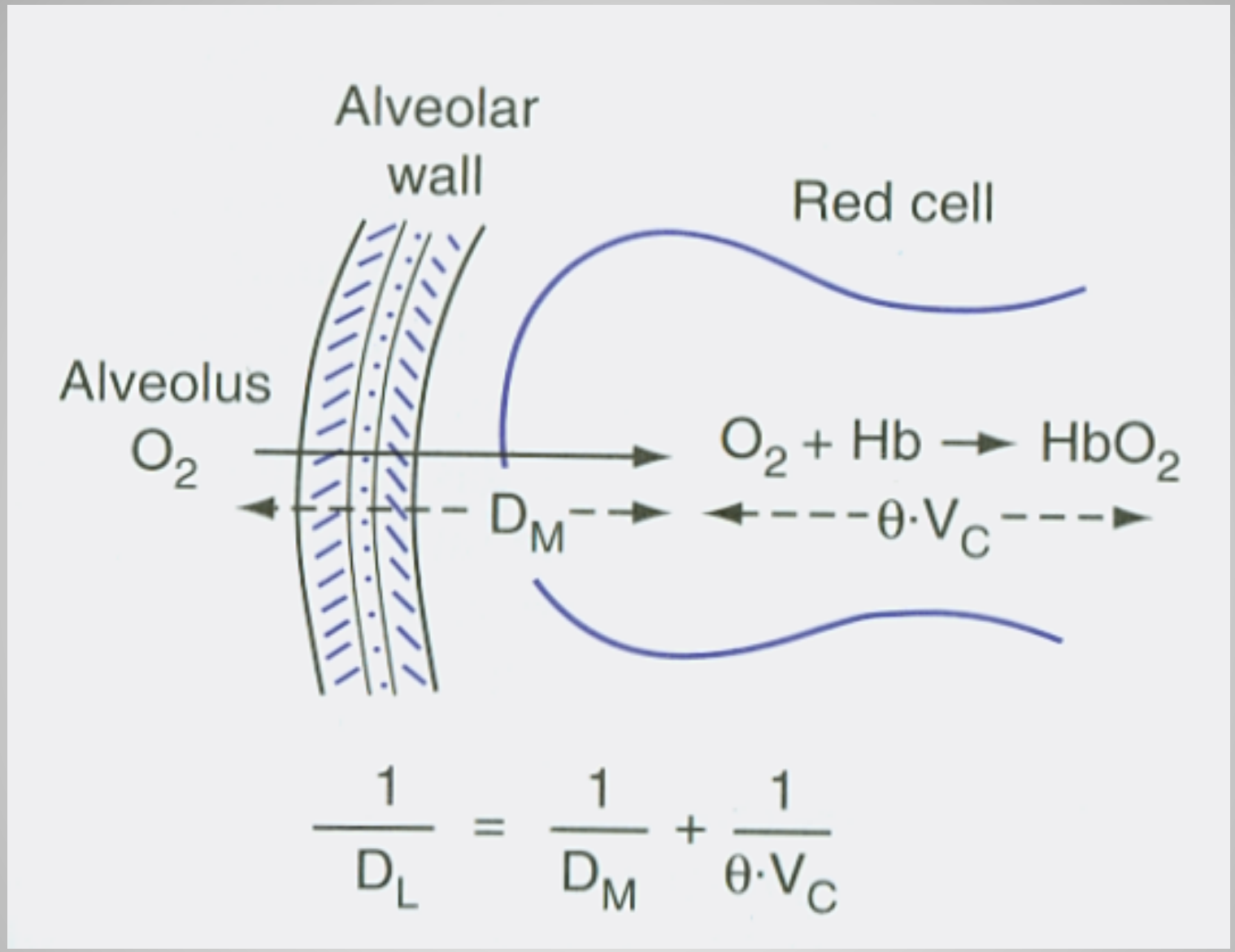
Gas Exchange

- Alveolar ventilation

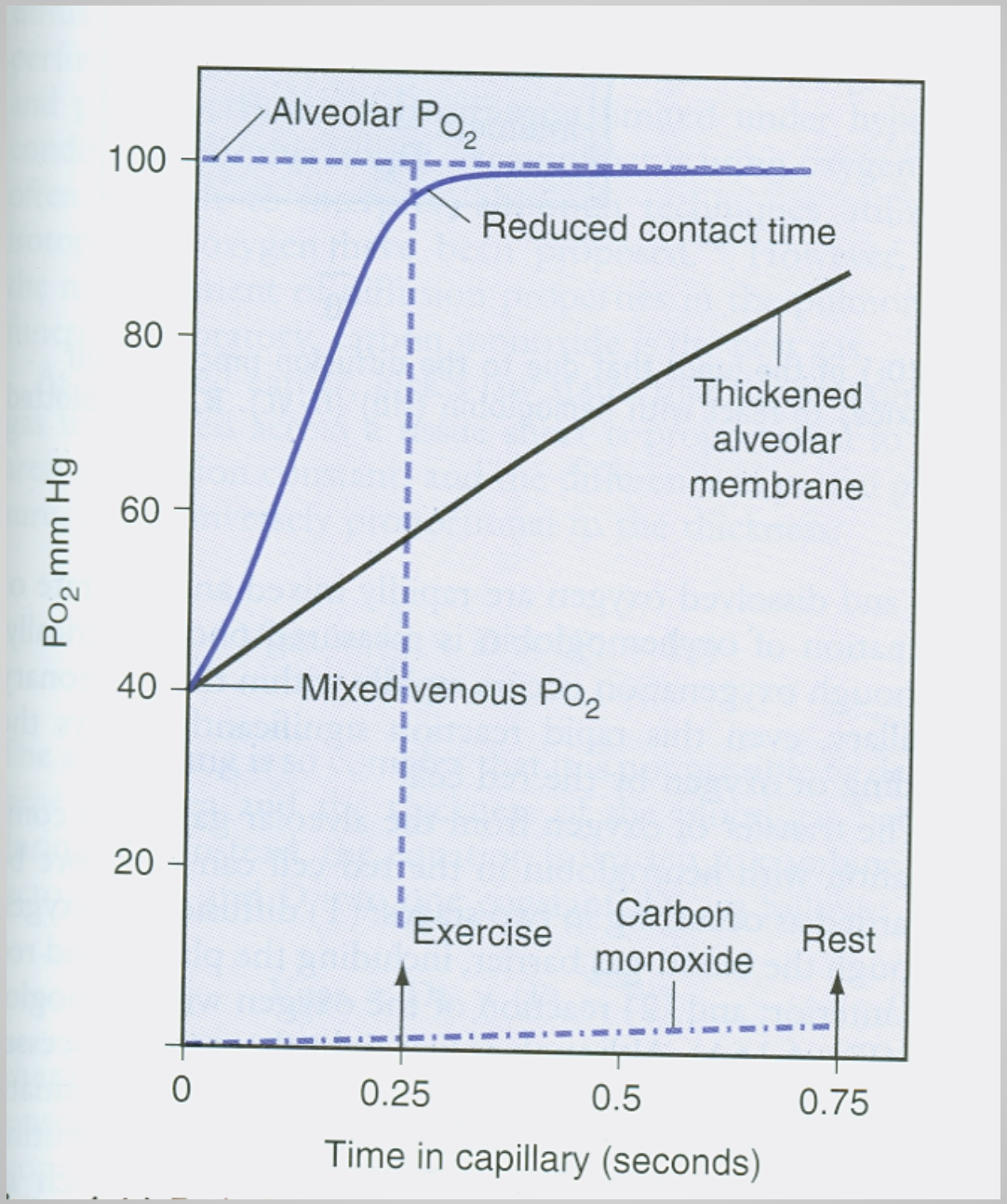
  VA = VE – VD. Anatomic VD = 1ml/lb

- Ventilation-perfusion matching
- Diffusion


140
120
100
80
60
40
20
0
PO_2, PCO_2 mm Hg
21
20
19
18
17
16
15
O_2 content mL/100 mL
O_2 content
PO_2
PCO_2
0
.01
0.1
1.0
10
100
∞
Ventilation-perfusion ratio

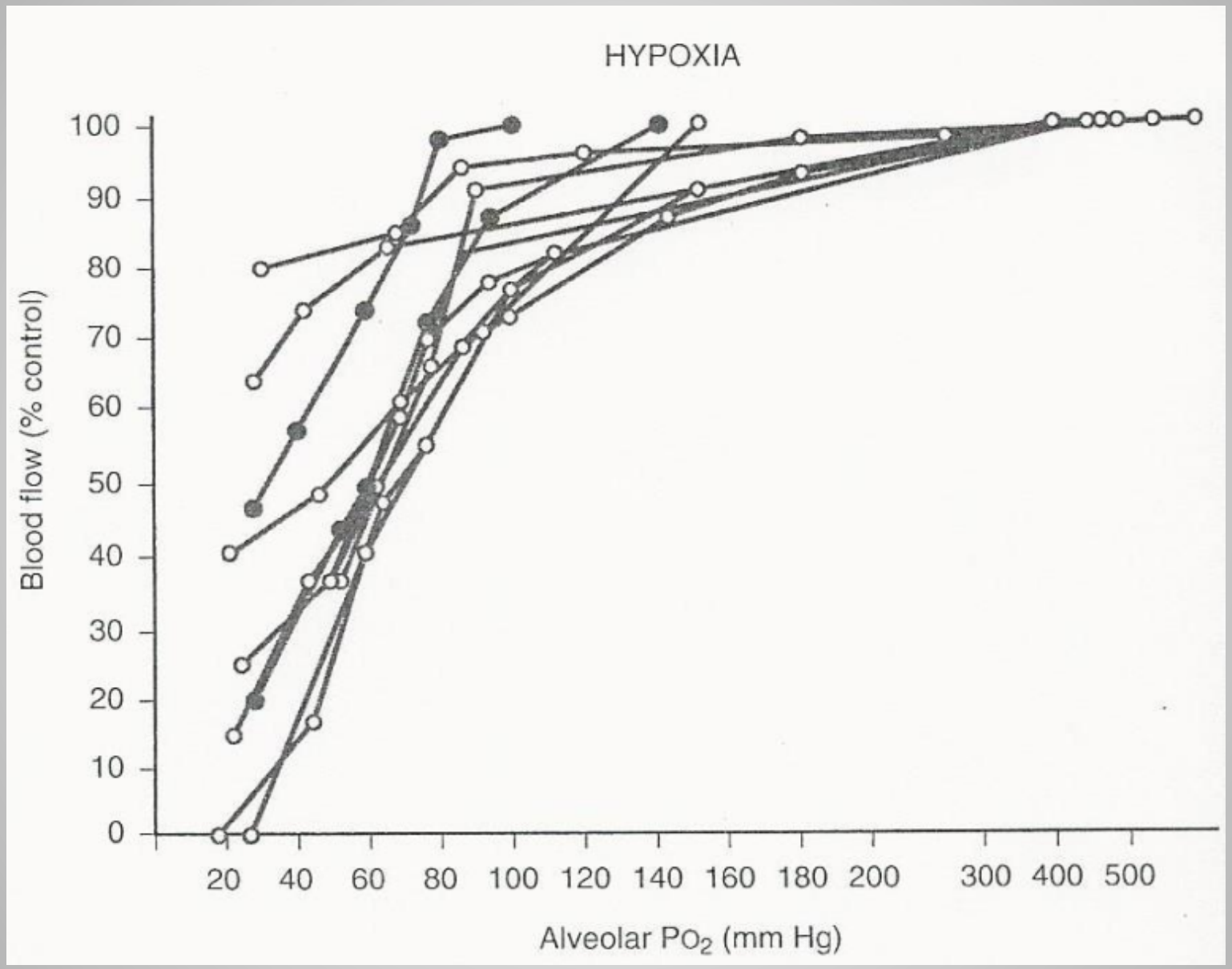


Gas transport impacted by alv-cap membrane (DM) and capillary blood volume (Vc)


Alveolar P_{O_2}
100
80
60
40
20
Reduced contact time
Thickened alveolar membrane
Mixed venous P_{O_2}
P_{O_2} mm Hg
Exercise
Carbon monoxide
Rest
0
0.25
0.5
0.75
Time in capillary (seconds)

Right Heart Function

- Pre-load
  - Fluid status, mean intrathoracic pressure
- Afterload
  - Mean intrathoracic pressure
  - Pulmonary vascular function – hypoxic vasoconstriction
- Adrenergic tone


HYPOXIA
Blood flow (% control)
100
90
80
70
60
50
40
30
20
10
0
20
40
60
80
100
120
140
160
180
200
300
400
500
Alveolar P_{O_2} (mm Hg)

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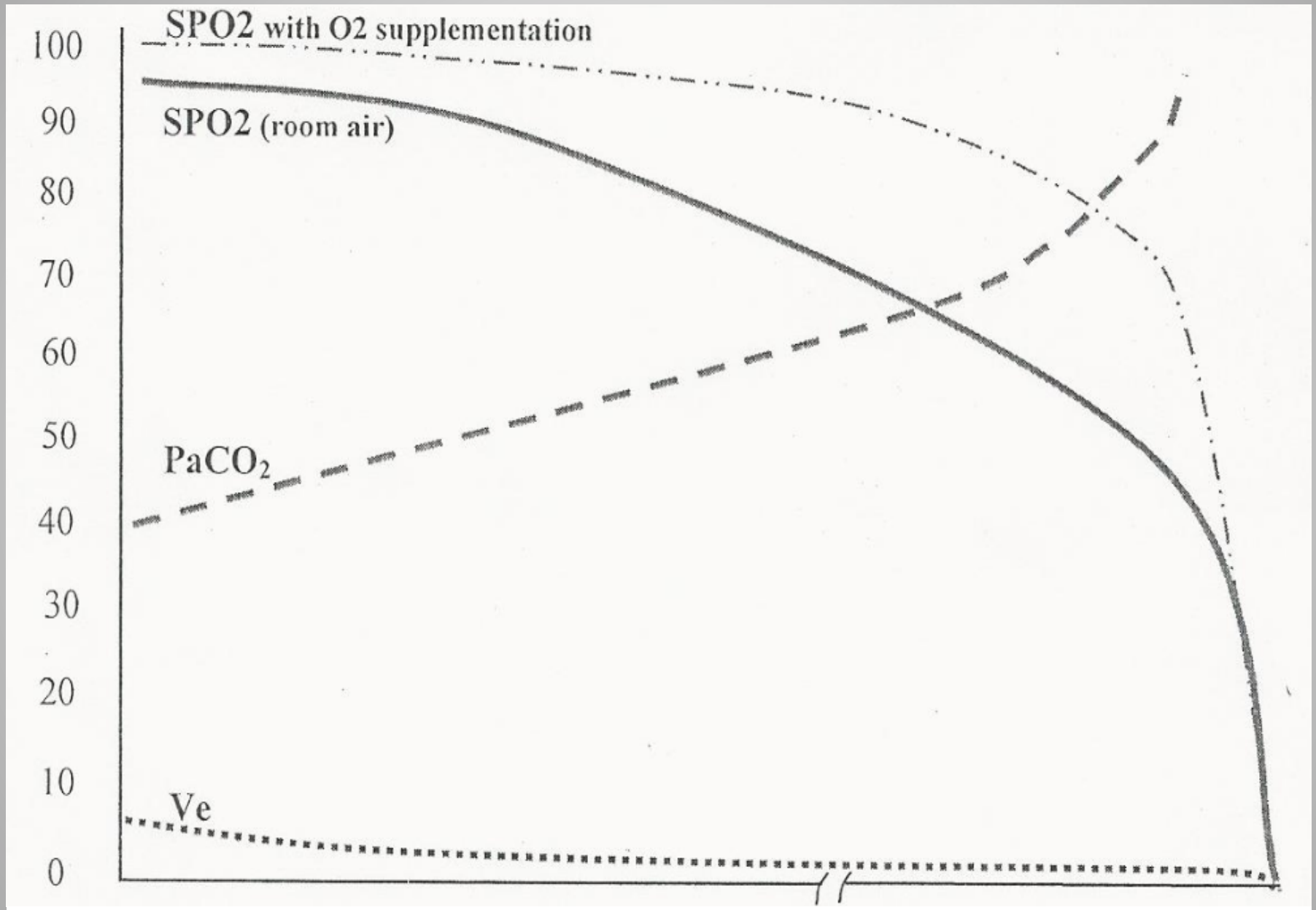
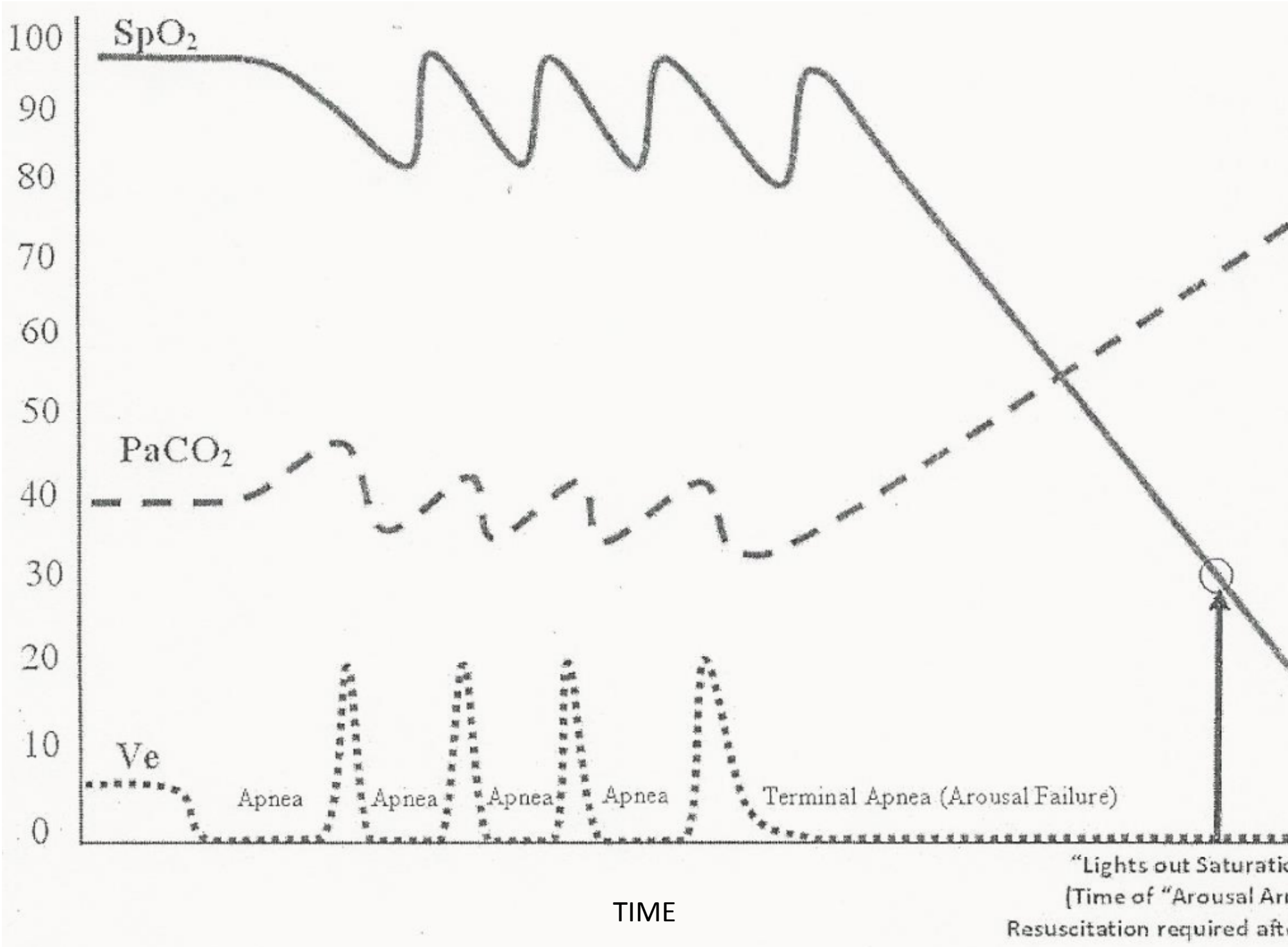
CNS Injury/CNS depressants
(Impaired Ventilator Controller)

- Hypoventilation and/or erratic breathing leads to reduced VA
  - Hypoxemia, acidosis
- Supine position, hypoventilation leads to atelectasis and VQ mismatch
  - Hypoxemia
- May be complicated by poor airway protection and aspiration
  - Hypoxemia, acidosis, mechanical loading


SPO2 with O2 supplementation
SPO2 (room air)
PaCO2
Ve
100
90
80
70
60
50
40
30
20
10
0
TIME

Sleep Disordered Breathing
(Impaired Ventilatory Controller with Sleep)

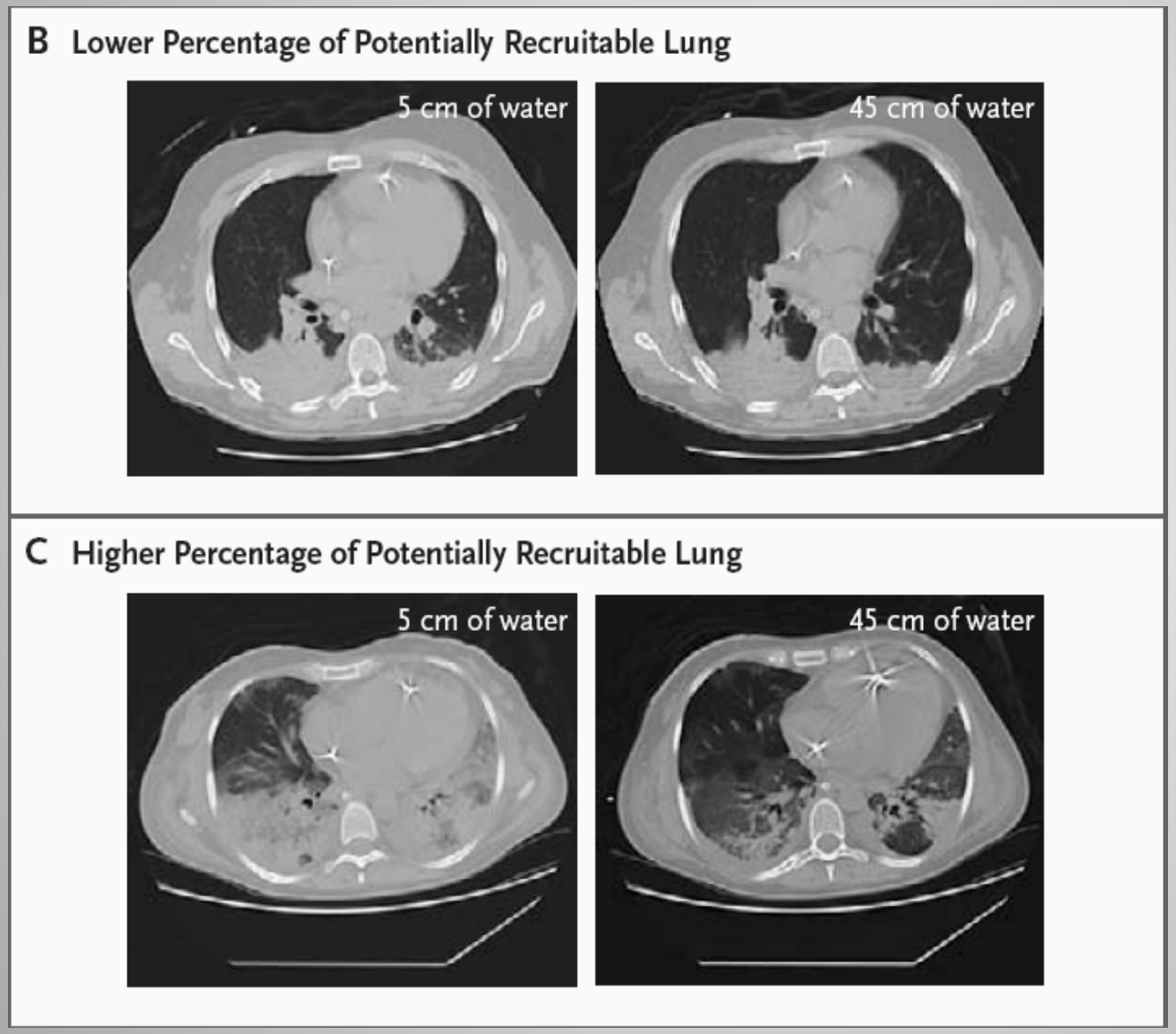
- Central and/or obstructive apneas/hypopneas lead to reduced VA
  - Hypoxemia, acidosis
- Failure of arousal reflexes
  - Hypoxemia, acidosis, respiratory arrest


100
90
80
70
60
50
40
30
20
10
0
SpO2
PaCO2
Ve
Apnea
Apnea
Apnea
Apnea
Terminal Apnea (Arousal Failure)
"Lights out Saturatio
(Time of "Arousal Ar
Resuscitation required aft
TIME

Compliance Loading

- Increased elastic WOB
  - Rapid shallow breathing pattern, dyspnea
- Reduced VA (reduced VE, increased VD)
  - Hypoxemia, acidosis
- Parenchymal inflammation/edema/collapse leads to VQ mismatch
  - Severe hypoxemia and RV impairment
  - Reduced FRC

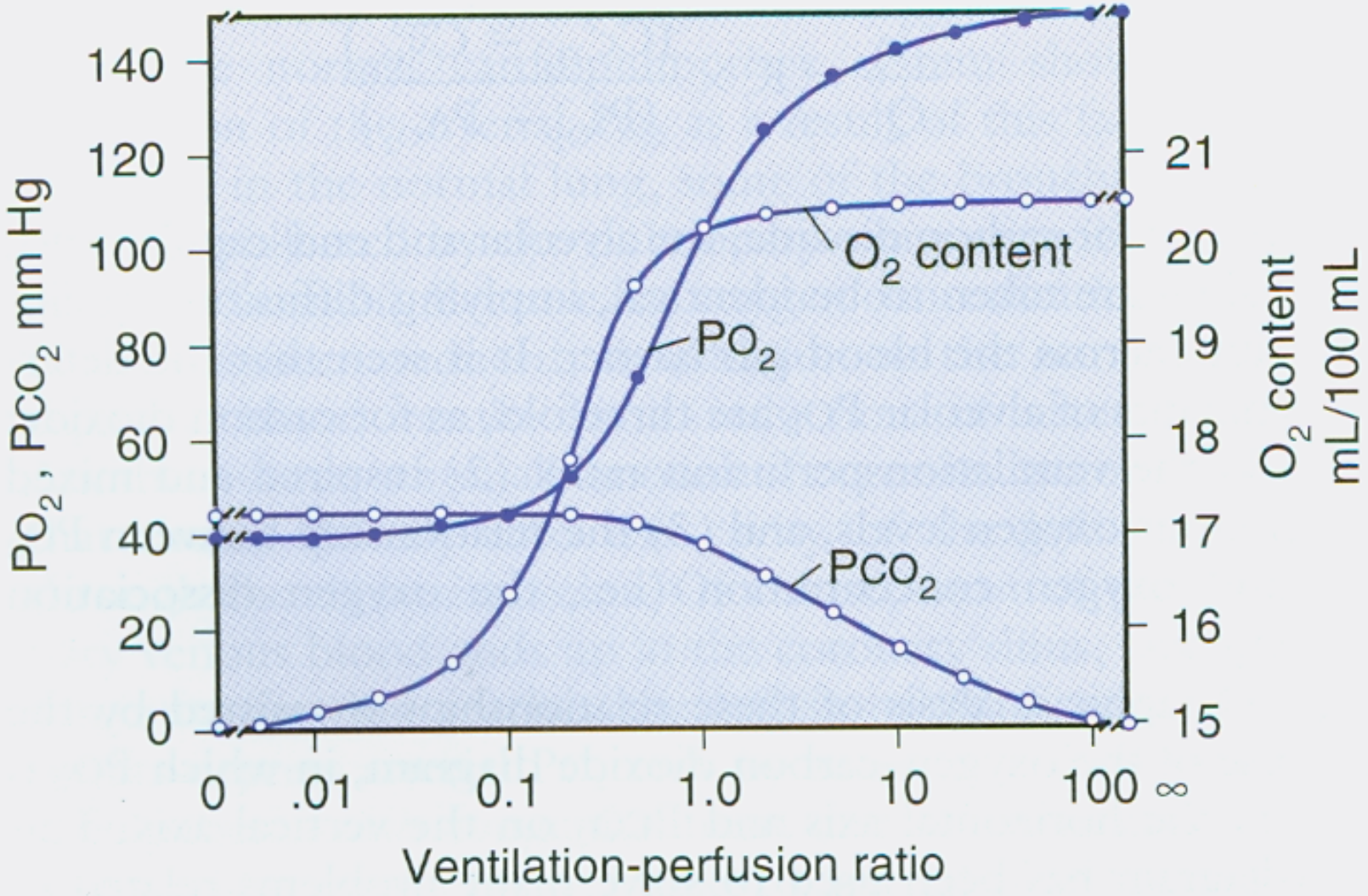
ALI and Compliance Loading



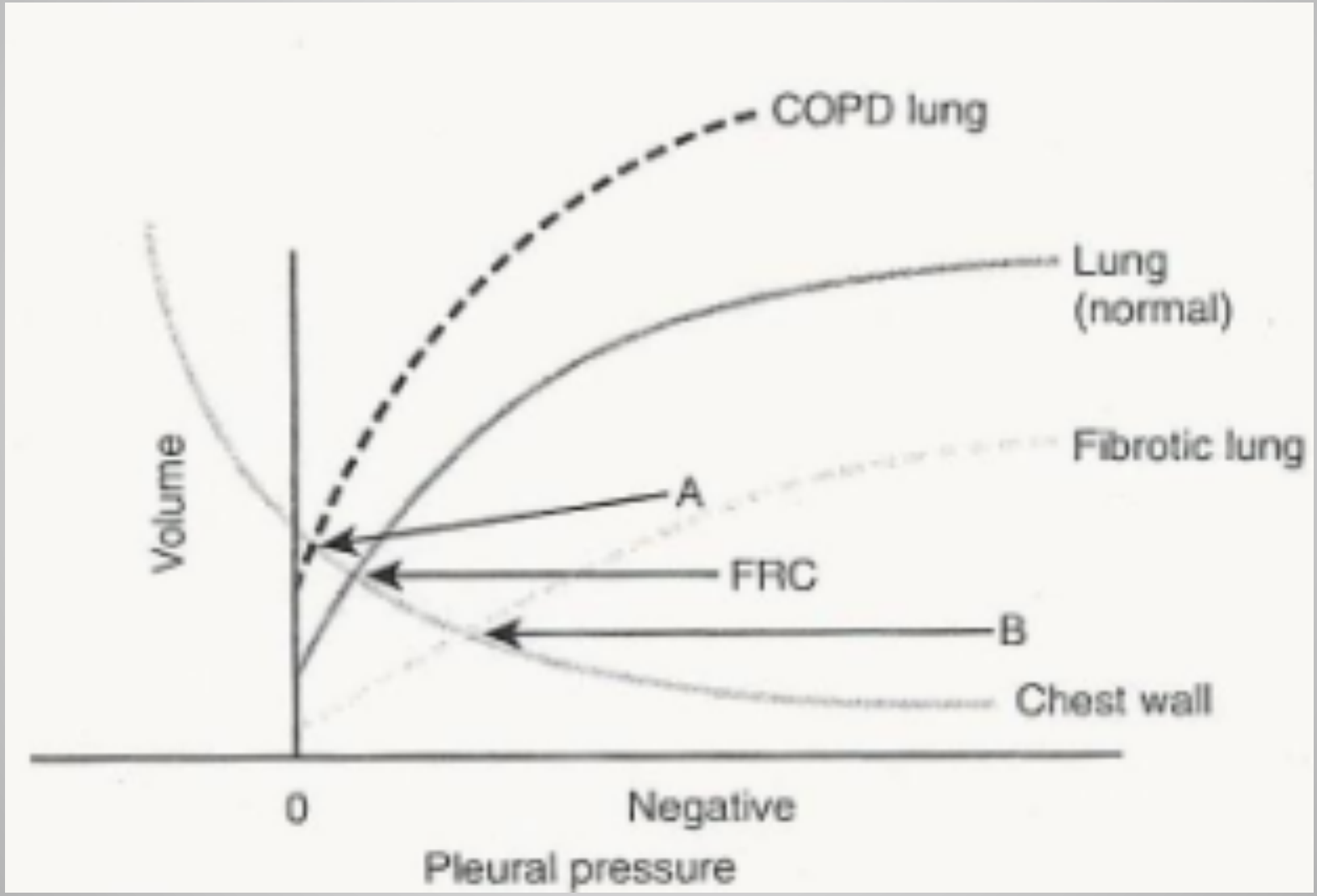
50% of pts
- 42% ALI
- 15% mortality

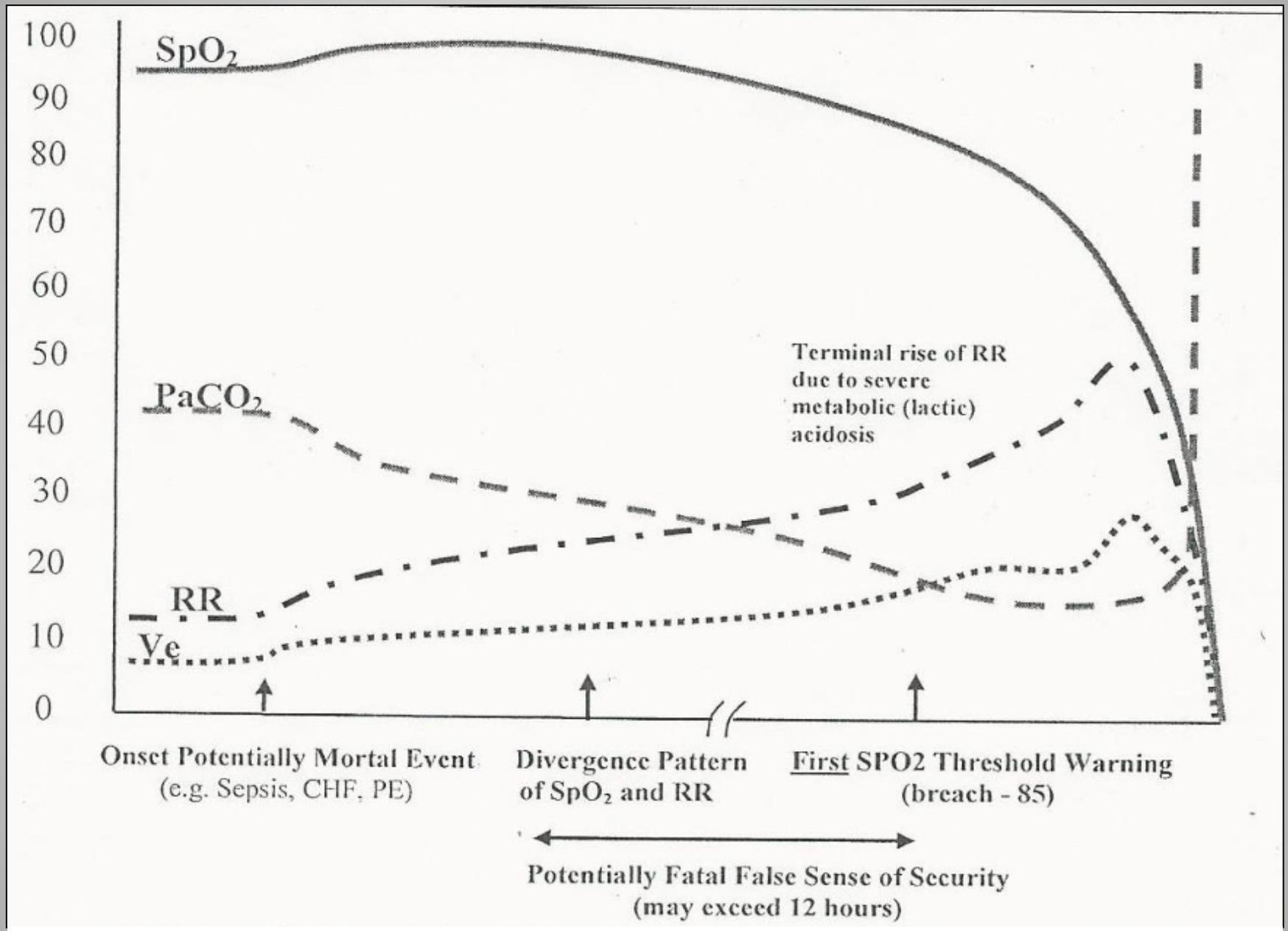
50% of pts
- 10% ALI
- 41% mortality

Gatttinoni NEJM 2006


140
120
100
80
60
40
20
0
PO_2, PCO_2 mm Hg
21
20
19
18
17
16
15
O_2 content mL/100 mL
O_2 content
PO_2
PCO_2
0
.01
0.1
1.0
10
100
∞
Ventilation-perfusion ratio

Lung Resting Size (FRC)

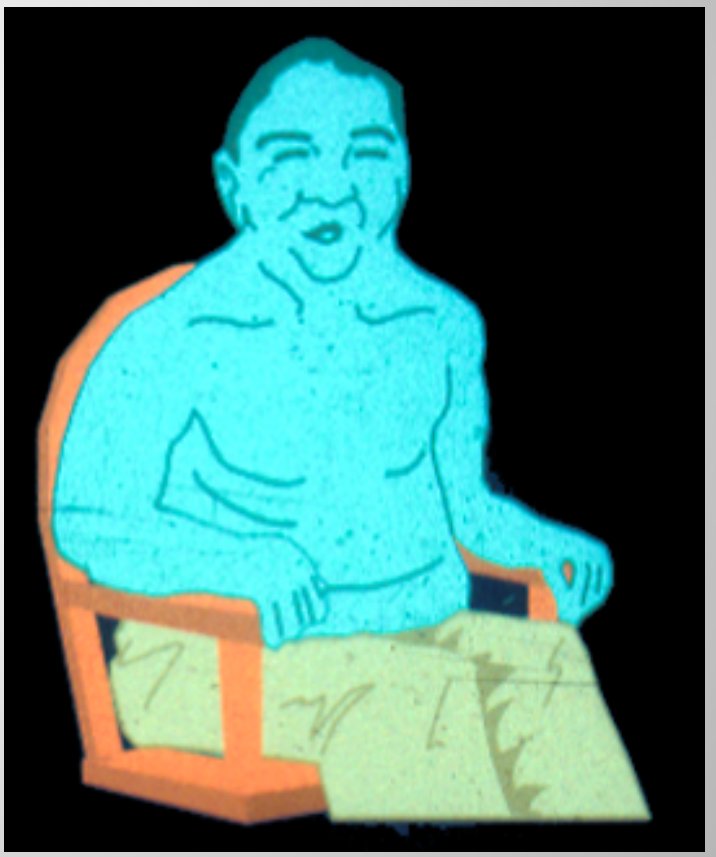


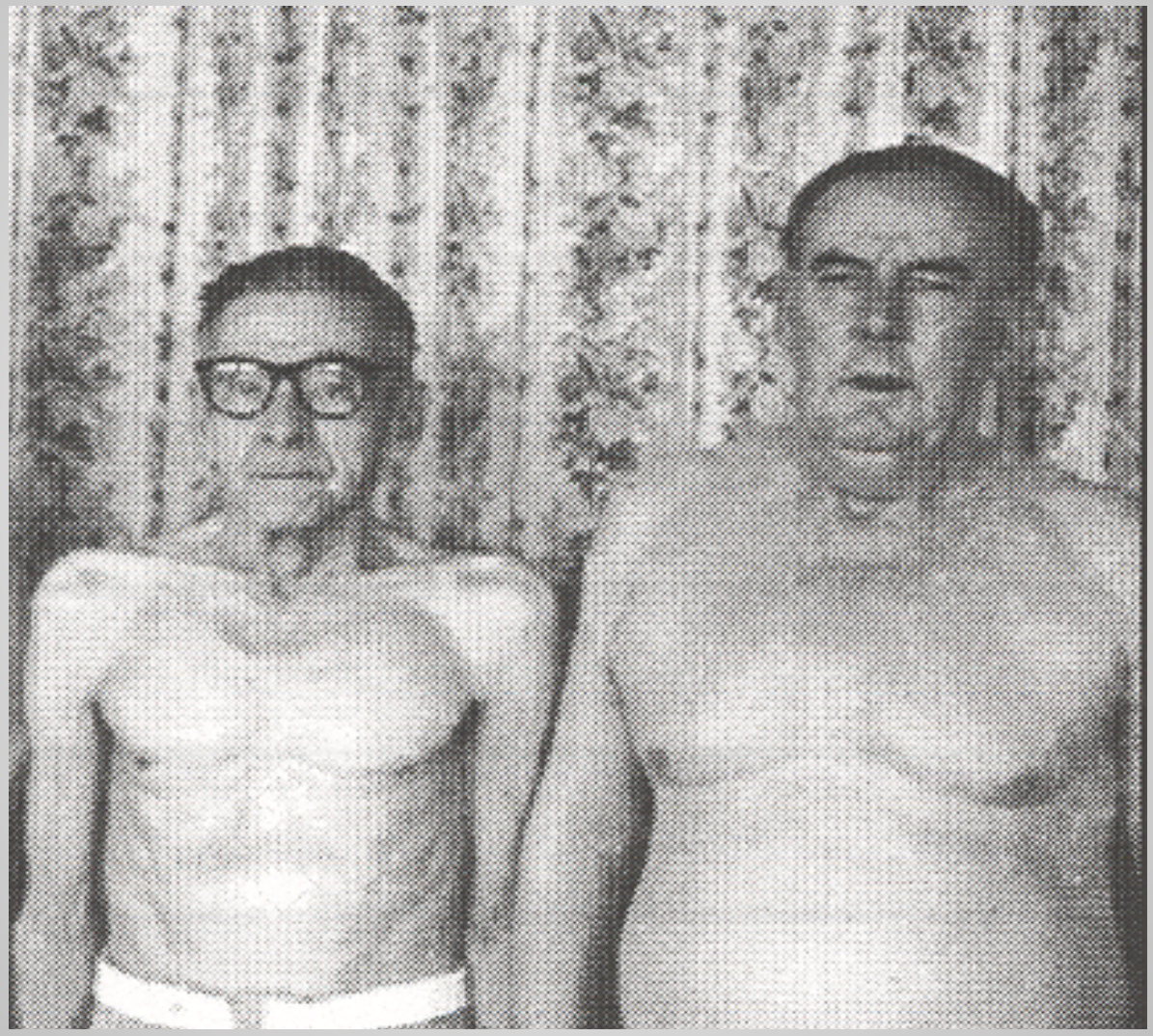

100
90
80
70
60
50
40
30
20
10
0
SpO2
PaCO2
RR
Ve
Terminal rise of RR due to severe metabolic (lactic) acidosis
Onset Potentially Mortal Event (e.g. Sepsis, CHF, PE)
Divergence Pattern of SpO2 and RR
First SPO2 Threshold Warning (breach - 85)
Potentially Fatal False Sense of Security (may exceed 12 hours)
TIME

Resistance Loading

- Increased resistive WOB and air trapping
  - Competing goals: VE vs air trapping
  - Longer expiratory time initially, then tachypnea with dyspnea, then bradypnea and ultimately arrest
  - Complicated by diaphragm malposition
- Reduced VA from reduced VE and markedly increased VD
  - Hypoxemia, acidosis,
- Intrinsic PEEP from Air Trapping
  - RV dysfunction

Ventilatory Pattern





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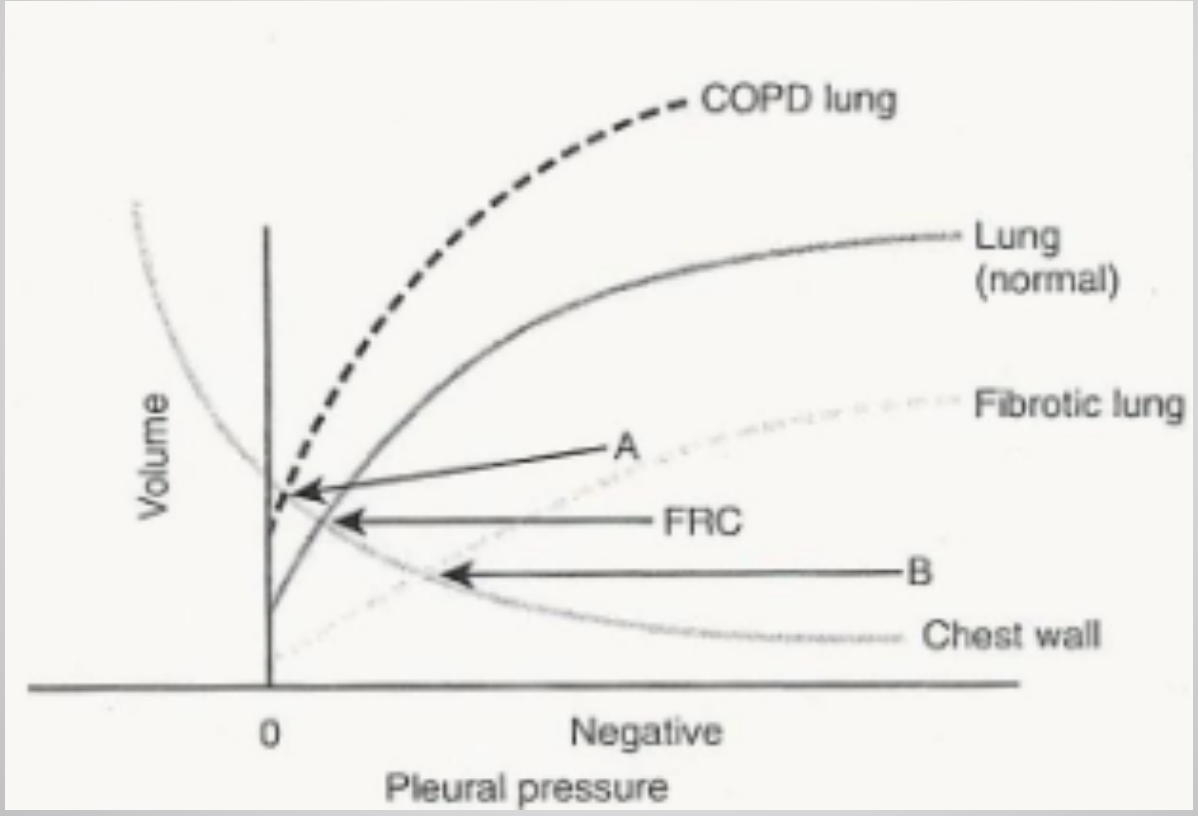
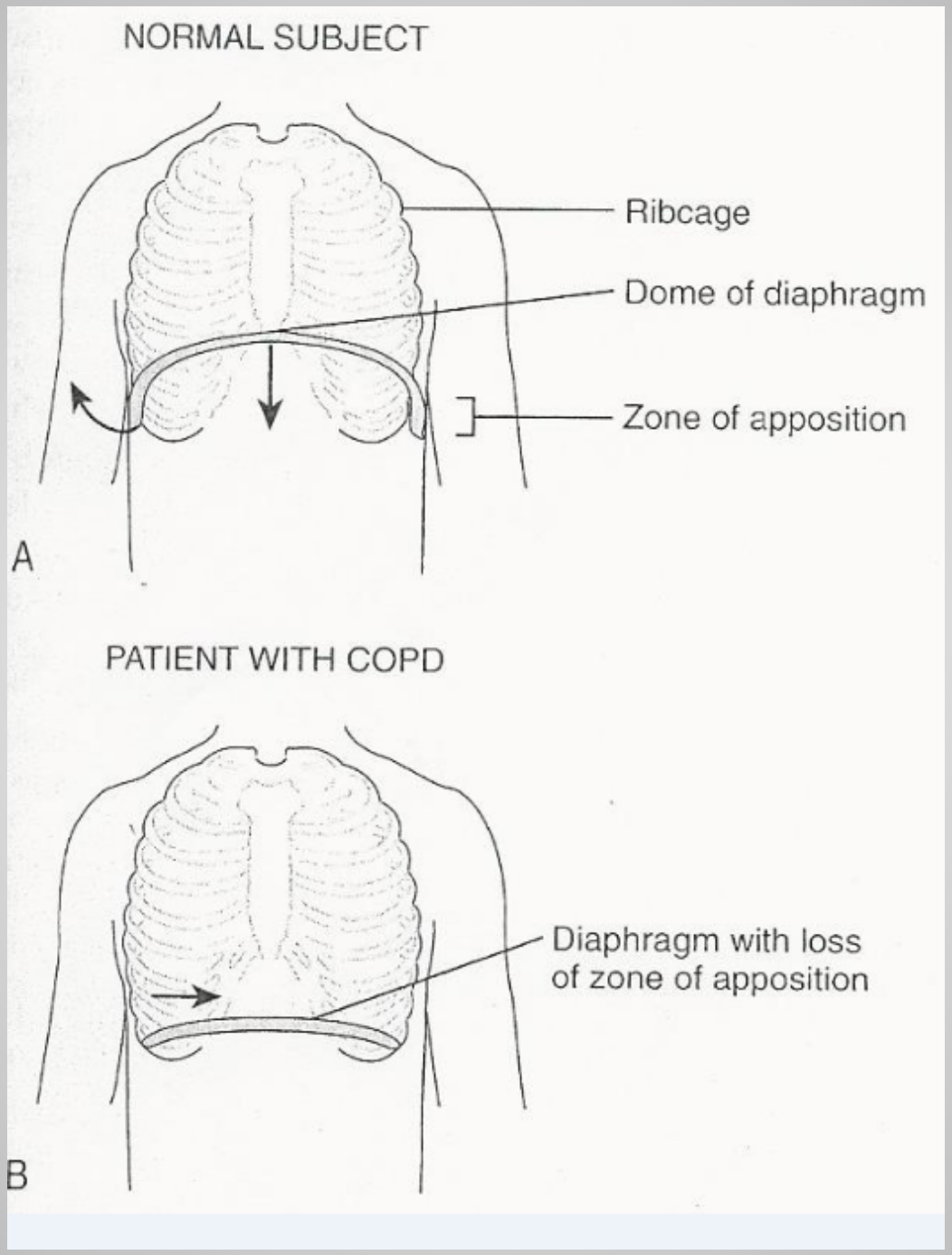
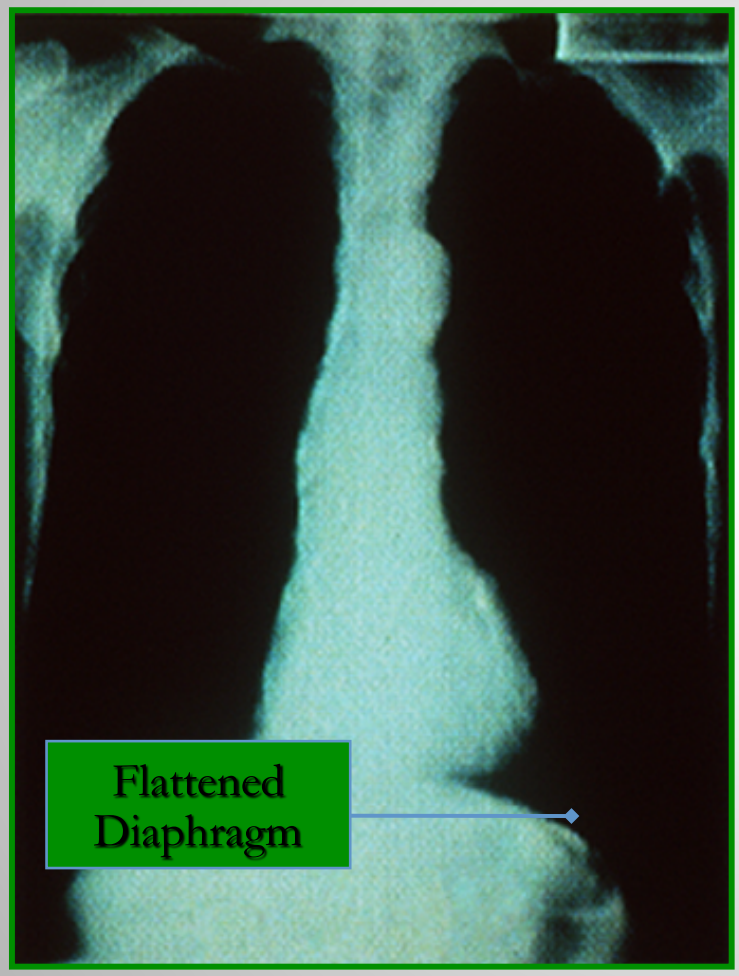
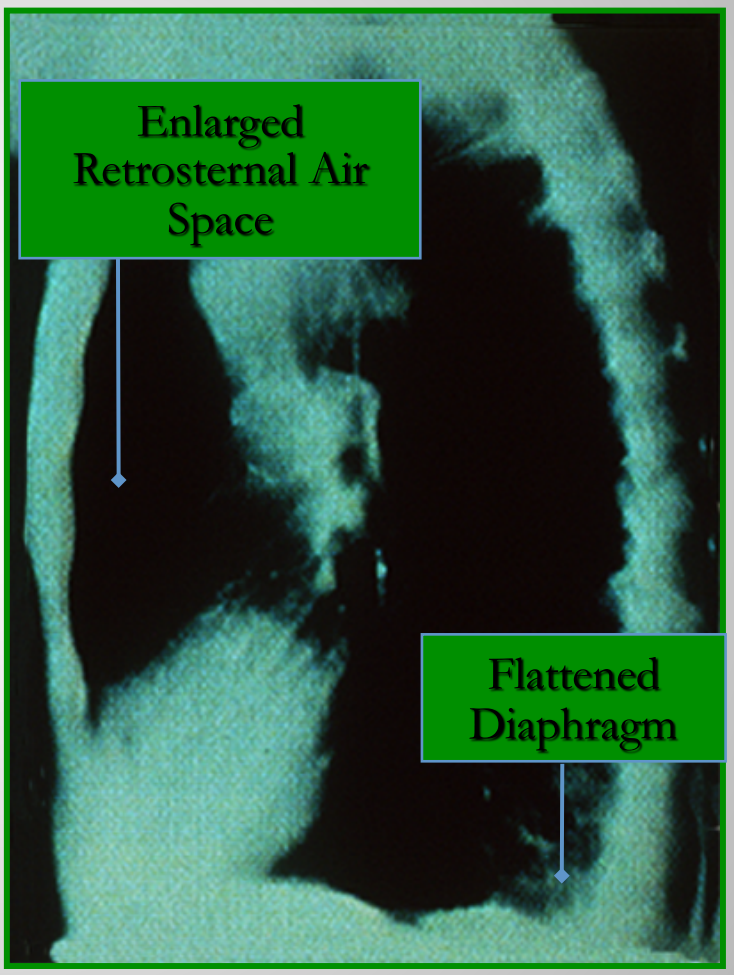



NORMAL SUBJECT
Ribcage
Dome of diaphragm
Zone of apposition
A
PATIENT WITH COPD
Diaphragm with loss
of zone of apposition
B

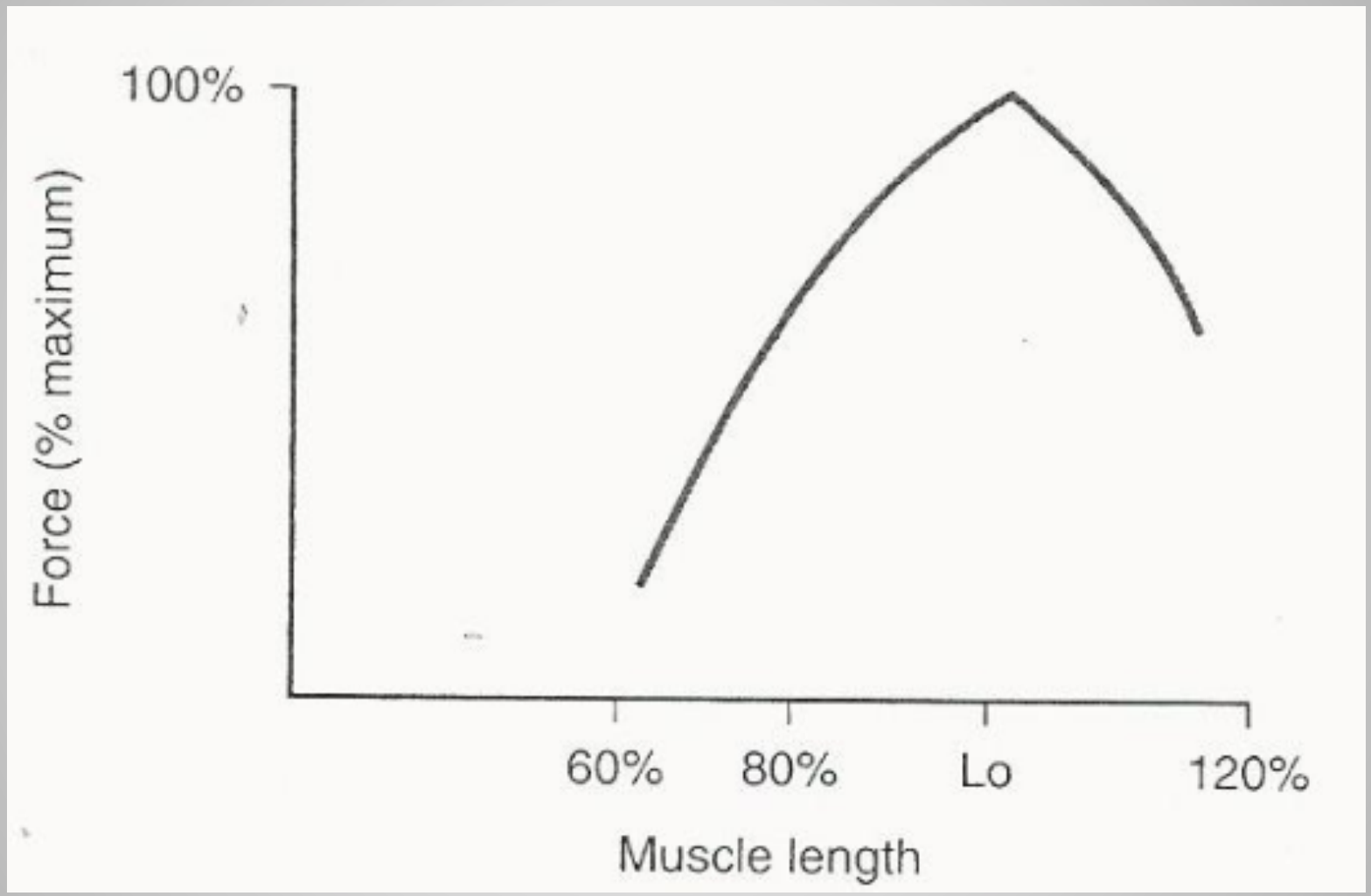
OAD: Chest radiograph



Posteroanterior



Lateral


100%
Force (% maximum)
60%
80%
Lo
120%
Muscle length

Vascular Loading

- Increased RV afterload (mechanical, hypoxia)
  - Hypotension, dyspnea
- Increased VD
  - Tachypnea, dyspnea
- Impaired VQ
  - Hypoxemia

Patterns of Respiratory Compromise

Etiology	Vent Pattern	FRC	Hypercapnia	Hypoxemia	RV dysfunction
CNS	Slow, erratic, dec VA	sl reduced	Yes	Later	Late
Crs Load	Rapid shallow dec VA late	reduced	Later	Yes	Yes
Raw Load	Short Ti, Incr R dec VA early	increased	Yes	Later	Yes
Vasc Load	Tachypnea	no change	No	Yes	Pronounced

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Systemic Effects of Respiratory Compromise from Any Cause

- Hypoxemia affects CNS
  - Mental status changes, confusion, agitation
- Severe hypoxemia can affect all organs (MODS)
- Acidosis affects cardiovascular and hemodynamic function
- Dyspnea and muscle loading produces stress response and adrenergic stimulation

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