Al mio segnale scatenate le vostre opinioni

Il Signor di mezza età,
molto noto ora in città
perché tutti, su per giù,
l'hanno visto alla Tivù,

ha un aspetto aristocratico,
e davvero sì simpatico
che fra i suoi ammiratori
ha non pochi imitatori.

Non respiro tanto bene

Uomo, 76 anni, tosse ed espettorazione

Viene in PS con le sue gambe

Ex fumatore

→...ha smesso due giorni fa

No documentazione con se'

Terapia: qualche "spruzzino"

Non respiro tanto bene

PA 165/95, fc 90 r, T 37.4°, SatO2: 93% in aa

Frequenza respiratoria: 20 cpm

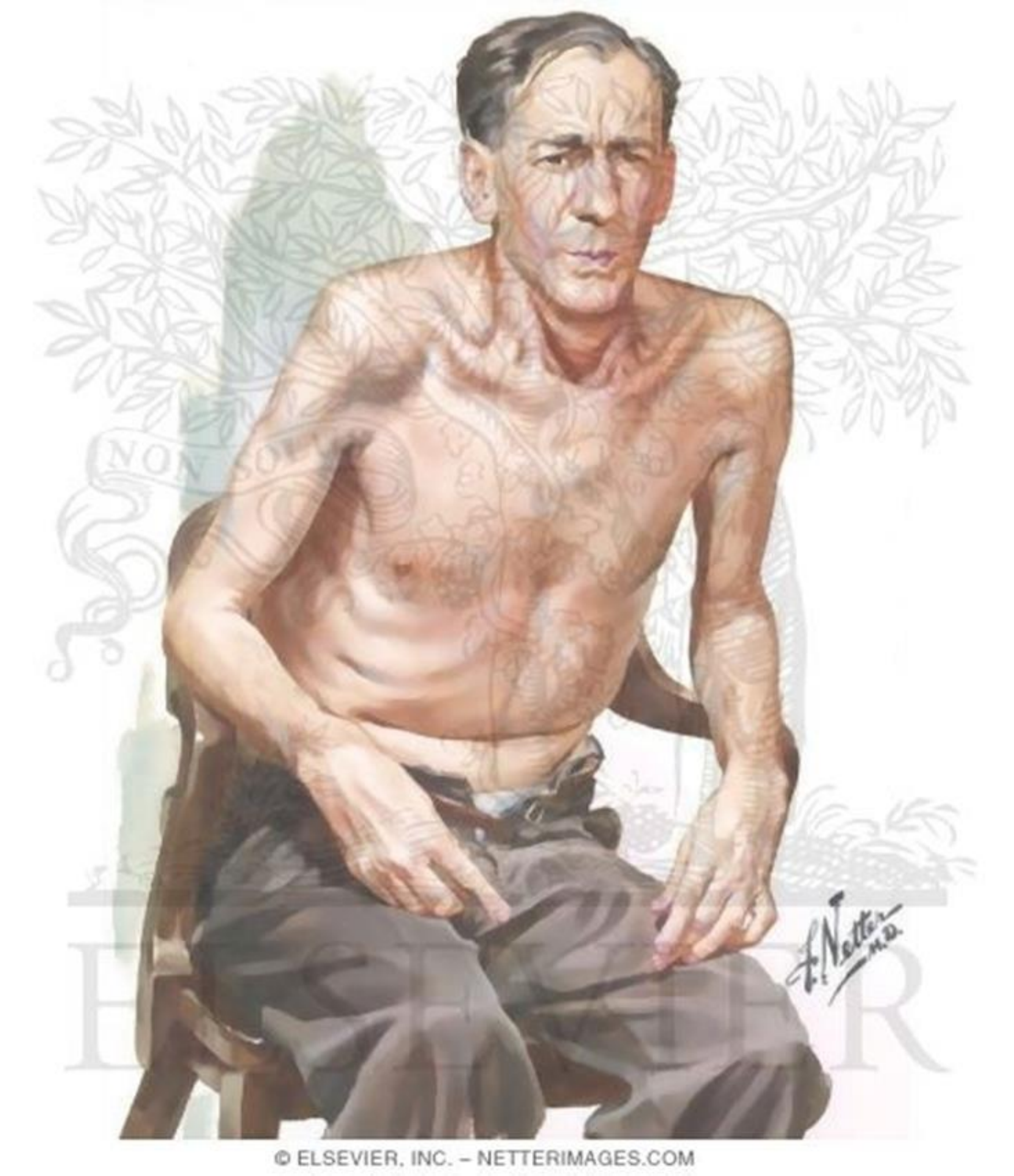
EO: ronchi e sibili

Non respiro tanto bene

→ Salbutamolo 6 puff ("al volo")

Meglio vero?

→ Dimissione, si rimanda al medico curante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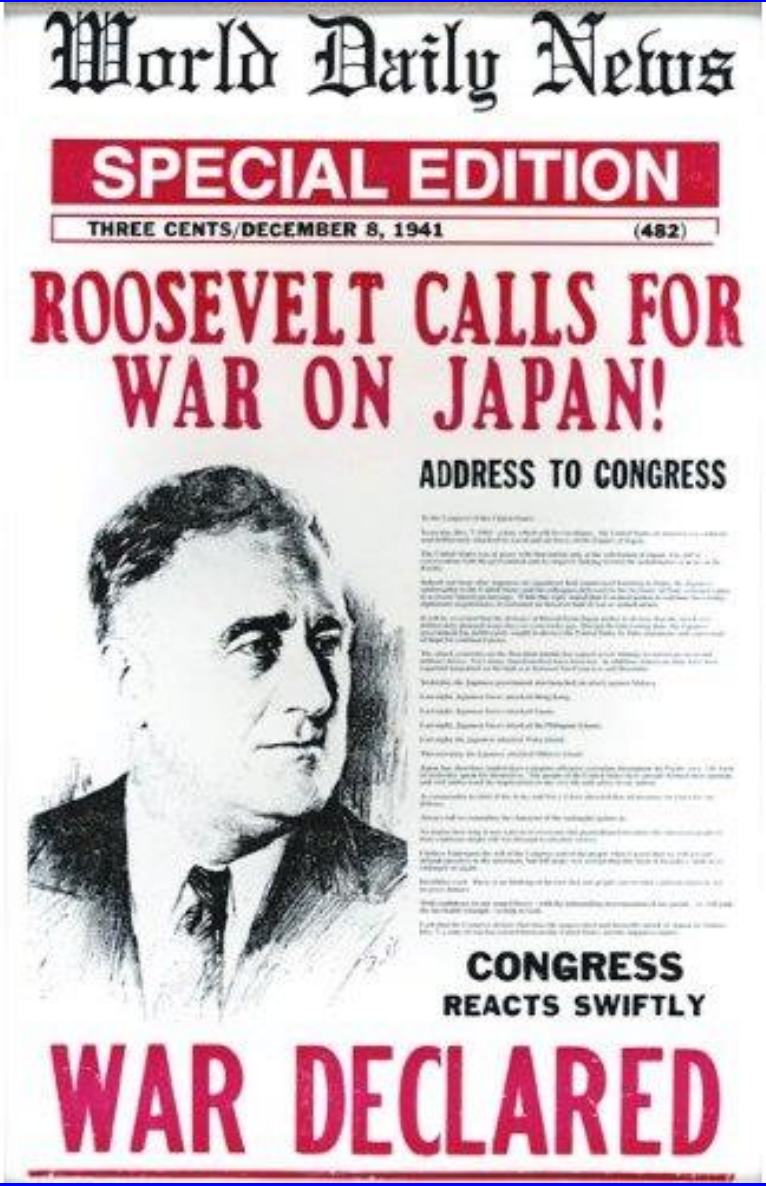
Il ritorno

48 h dopo (medicalizzata 118)

Frequenza respiratoria 34 cpm, SatO2: 86% in aa.

ABG!

- PaO_2 48 mm Hg
- $PaCO_2$ 66 mm Hg
- pH 7.24



World Daily News

SPECIAL EDITION

THREE CENTS/DECEMBER 8, 1941 (482)

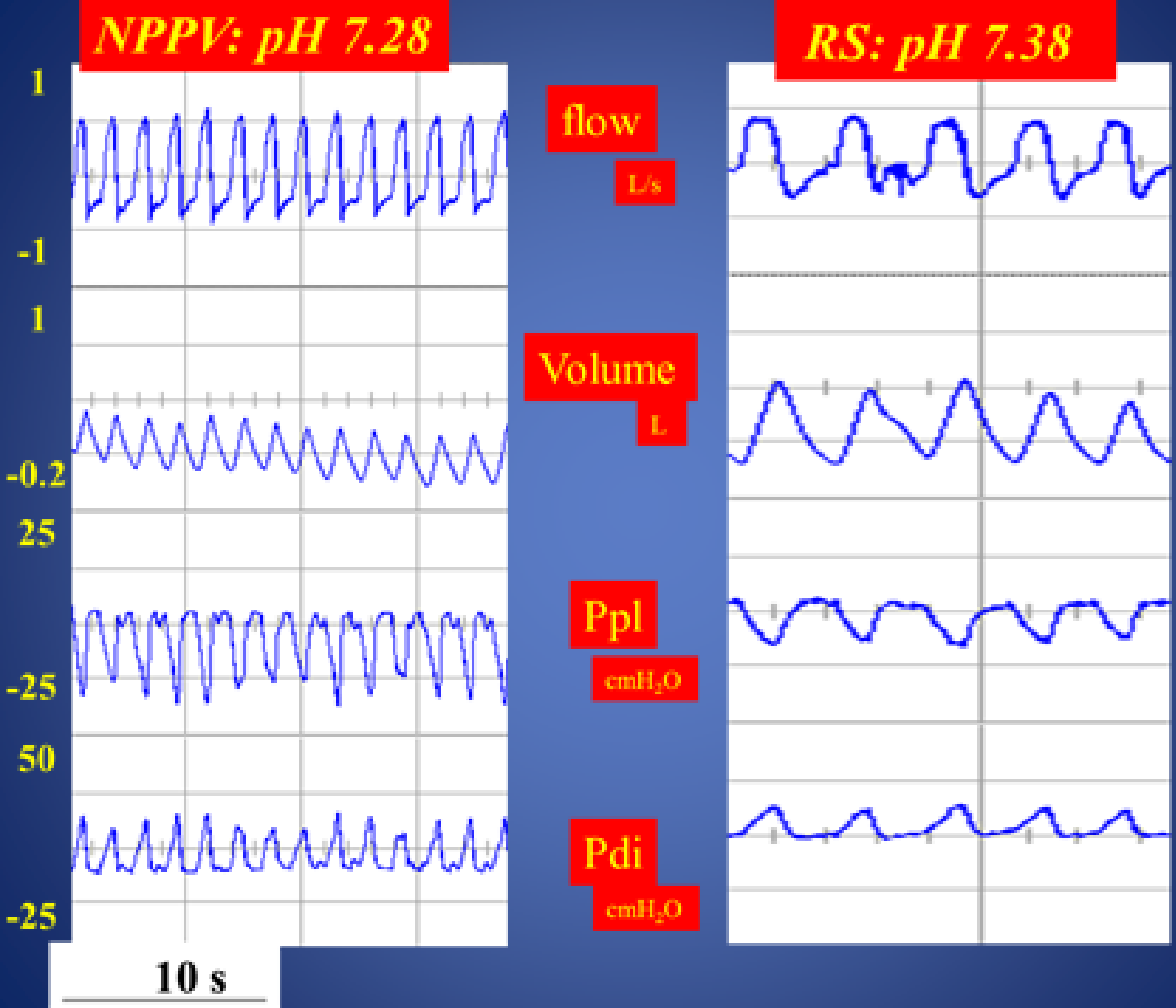
ROOSEVELT CALLS FOR WAR ON JAPAN!

ADDRESS TO CONGRESS

CONGRESS REACTS SWIFTLY

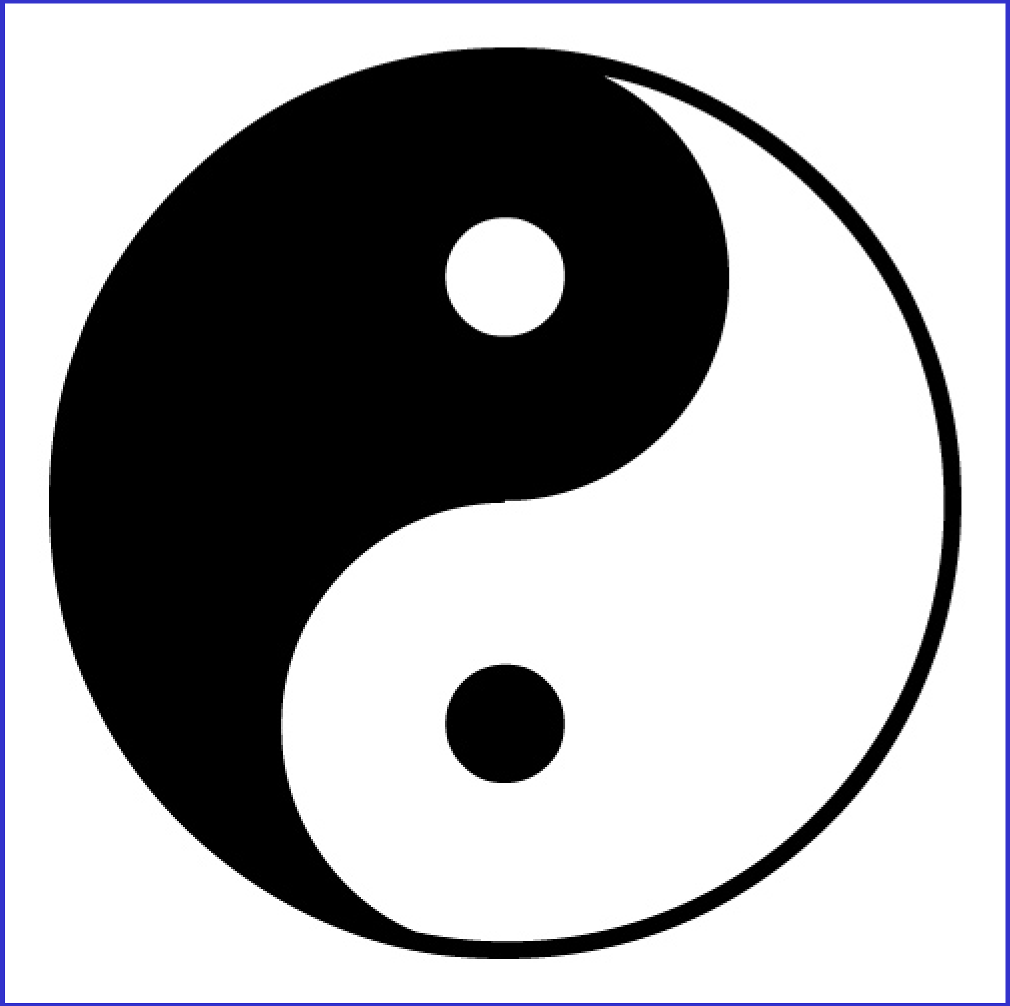
WAR DECLARED


IL SIGNORE
DI MEZZA ETA'
CHE BELL'ETA'
AH! SE AVESSI VENT'ANNI
DI MENO

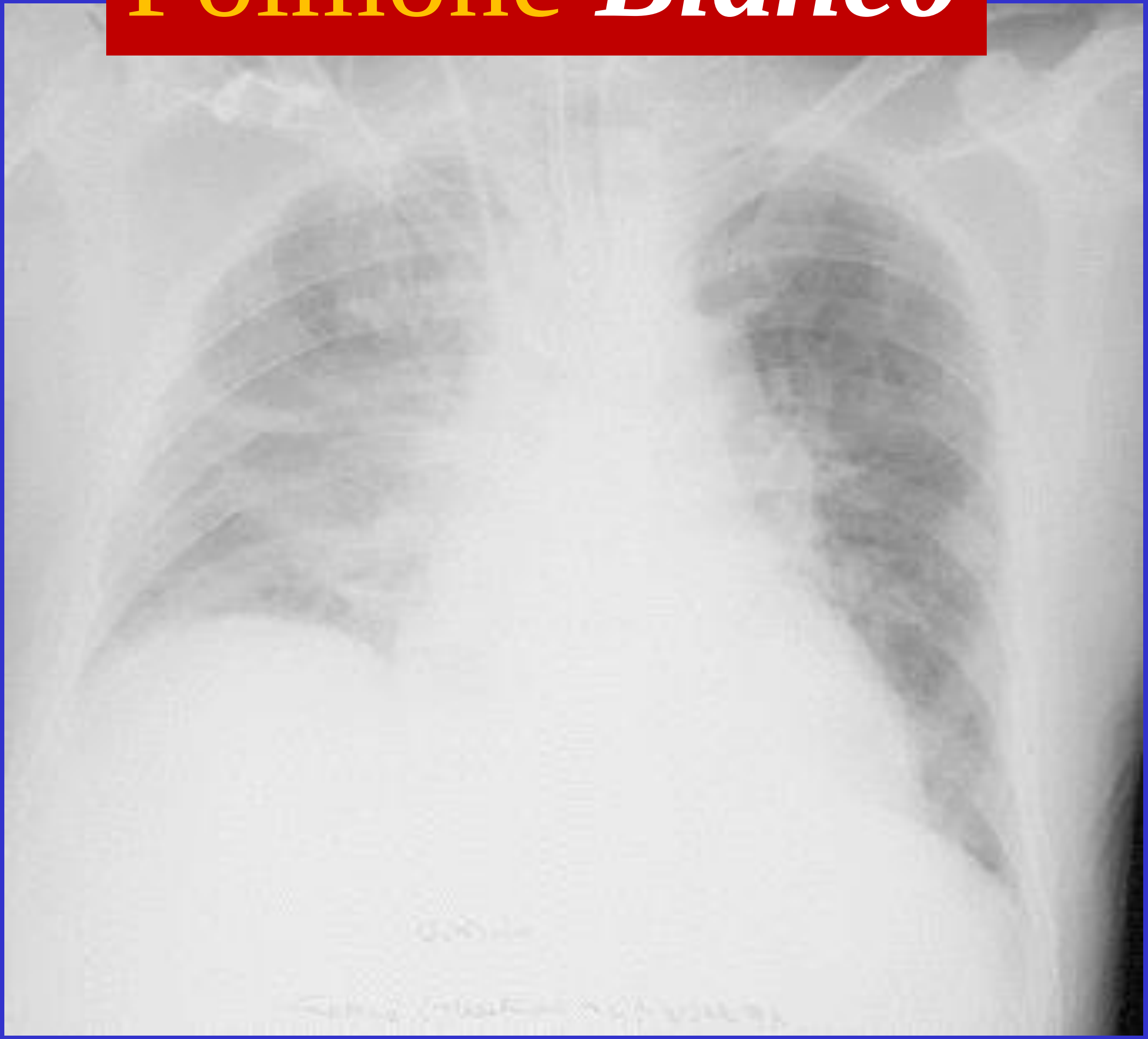

NPPV: pH 7.28
RS: pH 7.38
1
-1
1
-0.2
25
-25
50
-25
flow
L/s
Volume
L
Ppl
cmH2O
Pdi
cmH2O
10 s







Polmone ***Bianco***



Polmone *Nero*

Allo stesso modo?

FORSE CHE SI FORSE CHE NO · ROMANZO

DI GABRIELE D'ANNUNZIO.

PRESSO I FRATELLI TREVES IN MILANO. MCMX.

17.° migliaio.

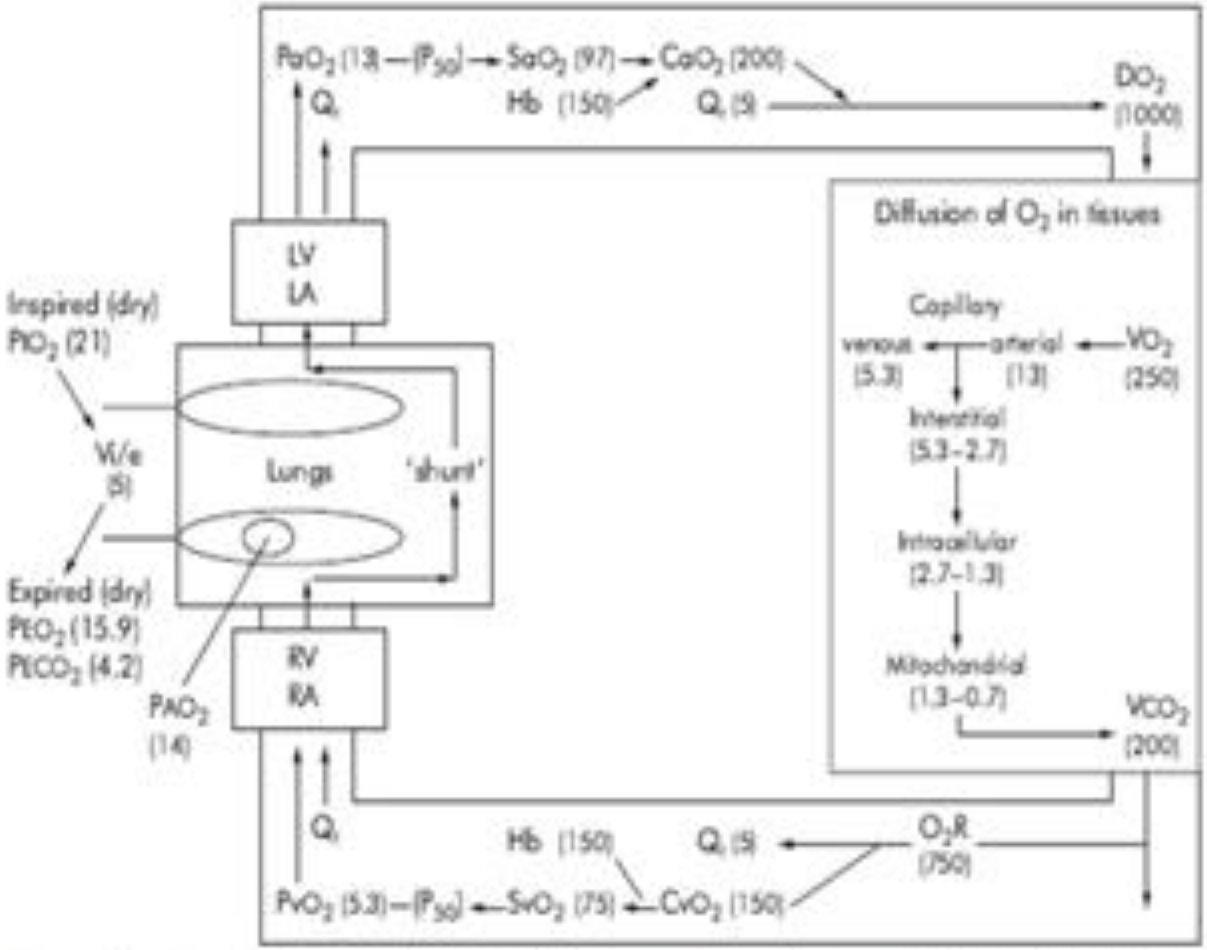


Figure 1 Oxygen transport from atmosphere to mitochondria. Values in parentheses for a normal 75 kg individual (BSA 1.7 m^2) breathing air (F_{IO_2} 0.21) at standard atmospheric pressure (P_B 101 kPa). Partial pressures of O_2 and CO_2 (P_{O_2}, P_{CO_2}) in kPa; saturation in %; contents (Ca_{O_2}, Cv_{O_2}) in ml/l; Hb in g/l; blood/gas flows (Qt, $V_{I/e}$) in l/min. P_{50} – position of oxygen haemoglobin dissociation curve; it is P_{O_2} at which 50% of haemoglobin is saturated (normally 3.5 kPa). D_{O_2} – oxygen delivery; V_{O_2} – oxygen consumption, V_{CO_2} – carbon dioxide production; P_{IO_2}, P_{EO_2} – inspired and mixed expired P_{O_2}; P_{ECO_2} – mixed expired P_{CO_2}; P_{AO_2} – alveolar P_{O_2}.


MECCANICA

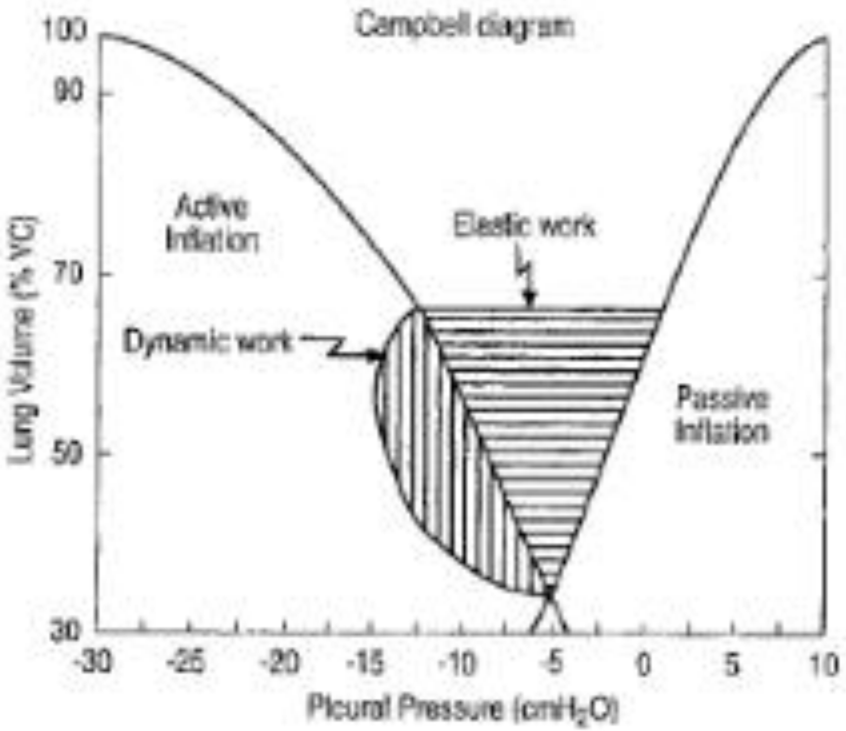
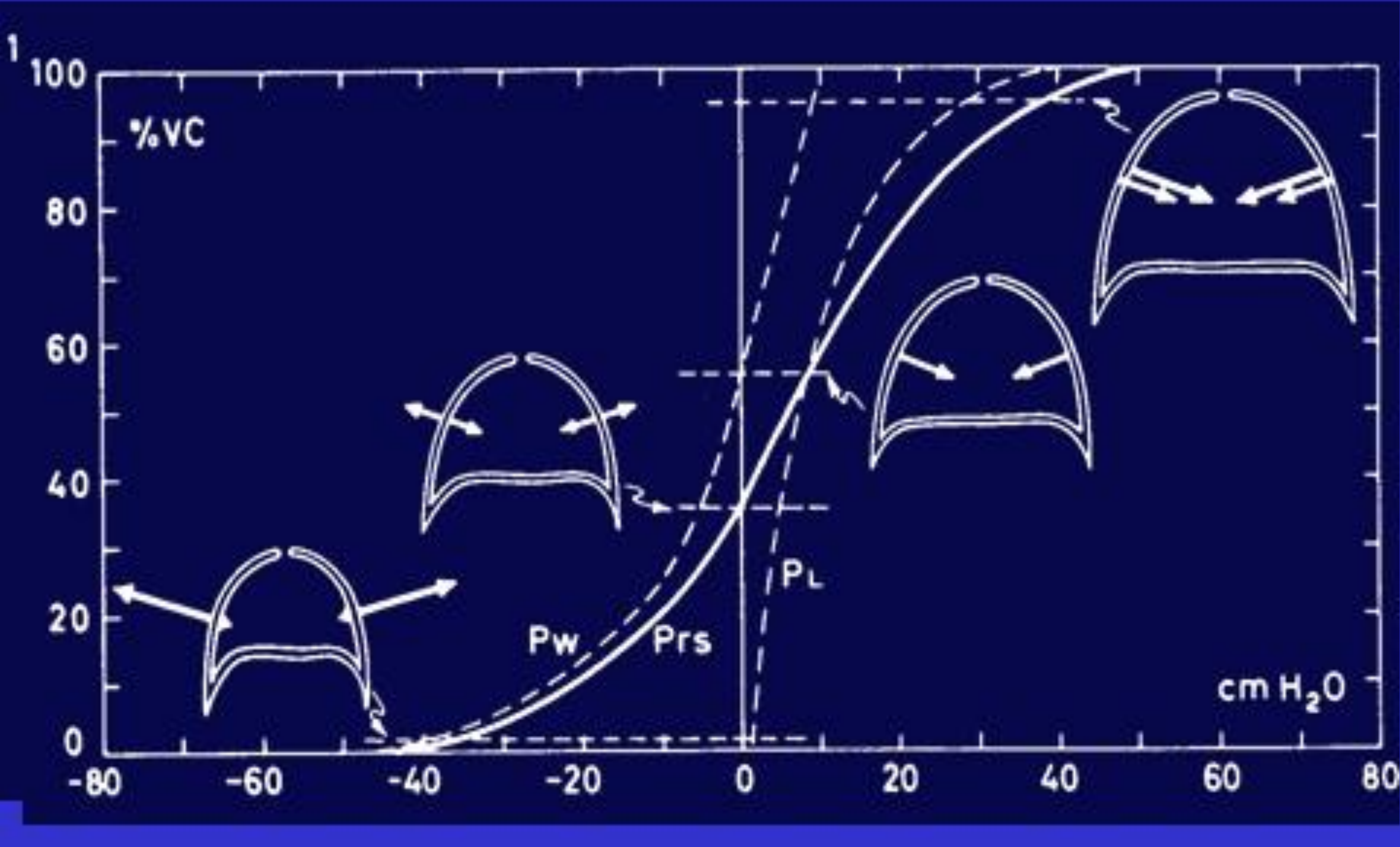
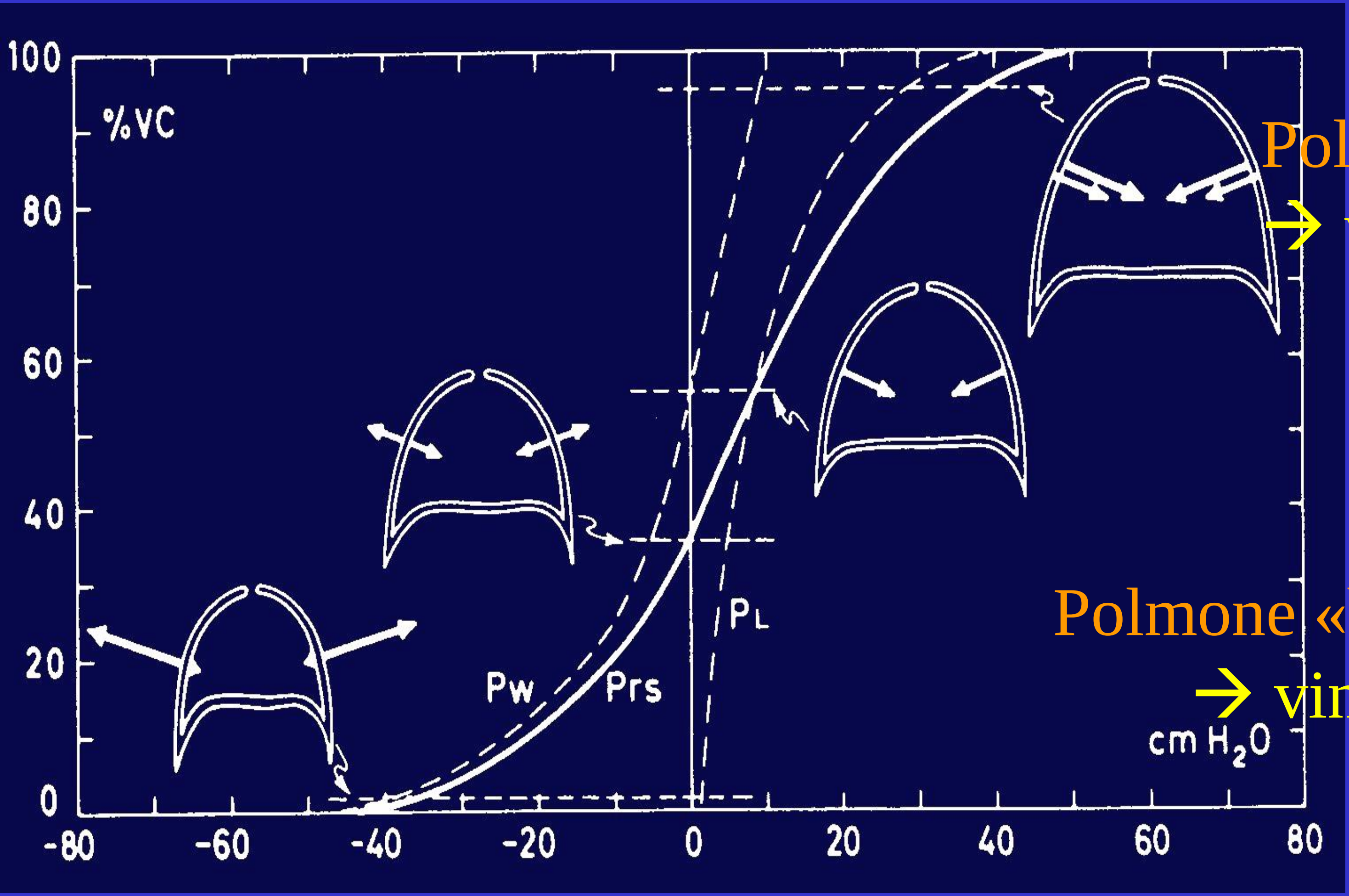


Figure 2. Campbell diagram. Graphical analysis of the work done during a breathing cycle by the inspiratory muscles. *Vertical hatching*: Work done to overcome flow resistance of the lungs. *Horizontal hatching*: Work done to overcome elastance of the lungs and chest wall. Modified by permission from Macklem PT, Mead J, editors. Handbook of physiology. Vol. 3: The respiratory system, Part 3. Bethesda, MD: American Physiological Society; 1986. p. 495.

CURVA P/V STATICA



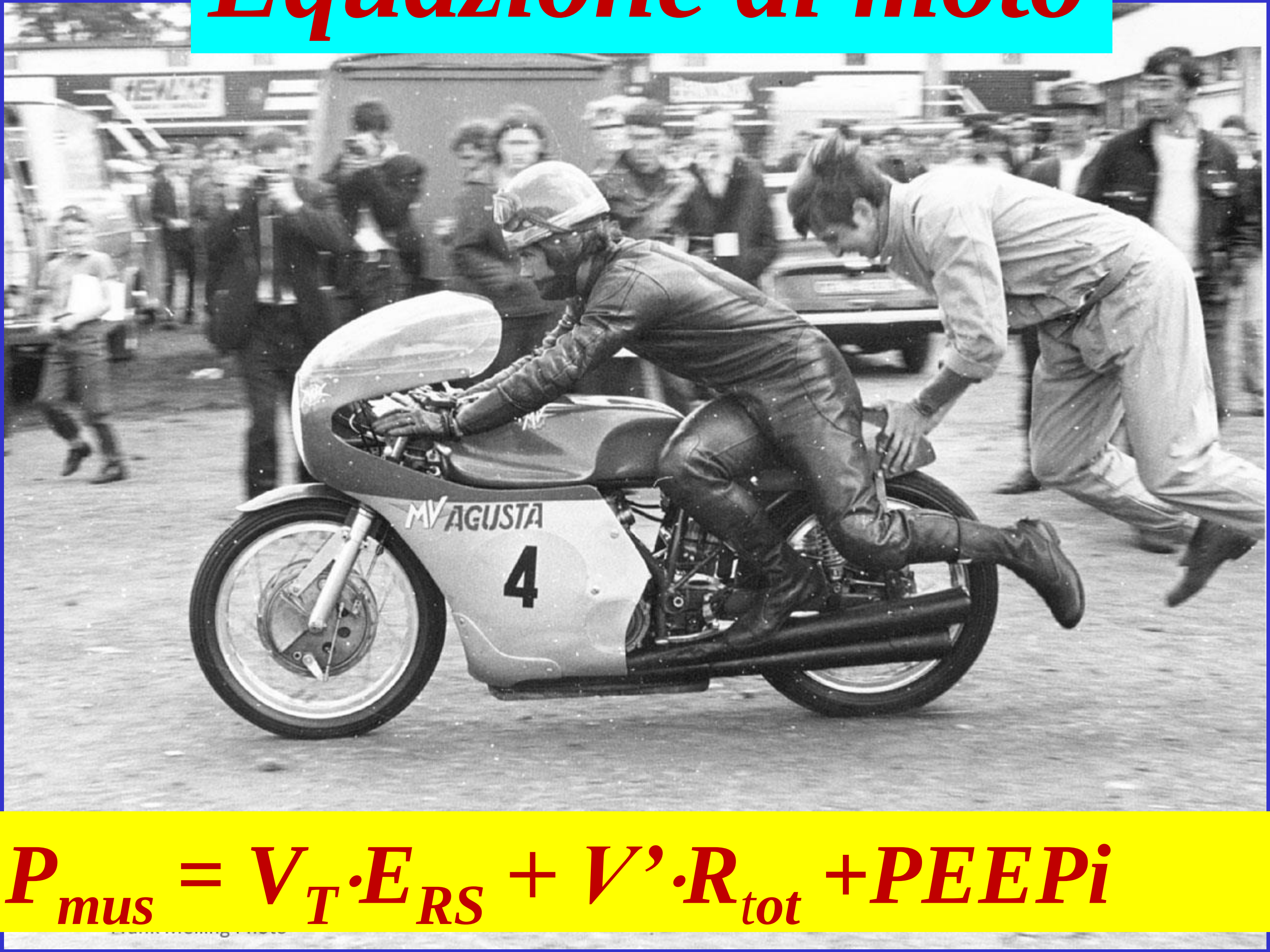
Curva P/V Statica : chi vince?



Polmone «nero»
→ vince ***Torace***

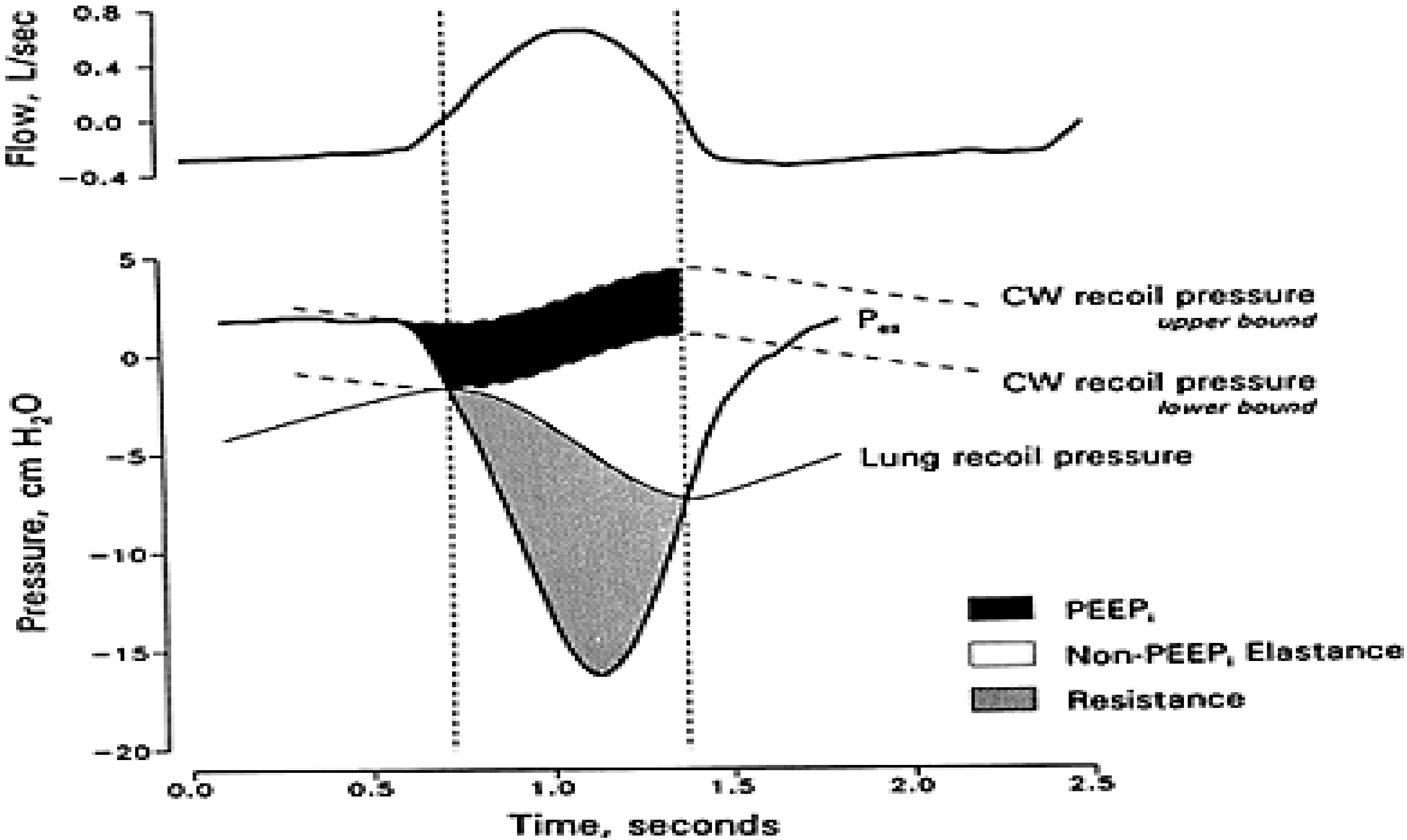
Polmone «bianco»
→ vince ***Polmone***

Equazione di moto

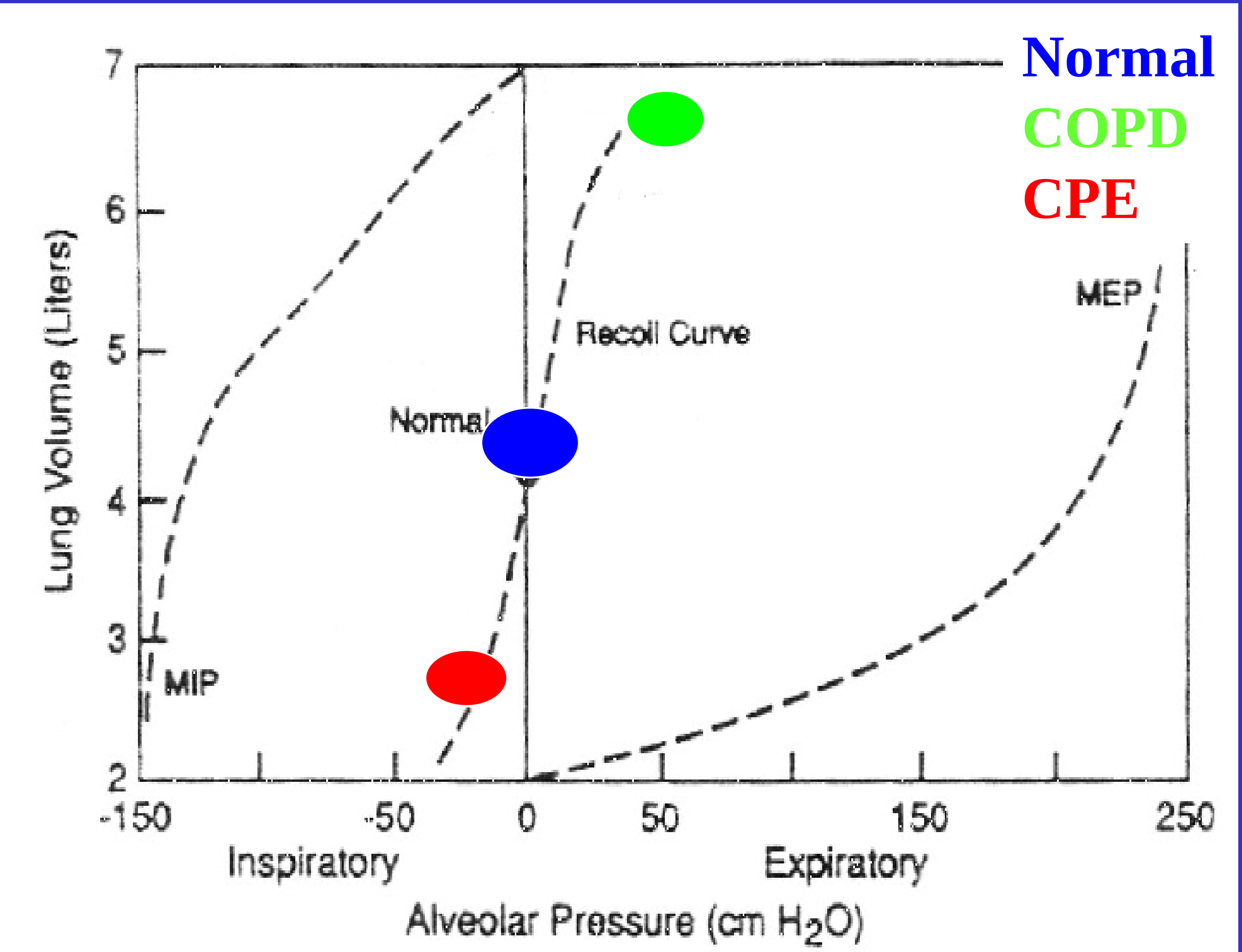


$$P_{mus} = V_T \cdot E_{RS} + V' \cdot R_{tot} + PEEPi$$

“CARICO” della VENTILAZIONE



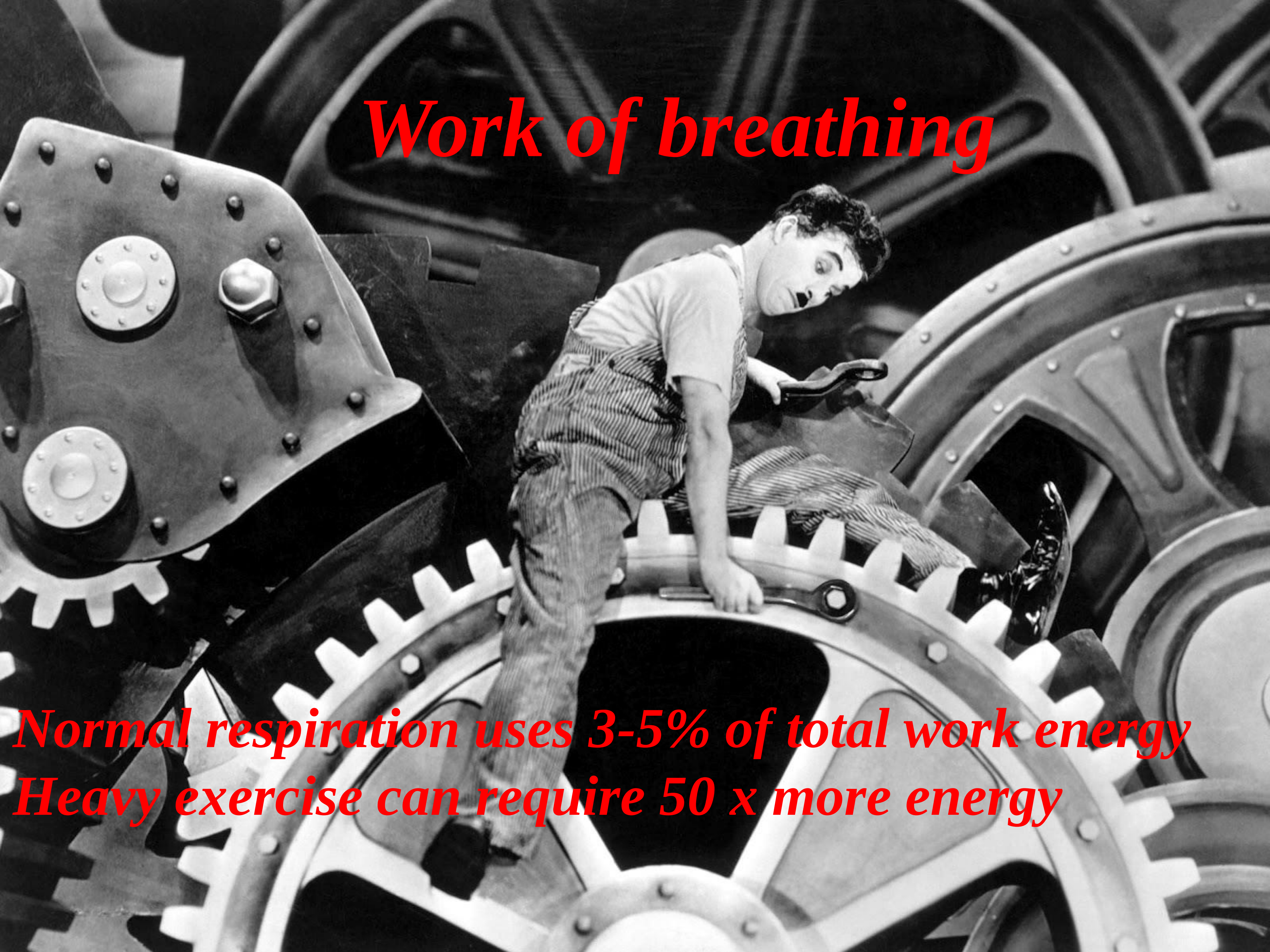
Am J Respir Crit Care Med 155:906



→*Ipossiemia*
+ *Ipercapnia*

→*Ipossiemia*

Work of breathing

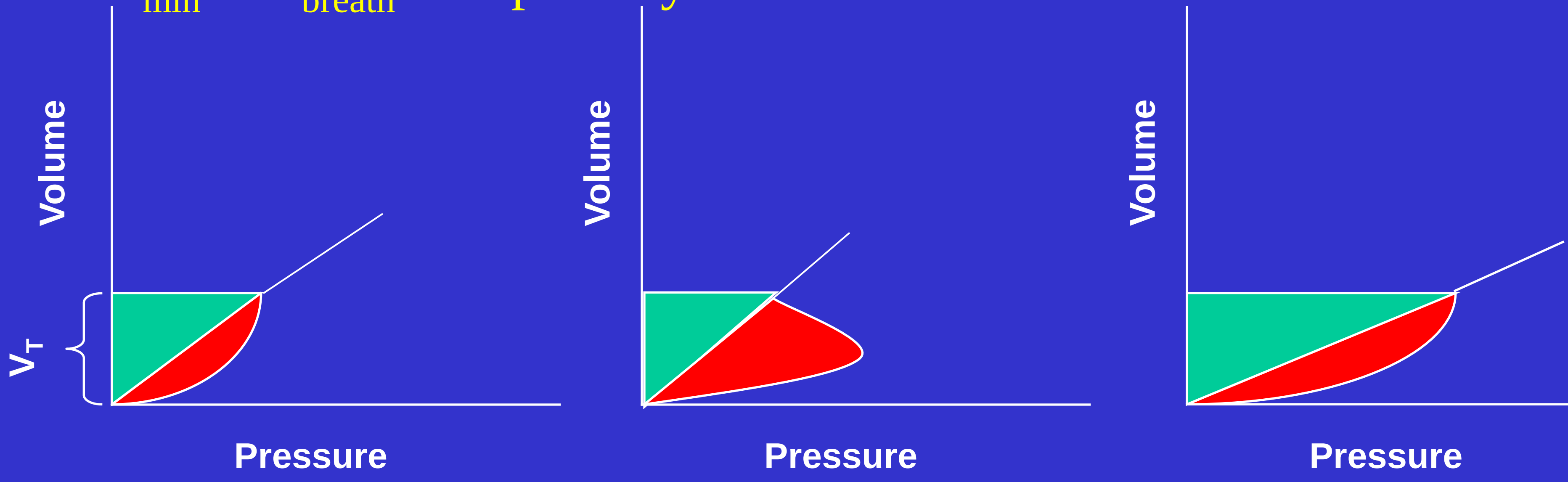


Normal respiration uses 3-5% of total work energy

Heavy exercise can require 50 x more energy

Work of Breathing

- Work per breath is depicted as a pressure-volume area
- Work per breath (W_{breath}) = P x tidal volume (V_T)
- W_{min} = w_{breath} x respiratory rate

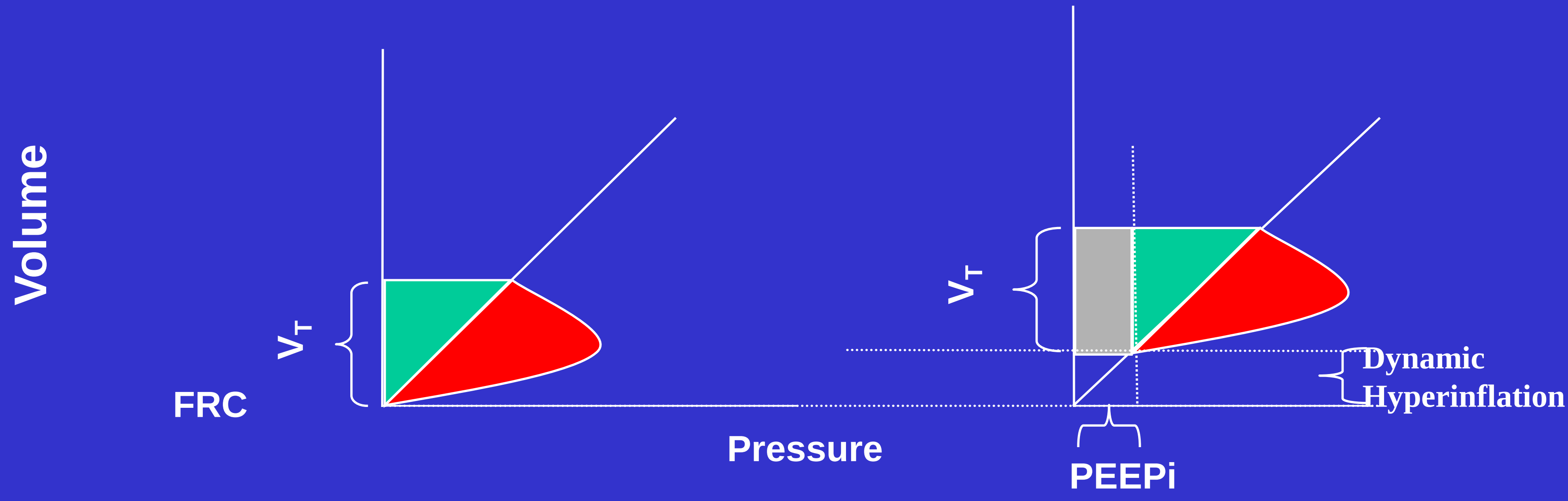


The total work of breathing can be partitioned between an elastic and resistive work. By analogy, the pressure needed to inflate a balloon through a straw varies; one needs to overcome the resistance of the straw and the elasticity of the balloon.

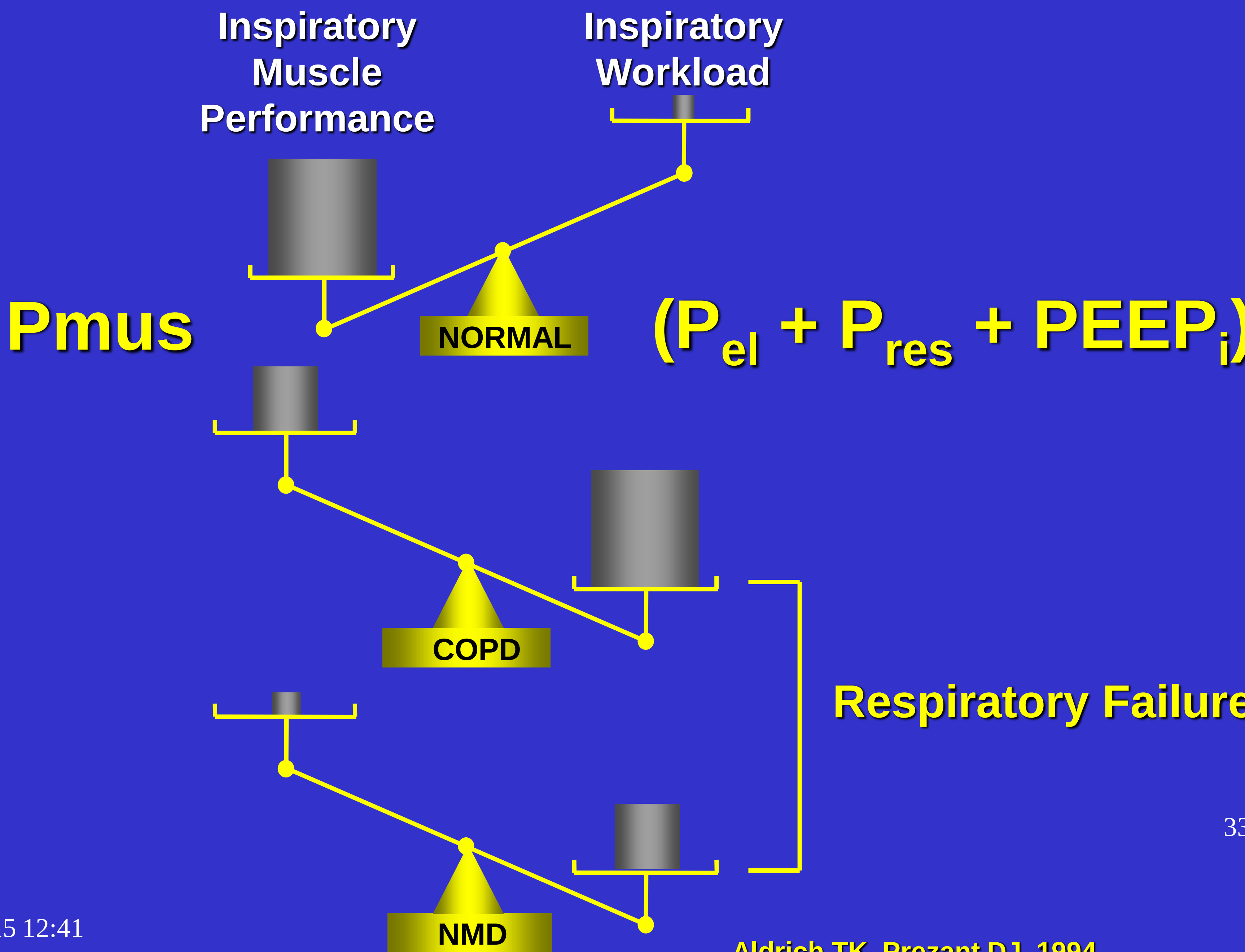
W_{EL} = elastic work *W_R = resistive work*

Intrinsic PEEP and Work of Breathing

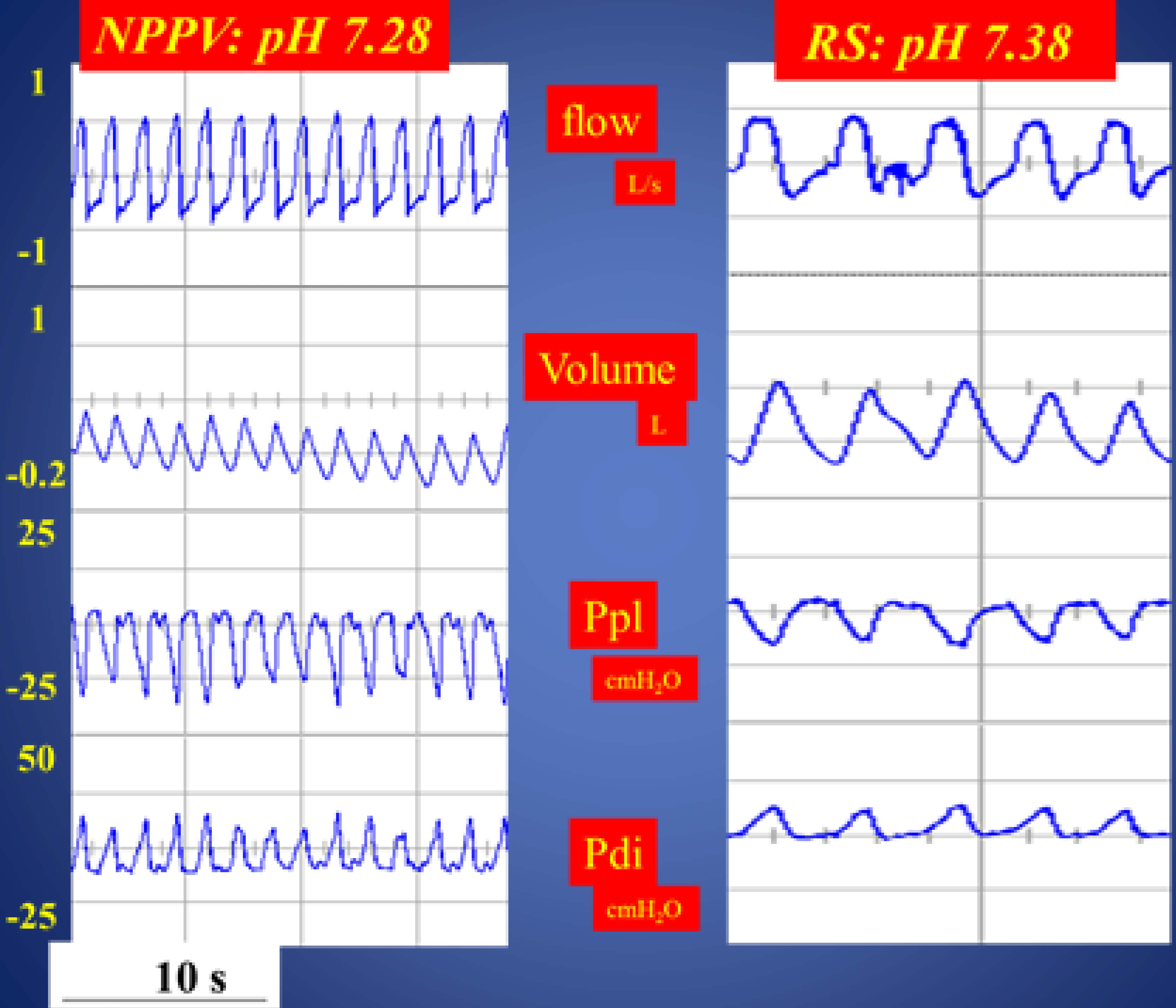
When present, intrinsic PEEP contributes to the work of breaking and can be offset by applying external PEEP.



PEEPi = intrinsic or auto PEEP; green triangle = tidal elastic work; red loop = flow resistive work; grey rectangle = work expended in offsetting intrinsic PEEP (an expiratory driver) during inflation

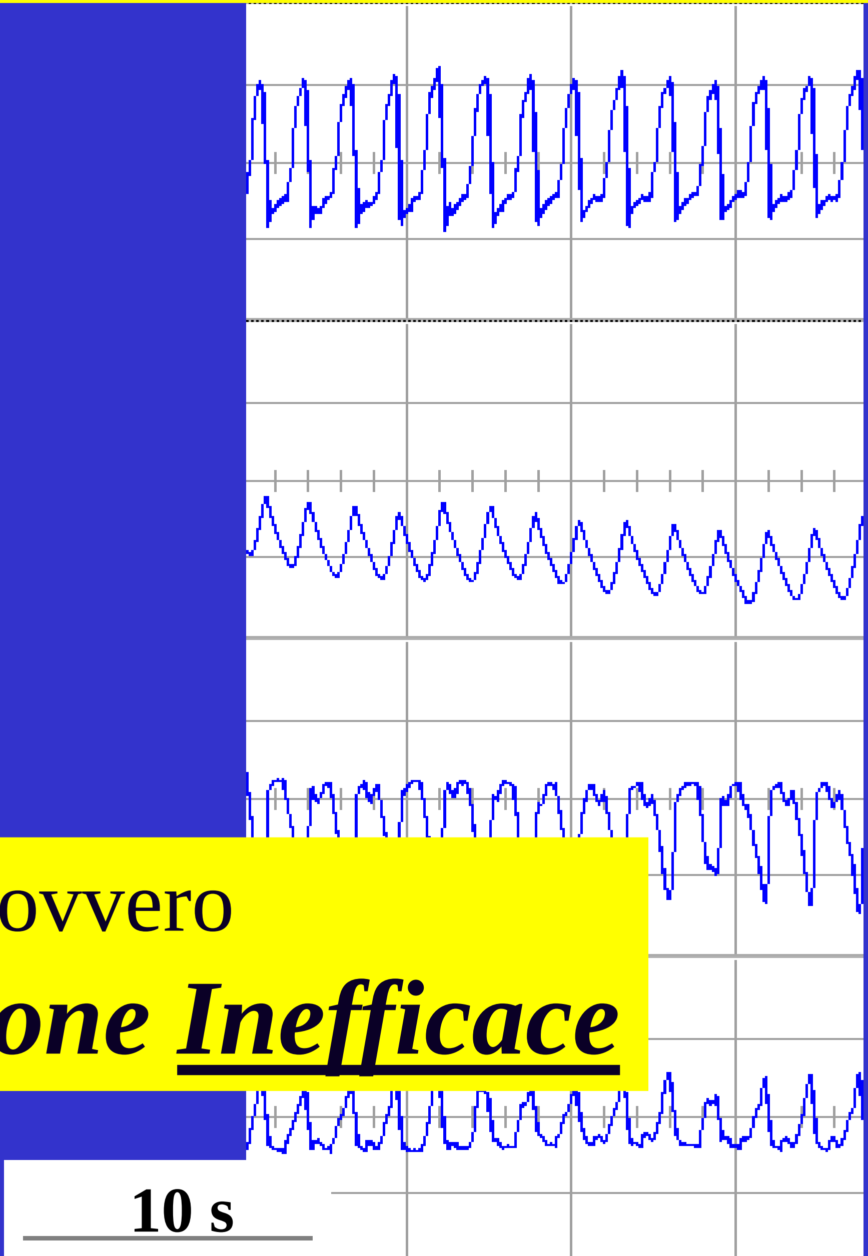


Aldrich TK, Prezant DJ. 1994



NPPV: pH 7.28
RS: pH 7.38
flow
L/s
Volume
L
Ppl
cmH2O
Pdi
cmH2O
1
-1
1
-0.2
25
-25
50
-25
10 s

→ *RAPID SHALLOW BREATHING*

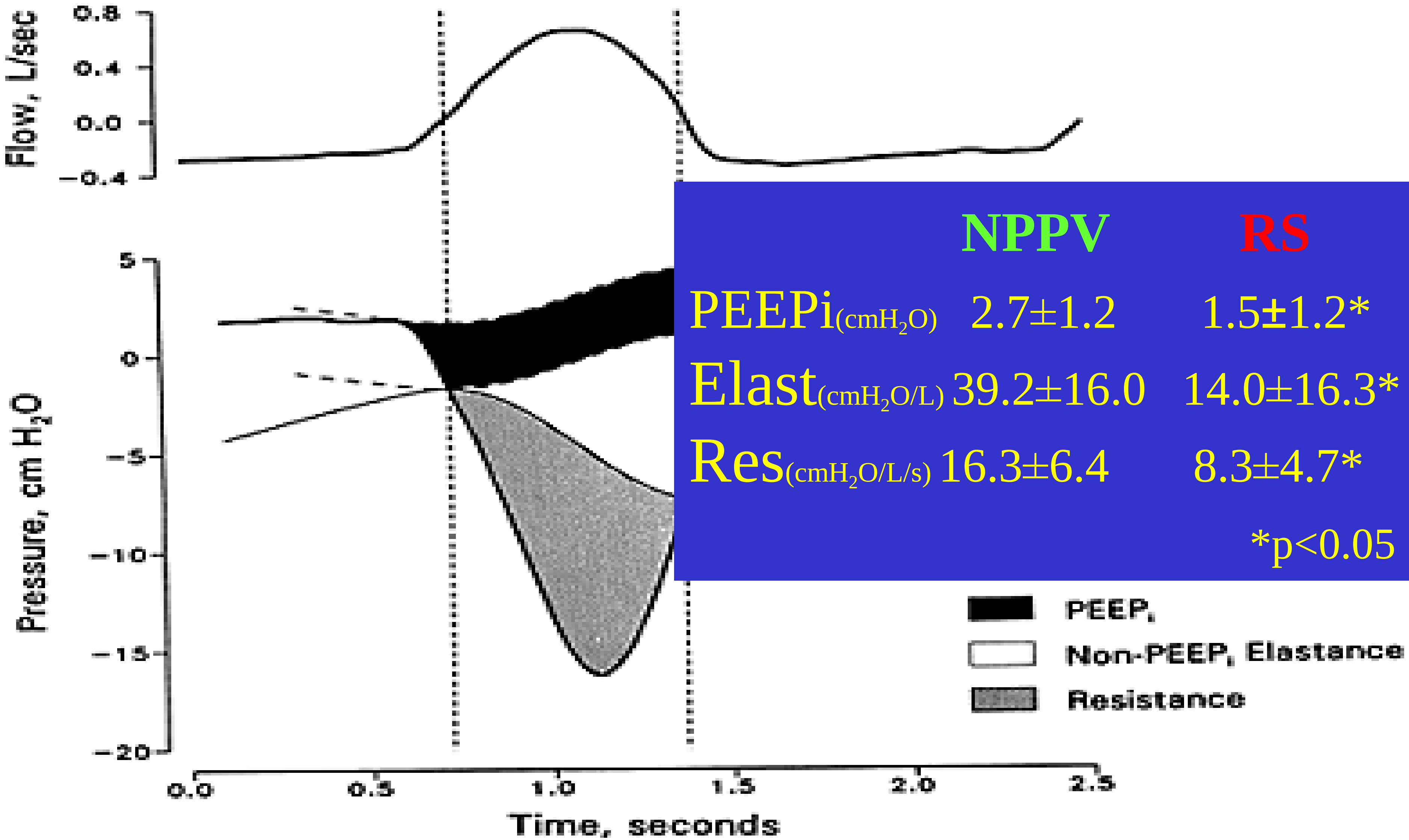


ovvero

Ventitazione Inefficace

→ pH acido!

“CARICO” della VENTILAZIONE

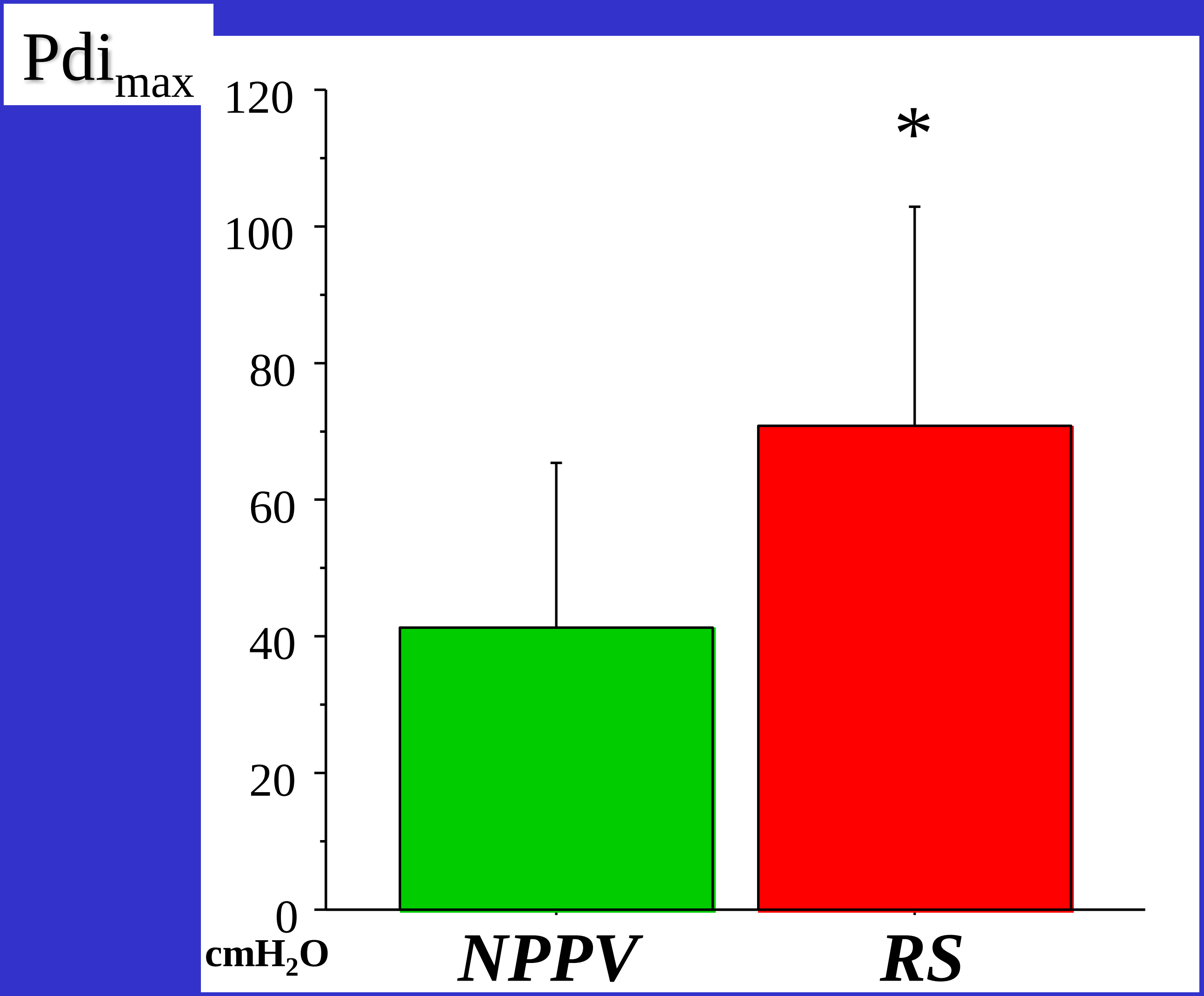


	NPPV	RS
PEEPi (cmH_2O)	2.7±1.2	1.5±1.2*
Elast (cmH_2O/L)	39.2±16.0	14.0±16.3*
Res (cmH_2O/L/s)	16.3±6.4	8.3±4.7*

*$p<0.05$

Am J Respir Crit Care Med 155:906

Forza dei Muscoli Respiratori



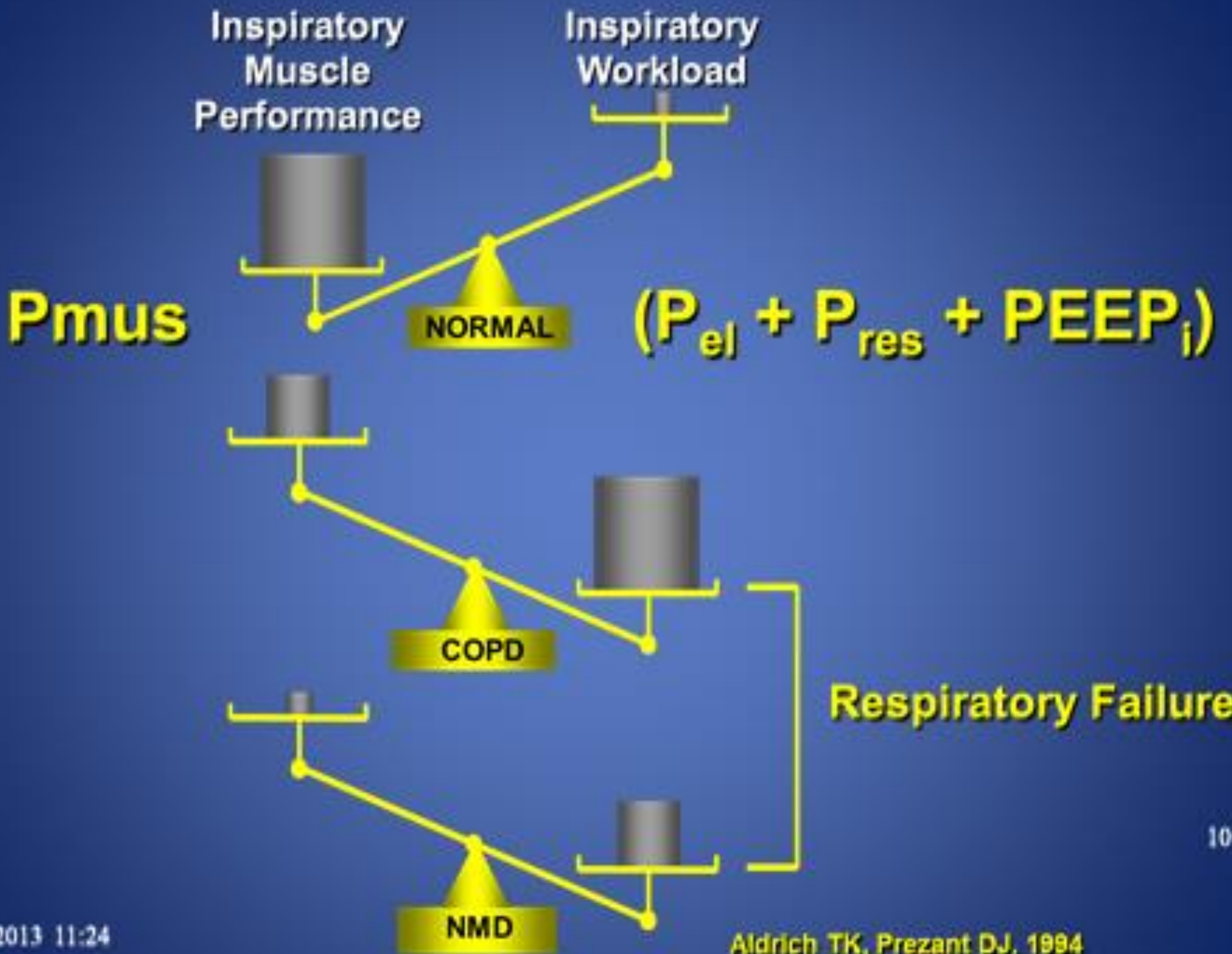
Muscoli Inspiratori - COPD

Forza Ridotta:

- BMI ridotto
- Alterazioni elettrolitiche
- Steroidi

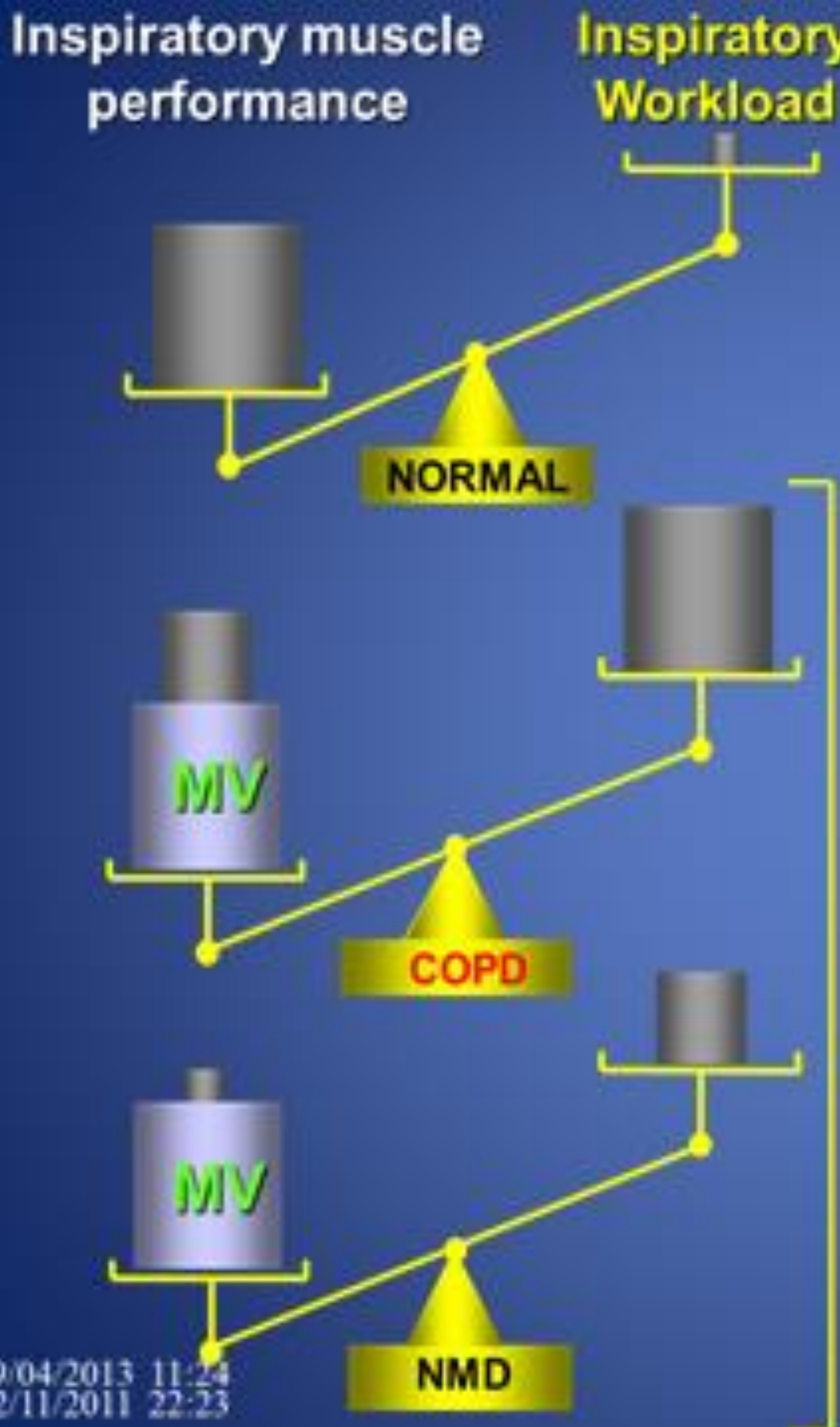
ma soprattutto:

IPERINFLAZIONE



Aldrich TK, Prezant DJ, 1994

09/04/2013 11:24



$$Pmus = P_{el} + P_{res} + PEEP_i$$

$$Pmus + Paw = P_{el} + P_{res} + PEEP_i$$

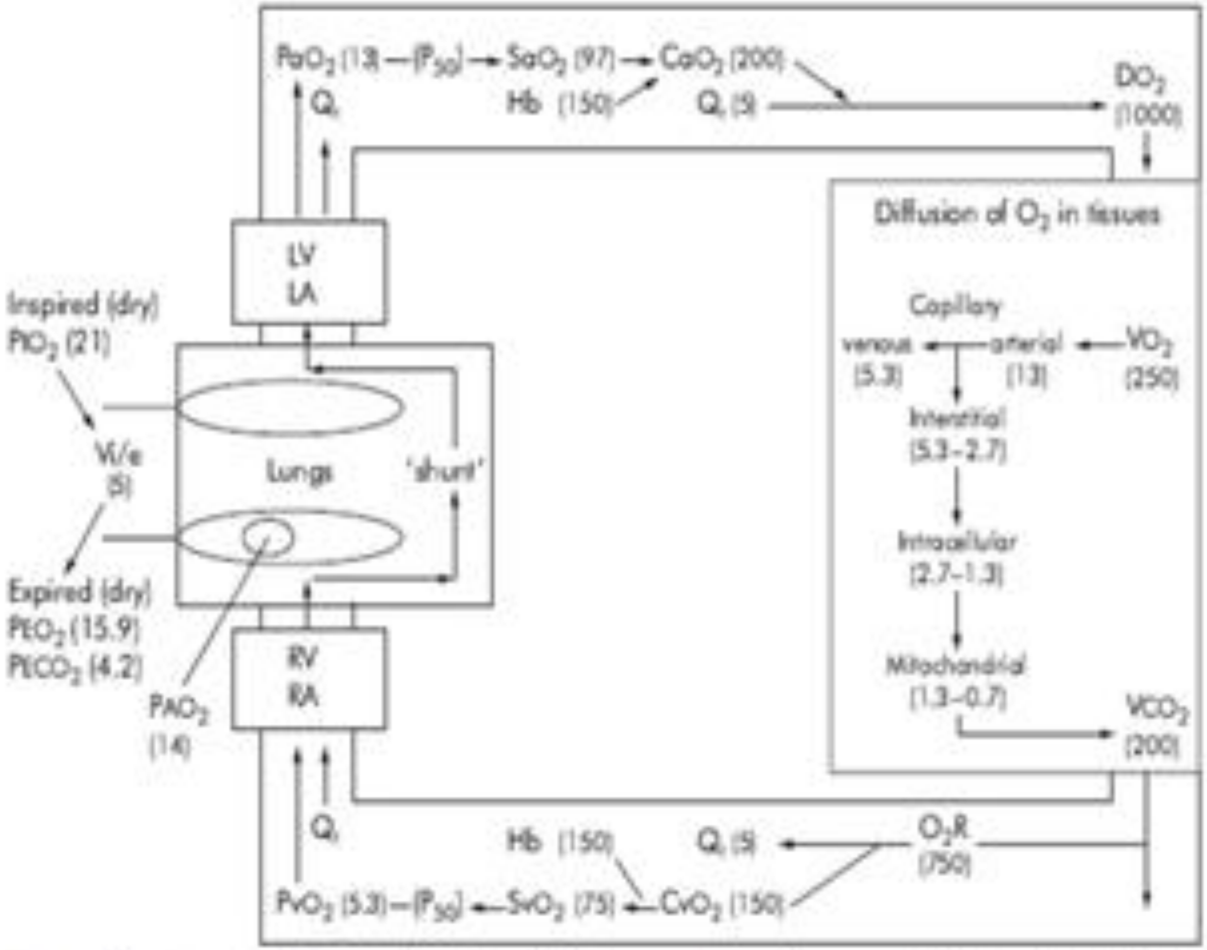


Figure 1 Oxygen transport from atmosphere to mitochondria. Values in parentheses for a normal 75 kg individual (BSA 1.7 m^2) breathing air (F_{IO_2} 0.21) at standard atmospheric pressure (P_B 101 kPa). Partial pressures of O_2 and CO_2 (P_{O_2}, P_{CO_2}) in kPa; saturation in %; contents (Ca_{O_2}, Cv_{O_2}) in ml/l; Hb in g/l; blood/gas flows (Qt, VI/e) in l/min. P_{50} – position of oxygen haemoglobin dissociation curve; it is P_{O_2} at which 50% of haemoglobin is saturated (normally 3.5 kPa). D_{O_2} – oxygen delivery; V_{O_2} – oxygen consumption, V_{CO_2} – carbon dioxide production; P_{IO_2}, P_{EO_2} – inspired and mixed expired P_{O_2}; P_{ECO_2} – mixed expired P_{CO_2}; P_{AO_2} – alveolar P_{O_2}.

Oxygen tranfert to tissues

DO_2 = 1000 mL/min

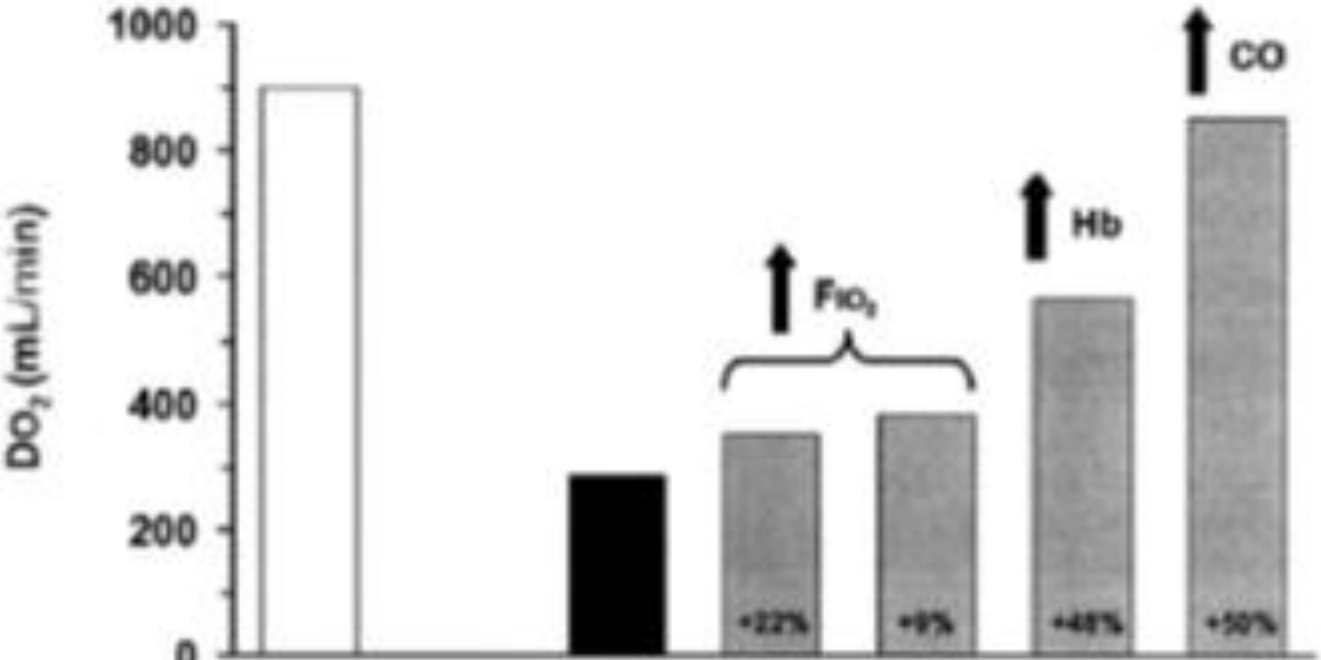
CO: 5 L/min
Hb: 15 gr/100 mL
SatO2: 100%

O2: 21 mL carried by the Hb, 0.3 mL with plasma

Table 1 Relative effects of changes in Pa_{O_2}, haemoglobin (Hb), and cardiac output (Qt) on oxygen delivery (D_{O_2})

	F_{IO_2}	Pa_{O_2} (kPa)	Sa_{O_2} (%)	Hb (g/l)	Dissolved O_2 (ml/l)	Ca_{O_2} (ml/l)	Qt (l/min)	D_{O_2} (ml/min)	D_{O_2} (% change)‡
Normal*	0.21	13.0	96	130	3.0	170	5.3	900	0
Patient†	0.21	6.0	75	70	1.4	72	4.0	288	−68
↑F_{IO_2}	0.35	9.0	92	70	2.1	88	4.0	352	+22
↑↑F_{IO_2}	0.60	16.5	98	70	3.8	96	4.0	384	+9
↑Hb	0.60	16.5	98	105	3.8	142	4.0	568	+48
↑Qt	0.60	16.5	98	105	3.8	142	6.0	852	+50

$D_{O_2} = Ca_{O_2} \times Qt$ ml/min, $Ca_{O_2} = (Hb \times Sa_{O_2} \times 1.34) + (Pa_{O_2} \times 0.23)$ ml/l where F_{IO_2} = fractional inspired oxygen concentration; Pa_{O_2}, Sa_{O_2}, Ca_{O_2} = partial pressure, saturation and content of oxygen in arterial blood; Qt = cardiac output. 1.34 ml is the volume of oxygen carried by 1 g of 100% saturated Hb. Pa_{O_2} (kPa) × 0.23 is the amount of oxygen in physical solution in 1 l of blood, which is less than <2% of total Ca_{O_2} for normal Pa_{O_2} (ie <14 kPa). *Normal 75 kg subject at rest. †Patient with hypoxaemia, anaemia, reduced cardiac output, and evidence of global tissue hypoxia. ‡Change in D_{O_2} expressed as a percentage of the preceding value.



FIO_2	0.21	0.21	0.35	0.60	0.60	0.60
PaO_2 (kPa)	13.0	6.0	9.0	16.5	16.5	16.5
SaO_2 (%)	96	75	92	98	98	98
Hb (g/dL)	13.0	7.0	7.0	7.0	10.5	10.5
CO (L/min)	5.3	4.0	4.0	4.0	4.0	6.0

FIGURE 2. Relative effects of changes in PaO_2, hemoglobin, and CO on DO_2 in a critically ill patient. DO_2 in a normal 75-kg subject at rest is shown in the white bar, and DO_2 in a patient with hypoxemia, anemia, and reduced CO is shown in the black bar. The gray bars show the effect of sequential interventions on DO_2. The numbers in each bar represent the calculated increase in DO_2 compared with the preceding value. FIO_2 = fraction of inspired oxygen; Hb = hemoglobin; CO = cardiac output. Data are from Leach and Treacher.[3]

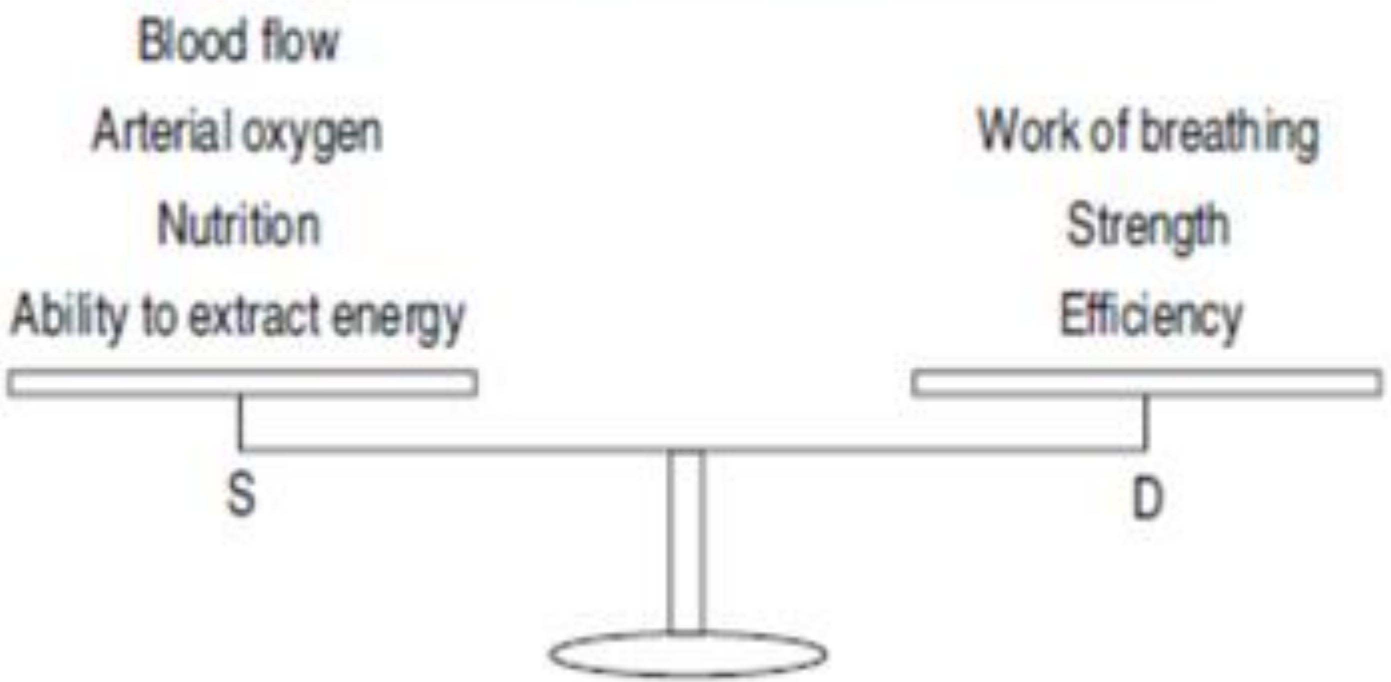


Fig. 3. – Respiratory muscle endurance is determined by the balance between energy supplies (S) and demands (D). Normally, the supplies meet the demands and a large reserve exists. Whenever this balance weighs in favour of demands, the respiratory muscles ultimately become fatigued, leading to inability to sustain spontaneous breathing.

Interactions

- Myocardial reserve
- Ventricular pump function
- Circulating blood volume
- Blood flow distribution
- Autonomic tone
- Endocrinologic responses
- Lung Volume
- ITP
- Surrounding Pressures (remainder of circulation)

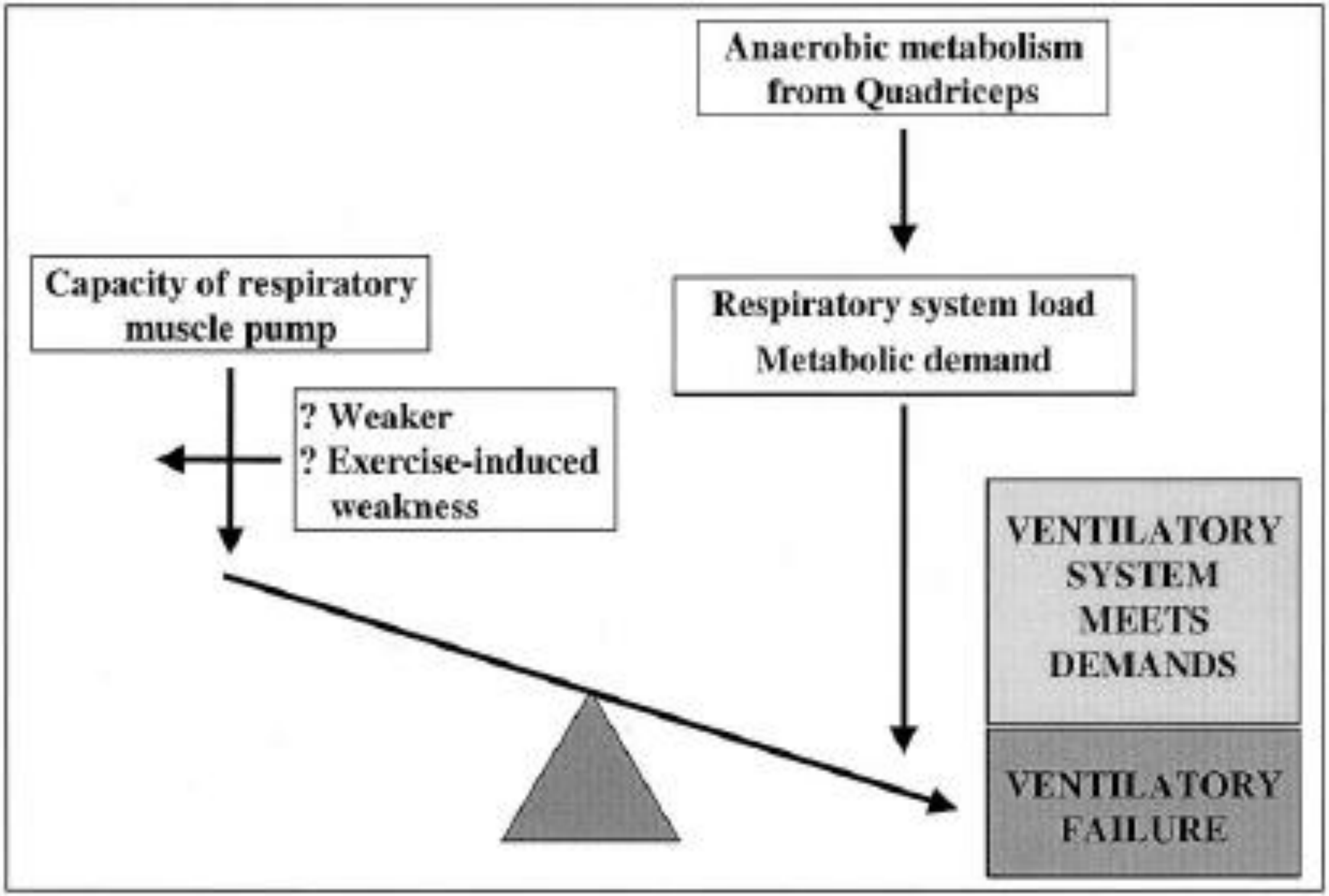
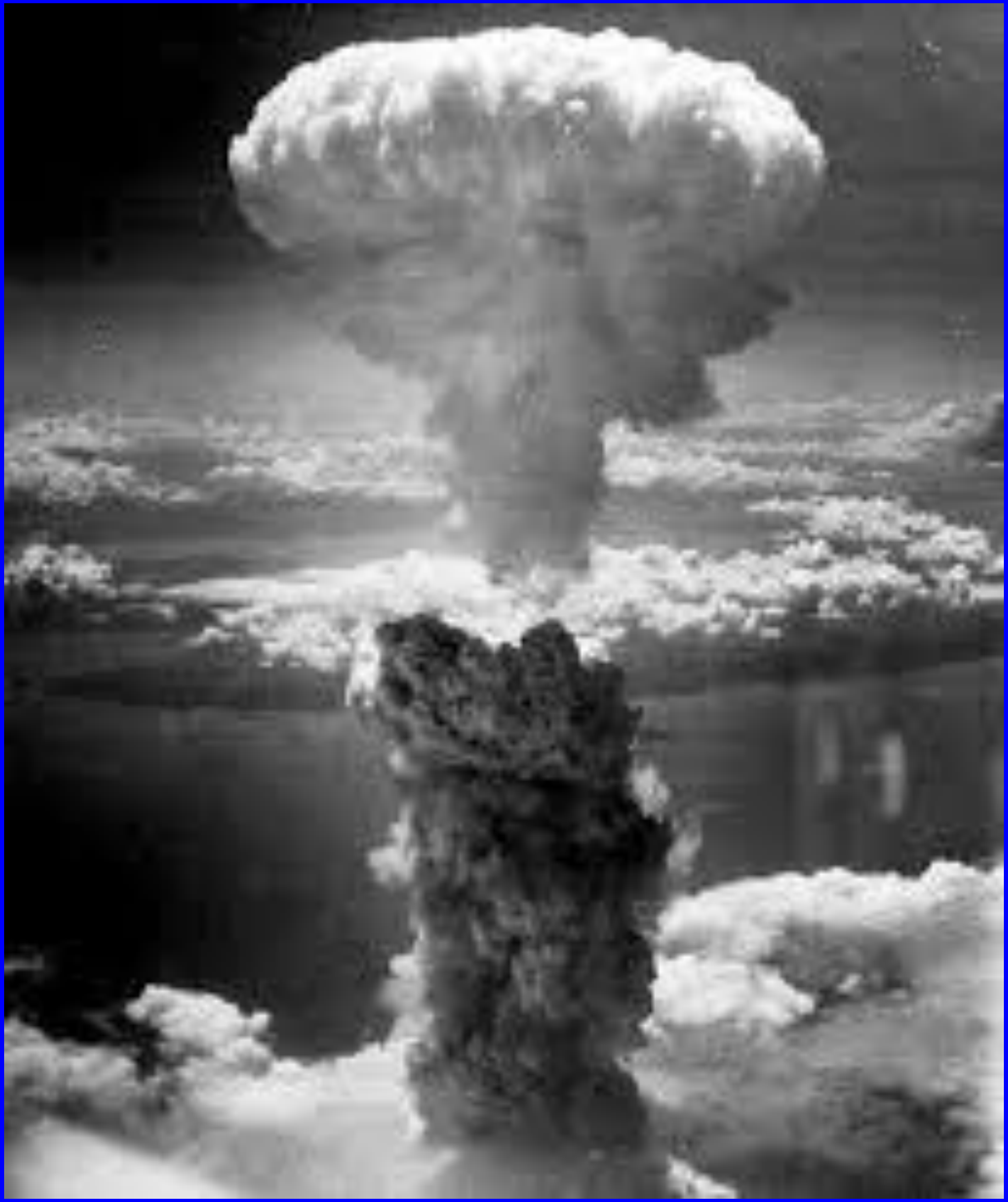


FIGURE 1. Schematic illustration of the effect of load and capacity on the respiratory muscle pump. If the quadriceps muscles metabolize anaerobically, the increased level of CO_2 needs to be cleared by the ventilatory system, imposing an additional load.

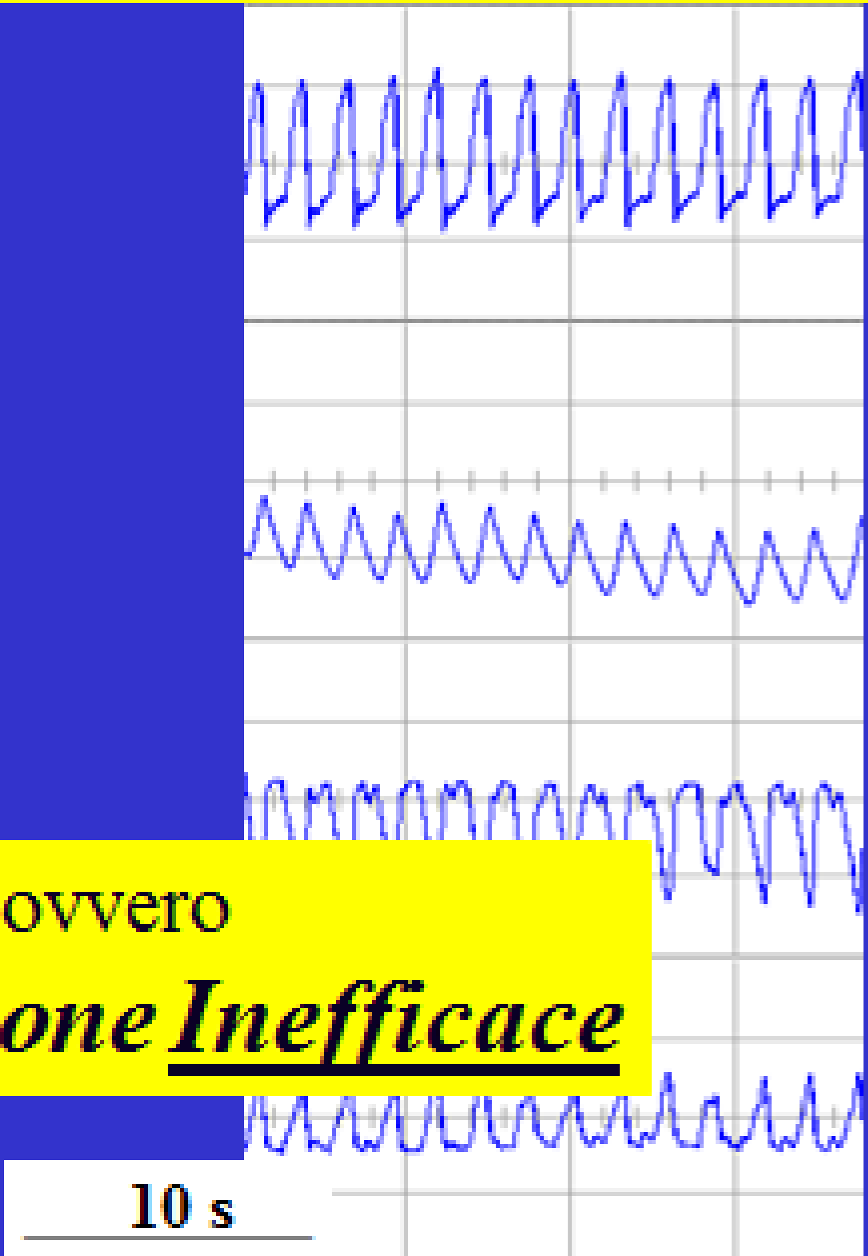
ὁδὸς ἄνω κάτω μία καὶ ὡυτή


DIEGO ABATANTUONO
ATTILA
FLAGELLO DI DIO
Cover DivX By Rono The Unstoppable (CDS)
DIVX
VIDEO




DUCTILE IRON
264

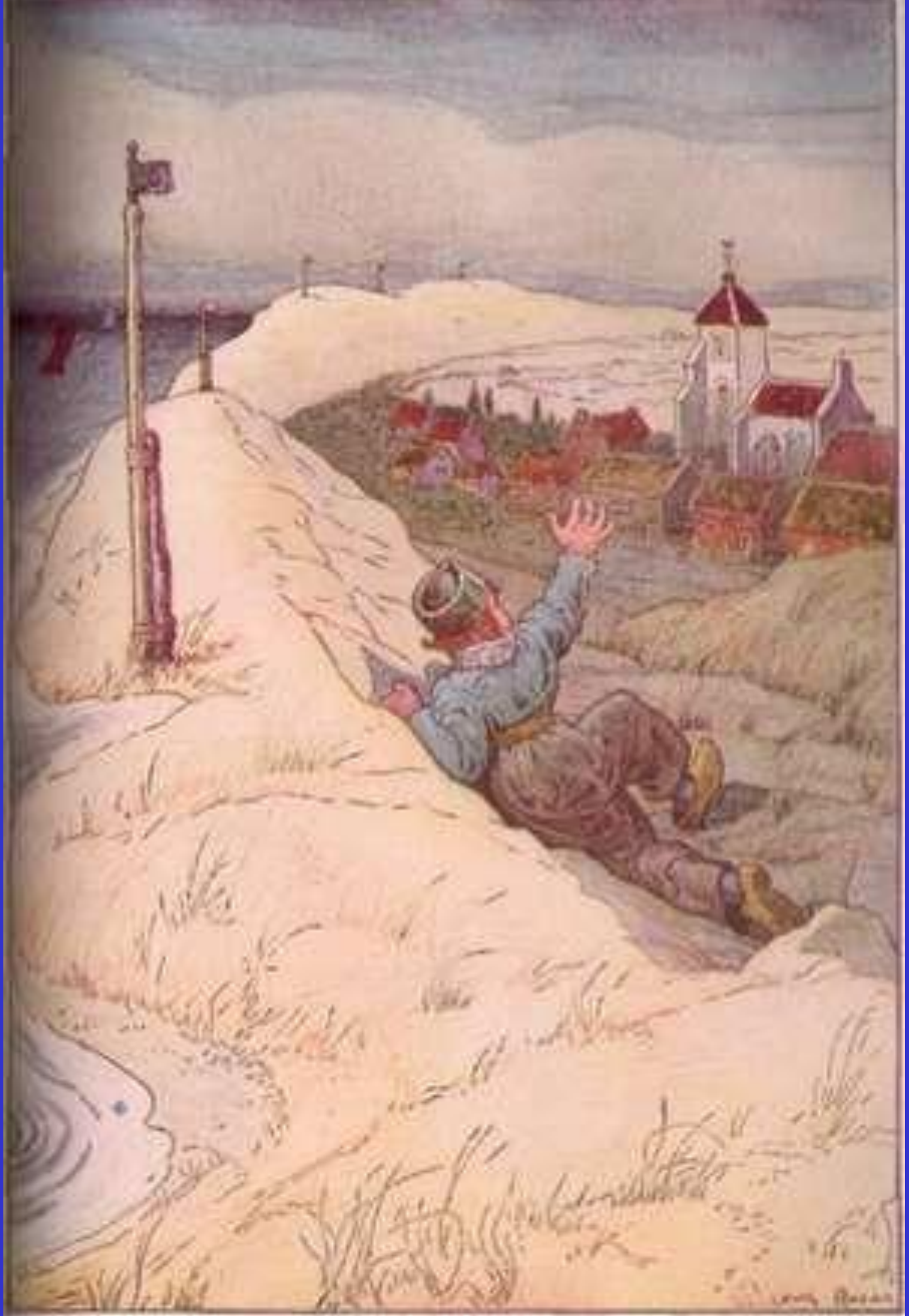
→ RAPID SHALLOW BREATHING



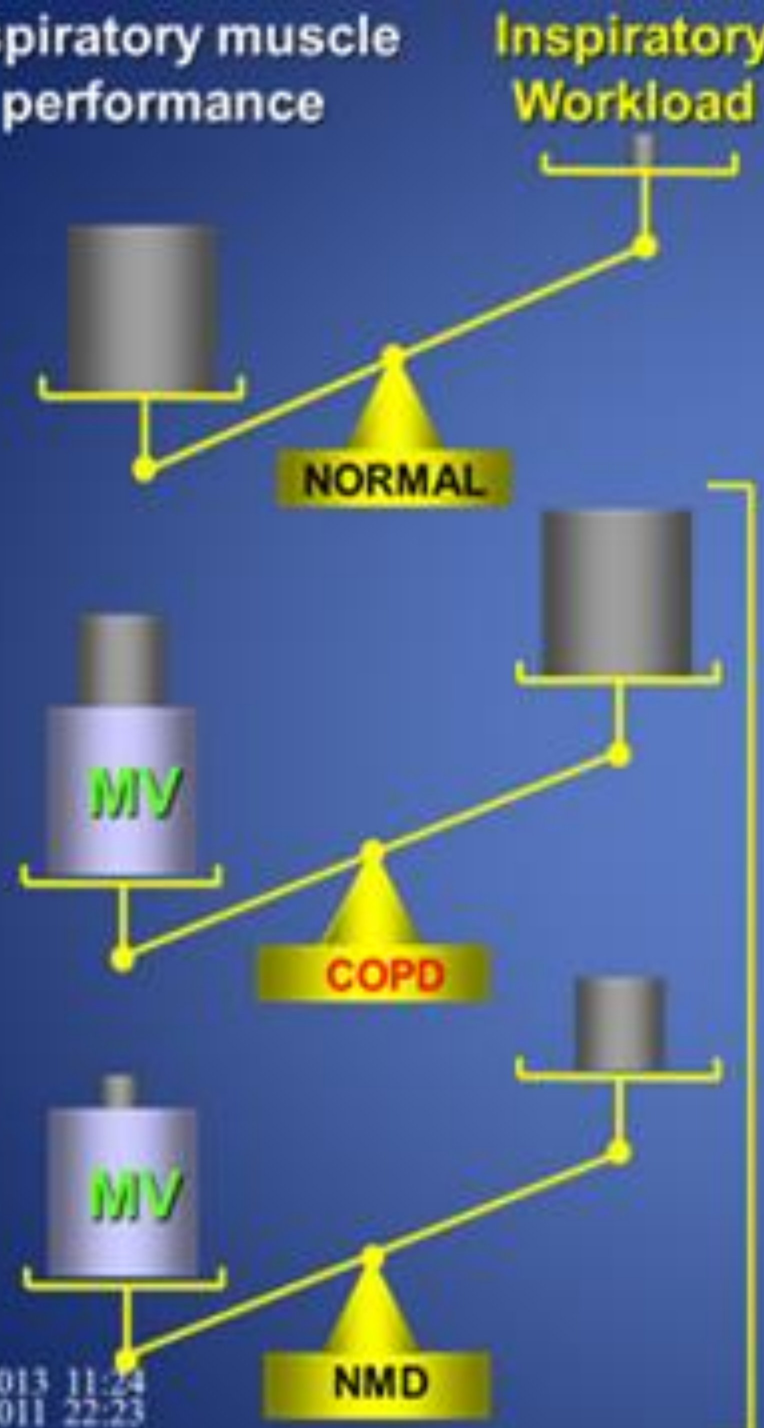
ovvero

Ventitazione <u>Inefficace</u>

→ pH acido!



A LEAK IN THE DYKE!



$$Pmus = P_{el} + P_{res} + PEEP_i$$

$$Pmus + Paw = P_{el} + P_{res} + PEEP_i$$

Fig. 2
Depiction of Acadian dyke construction at Grand-Pré by artist Lewis Parker. Courtesy of Parks Canada, Atlantic Service Centre, Halifax.

Lung Hyperinflation
→ impaires central hemodynamics

1) Pulmonary tamponade: ↑ right atrial, pulmonary capillary wedge, and left atrial pressures

2) Pulmonary blood volume ↓: due to PEEPi → intrathoracic hypovolemia

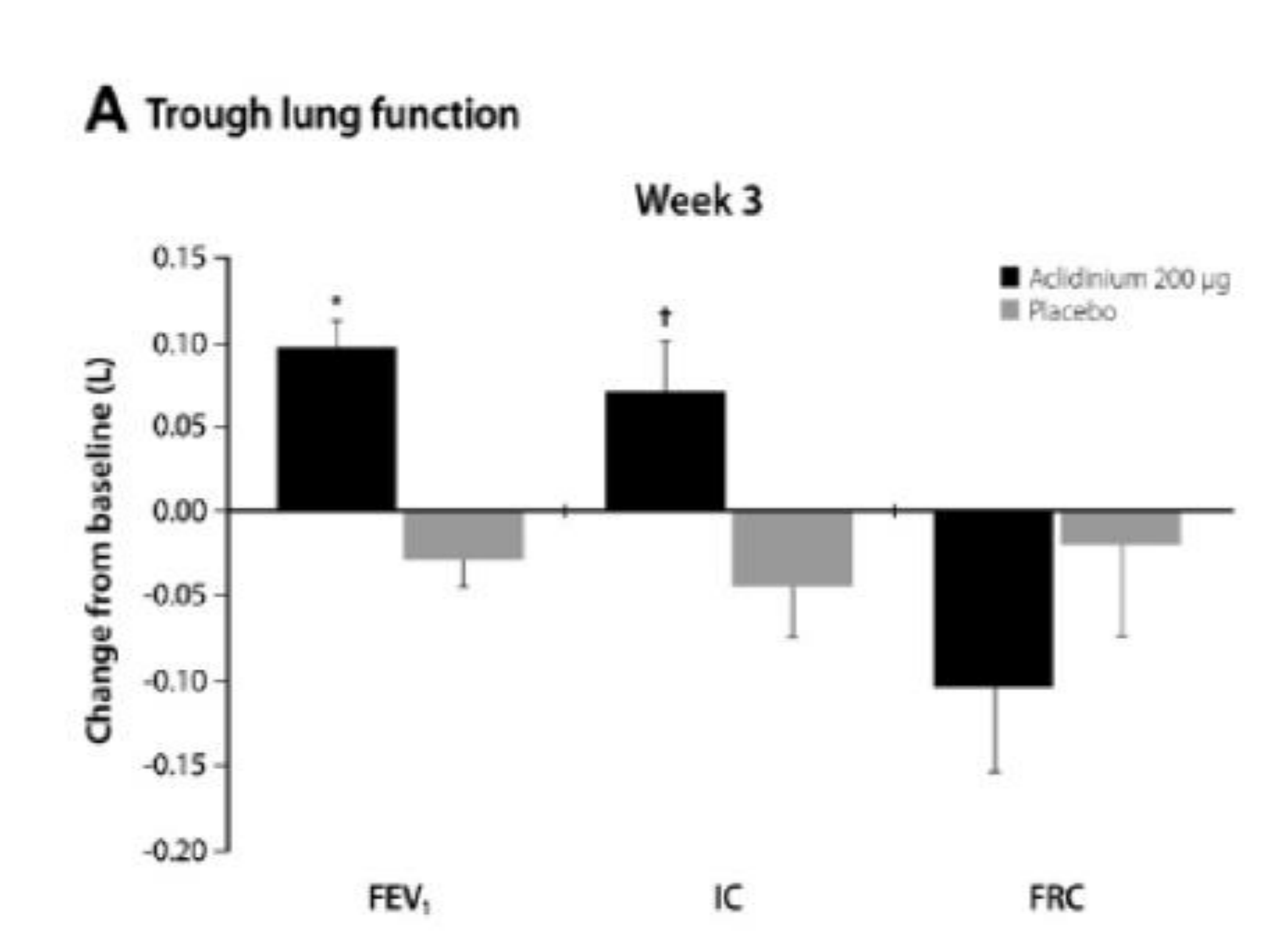
3) Pulmonary artery pressures ↑ : due to compression of intra-alveolar vessels by PEEPi

4) Left ventricular afterload ↑: negative inspiratory pleural pressure swings to overcome PEEPi

Therapy and Survival

Patients with very severe lung hyperinflation (ie, IC/TLC ratio <25%) have a very poor prognosis. It follows that successful lung deflation may positively influence survival

Air Trapping



Inhaled bronchodilators reduce dynamic hyperinflation during exercise in patients with COPD

In patients with COPD, inhaled bronchodilator reduces exercise DH and improves inspiratory pressure reserve and neuroventilatory coupling. Changes in DH and neuroventilatory coupling were the main determinants of reduced breathlessness.

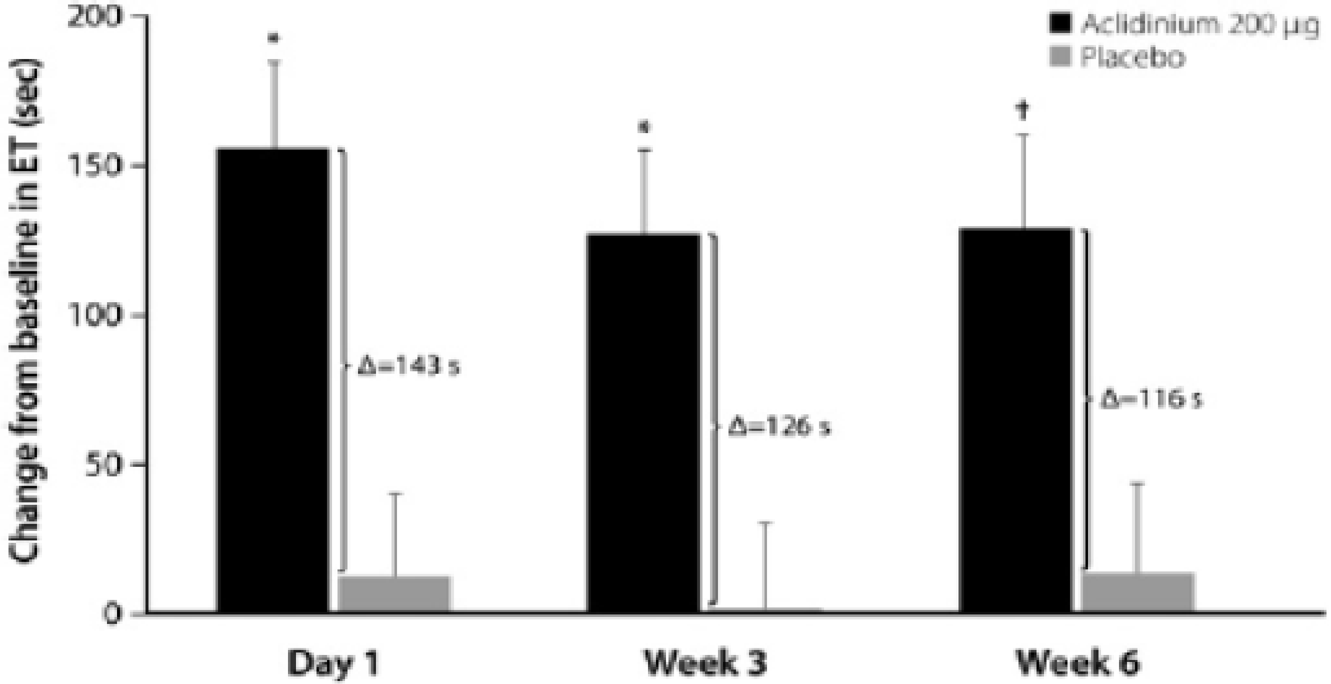
Am J Respir Crit Care Med, Vol. 153, No. 3 (1996), pp. 967-75

Bronchodilation

Successful lung deflation with maximal bronchodilator therapy should mitigate some of these negative effects on cardiac performance.

Tolleranza allo sforzo

(Maltais F et al. Respir Med 2011; 105: 580)



*P≤0.001, †P<0.005 vs placebo; change in ET measured at 180±10 minutes after administration of study medication

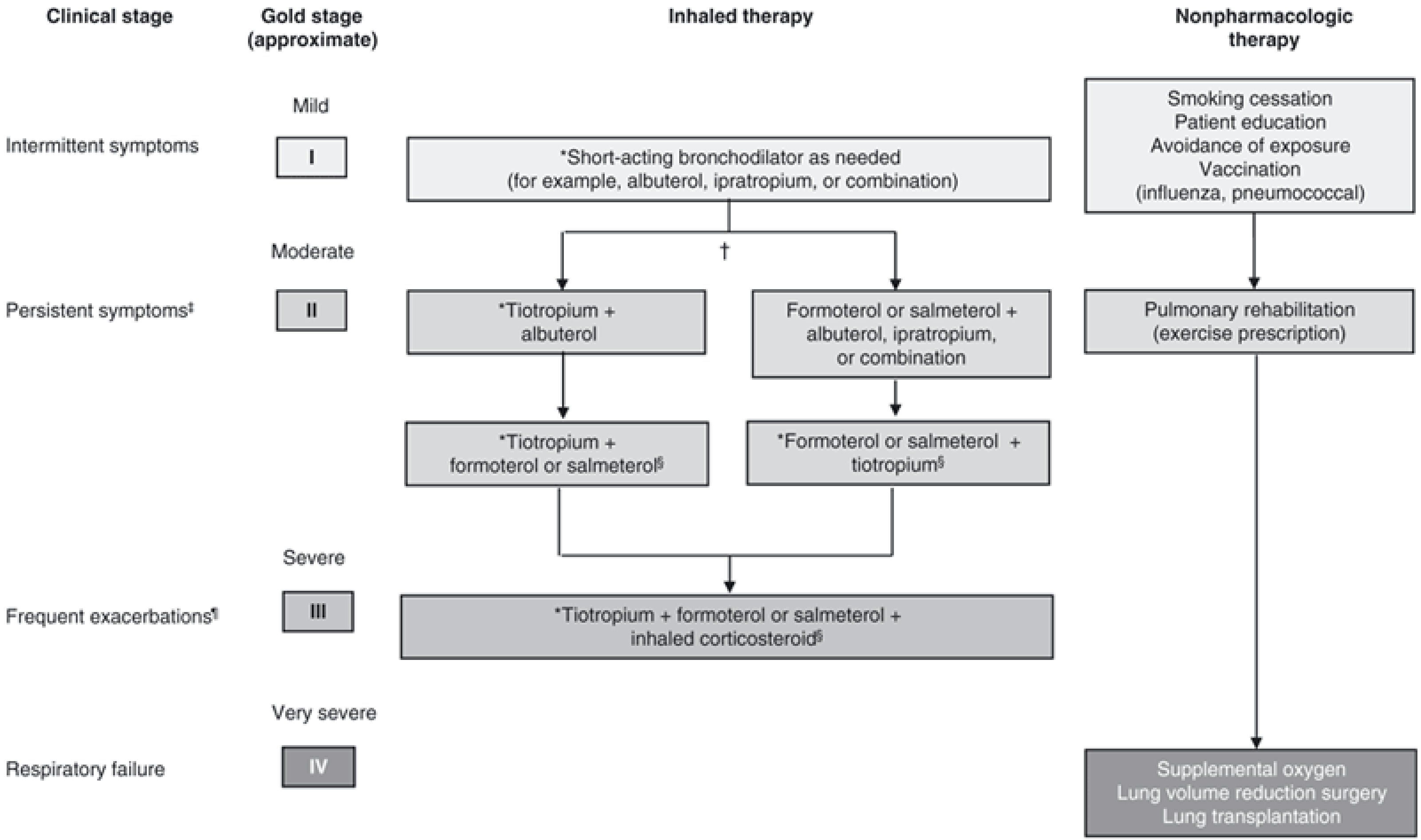
Bronchodilation

1) The suggestion that airflow obstruction in COPD is largely irreversible is no longer tenable
2) Clinically significant bronchodilation and lung deflation can be achieved following treatment with modern pharmacotherapy, even in those with the most severe COPD

Bronchodilation

3) Such therapy is consistently linked to sustained improvements in respiratory mechanics, exertional dyspnea, exercise tolerance, in both moderate and severe COPD.
4) Studies support the contention that additive physiological and clinical benefits accrue when using a combination of LABDs

Stage	0: At Risk	I: Mild	II: Moderate	III: Severe	IV: Very Severe
Characteristics	• Chronic symptoms • Exposure to risk factors • Normal spirometry	• $FEV_1/FVC < 70\%$ • $FEV_1 \geq 80\%$ • With or without symptoms	• $FEV_1/FVC < 70\%$ • $50\% \leq FEV_1 < 80\%$ • With or without symptoms	• $FEV_1/FVC < 70\%$ • $30\% \leq FEV_1 < 50\%$ • With or without symptoms	• $FEV_1/FVC < 70\%$ • $FEV_1 < 30\%$ or $FEV_1 < 50\%$ predicted plus chronic respiratory failure
	Avoidance of risk factors(s); influenza vaccination				
		Add short-acting bronchodilator when needed			
			Add regular treatment with one or more long-acting brochodilators *Add* rehabilitation		
				Add inhaled glucocorticosteroids if repeated exacerbations	
					Add long-term oxygen if chronic respiratory failure *Consider* surgical treatments



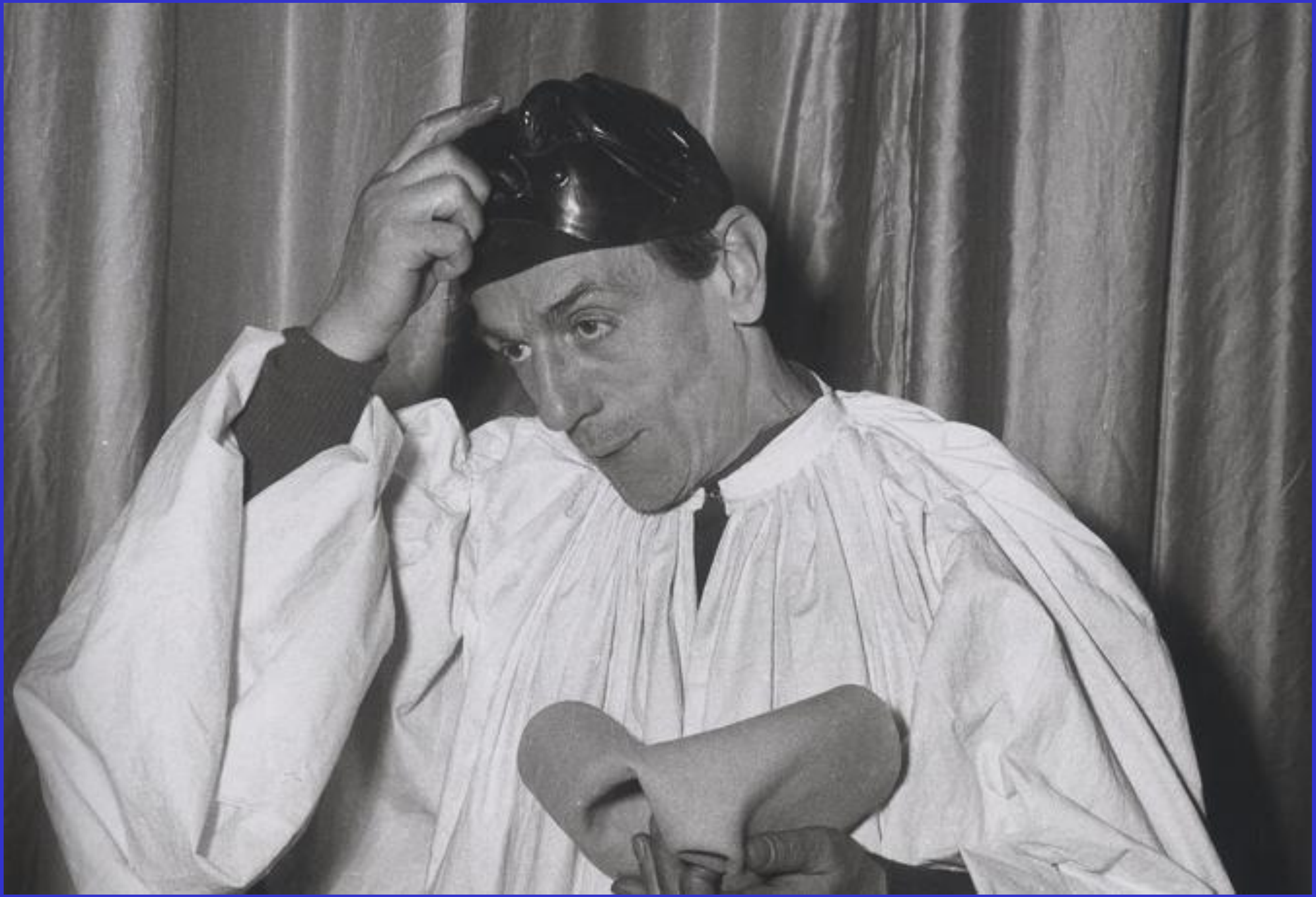
* Four-step algorithm for the implementation of inhaled treatment
† Pathway on left is recommended; pathway on right side is a valid alternative
‡ Defined as need for rescue medication on more than two occasions per week
§A short-acting bronchodilator can be used for rescue. Low-dose methylxanthines can be prescribed if the response to inhaled bronchodilator therapy is insufficient
¶ Defined as two or more exacerbations per year

Broncodilatazione

- Diminuzione delle resistenze
- Dimuzione dell'iperinflazione
  - A) PEEPi ↓
  - B) Carico elastico ↓

L’esperienza

Al mio segnale scatenate l'inferno



Roflumilast was approved in 2011 for COPD exacerbation reduction in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. This oral phosphodiesterase-4 (PDE4) inhibitor is thought to exert its pharmacologic action by increasing cyclic adenosine monophosphate in lung tissues and cells leading to an overall anti-inflammatory effect.[1] Currently, roflumilast is noted in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines as an appropriate add-on to a long-acting bronchodilator in patients with forced expiratory volume in 1 second (FEV1) < 50% predicted, chronic bronchitis, and frequent exacerbations.[2]

Roflumilast only provides a net benefit to patients at a high risk of severe exacerbations. Guideline developers should consider different recommendations for patients with COPD at different baseline risks for exacerbations.

Of additional interest regarding roflumilast therapy, evaluation of specific patient subset responders to this medication verifies the concept that there are different phenotypes of COPD. In the evolving world of personalized medicine, identifying those patient subgroups who respond to PDE4 inhibitors may allow for more targeted therapies in patients with certain phenotypes. Patients with a frequent exacerbator phenotype, defined as > 2 exacerbations per year, benefited from roflumilast therapy independent of long-acting bronchodilator or ICS use. These patients shifted from being frequent exacerbators to more stable infrequent exacerbators, which can be extrapolated to conclude that the anti-inflammatory effects of roflumilast can stabilize the disease in frequent exacerbator phenotypes.[7] The different mechanism of action of this agent compared with current COPD treatment options has the potential to provide additive benefits in the management of COPD.

Adverse effects associated with roflumilast include diarrhea, weight loss, nausea, anxiety/depression, and headache.[1] From clinical trial evaluations of these effects, associated diarrhea, nausea, and headache seem to be transient, but weight loss is maintained throughout roflumilast treatment

Statins in COPD: Useful or Not?

The study was terminated prematurely because interim analysis of the results showed that the frequency of acute exacerbations was almost identical in the 2 groups, as was the time to first exacerbation. Mortality and adverse events were also almost identical in the 2 groups. Blood lipid levels decreased by an average of 33 mg/dL in the statin group. This indicated the use of a statin and that it had the expected effect on blood lipid levels. The total study results were disappointing.

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Corticosteroids

The role of systemic corticosteroids in the treatment of exacerbations also remains contentious. There is no strong evidence to guide appropriate patient selection, route of administration or duration of treatment. Systemic corticosteroids reduce recovery time and treatment failures when used to treat acute exacerbations

The optimal dose and duration of therapy with corticosteroids has not been well established. GOLD guidelines recommended a dose of 30–40 mg prednisolone equivalent per day, preferably by the oral route, for 10–14 days

The role of inhaled corticosteroids (ICS) in the treatment of acute COPD exacerbation is even less defined.

Methylxanthines. Intravenous methylxanthines (theophylline or aminophylline) are considered second-line therapy, only to be used in selected cases when there is insufficient response to short-acting bronchodilators

Mucolytic Agents. The use of mucolytics and antioxidant agents (ambroxol, erdosteine, carbocysteine, iodinated glycerol) was investigated in numerous studies with controversial results

Anticholinergics have an important role in the acute treatment of COPD exacerbations. The anticholinergics reduce airway tone and improve expiratory flow limitation, primarily by blocking parasympathetic activity in the large and medium-sized airways. They also block the release of acetylcholine, which has been linked to increased bronchial smooth muscle tone and mucus hypersecretion.
Anticholinergic agents include short-acting agents appropriate for management of acute exacerbations (eg, ipratropium) and long-acting agents (eg, tiotropium, aclidinium, and umeclidinium).

Methylxanthines: These agents (eg, theophylline) increase collateral ventilation, respiratory muscle function, mucociliary clearance, and central respiratory drive. Despite this, many questions exist as to their true efficacy, and they have no real role in the acute exacerbation of COPD, except to increase the risk of adverse effects.[7]

Phosphodiesterase-4 (PDE-4) inhibitors: Selective PDE-4 inhibitors increase intracellular cyclic adenosine monophosphate (cAMP) and result in bronchodilation. Additionally, they may improve diaphragm muscle contractility and stimulate the respiratory center. Theophylline is a nonspecific phosphodiesterase inhibitor and is now limited to use as an adjunctive agent.

Magnesium: Though controversial, administration of magnesium is thought to produce bronchodilation through the counteraction of calcium-mediated smooth muscle constriction. The addition of intravenous magnesium is now considered to have class B evidence supporting its use in difficult and life-threatening exacerbations.

Heliox: Because of helium's low density, some class B evidence now exists for its use as the medium to drive nebulizer therapy. In theory, a mixture of helium and oxygen could improve gas exchange in patients who have an airway obstruction. In the realm of COPD exacerbations, however, the evidence is more slight, and more investigation is needed.

Leukotriene receptor antagonists: Intravenous leukotriene receptor antagonists have been shown to have benefit in asthma in limited studies, but, at this time, they have no role in COPD exacerbations.