The Importance of Spontaneous Breathing during Mechanical Ventilation

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Objectives

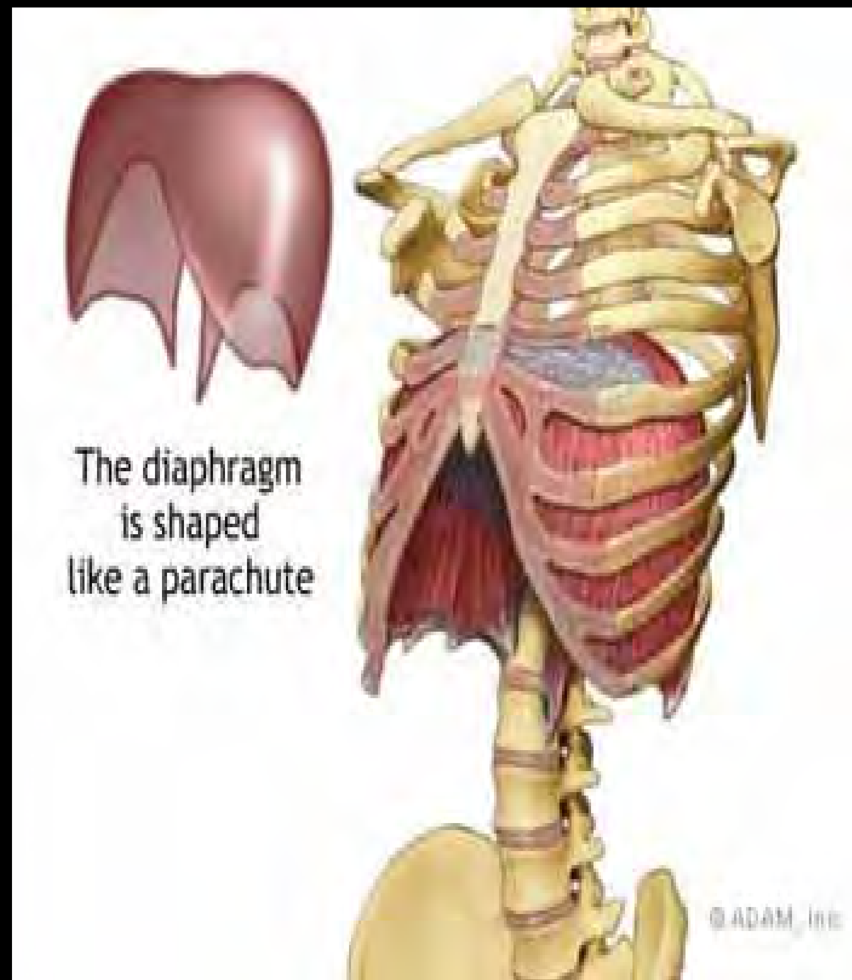
- Review the theoretical importance of spontaneous breathing on diaphragmatic function.
- Review the laboratory and human subject evidence of mechanical ventilation on diaphragmatic activity.
- Review the impact of daily SAT/SBT trials.

Author Disclosure/Conflict of Interest Statement

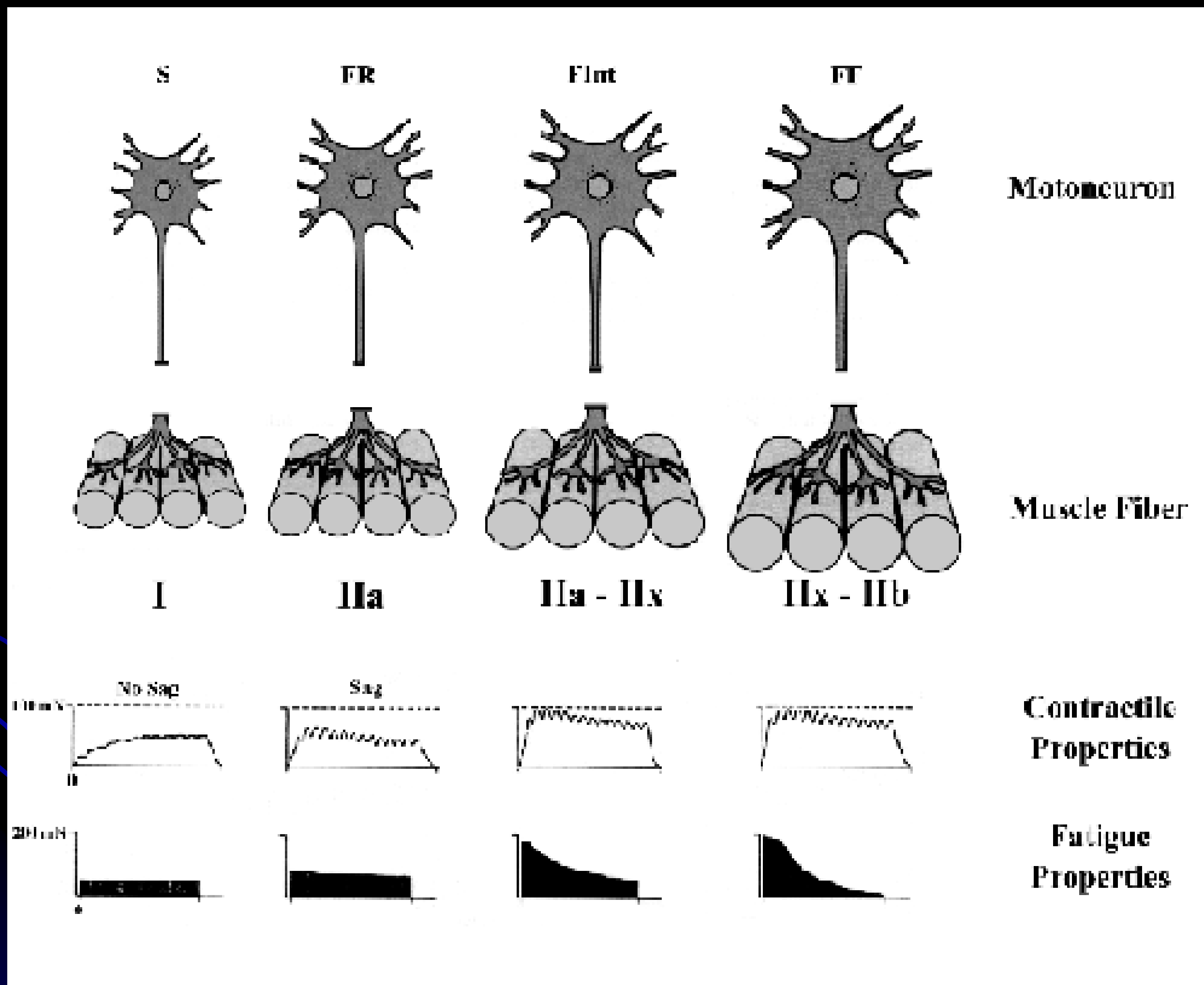
- I have no financial interests in the lucrative and profitable diaphragm-function industry nor do I work for the multiple for-profit or not-for-profit spontaneous breathing coalitions that exist on Capitol Hill…

Respiratory Power

- Diaphragm - extremely active muscle,(30- 40% activity, 24 hrs./day)
- Capacity to increase Ve 15 – 30-fold
- Composed of slow and fast twitch fibers
- Developmental and Disease specific modifications

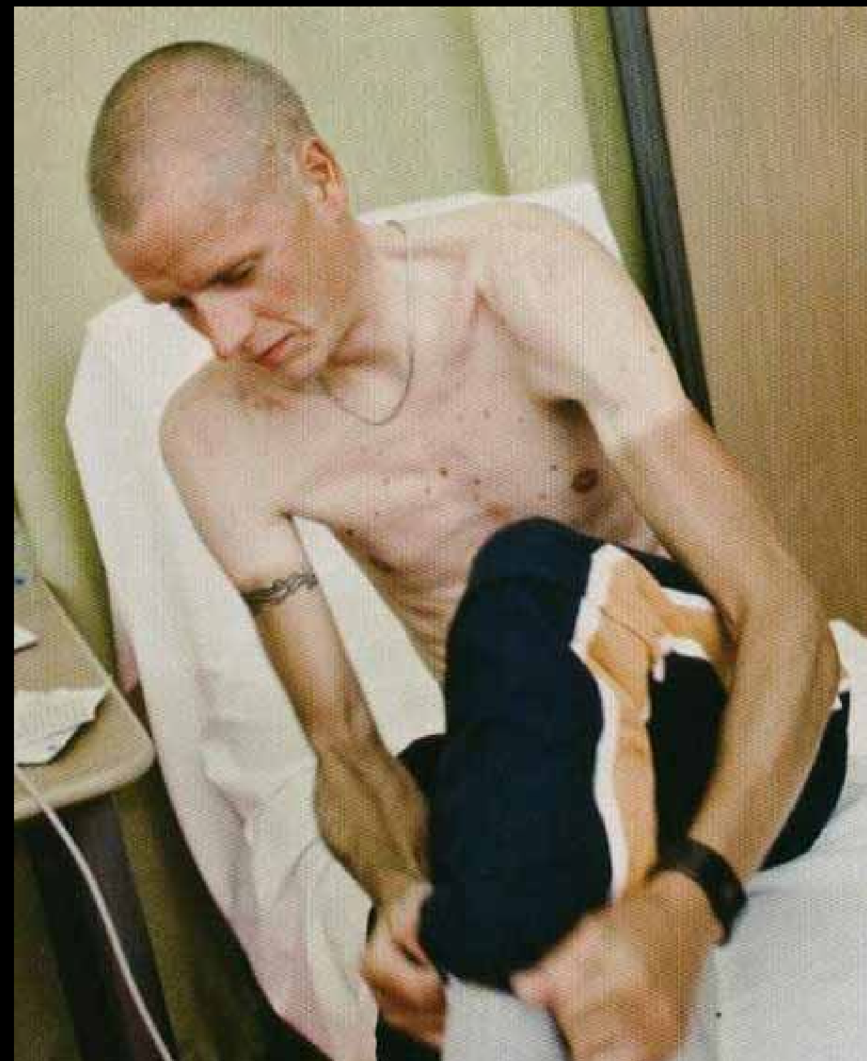


Characteristics of Diaphragm Muscle Fibers



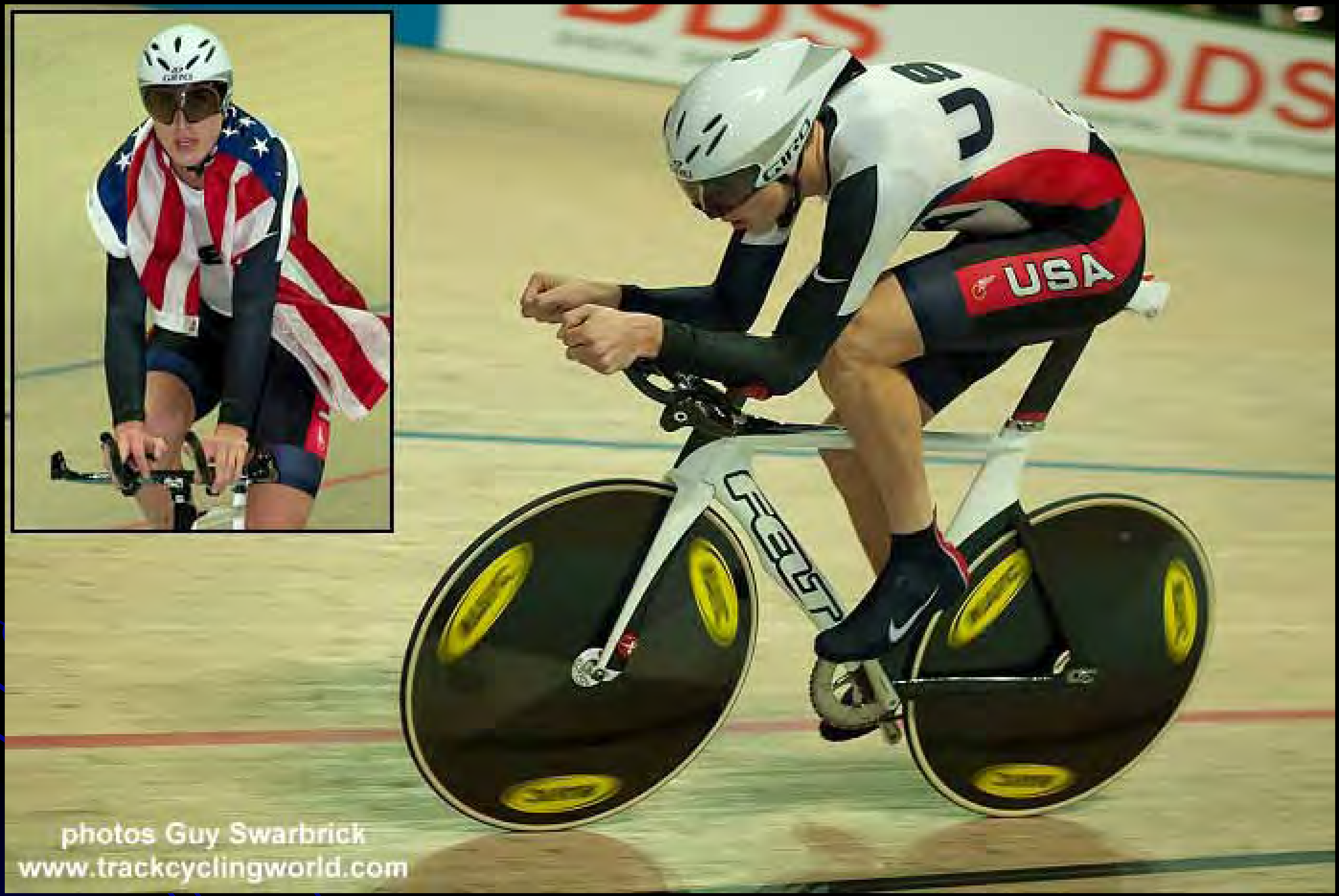
Form and Function

Pro Cycling ***tifosi***



Pro Cyclist

How Much Work are We Capable of?



Elite athletes - 185 - 200 LPM of Minute Ventilation

Premise – Pts. with Acute Respiratory Failure should be rested…

- Resting reduces pt work-of-breathing
- Resting reduces VO_2 by respiratory muscles
  - As much as 15-20% of total VO2 under extremis
- Resting prepares for weaning
- What possibly could be ***wrong*** with not breathing?

Ventilator Induced Diaphragmatic Dysfunction (VIDD)

- Adverse effect of mechanical ventilation on ventilatory muscles
- 40-50% reduction in pressure generating within 3-6 days of controlled mech vent.
  - Reduction in endurance
  - Reduction in force
- Not related to a change in nerve impulse

Ventilator Induced Diaphragmatic Dysfunction (VIDD)

- Characterized by a reduction in the force-generating capacity of the diaphragm.
  - Trans-diaphragmatic pressure generation is reduced
  - Reduction in endurance
- Usually time-dependent
- Majority of evidence from animal or *in vitro* studies

Probable Causes of VIDD

- Muscle atrophy – absence of use
  - Decreased protein synthesis
  - Protein breakdown
- Fiber Remodeling
  - Muscle specific proteins
  - Oxidative stress – protein oxidation
- Structural injury
  - Disruption of myofibrils
  - Abnormal mitochondria
- Metabolic enzymes – decreasing efficiency
- Gene expression – ultimate cause?

Muscle Atrophy

- Decreased protein synthesis
- Increased proteolysis
- 1 – 11 days
  - 40-50% reduction in diaphragmatic force
    - Baboon, piglet models
- Not related to lung volume, abdominal compliance, nerve impulse transmission

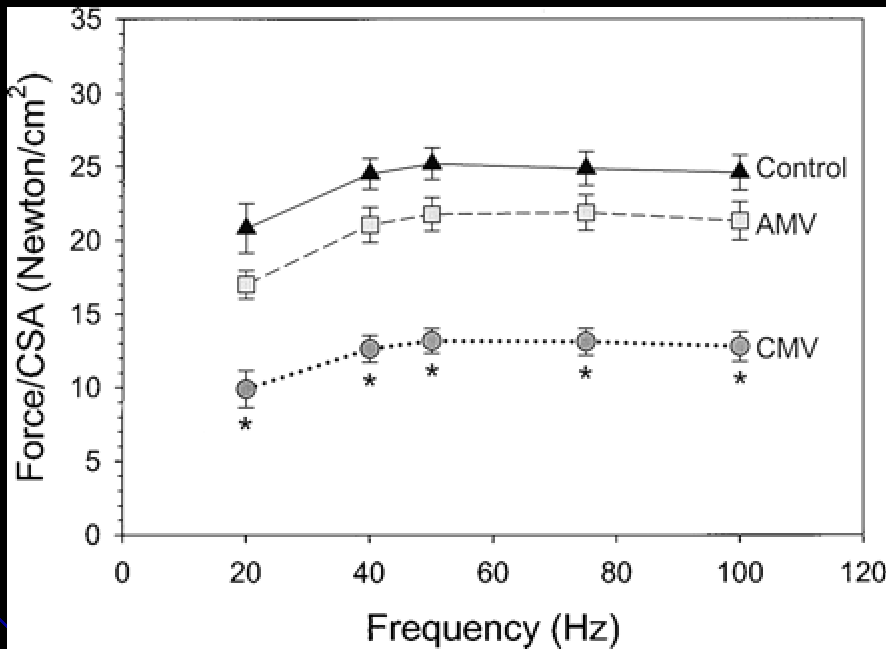
CCM 1997;25: 1187-1190

Intensive Care Med 2002; 28: 358-364

What is the Consequence of not Using the Diaphragm?

- The diaphragm fires 30-40% of the day
- More active than other skeletal muscle
- Normal exposure to a negative pressure
  - Stretch-like stimulus
- CMV = “Disuse”?
  - Unload the diaphragm
  - Cyclical inflation with PEEP, positive pressure

Impact of Assisted Ventilation vs. Controlled Ventilation

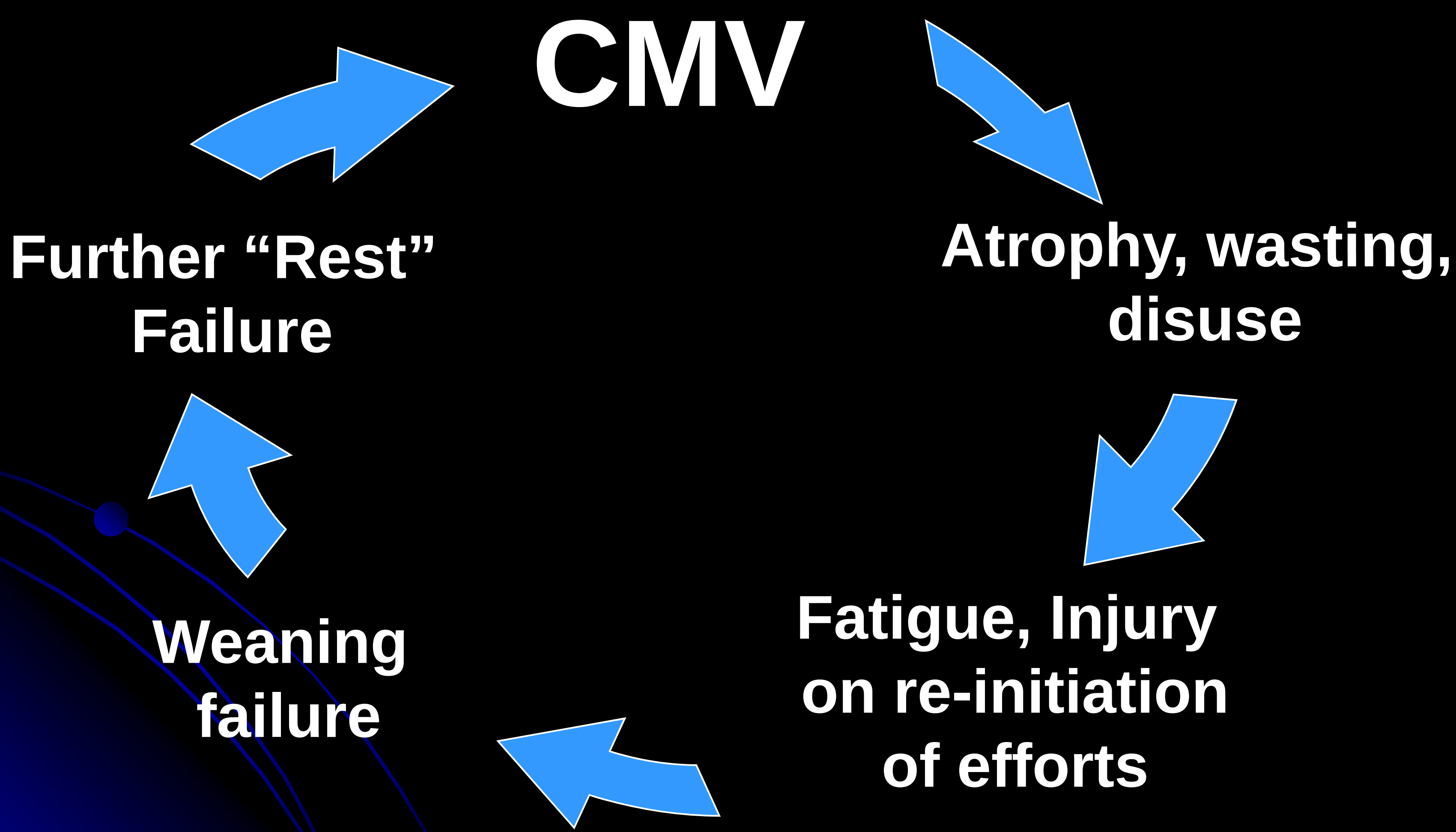


Sassoon, AJRCCM 2004; 170: 626-32

Conditions Increasing VIDD Risk

- Prolonged neuromuscular blockade
- Critical Illness Polyneuropathy
  - Sepsis
  - Hyperglycemia
  - Corticosteroids
  - Neuromuscular blockers

Hypothesis for weaning failure with controlled mechanical ventilation



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 27, 2008 VOL. 358 NO. 13

Rapid Disuse Atrophy of Diaphragm Fibers in Mechanically Ventilated Humans

Sanford Levine, M.D., Taitan Nguyen, B.S.E., Nyali Taylor, M.D., M.P.H., Michael E. Friscia, M.D., Murat T. Budak, M.D., Ph.D., Pamela Rothenberg, B.A., Jianliang Zhu, M.D., Rajeev Sachdeva, M.D., Seema Sonnad, Ph.D., Larry R. Kaiser, M.D., Neal A. Rubinstein, M.D., Ph.D., Scott K. Powers, Ph.D., Ed.D., and Joseph B. Shrager, M.D.

- Comparison of biopsy specimens
  - 8 control pts
    - 2-3 hrs. of mechanical ventilation
  - 14 brain-dead organ donors (case pts.)
    - 18 – 69 hrs. of CMV

Table 1. Summary of Demographic Characteristics, Reason for Surgery, and Medical History for Control and Case Subjects.*

Subject No.	Age (yr)	Sex	BMI	Reason for Surgery or Cause of Brain Death	Relevant Medical History
Control subjects					
1	79	M	31	Stage 1A adenocarcinoma of the lung	Prostate carcinoma, nonsmoker, farmer
2	64	M	36	Stage 1A adenocarcinoma of the lung	Peripheral arterial disease, rheumatoid arthritis, hypertension, coronary artery disease, smoked 90 pack/yr
3	55	F	23	Stage 1A benign fatty tumor	Hypercholesterolemia, osteoarthritis, smoked 10 pack/yr
4	76	M	27	Stage 1A adenocarcinoma of the lung	Coronary artery disease with history of myocardial infarction, macular degeneration, prostate carcinoma (radiation therapy, 1999), coronary-artery bypass graft (1988), pipe smoker (quit 30 yr ago)
5	58	F	30	Stage 1 carcinoid tumor	Hypercholesterolemia, primary hyperparathyroidism, kidney stones, smoked 40 pack/yr
6	25	F	27	Ganglioneuroma	Gallstones, nonsmoker
7	54	F	23	Ganglioneuroma	Glaucoma, seasonal allergies, nonsmoker
8	41	F	26	Hamartoma	Herniated lumbar disks, dysfunctional uterine bleeding, smoked 24 pack/yr (quit 2 yr ago)
Case subjects					
1	18	F	24	Motor vehicle accident	None
2	21	F	29	Drug overdose	Drug abuse
3	18	M	25	Gunshot wound to head	None
4	19	M	24	Respiratory arrest secondary to seizure	Seizure disorder with implanted pacemaker
5	49	M	24	Motor vehicle accident	Hypertension, peptic ulcer disease, depression, hypogonadism, smoker
6	33	F	44	Drug overdose	Drug and ethyl alcohol abuse, metronidazole and ceftriaxone for vaginitis
7	25	F	21	Motor vehicle accident	Pregnant
8	50	M	21	Stroke	Hypertension, ethyl alcohol abuse, smoked 30 pack/yr
9	23	M	20	Motor vehicle accident	Hypertension, ethyl alcohol abuse, marijuana abuse
10	53	F	45	Stroke	Hypertension, type 2 diabetes mellitus, gastresophageal reflux disease, atrial fibrillation (new onset)
11	45	M	32	Stroke	Hypertension, ethyl alcohol abuse, drug abuse
12	26	M	28	Cardiac arrest	Seizure disorder
13	56	F	26	Stroke	Smoked 80 pack/yr
14	58	F	36	Stroke	Hypertension, chronic obstructive pulmonary disease, hypothyroidism, schizoaffective disorder, bipolar disorder, smoked 25 pack/yr, obesity, oral corticosteroid prescription

* All control subjects had normal values for spirometry. BMI denotes body-mass index (defined as the weight in kilograms divided by the square of the height in meters).

NEJM 2008; 358:1327 -35

Table 2. Summary of Ventilator Settings, Arterial Blood Gas Measurements, and Vital Signs for Control and Case Subjects.*

Measurement	Control Subjects (N=8)	Case Subjects (N=14)	P Value
Ventilator settings and related measurements			
Tidal volume (ml/kg of body weight)	7.5±1.3	8.0±2.0	0.47
Ventilation frequency (breaths/min)	11±1.7	14±3.0	0.02
PEEP (cm H_2O)	0.0±0.0	6.0±1.0	<0.001
FiO_2 (%)	—	52±0.11	—
SaO_2 (%)	99±2.0	—	—
PaO_2 (mm H_2O)	—	147±88	—
$PetCO_2$ (mm Hg)	31±3.8	—	—
$PaCO_2$ (mm Hg)	—	34±6.0	—
Arterial pH (units)	—	7.39±0.05	—
PaO_2/FiO_2†	—	412±167	—
Vital signs			
Systolic pressure (mm Hg)	115±10	125±20	0.20
Diastolic pressure (mm Hg)	62±6.0	70±10	0.08
Heart rate (beats/min)	72±9.0	105±18	<0.001
Body temperature (°C)	35.7±0.3	36.4±1.1	0.06

* Plus–minus values are means ±SD. FiO_2 denotes fractional concentration of inspired oxygen, $PaCO_2$ arterial carbon dioxide pressure, PaO_2 arterial oxygen pressure, PEEP positive end-expiratory pressure, $PetCO_2$ end-tidal carbon dioxide pressure, and SaO_2 arterial oxygen saturation.

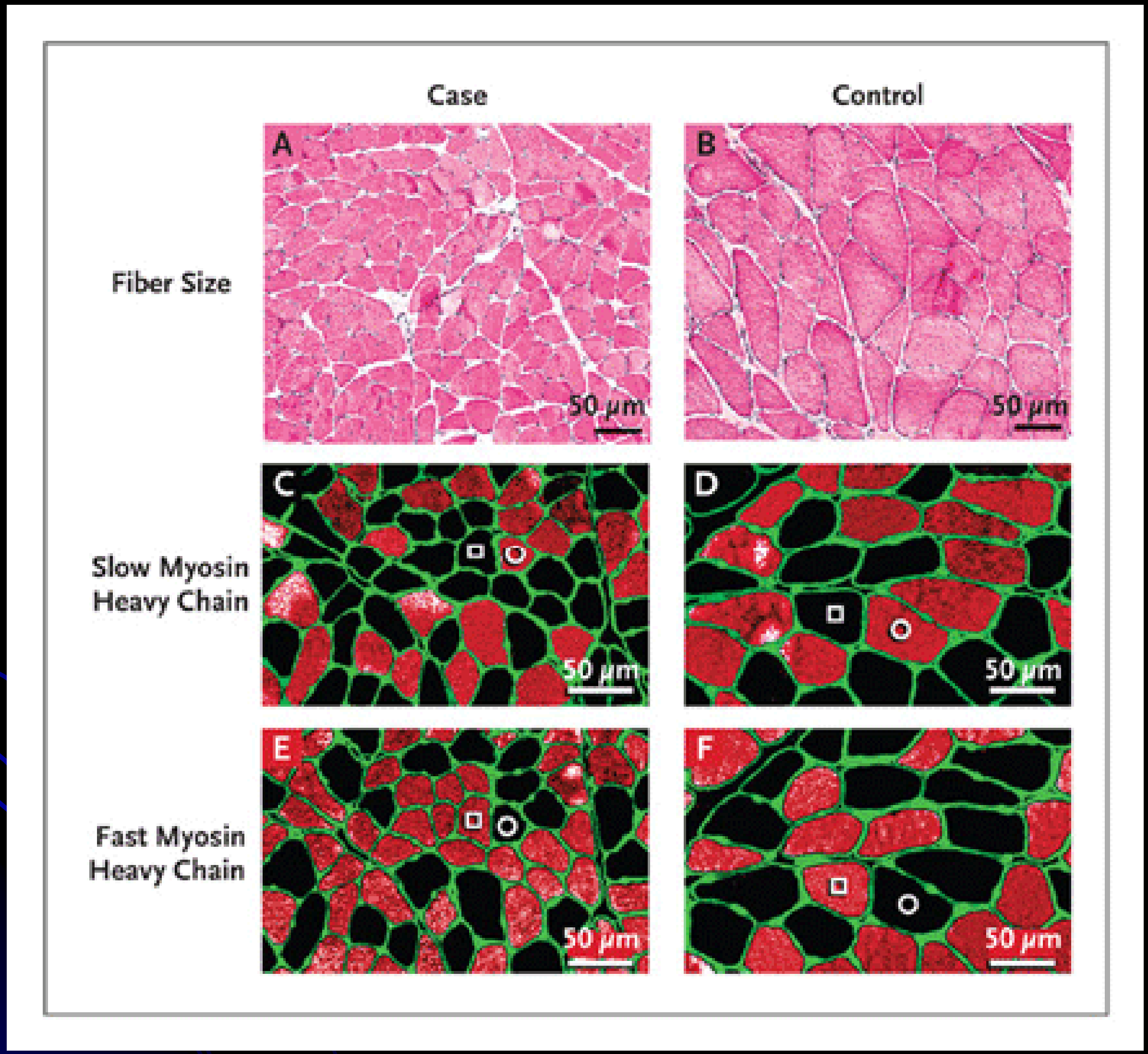
† These measurements were made at an FiO_2 of 1.0.

NEJM 2008; 358:1327 -35

18-69 hrs. of Diaphragmatic Inactivity and CMV

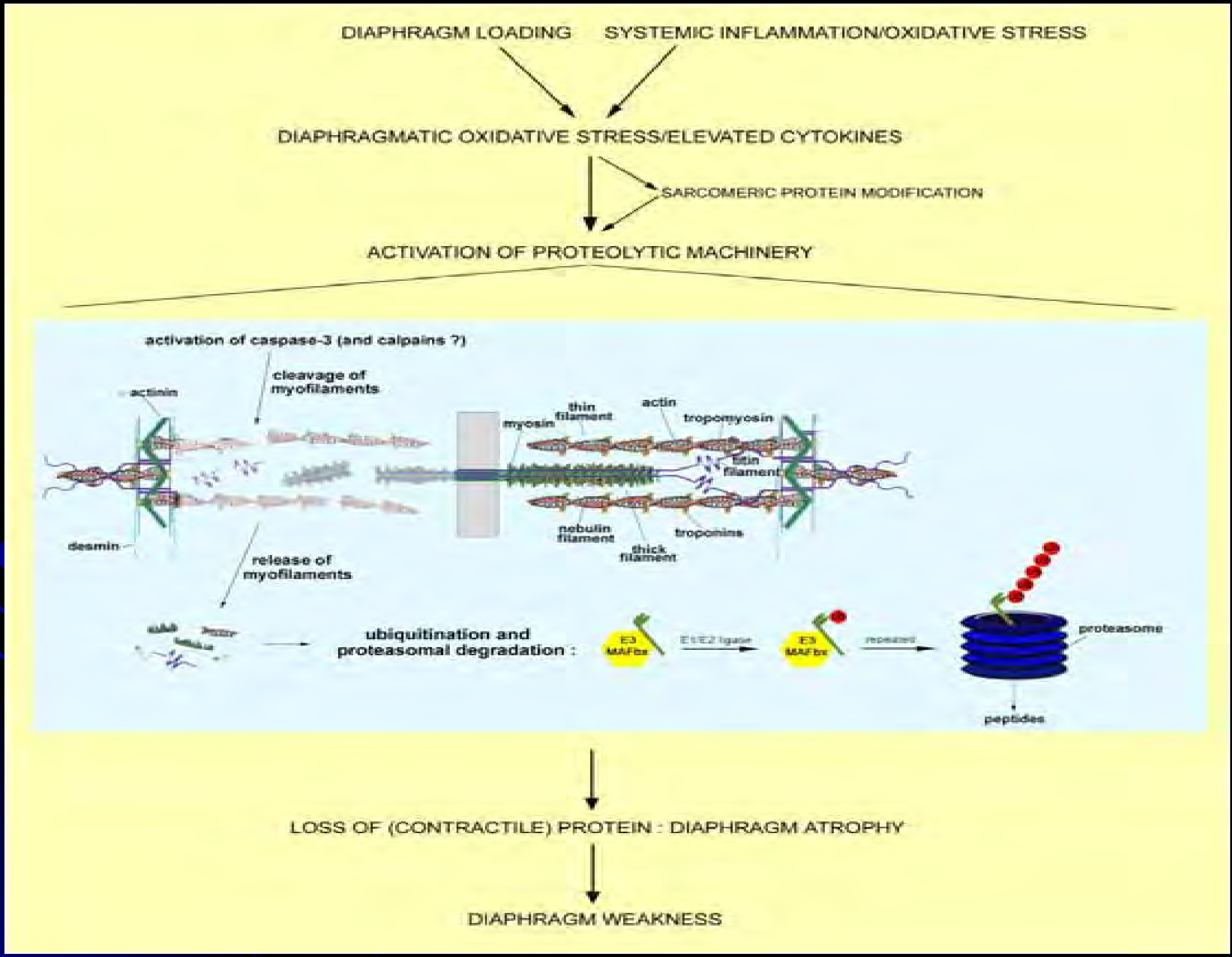
- Atrophy of both slow and fast-twitch fibers
- Increase in oxidative stress markers
- Increased proteolysis

Comparative Cross Section

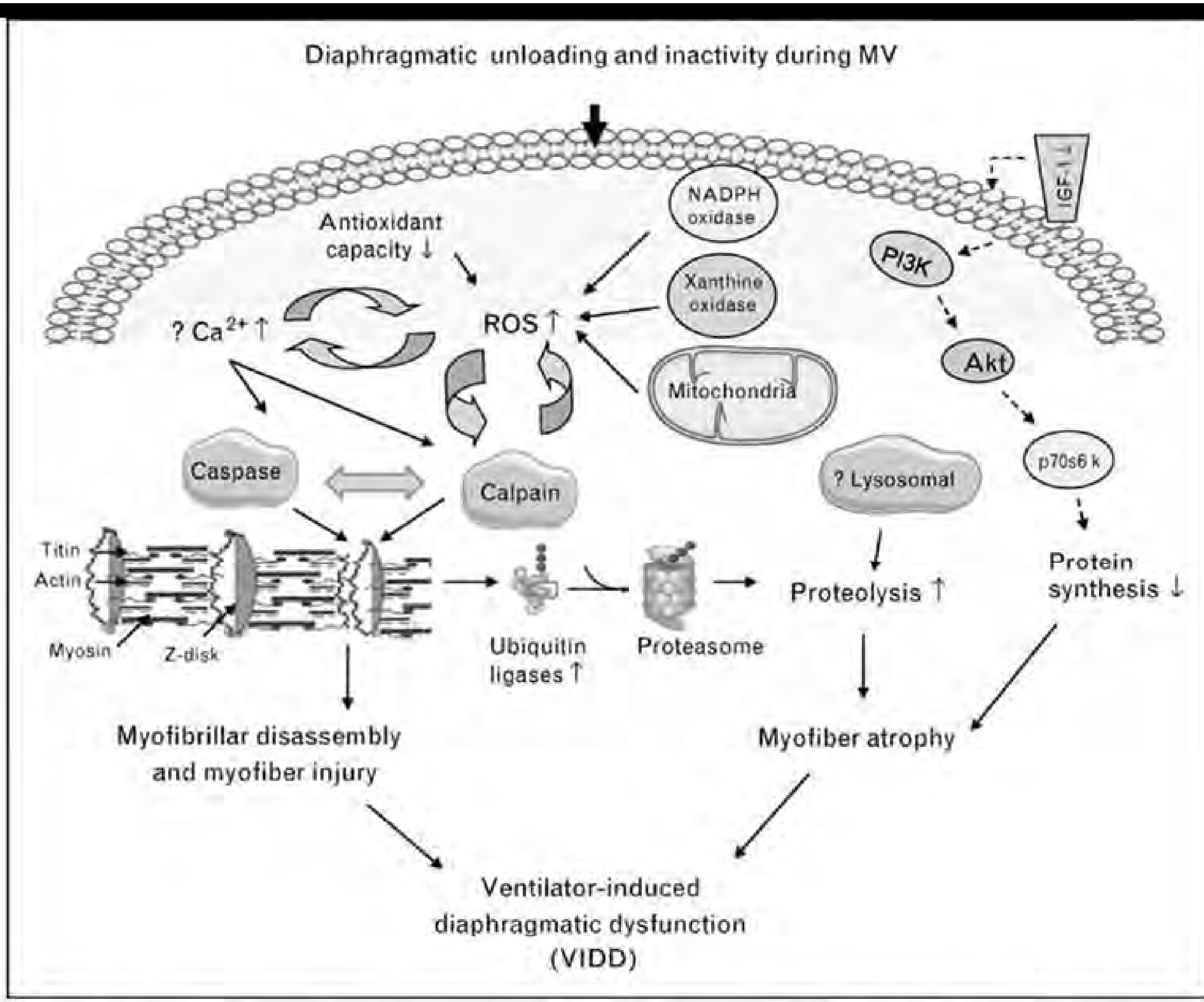


NEJM 2008; 358:1327 -35

Possible pathways of diaphragm atrophy and weakness



AJRCCM 2007;175: 1233-1240

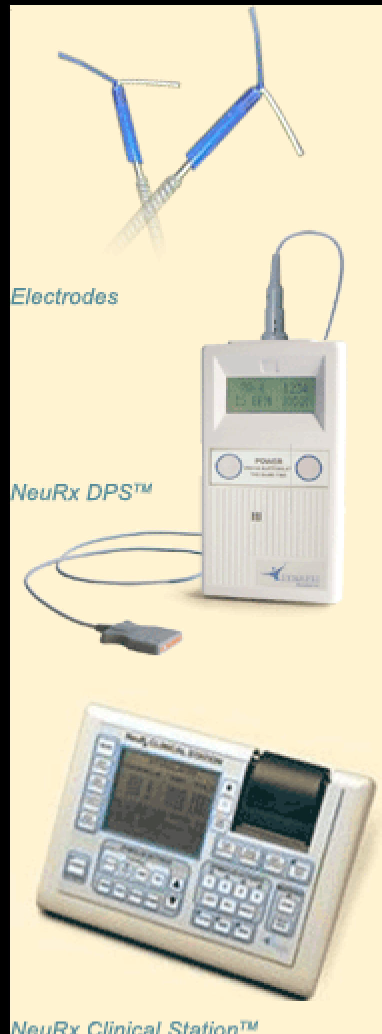


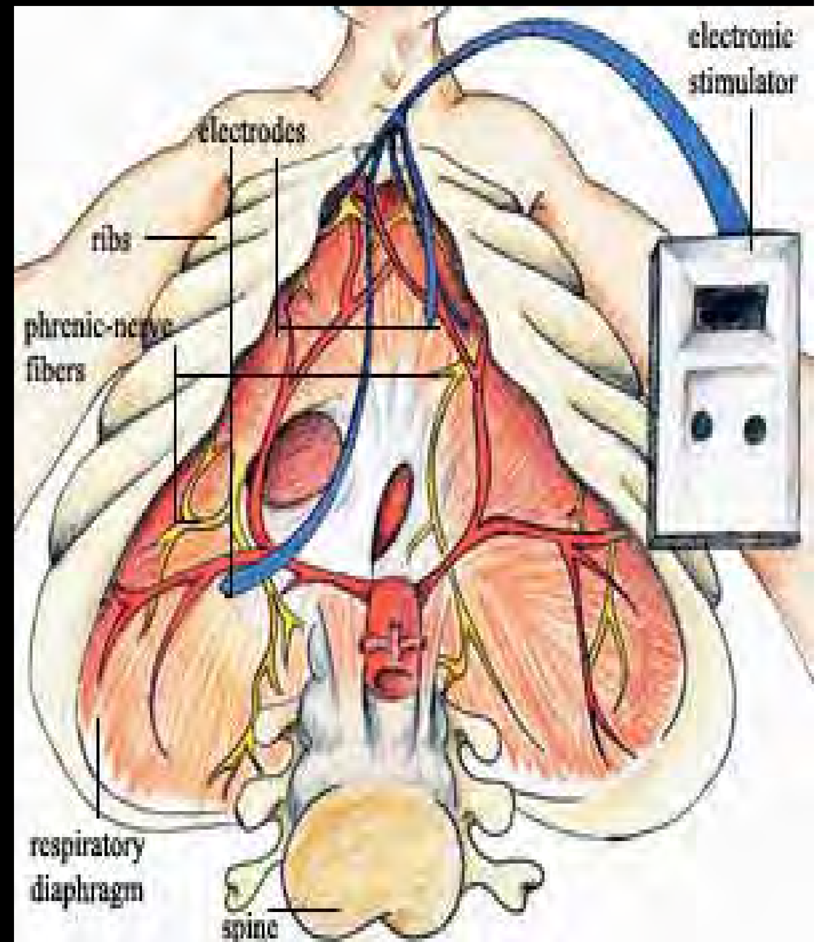
Several of the mechanistic pathways implicated in the development of VIDD are illustrated. Protein synthesis pathways are downregulated (indicated by dashed lines). In addition, ROS generated from several possible sources can activate downstream proteolytic pathways involved in myofiber injury and atrophy, including the calpain and caspase systems; these have the potential to be mutually reinforcing and to drive further ROS production. The role of lysosomally-mediated proteolysis, and particularly autophagy, remains to be explored. IGF-1, insulin-like growth factor-1; MV, mechanical ventilation; PI3K, phosphoinositide-3 kinase; ROS, reactive oxygen species.

Cur Opinion Critical Care 2010; 16: 19-25

Diaphragmatic Pacing

- Avoidance of muscle atrophy
- Improvement in tidal volume
- Augmentation of ventilatory support
- Site familiarity



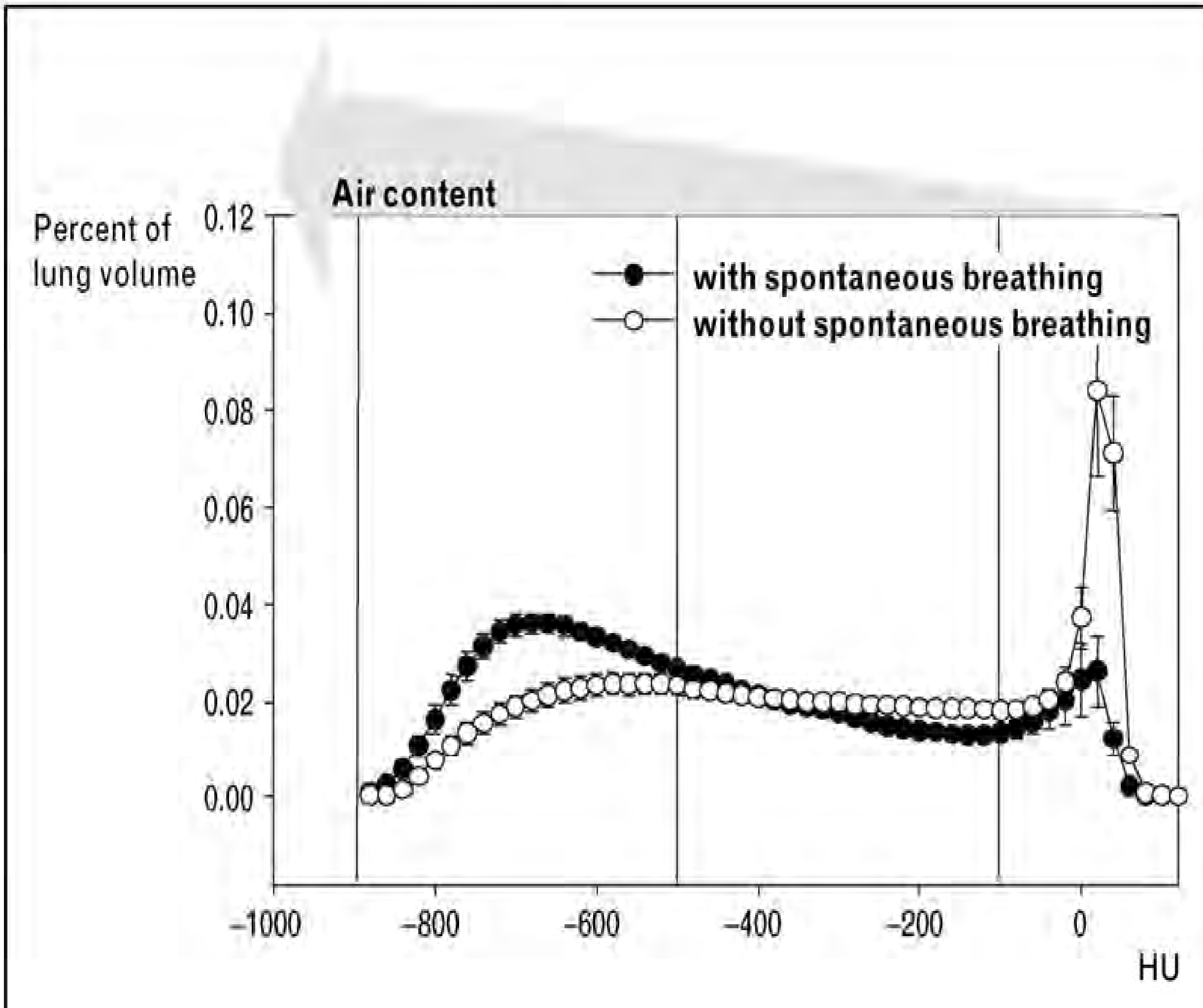


Spontaneous Breathing…It's just the right thing to do…

- Induces improvement in distribution of ventilation
- Improvement in V/Q
- Avoidance of alveolar collapse
- Preservation of muscular function, integrity

Spont breathing aerated lung units during ALI

Presence of spontaneous breathing resulted in a significant decrease in the lung volume with HUs ranging between −100 and 100, indicating nonaerated lung areas, while the lung volume with HUs ranging between −900 and −500 indicated normal aerated lung areas were increased. These observations indicate alveolar recruitment with spontaneous breathing.



Cur Opin Crit Care 2006;12: 13-18

Sedation Awakening and SBT

- Daily SBT demonstrated statistical and clinically significant ↓ in duration of CMV*.
- Daily interruption of sedation ↓ CMV duration and ↓ ICU LOS [Δ].
- Combining both sedation awakening and SBT produced ↓ in duration of CMV, ICU stay and ↓ mortality[±].

*Ely W, et. al, NEJM 1996; 335:1864-69

ΔKress J, et. al, NEJM 2000; 342: 1471-1477

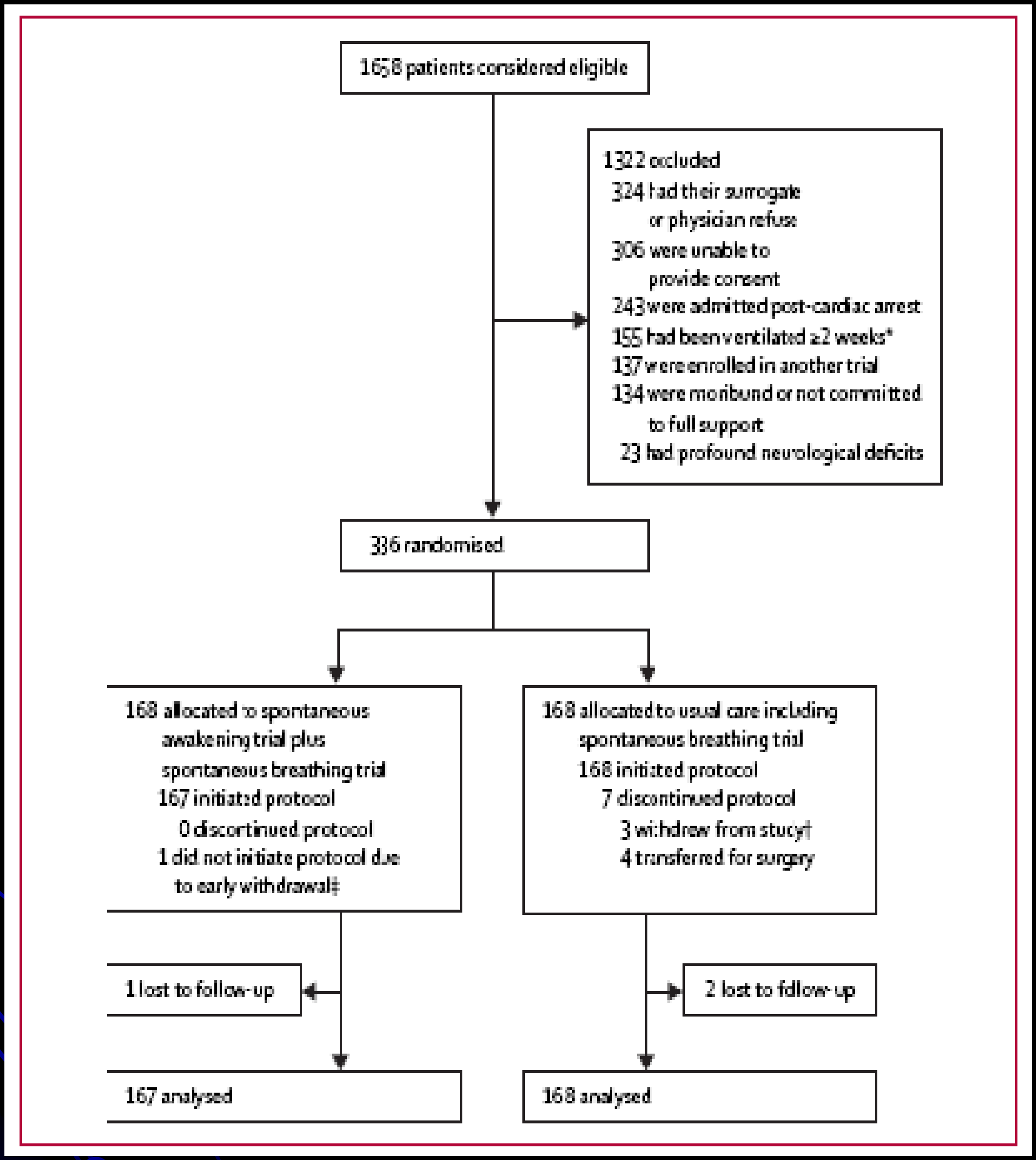
±Girard T, et. al, Lancet 2008; 371:126-34

Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

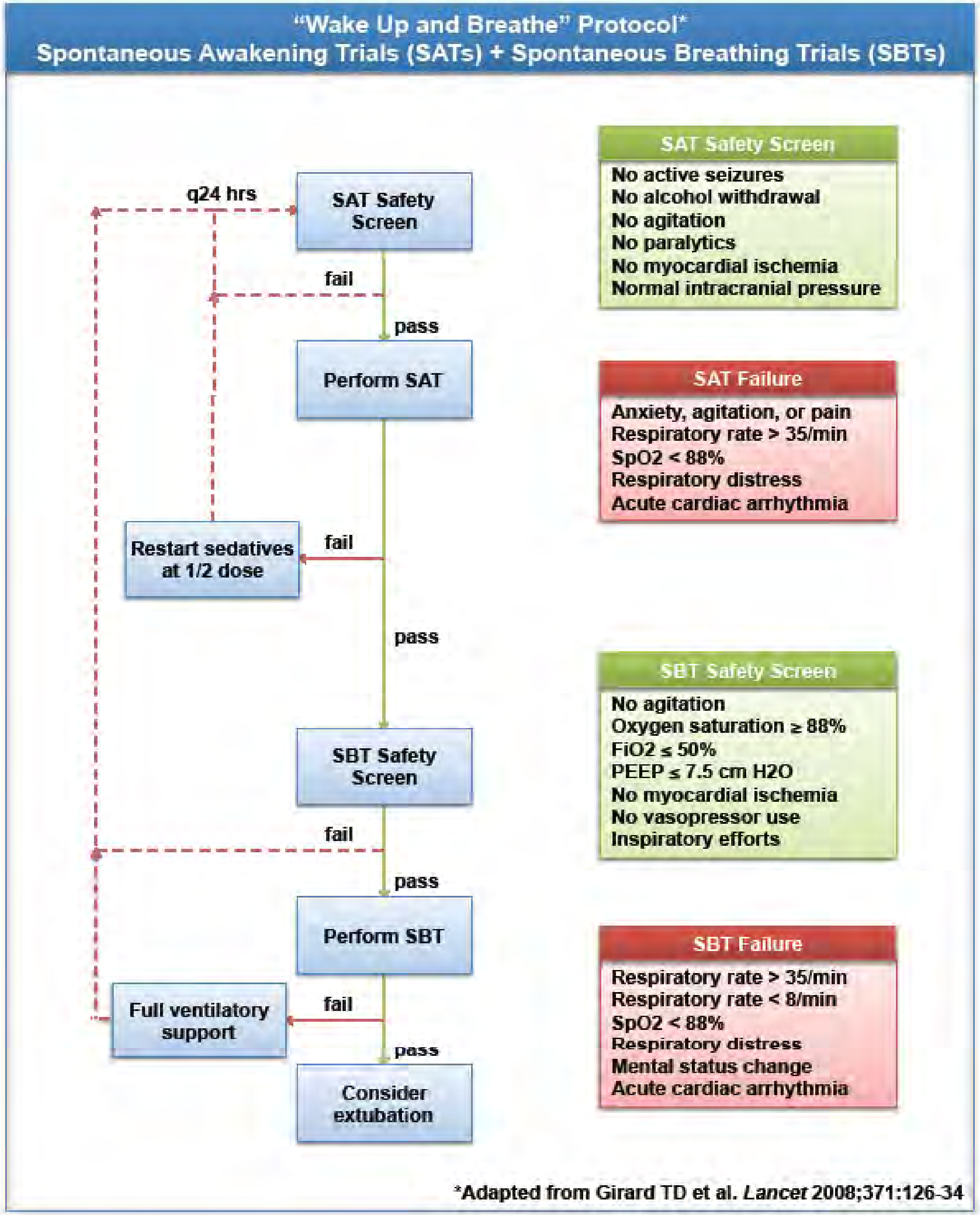
Timothy D Girard, John P Kress, Barry D Fuchs, Jason W W Thomason, William D Schweickert, Brenda T Pun, Darren B Taichman, Jan G Dunn, Anne S Pohlman, Paul A Kinniry, James C Jackson, Angelo E Canonico, Richard W Light, Ayumi K Shintani, Jennifer L Thompson, Sharon M Gordon, Jesse B Hall, Robert S Dittus, Gordon R Bernard, E Wesley Ely

- RCT in 4 hospitals
  - 336 patients
  - Control – Sedation as usual, daily SBT
  - Intervention – Daily SAT and SBT

Lancet 2008; 371: 126-34



Lancet 2008; 371: 126-34

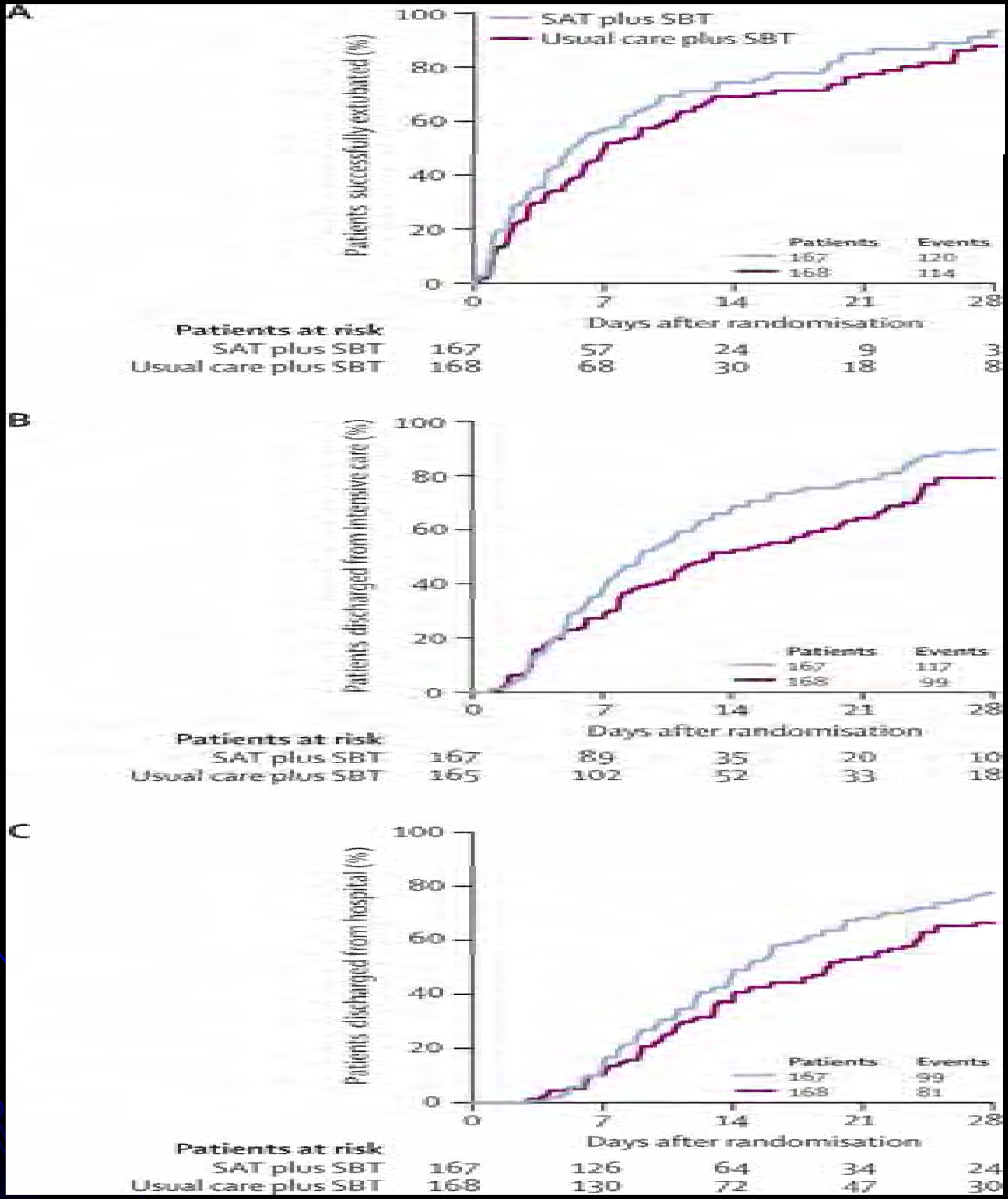

"Wake Up and Breathe" Protocol*
Spontaneous Awakening Trials (SATs) + Spontaneous Breathing Trials (SBTs)
q24 hrs
SAT Safety Screen
fail
pass
Perform SAT
Restart sedatives at 1/2 dose
fail
pass
SBT Safety Screen
fail
pass
Perform SBT
Full ventilatory support
fail
pass
Consider extubation
SAT Safety Screen
No active seizures
No alcohol withdrawal
No agitation
No paralytics
No myocardial ischemia
Normal intracranial pressure
SAT Failure
Anxiety, agitation, or pain
Respiratory rate > 35/min
SpO2 < 88%
Respiratory distress
Acute cardiac arrhythmia
SBT Safety Screen
No agitation
Oxygen saturation ≥ 88%
FiO2 ≤ 50%
PEEP ≤ 7.5 cm H2O
No myocardial ischemia
No vasopressor use
Inspiratory efforts
SBT Failure
Respiratory rate > 35/min
Respiratory rate < 8/min
SpO2 < 88%
Respiratory distress
Mental status change
Acute cardiac arrhythmia
*Adapted from Girard TD et al. Lancet 2008;371:126-34

	Intervention group (n=167)	Control group (n=168)	p value
Ventilator-free days*			
Mean	14·7 (0·9)	11·6 (0·9)	0·02
Median	20·0 (0 to 26·0)	8·1 (0 to 24·3)	
Time to discharge (days)			
From intensive care	9·1 (5·1 to 17·8)	12·9 (6·0 to 24·2)	0·01
From hospital	14·9 (8·9 to 26·8)	19·2 (10·3 to NA)†	0·04
28-day mortality	47 (28%)	58 (35%)	0·21
1-year mortality	74 (44%)	97 (58%)	0·01
Duration of brain dysfunction (days)			
Coma	2 (0 to 4)	3 (1 to 7)	0·002
Delirium	2 (0 to 5)	2 (0 to 6)	0·50
RASS at first successful SBT	−1 (−3 to 0)	−2·5 (−4 to 0)	0·0001
Complications			
Any self-extubation	16 (10%)	6 (4%)	0·03
Self-extubation requiring reintubation‡	5 (3%)	3 (2%)	0·47
Reintubation‡	23 (14%)	21 (13%)	0·73
Tracheostomy	21 (13%)	34 (20%)	0·06

Data are mean (SD), n (%), or median (IQR). RASS=Richmond agitation-sedation scale. SAT=spontaneous awakening trial. SBT=spontaneous breathing trial. *Ventilator-free days from study day 1 to 28. †Greater than 25% of patients in the SBT group remained in the hospital at study day 28. ‡Reintubation within 48 hours of extubation.

Table 3: Main outcomes

Lancet 2008; 371: 126-34



Lancet 2008; 371: 126-34

Spontaneous Breathing Trial (SBT)

Source Order

Intervention Type

Patient Evaluation:

Patient Presentation

READINESS TO WEAN

Has This patient previously failed weaning or extubation?

Spontaneous Awakening Trial(SAT) Criteria | SAT

- ☐ Sedation infusion for seizures, ETOH withdrawal
- ☐ Increasing sedation doses for ongoing agitation
- ☐ Neuromuscular blockers
- ☐ Evidence of MI within 24 hours
- ☐ Evidence of increased ICP
- ☐ Sustained anxiety, agitation or pain
- ☐ Resp rate >35 for > 5 min
- ☐ SpO2% <88% for > 5 min
- ☐ Cardiac dysrhythmia
- ☐ 2 or more signs of resp distress (tachy/bradycardia, accessory muscle

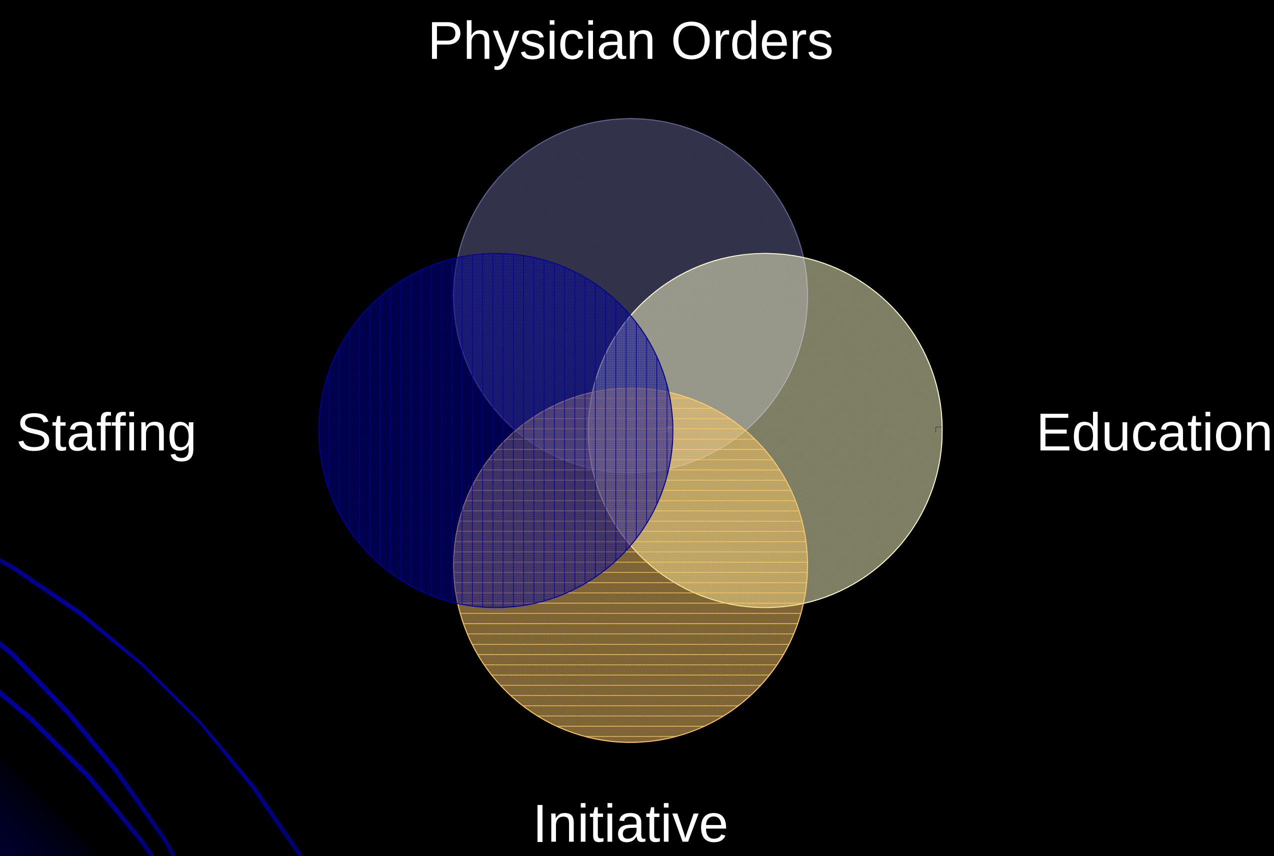
Spontaneous Breathing Trial(SBT) Criteria | SBT

- ☐ SpO2 % < 88% on FIO2% > 50%
- ☐ PEEP > 9 cm H2O
- ☐ Significant pressors/inotropes
- ☐ Evidence of increased ICP
- ☐ Sustained anxiety, agitation or pain
- ☐ Respiratory rate > 35 for > 5 min
- ☐ SpO2% < 88% for > 5 min
- ☐ Cardiac dysrhythmia
- ☐ 2 or more signs of respiratory distress (tachy/bradycardia, accessory m

Goals:

Target Trial Time | Minutes

Reasons for “Missed Opportunities” with SAT or SBT Attempts



Mechanical Ventilation without Initiation of Inspiratory Efforts…

- Leads to disuse, atrophy
  - Reduction in tidal volume, inspiratory capacity
- Leads to fatigue
- Leads to “resting” without work
- Leads to injury with a return to normal work levels and subsequent weaning failure

Take Home

- Patient initiation of breathing is a good thing
- Multiple factors influence weaning
  - Pharmacologic, Pathophysiology
  - Ventilator management
- Animal, human data imply diaphragmatic wasting occurs in a very short period of time (< 24 hrs.) with controlled MV.
- No evidence of PS, A/C, IMV superiority
- There is strong evidence that daily SAT/SBT's are the right thing to do…

References

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