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Authors’ response: Origin of the 24-h rest arm

Accepted: 13 August 2014
 Published online: 22 August 2014
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Dear Editor,
 The source of an idea that gives rise to a new discovery can be hard to

pinpoint [1], but no difficulty arises in tracking the origin of the idea for including a 24-h rest arm in the above-cited randomized clinical trial.

The truncated left axis on the figure of Esteban and colleagues betrays their misunderstanding of the origin of that idea.

From 1982 onwards, Tobin had been undertaking research on the influence of the respiratory controller and respiratory muscles on mechanical ventilation and weaning. His laboratory presented this research annually (Table 1). Studies revealed a Janus-like relationship: too much ventilation risked atrophy, too little hindered recovery from fatigue.

To determine optimal rest, Tobin’s laboratory investigated the pace of diaphragm recovery after incurring

fatigue. In spring 1992, Laghi began experiments which showed the diaphragm needed 24 h to recover from fatigue. This work was submitted to ATS in November 1992. These facts belie Esteban and colleagues’ claim that the results “were probably obtained in the late 1993 or early 1994.”

In May 1991, Brochard’s group presented an RCT of three weaning techniques: T-tube trials repeated several times a day, SIMV, pressure support. Rest between each failed T-tube trial could be as brief as 1 h. When published, Brochard’s group did not mention that longer rest between T-tube trials might be beneficial.

When Tobin first met Esteban in August 1992, he already knew the

Table 1 Chronology of events pertaining to 24-h rest arm in RCT of weaning techniques

1982	May 17	ATS: Development of breathing pattern analysis (Los Angeles) ^a
1984	May 22	ATS: Breathing pattern during weaning (Miami Beach) ^b
1985	May 14	ATS: Monitoring respiratory muscle function—Invited lecture (Anaheim)
1986	May 12	ATS: Chest-wall motion in weaning-failure patients (Kansas City) ^c
1987	May 11	ATS: Ventilator-induced respiratory muscle atrophy (New Orleans) ^d
1988	May 10	ATS: Effect of ventilator tidal volume on respiratory controller (Las Vegas) ^e
1989	October 24	ACCP: Is respiratory muscle rest necessary when weaning?—Invited lecture (Toronto)
1990	May 25	SCCM: Weaning from mechanical ventilation—Plenary lecture (Washington)
1991	May 13	ATS: ROC curve analysis of weaning prediction (Anaheim) ^f
	May 14	Brochard presents RCT of 3 techniques—Repeated T-tube trials, SIMV, PS—at ATS ^g
1992	January	Laghi visits Brompton to train in magnetic stimulation
	April	Laghi performs preliminary experiments on twitches
	June 29	IRB approves “Evaluation of diaphragmatic fatigue” protocol
	July	Laghi begins formal data collection on recovery from diaphragmatic fatigue
	August 23–27	Tobin and Esteban discuss undertaking RCT at VII Congreso Terapia Intensiva (Buenos Aires) Esteban lectures on “Monoclonal antibodies in postoperative abdominal sepsis” Benito lectures on “Gasometric indices in respiratory insufficiency” Tobin lectures on “Muscle fatigue,” “Weaning,” “Monitoring neuromuscular function”
	October	Spanish Lung Failure Collaborative Group begins RCT of four weaning techniques
	November 11	Laghi submits recovery from diaphragmatic fatigue to ATS (San Francisco)
1993	May 19	Laghi presents recovery from diaphragmatic fatigue at ATS (San Francisco) ^h
1994	May 3	Tobin mails RCT paper to <i>NEJM</i> ⁱ
	June 10	Tobin mails twitch paper to <i>JAP</i> ^j
	October 5	Tobin mails revision of RCT paper to <i>NEJM</i>
	December 19	Tobin mails revision of twitch paper to <i>JAP</i>

ATS American Thoracic Society, ACCP American College of Chest Physicians, ARRD American Review Respiratory Disease, IRB institutional review board, JAP Journal of Applied Physiology, NEJM New England Journal of Medicine, RCT randomized controlled trial, ROC receiver operating curve, SCCM Society of Critical Care Medicine, SIMV synchronized intermittent mandatory ventilation

^a ARRD 125:A122, 1982

^b ARRD 129:A106, 1984

^c ARRD 133:A123, 1986

^d ARRD 135:A201, 1987

^e ARRD 137:A266, 1988

^f ARRD 143:A684, 1991

^g ARRD 143:A602, 1991

^h ARRD 147:A956, 1993

ⁱ NEJM 332:345, 1995

^j JAP 79:539, 1995

diaphragm required 24 h of rest to recover from fatigue, and that T-tube trials in Brochard's RCT entailed as little as 1 h rest. On the basis of years of researching the respiratory muscles, Tobin impressed upon Esteban the importance of a 24-h rest period in the design of an RCT of weaning techniques.

Three arms in the Spanish RCT were largely a copy of the Brochard design (Benito was an author on both), thus entailing zero novelty. Research lacking originality is, of course, otiose. The only novelty in the Spanish RCT was the idea for the fourth arm: patients who failed a T-tube trial would not undergo another until they had rested on assist-control ventilation for 24 h.

For unclear reasons, Esteban and colleagues believe that a sentence in the *NEJM* paper supports their claim to priority of ideas. That sentence simply provides a scientific base to the observation that a daily challenge,

followed by 24 h of rest, enhances muscle plasticity. Deciphering the author of the sentence hardly requires expertise in stylometric forensics.

They note that the RCT paper does not reference the twitch paper. The reason is simple. The *NEJM* and *JAP* manuscripts moved in parallel, not in series (Table 1).

They preface their letter with lines from Lepera; more apt might be Tacitus, "Men are more ready to repay an injury than a benefit because gratitude is a burden and revenge a pleasure."

The above chronology and litany of facts should be enough to allow each reader of *ICM* to form his or her own conclusion as to the source of the idea for including the 24-h rest arm in the RCT.

Conflicts of interest Dr. Laghi's research laboratory has received research grants from the National Institutes of Health, VA Research Service, Liberate Medical LLC,

and the National Science Foundation. Dr. Tobin receives royalties from McGraw-Hill for two books published on critical care medicine.

Ethical standard Approval by an ethics committee is not applicable.

Reference

1. Bliss M (1984) The discovery on insulin. University of Chicago Press, Chicago

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