

In summary, RR measurement studies would benefit from an uncertainty (probabilistic) approach to the reference standard, including procedures to measure and reduce this uncertainty (5). Continuous RR measurements, rather than single-threshold values, should be used to assess clinical uncertainty and corrections considered for other known covariates such as core body temperature. ■

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J. Mark Ansermino, M.B. B.Ch.
Guy Dumont, Ph.D.
The University of British Columbia
Vancouver, British Columbia, Canada

Amy Sarah Ginsburg, M.D., M.P.H.*
Save the Children Federation, Inc.
Fairfield, Connecticut

*Corresponding author (e-mail: aginsburg@savechildren.org).

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Ⓢ PC₂₀ versus PD₂₀: Why Change a Scientifically Well-Established and Clinically Relevant Test?

To the Editor:

We read with interest the article by Coates and colleagues (1). The authors elaborate on the recently published “ERS Technical Standard on Bronchial Challenge Testing: General Considerations and Performance of Methacholine Challenge Tests” (2) and suggest that PD₂₀ (the provocative dose of methacholine [MCh] that results in a 20% fall in FEV₁) should replace PC₂₀ (the

provocative concentration of MCh that results in a 20% fall in FEV₁). We have the following comments:

1. MCh dose versus concentration: Based on the suggested new standard for using dose instead of concentration of MCh to evaluate and report airway reactivity, the authors recommended using a mechanical breath simulator to collect MCh on a filter representing the mouth and calculate the deposited dose. Alternatively, they suggest that nebulizer manufacturers should provide those who perform MCh challenge tests with information regarding the aerosol output characteristics of their nebulizer. No mechanism is suggested regarding how to make this happen, and pulmonary function testing (PFT) laboratories are left with considerable confusion as to how to proceed.
2. Nebulizer replication studies: The authors cite recent articles comparing the original Wright nebulizers with newer nebulizers (specifically the SOLO Aerogen vibrating mesh device and the Aero Eclipse). These papers showed that PD₂₀, but not PC₂₀, was independent of the delivery system used. However, these nebulizers are infrequently used in most PFT laboratories. We wonder if it is not essential to replicate their findings against other commonly used nebulizers.
3. Nebulizer cost and durability: Vibrating mesh nebulizers are expensive and have well-known problems involving mesh clogging and circuit issues. Also, their mass median aerodynamic diameter is considerably larger than that of the Wright small-volume nebulizer.

We wonder how replacing concentration × 2 minutes at each doubling concentration with the hyperprecision “dose” would improve our ability to provide more clinically relevant answers. In particular, we have found no studies that showed this change to be of sufficiently increased benefit to offset the considerable increase in cost and difficulty of obtaining similar data in virtually all current PFT labs.

If the authors’ recommendations are adopted before such evidence is available, a widely used important test for airway hyperreactivity would become a test that is exclusive to a relatively small number of academic PFT labs in large centers, thus inconveniencing patients in smaller communities who must travel, often many miles, to the centers that are able to implement the change! ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Israel Amirav, M.D.*
University of Alberta
Edmonton, Alberta, Canada
and
Dana-Dwek Children’s Hospital
Tel Aviv, Israel

Michael T. Newhouse, M.D.
McMaster University
Hamilton, Ontario, Canada

ORCID ID: 0000-0002-6917-5285 (I.A.).

*Corresponding author (e-mail: amirav@ualberta.ca).

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Reply to Amirav and Newhouse

From the Authors:

We thank Drs. Amirav and Newhouse for their letter and interest in our editorial on characterizing nebulizer performance for methacholine challenge tests (1). We respectfully disagree with the premise of their letter. We believe that the science and clinical relevance of the previous 1999 guidelines need to be updated. The main problem is that the English-Wright nebulizer is no longer widely available, and if pulmonary function labs were to use as a substitute currently available nebulizers that have much higher aerosol output than the English-Wright nebulizer, every concentration step would deliver a much higher stimulus dose than intended by the 1999 guidelines.

Regarding the need to calculate a delivered methacholine dose, the authors state that we offered no mechanism for how to compel nebulizer manufacturers to characterize the performance of their nebulizer. This was, in fact, the main purpose of our letter: to call out to the manufacturers to provide this essential service. We acknowledged that this would be beyond the capabilities of most pulmonary function labs, but it should be very much achievable by nebulizer manufacturers and aerosol scientists. Our hope was that this letter would emphasize to manufacturers that the American Thoracic Society and European Respiratory Society are counting on them to help the pulmonary function lab community.

The authors also suggest that the data cited regarding the comparison of the English-Wright nebulizer with other nebulizers should include information about other commonly used nebulizers. We certainly agree, and remain hopeful that such data will be forthcoming. The data we cited, including those obtained with a vibrating mesh nebulizer, were simply meant as examples of how dose, not concentration, should be the common unit of measurement across devices.

Regarding the point made about how the current recommendations might not provide more clinically relevant information, we would like to emphasize that at present there is significant variability in the way methacholine challenge tests are performed, resulting in the potential for imprecision and diagnostic error. No other diagnostic test in modern medicine would allow such a lack of rigorous standards or interlaboratory variation. With

better defined and updated methodology, physicians can now have more confidence in the results of testing. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

David Kaminsky, M.D.*
University of Vermont College of Medicine
Burlington, Vermont

Allan Coates, M.D.
University of Toronto
Toronto, Ontario, Canada

Bruce Culver, M.D.
University of Washington
Seattle, Washington

Donald Cockcroft, M.D.
University of Saskatchewan
Saskatoon, Saskatchewan, Canada

Teal Hallstrand, M.D., M.P.H.
University of Washington
Seattle, Washington

Jeffrey Haynes, R.R.T., R.P.F.T.
St. Joseph Hospital
Nashua, New Hampshire

Neil MacIntyre, M.D.
Duke University Medical Center
Durham, North Carolina

Jack Wanger, M.Sc., R.R.T., R.P.F.T.
Pulmonary Function Testing and Clinical Trials Consultant
Rochester, Minnesota

*Corresponding author (e-mail: david.kaminsky@uvm.edu).

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Interstitial Lung Disease and Mediastinal Lymph Nodes: A Computed Tomography–based Biomarker beyond Nosological and Etiological Borders?

To the Editor:

We read with great interest the article by Adegunsoye and colleagues (1) recently published in the *Journal*. Using a rigorous

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