



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

or repetitive antigenic stimulations, combined with advancing age. Epithelial cells could be a significant source of neutrophil chemoattractants, which contributes to a low-grade inflammation in older subjects. Persistent, low-grade inflammation could damage elastin and perhaps lead to the age-associated loss of elastin fibers. Therefore, considering that many patients affected by asthma or COPD who increasingly perform induced sputum are often > 50 years old, these findings deserve further investigations.

Mario Malerba, MD
University of Brescia
Bruno Balbi, MD
Istituto di Gussago Brescia
Brescia, Italy
Antonio Spanevello, MD
Istituto di Cassano Murge
Bari, Italy

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Mario Malerba, MD, Department of Internal Medicine, University of Brescia, I Medicina, Spedali Civili di Brescia, P.zza Spedali Civili n 1, Brescia, Italy; e-mail: malerba@master.cci.unibs.it

REFERENCES

- 1 Thomas RA, Green RH, Brightling CE, et al. The influence of age on induced sputum differential cell counts in normal subjects. *Chest* 2004; 126:1811–1814
- 2 Meyer KC, Ershler W, Rosenthal NS, et al. Immune dysregulation in the aging human lung. *Am J Respir Crit Care Med* 1996; 153:1072–1079
- 3 Ammann AJ, Schiffman G, Austrian R. The antibody responses to pneumococcal capsular polysaccharides in aged individuals. *Proc Soc Exp Biol Med* 1980; 164:312–316
- 4 Thompson AB, Scholer SG, Daughton DM, et al. Altered epithelial lining fluid parameters in old normal individuals. *J Gerontol* 1992; 47:M171–M176
- 5 Abramson SL, Malech HL, Gallin JI. Neutrophils. In: Crystal RG, West JB, ed. *The lung: scientific foundations*. New York, NY: Raven Press, 1991, 553–563

Ribavirin Should Be Tested in Clinical Trials in Combination With Other Antiviral Agents for Severe Acute Respiratory Syndrome

To the Editor:

We read with interest the article in *CHEST* by Chiou et al (July 2005)¹ and offer the following comments. The ribavirin-treated patients had higher lactate dehydrogenase levels, a well-known adverse prognostic factor in severe acute respiratory syndrome (SARS). The nonsignificantly higher mortality could be due to the more severe disease in this group. Viral load, another important predictor of mortality, was not available.² Moreover, Figure 1 seemed inaccurate: the survival in ribavirin-treated patients should be 0.88 at day 30 (5 of 44 patients died) instead of 0.71.

Classifying the ribavirin-treated patients into hypoxemic and nonhypoxemic subgroups (Table 2) and attributing the higher mortality in the hypoxemic subgroup to ribavirin was problematic, as both subgroups were treated with an identical protocol of ribavirin. From the data presented, a more likely explanation for

the more severe drop in hemoglobin in the hypoxemic subgroup was that they had more severe disease. The survival curves in Figure 4 also appeared inaccurate: the survival in patients with drop in hemoglobin > 2 g/dL should be 0.69 (5 of 16 patients died) instead of 0.45. Hence, the result of the log-rank test ($p = 0.007$) needs to be justified.

Only factors that were potentially associated with hypoxemia were analyzed in Table 2. No univariate or multivariate analyses on factors related to death were reported. The conclusion that hemoglobin level was the only factor associated with death was not supported by the data presented.

In Figure 6, the shaded triangles were supposed to represent the hemoglobin of patients who were hypoxemic and had received ribavirin. There were 22 triangles, but there should only be 17 patients. In addition, expressing the survival of individual patients by proportion (y-axis) is difficult to understand.

Therefore, there is no convincing evidence that ribavirin has contributed to a life-threatening drop in hemoglobin or mortality in this report. As of today, three independent studies^{3–5} have shown ribavirin to have *in vitro* activities against SARS-coronavirus, alone or in combination with other agents. Ribavirin should be tested in future randomized controlled studies in combination with other potential antiviral agents for SARS.

REFERENCES

- 1 Chiou HE, Liu CL, Buttrey MJ, et al. Adverse effects of ribavirin and outcome in severe acute respiratory syndrome: experience in two medical centers. *Chest* 2005; 128:263–272
- 2 Chu CM, Poon LL, Cheng VC, et al. Initial viral load and the outcomes of severe acute respiratory syndrome (SARS). *Can Med Assoc J* 2004; 171:1349–1352
- 3 Chu CM, Cheng VC, Hung IF, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax* 2004; 59:252–256
- 4 Chen F, Chan KH, Jiang Y, et al. *In vitro* susceptibility of 10 clinical isolates of SARS coronavirus to selected antiviral compounds. *J Clin Virol* 2004; 31:69–75
- 5 Morgenstern B, Michaelis M, Baer PC, et al. Ribavirin and interferon- β synergistically inhibit SARS-associated coronavirus replication in animal and human cell lines. *Biochem Biophys Res Commun* 2005; 326:905–908

Chung-Ming Chu, MD, FCCP
Kin-Sang Chan, MBBS, FCCP
United Christian Hospital
Hong Kong

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Chung-Ming Chu, MD, FCCP, United Christian Hospital, Hong Kong, PRC

A Modified Percutaneous Tracheostomy Technique Without Bronchoscopic Guidance

A Note of Concern

To the Editor:

We read with interest the article in *CHEST* by Paran and colleagues (September 2004)¹ on a modified percutaneous tra-