

CHEST[®]

Official publication of the American College of Chest Physicians



Adrenomedullin: A Player at High Altitude?

Marcell Toepfer, Gunther Hartmann, Maximilian Schlosshauer, Hubert Hautmann, Matthias Tschöp, Rainald Fischer and Rudolf M. Huber

Chest 1998;113:1428
DOI 10.1378/chest.113.5.1428

The online version of this article, along with updated information and services can be found online on the World Wide Web at:
<http://chestjournal.chestpubs.org/content/113/5/1428.2.citation>

Chest is the official journal of the American College of Chest Physicians. It has been published monthly since 1935. Copyright 1998 by the American College of Chest Physicians, 3300 Dundee Road, Northbrook, IL 60062. All rights reserved. No part of this article or PDF may be reproduced or distributed without the prior written permission of the copyright holder.
(<http://chestjournal.chestpubs.org/site/misc/reprints.xhtml>)
ISSN:0012-3692

A M E R I C A N C O L L E G E O F



C H E S T

P H Y S I C I A N S[®]

of aerosolized albuterol in acute asthma. *Am J Respir Crit Care Med* 1997; 155:454-58

6 National Asthma Education and Prevention Program Expert Panel Report 2: guidelines for the diagnosis and management of asthma (Publication 55-4051). Bethesda, Md: National Institutes of Health, 1997

Adrenomedullin: A Player at High Altitude?

To the Editor:

Adrenomedullin is a potent vasodilating peptide first isolated from pheochromocytoma.¹ Adrenomedullin induces vasorelaxation by activating adenylate cyclase and by stimulating the release of nitric oxide via specific receptors.^{2,3} The messenger RNA is strongly expressed in the human lungs but also in various tissues including heart, aorta, kidneys, thyroid, and adrenal medulla.² Adrenomedullin plasma levels are raised in experimental pulmonary hypertension.⁴ Hypoxemia at high altitude induces increased pulmonary arterial resistance with subsequent increase in pulmonary arterial pressure and can result in life-threatening pulmonary edema.⁵

To examine the pathophysiological significance of adrenomedullin in hypoxic conditions, we measured plasma adrenomedullin concentrations in 10 healthy mountaineers (three women and seven men; mean \pm SD age, 32 ± 5 years) at Capanna Regina Margherita high-altitude research laboratory at Monte Rosa, Italy (altitude, 4,559 m above sea level). Three days after baseline examination at 540 m (barometric pressure, 740 mm Hg), the subjects ascended to 4,560 m (barometric pressure, 410 mm Hg) within a period of 72 h. The ascent consisted of transport by cable car to an altitude of 3,200 m and a 2-h climb to an altitude of 3,600 m, where the subjects stayed for 2 nights. Then another 5-h climb brought the subjects to the high-altitude research laboratory at 4,560 m. The subjects were examined after a 4-h rest on the day of arrival (day 1) and the next morning (day 2). Blood samples were taken with tubes that contained 1 mg/mL disodium EDTA and 500 U/mL aprotinin, centrifuged immediately and stored at -20°C . Plasma ADM levels were measured by specific radioimmunoassay (Phoenix Pharmaceuticals; Mountain View, Calif; intra-assay CV, $<5.0\%$; detection limit, 3.01 pg/mL).

All subjects had severe hypoxia at high altitude (arterial oxygen saturation, $78 \pm 5\%$; partial pressure of oxygen, 45 ± 4 mm Hg; partial pressure of carbon dioxide, 32 ± 3 mm Hg). All subjects developed symptoms of acute mountain sickness (Lake Louise acute mountain sickness score, range, 4 to 9; mean \pm SD, 6.0 ± 1.1), but none of the subjects developed high-altitude pulmonary edema or high-altitude cerebral edema. Plasma adrenomedullin concentrations were significantly higher at high altitude (day 1, mean \pm SD, 32.4 ± 8.3 pg/mL; day 2, 34.1 ± 9.1 pg/mL) as compared with baseline measurements (18.4 ± 3.5 pg/mL; $p < 0.001$) (Figure 1).

These results suggest that adrenomedullin is involved in pathophysiologic changes at high altitude. Exposure to an altitude of 4,560 m leads to a twofold increase in pulmonary arterial pressure.⁵ The role of adrenomedullin in the regulation of pulmonary circulation at high altitude is not clear at present, but high levels of adrenomedullin may be a response to counter hypoxic vasoconstriction in the pulmonary arterial circulation.

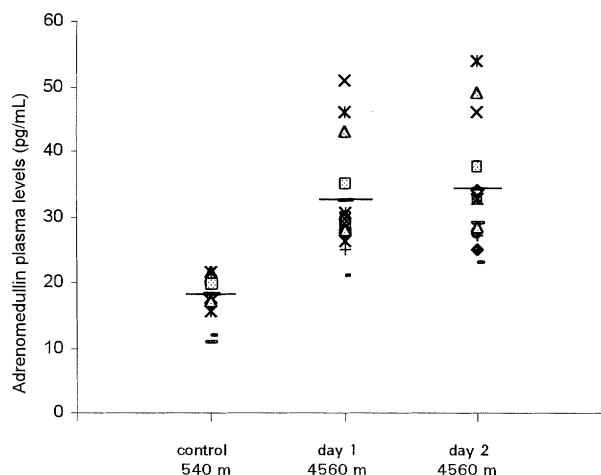


FIGURE 1. Adrenomedullin plasma levels at 540 m before ascent to high altitude (barometric pressure, 740 mm Hg) and on day 1 and day 2 after arrival at 4,560 m (barometric pressure, 410 mm Hg).

The pathophysiological significance of adrenomedullin in the development of high-altitude pulmonary edema needs to be elucidated in further studies.

Marcell Toepfer, MD
Gunther Hartmann, MD
Maximilian Schlosshauer, MD
Hubert Hautmann, MD
Matthias Tschöp, MD
Rainald Fischer, MD
Rudolf M. Huber, MD
Department of Medicine
Klinikum Innenstadt
Ludwig-Maximilians-University
Munich, Germany

REFERENCES

- 1 Kitamura K, Kangawa K, Kawamoto M, et al. Adrenomedullin: a novel hypotensive peptide isolated from human pheochromocytoma. *Biochem Biophys Res Commun* 1993; 192:553-60
- 2 Ichiki Y, Kitamura K, Kangawa K, et al. Distribution and characterization of immunoreactive adrenomedullin in human tissue and plasma. *FEBS Lett* 1994; 338:6-10.
- 3 Shimekake Y, Nagata K, Ohta S, et al. Adrenomedullin stimulates two signal transduction pathways, cAMP accumulation and Ca^{2+} mobilization, in bovine aortic endothelial cells. *J Biol Chem* 1995; 270:4412-17.
- 4 Shimokubo T, Sakata J, Kitamura K, et al. Augmented adrenomedullin concentrations in right ventricle and plasma of experimental pulmonary hypertension. *Life Sci* 1995; 57:1771-79.
- 5 Scherrer U, Vollenweider L, Delabays A, et al. Inhaled nitric oxide for high-altitude pulmonary edema. *N Engl J Med* 1996; 334:624-29.

Solitary Pulmonary Lesion Evaluations

To the Editor:

The article by Goldberg-Kahn et al (April 1997)¹ in which the authors compared the cost-effectiveness of four different strate-

Adrenomedullin: A Player at High Altitude?

Marcell Toepfer, Gunther Hartmann, Maximilian Schlosshauer, Hubert Hautmann, Matthias Tschöp, Rainald Fischer and Rudolf M. Huber

Chest 1998;113; 1428

DOI 10.1378/chest.113.5.1428

This information is current as of April 12, 2012

Updated Information & Services

Updated Information and services can be found at:

<http://chestjournal.chestpubs.org/content/113/5/1428.2.citation>

Cited By

This article has been cited by 1 HighWire-hosted articles:

<http://chestjournal.chestpubs.org/content/113/5/1428.2.citation#related-urls>

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:

<http://www.chestpubs.org/site/misc/reprints.xhtml>

Reprints

Information about ordering reprints can be found online:

<http://www.chestpubs.org/site/misc/reprints.xhtml>

Citation Alerts

Receive free e-mail alerts when new articles cite this article. To sign up, select the "Services" link to the right of the online article.

Images in PowerPoint format

Figures that appear in *CHEST* articles can be downloaded for teaching purposes in PowerPoint slide format. See any online figure for directions.

A M E R I C A N C O L L E G E O F



P H Y S I C I A N S[®]