ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

Volume 151

REGULATION OF PHOSPHATE AND MINERAL METABOLISM

Edited by Shaul G. Massry, Joseph M. Letteri, and Eberhard Ritz

REGULATION OF PHOSPHATE AND MINERAL METABOLISM

Edited by

Shaul G. Massry

University of Southern California
Los Angeles, California

Joseph M. Letteri

State University of New York at Stony Brook and
Nassau County Medical Center
East Meadow, New York

and

Eberhard Ritz

University of Heidelberg
Heidelberg, Federal Republic of Germany

PLENUM PRESS • NEW YORK AND LONDON

Library of Congress Cataloging in Publication Data

Main entry under title:
Regulation of phosphate and mineral metabolism.

(Advances in experimental medicine and biology; v. 151)
"Proceedings of the Fifth International Workshop on Phosphate and Other Minerals, held September 23-27, 1981, in New York City, New York"—P.
Bibliography: p.
Includes index.
1. Phosphorus—Metabolism—Disorders—Congresses. 2. Phosphorus—Metabolism—Congresses. 3. Mineral metabolism—Disorders—Congresses. 4. Mineral metabolism—Congresses. I. Massry, Shaul G. II. Letteri, J. M. (Joseph M.) III. Ritz, Eberhard. IV. International Workshop on Phosphate and Other Minerals (5th: 1981: New York, N.Y.) V. Series. [DNLM: 1. Phosphates—Congresses. 2. Minerals—Congresses. W1 AD559 v. 147/ QV 285 I61 1981m]
RC632.P56M47 599.01'33 82-7602
ISBN 0-306-41020-6 AACR2

Proceedings of the Fifth International Workshop on Phosphate and Other Minerals, held September 23-27, 1981, in New York City, New York

A Division of Plenum Publishing Corporation
233 Spring Street, New York, N.Y. 10013

Printed in the United States of America

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TO OUR WIVES

Meira Massry
Mary Letteri
Christina Ritz

AND TO OUR CHILDREN

PREFACE

We are pleased to present to our readers the Proceedings of the Fifth International Workshop on Phosphate and Other Minerals which was held in New York City, New York, U.S.A during September 23-27, 1981. It was hosted by Joseph M. Letteri, M.D., Professor of Medicine at the State University of New York at Stonybrook School of Medicine, and Chief, Division of Nephrology, Nassau County Medical Center.

As in the previous Workshops, this meeting provided an opportunity for interested scientists from interrelated fields, including nephrology, endocrinology, physiology, biochemistry and nutrition, to get together and discuss the recent advances in the field of phosphate and mineral metabolism. There were 29 invited presentations by leading scientists and 40 oral and 90 poster presentations selected from over 250 abstracts submitted to the Organizing Committee. The Workshop was attended by 250 scientists from 14 countries including Austria, Australia, Canada, Denmark, England, France, Germany, Holland, Israel, Italy, Japan, Sweden, and the United States of America.

The Sixth International Workshop on Phosphate and Other Minerals will be held during June 24-26, 1983 in Verona, Italy. It will be hosted by Professor Giuseppe Maschio, Director, Division of Nephrology, Istituti Ospitalieri, Verona, Italy. The theme of this coming Workshop will continue to focus on the pathophysiology of phosphate homeostasis and the metabolism of other minerals.

We would like to express our thanks and gratitude for all those who have stimulated, encouraged and supported us to hold the Fifth International Workshop in New York City. This endeavor could not have been possible without the generous financial support of the National Institutes of Health, Institute of Arthritis, Diabetes, Digestive and Kidney Diseases (USA), National Kidney Foundation of New York (USA), New York Kidney Disease Institute (USA), Ciba-Geigy Pharmaceutical Company (USA), Cobe Laboratories, Inc. (USA), Gambro, Inc. (USA), Hoffman-LaRoche, Inc. (USA), Plenum Publishing Corporation (USA), S. Karger AG, Basel (Switzerland), The Cordis Dow Corporation (USA), The Proctor and Gamble Company (USA), The Upjohn Company (USA), and Travenol Laboratories, Inc. (USA).

A special tribute goes to Ms. Gracy Fick, Ms. Jeannie Scileppi, and Ms. Claire Ciaccio for their tremendous and invaluable contribution for the organization of the Workshop. Last, but not least, we would like to express our deepest appreciation for Mrs. Mary Letteri for the arrangement of the wonderful and exquisite social events during the Workshop; these were truly memorable occasions.

Shaul G. Massry
Joseph M. Letteri
Eberhard Ritz

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THE ADAPTIVE SYSTEM OF THE TUBULAR TRANSPORT OF PHOSPHATE

J.-P. Bonjour, J. Caverzasio, H. Fleisch,
R. Mühlbauer, and U. Troehler

Department of Pathophysiology
University of Berne
Berne, Switzerland

The present report is an attempt to review the state of our knowledge concerning the adaptation of the tubular transport of Pi in relation with the homeostasis of Pi.

DEFINITION OF ADAPTATION

According to the Webster's New World Dictionary (1), the term "adaptation" when used in biology is defined as "a change in structure or function that produces a better adjustment to environment". Therefore, adaptation of the system responsible for the renal tubular transport of inorganic phosphate (Pi) means a change in its function, i.e. an adjustment of its transport capacity. The Pi transport system in the mammalian nephron is characterized by a maximal rate at which this ion can be transferred across the tubular epithelium from lumen to blood (2). As it will be reemphasized later on, this maximal rate (Tm or max.TRPi) is not an absolute constant since it can be set at different levels according to the physiological or pathological conditions. The renal Pi transport system is essentially a saturable process with no appreciable first order component. This feature implies that Pi can completely disappear from the urine as a consequence of a very small decrement in its plasma concentration, i.e. without any change in the transport capacity at the tubular level. In such a condition, it would be inappropriate to use the term "adaptation", even though the kidney excrete a Pi-free urine.

ASSESSMENT OF OVERALL TUBULAR Pi TRANSPORT CAPACITY AND ADAPTATION

The best and only way of estimating the capacity of the tubular Pi transport system of the whole kidney is to determine the maximal net reabsorption of Pi per unit volume of glomerular filtrate under acute Pi infusion. In clinical practice an indirect estimate of the tubular Pi reabsorption capacity can be obtained by the use of a nomogram based on the relationship between the plasma concentration and the fractional excretion of Pi (3). However, in Pi depletion where the endogenous plasma Pi concentration is usually below the threshold value beyond which Pi appears in the urine, this nomogram cannot be used for estimating the tubular Pi reabsorptive capacity. Therefore, in studies concerning the tubular adaptive response to Pi restriction it is necessary to determine max.TRPi(Tm)/GFR directly by infusing acutely Pi until this value is reached.

EVIDENCE FOR ADAPTATION

That Pi can disappear from the urine in response to a restriction in the alimentary Pi supply has been known for many years (4,5, see also for review ref. 6). However, the definitive proof that this phenomenon was associated with an actual adaptation, i.e. an increase in the overall tubular capacity to reabsorb Pi was brought forward only recently (6,7) with the demonstration that this adaptation was independent of the parathyroid hormone (PTH). It has been shown that the absolute increase in max.TRPi/ml GF induced by a given Pi restriction was virtually the same in intact and chronically thyroparathyroidectomized (TPTX) rats (10). A PTH-independent adaptive increase in the tubular Pi reabsorptive capacity of the whole kidney in response to Pi restriction has been demonstrated in other mammalian species such as the pig (8), and the mouse (9). To our knowlege the demonstration of a PTH-independent change in the tubular Pi transport capacity in response to Pi deprivation in man has not been yet reported.

RENAL ADAPTATION AND Pi HOMEOSTASIS

The fact that the renal tubule can react to the amount of Pi supplied by adjusting its Pi transport capacity has some important consequence for the homeostasis of Pi. It is obvious that because of this adaptive mechanism the plasma Pi concentration will be less dependent upon variations in the amount of Pi supplied in the diet. Another homeostatic consequence of the adaptive response is related to the conservation of the Pi mobilized from body stores during the daily fasting or postabsorptive period. Indeed, in Pi deprived animals this amount of Pi which enters the extracellular compartment from body stores