The Transfer of Calcium and Xontium
Riological

Edited

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The Transfer of Calcium and Strontium Across Biological Membranes

Proceedings of a Conference held at Cornell University Ithaca, New York, May 13–16, 1962

Edited by

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PREFACE

The present volume represents the proceedings of a Conference held at Cornell University, Ithaca, New York, May 13–16, 1962. The Conference, being of the same name as the title of this book, was organized upon the recommendation of a number of experts in the field. It was felt that there was enough new information and concepts becoming available to warrant a gathering of investigators for purposes of discussion and exchange of information. With the kind support of the U. S. Atomic Energy Commission, the National Institute of Dental Research, the National Science Foundation and Cornell University, such a meeting was made possible.

Calcium, of course, is an essential cation necessary for the functioning of several enzyme systems, for blood clotting, for normal nerve and muscle function, for bone formation and for maintaining the integrity of biological membranes. Its concentration in blood and other body fluids is closely controlled primarily by the action of the parathyroid glands. Strontium, not known to have any biological function, is of interest because of its presence in fissionable material and, for this volume, because of its similarity (chemical, physical and biological) to calcium. Considerable time and effort has (and is) being given to the problem of how calcium functions in these several systems. Perhaps related to this and of equal importance, is the question of how calcium moves across cells and cellular membranes. One may ask, for example, what types of transfer processes are involved and which predominates under normal physiological and nutritional situations? In reference to intestinal absorption, what mechanisms are available for altering the degree of calcium transfer in response to varying calcium intakes. How does vitamin D exert its effect? And what of the other factors, such as lactose, that also influence these processes? Is calcium reabsorbed from the kidney tubule by the same mechanism that operates in the intestine?

The problems concerning radiostrontium (Sr⁸⁹ and Sr⁹⁰) are perhaps somewhat different but just as significant. After these radionuclides have been absorbed and deposited in bone, only a small amount can be removed except by exceedingly drastic measures. A more promising approach would be to prevent or depress their intestinal absorption as quickly and as efficiently as feasible. In order to attack this problem intelligently, one should know by what process or processes strontium is actually absorbed.

It was to such problems and questions as alluded to above that the theme of this volume (and the Conference) was addressed. Certainly, all of the answers are not yet available and many of the solutions are still many years away. It is hoped that this undertaking will serve to shorten, if only briefly, the lag time.

xii PREFACE

With gratitude, the fine cooperation of the program committee, consisting of Dr. R. H. Barnes (Cornell University), Dr. C. L. Comar (Cornell University), Dr. D. H. Copp (University of British Columbia), and Dr. H. E. Harrison (Johns Hopkins University) is acknowledged. Sincere appreciation is extended to the session chairmen who also served as sectional editors, these being: (I) Dr. A. K. Solomon and Dr. P. F. Curran (Harvard University), (II) Dr. B. B. Migicovsky (Canada Department of Agriculture, Ottawa), (III) Dr. R. Nicolaysen (University of Oslo, Norway), (IV) Dr. Bertil Lindquist (University of Umea, Sweden), (V) Dr. Felix Bronner (Hospital for Special Surgery, Cornell Medical Center), (VI) Dr. F. C. McLean (University of Chicago), (VII) Dr. D. H. Copp (University of British Columbia). Many others, particularly Howard Spicer, Jennifer Wheldon, Ruth Ditzell and Eleanor Rosica, were most helpful in the organization of the Conference and in the preparation of the discussion for the publisher. The suggestions and advice of Dr. C. L. Comar proved most valuable and his contributions are acknowledged with many thanks.

Ithaca, New York October, 1963 R. H. WASSERMAN

INTRODUCTORY COMMENTS

Rapid progress in the gaining of fundamental knowledge is bound to result from a happy convergence of men with ideas and motivation, an opportunity for personal communication, a highly developed state of the art, and availability of material capabilities. The men with ideas are well represented here as contributors to this conference on calcium and strontium transport. The conference itself provides the market-place for ideas where sparks are expected from the clash of minds. Over the years there has been a sustained research interest in the nutritional and physiological aspects of calcium metabolism. Nevertheless, it is fair to state that the problems posed by the advent of atomic energy on a large scale provided considerable motivation and stimulation that led to intensification of studies of both calcium and strontium. Ironically, but perhaps with a measure of poetic justice, the same developments that brought the issue into being have also provided specific experimental tools and material capabilities that have furthered the solution of these problems as well as of many others.

Since the very early experiments, it has been generally accepted that calcium and strontium are interrelated in metabolic behavior. This means first of all that possible effects of radioactive strontium should be looked for in relation to those functions known to be dependent upon calcium:—skeletal processes, coagulation of blood, contractility of muscle, reactivity of the nervous system, and linkage in the nucleus of the cell. There is still a mild controversy about whether the behavior of adventitious radiostrontium in the mammalian organism is governed by the levels of stable strontium or by the homeostatic action of calcium plus strontium. Though many incline to the latter view, numerous observations yet remain to be explained. Hopefully, clarification will be provided by an understanding of the details of transport (e.g. competition, if any, for binding sites; carriers; energy sources). This conference, not entirely by chance, comes at a time when research in the broad area of mineral metabolism is about to take another tack. We know reasonably well what happens in the body under certain conditions to minerals such as calcium and strontium. Now we require to know why it happens and how we can change the pattern of events at will.

When the strontium problem first blossomed, it was optimistically thought that all the necessary information was existent in the voluminous literature on calcium:—ready for the taking. But the welter of conflicting views on even the most mundane aspects of calcium metabolism was disillusioning. It appeared that, if generalizations were to be possible, there must be much more basic information provided to shore-up the innumerable ad hoc findings.

It has been gratifying in a sense to see in recent years the interplay between practical needs and the fundamental approach. There has been general recognition and acceptance of the idea that feasible practical solutions will most likely be attained only if there is basic understanding of many aspects. The research that has been stimulated is no less fundamental or imaginative because of foreseeable relevance.

C. L. Comar

The Transfer of Calcium and Strontium Across Biological Membranes

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SECTION I.

Fundamentals of Ion Transfer Across Membranes