Meetings

Calcified Tissues

Regular meetings at which progress in research is reported are needed in all fields but especially by those which attract the interest of workers from many disciplines. Those interested in calcified tissue research have come to depend on the annual Gordon Research Conference on the Chemistry, Physiology, and Structure of Bones and Teeth and more recently on the annual European Symposia on Calcified Tissues to keep in touch with the work and views of colleagues from other centers on both sides of the Atlantic. While various areas of the field have recently been covered in depth by special symposia these two series of conferences provide the only forums where the full breadth of applicable research is covered and the many disciplines represented meet regularly.

The fifth in the series of European symposia was organized at the invitation of the French workers in Bordeaux, 5–8 April 1967. Most of the western European countries were represented and a number of investigators from the United States, Canada, and Israel attended. Crystallographers and inorganic chemists, cell physiologists, and biophysicists shared the podium with internists, orthopedic surgeons, and anatomists. Unlike the Gordon Conference these programs have been largely composed of short communications selected by the organizing committee from among those submitted by the participants. Each section also contained one longer presentation designed to bring the audience up to date with the current status of work in the area under discussion as well as to present the invited speaker's own investigations.

The mineral phase received the major emphasis in discussions of skeletal physiology and structure at the molecular level. Chemical studies of the kinetics of precipitate formation and crystallographic evidence of an amorphous as well as a crystalline phase in calcium phosphate precipitates in vitro and bone mineral are beginning to combine to indicate that the deposition of bone mineral is probably a three-phase process. This process begins with the formation of primary nuclei which then serve as secondary nucleation centers and ends with "maturation" of amorphous material into ordered crystals. Several lines of evidence suggest that local supersaturation with either calcium or phosphate may be required to initiate this process although so far the nature of the mechanisms which might be responsible remains unclear. In this connection the old idea that alkaline phosphatase might somehow be involved was revived once more by the interesting observations of two laboratories (Hekkelman in Leiden and Russell *et al.* in Davos) that alkaline phosphatase, adenosine triphosphatase, nicotinamide-adenine dinucleotide phosphatase, and pyrophosphatase in bone may well be the same enzyme.

Several observations regarding collagen turnover, changes in glycolytic activity of bone cell, and content of nucleic acid in various states were recorded, thus indicating that interest in the biology of the organic phase remains active. Of particular interest to a number of workers was the excellent summation provided by Travis of the interrelations of organic and mineral phase structures at the submicroscopic level. The close correlations between tubules of organic material which seem to serve as sheaths for the prismatic macrocrystals of dental enamel were a striking new observation in this area.

Disturbance in genetic mechanisms as a possible cause of skeletal disorders has received little attention. Eisenberg's careful study of the genetic background of a family afflicted with hypophosphatasia not only provided useful new information about this disease but also could serve as a good model for this type of work. Hurley observed that a deficiency in manganese reproduced a genetically determined ataxia in mice. The ataxia turn seemed to be caused by a failure of otolith formation. Such results raised a lot of speculation about the relation of manganese to calcification mechanisms on the one hand and possible genetic effects on transport mechanisms on the other.

Once again bone disease whether induced by dietary deficiency or other causes provided experimental models which helped provide new insights into normal mechanisms. New observations on the effects of vitamin D in pregnancy, in resistant rickets, on calcium homeostasis, and in stress were reported in this area.

The effects of hormones on skeletal systems have long been a subject of study. The session on hormones and their effects was largely dominated by discussions of thyrocalcitonin. Particularly noteworthy was the excellent summation of the present state of knowledge about this newly discovered hypocalcemic material provided by MacIntyre. Potts indicated that it is now possible to prepare thyrocalcitonin in a high state of purity which permits its size and amino acid sequence to be quite accurately determined. The importance of these observations to the measurement of the hormone in vivo and in vitro and to investigations of its mode of action are obvious.

A variety of observations regarding the presence of this hormone and its biological effects were reported. Arnaud was able to find thyrocalcitonin activity in plasma of normal pig suggesting that significant levels are normally to be found in the circulating body fluids. It was of interest that despite general agreement that the effects of thyrocalcitonin are mediated through skeletal mechanisms—specifically bone resorption—no incontrovertable evidence has yet been obtained as to its precise site or mode of action in the skeletal system.

Not unexpectedly, parathyroid hormone received considerable attention. Further work of purification and characterization especially of human hormone was reported from Aurbach's laboratory. This work indicates that human hormone is very similar to bovine, but minor differences in amino acid composition appear to be present which could explain observed differences in immunogenic activity. Relationships between parathyroid activity and acidosis were reported which recalled older work suggesting an interrelationship between these two factors in the production of renal osteodystrophy. Modification of glucose transport

activity in the renal tubule by parathyroid hormone was also reported, a finding which might have importance as a means of determining parathyroid activity in clinical situations.

Although absorption of calcium and phosphate from the gastrointestinal tract has been a favorite topic of investigation for many years no real progress in understanding the mechanisms involved occurred. It was not surprising, therefore, that Wasserman's report of a calcium-binding protein in the intestinal mucosa of chicks was greeted with such interest when it first appeared 2 years ago. Participants were particularly grateful, therefore, to be brought up to date on the most recent developments in this work. This protein appears to constitute 2 percent of the total protein in the soluble supernate of homogenates of isolated mucosal cells. It has a molecular weight of around 28,000, a very high electrophoretic mobility and a high affinity for calcium.

An important physiological role is suggested for it since the amount present seems directly proportional to the amount of vitamin D present in the organism and to the rate of calcium absorption as measured in vitro. Experimental manipulation of calcium absorption by vitamin D deprivation, and by adaptation to diets low and high in calcium content with subsequent measurement of this protein appear to confirm this point of view, as do the relative concentrations to be found in various parts of the small bowel. For example, the highest concentration is in the duodenal mucosa which has been shown by a number of workers to be the site of the greatest active transport of calcium along the gut. A 55-fold purification of the material has permitted a preliminary estimate of amino acid composition. These analyses indicate a high carboxylic acid content which may well be related to its strong chelating action. Finally it was of more than passing interest to learn that the relative binding constant for calcium is higher than that for strontium by a factor of approximately 25 percent, an observation which may provide the explanation for the ion discrimination in gut absorption.

A number of new techniques for examining bone were discussed. The enormous potential for examining the amount and composition of bone mineral at microscopic sites offered by electron probe analysis, and the measurement of skeletal density by absorption of a photon beam both evoked marked interest. The electron probe technique will provide a visual map of the distribution of any element in a thin section of undecalcified bone with a precision of one micron or less. Sensitivity is of a very high order but there are many pitfalls which must be avoided which include errors arising from uneven thickness of the section, irregularities in the surface plane of the section and other factors.

The new technique of photon beam densitometry has been brought to a high level of precision and practicality. Two groups reported on this technique (Nilsson in Malmö, and Cameron *et al.* in Madison). It appears that it is soon to become the standard method for estimating change in skeletal mass in vivo.

The organizing committee reported that it intended to publish the proceedings of the conference. It was announced that the sixth symposium would be held in Lund, Sweden, at the end of August or early September 1968. The seventh symposium was tentatively scheduled for Italy, probably to be held in the spring of 1970.

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Indian Ocean

That oceanography has come of age in recent years is evident from the increasing interest many nations are taking to study the oceans. It is increasingly evident that man's future lies in harnessing the vast food and mineral resources of the world's oceans. The Indian Ocean, which was until recently the least studied and was hence a mare incognito, is by virtue of international expeditions for several years (1960–65) now better understood. In order to assess the results achieved by the International Indian Ocean Expedition a symposium on the Indian Ocean was held in New Delhi, 2–4 March 1967.

A concerted use of marine resources —both food and mineral—were advocated by D. N. Wadia (Indian National Committee of Oceanographic Research), Atama Ram (C.S.I.R.), T. R. Seshadri (National Institute of Sciences of India), and N. K. Panikkar (National Institute of Oceanography, India). Seshadri, while pointing out that the sea was an immense source of food and minerals, remarked that even the seaweeds, now considered useless, could provide valuable materials such as algin and agar.

In the field of physical oceanography the symposium brought out the finding based on the cruises of the I.N.S. *Kistna* that the concentration and the thickness of the oxygen-rich layer were greater in the Arabian Sea than those in the Bay of Bengal. This is noteworthy because there are certain regions in the Arabian Sea where the supply of oxygen is low causing the large-scale death of marine fauna. In the Bay of Bengal the thickness of the oxygen-poor layer appeared to be increasing toward the north.

On the basis of the first cruise of the R. V. *Anton Bruun* in the spring of 1963 and studies by other vessels, E. C. Lafond (U.S. Navy Electronics Laboratory) remarked that the northeasterly and southwesterly monsoon winds largely control the surface circulation, resulting in clockwise or counter-clockwise circulation of the entire bay as well as large gyral circulations in different areas of the bay. Lafond reported occurrence of peripheral upwelling along the Burmese coast when the northeasterly monsoon prevailed. Upwelling developed along the east Indian coast when the southwestern monsoon became strong. These upwellings, though short-lived, affect organic production in the Bay of Bengal.

L. V. Gangadhara Rao and R. Jayaraman (National Institute of Oceanography) reported the existence in the upper 50 meters of the Eastern Bay and the Andaman Sea, a low salinity water mass. The Indian Ocean equatorial water (temperature, 4° to 16°C; salinity, 3.48 to 3.52 percent) was encountered as the major subsurface water mass below 100 to 150 meters in depth. They also detected traces of Persian Gulf water and regions of convergence and divergence in the Bay of Bengal. These authors reported some of the interesting findings such as the core of high salinity water and spreading of thermocline in the region of the equatorial under current where a few sections were worked by the I.N.S. *Kistna.*

Scientists from the Indian Naval Physical Laboratory (Cochin), K. V. Sundararamam, C. K. B. Kurup, and K. V. Sriramamurty, identified various