may be considered as a relatively simple biological analog of the kidney. The stimulatory effect of the hormone vasopressin on the transport of Na^+ requires that the hormone be on the serosal side of the membrane in spite of the fact that the rate-limiting step apparently occurs in the mucosal barrier. Similar experiments may shed light on the role of K^+ in the transport of Na^+.

Because of the great difference in complexity of the organisms under study, it is unlikely that the remarkable progress characteristic of recent microbial investigations will soon be paralleled in studies on animals. Nonetheless, it was apparent from the meeting that the results obtained from microbial studies are rapidly finding application in animal work and that noteworthy advances are being made in elucidating control mechanisms in the higher species.

The program was arranged by D. Stetten, Jr., and O. Touster in collaboration with the session chairmen. The National Institutes of Health awarded a generous grant in support of the symposium.

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Endocrine Control of Growth

A symposium on growth, sponsored by the Division of Comparative Endocrinology of the American Society of Zoologists, was held on 28 December 1962 in Philadelphia. Interest in comparative endocrinology has steadily increased in the last decade. The Division now has close to 400 members, and attendance at this symposium was large.

Previous work has shown that systems analysis of endocrine control of lower animals might very well be extrapolated to an analysis of endocrine control in the higher vertebrates. A prime example of this is neuroendocrine integration and the structure of neurosecretory cells. Although previous symposia on comparative endocrinology, including three international congresses, have been successfully conducted in recent years, none has been primarily concerned with growth processes. The present symposium had as its aim the discussion of not only those well-known vertebrate hormones that may act on growth but also substances affecting growth in lower animals, and even plants, where the classical definition of a hormone could not possibly apply. In addition, speakers invited to participate were, in general, established workers in the field who had not presented similar material at the last two international congresses of comparative endocrinology.

The plant growth substances, discussed by Bruce Stowe (Yale), proved to be most stimulating to the zoologists present. Because the indoles are the major auxins, a technique was developed whereby neutral indoles could be separated and identified by gas chromatography with a Versamid 900 column. Since this technique is specific for neutral indoles, any indole acids to be studied must first be converted to neutral products. Since gas chromatography by flame ionization can detect parts per billion, this technique could allow detection of auxins in specific growth regions and perhaps obviate the use of bioassays. Although the structure of some gibberellins is now known, their mode of action in restoring normal growth to mutant dwarf plants is still an open question. It is now believed that the gibberellins interact with the auxins and kinetin-like substances to bring about homogeneous growth in some plants. A most interesting series of experiments involving the local application of kinetin-like substances to plant leaves was discussed in detail by Stowe. The results indicate that these substances act to mobilize amino acids in the plant and thus result in enhanced protein synthesis. Of great interest was the report that certain lipids enhance the synergistic action of auxin and gibberellic acid in promoting plant growth. Substances such as methyl linoleate have a profound effect when applied with the plant growth substances, and although the reason for this effect is still not known, it is reminiscent of the action of certain lipids in enhancing the effect of insect growth hormones.

The "immortal" hydra was the subject of Burnett's (Western Reserve) discussion. Although hydra is a vigorously polarized animal, grafting experiments have indicated that the polarity can be inverted. A substance is produced in hydra which has the capacity to induce head formation. Assay animals placed on an agar block containing an extract of this material form many heads and in some cases appear to be a mass of heads. Burnett believes that growth in hydra is controlled by both growth-promoting and growth-inhibiting substances, although the presence of two different substances has not been conclusively demonstrated. Burnett argued that the rapidly proliferating hypostomal region of hydra contains neurons that may be neurosecretory. Neurosecretory stains indicate that there are granules in the cell bodies and in the axons. In the discussion following this paper it was pointed out that neurosecretory-like elements have been noted in hydra under the electron microscope. If these observations are confirmed, it will mark the first demonstration of neurosecretion in the Cnideria, a phylum where the occurrence of any type of neuron at all has been a matter of conjecture for a long period of time. Whether the activity of these "neurosecretory cells" is requisite to growth in hydra is not yet known.

Although the basic endocrine control of molting in decapaod crustaceans remains as postulated several years ago, Bliss's (American Museum of Natural History) recent studies have indicated the extreme importance of environmental conditions on the pre-molt (proecdysis) stage. She reported on her recent studies which indicate that photoperiod, moisture, temperature, and the presence or absence of other crustaceans affect the onset of proecdysis. That is, the animal will only enter proecdysis when it is more or less assured that environmental conditions are favorable for surviving those critical days following the shedding of the exoskeleton when it is no longer protected by its hard outer skin. Thus stress situations will prevent the onset of this hormonally-controlled process. The ability of the crustacean to alter its molting cycle in this manner may be one reason for the long survival of this class of animals.

One of the highlights of the symposium was Howard Schneiderman's (Western Reserve) penetrating analysis of recent developments regarding insect hormones. A dozen pure compounds have been found to possess juvenile hormone activity; the majority of them are terpenes. All these substances have the ability to prevent certain parts of the insect from assuming their adult aspect. It is of great interest to note that although these compounds do have juvenile hormone activity, it is very unlikely that any is the true insect juvenile hormone since all are far less active than crude insect juvenile hormone extracts. Further work has shown that a whole host of steroids possess brain hormone activity and that one compound has both brain hormone and juvenile hormone activity. If terpenes (steroid precursors) and steroids prove to be the materials from which insect hormones are synthesized, it is possible that steroid hormones are not a recent innovation of the vertebrates but may have controlled physiological processes in animals from earliest times. In this connection it was noted that insects cannot synthesize steroids, at least by way of the conventional biosynthetic pathways, but do possess the mechanisms necessary to modify dietary sterols. The mode of action of the insect molting hormone appears to be on the chromosomes of the cells affected. The report on Clever's recent experiments with the giant polytene chromosomes of flies revealed that the insect growth hormone may actually cause enhanced metabolic activity of specific gene loci within minutes of being administered. Since the juvenile hormone acts in conjunction with the molting hormone and modifies the route of the molt, it may also act on the genetic machinery or on messenger compounds whose ultimate information comes from the genes.

On the basis of pituitary grafts and histological examination, Etkin (Albert Einstein College of Medicine) has demonstrated that implanted pituitary tissue cannot cause metamorphic climax in tadpoles although growth occurs. Etkin proposed that the thyroid hormone stimulates the hypothalamus resulting in an increased titer of neurosecretory substance and hypothalamic maturation. Thyroidectomy prevents development of the median eminence, whereas exogenously administered thyroid hormone causes metamorphosis and median eminence development. The hypothalamus in turn inhibits release of the growth hormone while release of thyrotropin is stimulated. In this manner the rising titer of thyroid hormone in the tadpole inhibits growth and favors the attainment of thyroid hormone levels which will produce metamorphic climax. Baker-Cohen (Albert Einstein College of Medicine) discussed growth hormone in fishes in relation to thyroid hormone and thyrotropic hormone. A synergistic effect was noted when growth hormone and thyrotropic hormone were administered simultaneously, but it is due most likely to the fact that the thyroid hormone itself sensitizes the target tissues to growth hormone. In addition, the thyroid hormone most likely aids in maintaining proper pituitary function.

After discussing an exception to the generally accepted postulate that growth hormone controls growth in mammals, Ernst Knobil (Pittsburgh) presented a stimulating talk on the mode of action of growth hormone in monkeys and rats. The exception is the guinea pig, where hypophysectomy does not arrest growth and administration of exogenous growth hormone is ineffective. Recent studies indicate that growth hormone in mammals acts to increase protein metabolism perhaps by increasing the active uptake of amino acids in target organs. In vitro studies on the rat diaphragm, with labeled α-aminoisobutyric acid (AIB), have demonstrated that growth hormone stimulates the active transport of amino acids into the cell. However, not all amino acids are so stimulated. It is therefore possible that growth hormone has an indirect effect upon protein anabolism by stimulating the active transport mechanism in the cell, and may not play a role in the actual formation of protein from precursor amino acids. These studies on the mobilization of amino acids in the cell are in many ways similar to the proposed action of the kinetin-like substances as discussed by Stowe.

The remainder of the symposium was devoted to three papers on diverse subjects. One by Price (Chicago) was concerned with hormonal control of embryonic gonad growth. Past studies have shown that the female is the neutral sex in mammalian embryos and that the gonadal hormones of the male act to bring about the differentiation of the male condition. Price summarized her studies on the bioassay of embryonic gonadal hormones by organ culture techniques and then in a truly comparative review discussed the size and hormone activity of the embryonic gonads in mammals as diverse as the horse, giraffe, elephant, and seal. It appears that in all of these organisms the fetal ovary is actually larger than that of the mother. It has been demonstrated in the horse that this fetal ovarian hypertrophy is associated with a concomitant release of estrogens. Since most endocrinologists (including those working on invertebrates) utilize animals in the postembryonic state, Price's paper suggested crucial experiments with other animal forms.

Edgren (Wyeth Laboratories) discussed his experiments on the effects of combinations of estrogens and of estrogens with other steroidal agents on mouse uterine growth. On the basis of a mass of statistically interpreted data, Edgren has conceived a theory regarding the competition of these steroids for uterine "sites." He believes that there are two receptor sites for estrogens in the uterus, analagous to the active sites of enzymes. One site would accept estrone and certain other steroids, whereas the other site would accept estriol and testosterone. Edgren suggests that this interpretation would explain how the uterus responds to a shifting pool of steroid hormones which may have synergistic or antagonistic interactions. The last paper dealt with the local effect of thyroxin on amphibian metamorphosis and was presented by Jane Kaltenbach (Mt. Holyoke). By implanting cholesterol pellets containing thryoxin, local metamorphosis can be obtained, even in the muscles responsible for movement of the eyeball. This suggests a direct action of thyroxin on the target tissues and organs and is similar in many respects to bioassays of certain insect growth hormones where only those cells in immediate contact with the hormone respond. Perhaps an in vitro system utilizing tadpole tissues and thyroid hormone will be extremely useful for those biochemists interested in growth processes.

According to comments received from participants, senior members of the audience, and graduate students, this symposium was extremely successful. Many of us attending the symposium returned to our laboratories convinced that comparative endocrinology has only recently entered its logarithmic phase of growth. Similar symposia sponsored by the Division of Comparative Endocrinology are planned for the International Congress of Zoology and for future annual meetings of the division.

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