Comparative Vertebrate Endocrinology

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Preface

This book has been written primarily for use as a textbook by undergraduate, as well as graduate, students. It is hoped that it may serve as a basis for course work in Comparative Endocrinology and also as an auxiliary text to aid the teaching of Comparative Animal Physiology. In order to gain most from this book, the reader should have a basic knowledge of zoology and animal physiology. I have, nevertheless, attempted to put the endocrinology that is described into a broader biological framework by relating it to the animal's physiology, ecology and evolutionary background. This is one of the reasons why I have departed from the more usual format of previous textbooks in this area which generally deal with each endocrine gland in succession, chapter by chapter. Instead, I have attempted to describe certain broad and basic biological processes the functioning of which is often coordinated by the secretion from several endocrine glands.

No attempt has been made to describe invertebrate endocrinology as the rapid growth of this area really justifies a separate textbook. The book by K. G. Highnam and L. Hill (*Comparative Endocrinology of the Invertebrates*, Elsevier: Amsterdam, 1970) deals admirably with this subject.

It has not been possible in a book of this nature to give a complete list of original references. There are far too many of these and many of the earlier observations are already a part of the 'classical literature'. Instead, I have attempted to refer the reader to more recent papers and reviews that contain references to the material described and can act as useful 'starting points' for those students who wish to study the subject further. In order to keep abreast of developments in the various subject areas described, the current literature should be consulted. The principal journals where papers on these subjects are published are: *General and Comparative Endocrinology*, *Journal of Endocrinology*, *Endocrinology and Comparative Biochemistry and Physiology*. There are, in addition, many papers that appear in the standard physiological journals, especially *Journal of Physiology* and *American Journal of Physiology*.

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Some commonly used abbreviations in endocrinology

ACTH	adrenocorticotrophic hormone
ADH	antidiuretic hormone
AMP	adenosine 3′,5′-monophosphate
AVP	arginine-vasopressin
CBG	cortisol-binding globulin
COMT	catechol-*O*-methyl-transferase
CRH	corticotrophin-releasing hormone (= CRF)
CT	calcitonin
FSH	follicle-stimulating hormone
GH	growth hormone
Gn-RH	gonadotrophin-releasing hormone (= LH/FSH-RH)
HCG	human chorionic gonadotrophin
HCS	human chorionic somatomammotrophin (= HPL)
HIOMT	hydroxyindole-*O*-methyl-transferase
HPL	human placental lactogen
HTF	heterothyrotrophic factor
ICSH	interstitial cell-stimulating hormone (= LH)
-IF	– inhibiting-factor
-IH	– inhibiting-hormone
LH	luteinizing hormone (= ICSH)
LTH	luteotrophic hormone (= prolactin)
LVP	lysine-vasopressin
MAO	monoamine oxidase
MI	melanophore index
MSH	melanocyte- (or melanophore-) stimulating hormone
MRH	melanocyte-stimulating hormone-releasing hormone
PNMT	phenylethanolamine-*N*-methyl-transferase
P-	prolactin (prefix as in P-RH)
PTH	parathormone
-RF	– releasing factor
-RH	– releasing hormone
-R-IH	– release-inhibiting hormone
SHBG	sex hormone-binding globulin
T_3	tri-iodothyronine

T_4	tetra-iodothyronine (= thyroxine)
TBG	thyroid hormone-binding globulin
TRH	thyrotrophin-releasing hormone
TSH	thyroid-stimulating hormone (= thyrotrophin)

Contents

1. Introduction

This book describes a method of transferring information within vertebrates. Such communication is necessary in order to coordinate physiological processes with each other and to the happenings in the external environment. Even unicellular organisms synchronize their various internal life processes. In such small creatures, however, local accumulations of metabolites may exert a direct control on biochemical reactions, while external stimuli have relatively widespread effects so that specialized pathways for communication may not be as necessary. Thus when the distances involved are short, physical processes such as conduction, convection and diffusion may be adequate for the integration of the physiological processes. Nevertheless, even unicellular organisms possess specific coordinating systems such as that seen in the protozoan *Tetrahymena* (Blum, 1967) which possesses adrenaline. This hormone has similar metabolic actions in this protozoan to those which it has in vertebrates.

The problems of communication and coordination are greater in multicellular than in unicellular organisms. There are several reasons for this, especially their larger size. As the linear distances between the different parts of an animal increase, simple physical communications become relatively slower and less precise, and so not as effective. In multicellular organisms, the cells are usually specialized and perform different functions which, in combination, are essential for the animal's life. Thus some tissues may be concerned with the formation of reproductive germ cells, several others with the preparation of suitable nutritive materials and yet others with building morphological structures. The ultimate successful completion of these processes will be determined by the effectiveness of the communication between the tissues themselves and the external environment.

The transfer of information in animals

There are three principal ways by which cells in multicellular organisms can communicate with each other. Firstly, when they are in close juxtaposition, and are only separated by narrow fluid-filled spaces, direct electrical and chemical interactions can occur. Cells also maintain some structural connections with each other across which they may also communicate. Secondly, contact between more remote cells can be maintained along tracts of nerve cells which are merely tissues that are specialized for such exchanges of information. Thirdly, chemicals may be released, for example from the endocrine glands, into the blood which carries them to special sites that are physicochemically programmed to react and respond to them.

The endocrine glands are tissues that, unlike exocrine glands, have no ducts but release their secretions, called 'hormones', directly into the blood passing through them. It is with the diversity of such hormonally controlled processes that we are going to be principally concerned in this book. It should, however, always be recalled that the endocrine gland represents only a single facet of the animal's communication network, and that nerves are also important. Endocrinologists and neurophysiologists have often only concentrated on their own special fields of study to the relative exclusion of the rest of the animal's physiology. This is unfortunate as the complete animal is an academically and esthetically pleasing thing to see and contemplate, and any single facet taken from the whole becomes less interesting and is physiologically nonsensical. The relations of nerves and endocrines, however, can also be considered from a more direct standpoint as it is apparent that the functions of each are related to each other. They are often mutually interdependent and may even act together to control a single process. Nerve cells thus can respond to hormones in a manner that influences behavior and endocrine glands often receive information and directions from the brain. Both hormones and nerves can act together to control the melanophores in certain fishes. Some hormones, including adrenaline, vasopressin and oxytocin, are even made by nerve cells.

Neural versus humoral coordination

It is uncertain which came first; nerves or hormones. Why do animals have both? It may help us to understand hormones if we compare their respective properties and roles in the body.

The neural transfer of information occurs along distinct morphological pathways made up of chains of nerve cells with their long axons. Transmission along these avenues is fast (up to about 100 m/sec) and is directed precisely to specific sites in the body. Neural transmission involves a series of electrical events interrupted at intervals by a local release of chemicals (transmitters), and is concluded by the release of these, principally acetylcholine or a catecholamine (such as noradrenaline) close to the effector tissue. Such a transmitter is then rapidly destroyed near its site of action. Further stimulation will be dependent on subsequent neural transmission.

The effect is thus rapid in onset, short in duration and can be localized with considerable accuracy.

The hormones, on the other hand, are released into the blood which carries them towards their effector site(s). In most instances this is outside the cardiovascular system so that the hormone must also cross capillaries and diffuse through the intercellular spaces to the site of its action. Not surprisingly, hormonal responses are slower than those mediated by nerves. Hormones are dispersed very widely in the body and so come into contact with a great variety of cells with which an interaction, in most instances, would not be fruitful. The problem of ensuring that hormones only act at specific sites is largely solved by the multiplicity in their chemical structures. (There are over 40 different known hormones in a mammal.) Complementing such variations are parallel differences in the chemical structures of the sites where they interact ('receptors') with their target (or 'effector') cells.

A hormone can exert widespread effects by interacting with different effector tissues (for instance estrogens act on the uterus, mammary glands, liver, brain, etc.). The characteristics of the receptors in each may differ just as the response will vary. A hormone thus may act very specifically at each of several sites in the body and yet, at the same time, exert many different actions.

Perhaps the most physiologically significant difference between neural and humoral communication is in the duration of the actions of the transmitters involved. Because their transmitters are rapidly destroyed, nerves must be repetitively stimulated if their effects are to be prolonged. While hormones also have a finite period of survival, the duration of their effects varies from less than a minute to several days. Some hormones, once released into the circulation, survive in it for many hours. When some reach their receptor sites, the initiated response may be of a persistent nature that is not readily terminated. Thus if an endocrine gland is removed, it may be several days before physiological signs of its absence became apparent. Hormones are thus sometimes described as exerting their effects slowly but persistently, in contrast to the more rapid and transient actions of nerves. There are, however, exceptions to such a generalization.

What is comparative endocrinology?

Comparative endocrinology concerns the study of the endocrine glands in different species of animals, both vertebrates and invertebrates. Its aims are analogous to the older and more classical disciplines of comparative anatomy and comparative physiology. The prime academic objective is to reconstruct evolutionary pathways by the study of extant species. Fig. 1.1 shows the phylogenetic relationships of the vertebrates and this emphasizes

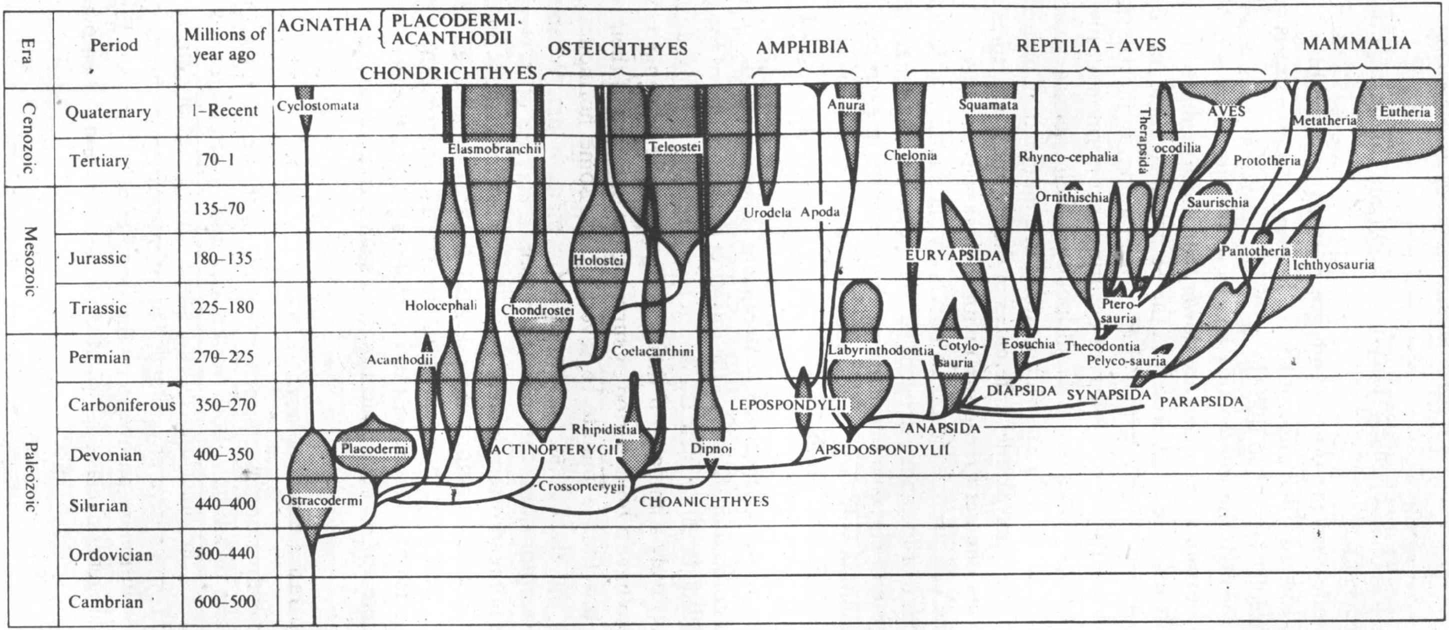

Fig. 1.1. A classification of vertebrates in relation to their phylogenetic origins and a time scale, in terms of paleontological periods. (From Torey, 1971.)

the extant groups which may be particularly interesting in such studies. The mere examination of the endocrine system of some bizarre and exotic vertebrate does not alone constitute 'Comparative Endocrinology' (it may be 'Animal Endocrinology') unless the data can be considered in relation to that in other, phyletically related species. Such information can be used to help confirm, complete and even extend our knowledge of the phylogenetic relationships between vertebrates and to follow the evolution of endocrine mechanisms. The lungfishes (Dipnoi) may afford us an example. These fishes have long been considered, on the basis of morphological information, to be close to the original line of evolution connecting the bony fishes (Osteichthyes) and the Amphibia. As we shall see later, homologous vertebrate hormones often exhibit considerable differences in their chemical structure. Many such differences are apparent between the hormones in fishes and tetrapods. The structure of several hormones present in lungfishes, however, show a greater similarity to those in tetrapods than those in other fishes. For instance, a neurohypophysial hormone called mesotocin is present in amphibians, reptiles and birds but in bony fishes the homologous hormone is isotocin (which differs from mesotocin by a single amino acid substitution) with the exception of the lungfishes, which have mesotocin. It has also been found that the growth hormone and prolactin present in lungfishes are more like those in tetrapods than in other fishes.

Apart from contributing to the over-all phyletic study of vertebrates, the comparative endocrinologist aspires to reconstruct the lines of evolution within the endocrine system itself. This can be done by examining and comparing in different species, the morphology of the endocrine tissues, the structures and activities, both immunological and pharmacological, of their secreted hormones and their different physiological roles.

The uses of comparative endocrinology

The classic, or academic aims, of comparative endocrinology have been described above. The provision of such intellectual satisfaction is not, however, sufficient justification for all! There are, indeed, a number of other contributions that such studies can make to biology, and some examples of these are given below.

The process of reproduction in vertebrates is dependent on the endocrine secretions and an understanding of this relationship can provide information that may be usefully applied when, for esthetic or economic reasons, we may wish to increase, or decrease, the fecundity of a species. This type of study thus constitutes a contribution to the field of 'biological control' (Bern, 1972).

Knowledge of the endocrine system in man has largely been made possible by experiments on other animals. This has principally involved mammals like rats, rabbits, and monkeys but also some more exotic and bizarre creatures. Quantitative measurements of gonadotrophins and melanocyte-stimulating hormone (MSH) were originally made (and sometimes are still) using the responses of the clawed toad (*Xenopus laevis*), while prolactin levels can be measured by its effects on the pigeon's crop-sac or on the behavior of a newt. Oxytocin is assayed by utilizing its ability to decrease the blood pressure of chickens, and the rate of water movement across the toad's urinary bladder can be used to distinguish between two, chemically different, mammalian antidiuretic hormones (ADHs).

The responsiveness of a toad's urinary bladder to ADH and aldosterone is used to study the 'mechanism of action' of these hormones on membrane permeability. Such preparations provide useful 'models' of hormonal effects on the mammalian kidney.

The relationship of the structure of a molecule, to its biological activity, is a field of considerable interest to biologists. The diversity, or polymorphism, in the structure of vertebrate hormones, together with their disparate effects on different tissues and in various species, offers a natural 'laboratory' for such studies. Nature has had a long time and wide opportunities to experiment with the effects of changes in molecular structures on the activities of such excitants. At present, this is most clearly seen among the neurohypophysial hormones of which there are at least nine known chemical variants among the vertebrates. These hormones are peptides containing eight amino acids and often only differ from one another by a substitution at a single chemical locus. They are very reactive molecules and can exert actions at many different sites ranging from the uterus and mammary gland to blood vessels, the kidney, and the amphibian skin and urinary bladder. Analogous effector tissues in different phyletic groups exhibit different abilities to respond to each such hormone, be it a natural one or a variant made in the chemist's laboratory. There are available, and in use, more than 20 different effector-preparations that can be used to study the effects of changes in chemical structure among these hormones on its biological effectiveness. Natural variants of hormones, in which the biological activity has been altered in some way, may be of potential use to man. For instance, calcitonin (a hormone concerned with the regulation of calcium in the body) from the salmon ultimobranchial bodies is far more potent in man than the natural hormone he possesses.

The diversity of vertebrates as a background for endocrine variation

There are some 42 000 extant species of vertebrate animals. The vertebrates originated some 400 million years ago as creatures who apparently lived in the sea or, possibly, in fresh water. They subsequently evolved and occupied almost every conceivable habitat in the oceans, in fresh-water rivers and lakes, and on the land. Their abodes range from the cold polar regions to hot equatorial ones, from deserts to swamps, from high mountains to the ocean deeps. The considerable morphological and physiological diversity of vertebrates mirrors their success in this multitude of environmental conditions. It is thus not surprising to find that the endocrine system exhibits inter-specific differences that reflect adaptations to such different environments. Nevertheless, it is also somewhat unexpected to find that considerable similarities are still apparent in the endocrine systems of species as distantly related as the hagfish (Cyclostomata) and man.

The endocrine glands of vertebrates have special roles to play in the regulation of many types of physiological processes which include reproduction, osmoregulation, intermediary and mineral metabolism, and growth and development (Table 1.1). The nature of the responses to hormones differ considerably but can be classified into several major groups including their actions on membrane permeability, muscular contraction, the transformation of substrates involved in intermediary metabolism and growth, and a controlling (or trophic) action on other endocrine glands (Fig. 1.2).

Many, though not all, of the endocrine glands are essential for life and the reproduction and survival of the species. In other instances, however, their immediate importance for survival is not clear. Animals cannot reproduce if the endocrine function of their gonads is compromised and death soon follows complete destruction of the adrenal cortex. Life may be shortened if the Islets of Langerhans fail to produce sufficient insulin and normal growth, development and maturation of the young will not occur if the secretion of pituitary growth hormone or thyroid hormone is inadequate. On the other hand, antidiuretic hormone from the neurohypophysis, is not essential for life though in its absence very large volumes of urine are secreted by the kidney. In man this is an annoying condition as prolonged sleep is not possible and even during the waking hours it can lead to social difficulties but it is not fatal. If drinking water were in limited supply, however, dehydration could be a potential problem and absence of this hormone may then affect survival. It should also be remembered that while too little of a hormone can constitute a problem, too much may also result in physiological difficulties. Hormone imbalances can result from genetic abnormalities, the presence of tumors, and accidental disruption of the events controlling secretion of the hormone. A few examples of such endocrine dysfunction and their effects are summarized in Table 1.2.

Endocrine glands, or tissues, have been identified among all of the vertebrates. Those common to the major groups (from the Cyclostomata to the Mammalia) are the pituitary, thyroid, endocrine pancreas, adrenal

TABLE I.I. *The secretions of the endocrine glands*

Gland	Hormones	Target tissues
Pituitary		
Adenohypophysis		
Pars distalis	Follicle stimulating hormone, FSH	Ovary and testis
	Luteinizing hormone, LH (also called interstitial-cell stimulating hormone, ICSH)	Ovary and testis
	Thyrotrophic hormone, TSH	Thyroid
	Corticotrophic hormone, ACTH (adrenocorticotrophic hormone)	Adrenocortical tissue
	Growth hormone, GH (somatotrophic hormone)	Liver forms somatomedins which alter tissue metabolism (liver, muscle, adipose tissue)
	Prolactin (luteotrophic hormone, LTH)	Mammary glands, fish gills, tadpole metamorphosis, corpus luteum, kidney, skin, etc.
	Lipotrophin	Adipose tissue
Pars intermedia	Melanocyte stimulating hormone, MSH	Melanocytes, pigmentation and color change
Neurohypophysis		
Pars nervosa	Vasopressin, ADH, vasotocin	Kidney, amphibian skin and urinary bladder
	Oxytocin	Mammary gland, uterus
Hypothalamus	Pituitrophins; FSH/LH-RH, P-IH, MSH-R-IH, CRH, TSH-RH, GH-RH, etc.[1]	Release of hormones by the adenohypophysis