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EMPIRICISM IN ENDOCRINOLOGY
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Since the time when the bacterial origin of disease was promulgated as a theory there has been no concept that has dominated modern medicine more than that of the endocrine regulation of bodily activities. The science of endocrinology may be said to have its origin in classical times as we may gather from the advice given by Pliny who suggested the use of donkey and stag gonads as good aphrodisiacs. But it remained for Claude Bernard and the erroneous but stimulating work of Brown Seward to demonstrate the potentialities of the endocrine system. From that time onwards the literature has swollen to enormous dimensions as a result of the important contributions appearing constantly in the medical and biological journals of every civilised country. To-day it is fully appreciated that what we are bodily, mentally, sexually, emotionally and facially largely determined by the harmonious interaction of all the endocrines which are pouring their active secretions in minute quantities into the blood stream.

Anatomists have been aware of the existence of these glandular structures for a long time past and their observations paved the way for the great physiological and medical progress made in the last four decades in regard to this system. It would have been fantastic for a Banting or a Best to have isolated insulin from the pancreas, or a Murray to have prepared a desiccated thyroid extract, without the preliminary information concerning the histological structure of these organs.

Some of the most significant data in regard to internal secretions have been obtained by careful observations made by clinicians in patients suffering from hyperactivity and underactivity of the endocrines. The most classical example is the observation of Addison who first described the physical changes produced by pathological destruction of the suprarenals. Basing their work on the facts established, by the clinician, and the anatomist, physiologists have prepared many thousands of extracts of the various glands. Some of these products, particularly thyroid extract and insulin, have certainly yielded most sensational results in hormonal therapy and these have come to stay for all time; but the majority of the extracts still used at present are of dubious value. With the first flush of success the customary sensation monger, armed with the usual weapons of empiricism and brilliant theories has created a chaotic environment which tends to impede real advances in our knowledge. It is quite clear that if we are to extricate the science from the hands of empiricists we require constantly to revert to the necessary preliminary stage of collecting anatomical data and exploiting to the full the knowledge of such facts as are already established. The anatomist has been fully aware of this situation all the time and certain basic principles established by him are gradually being accepted.

First of all it is being demonstrated that glandular extracts prepared from animals at varying times after death vary in potency. This is to be expected because living tissue is made up of a highly complex labile substance which changes physically and chemically during the process of cellular death. This produces a disintegration of the complex substances of the living cell into the equally complex molecules which may be regarded as products of decomposition. These changes are recognisable histologically within 10 minutes after death. Distinct but subtle changes occur in the mitochondria and Golgi's reticular network of the dying cells. If then visible changes occur in a tissue soon after death it can be appreciated readily that the physiological make up of the cell must be also profoundly influenced. It is evident then from the nature of this situation that when tissues are collected indiscriminately post-mortem all sorts of possible extractives may appear depending on the degree of post-mortem change that has occurred in the gland before preparation. But if post-mortem effects are so easily
demonstrated there are other changes which are produced in the endocrine glands by slight changes in the environment of the animal. Numerous researches, particularly in the thyroid gland reveal that diet, variations in the activities of other endocrine organs, variations in temperature, unhygienic conditions and inanition produce constant changes which can be demonstrated histologically. If an animal is kept in captivity with an unrestricted diet the thyroid gland becomes hyperplastic. This condition is characterised by enlargement of the cell, increase in size of the Golgi network and abundance of large mitochondria, with disappearance of colloid from the vesicle. Iodine included in the diet produces flattening of the cell, whereas pituitrin stimulates the gland to activity. An environment of constant high temperatures produces a state of underactivity whereas hyperactivity may be produced by exposure to cold. Both unhygienic conditions and inanition produce in the majority of cases changes indicative of thyroidic hyperactivity. The significance of the results of these carefully planned experiments is very great, and when these established facts have been applied to the preparation of thyroid extracts, the character and stability and uniformity of extract must certainly improve.

There are still other factors which determine the structure of the endocrine glands. The most important to be considered is growth changes. It is being maintained with increasing emphasis that endocrines undergo great modifications during growth and certain reactions occur in the cells which are characteristic of the particular periods of growth under consideration. The cells, distribution and structure of Golgi apparatus and mitochondria vary. It is possible with a little experience to assess the age of a person by an histological examination of the glands. The second important factor affecting internal glandular secretions is the variations the endocrine glands undergo in structure during the rhythmically recurring stages of the sex cycle and these are also being gradually established. The gross changes taking place in glands according to their age and sexual rhythm is not at present considered seriously by those who make extracts. In the literature on this subject it is commonly quoted that extracts are prepared from the glands of young animals. But if these extracts are administered to subjects of a different age from which the extracts are prepared, one may be administering something which is different from what the individual actually requires and the therapy is therefore empirical.

But apart from these changes which occur in the endocrines in growth, sex and variations in environment there is still another important aspect of this subject which is not appreciated. The histologist is elaborating delicate microchemical tests to identify numerous substances located in the cytoplasm of cells of the various glands. Adrenaline to-day may be readily recognised in the suprarenal. Armed with the knowledge available of the chemical nature of the cytological constituents of the cell, a solvent for the extraction of the active substances immediately suggests itself. This is a scientific and logical approach. Such a method of approach will eliminate the empirical methods of investigators who in the past have freely used all sorts of reagents, be they strong acids or alkalies, ether or acetone, alcohol or water, always hoping that at least one of these solvents will contain the active ingredient.

Although these various omissions mentioned arise during the preparation of the extracts, empirical methods are further multiplied when these extracts are used by the clinician. The administration of these substances is never controlled. This is well demonstrated where thyroxin, originally introduced for disturbances in the thyroid gland is to-day applied in many conditions such as congenital under-development of the uterus, amenorrhoea, hyperemesis gravidarum, eclampsia, nephritis, high blood pressure, psoriasis, eczema, acne, baldness, chilblain, enuresis, epilepsy, tetany, migraine, infantile diarrhoea, constipation, fibrositis, arthritis. Similar lists accompanying a patent medicine are held up to ridicule by the clinician!

Only a few of the salient fallacies and shortcomings of endocrine preparation and therapy have been cited. The whole field of endocrinology must be treated scientifically. This involves the most rigid and exhaustive methods of standardisation both in the preparation of extracts and in therapeutics. If stable and uniformly acting hormones are to be prepared the state of the tissue used requires to be determined by histological procedures. The establishment of the actual morphology and the range of morphological variations in different physiological states must be determined, before we can fully understand the actions of the glands in health and disease.