SOME ASPECTS OF SYSTEMIC STRESS

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ABSTRACT

Certain aspects of systemic stress have been discussed in the light of available information, with the purpose of indicating the importance of carrying out an investigation on stress as encountered in every day life by our civilians and defence forces. The various scientific problems worth studying in this connection have also been pointed out.

Introduction

Life passes through many stressful situations. Sometimes it is threatened and sometimes it is not, but the question is how the system reacts to stress. To throw light on this point a large number of investigations have been carried out so far and the results are summarised in several reports (1-3). The role of endocrine and nervous systems in supporting the internal environment was postulated long time back, but the adrenal gland and the hypophysis have been assigned subsequently the most significant functions in this connection (2). When animals are subjected to intensive stress, there occur involution of the thymico-lymphatic apparatus, gastrointestinal erosion and enlargement of the adrenal cortex. The result of exposing hypophysectomized or particularly adrenalectomized animal to even mild stress is fatal. Replacement therapy with appropriate extracts of these glands helps these animals to overcome the stress. Activity of the cortical extracts has been ascribed to some steroids and their derivatives, and that of the pituitary extract being due to adrenocorticotrophic hormone (ACTH). The chemical composition of the adrenal gland with respect to some essential nutrients such as ascorbic acid, pantothenic acid, lipids and some minerals also changes. All these observations have paved the way for throwing more light on the subject.

What is meant by stress

According to Selye (2) stress may be considered as the harmful state of homeostasis and the agent causing it may be called a stressor. The latter exerts dual effects. When a limited number of cells reacts with the agent in a selective manner, the effect is specific. In connection with systemic stress it is, however, the non-specific effect which is more important. In this case, morphological, functional and biochemical changes elicited by various systemic stressors are found to be essentially the same irrespective of the specific nature of the eliciting stimulus. The effects are not localized, rather extensive regions of the body deviate from their normal resting stage. Specific effects under certain circumstances may also produce non-specific changes. Before discussing the mechanism of response to stress or how the non-specific stressors act upon the body, it might be worth giving a list of non-specific stress factors.

The Various Non-specific Stress Factors

The list of such factors is undoubtedly long and the following ones quoted from pertinent literature (2-5) may be considered quite illustrative.

(*i*) Environmental factors, such as extremes of heat and cold, anoxia, and extremes of high and low humidity.

(*ii*) Physiological factors, such as pregnancy, fatigue, excessive work, dehydration, calorie deficiency, and stresses created by emotional states of various kinds.

(*iii*) The effects of various drugs such as atabrine, atropine, nicotine, morphine, thyroid and dinitrophenol.

(*iv*) Pathological states such as infections, fevers, intoxication of various kinds, shock, surgery, burns, hemorrhage etc.

(*v*) Metabolic disorders that involve the hyper-activity of the various endocrine glands, or the administration of large doses of hormone to compensate for underactivity of the endocrine glands.

Mechanism of Response to Stress Factors

The picture describing the response of an animal to a stress factor is visualised as follows (2, 3). When a stressor acts upon some part of the body, a stimulus travels through some unknown pathway from the injured area to the anterior pituitary which is induced thereby to discharge ACTH. To most stressors the first response may possibly be the secretion of adrenaline by the adrenal medulla (6). The adrenaline stimulates the pituitary to secrete more ACTH, which in turn acts on the adrenal cortex, causing an increased secretion of adrenocortical hormones. It is through the influence of adrenocortical hormones that many different biochemical processes are set in motion to enable the animal to resist the action of a wide variety of stressors. The various biochemical processes constitute, in other words, a metabolic phase characterising an increased rate of utilization of cortical hormones in the body. The other phase involved is the autonomic phase which depends on the activation of the sympathetic nervous system. The sympatho-adrenal system is reported to initiate, whereas the pituitary-adrenocortical system supports cellular activities (3].

Principal Biochemical Reactions Essential for Survival

The main biochemical reactions which appear to be necessary for survival and which take place during numerous physiological adjustments have been summarised as follows (2, 3, 5). Mention has, however, been made above that these are the consequences of increased outflow of cortical hormones.

(*i*) Breakdown and metabolism of tissue protein, resulting in an increased output of nitrogen in the urine.

(*ii*) Stimulation of gluconeogenesis and the carbohydrates thus formed increase the levels of blood sugar and liver glycogen.

(*iii*) Decreased utilization of carbohydrates by the tissue and increased utilization of fat, accompanied in part, by decreased sensitivity to insulin.

(*iv*) Possible loss of essential nutrients, other than amino acids.

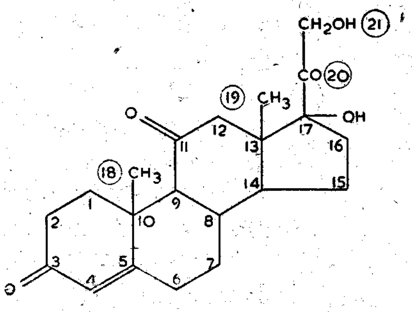
How the cortical hormones actually elicit such chemical changes is not known. It has been indicated that their action probably lies in increasing the permeability of cells or they may participate in the enzymic systems in some way(3).

Although the importance of cortical secretion has been greatly realised further work has to reveal the presence of no less than thirty steroids in the cortex (7). Of these, only corticosterone, hydrocortisone and an unidentified steroid probabl ypresent also in the amorphous fraction, have been detected in the blood(8). Traces of cortisone and 11-desoxycorticosterone may also be present but further proof appears necessary. Moreover, only six members which have been obtained in crystalline form are active in keeping adrenalectomized animals alive and in good condition. The amorphous fraction of cortical extract also possesses very high activity, but the part played by other members is not adequately known. The metabolic effects of the crystalline members as found out after administering them into laboratory animals have also been studied to corroborate the results enumerated above. On the basis of the actions of the individual members, they have been classified as follows (9).

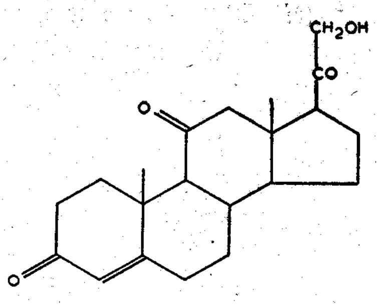
Classification of Active Corticoids

A. Glucocorticoids

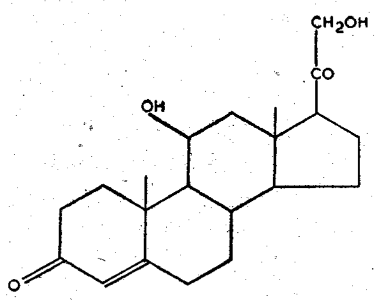
(*i*) Cortisone (Kendall's compound E) or 11-dehydro-17-hydroxy-corticosterone.



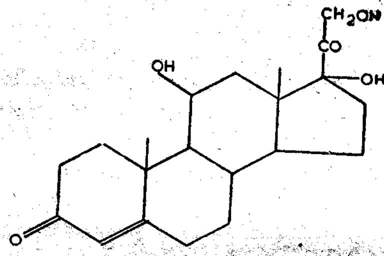
(*ii*) 11-Dehydrocorticosterone (Kendall's compound A)



(*iii*) Corticosterone (Kendall's compound B)



(*iv*) 17-Hydroxycorticosterone(Kendall's compound F)



They are characterised by having an oxygen atom attached to the 11th-carbon atom and are concerned with the intermediary metabolism of protein and carbohydrate.

Actions—

(*i*) Increased conversion of exogenous protein to carbohydrate (Gluconeogenesis).

(*ii*) Increased conversion of exogenous carbohydrate to glycogen.

(*iii*) Rise in blood sugar level.

(*iv*) More mobilization and utilization of fat, with less oxidation of available carbohydrates.

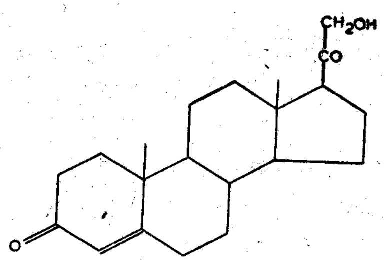
(*v*) Production of negative nitrogen balance either as a result of increased protein catabolism, decreased protein anabolism, or both.

(*vi*) Moderate sodium and water retention power but not comparable to that of mineralo-corticoids.

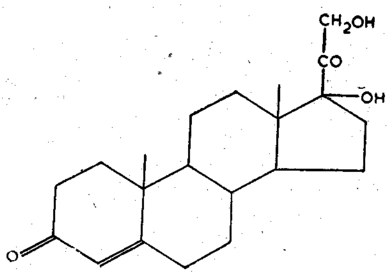
(*vii*) Destruction of lymphocytes and eosinophils.

B. *Mineralo-corticoids.*

(*i*) Desoxycorticosterone or Deoxycortone



(*ii*) 11-Desoxycortisone (Reichstein's compound S) or 11-desoxy-17-hydroxy-corticosterone



They have predominant effect on electrolyte and fluid balance.

Actions—

(*i*) Urinary retention of sodium and chloride.

(*ii*) Increase of plasma volume.

(*iii*) Increase of extra cellular fluid volume.

(*iv*) Decrease of sodium and chloride concentrations in perspiration.

The effects on water and electrolyte balance are approximately thirty times as great as those of cortisone.

(*v*) Increase of urinary excretion of potassium possibly as a result of intracellular potassium loss due to protein breakdown and displacement of intracellular potassium by retained sodium.

C. "*N*" *Hormones*

The members are sex hormones like progesterone, oestrogens and androgens with power to exhibit androgenic or anabolic activity. One of the androgens isolated from the adrenal is called adrenosterone. Though their action may lie in the retention of nitrogen, phosphorus, potassium, sodium and chloride, normally such action is not so significant.

The above classification cannot be considered a rigid one. There may however, be overlapping of properties, though of a relatively less degree. But the activity of one member may be enhanced or inhibited to some extent by the presence of a member of another group(10). Before proceeding further it may be well to state also the functions of adrenaline in a general way. Its role is ubiquitous (3). Its blood sugar raising action is almost immediate and of very short duration. The main action of this hormone is on liver and muscle glycogenolysis, and it may also liberate cortical steroids(10*a*).

General Adaptation Syndrome

The reactions essential for survival have been mentioned above. It remains to be seen, however, what happens physiologically throughout the period of long exposure to an abnormal condition. To understand the entire process Selye (2) has introduced the concept of general adaptation syndrome which represents in fact the whole response comprising three phases, namely, the alarm reaction (A-R), the stage of resistance and the stage of exhaustion. These phases occur one after another, the alarm reaction being the first stage of performance.

The alarm reaction is set in by sudden exposure to stimuli to which the organism was not adapted. This has been divided into two phases, namely, the shock phase and the counter shock phase. The former is characterised by hypothermia, hypotension, depression of the nervous system, decrease in muscular tone, hemoconcentration, deranged capillary and cell membrane permeability, generalised tissue breakdown, hypochloremia, hyperkalemia, acidosis, a transitory rise followed by leucocytosis, eosinopenia and acute gastrointestinal erosions. The shock phase may vary from a few minutes to about twenty four hours depending on the intensity of the damage inflicted.

In the counter shock phase most of the changes noted during the shock phase are reversed. The cortex which becomes depleted of lipids gets recharged during the counter shock phase. Other biochemical changes in this phase have already been stated. If this phase can last for a long time, the subject is understood to have developed the stage of resistance against the aggressive agent. The stage of resistance is the stage in which adaptation is maximum.

In case the exposure to abnormal condition is prolonged, adaptation may wear out and further resistance becomes impossible. This is the stage of exhaustion, when life becomes incompatible. This stage is morphologically identical with those signs manifested during the alarm reaction. Whether or not the above theory is free from criticism remains to be seen.

The question that arises next is concerned with the diseases of adaptation. During adaptation to any kind of stress such as the strain and anxiety of every day life, some derangements of the endocrine and metabolic mechanism responsible for building up of adaptation can lead to pathological responses characteristic of certain diseases known as the diseases of adaptation. Imperfections and inadequacies of the general adaptation syndrome appear to be their cause (2, 10b, 11). What etiological relationship exists between the diseases of adaptation and the hormones elaborated during the stage of resistance and exhaustion has in fact formed the subject of current research in many laboratories. Further elucidation regarding the secretion, functions and metabolism of such hormones as the somatotrophic hormone (STH), prophlogistic corticoids (P-Cs) or mineralo-corticoids and antiphlogistic corticoids (A-Cs) or glucocorticoids is needed in this connection. There are a number of problems in connection with the subject of stress which require further study and a few of them may be mentioned below.

Some Problems for Further Study

Detailed information regarding the nature of cortical secretion, the manner of utilization of the secretory products and the fate of the biologically active corticoids not traceable in blood, is lacking. It will be desirable, therefore, to give more attention on these aspects. If the activation of the adrenopituitary axis is to be tested, the levels of adrenaline, ACTH, cortical hormones and some metabolic products, in blood need determination. Though there are methods to analyse some of these hormones in blood (12-15), further work to improve them may also be indicated. The work of Thorn et al (10c) with human subjects gives emphasis on the determination of eosinophil count in blood and 17-hydroxy corticoid excretion in urine. Eosinopenia has been used as an index of stress in most studies but the degree of eosinopenia due to cortical activation alone remains to be worked out. It has been stated that if the fall in eosinophil count is less than fifty per cent, activation of the cortex is in doubt and under this condition the secretion of ACTH may also be considered minimum. In studies on the metabolism of cortical hormones (10c, 16), the necessity for developing suitable methods for determining 17-hydroxy corticoids in urine is also obvious. Similarly, development of method for the analysis of adrenocortical steroids will prove extremely useful (10d).

Lastly, it may be pointed out that stress may create some nutritional problems (5, 11, 17). To quote Lepkovsky (5), it is not certain whether it is the new carbohydrates that are essential to the survival of the animal under stress, or whether it is some other unknown compounds formed by the reactions set in motion by the activated pituitary-adrenal system. Even less is known of the price the animal pays, in terms of nutrients, for protection against the various non-specific stresses that are part of the hazards of living. Evidence is accumulating to indicate that, in order to restore the protein lost to the body, the protein intake must be increased, but it is also necessary to make certain that the dietary protein reaches the cell, where it is to be laid down as tissue protein. The diet plays an important role in meeting the losses of essential nutrients during stress,but the exact nature of this role remains largely to be determined.

In diseases of adaptation the nature of the diet has profound influence. For instance, if the animals are exposed to stress, such as cold, for a sufficiently long time, diets rich in protein or sodium will favour the development of lesions characteristic of rheumatic fever, nephropathies etc. (11). A great deal of work has, however, been carried out recently to prove the importance of sodium free diet in controlling hypertension. The relationship between stress and nutrition has formed, therefore, a very important subject of investigation.

CONCLUSION

In conclusion it may simply be said that the problem of stress encountered by human beings of different occupations should receive the attention it deserves. Investigations on this subject will give results of immense value.

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