CHAPTER I

INTRODUCTION
Upto 1952, desoxycorticosterone was the only mineralocorticoid known to science. In 1953, Simpson et al. announced the crystallization of a new steroid which was from 30 to 100 times more active than desoxycorticosterone in promoting sodium retention in the rat in amounts of 0.1 ug or even less. This new steroid was named aldosterone due to the presence of an aldehyde group at position 18. The amount of secretion of adrenal cortex is regulated by circulating adrenocorticotropic hormone (ACTH) from the pituitary. In addition to its effect on adrenal corticosteroids, ACTH brings about the reduction in the cortical cholesterol and ascorbic acid. The cholesterol contents fall by half in about 5 to 6 hours and require some 24 hours after administration of ACTH for restoration of the normal level. This response is considered to be unique effect of ACTH since no similar reduction in the cholesterol contents of other organs has been observed so far. However the present study for the first time on adrenal and recent allied studies on frog brain (Shrivastava, 1979), fish brain (Jain, 1985), rat liver (Pacholi, 1985), fish liver (Shukla, 1985) and rat pituitary (Sil, 1985) show that NaCl and certain amino acids do bring about reduction in the amount of cholesterol in the mammalian adrenal and the above organs in in-vitro experimentation.
Unlike other adrenal corticoids, the secretion of aldosterone appears to be controlled by more than one factor, ACTH being only one of them. Aldosterone secretion decreases after hypophysectomy but can be raised in such animals by lack of sodium in the diet or by a fall in circulating blood volume. Such falls may be produced, for example, by bleeding or by obstruction of thoracic inferior vena cava, resulting in the formation of ascites. The agent believed to be responsible for stimulating aldosterone production in states of reduced blood volume is renin, an enzyme, present in kidneys and found in renal blood after haemorrhage. Renin, in turn forms angiotensin in the blood stream, a polypeptide shown to stimulate secretion of aldosterone by direct action on the adrenal tissue (Davis et al., 1961). Severe changes in blood electrolytes may act directly on adrenal tissue and elicit accelerated secretion of aldosterone (Denton, 1964). According to Debreceni and Crete (1973) the salt depletion induced increase in aldosterone secretion is not direct effect of the changes in sodium space at the adrenocortical level but mediated through extra-adrenal factor or factors. The factors, renin and angiotensin, may be true for kidney, but, in the adrenal itself, indirect evidence points to the correlation between certain amino acids, NaCl concentration and ACTH effects (aldosterone production). The results, which can be presumed from the present study, are shown in Fig.1. Llorëns, Borrell and Borrell (1973) found significant increase of corticosteroids after peritoneal injections.
of ACTH or insulin but a decrease was noticed after glucagon administration in cats. Increase in corticosteroids means primarily increase in levels of cholesterol. Thus, other factors, including hormones apart from ACTH, may effect adrenocortical function.

While there is sufficient work on mammalian adrenal and pituitary, there is practically no information on the behaviour of adrenal tissue under the normal conditions and under the influence of various ionic concentrations. Cholesterol synthesis and its depletion has been studied mainly with reference to ACTH and ascorbic acid (Misra and Shrivastava, 1974). The present study for the first time not only shows a direct relationship in the NaCl concentration, amino acids and oxygen consumption but also on cholesterol contents of the adrenal which in its turn influences the rate of synthesis of corticosteroid.

This work then has been further planned to evaluate the influence of various concentrations of sodium chloride corresponding to normal physiological saline and two steps higher and lower with a difference of one gram per litre at each step. The results point out a constant increase in relation to ionic concentration. Further, the effect of all important amino acids on the oxygen consumption of adrenal has so far not been studied in any class of vertebrates. Special interest has been taken in those amino acids whose
metabolic defects are inherited and lead to mental
delay retardation and malfunction of the central nervous
system like phenylpyruvic oligophrenia, citrullinuria,
hyperprolinemia hydroxyprolinemia etc. (Howell and
Lee, 1963; Holden, 1962). That such a work has
applied value is shown by the researches of Laborit
(1966) and Laborit, Thuret and Lamothe (1972) on the
aspartic acid and its potassium and magnesium salts.
Udintsev (1970) found stimulation of steroid synthesis
in vitro and in vivo in man and animals by glutamic
acid.

Another interesting feature presented herein
is the influence of ionic concentration and amino acids
on the quantity of cholesterol in the adrenal. The
relationship between oxygen consumption and cholesterol
production has not still been worked out in any class
of vertebrates. To find out a probable explanation
of this relationship, minute changes in hydrogen ion
concentration have been estimated for the whole data.
The statistical studies point out a very high correla-
tion and regression not only between oxygen uptake and
quantity of cholesterol but also between adrenal and
pituitary and between adrenal and liver. Since
acetyl-CoA is the starting point for the biosynthesis
of cholesterol and since it also takes part in the
tricarboxylic acid cycle, these studies of special
significance as indicating the ratios of acetyl-CoA
entering in each cycle under a particular set of
conditions.
Fig. 1: Probable relationship of factors acting on adrenal cortex based on direct and indirect evidence.

Central Nervous System

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\text{Liver \quad NaCl & certain amino acids \quad (Pacholi, 1985)}
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\text{Blood \quad & Sil, 1985}
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\text{Extra cellular space \quad NaCl, certain amino acids \quad (Jain, 1985)}
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Adrenal Cortex

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\text{Pancreas \quad (Insulin etc.) \quad Aldosterone}
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\text{Fall in Cholesterol & Ascorbic acid.}
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Angiotensin

Kidney

Renin