that the improvement or lack of improvement in diseases treated with ACTH or cortisone can be attributed to metabolic or electrolytic changes. Nevertheless, although these effects are relatively unimportant in terms of therapeutic responsiveness, they may be of major importance when they appear during treatment with ACTH, cortisone or similar steroids. With a full understanding of the physiological actions which result from an insufficiency or an excess of circulating corticoids, the management of patients during ACTH and cortisone treatment will become less of a problem.

UNTOWARD PHYSIOLOGICAL EFFECTS

In this discussion the term "untoward effects" refers to physiological alterations which accompany ACTH and cortisone administration but which at present appear to be of no therapeutic benefit. Occasionally the early preparations of ACTH, due to posterior pituitary contamination, caused blanching of the skin and abdominal cramps, but with the improved preparations of ACTH now available these reactions, as well as antigenic reactions to ACTH, are now so rare that ACTH may be safely administered intravenously.[2] The intramuscular administration of cortisone may rarely cause local irritation, erythema and skin rashes. These are probably due to the vehicle in the preparation used rather than to the cortisone molecule per se.

The untoward physiological effects associated with the administration of ACTH and cortisone may be conveniently considered under the following headings.

Alterations in Electrolyte Metabolism.—One of the characteristic chemical blood findings which has been observed in hyperadrenocorticism, and from ACTH or cortisone, is hypopotassemic, hypochloremic alkalosis. This is noted particularly when the dosage is high and the course of therapy prolonged. One of the characteristic physiological actions of the majority of adrenal steroids is to increase potassium excretion, and the changes in serum chloride and serum pH follow. The presence of this abnormal serum electrolyte pattern, particularly hypopotassemia, is suggested clinically by the development of lethargy, muscular weakness and cardiac irregularities. Early chemical evidence consists of a lowered serum chloride and an elevated carbon dioxide-combining power. If the level of serum chloride and the CO_2 combining power are significantly altered in this way, it is likely that the serum potassium is low. The latter produces characteristic changes in the electrocardiogram (chart 1), which thus becomes a useful substitute for chemical determinations of serum potassium concentration.

In order to prevent hypopotassemia, hypochloremic alkalosis, potassium chloride should be administered. Not only does it supply the required potassium and chloride ions but, in addition, its diuretic action reduces water retention, which generally accompanies adrenal hormone treatment. The usual dosage is 0.9 Gm. three times a day as enteric-coated tablets. This will suffice in most cases. With an occasional patient it will be necessary to increase the potassium chloride to a total daily dose of 5.4 Gm. It appears that the amount of potassium required in some patients is related to the level of adrenal cortical hormone attained from ACTH stimulation or cortisone treatmeint. The greater the elevation of the hormone levels the greater the possibility of hypopotassemia. While hypopotassemia calls for prompt treatment, it should be pointed out that overzealous administration of

2. Renold, A. E.; Forsham, P. H.; Maisterrena, J., and Thorn, G. W.: Intravenous ACTH (Preliminary Report), New England J. Med. **244**:796-798, 1951.