RECENT PROGRESS IN ALDOSTERONE RESEARCH

The sodium-retaining action of aldosterone is now well known and its importance in the homeostatic regulation of electrolyte and, indirectly, fluid balance has been clearly demonstrated. However, there are still many problems to be solved and it appears that the answers will not be long delayed, judging from the intense research activity in this field.

One of the main problems upon which some light has recently been shed, is the mechanism by which aldosterone secretion of the adrenal is initiated. Denton et al., in a neat series of experiments, showed that the denervated transplanted adrenal can adequately secrete aldosterone. The conclusion to be drawn from this work is that the stimulus to the adrenal must be on a humoral basis, especially because in cross-circulation experiments the transplanted adrenal responded equally well. The identity of the hormone responsible is unknown and other work has shown that it is not ACTH. The site of production of the hormone is also unknown, although there is some very good evidence that the centre which controls its secretion is probably situated in the region of the pineal and the subcommissural body in the diencephalon.

The stimuli affecting the central receptor have been demonstrated to be changes in extracellular volume. Experiments illustrating the part played by the vagus in transmission of stimuli set up by volume changes are of great interest. Constriction of the inferior vena cava (which locally reduces intravascular volume) produces an increase of aldosterone, whether the vagus is sectioned or not. But when the constriction is released, the aldosterone level does not fall unless the vagus is intact. It appears, then, that the stimulus for the increase in aldosterone level is independent of the vagus and is transmitted by other pathways, but this is not the case in decrease in the aldosterone level.

Another well-known fact is that urinary aldosterone is increased in amount in oedematous states. It is presumed, therefore, that aldosterone is directly implicated in the production of oedema. However, the fact that there is no oedema in some cases of aldosterone-secreting tumour (Conn's syndrome) raises a serious difficulty. To complicate matters further, it has been clearly shown that some patients with gross oedema due to congestive cardiac failure have low aldosterone levels in the urine. Explanations offered as a solution to these problems do not appear to be very convincing. It is predicted that a further search in the 'amorphous fraction' of adrenal secretion may yield more hormones of vital importance which, together with aldosterone, influence electrolyte metabolism.

From the practical point of view, two substances which antagonize aldosterone, and hence diuretic properties, have been under investigation. Amphenone and derivatives act directly on adrenal steroidogenesis, reducing, among other hormones, the output of aldosterone. The toxicity of this compound, however, precludes its general usefulness. The spiroloactones, which are also steroid compounds, appear to produce their effects by blocking the sodium-retaining action of aldosterone and DOCA on the renal tubules. Although the application of these substances is still very much in the experimental stage, the work provides some indication of the direction in which diuretic therapy of the future is progressing.

ADRENAL VIRILIZING TUMOUR AND PREGNANCY

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Many cases of adrenal virilism have been described, but the occurrence of a successful pregnancy and the birth of a normal female child in this condition has not been reported.

CASE HISTORY

First Admission

The patient, a White female at that time 32 years old, presented in 1955 at another hospital with a history that during the previous 2 years she had noticed progressive growth of facial hair as well as temporal recession of her scalp hair. Her voice had become 'deeper and masculine'. The menstrual cycle remained regular and normal. She had 2 children (3 and 3 years) both of whom had been breast fed.

The available relevant details of this admission (Table 1) show a persistently high 17-ketosteroid excretion. No abnormality was seen on intravenous pyelogram. At laparotomy a wedge of the right ovary was removed, which on histological section showed a normal corpus luteum. Unfortunately there is no record of the adrenal gland having been examined. Post-operatively there was no improvement in the hirsuties; the estimation of the excreted 17-ketosteroids gave a high normal figure.

During the next few years the hirsuties extended to the chest, abdomen and extremities. The menstrual cycle remained normal. Although there was difficulty in becoming pregnant, she gave birth in 1956 to a live premature child, which she breast fed. This pregnancy was complicated by threatened miscarriages. The birth of the child was 2 years after the second admission.

Second Admission

The patient was referred to the Johannesburg Hospital in 1958 because of a change in her symptoms. She stated that for the previous 7 months she had developed amenorrhoea, severe acne of her body and face, progressive hirsuties, increasing strength and libido, and a gain in weight.

Examination showed a slightly 'moon-faced' young woman with extensive acne of face and body. The scalp hair was profuse and dark. The trunk and extremities were hirsute and the pubic hair was of male distribution. The blood pressure was 120/70 mm. Hg. Gynaeucological examination showed a markedly enlarged clitoris. The vagina, cervix and uterus were normal. The left ovary was palpable, but not the right. The patient's 2-year-old child was examined and found to have normal external female genitalia.

Special investigations. The results of the steroid investigations are incorporated in Table 1. The following laboratory data were also obtained: Haemoglobin, 16 g./100 ml. Leucocytes, 8,600/ c.mm (neutrophils 61%, monocytes 6%, lymphocytes 33%).