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Sodium and Potassium Excretion in Pinealectomized and Adrenalectomized Rats.* (27212)

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It has been suggested that the pineal gland may be involved in regulation of aldosterone secretion(1,2) or in regulation of body electrolytes(3). Farrell(2) reported that administration of various pineal extracts augmented or decreased the amount of aldosterone in adrenal venous blood of dogs and postulated that the pineal gland contained both an "adrenoglomerulotropic" hormone and an adrenal inhibiting substance. Panagiotis and Hungerford(3) reported that the stainable fat in the pineal gland was depleted as a result of feeding a diet deficient in sodium. This response of the pineal seemed to be specific for sodium deficiency since equally severe regimens of magnesium deficiency or potassium deficiency were without effect. Wurtman, Altschule and Holmgren(4) reported adrenal hypertrophy after pinealectomy and atrophy after administering pineal extract.

The salt balance studies reported here were designed to determine whether or not the pineal gland has an effect upon excretion of sodium or potassium. The results indicate that the pineal acts to cause loss of sodium and it is suggested that it acts via the adrenal gland.

Methods. Male rats of the Holtzman strain weighing 90-100 g at operation were used in these experiments. Pinealectomy was performed by a technic used in this laboratory (3) and adrenalectomy by the usual dorsal approach. Completeness of operative removal of the glands was checked at autopsy. Intact, pinealectomized, sham-pinealectomized, adrenalectomized and adrenalectomized-pinealectomized rats were placed in individual metabolism cages on the day of operation and 24-hour urine samples were collected for the first 5 post-operative days. They were fed a purified diet deficient in sodium and potassium and were given distilled water to drink. The diet has been reported elsewhere(3) except that the sodium and potassium salts were replaced with dextrose. The animals received daily intraperitoneal injections of a solution which contained 600 μeq. of sodium and 300 μeq. of potassium in a 4.0 ml volume (NaCl and K_2HPO_4).

Sodium and potassium concentrations were determined by flame photometry and total daily urinary sodium or potassium was calculated (using 24-hour urine volume) and expressed in microequivalents per day. At autopsy blood was obtained from the abdominal aorta and sodium and potassium concentrations were determined on the plasma.

To avoid the effect of post-surgical sodium retention, sham-pinealectomized and pinealectomized groups were subjected to same experimental procedure, except that the groups were started on the regimen on the 17th post-operative day and continued to the 21st post-operative day.

Conclusions. The sham-operated and pinealectomized rats (Table I) exhibited a post-surgical retention of sodium during the first 5 post-operative days when compared with the unoperated controls ($P = <.01$). On the 4th and 5th days, the urinary sodium of the sham-operated rats appeared to be returning toward normal values. However, only the 4th day was significant ($P = <.01$) when compared with the pinealectomized

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TABLE I. Electrolyte Excretion from Post-Operative Day 1-5.

Group	Daily sodium excretion — Day 1	2	3	4	5	Daily potassium excretion — 1	2	3	4	5	No. rats	Final B.W. (g)
Intact	957 ±49	223 ±32	389 ±44	497 ±23	407 ±38	485 ±46	57 ±3	59 ±5	29 ±3	16 ±2	8	128
Pinealectomized	465 ±90	180 ±40	289 ±24	226 ±32	193 ±30	360 ±87	56 ±11	30 ±5	49 ±4	23 ±4	8	132
Sham-operated	436 ±72	212 ±38	272 ±51	392 ±44	243 ±25	290 ±19	37 ±6	53 ±8	33 ±5	26 ±2	5	126
Adrenalectomized	804 ±42	563 ±51	601 ±55	574 ±41	508 ±17	434 ±67	128 ±26	117 ±26	212 ±35	263 ±21	8	115
Pinealectomized–adrenalectomized	649 ±60	634 ±66	563 ±39	547 ±31	523 ±40	396 ±33	152 ±35	74 ±22	188 ±71	230 ±62	7	120

Mean values ± stand. error.
Total sodium and potassium expressed in microequivalents/day.

group. If an "adrenoglomerulotropic" factor had been removed by pineal ablation, one would have expected an increased sodium excretion such as the natriuresis seen after adrenalectomy during the same 5-day period. While these experiments are not exactly comparable to those of Farrell(1,2) they do not lend support to the proposal that an "adrenoglomerulotropic" hormone is elaborated by the pineal gland. Characteristic changes in the zona glomerulosa of the adrenal gland which occur after sodium deficiency were not prevented by pinealectomy(3), and would also fail to confirm existence of an "adrenoglomerulotropic" hormone. Wurtman *et al.* (5) also failed to confirm existence of an "adrenoglomerulotropic" hormone using adrenal zona glomerulosa width and potassium excretion studies.

Sham-operated and pinealectomized rats were allowed to recover from the surgical procedure before being placed on the known sodium and potassium intake regimen. The data presented in Table II clearly demonstrate that the sham-operated group returned to normal levels of sodium retention while pinealectomized rats still retained significantly more sodium ($P = <.01$). During the 5 days of controlled electrolyte intake, day 1-2 would represent a leveling off period. The difference between the groups was revealed during the last 3 days. This observation would suggest that a pineal hormone acts in some way to cause loss of sodium. If a pineal hormone has its action by inhibiting the adrenal zona glomerulosa, then the amount of sodium retained by adrenalectomized-pinealectomized rats would not be different from that of adrenalectomized rats. The data in Table I demonstrate that the amount of sodium excreted by these 2 groups did not differ, tending to confirm the suggestion that a pineal hormone exists which acts via the adrenal gland, perhaps inhibiting the zona glomerulosa.

No effect of the pineal gland on potassium retention could be demonstrated by these experiments (Tables I and II). The amount

TABLE II. Electrolyte Excretion from Post-Operative Day 17-21.

Group	Daily sodium excretion — Day 17	18	19	20	21	Daily potassium excretion — 17	18	19	20	21	No. rats	Final B.W. (g)
Sham-operated	1991 ±206	448 ±41	309 ±38	395 ±28	401 ±28	764 ±68	92 ±12	48 ±6	47 ±8	37 ±4	6	188
Pinealectomized	1518 ±96	445 ±53	180 ±44	234 ±17	184 ±18	697 ±94	136 ±12	76 ±5	48 ±3	44 ±5	5	198

Mean values ± stand. error.
Total sodium and potassium expressed in microequivalents/day.

of potassium administered in these experiments proved to be marginally adequate, which may have masked any effect the pineal may have exerted. Wurtman *et al.*(5) reported a slight increase in potassium excretion in pinealectomized rats. They did not control potassium intake, however.

The concentration of plasma sodium in pinealectomized rats appeared to be slightly elevated (to 149 meq./l compared with 142 meq. l) but no differences in plasma potassium levels were noted. Yamada(6) found no change in plasma sodium or potassium levels after pinealectomy and ablation of the habenular nucleus.

In these experiments the pinealectomized rats retained close to 180 μeq. per day more sodium than the control groups while adrenalectomized rats lost about 180 μeq. per day more than the control groups. These results strongly suggest that the pineal gland has an influence on the regulation of body sodium.

Summary. 1. Pinealectomized rats retained more sodium than sham-operated or unoperated control rats. 2. The amount of sodium retained by adrenalectomized-pinealectomized rats was not different from that retained by adrenalectomized rats. 3. No effect of the pineal gland on potassium retention was observed in these experiments. 4. It was concluded that the pineal gland may elaborate a hormone which causes loss of sodium and evidence is presented to suggest that it acts via the adrenal gland.

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Influence of Sex and Hair Growth Cycle on Lipid Composition of Mouse Epidermis.* (27213)

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Recent evidence indicates that the lipid (phospholipid, neutral lipid, cholesterol, cholesterol esters, and triglyceride fractions) composition of epidermis of Swiss female mice at the 12th (anagen II) and 22nd (telogen) days of the hair growth cycle does not differ appreciably(1). The epidermis of the 2nd to the 5th day (anagen I to anagen III) of the cycle is several times thicker than that on the 12th to the 22rd days of the cycle(2). This pronounced increase in epidermal thickness is associated with some interesting chemical changes. For example Carruthers *et al.*(3) showed that the activity of cytochrome oxidase at the 4th day of the cycle is twice that of the 12th and 22nd days, and appears to be related to cell division. Also Griesemer(4) has shown that the activity of cytochrome oxidase, succinic dehydrogenase and ribonucleic acid content of the epidermis of the 4th day of the cycle of the rat are significantly higher than at 6 days (telogen). Sex also appears to play a role in the lipid composition of mouse epidermis since methylcholanthrene (MC) treated male epidermis has a much higher cholesterol content than similarly treated female epidermis(5). These differences in enzyme activity and lipid composition prompted an investigation of the lipids of the epidermis at 3 distinctly different stages of the hair growth cycle, the results to which are reported here.

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