icular stomatitis virus in the homologous chick cell culture system but showed no activity against this virus in mouse embryo, grivet kidney, bovine kidney or rabbit kidney cell cultures. The remarkable similarity of chick DNA-interferon to RNA-interferon, even though induced by basically different agents, is consistent with the concept that interferon is synthesized by resident host mechanisms rather than under the viral genetic code.

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Vasopressin Effect on Urinary Concentration in Rats with Hereditary Hypothalamic Diabetes Insipidus (Brattleboro Strain).* (29871)

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Patients with hypothalamic or neurohypophysial diabetes insipidus (D.I.) respond to administration of exogenous vasopressin with increased concentration of the urine; such a response, in fact, distinguishes these conditions from nephrogenic diabetes insipidus. However, even with administration of vasopressin many patients with hypothalamic or neurohypophysial D.I. fail to achieve the urine osmolalities which normals attain(1). Rats with surgically induced D.I. do not concentrate the urine normally when given exogenous vasopressin in acute experiments(2). The same is true of rats with hereditary hypothalamic D.I., which probably can synthesize no vasopressin whatsoever(3,4).

We have recently discovered that the sub-

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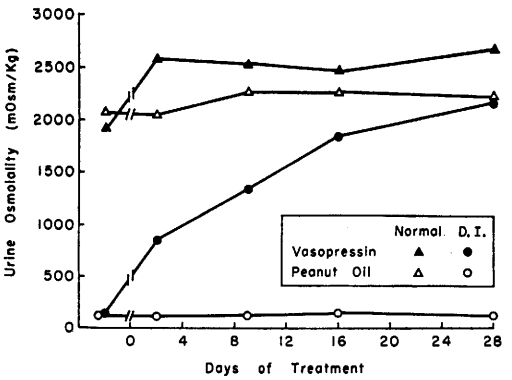

FIG. 1. Mean urine osmolalities of normal and D. I. rats, before treatment (points to left of day zero) and during course of 28 daily injections of vasopressin or peanut oil.

normal response to vasopressin in rats with hereditary D.I. is gradually corrected by the daily administration of vasopressin for a period of 4 weeks. So far as we know, this phenomenon has not been reported previously.

Materials and methods. Four rats with D.I. were given 1.0 unit of vasopressin tannate in oil (Pitressin tannate in oil, Parke, Davis & Co.) subcutaneously daily for 28 days. Water intake, and volume and osmolality of 24-hour urine specimens were measured during the second day of this treatment and thereafter every 6 or 7 days. There were 3 control groups: 1) 4 rats with D.I. given daily injections of 0.2 ml of vehicle (peanut oil); 2) 2 normal rats given 1.0 unit daily of Pitressin tannate in peanut oil; and 3) 2 normal rats given daily injections of peanut oil. All the animals used in this experiment were females 6 months old. All had free access to water and to the standard laboratory diet (Purina Labena rat chow) throughout the experiment.

Results. Fig. 1 shows the average osmolality of 24-hour urine specimens for each group. Initial failure of D.I. rats given vasopressin to achieve normal urine concentration is seen in the average value of 860 mOsm/kg on the second day of treatment; this is less than half the osmolality achieved by normal rats given peanut oil injections. With continued vasopressin administration, however, average urine osmolality in D.I. rats progressively increased to 2172 mOsm/kg on the 28th day. This progression is statistically significant. Normal rats maintained on vasopressin showed an immediate elevation of urine osmolality which was not progressive. D.I. rats given peanut oil continued to produce copious amounts of dilute urine with no significant change of osmolality.

Urinary osmolal excretion in D.I. rats given peanut oil averaged 12.5 mOsm per 100 g body weight per 24 hours and did not change during the 28 days. Osmolal excretion was 6 mOsm/100 g/24 hours in both groups of normal rats throughout the experiment. In D.I. rats given vasopressin, osmolal excretion decreased to 9 mOsm/100 g/24 hours on the second day and remained at this level. The reasons for these differences in osmolal excretion are not known.

Discussion. Neither the subnormal response of D.I. rats to exogenous vasopressin given acutely nor the correction of this response with prolonged administration of vasopressin is explained by these data. The diluting effect of increased osmolal excretion cannot be invoked, for, although D.I. rats given vasopressin excreted more osmoles than normals, their ability to concentrate urine continued to improve and became normal despite maintained higher osmolal excretion. Nor is progressive accumulation of the hormone a likely explanation, since the daily doses used throughout the experiment were much higher than those considered necessary for maximal antidiuretic effect.

De Wardener and Herxheimer observed that prolonged overhydration in humans diminished the ability of the kidneys to concentrate urine in response to exogenous vasopressin(5). They suggested that this effect might have been related to expansion of the extracellular fluid space, but such an explanation seems unlikely in D.I. rats in which the primary event is polyuria rather than polydypsia. Serum osmolalities and sodium concentrations in these animals show, rather, that they are in a state of chronic dehydration with probable contraction of the extracellular fluid volume(3).

A striking feature of these results is the long period of vasopressin replacement required to correct the concentrating defect.

This might reflect a slow reversal of anatomical changes in the kidneys. By light microscopy the kidneys of D.I. rats appear normal, but ultra-microscopic changes in the nephrons of normal rats undergoing acute water diuresis were described recently(6). Adaptation of an enzyme system(s) needed for the action of vasopressin might also require considerable time.

We have observed striking hypertrophy of neurons in the supraoptic and paraventricular nuclei of untreated hereditary D.I. rats and partial reversal of these changes after 28 days of vasopressin administration(7). These changes might reflect adjustment to a new steady state in the feed-back system which regulates activity in the hypothalamo-neurohypophysial system. For example, either oxytocin, which these D.I. rats probably produce and release in excess(4), or an analogue of vasopressin which these rats might synthesize in lieu of this hormone, might inhibit the antidiuretic effect of vasopressin, perhaps by competition for binding sites(8). Initially, under the influence of constant osmotic stimulation, either or both of these compounds might be released in excessive amounts. Then, as normal fluid balance is approached under treatment with exogenous vasopressin, progressively less hypothetical inhibiting compound(s) might be released until finally the urine was concentrated normally.

These possible mechanisms, which might influence the degree of hypertonicity of the renal medullary interstitium and/or the permeability of various renal membranes to water, are speculative and by no means mutually exclusive.

Summary. When given large doses of vasopressin tannate in oil, rats with hereditary hypothalamic diabetes insipidus at first do not concentrate urine normally. This defect is progressively corrected as daily injections of hormone are continued for 4 weeks.

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Alterations of Lipogenesis in the Intact Chick by Dietary Malonic Acid.* (29872)

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Previous experiments have shown that dietary biotin deficiency can depress the rate and alter the pattern of lipogenesis in the intact chick as measured by total carcass fatty acids, fatty acid composition and acetate incorporation into long-chain fatty acids (LCFA). The inhibition of lipogenesis appeared to be at the acetyl-CoA to malonyl-CoA step(1). Malonic acid has been shown to stimulate LCFA synthesis *in vitro*(2,3).

This paper reports the effects of dietary malonic acid on LCFA synthesis in normal and biotin-deficient intact chicks.

Methods. Day-old female White Rock

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