According to findings of PAS reaction in epidermis of our cases, its value ranged from positive (+), uncertain (+ −) to negative (−) as shown in the Table.

By comparing the relation between glycogen in epidermis (PAS reaction) and blood sugar levels, we have shown that PAS positivity of epidermis is directly proportional to the high blood sugar. Satistically, by use the test x^2, we could establish that PAS positivity was significant in cases with high blood sugar ($X^2 = 12.93$ $P < 0.01$).

Discussion. There are in the litterature divergent opinions about relation of diabetes and the skin. Some authors are of the opinion that there is not any connection between the two[5], but others thought that the number of dermatoses in diabetes is augmented[6–8].

We found that in the dermatological praxis it is generally known that the number of diabetics injured from mycosis is augmented. This we could explain by the fact that such skin possesses greater quantities of carbohydrates for better growth of these fungi.

Conclusion. By histological analysis of material from the earlobe of diabetics and border-line cases of diabetes, we established that the PAS positivity in epidermal cells is stronger than in healthy epidermis, and that it is stronger in diabetics than in border-line cases. By comparing the level of blood sugar and PAS-positivity in epidermal cells, we find that the strenght of PAS-positivity is proportional to the level of blood sugar, and that the difference between PAS-positivity in persons with less blood sugar and those with more blood sugar is statistically significant.

PAS reaction in epidermal cells at different diagnoses

Diagnoses	No of diagnoses	PAS reaction (No of cases)
Borderline cases	26	− (6), + − (12), + (8)
Diabetics	33	− (3), + − (9), + (21)
Normals	41	− (14), + − (18), + (9)

Résumé. Après une analyse histologique de la peau du pavillon de l'oreille des diabétiques et cas limites de diabète, nous avons conclu que la positivité PAS de leurs cellules épidermales est beaucoup plus forte que dans l'épiderme sain, et qu'elle est plus forte chez les diabétiques que dans les cas limites de diabète. Nous avons trouvé que l'intensité de la positivité PAS est proportionelle au taux du sucre dans le sang et que la différence entre la positivité PAS chez les personnes ayant un taux bas de sucre et celles qui en ont un taux élevé est statistiquement significative.

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Selective Potentiating Effects of Metal Ions on Vasopressin[1,2]

Extensive literature exists demonstrating the influence of mono- and divalent cations on the sensitivity of various bioassay systems to neurohypophyseal hormones (e.g., [3–6]). These phenomena have usually been associated with a direct effect of the cations on the tissue rather than on the hormones. Neurohypophyseal hormones have been demonstrated to form complexes with paramagnetic ions such as Cu^{++}, Ni^{++} and Co^{++}, involving displacement of specific protons attached to nitrogen atoms[7–9]. However, using the isolated toad urinary bladder as assay system, both the Cu^{++}-vasopressin complex and the free hormone showed identical hydroosmotic activity[10].

In the present study we investigated the possible interactions of Na^+, NH_4^+ and Ca^{++} with arginine vasopressin (AVP) as reflected by selective changes of the rat blood pressure response to the hormone.

Methods. The AVP used had a rat bp activity of 460 ± 13 USP U/mg as determined by four-point assay (n 6). The *stock solution* was comprised of 1 µg AVP/ml water (mean pH 6.6). The water contained less than 0.05 meq/l Na^+. Dilutions used were a) 1 ml stock solution plus 9 ml water equals *control solution*, which contains 100 ng AVP/ml water; b) 1 ml stock solution plus 9 ml electrolyte (Na^+, NH_4^+ or Ca^{++}) solution at 111% final concentration equals *test solution*. The mean pH of the control and test solutions was 6.6. Control and test solutions of AVP were made by using mechanical mixing

1 Supported by USPHS Grant No. AM-13567.

2 Abbreviations used are: AVP, arginine-vasopressin; bp, blood pressure; U, unit; n, number of experiments; $\bar{x}$, mean value; S.E. standard error; p, level of significance; NS, not significant.

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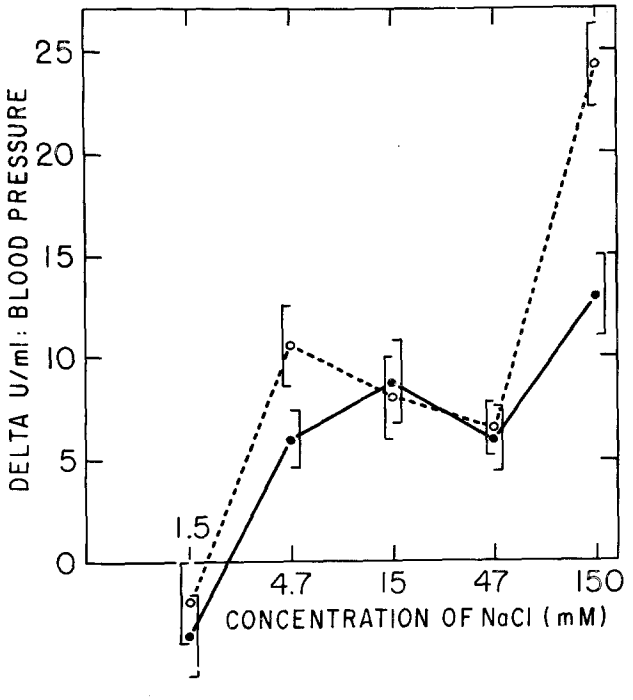
2 min prior to injection and the left-over solutions were then discarded.

Both kidneys of male Wistar strain rats (wt. 180–250 g) were removed from ether-anesthetized animals 12–16 h prior to use. Water and standard laboratory diet were offered *ad libitum* after nephrectomy. For the assay the animals were anesthetized with 1.4 g/kg urethane s.c. (7 ml/kg of a solution containing 0.2 g/ml). 30 min later the rats received pentolinium tartrate 15 mg/kg i.p. (1.5 ml/kg of Anolysen®-Wyeth in a concentration of 10 mg/ml). After a further 30-min period tracheotomy was performed and a PP20 polyethylene catheter (Portland Plastic Ltd) filled with 150 m*M* NaCl was inserted into a jugular vein. A hypodermic needle was sealed into the external end. Another catheter (PP20) was placed into the right common carotid artery, filled with 4 mg (500 U) heparin/ml 150 m*M* NaCl, and attached to a Statham P23AC transducer connected to a Grass Model 7 polygraph. Chart speed: 2.5 mm/min. There was no regulation system for body temperature. AVP injections were made with 500 µl syringes (Inaltera®). Standard, control and test solutions (0.1 ml) were administered over 1 sec, followed by 0.05 ml of 150 m*M* NaCl solution. The injection sequence was as follows: 5 to 15 AVP standard injections at equal and at increasing concentrations in order to test for reproducibility of response and acceptable dose-response relationship, respectively; then AVP standard, AVP test solution, AVP control, AVP standard, AVP control, AVP test solution, etc. AVP standards (containing 50, 100 and 150 ng/ml) were made up in 150 m*M* NaCl and not used beyond 2 h.



Effect of increasing concentrations of Na^+ on the rat pressor response to AVP. The activity of 100 ng AVP/ml dissolved and injected in NaCl solutions ranging from 1.5 to 150 m*M* have been compared with the activity of 100 ng AVP/ml H_2O as control. The ordinate gives the difference in activity between standardized test and control solution expressed in delta values: Δ = activity/ml of AVP test solution minus activity/ml of control (●—●). NaCl concentration is plotted on the abscissa. The results of analogous experiments using equimolar concentrations of angiotensin II[11] are given for comparison (○---○).

The recorded amplitudes of bp increase are expressed in terms of the AVP standards. This minimizes possible errors deriving from changes in sensitivity of the test system in the course of the experiment. The activity recorded with 100 ng AVP/ml 150 m*M* NaCl is denoted arbitrarily as 100 U/ml (note that U does not refer to USP U); this was necessary because of the solvent dependence of AVP activity (see below). Since each test solution was preceded or followed by a control solution (identical amount of AVP dissolved in distilled water) delta values can be given: Δ = activity/ml test solution minus activity/ml control. Paired samples were compared by a *t*-test and different series by the non-parametrical Wilcoxon test.

Results. Characteristics of the rat bp assay. A total of 31 rats was used for the study. 4 rats had to be eliminated because of unacceptable dose-response relationships. With the remaining 27 rats a total of 384 bp determinations (14.2/rat) was obtained. Intravenous injections of 50 ng AVP/ml 150 m*M* NaCl, or 100 ng AVP/ml 150 m*M* NaCl at the beginning of the tests increased the bp by 14.0 ± 0.9 mmHg (*n* 27) and 25.6 ± 1.3 mmHg (*n* 27), respectively. At the end of the tests the response to the identical standards was 15.1 ± 1.1 mmHg (*n* 27) and 25.7 ± 1.6 mmHg (*n* 27) indicating the lack of detectable tachyphylaxis. Injections (0.1 ml) of water, increasing concentrations of NaCl (1.5 to 470 m*M*), 150 m*M* NH_4Cl and 15 m*M* $CaCl_2$, all without AVP, gave only minimal (2–3 mmHg) and equal pressor responses. The bp increase after injection of the control solutions (100 ng AVP/ml water) was 23.4 ± 0.5 mmHg (*n* 192) corresponding to 87.7 ± 0.8 U/ml (*n* 192).

Ion effects. It can be seen from the Figure that injections of constant amounts of AVP dissolved in increasing concentrations of NaCl give rise to an increase in the bp response. This ion-induced enhancement of activity is non-linear within a range of NaCl concentration of 1.5 to 150 m*M*. In addition there is a further increase in the bp activity amounting to a Δ of 16.2 ± 1.7 (*n* 24) when the NaCl concentration is increased from 150 to 470 m*M*. Analogous studies with NH_4Cl show this cation to be less effective than NaCl in enhancing the bp activity of AVP. In contrast, $CaCl_2$ is as effective as NaCl (Table).

Discussion. This investigation shows that bp response to AVP in nephrectomized rats can be potentiated by Na^+, Ca^{++} and, to a lesser degree, NH_4^+ (Figure and Table). Various activities of Val^5-angiotensin II-Asp^1-β-amide (angiotensin II) are also potentiated by Na^+[11–14] and the enhancement of angiotensin II activity by Na^+, Ca^{++}, NH_4^+ and other ions was studied in detail in the rat bp system[11]. While the potentiation of the pressor activities of AVP and angiotensin II by Na^+ is the same in the concentration range of 1.5 to 47 m*M*, it is clearly less for AVP at higher NaCl concentrations (see results). Moreover, the potentiation of AVP by Ca^{++} is considerably less than in the case of angiotensin II, where it was about two-fold that induced by Na^+[11].

Studies with angiotensin II suggested that ions modify the preferred conformation of the peptide in solution and that these conformational changes are detected by the hormone receptors, thus leading to changes in the biological activity of angiotensin II[11,12].

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If a similar interpretation is adopted to account for metal-ion induced potentiation of the AVP activity, the reduced effectiveness of Na^+ and Ca^{++} in the case of AVP could be due to differences in structure of the two hormones. The cyclic neurohypophyseal hormones possess a more rigid solution conformation[15,16] than the linear peptide antiogensin II[17–19], and their topography may therefore be less susceptible to ion-induced perturbations.

Zusammenfassung. Der Effekt von Na^+-, NH_4^+- und Ca^{++}-Ionen auf die Blutdruckaktivität von Arginin-Vasopressin wurde untersucht und mit analogen Experimenten (Val[5]-Angiotensin II-Asp[1]-β-Amid) verglichen. Die Wirkungsweise der Ionen-induzierten Potenzierung von Vasopressin wird diskutiert.

Effect of NaCl, NH_4Cl and $CaCl_2$ on the pressor activity of AVP[a]

Test solution	n	Δ	P	Intergroup p
150 mM NaCl	24	13.0 ± 2.0	<0.001	<0.05
150 mM NH_4Cl	24	6.8 ± 1.9	<0.005	
15 mM NaCl	24	8.8 ± 2.0	<0.001	NS
15 mM $CaCl_2$	24	8.2 ± 2.5	<0.005	

[a] The test solutions consist of 100 ng AVP/ml; Δ represents activity of test solution minus activity of control (100 ng AVP/ml H_2O) in arbitrary U/ml.

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Effect of Dosage of Oestradiol-17β on the Life-Span of the Rabbit Corpus luteum

Luteolysis in the rabbit cannot be clearly ascribed either to a luteolytic factor or to withdrawal of luteotrophic support[1]. Thus the corpora lutea persist until 31 days in the presence of a placental unit[2], evidently solely or partly due to the promotion of oestrogen production[3–5]. In the pseudopregnant doe luteal regression occurs after 14–15 days, and hysterectomy does prolong the life-span to 24 days[6]. However, asynchronous regression of 17 day old corpora lutea may occur even in the presence of the uterus[7,8], an observation which is difficult to explain on the basis of a luteolytic factor. A relationship between oestrogen level and the life-span of the corpus luteum might adequately explain these observations. Thus a 'permissive' level of oestrogen production could be postulated to give a life of about 24 days. Depression of oestrogen levels, perhaps as a result of utilization by the pseudopregnant uterus, would shorten luteal life. In contrast the pregnant uterus or fetoplacental unit, by augmenting oestrogen production, would correspondingly prolong luteal life. We have therefore looked for such a dose-response relationship.

Materials and methods. New Zealand White does, weighing 3–5 kg were used. The oestradiol-17β was administered s.c. in propanediol. All hysterectomies were performed prior to 7 days post coitum (p.c.) unless otherwise indicated. One ovary was examined by laparotomy every 4–5 days and the number, size and location of corpora lutea recorded.

Corpus luteum life in intact and hysterectomized pseudopregnant rabbits treated with oestradiol-17β

Treatment	No. of animals	Oestradiol-17β-dose (μg/5 lbs/day)	Mean corpus luteum life (days + S.E.)
Hysterectomy only	3	–	24.3 ± 0.9
Late hysterectomy days 12, 14, 15, 15, 15	5	–	23.9 ± 1.1
Hysterectomy and oestradiol-17β	3	–	25.3 ± 0.3
Hysterectomy and oestradiol-17β	3	1	35.0 ± 2.9
Hysterectomy and oestradiol-17β	2	2	39.5 ± 6.5
Hysterectomy and oestradiol-17β	3	5	> 56.5 ± 4.5
Hysterectomy and oestradiol-17β	2	10	> 58.5 ± 0.5
Intact + oestradiol-17β	3	–	15.8 ± 1.2
Intact + oestradiol-17β	3	1	15.2 ± 2.1
Intact + oestradiol-17β	2	2	18.4 ± 1.8
Intact + oestradiol-17β	3	5	34.9 ± 2.3
Intact + oestradiol-17β	3	10	> 50.8 ± 2.1