show the *pars buccalis* to be entirely lacking in its normal location beneath the infundibulum. It is present, however, as a distant and characteristic body of cells closely applied to the floor of the myelencephalon, where it appears to have induced an hyperplasia of the adjacent tissue of the hindbrain. At this position, a section of the notochord is missing, but this segment of the notochord is to be found just anterior to the infundibular recess, beneath the forebrain. It is to be remembered that the rudiment of this piece of chorda was placed in the position normally occupied by that of the *pars buccalis* in the gastrula stage. Since at that time chordal material was irreversibly determined, its occurrence in this anterior situation was to have been expected.

By the first experiment it is shown that prevention of contact between the *pars buccalis* and nervous tissue, by microsurgical intervention at an early embryonic stage, is equivalent to removal of the *pars intermedia* at a later stage, since the development of the *pars intermedia* is suppressed. The second experiment establishes the location in the late gastrula of the presumptive *pars buccalis,* and indicates that the neural tissue necessary to cause the differentiation of the *pars intermedia* is more or less specific. Although it cannot be said at this time that the infundibular region of the brain possesses the inductive power exclusively, it is believed that tissue with this power must be similar to that of the infundibulum. It is suggested that the ependymal cells may have this capacity.

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Adrenal Cortical Hormone (Cortin) in Blood and Urine of Patients with Cushing's Disease.*

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Evidence has been accumulating which tends to support the hy-

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pothesis that the symptoms of Cushing's disease are due to a hyperfunction of the adrenal cortex.[1] If this is true, one might expect to find an increased amount of adrenal cortical hormone (ACH) in the blood of these patients. We have previously shown that the sera of patients with Cushing's disease, when injected into adrenalectomized rats, prolong the survival period of these animals beyond that of untreated controls.[2] The present communication reports the fact that extracts of the patients' blood and urine prepared by a method used for extracting ACH from adrenal tissue will also prolong the lives of adrenalectomized rats. This would seem to add further support to the hypothesis that Cushing's disease is due to an overproduction of the adrenal cortical hormone.

Grollman and Firor[3] have demonstrated that ACH can be obtained from the urine of normal adults in very small amounts. Utilizing as their standard the growth and the prolongation of life in adrenalectomized rats, they found that one liter of urine contains an amount of hormone (ACH) corresponding to 0.5 g of glandular tissue.

Extracts were made of the blood of 3 patients with unmistakable Cushing's disease. In one case the urine was also extracted. In a fourth patient, a girl of 5 with an adrenogenital syndrome, the urine was tested in the same way. The extraction was carried out according to the method of Grollman and Firor, using benzene. The residue from 100 cc of blood was taken up in 10 cc of olive oil. The residue from a 24-hour urine specimen was also taken up in 10 cc olive oil. The extract was injected subcutaneously in doses of 0.1 cc daily into male rats adrenalectomized at one month of age. Only those rats which had gained at least 5 g in weight by the fifth postoperative day were used for the assay. It was found that rats which had not gained this amount were likely to die in 2 or 3 days, probably as the result of the operation, even when significant amounts of ACH (Upjohn's preparation) were given. The assay injections were started on the fifth day.

The test animals were fed a stock diet consisting of:

Whole wheat	67.5
Casein	15.0
Whole milk powder	10.0
NaCl	1.0
$CaCO_3$	1.5
Milk fat	5.0

[1] McQuarrie, I., Johnson, R. M., and Ziegler, M. R., *Endocrinol.*, 1937, **21**, 762.

[2] Anderson, E. M., and Haymaker, W., *Science*, 1937, **86**, 545.

[3] Grollman, A., and Firor, W. M., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 669.

TABLE I.
Survival of Adrenalectomized Rats Treated with Extracts of Blood and Urine of Patients with Cushing's Disease.

Daily	Daily Dose Equivalents	No. of Test Animals	Age at Time of Adrenalectomy, days	Days Survival After Adrenalectomy	
				Range	Median
Control Groups					
1. No injections		28	29†	6-15	8.1
2. Injected with olive oil	.2 cc	11	29	7-14	9.1
3. " " ACH (Upjohn)	.1 cc aq. soln. = 4 g fresh gland	4	28	10-14	11.8
4. " " " "	.2 " " " = 8 " " "	2	29	10-17	13.3
5. " " " "	.2 " " " = 8 " " "	12	29	23-33*	26.6*
Experimental Groups					
1. Extract of blood, Patient A (Cushing's Disease)	.1 oil soln. = 1 cc blood	10	27†	7-30	14.5
2. Extract of blood, Patient B (Cushing's Disease)	.1 " " = 1 " "	2	26†	16	16.0
3. Extract of urine, Patient B	.1 " " = .01 of total 24-hr urine	23	27	8-32	16.1
4. Extract of blood, Patient C (Cushing's Disease)	.1 " " = 1 cc blood	5	27	9-20	14.2
5. Extract of urine, Patient D (Adrenogenital syndrome)	.1 " " = .01 of total 24 hr urine	8	27	7-15	10.4
6. Extract of urine, Normal Adult	.1 " " = .01 " " " "	7	29	6-12	8.5
7. Extract of Blood, Normal Adult	.1 " " = 1 cc blood	8	28	7-13	9.6

*Injections of ACH were stopped on 20th day postoperative. The average survival period after stopping the hormone was 6.6 days.
†Age differences of 2 or 3 days at this period of life influence survival periods, the older rat having a longer survival period.

On this diet the average survival period of adrenalectomized rats from our colony and of this age was 16 days. In order to shorten the survival period, a solution of 0.5% KCl was given in the drinking bottles in place of tap water. This reduced the average survival period to 8.1 days.

The results of this study are given in Table I. It is evident that the adrenalectomized rats receiving extracts of blood and urine from patients with Cushing's disease survive a longer period that the untreated controls. An attempt has been made to estimate roughly the potency of these extracts by comparison with known amounts of ACH (Upjohn). It would appear that 1 cc of blood from a patient with Cushing's disease contains an amount of ACH equivalent to slightly more than the hormone content of 4 g of fresh adrenal glands. A 24-hour urine specimen may contain an amount equivalent to 400 g of tissue. The urine of the patient with the adrenogenital syndrome showed no significant amount of ACH; however the patient did excrete androgenic hormone as follows per 24 hours: 5 IU of free androgenic hormone and 33 IU of hydrolyzable androgenic hormone.

The question might be raised whether the presence of oestrin or of prolan, which may both be present in the urine, might prolong the life of adrenalectomized rats, but Grollman and Firor found that these substances had no effect upon prolonging the lives of these animals. This is being checked further in a special study.

Conclusion. Patients with Cushing's disease have in their blood an excess amount of a substance which resembles adrenal cortical hormone in its ability to prolong the life of the adrenalectomized rat. Furthermore, this substance is excreted in significant amounts by the kidneys.

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Effect of Vitamin A Deficiency upon Rate of Pupil Dilation During Dark Adaptation.

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Wald has recently shown that there is a definite chemical relationship between visual purple in the retina and vitamin A. The