one. Previous work has shown that large amounts of saline have no demonstrable effect on the resistance of suprarenalectomized rats. Repeated injections of epinephrin have only a very slight effect.[8] An extract of the spleen made in the exact manner as the cortical extract failed to produce any increase in resistance of suprarenalectomized rats. The female sex hormone of Doisy (Theelin, Parke, Davis and Co.) did not raise the resistance of suprarenalectomized rats. Through the kindness of Prof. Harrow of the College of the City of New York, we tested the effect of the male sex hormone on the resistance of suprarenalectomized rats with negative results. We believe, therefore, that the action of cortin on the resistance of suprarenalectomized rats to histamine and other toxins and poisons is a measure of specific activity of the life prolonging hormone of suprarenal cortex.

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A Substance in Urine of Normal Human Adults That Raises the Resistance of Suprarenalectomized Rats.

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Though potent extracts of the suprarenal cortex as made by F. A. Hartman[1] and Swingle and Pfiffner[2] will prolong the life of suprarenalectomized cats, enormous quantities of suprarenal glands are necessary for the recovery of small amounts of the active substance. A more efficient method should be found for obtaining the substance in larger amounts in order to make the use of cortical hormone available.

It occurred to us that the cortical hormone may be eliminated in the urine in large amounts. A lipoid extract of the urine of normal young adults, males and females, was made. The urine of young male and female adults is extracted with benzene. The benzene is allowed to separate. The benzene fractions are evaporated at 40° *in vacuo* to dryness, the residue taken up in ether, the ether evaporated off *in vacuo* and the residue taken up in water or oil. The final

[7] Hartman, F. A., *Endocrinol.*, 1930, **14**, 229.

[8] Perla, David, and Marmorston-Gottesman, J., *Am. J. Phys.*, 1929, **89**, 152.

[1] Hartman, F. A., *Endocrinol.*, 1930, **14**, 229.

[2] Swingle, W. W., and Pfiffner, J. J., *Am. J. Phys.*, 1931, **96**, 153.

aqueous product is colorless and turns faintly pink in 24 hours. There is no epinephrine present. It is non-irritating when injected subcutaneously or intraperitoneally and has no odor of urine. The procedure takes 36 to 48 hours. The final product was made up so that 1 cc. of the extractive was equivalent to 300 cc. of urine.

The effect of repeated daily injections of the extract on the resistance of suprarenalectomized rats to histamine poisoning was determined in the same manner and under the same conditions as extracts of the suprarenal gland in our previous experiments[3, 4, 5] with cortin prepared from the cortex of the whole gland according to the method of F. A. Hartman. Repeated injections of cortical hormone raise the resistance of suprarenalectomized rats to histamine poisoning administered on the 6th day after the operation. An arbitrary standard unit was established as that quantity of cortex administered on the 5th and 6th day after suprarenalectomy necessary to protect these rats against 200 mg. of histamine per kg. The minimal lethal dose of histamine for untreated suprarenalectomized adult rats is 100 to 120 mg. per kg. when given on the 6th day after suprarenalectomy.[6]

Thirty suprarenalectomized, 3 months old rats were used. Three received daily injections of 1 cc. of the urine extract from the first to the 6th day after operation. On the 6th day, these received 200 mg. of histamine per kg. Two survived and one died. Three rats received daily injections of 1 cc. of the urine extract and on the 6th day were given 300 mg. of histamine per kg. Of these, 2 survived and one died. Six rats received 1 cc. only on the 5th and 6th day after the operation and were given 200 mg. of histamine per kg. Four survived and 2 died. Five rats received 2 cc. only on the 5th and 6th day after operation and were given 200 mg. of histamine per kg. All survived. Two were given 2 cc. of extract on the 5th and 6th day and were injected on the 6th day with 300 mg. of histamine. One died and one survived. Two suprarenalectomized rats received 2 cc. of extract on the 5th and 6th day and were given 400 mg. of histamine. One died and one survived.

As controls, the protective effect of the male sex hormone of Funk and Harrow[7] was tested. We obtained a small quantity of the

[3] Perla, David, and Marmorston-Gottesman, J., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 648.

[4] Perla, David, and Marmorston-Gottesman, J., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 650.

[5] Marmorston-Gottesman, J., and Perla, David, PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 1022.

[6] Marmorston-Gottesman, J., and Gottesman, J., *J. Exp. Med.*, 1928, **47**, 503.

[7] Funk, C., and Harrow, B., PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 325.

male hormone through the courtesy of Prof. Harrow. Four rats injected daily with 1 cc. of the extract were given 200 mg. of histamine on the 6th day. One rat survived 48 hours and 3 died within 8 hours. Two rats were injected daily with 10 units of "theelin," the female sex hormone of Doisy, and both died with 200 mg. of histamine per kg. Five suprarenalectomized rats were untreated and were given 200 mg. of histamine on the 6th day after operation. They all died.

TABLE I.

Effect of repeated injections of an extract obtained from urine on resistance of suprarenalectomized rats to histamine poisoning.

No. of rats	Sex		Extract of Urine* (days)						Histamine (mg. per kg.)	No. Survived	No. Died
	M	F	1 cc.	2 cc.	3 cc.	4 cc.	5 cc.	6 cc.			
3	2	1	1	1	1	1	1	1	200	2	1
3	1	2	1	1	1	1	1	1	300	2	1
6	3	3	0	0	0	0	1	1	200	4	2
5	3	2	0	0	0	0	2	2	200	5	0
2	1	1	0	0	0	0	2	2	300	1	1
2	1	1	0	0	0	0	2	2	400	1	1
			Funk-Harrow Male Hormone†								
4	2	2	1	1	0.5	0.5	1	1	200	1§	3
			Theelin (Doisy Female Sex Hormone)‡								
2	1	1	10un.	10u.	10u.	10u.	10u.	10u.	200	0	2
			Untreated Controls								
5	2	3	0	0	0	0	0	0	200	0	5

* 1 cc. equals extractive of 300 cc. of urine of young normal adults.
† 1 cc. equals extractive of 400 cc. of urine of adult males.
‡ Expressed in Allen Doisy rat units.
§ This animal survived 48 hours.

Comparing the results with extracts of suprarenal cortex with these experiments, it is estimated that one liter of urine furnished an equivalent amount of protective substance in about ½ pound of whole gland.

The extractive obtained from the urine contains a substance that has some of the physiological properties of cortex of the suprarenal gland. In previous experiments we found that an increase in resistance in suprarenalectomized rats following administration of cortin is a specific one. As with the cortical preparations, young adult suprarenalectomized rats injected with the extract from the urine gained from 8 to 10% in weight during the first week following suprarenalectomy. The suprarenalectomized untreated rats either lost weight or their weight remained stationary.

Preparations made from other organs such as the spleen in the manner of cortin; and theelin, the female sex hormone of Doisy, and the male hormone of Funk and Harrow, fail to raise the resistance of suprarenalectomized rats.

Experiments are in progress to determine the effect of this extract of the urine on suprarenalectomized cats.

A substance has been extracted from the urine of young human adults which has some of the physiological properties of the cortical hormone of the suprarenal gland.

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Experimental Inoculation of Man and Guinea Pigs with the Virus of Cattle Warts.

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The etiological agent of human verrucae has been established as a filterable virus by a number of investigators. This was suggested first by Ciuffo[1] and firmly established by Wile and Kingery[2] and by Kingery.[3] Schultz[4] reported that he had succeeded in transmitting cattle warts to man but the filterable nature of the cattle wart virus was not proven until the work of Creech.[5] Creech succeeded in producing experimental wart lesions in 15 out of 22 calves with both filtered and unfiltered cattle wart material.

It is becoming more and more apparent that there are many similar diseases to be found in the different species. Studies should be directed towards the discovery of common etiological agents in many of these conditions. The so-called pox diseases of man and animals represent good examples which suggest common or at least closely related etiological factors. Information concerning the relationship of these agents is particularly valuable.

We have attempted to determine a possible relationship between the virus of cattle warts and of the common wart in man. Usually

[1] Ciuffo, G., *Gior. Ital. delle Malattie Venere e della Pelle*, 1907, **48**, 17.

[2] Wile, U., and Kingery, L. B., *J. Am. Med. Assn.*, 1919, **73**, 970.

[3] Kingery, L. B., *J. Am. Med. Assn.*, 1921, **76**, 440.

[4] Schultz, F., *Deut. Med. Wchnschr.*, 1908, **34**, 423.

[5] Creech, G. T., *J. Agric. Res.*, 1929, **39**, 723.