15831

Effect of Ergotamine Tartrate on Potassium Changes in Histamine Shock.*

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Serum potassium changes in histamine shock were investigated in rats treated with ergotamine tartrate (ET-rat) and compared with the previous findings on intact rats and rats with autoplastic grafts of adreno-cortical tissue (ACT-rat)[1] as an approach to the question of the relative importance of medullary and adrenocortical factors concerned with the release of potassium in histamine shock.

Methods. Serum potassium was determined for adult male rats (Long-Evans strain) at 30 and 60 minutes following intraperitoneal injections of histamine phosphate† (10 mg/100 g body weight). Parenteral administration of ergotamine tartrate‡ (0.5 mg/100 g body weight) was given one-half hour prior to the injections of histamine. The dosage of ergotamine used was sufficient to depress adrenergic activity, as determined by epinephrine reversal, for the strain used. Details of operative procedure and chemical methods of analysis were identical with those previously described.[1]

Results. Experiments to date have led to the following observations on the rat treated with ergotamine:

1. Some reduction of the normal fluctuation of serum potassium was indicated by the decrease in the standard deviation.

6 cases, average 21.3±0.8 mg/100 ml
cf. controls 21.3±1.3 mg/100 ml

2. No significant effect upon the rising trend of serum potassium during development of histamine shock (30-minute values) was obtained.

5 cases, average 24.0±1.9 mg/100 ml
cf. controls, 24.5±1.7 mg/100 ml

3. A possible accentuation in fall of serum potassium occurred during subsidence of histamine shock (60-minute values).

5 cases, average 19.8±2.5 mg/100 ml
cf. controls 22.8±3.5 mg/100 ml

4. A possible exacerbation of the rise in serum potassium ensued upon repeated or extensive bleeding (see 6, below).

3 cases, average 27.9±0.26 mg/100 ml
cf. controls 23.8±1.4 mg/100 ml

The determinations were made on a second blood specimen of 4 ml taken immediately after the first 4 ml bleeding.

5. An elevation of serum potassium followed upon higher dosages of histamine. After 20 and 40 mg histamine in single paired experiments the values obtained 60 minutes later were respectively:

26.8 mg/100 ml and 30.6 mg/100 ml for the ET-rats;
cf. 24.4 mg/100 ml and 24.0 mg/100 ml for controls.

6. No marked influence on gross symptoms was found. Atonia appeared slightly aggravated; under anesthesia respiratory failure upon bleeding was more easily induced than in the controls. The higher values for serum potassium as found in (4) and (5) above correlated with this observation. Toxic reactions from ergotamine alone were not especially apparent in the rat and were in no way as severe as reported for the dog (2).

Some observations were made on rats bearing grafts of adrenocortical tissue and similarly treated with ergotamine. Blood samples were analyzed for potassium at 30 minutes (3 cases) and at 60 minutes (4 cases) following the injection of histamine (10 mg/100 g). The potassium averages for the 2 groups were comparable to those obtained in histamine-shocked rats with only regenerated cortex: *e.g.*

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1 tum-Suden, C., Wyman, L. C., and Derow, M. A., *Am. J. Physiol.*, 1945, **144**, 102.

† Burroughs Wellcome and Company.

‡ Gynergen, kindly supplied by Sandoz Chemical Works, Inc.

35.5±0.5 mg/100 ml at 30 min., ergotamine;
34.2±5.8 " " " " " , no ergotamine;
41.0±2.4 " " " 60 " , ergotamine;
38.5±6.5 " " " " " , no ergotamine;

The ergotamine-treated preparations differed from the nontreated in showing less variability in potassium levels. Survival, as judged both by time and number, seemed slightly better than expected for this class of animal receiving a dosage of histamine (10 mg) which previously was fatal to 60% of the nontreated within one hour.

Discussion. The data obtained indicated that fluctuations in serum K tended to be suppressed by ergotamine tartrate. In the dosage used the difference from the untreated controls was not significant. However, if maximum amounts of ergotamine had been employed a slight lowering of the potassium levels might have been established as found by Houssay for the dog.[2]

Symptomatically, the course of histamine shock following upon the administration of 10 mg intraperitoneally appeared unchanged both in the intact rat and the rat bearing adrenocortical grafts. There was no evidence of a potentiation or synergism between cortical hormones and epinephrine as might be surmised from the findings of Vogt that the latter prolongs cortin secretion.[3] The lack of such interaction therefore cannot account to any extent for the high susceptibility in rats possessing only adrenocortical tissue. The experiments serve to emphasize the inefficiency of regenerated cortical substance, the relation of the rise in extracellular potassium to level of cortical activity and the minor influence of the sympathico-adrenal mechanisms upon potassium release in histamine shock.

Summary. Ergotamine tartrate in the dosage used did not significantly modify serum potassium changes characteristic of histamine shock in the rat. It did not influence histamine tolerance in either the normal or the demedullated animal.

2 Houssay, B. A., and Gerschmann, R., *Rev. Soc. Argent. de Biol.*, 1939, **15**, 327.

3 Vogt, M. J., *J. Physiol.*, 1945, **103**, 319.

15832

Effect of Sex Hormones on Pituitary Lactogen and Crop Glands of Common Pigeons.*

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Estrogens, testosterone propionate and progesterone can exert a dynamic stimulus to the secretion of lactogenic hormone by the anterior pituitary. This is particularly true of the estrogens which have been shown to increase the pituitary lactogen content of rats,[1-3] guinea pigs[3,4] and rabbits[5] from 200 to 500%. A 40% increase has been obtained with testosterone propionate in rats.[6] Progesterone apparently has no effect on the lactogen content of the A.P. when administered in small or moderate dosages, but amounts well above the physiological level in rats (15.0 mg per day for 10 days) have increased it about 74% on a body weight basis.[7] Selye

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1 Reece, R. P., and Turner, C. W., *Mo. Agr. Exp. Sta. Res. Bull.* No. 266, 1937.

2 Lewis, A. A., and Turner, C. W., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 439.

3 Meites, J., Trentin, J. J., and Turner, C. W., *Endocrinology*, 1942, **31**, 607.

4 Meites, J., and Turner, C. W., *Endocrinology*, 1942, **30**, 711.

5 Meites, J., and Turner, C. W., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 190.

6 Reece, R. P., and Mixner, J. P., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 66.