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Influence of the adrenals and gonads on the plasma kininogen concentrations in male and female rats

A relation has been established between the concentration of reproductive hormones and the plasma kininogen concentrations in the rat. Previous work has shown that oestrogens will raise plasma kininogen concentration in the rat and progesterone will lower the kininogen concentration in either intact or ovariectomized female rats (McCormick & Senior, 1974; Senior & Whalley, 1974). In the male rat a relation has been established between the plasma kininogen concentration and treatment with androgens. If androgens are administered to the male or female then the plasma kininogen concentration is lowered in intact rats (McCormick & Senior, 1974). The actual mechanism by which these factors influence plasma kininogen values has not yet been elucidated but the evidence so far suggests that reproductive hormones are mediators in the normal maintenance of the kininogen concentrations. Other workers have noted that following adrenalectomy in the rat there is an increase in plasma kininogen concentration (Rosa, Rothschild & Rothschild, 1972). This increase following adrenalectomy could result from a change in the reproductive hormone concentrations and the work reported here was undertaken to investigate the interrelation between the gonads and adrenals in the regulation of plasma kininogen concentrations.

The work was divided into two sections, one involving female and the other male rats. The animals used all weighed 200–250 g and were housed in groups of six in light- and temperature-controlled conditions. They were allowed free access to food and were all given normal saline to drink from the day of operation. Adrenalectomy

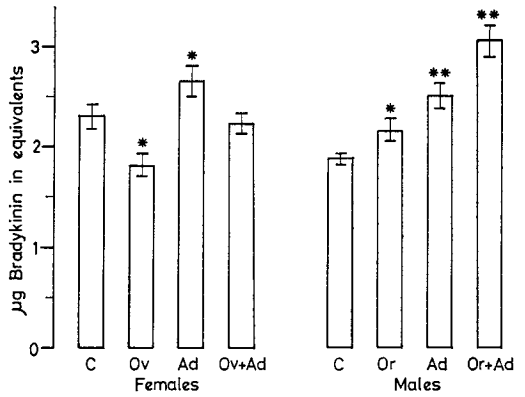

FIG. 1. Changes in plasma kininogen concentrations 6 days after ovariectomy (Ov) and adrenalectomy (Ad) in the female rat and orchiectomy (Or) and adrenalectomy (Ad) in the male rat. C = sham operated rats. Each group represents 6 animals. Vertical bars represent the s.e.m. $^{*}P < 0{\cdot}05$, $^{**}P < 0{\cdot}001$.

and ovariectomy were performed bilaterally by the dorsal route, orchiectomy was performed by removing the testes from the scrotal sac by the anterior route. The control animals received sham operations for adrenalectomy and castration. All operative procedures were performed under halothane anaesthesia. Each group contained six rats, which were then used for plasma kininogen determinations 6 days after the operation. The kininogen values were obtained by the method described previously (Senior & Whalley, 1974), and are expressed in μg ml^{-1}, 1 μg referring to the amount of liberated free kinin which was equivalent to 1 μg synthetic bradykinin (BRS640, Sandoz Products Ltd.). The method is essentially that of Diniz & Carvalho (1963) which uses trypsin to convert total kininogen to free kinin.

The results are presented in Fig. 1, statistical comparisons were determined using Student's *t*-test. It can be seen that in the sham operated control rats the female kininogen concentration is 2·3 μg ml^{-1} of plasma which is significantly higher ($P < 0{\cdot}05$) than that found for the male (1·9 μg ml^{-1}). Removal of the ovaries in the female results in a significant ($P < 0{\cdot}05$) decrease in the plasma kininogen concentration. In the male, however, castration results in a significant ($P < 0{\cdot}05$) increase in the plasma kininogen concentration. Adrenalectomy alone, in both sexes causes a significant increase in the plasma kininogen content when compared with control values, the effect being more marked in the male than in the female. When castration and adrenalectomy are carried out simultaneously, then the effect on the plasma kininogen concentration is again sex dependent. In the female following the double ablation the plasma kininogen concentration is not significantly different from the control value. However, in the male removal of the testes and adrenal glands together results in an even greater increase in the plasma kininogen concentration to 3·0 μg ml^{-1}.

The observations show that in the female gonadectomy and adrenalectomy result in opposite effects on the plasma kininogen concentrations. Thus, when the two ablations are performed simultaneously the changes in the kininogen concentration caused by removal of each pair of endocrine glands are negated resulting in values which are similar to the values for the control (intact) animals. In the male, where gonadectomy and adrenalectomy both result in an increase in plasma kininogen concentration, the effect of performing the ablation of both pairs of endocrine glands simultaneously results in an additive effect.

It has previously been shown that, after ovariectomy, treatment with oestrogen in physiological doses can restore the plasma kininogen concentration to that normally found in the mature female rat (McCormick & Senior, 1974). The increase in kininogen concentrations in the female as a result of oestrogen treatment can be modified by progesterone (Senior & Whalley, 1974), thus suggesting that in the female rat the ratio of oestrogen : progesterone will affect the kininogen concentration. This is substantiated by work on the immature female in which the kininogen values are low before sexual maturity defined by the onset of vaginal oestrus (McCormick & Senior, 1974). Similarly, Rothschild & Castania (1970) have shown that the kininogen concentration in young rats is lower than that found in the adult. In the male, the changes in plasma kininogen concentration resulting from castration can be accounted for by the influence of the androgenic hormones. Testosterone, has been shown to reduce the plasma kininogen content in the male (McCormick & Senior, 1974), consequently, removal of the major androgenic influence by orchiectomy results in an increase in plasma kininogen concentration. How does the increase in kininogen values in both male and female rats following adrenalectomy fit into this hypothesis? Castania & Rothschild (1974) have shown that adrenaline, and to a less extent noradrenaline, will reduce the plasma kininogen content in the anaesthetized rat. It is possible that by removing the whole adrenal gland the change in catecholamine concentration would result in less kininogen being mobilized. Another explanation for the rise in plasma kininogen in both sexes following adrenalectomy could be as a result of changing sex hormone patterns. The administration of corticosterone to rats appears to have little effect on the plasma kininogen content (Senior & Whalley, unpublished observation). However, the adrenal glands have been shown to contribute substantially to the peripheral plasma progesterone pool in the rat (Fajar, Holzbauer & Newport, 1971; Feder, Resko & Goy, 1968; Mann & Barraclough, 1973). Hence adrenalectomy would decrease the circulating progesterone thereby removing an influence which normally lowers the rat plasma kininogen content.

School of Studies in Pharmacology,
University of Bradford,
Bradford BD7 1DP, U.K.

JUDITH SENIOR
E. T. WHALLEY

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