thermal characteristics of the skin are changed in a way to combat these heating effects. Therefore, the harmful effects of high energy and long term radiation are decreased. 4. Pain threshold is frequently measured as temperature elevation or as reaction time, and then it is markedly affected by changes in blood flow and rate of sweating. However, if it is studied in terms of tissue temperature, it is independent of these physiological variables.

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Antagonism of Diuretic Action of Thyroxine by Ethanol. (22442)

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Pretreatment with thyroxine causes an increase in the rate of excretion following the administration of a water load in the dog(1) and in the rat(2). Since ethanol also elicits a diuresis(3,4), these two substances were combined in an attempt to produce a diuretic response suitable for use in the biological assay of the antidiuretic hormone (ADH). Contrary to expectations, ethanol was found to abolish the diuretic action of thyroxine.

Materials and methods. Four groups of animals, each containing 12 female rats weighing approximately 200 g, were used in this experiment. The control groups and the rats that were pretreated with thyroxine were gavaged with distilled water or 8.5% ethanol in an amount equivalent to 7% of the body weight. The resulting diuresis was quantified by placing 4 rats in each urine collection cage and measuring the volume of urine from each cage at 15 minute intervals until the urine flow returned to normal. The cumulative volume of urine excreted by each group of rats was then converted to the per cent of the total water load excreted and plotted as a function of time. Pretreatment with thyroxine consisted of the daily intraperitoneal injection of 20 μg of thyroxine for 7 days prior to the gavage with distilled water or ethanol. Two groups of pretreated rats were given the water and ethanol loads intraperitoneally in order to determine if the ethanol was interfering with the absorption of the fluid from the intestine.

Results. As shown in Fig. 1, ethanol prolongs the diuresis following the administration of a water load whereas pretreatment with 20 μg of thyroxine per day results in an increased rate of excretion. Both of these treatments lead to the excretion of a greater percentage of the water load than that observed in the untreated controls. However, when pretreated rats are gavaged with ethanol, the diuretic response is similar to that observed in the rats which received no pretreatment with thyroxine. Thus the ethanol abolishes the diuretic action of the thyroxine.

Since the excretion of the water load by all 4 groups of animals is linear from 75 to 135 minutes after the gavage, the differences in the rates of excretion observed during this period were analyzed statistically using the Analysis of Variance (2 way classification) method(5). The rate of excretion of the water load by the rats pretreated with thyroxine differs significantly ($P<0.005$) from the rates exhibited by the other groups but

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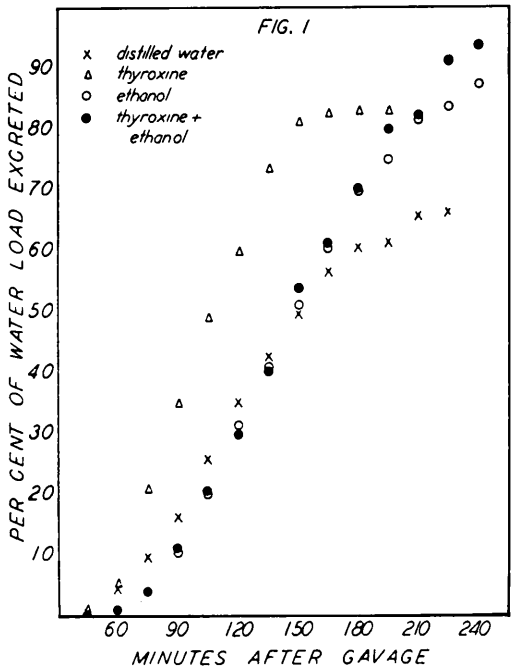

FIG. 1. Effect of ethanol, thyroxine, and combined treatment with ethanol and thyroxine on excretion of water load by the rat.

the diuretic responses of the rats gavaged with ethanol following pretreatment with thyroxine and the rats receiving only ethanol or water gavages do not differ significantly from each other.

As thyroxine is known to increase the rate of absorption of fluids from the intestines, water loads were administered intraperitoneally in order to determine whether the ethanol block occurred at this point. Since a differential rate of excretion was observed in thyroxine treated rats gavaged with distilled water and with 8.5% ethanol, the ethanol antagonism does not appear to occur in the intestine.

Available evidence indicates that the diuretic action of thyroxine is due, at least in part, to a direct action on the kidney(6) and is not dependent upon the increased BMR(7). This action of thyroxine is best explained by assuming that thyroxine increases the number of functional nephrons in the kidney(8).

Ethanol is presumed to cause a diuresis by decreasing the normal sensitivity of the supraoptico-hypophyseal mechanism to changes in the tonicity of the body fluids(3). This action is not a function of the actual amount of ethanol in the blood but rather, it is associated with an increasing concentration of ethanol in the blood. Thus a slow increase in the concentration of ethanol in the blood results in a greater diuresis than a rapid one (4).

On the basis of the accepted mechanisms by which these substances elicit a diuresis, it is difficult to explain the block of the diuretic action of thyroxine by ethanol. Since ethanol depresses the release of ADH, it is doubtful that the ethanol block of the thyroxine effect occurs at the hypophyseal level. However, it is equally difficult to explain this mechanism at the kidney level. As the ethanol block does not depress the rate of excretion below that of the untreated controls, the ethanol would have to act only on the "extra" nephrons mobilized by the thyroxine pretreatment. On the basis of the available data, it is not possible to explain this phenomenon.

Summary. Although thyroxine and ethanol possess diuretic activity when administered alone, the administration of 8.5% ethanol to rats pretreated with 20 μg of thyroxine per day for 7 days abolishes the diuretic action of the thyroxine. The ethanol block is not caused by a decrease in the rate of absorption of fluid from the intestine. The mechanism by which ethanol blocks the diuretic action of thyroxine is not apparent from the available data.

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