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FIELD RESEARCH LABORATORY

Fort Knox, Kentucky

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THE RESPONSE OF THE THYROID GLAND TO A LOW ENVIRONMENTAL TEMPERATURE AS STUDIED WITH RADIOIODINE*

*Sub-project under Study of Physiological Effects of Cold. Approved 24 Sept. 1942. (MDFRL Project No. 6-64-12-02-(6).

(6) THE RESPONSE OF THE THYROID GLAND TO A LOW ENVIRONMENTAL TEMPERATURE AS STUDIED WITH RADIOIODINE*

by

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ABSTRACT

THE RESPONSE OF THE THYROID GLAND TO A LOW ENVIRONMENTAL TEMPERATURE AS STUDIED WITH RADIOIODINE

OBJECT

Limited studies by this laboratory of basal metabolic rates of men exposed to cold in an Arctic environment did not reveal any demonstrable change in energy metabolism. In order to determine the effects of varying amounts of cold exposure on thyroid function, studies were carried out on rats using the uptake of radioiodine as a measure of the functional activity of the gland.

RESULTS

The studies of Leblond et al. (2) were extended to shorter and longer time intervals of exposure to ~~cold~~ Male rats were exposed to 4° ± 0.5°C for periods of from 2 hours through 60 days. A diminished amount of radioiodine was found to be present in the experimental animals at exposure intervals under 6 hours. The amount present at about 6 hours was the same as for the controls and increased after 12 to 24 hours. The increased uptake was most pronounced at 7 to 9 days and gradually returned to control values by 40 days.

RECOMMENDATIONS

The causes of the apparent inhibition at short intervals of exposure should be investigated. The relationship between body temperature and thyroid function should be studied further.

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I. INTRODUCTION

It is a well established fact that the thyroid gland, because of its influence on metabolism, plays an important role in the regulation of body temperature. That the function of this endocrine gland is affected by the environmental temperature has also been recognized for many years. This response of the thyroid to cold has been studied by various methods, the most common method of study being histological (1).

Leblond et al. (2) used radioactive iodine (I^{131}) to estimate the activity of the thyroid gland. They studied the uptake of radioactive iodine by the thyroid and its degree of conversion to diiodotyrosine and thyroxine in rats exposed to cold (0-2°C) for periods up to 40 days. Using a carrier dose of radioiodine (5 micrograms) and studying three exposure intervals, it was demonstrated that there was an apparent increase of uptake following 7 days exposure, maximal at 26 days and absent after 40 days of exposure.

It was felt desirable to extend this study of thyroid function at low environmental temperatures to shorter and also longer time intervals. The uptake of radioactive iodine (I^{131})* was used as a measure of the functional activity of the thyroid gland.

II. EXPERIMENTAL

A. Apparatus and Methods

Male rats of the Wistar strain were used. On arrival at the laboratory, they were immediately placed on Purina laboratory chow ad lib., and on water that was redistilled from alkaline solution. They were maintained on this regimen for at least 10 days before experimental procedures were attempted. Experimental animals were kept in wire mesh cages with 6 individual compartments. These cages were kept on a rack that permitted free air circulation. The temperature of a large walk-in refrigerator in which the rats were kept was maintained at 4° ± 0.5°C for periods up to 60 days. A constant record of the temperature was made on a Taylor thermograph. The light in the cold room was left on throughout the working day.

Control animals were kept together until one week before use at which time they also were placed in individual cages.

All animals were allowed water but were deprived of food for a period of 24 hours prior to sacrifice. Two hours before being sacrificed they were injected intraperitoneally with about 5 microcuries of radioiodine (I^{131}) made up in Krebs phosphate buffer (pH 7.4). The following

* Supplied by Oak Ridge National Laboratories.

was used for preparing the necessary radioiodine. The required amount of I^{131} solution (about 5 microcuries/rat) was pipetted into a small Erlenmeyer flask and then the necessary volume of Krebs phosphate buffer added so that 1 ml. of solution was available per animal and also for a standard. The liquid was agitated by flushing the injection syringe several times with this solution. One milliliter aliquots were used for the intraperitoneal injections and also for the standard. The standard was used to determine precisely the amount of radioactive iodine used for injection. It was made up as follows: 1 ml. of the solution was made up to a 1000 ml. volume with distilled water and later a 1 ml. aliquot was counted along with the fractionated thyroid.

Precisely two hours after injection of the radioiodine (experimentals were injected in the cold room) the animals were sacrificed by a sudden sharp blow at the base of the skull. They were immediately exsanguinated by cutting into the chest and the thyroids were rapidly excised and placed in 2 ml. of 2 N sodium hydroxide, then heated on the steam bath for 2 hours and the hydrolysate made up to a given volume. An aliquot was counted for determination of per cent of total uptake of the injected dose. A known portion of the remaining hydrolysate was then taken for fractionation into organic bound and inorganic radioiodine components. The inorganic fraction was usually discarded. However, to check the extraction procedure, on several occasions the inorganic fractions were also extracted and the results when added with the organic-bound determinations gave close agreement (2-3%) with the total count.

All animals were autopsied and if any gross abnormalities were noted, they were excluded from the experiment. Altogether, more than 250 animals were used in this investigation.

B. Results

The first experiments were made after relatively short exposures to cold ($4^{\circ} \pm 0.5^{\circ}C$); namely 1, 3 and 7 days. The results obtained showed that there was an increased uptake even at one day.

In numerous repeat experiments of rats exposed to $4^{\circ} \pm 0.5^{\circ}C$ for 1 day, it was confirmed that there was a definite increase of uptake by the thyroid of the injected I^{131} tracer dose as compared with controls. The uptake noted was almost equal to that reported by Leblond et al. (2) for longer time intervals (7 and 26 days). For comparison, data have been extracted from the literature and are plotted with all of those obtained in this investigation. (See Figure 1).

1. Short Exposures to Cold:

As the values obtained after exposure to $4^{\circ} \pm 0.5^{\circ}C$ for 24 hours indicated a definite stimulation of the thyroid, it was of interest to determine how early this increased uptake took place.

The next group of animals studied are here referred to as the short time exposures, i.e. less than 24 hours. As can be seen from the graph (Figure 1) after only 2 hours exposure to $4^{\circ} \pm 0.5^{\circ}C$ there was an

apparent decrease in the uptake of radioiodine. At 4 hours, it increased somewhat and after 6 hours in the cold it came up to control values. It was only after 6 hours that an increased iodine content occurred and at 12 hours was comparable to the 24 hour values. From the graph (Figure 2) it can be seen that the organic component followed the general outline of the total I^{131} uptake curve.

To eliminate the possibility that the decreased uptake at the early time intervals could be due to circulatory changes, the following experiment was done. A group of 12 rats had their back legs shaved over a superficial vein 3 days before they were to be injected intravenously. Two groups of 4 each were placed in the cold room at $4^{\circ} \pm 0.5^{\circ}C$ for 2 and 4 hours respectively. Then, while still in the cold, they were injected with the usual 1 ml. aliquot of I^{131} solution intravenously and were allowed to stay in 2 hours longer, after which time they were sacrificed. Controls were likewise injected intravenously and were sacrificed 2 hours later. The results obtained with the intravenous administration of I^{131} were in close agreement with those by the usual intraperitoneal injection and are incorporated in the graph.

2. Long Exposure to Cold:

Animals were maintained in the cold for periods up to 60 days. As mentioned previously, it has been possible to show earlier stimulation of thyroid activity than has previously been reported in the literature. The per cent of an injected dose of radioiodine taken up was used as an index of activity. There was increased uptake as early as 12-24 hours. The data obtained from the 3 and 7 day runs also showed enhanced uptake, whereas at 40 days, the uptake of I^{131} was again at control values. Every experimental group of rats was controlled by animals of the same shipment and also of the same age. A 60 day interval showed that the gland was still at essentially control values.

III. DISCUSSION

The data obtained have been grouped into proper exposure intervals and have been plotted with standard error. The curve may arbitrarily be broken up into three components.

The first part is from 2 to 6 hours. It shows that there was a decreased amount of I^{131} present in the gland and that the amount present gradually increased. The second portion of the graph began at about 6 hours where the experimental values were equal to controls. Uptake rapidly increased so that by 12-24 hours, the amount of I^{131} present in the gland was above control values. The difference was increasing up to 7 days and then progressively fell so that after 40 days of exposure to $4^{\circ} \pm 0.5^{\circ}C$ the experimental values were essentially those obtained for the control.

The return to normal values after 40 day exposure has been reported previously by Starr and Roskelley (1a) and by Leblond *et al.* (2).

IV. CONCLUSIONS

1. The per cent uptake of radioiodine by the thyroid glands of Wistar male albino rats that have been exposed to $4^{\circ} \pm 0.5^{\circ}C$ for periods varying from 2 hours through 60 days has been studied.

2. There was a diminished amount of radioiodine present in the experimental animals at intervals under 6 hours. The amount present at about 6 hours was the same as for the controls and was increased after 12-24 hours.

3. After 24 hours, this increased uptake was most pronounced at 7-9 days and gradually returned to control values by 40 days.

V. RECOMMENDATIONS

1. The causes of the apparent inhibition at short time intervals should be investigated.

2. Relationship between body temperature and thyroid function should be studied further.

3. The function of the thyroid during adaptation (BMR measurements) should be determined.

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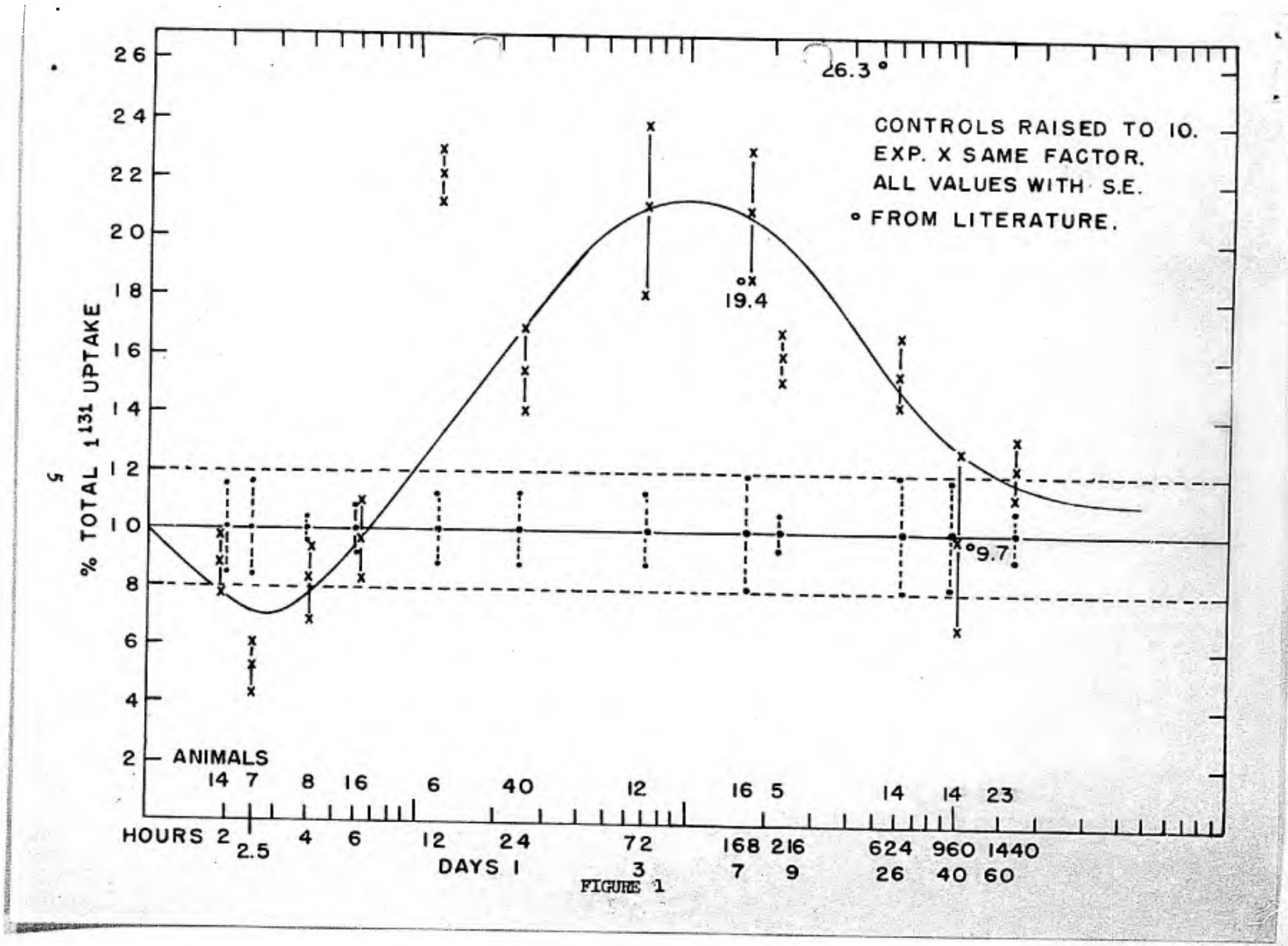
26.3°
CONTROLS RAISED TO 10.
EXP. X SAME FACTOR.
ALL VALUES WITH S.E.
° FROM LITERATURE.
19.4
9.7
% TOTAL I131 UPTAKE
26
24
22
20
18
16
14
12
10
8
6
4
2
ANIMALS
14 7 8 16 6 40 12 16 5 14 14 23
HOURS 2 2.5 4 6 12 24 72 168 216 624 960 1440
DAYS 1 3 7 9 26 40 60

FIGURE 1

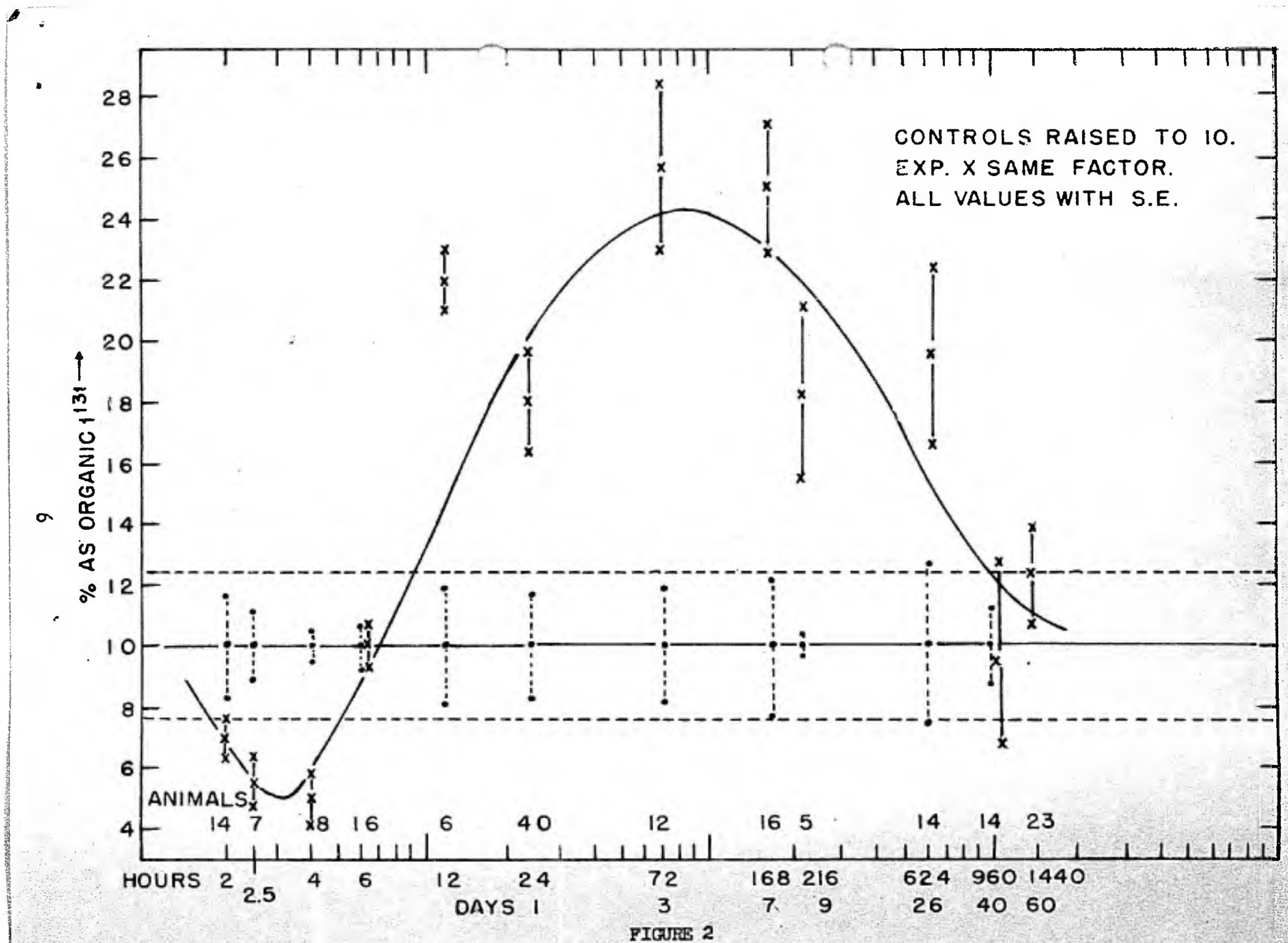
CONTROLS RAISED TO 10.
EXP. X SAME FACTOR.
ALL VALUES WITH S.E.
% AS ORGANIC I131
28
26
24
22
20
18
16
14
12
10
8
6
4
ANIMALS
14 7 8 16 6 40 12 16 5 14 14 23
HOURS 2 2.5 4 6 12 24 72 168 216 624 960 1440
DAYS 1 3 7 9 26 40 60

FIGURE 2