produces nuclear damage. Although this damage resembles nuclear damage which occurs when the entire cell is irradiated, it is less severe due to the protection of the cytoplasm from the effects of irradiation. (2) Continuous ultraviolet irradiation of the nucleus of a living cell produces cytoplasmic damage resembling that which occurs when the entire cell is irradiated, but is less pronounced.

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Septal and Anterior Hypothalamic Lesions: Some Effects on Sleep and Body Metabolism in Cats.* (26943)

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It is currently hypothesized that the posterior hypothalamus and ascending reticular formation are concerned with the state of wakefulness. In accordance with this, it has been postulated that somnolence is due to periods of depressed activity within these regions. Some authors, although supporting the relationship of these areas to wakefulness, have preferred to regard these periods of depressed function as due to influences from specific mechanisms which may be subject to extrinsic rather than intrinsic factors.

Ranson and Ingram(1), and again Ingram *et al.*(2) reported that lesions placed in a number of areas of the cat's hypothalamus caused somnolence, but no sleeplessness was noted. Kabat *et al.*(3), stimulated the preoptic region of cats without producing sleep. Ranson and Magoun(4) partly destroyed this latter region (in cats) and observed no change in sleep-wakefulness cycles. Insomnia was not mentioned by Ranson(5) after lesions in the hypothalamus of monkeys.

Nauta(6) described a condition of sleeplessness produced by elimination of the suprachiasmatic and preoptic areas in rats. Postoperatively these animals behaved more or less normally, but would not sleep and after a few days lapsed into a state of exhaustion and died. Nauta concluded that there might be an area in the preoptic region which served as a "sleep center", as opposed to a "waking center", referring to a region in the posterior hypothalamus around the mammillary nuclei. This latter area, when removed, would produce somnolence, and Nauta believed that the "sleep center" functionally inhibited the "waking center" to produce a state of sleep. Heath(7) placed lesions somewhat rostral to those of Nauta, but including some areas in common, and no sleeplessness was reported.

Considering Nauta's findings from the standpoint of metabolic and hypothalamic re-

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lationships one wonders if disturbances of metabolism could have been induced and contributed to a truly sleepless state.

This work concerns an attempt to reproduce Nauta's results in cats, and to uncover any gross metabolic disturbances that might be related to it.

Methods. Bilateral electrolytic lesions were placed by stereotaxic means in the suprachiasmatic and preoptic region of 24 cats. These were designed to conform as closely as possible to the area which Nauta incised surgically in rats.

Criteria for determining alterations in sleep and wakefulness cycles in cats present serious difficulties since each animal has its own particular pattern. Two approaches to the problem were used. One method was the observer's subjective impression. Evidence of sleep was judged on the basis of posture, position of the head, eyes open or closed, and respiratory depth and rate. A second method involved the use of an activity recorder, patterned after the description by Mitchell(8). Controls were run on the recorder for each cat before the operations. The instrument provided an easily standardizable method for determining whether a cat moved around the cage more after operation than before. Records were run on some animals throughout the day and night during alternate 15-minute intervals, by means of a timing device, and random recordings were made throughout the postoperative period. Visual observation combined with electrical recording provided an index of activity, and also presumptive evidence for sleep in these animals.

Five animals were fed a special diet prior to operation to determine the range of normal values for certain contemplated blood and urinary chemistry determinations. The diet consisted of 100 g of horse meat, 100 ml milk and 100 ml water per day. These animals were kept in metabolism cages which allowed accurate determination of urinary output. Daily rectal temperatures were also taken.

By means of cardiac puncture repeated samples of blood were obtained. Serum sodium and potassium were determined by flame photometry and chlorides by a Chloridometer. (Blood sugars were not determined in this experiment.) The values so obtained correlated well with those of other authors. Urinary chlorides were monitored using the "Fantus Test," and urinary reducing substances were determined by means of the Clinitest. The other 19 animals were fed a regular animal house diet. During the first 24 hours postoperatively 50 ml normal saline and 50 ml of a 5% glucose solution were administered subcutaneously.

The brains were removed after perfusion with 10% formol-saline. Alternate microscopic sections were stained by the Nissl and Weil technics for determination of the location and limits of the lesions.

Results. Microscopic evaluation of the 24 animals revealed that the lesions desired had been obtained in 11. This group displayed 2 forms of postoperative behavior. Seven of these 11 animals recovered uneventfully; however, it was noted and confirmed by the activity recorder that marked hyperactivity, *i.e.*, agitation and increased pacing associated with decreased sleeping time, occurred from the fourth to the seventh day. The remaining group of 4 recovered promptly but did not show this phase of hyperactivity.

Five of the 7 animals previously described, and 2 from the latter group of 4, began to decline physically after the seventh postoperative day, concomitant with failure to eat or drink, so that they had either died or were moribund at the time the brains were removed. Blood serum and urine chemistries failed to reveal any significant trends in the values obtained other than those which might be expected because of decreased oral intake, or the necessity for continued administration of subcutaneous fluids beyond the first postoperative day.

No abnormalities in temperature control, other than the transient drop found after pentobarbital anesthesia, was found in 5 animals so studied. Three of these were included in the group which declined to the moribund state.

The largest extent of a typical lesion is shown in Fig. 1. Rostral limits of the lesions in all 11 animals were at the level of the anterior commissure, as it crosses the midline,

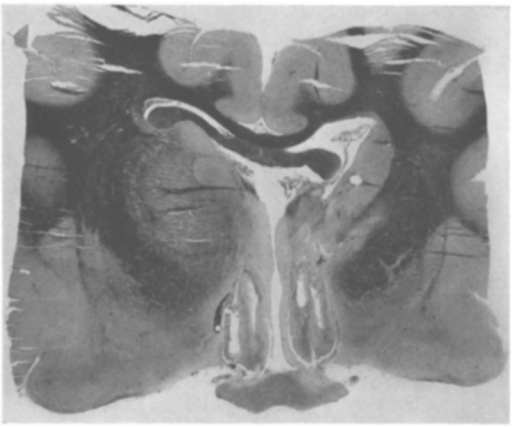

FIG. 1. Photomicrograph showing the greatest dimensions of satisfactory lesions in a typical animal. Weil stain.

and they extended caudally through the whole of the anterior hypothalamic area. Ventrally they reached the level of the optic chiasm and dorsally the roof of the third ventricle. However, when obvious microscopical differences were sought between the group of 7 cats that declined and the 4 that showed no change, no variations were readily apparent.

Discussion. Lesions located in presumably similar areas in the cat and rat appear to be without comparable effects on the sleep-waking cycle in the 2 species. The unexpected pattern of a sudden physical decline, beginning about the eighth postoperative day in a large percentage of cats, was interesting, but unexplained by such metabolic disturbance as might be indicated by the chemical methods herein used.

Without going into a minute analysis of fiber and nuclear damage and/or volumetric estimates of tissue damage, there appears to be no ready anatomical evidence for the difference in outcome of the 2 groups. Perhaps the eventual gathering of specifically meaningful knowledge of the area may help to account for these findings.

Summary. Eleven cats were subjected to lesions which were thought to correspond to Nauta's preoptic brain transections in rats. Seven of these exhibited a brief period of hyperactivity from the fourth through the seventh postoperative day, whereas 4 showed no change. Seven also declined physically, ceased drinking and eating, and died(2) or approached death before sacrifice. This decline could not be correlated directly with the periods of hyperactivity. There was no persistent alteration in sleep-wakefulness cycles. The only gross effect on serum electrolytes was concentration concomitant with dehydration. Potassium levels fell corresponding to a decrease in intake.

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Goldthioglucose-Induced Hypothalamic Lesion and ACTH Release.* (26944)

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Goldthioglucose (GTG) when administered to mice in appropriate concentrations will produce localized destruction in the hypothalamus(1,2,3) and other areas of the

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