autosomal alleles which are not closely linked with the brown-black locus (linkage group VIII) and the dilute-dense locus (linkage group II). 4. Substrain STR/N has the As_a^1 allele whereas STR/1N has the As_a^2 allele indicating the second known gene difference between these two substrains.

We gratefully acknowledge the technical assistance of Mr. William Humphrey, Jr.

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Received May 6, 1963. P.S.E.B.M., 1963, v113.

Anatomical Changes in Middle Ear and Cochlea of the Rat Following Stimulation with High Intensity Sound. (28412)

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High intensity sound is a potent stressor. As such it affects experimental animals by producing an increased secretion of adrenal cortical hormone(1-3). This effect might be mediated through (1) physical damage to the animal, *e.g.*, through trauma to the acoustical apparatus, (2) production of epileptiform seizures, and/or (3) activation of a complex neuroendocrine mechanism. This last interaction has been demonstrated in a previous study which showed that high intensity sound, like other stressors (immobilization, scalding) produces marked changes in the secretion rate of corticosterone in the rat(3,4). A marked increase of secretion is observed after 2 or 48 hours of sound exposure, while a marked decrease in corticosterone secretion is observed after 12 hours of exposure(3). This effect was noted without the occurrence of any type of seizure (3). As the increase of corticosterone secretion could be prevented by destruction of the middle ear bilaterally, it is clear that intense sound is effective only through the auditory apparatus(3). The present study was done to evaluate anatomical effects of high intensity sound on the middle ear and

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cochlea of rats, and thus to determine whether physical, anatomical trauma might be in part responsible for the observed changes in corticosterone secretion rate.

Methods. Six Sprague-Dawley female rats weighing 200-250 g were exposed to sound of sinusoidal character at a frequency of 200 cycles per second (cps) and an intensity of 130-135 decibels (db). The animals were studied in pairs, each pair exposed to sound for either 2, 12 or 48 hours. Each animal was placed in an individual cage for 7 days prior to study and kept there throughout the experiment. Twenty-four hours prior to sound stimulation the animals were placed in a room where they could be completely surrounded by a sound field. The sound was monitored by a condensor microphone and oscilloscope to maintain constant intensity and sinusoidal wave characteristics.

Two Sprague-Dawley female rats weighing 200-250 g received identical treatment except that they were not exposed to sound. Immediately after stimulation, the animals were sacrificed by decapitation. Temperoparietal areas of the skull were removed bilaterally and placed in 5% trichloracetic acid for decalcification and dehydration. After 3 weeks the temporal bones were isolated and placed in fresh 5% trichloracetic acid for an additional 2 weeks. The areas of the middle and inner ears were then isolated and embedded in celloidin. Sections were made at 5 μ intervals extending from the middle ear to the cochlea (from the basal portion to the apex). All sections were made parallel to the modiolus of the cochlea to provide representative mid-modiolar sections in a vertical plane. Every fifth section was mounted and stained with hematoxylin-eosin. Evaluation of anatomical changes was made, using light microscopy, by the author and by a pathologist who had no prior knowledge of the experimental design. Independent judgments of anatomical changes were in agreement in each case.

Results. No anatomical changes were noted in the middle ears of any of the animals. The cochleas of the animals exposed to 2, 12 or 48 hours of sound, when compared to those of normal controls, showed a mild degree of edema in the external hair cells along the basilar membrane (Fig. 1).

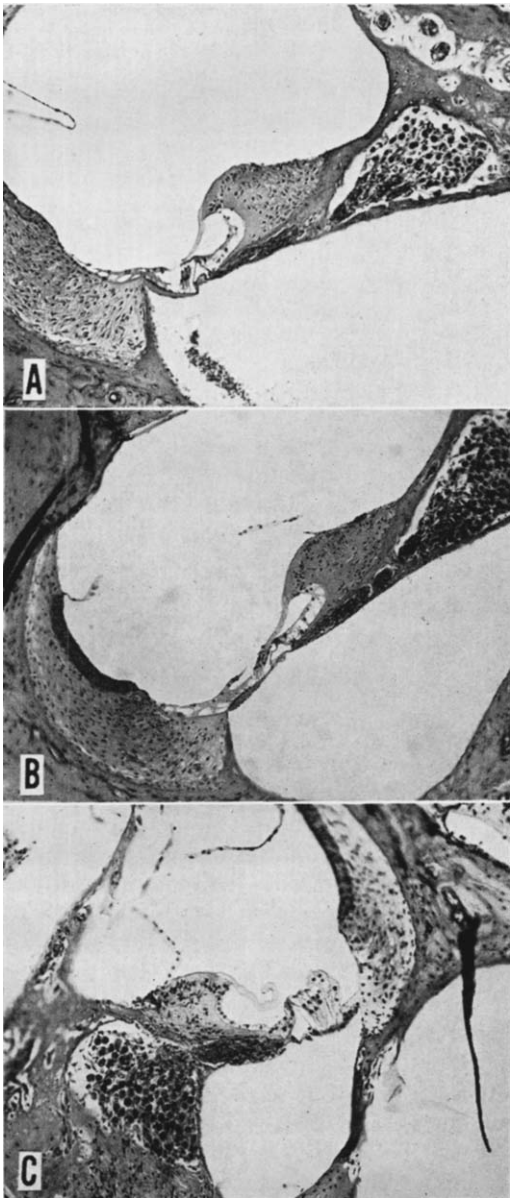

FIG. 1. A. Photomicrograph of a mid-modiolar section of right cochlea of a control rat (H and E, 150 ×). B. Photomicrograph of a mid-modiolar section of right cochlea of a rat after 12 hr of high intensity sound. Note slight edema of hair cells along basilar membrane. No other significant anatomical changes can be identified (H & E, 150 ×). C. Photomicrograph of a mid-modiolar section of right cochlea of a rat after 48 hr of high intensity sound. Note edema of hair cells along basilar membrane. No other significant anatomical changes can be identified (H and E, 150 ×).

After 48 hours of continuous high intensity sound the hair cells were slightly more edematous than after 12 hours of sound. No other changes were observed. No damage to the mesothelial cells beneath the basilar membrane was noted in any section.

After 2 or 48 hours of continuous, high intensity sound there was a marked increase in corticosterone secretion(3). After 12 hours of continuous high intensity sound there was a significant decrease in corticosterone secretion(3).

Discussion. Röhr(5) and Marx(6) exposed guinea pigs to sound of sufficient intensity to produce degenerative cochlear changes. They noted, however, that in mice exposed to sound of this same intensity there were no histological changes of any kind. Kimura reported that degenerative cochlear changes were produced following intense sound in pigeons, guinea pigs and mice(7). He attributed failure of previous workers to produce changes in mice to inadequate methods of exposure. It is not clear whether the species differences are in fact real because subsequent studies dealing with cochlear and hearing changes following intense sound have been carried out mainly in guinea pigs.

The middle ears and cochleas of the rats exposed to high intensity sound in the present study, for as long as 48 hours, showed very little histological change as compared to those of non-exposed rats, and there was no indication of significant acoustical trauma. Rat cochleas may be more resistant to the trauma caused by high intensity sound than those of other species. As there are no published data available for the rat, comparable to the guinea pig, interpretation of the present findings is difficult.

Most investigators agree that continuous sound stimulation at an intensity less than 100 db and a frequency less that 1000 cps, even for as long as 70 days, produces no cochlear damage in guinea pigs and cats and does not interfere with hearing as estimated from cochlear microphonic thresholds (CMT) (8-10). At the same intensity and a frequency of 2500 cps cochlear changes have been observed and their incidence is correlated with decreases in CMT(9). Other workers have noted cochlear changes in guinea pigs after exposure at 134 db but have found that these changes could not always be correlated with decreases in CMT (11-13). Exposure of guinea pigs to sound of 140 db or above produced significant cochlear changes correlated with hearing loss (14-17). Workers generally agree that one of the mildest unquestioned anatomical changes in guinea pig cochleas following intense sound is the stripping of the mesothelial cells from under the basilar membrane(16-18). This stripping has been found without any other evidence of cochlear trauma. The absence of these cells, however, does not preclude normal or nearly normal auditory function in guinea pigs(19). Changes in the protoplasm of the external hair cells of the organ of Corti are also sensitive indicators of acoustical trauma, but these changes are reversible and variable and not specifically related to hearing loss (16,18). One of these early changes is edema of the external hair cells.

In the present study a slight degree of edema of the hair cells along the basilar membrane was observed in the stressed, but not in the unstressed animals. No other anatomical changes were observed. The meaning of the edema cannot be fully interpreted. The absence of degenerative anatomical changes does not mean unequivocally that there was no cochlear trauma. It is always possible that anatomical changes would have become more apparent if the animals had been allowed to survive for a longer time(15,17), although this appears to be unlikely(20). In any event, after 48 hours of continuous exposure to intense sound no significant anatomical changes could be observed.

The intense sound field into which the animals of the present study were placed effected marked changes in the secretion of corticosterone. After 2 or 48 hours of continuous high intensity sound there was a marked increase in corticosterone secretion but no significant cochlear trauma. After 12 hours of continuous high intensity sound there was a marked decrease in corticosterone secretion to levels below those of the

non-stressed animals and at this time there was also no significant cochlear trauma. Thus the increase in steroid secretion does not appear related to any anatomical cochlear changes. Rather it results from activation of neuroendocrine mechanisms involving the hypothalamic-pituitary-adrenal axis.

Summary. Rats were exposed to sound of 200-220 cps at an intensity of 130-135 db for 2, 12 or 48 hours. A marked increase in secretion of corticosterone was observed after 2 or 48 hours, and a marked decrease after 12 hours. Significant anatomical changes were not observed in the middle ears or cochleas of any of the animals. The data suggest that the changes in secretion rate of corticosterone do not depend on anatomical changes in the rat cochleas.

The author is deeply indebted to Dr. Drake W. Will for his assistance in interpreting the cochlear photomicrographs.

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Received May 10, 1963. P.S.E.B.M., 1963, v113.

Fat-Mobilizing Effect of Growth Hormone in the Guinea Pig.* (28413)

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The rise in plasma free fatty acids (FFA) after parenteral administration of somatotropin preparations has been well-documented in several species tested with material from various sources(1-3). It is recognized that growth hormone preparations available are contaminated with small amounts of other pituitary principles; for brevity, the term somatotropin (or growth hormone) will be used in place of somatotropin preparation. This report concerns the response to an ovine (sheep) somatotropin in the guinea pig, a test animal heretofore not found responsive to several somatotropins (4).

Materials and methods. Male guinea pigs of mixed color, initial weight varying from 250-300 g, were used. Somatotropin used in these studies included ovine‡ and bovine§

* This investigation was supported by a Public Health Service training grant from Nat. Inst. of Arthritis and Metab. Dis.

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‡ Kindly supplied by Endocrinology Study Section, Nat. Inst. of Health, N.I.H.-GH-S-4.

§ Kindly supplied by Endocrinology Study Section, Nat. Inst. Health, N.I.H.-GH-B-2.