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7. I am grateful to Armour Research Laboratories and to Dr. I. I. Geschwind for supplying, respectively, the Armour MSH #D216-155C and the purified β -MSH used in this investigation.
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9. I am grateful to Dr. Aaron B. Lerner of Yale University School of Medicine for supplying the melatonin used in these experiments.
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Experimental Study of Teratogenic Effect of Emotional Stress in Rats

Abstract. The teratogenic effect of audio-visual and immobilization stress was studied in rats. Groups of 15 animals were subjected from the 9th to the 12th day of pregnancy to one or the other of these types of stress or to stress combined with administration of vitamin A. It was shown that the stresses alone had no effect on congenital malformations. Immobilization stress seemed to potentiate the teratogenic effect of vitamin A.

Rats of the Holtzman strain, ranging in weight from 250 to 320 g, were used in the experiment reported here (1). The female animals were kept together with males. Vaginal smears were taken every night and examined for spermatozoa. The day on which spermatozoa were found was regarded as the first day of pregnancy. The pregnant rats were divided at random into six groups with 15 animals in each group. The groups were treated as follows. Group 1 consisted of control animals. Rats in group 2 were subjected to intermittent ringing of bells and flashing of light (2) from the 9th to the 12th day of pregnancy for 6 hours daily. Rats in group 3 were subjected to immobilization, as described by Renaud (3), for 3 hours on the 9th day and for 4 hours from the 10th to the 12th day of pregnancy. Each rat in group 4 received, by intubation, 15,000 international units of vitamin A in oily suspension (4) daily from the 8th to the 12th day of pregnancy. Rats in group 5 were also given the vitamin A and, in addition, were subjected to audio-visual stress, like those in group 2. Rats in group 6 received the vitamin A and, in addition, were subjected to immobilization, like those in group 3.

All animals were allowed to eat Purina laboratory chow ad libitum and were also fed raw potatoes and dry bread three times a week. The animals were killed on the 20th day of pregnancy. The young were removed,

weighed, and preserved in 10-percent Formalin until they had been examined macroscopically. Deformities of the brain and calvaria as well as cleft palate were recorded.

The results are shown in Table 1. No congenital malformations were found in young of the control group or of the groups which were subjected to stress only (groups 2 and 3). In the group fed vitamin A but not subjected to stress (group 4) there was a low incidence of malformations; these were confined to about one-third of the litters. About the same proportion of malformations occurred in the group in which feeding of vitamin A was accompanied by audio-visual stress (group 5). In the young of rats that had been fed vitamin A and had also been immobilized (group 6), the percentage of cleft palates was eight times as high as in the young of those that had only been given the vitamin, and the percentage of young with some malformation was about five times as high. The percentage of resorbed embryos in group 6 was relatively high—a fact which explains the lower number of young per litter in the group. This may also explain the small number of young with deformities of brain and calvaria in this group, since it is known that embryos with severe malformations tend to die and are then resorbed.

Animal experiments have shown that administration of cortisone during pregnancy increases the teratogenic effect of vitamin A hypervitaminosis in rats (5). Cortisone has also been found to increase the incidence of cleft palate in mice of a genetic strain in which there is normally a low incidence of cleft palate (6). Since stimuli causing nervous excitement are known to increase

adrenal cortical secretion (7), a similar, teratogenic effect might be expected as a result of emotional stress.

Although the audio-visual stress had some effect on the behavior of the animals in our experiment, causing them to hide under each other and to wash their faces (8), it did not increase the frequency of vitamin-A induced deformities. Possibly it was not severe enough. Immobilization is a severe stress in rats; it causes a typical alarm reaction, with enlargement of the adrenals within a few hours (3, 9). Its severity, even if applied for 3 to 4 hours on 4 days only, is shown by the fact that a vaginal bleeding with coagula was observed in four animals during immobilization. The bleeding appeared on the 11th or 12th day of pregnancy and almost certainly was a sign of abortion. It differed radically from the small physiological uterine bleeding which is a characteristic sign of pregnancy in rats and appears usually on the 14th day of pregnancy (10). Since the uteri of the animals with observed bleeding looked like the uteri of the other nonpregnant animals, it is quite probable that immobilization had caused a miscarriage in most of the nonpregnant animals of groups 3 and 6.

Immobilization alone did not cause any malformations, but it seemed to increase the teratogenic effects of vitamin A. This result is similar to the findings of Millen and Woollam (5), that cortisone administration increases the teratogenic effect of vitamin A hypervitaminosis in rats but does not itself cause malformations. Immobilization has been called a pure emotional stimulus (3, 9), but this can be argued, of course, and the same authors have also called it a "neuromuscular exer-

Table 1. Effect on congenital malformations in the offspring of rats of audio-visual stress, immobilization stress, and vitamin A plus stress. Figures in parentheses, percentages of total.

| Item | Controls | Stress | | Vitamin A | Vitamin A plus stress | |
|--|------------------|------------------|------------------|------------------|-----------------------|------------------|
| | | Audio-visual | Immobilization | | Audio-visual | Immobilization |
| Rats with spermatozoa in vaginal smear (No.) | 15 | 15 | 15 | 15 | 15 | 15 |
| Mean weight of rats on 1st day of pregnancy \pm standard error (g) | 266.3 \pm 6.25 | 269.0 \pm 8.51 | 262.3 \pm 6.87 | 272.3 \pm 6.75 | 271.2 \pm 6.12 | 270.7 \pm 4.76 |
| Rats with young (No.) | 14 | 13 | 8 | 14 | 14 | 5 |
| Rats with vaginal bleeding (observed abortions) (No.) | | | 2 | | | 2 |
| Totally resorbed embryos (No.) | | 7 | 3 | 2 | 1 | 9 |
| Young (total No.) | 182 | 152 | 102 | 178 | 162 | 49 |
| Mean weight of young (g) | 2.40 | 2.47 | 2.45 | 2.46 | 2.65 | 2.41 |
| Young per litter (No.) | 13.0 | 11.7 | 12.8 | 12.7 | 11.6 | 9.4 |
| Litters with deformities (No.) | | | | 5 | 5 | 3 |
| Young with deformities (total No.) | | | | 13 (7.3) | 7 (4.3) | 18 (36.7) |
| Young with deformities of brain and calvaria (No.) | | | | 11 (6.2) | 3 (1.9) | 1 (2) |
| Young with cleft palate (No.) | | | | 8 (4.5) | 4 (2.5) | 18 (36.7) |

tion" (11). The struggling of properly immobilized animals was minimal after the first day, and lesions or tourniquet effects in the extremities were avoided through adequate technique. If this particular form of stress is regarded as mainly emotional, the results support the opinion that emotional factors may under certain circumstances favor the manifestation of congenital defects (12).

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References and Notes

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Perturbations of the Orbit of the Echo Balloon

Abstract. The motion of the Project Echo communications satellite during its first 12 days clearly confirms previous predictions of the influence of solar radiation pressure. During this time, solar pressure reduced perigee height by 44 km. The approximate value of 1.1×10^{-18} g/cm³ has been obtained for the average air density at the 1600-km altitude of the satellite.

The successful launching of the Echo I balloon on 12 August 1960 provided the first definitive test of the effect of solar radiation pressure on satellite orbits. The importance of this effect on the orbits of large, lightweight satellites was originally discovered and first demonstrated theoretically in the spring of 1959 by the authors, in collaboration with R. W. Parkinson (1).

As reported by the National Aeronautics and Space Administration (NASA), Echo I is an aluminum-coated, half-mil Mylar sphere, 100 ± 1 feet in diameter. Its weight when launched was 157.00 lb, including 33.34 lb of sublimating powders. Hence

its cross-sectional area-to-mass ratio (A/M) was initially 102 cm²/g. Small holes introduced before launching, and meteoric punctures, will permit gas to escape, reducing the mass at a rate difficult to predict. The acceleration due to solar radiation is $K(I/c)$ (A/M), where I is the solar energy flux (2), c is the velocity of light, and K is a constant ($0 \leq K \leq 2$) whose value depends on the reflecting characteristics of the surface. For specular reflection from a perfect sphere, $K = 1$. Small irregularities in the shape or any diffuseness in the reflection of sunlight will tend to increase K . (For a sphere whose reflection is completely diffuse, $K = 1.44$.) In addition, if the balloon surface nearest the sun is at a higher temperature, the emitted infrared radiation will be nonisotropic and will have the effect of increasing K .

At the time of writing of this report, orbit data were available only for the first 12 days. Orbital elements were computed from the data by P. Zadunaisky of the Smithsonian Astrophysical Observatory (3, 4). Zadunaisky used only unrefined angular data obtained by the Baker-Nunn cameras. Each computed set of elements was determined from two days of observations, centered about the epoch of the elements. The trial expressions for the mean anomaly, the eccentricity, and the argument of perigee consisted of second order polynomials. However, in the latter two cases, all but the lowest order coefficient were held fixed throughout the computation (5). The data obtained each day were well distributed about the orbit, and hence the residuals are rather small; the probable errors of the elements are indicated on the appropriate graphs (see Figs. 1 and 2). Short-period terms appear neither in the elements computed from observations nor in our theoretical results, since these terms are averaged out in both cases.

In Fig. 1, we have plotted the orbit eccentricity (e) versus time through

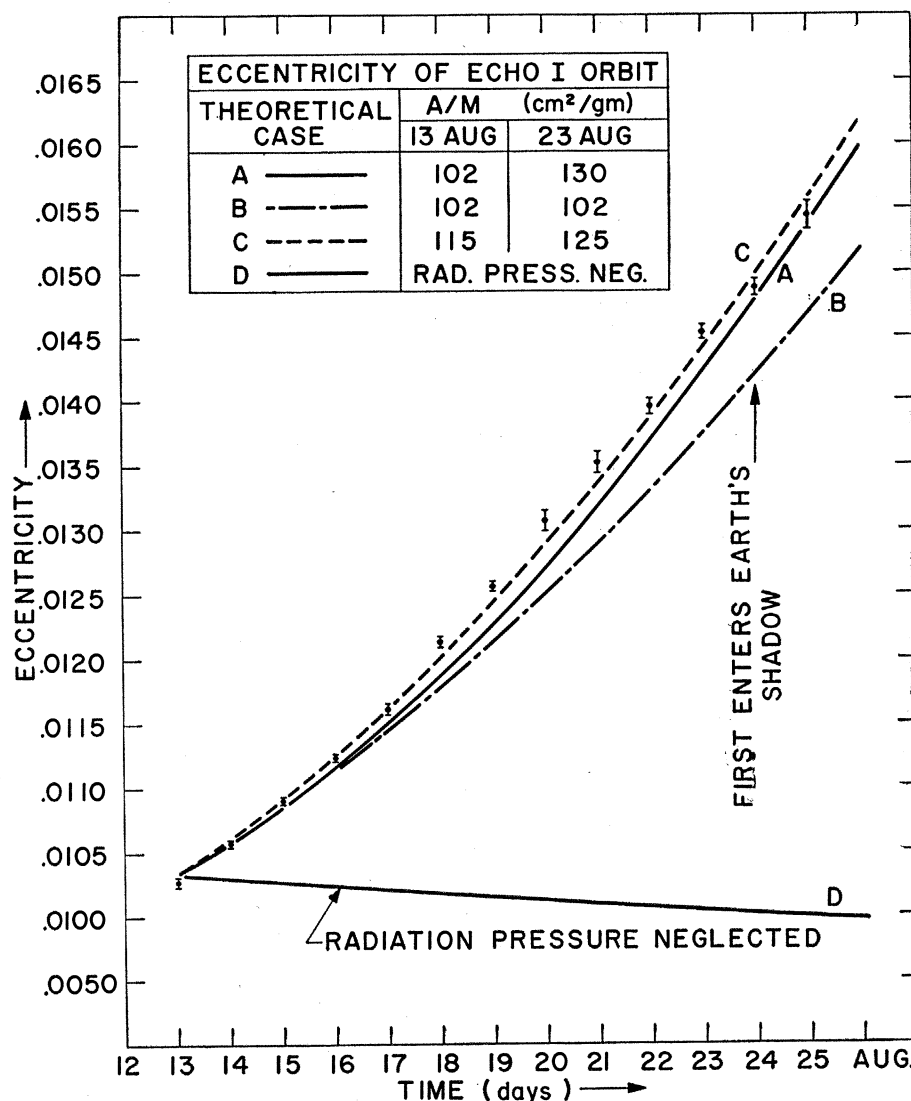


Fig. 1. Time variation of eccentricity.