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To: J. G. Gaume

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From: R. H. Edgerley

Subject: "Living Clocks" and Manned Space Flight
Biological

Dr. H. Strughold of the USAF School of Aviation Medicine (Brooks AFB, Texas) has repeatedly called attention to one possible problem area of space flight which to the best of my knowledge has gone more or less unheeded. His earliest warning that I know of refers more specifically to "The Physiological Day-Night Cycle in Global Flight" and was presented at the school in 1952. The problem is whether or not such flight would affect the diurnal cycle and, if so, what might be the consequences.

Over a period of years, it has been increasingly apparent that the magnitude of almost any biological measurement is a function of the particular time of day it is made. In addition, there are many examples of organisms showing certain activities with remarkable periodicity. The cyclic nature of these changes has led to the concept of a biological clock possessed by every living organism. It is my impression that most biologists (those not working in this field) have considered this clock as reflecting the influence of temperature and light and that changes in the cycles brought about by these factors are not too important so far as the organisms themselves were concerned. Some of the rather well-known photoperiodism phenomena might be an exception, but most reports deal with a response of more importance to the species than to the individual. Profound effects on the individuals through alteration of their cycles were, however, demonstrated by F. Halberg and his associates (Science, 128(3325):657, 19 September 1958). These investigators reversed light and darkness for a strain of mice subject to audiogenic seizures. A noise stimulus now caused a very striking increase in responses, including convulsions and death, as compared with the un-reversed controls. The effect depended on the stimulus being applied at a particular time of the cycle. The work would indicate that "resetting the timer" in an organism may markedly enhance susceptibility to stress. As long as the clock seemed subject only to temperature and light, this report still did not seem of any great consequence to manned space flight. Since these factors must be under control anyway in a space vehicle, there appeared to be no reason why they could not be controlled in such a way as not to affect the crew adversely.

Recently, a new theory of biological clocks was advanced which has seriously jogged my own complacency. Dr. F. A. Brown, Jr. of the Biology Department of Northwestern University (Evanston) has advanced evidence that the basic timing of the living clock "depends upon a continuous inflow of cyclic information of the natural cosmic frequencies". (Science, December 5, 1959, 130(3388):1535. 1544) These frequencies also referred to as "external geophysical rhythms" apparently include diurnal variations in secondary cosmic radiation. Light and temperature are relegated to secondary importance as "phasing agents". Since the variations of cosmic radiation reaching the ground are a function of the diurnal changes in the atmospheric attenuation of the primary cosmic particles, it would appear that flight above the atmosphere could very well affect the "primary clock". If this is true, the experiments of Halberg and his co-workers provide us with an indication that such an effect could be very serious.

Besides presenting the correlations between the activities of fiddler crabs and potatoes and the daily variation in cosmic radiation, Dr. Brown points out certain other correlations of especial interest to me. One is the dependency of oxygen consumption in both potatoes and fiddler crabs on barometric pressure changes. The other is the information that Stoppel, back in 1916, hypothesized that the daily rhythm in air ionization was responsible for the biologic cycles.

R. Nagy in his review "Air Ionization" (Westinghouse Electric Corporation Research Paper BL-R-8-0099-6G6,1, Feb. 18, 1959) quotes a report which explains how barometric changes could cause "relatively rapid and large changes in the ionization of the air". Although his source appears rather unscientific biologically, the proposed mechanism (ionization of the air by the earth as the air is "breathed" in and out of the ground) appears possible. While this is of interest in itself, it is not directly related to Brown's experiments since the experimental organisms were maintained under constant pressure during the time they apparently responded to external barometric changes.

Allan H. Frey in a paper relating atmospheric ionization to Selye's stress concept (Behavior and Atmospheric Ions; General Electric Company, T.I.S., #R59 ELC-121, December 1959, Ithaca, New York), cites Tchijevsky as reporting that lack of air ions in a carefully controlled environment caused lethargy and death in his experimental animals (Academia Colombiana de ciencias exactas fisicas y naturales bogata, 1940, 4, N.13-16, 182-194). Apparently, no one has tried repeating this work which might now be construed as indicating that the animals may have been deprived of any input to their "clock" and died as a consequence. It is possible that the biological effects of ionized air have been so difficult to pin down because of their being a function of how the ionization is imposed on the existing diurnal cycle.

In our work, we have postulated that ionized air acts similarly to ionization in the tissues, i.e. that energetic free radicals (O and N) produced by the recombination of ionized air moledules, are responsible for ionized air effects just as the free hydrogen and hydroxyl radicals produced from ionized water, are primarily responsible for the effects of penetrating radiations. As we have previously pointed out, most of the biological work on

ionizing radiations has confounded the effects of ionized air and ionization in the tissues. It is possible in Brown's experiments that cosmic radiation determined the response either by ionizing the air or the tissues.

From these considerations, which appear to correlate with Dr. Brown's article, it would seem likely that either ionized air or ionizing radiations might affect the timing mechanism of biological systems. It may well be that there is already evidence in the literature relating the effect of X-rays for example to the diurnal cycle. I know this is true of mitotic cycles, but this is not as satisfying as might be other examples.

The movements of potassium (some of which is naturally radioactive) in organisms is another area in which to look for influences on the diurnal cycle. Variations in total potassium among organisms might also affect their sensitivity to external radiations in this respect.

Aside from watching the literature for such effects, it will be well to examine our experimental records for evidences of cyclic changes and their relation to the results of our experiments. It is possible that our existing and presently planned work will provide information on this subject without any modification or new equipment.

In summary, we can say that present evidence indicates the possibility that organisms in a space environment may suffer injurious effects from ordinarily inocuous agents as a result of disruption of their timing mechanism by cosmic radiation.

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