ing wakefulness which seems to be characteristic of the midpontine preparation deserves more attention, and its mechanisms are being presently investigated (*7*). Suffice it to say here that the behavioral and electroencephalographic patterns of the "midpontine" animal do not appear to result from hypoventilation and consequent hypercapnia, as demonstrated by blood gas measurement before and after appropriate brain-stem transection (*7*). A synchronizing, or possibly sleep-inducing, influence exerted by some structure in the caudal brain stem can be tentatively envisaged, and its existence will be tested experimentally. This might provide a new interpretation of Roger, Rossi, and Zirondoli's finding (*5*) that trigeminal deafferentation precipitates electroencephalographic sleep patterns in the *encéphale isolé* cat.

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30 January 1958

Delayed Deaths in Sublethally X-rayed F_1 Hybrid Mice Injected with Parental Strain Spleen Cells

Essentially permanent protection against death from radiation exposure (that is, protection for a large fraction of the normal life span) is afforded in mice subjected to amounts of x-irradiation that would otherwise be lethal, by the injection of normal bone marrow cells taken from isologous mouse donors (mice of the same inbred strain). Following the injection of hematopoietic cells from homologous donors (mice of a different genetic strain), protection against radiation death is either greatly decreased (*1*) or is of only temporary duration, and the phenomenon of "late" or "homologous deaths" during the fourth week and later becomes evident (*2*). During the course of studies (*3*) on the role of the lymphoid tissues in this "homologous disease" (*4*), it was observed that the injection of normal parental strain spleen cells into nonirradiated, or into sublethally x-irradiated, F_1 hybrid mice resulted in delayed deaths (*5*).

Ten-month-old male mice (strain C57L × A, F_1 hybrids) were the recipients. The donors of the spleens were 10- to 25-week-old mice of the A strain. Nonirradiated LAF_1 mice, and also mice exposed to a sublethal radiation dose [500 r of 250-kvp (peak) x-rays] received a single intraperitoneal injection of A-strain spleen cells, as homogenate, in Tyrode's solution containing 4 mg of penicillin. The results are summarized in Table 1. It is evident that the injection of A-strain spleen cells leads to delayed deaths—in mice irradiated with 500 r during the second, third, and fourth weeks and in nonirradiated mice, at 3 to 8 weeks. The lethal effect in the nonirradiated mice appeared to be dependent in part on the size of the spleen cell inoculum—the larger the number of cells injected, the earlier the deaths. The general appearance of these mice (Fig. 1) is reminiscent of that of irradiated mice with homologous disease following injection of homologous bone marrow; debilitation, body-weight loss, and atrophic spleen and thymus were noted. The lethal effect could not be duplicated by the injection of LAF_1 spleen cells into other LAF_1 mice or into A-strain mice.

It seems plausible that the above-described phenomenon is in the nature of a reaction against the host—possibly the homograft type of reaction (*6*)—of injected spleen cells capable of producing immunoreaction. Since A-strain mice are known to have the specific histocompatibility antigen (designated *H-2*^{a}) at the *H-2* gene locus (*7*), and since C57L mice are known to have a different specific antigen (*H-2*^{b}), it is evident that LAF_1 mice contain both antigens and, therefore, that A-strain spleen cells are not "foreign" antigenically to the immunological apparatus of LAF_1 mice. On the other hand, the tissues of the LAF_1 host contain an antigen (*H-2*^{b}) that is "foreign" to the A-strain spleen cells injected

Fig. 1. Typical "homologous disease" in mouse of strain LAF_1 previously subjected to sublethal dose (500 r) of x-irradiation, 35 days after injection of 12×10^6 nucleated cells from A-strain mice.

into their midst. Under these circumstances, immunological reactivity can take place only in one direction, and we see, in effect, the "rejection" of the host tissues by the injected A-strain spleen cells.

The similarities between the above phenomenon and that of "homologous disease" in x-irradiated mice (at LD_{100} doses) injected with homologous bone marrow cells is perhaps more than fortuitous. It is suggested that this latter syndrome may be a consequence, at least in part, of transfer of cells in the injected bone marrow suspension, capable (or potentially capable) of producing immunoreaction. According to this view, attempts to remove or inactivate such cells in the donor bone marrow could conceivably reduce the potential hazard of homologous reactions following the administration of nonisologous marrow as therapy for acute radiation sickness.

Note added in proof. It has been found (*8*) that the lethal effect of injected parental spleen cells is not duplicated by the injection of A-strain spleen cells lysed in distilled water, nor by injection of 40 mg of A-strain liver as a homogenate in Tyrode's solution. Thymus cells have been found to be much less active than cells from spleen. Thus 12×10^6 nucleated thymus cells (from

Table 1. Lethal effect of injected spleen cells from A-strain mice in normal and irradiated LAF_1 mice. Mice were injected a few hours after irradiation unless otherwise indicated; the number of test animals is shown in parentheses.

No. or wt of A-strain spleen cells injected	Radiation dose to recipient (r)	Mortality	
		No.	Days after irradiation
6.5×10^6	500 r	5 (5)	9, 10, 10, 12, 12
3.2×10^6	500 r	4 (4)	12, 12, 12, 28
16×10^6	500 r	1 (1)	12
(85 mg)	500 r	7 (7)	14, 17, 19, 19, 25, 26, 26
(82 mg)*	500 r	6 (6)	24, 26, 27, 31, 31, 20
6.5×10^6	None	1 (5)	55
16.4×10^6	None	5 (5)	24, 27, 28, 42, 42
33×10^6	None	4 (4)	17, 20, 20, 20

* Injected 6 days after irradiation.

9-week-old A-strain mice) elicited death (at 49 days) in only one of seven sublethally x-rayed 4-month-old LAF_1 mice, whereas 12×10^6 spleen cells produced deaths in all of 17 similarly irradiated LAF_1 mice. Of considerable interest, furthermore, is the observation that injection of 12×10^6 cells taken from newborn (1 to 4 days old) mice of strain A did not elicit any deaths (by 5 months, at this writing). On this basis, experiments are now in progress to test the feasibility of preventing the secondary "homologous disease" in lethally x-irradiated LAF_1 mice (870 r) by injection of spleen cells from newborn strain-A mice. It appears, thus far, that such cells afford 100 percent protection against deaths during the three months after irradiation.

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13 January 1958

New Technique for Recording Skin Resistance Changes

The aspects of skin resistance commonly measured are specific responses (psychogalvanic reflex), nonspecific fluctuations, and basal resistance level. The basal resistance is usually noted periodically and is regarded chiefly as a reference level for specific and nonspecific responses. This report describes information obtained when basal skin resistance is recorded continuously.

A specially constructed skin resistance meter (*1*) receives the input from the subject. Output from this meter is passed through a Brush amplifier to a Brush two-channel magnetic oscillograph. The write-out is calibrated at 1 cm/12 min on the abcissa and at 1 cm/10,000 ohm on the ordinate. Classical galvanometric measurement of skin resistance, on the other hand, is often recorded at 1 cm/2 sec on the abcissa and at 1 cm/250 ohm on the ordinate. The continuous basal resistance recording is, therefore, 1/180 of the abcissa as recorded by the classical procedure and 1/40 of the ordinate.

Dry plantar electrodes (*2*), measuring approximately 7 by 10 cm, are employed. These are made of silver conductive cloth, sewed into individually fitted socks, and secured in place by well-fitting shoes. When the environmental temperature is controlled, records are virtually free of artifacts, regardless of whether the subject is standing, sitting, lying, or walking.

This technique gives a clear record of periods of sleep by demonstrating graphically a rise of basal resistance (see Fig. 1, tracing *A*). Alertness is revealed by a line of relatively low resistance. Relaxation and drowse are indicated by gradually rising resistance with infrequent, large fluctuations. This may progress to the high stable resistance of sleep. Fitful sleep is shown by large drops interrupting the high stable line. Periods of arousal during sleep are marked by sharp drops and slow recovery.

The exact point of onset of sleep is not clearly indicated but can be closely approximated by correlation with ability to respond to stimuli such as light flashes or verbal requests. The onset of awakening is clearly indicated on the tracing and is confirmed by behavioral observation. The period of drowse is distinctly different from the awake period. Thus, electronic monitoring of alertness is possible. This is particularly useful in research such as studies of human isolation, where the usual means of observing subjects are not feasible.

A clear graphic picture of activity may be obtained, as illustrated in tracings *B* and *C* of Fig. 1. The difference between the work and relaxation periods is apparent. Since identical experimental procedures were used for making these tracings, the extent of individual variation in the tracings is emphasized. It is also noted that the individual of tracing *C* was "relaxed" when his resistance was higher than that shown by the individual of tracing *A* when asleep.

Tracings *D*, *E*, and *F* are individual records obtained from three additional subjects while alert, with minimal external stimulation. The degree of basal resistance reactivity was judged qualitatively, as shown in the figure. Recordings have been obtained from 22 subjects. Seven have been judged hyporesponsive, eight normoresponsive, and seven hyperresponsive. Five subjects have been tested repeatedly. While mild variability in response pattern was noted, their tracings always fell in the original categories.

In general, hyperresponsive tracings are obtained from subjects who can relax easily, while hyporesponsive tracings are obtained from subjects who do not relax easily. Work is now under way to correlate these skin resistance response

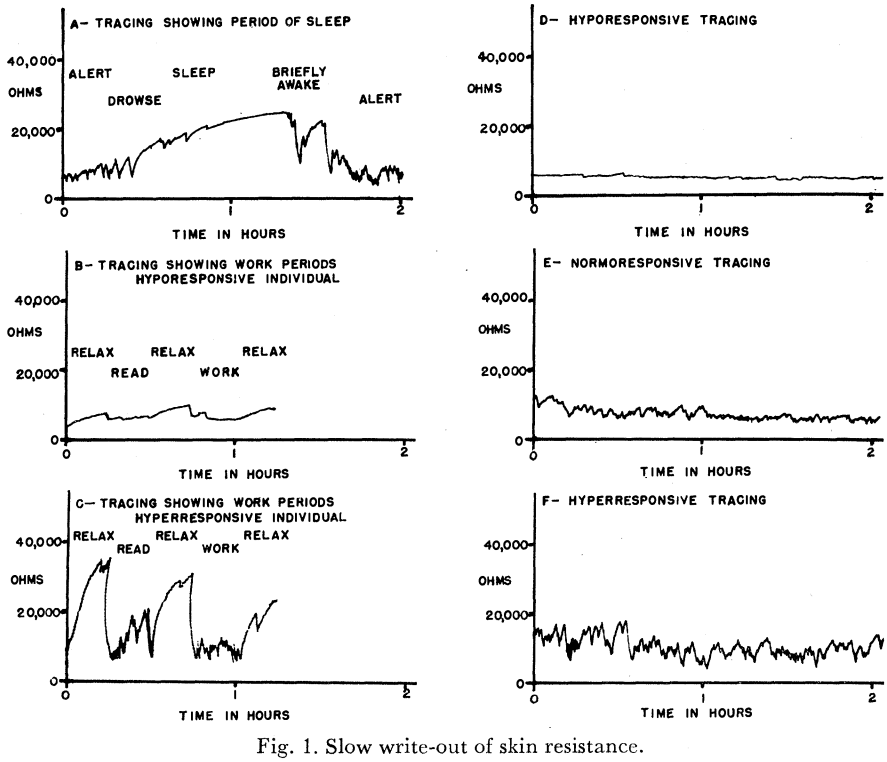

Fig. 1. Slow write-out of skin resistance.