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In a previous review (1) the author evaluated the intensity of cosmic radiation near the top of the atmosphere in order to estimate the hazards involved to aviators and found that even with intense daily flights the radiation exposure remains below the permissible limit.

During the past five years, potentialities of space travel have greatly increased and new knowledge has become available regarding the nature of cosmic radiation. In the present article the knowledge pertinent to dose evaluation is reviewed for conditions of flight in space in the vicinity of the earth but away from the influence of its atmosphere or magnetic field. Certain properties of the heavy nuclei are also discussed as well as some of the available information on their actual biological effects. Development and completion of the new Heavy Ion Linear Accelerator allows extension of quantitative biological work with these particles. Finally, the statistical nature of the hazard from cosmic radiations and the limitations of space flight due to such rays are discussed.

I. The Primary Cosmic Radiation.

Our present picture of the primary cosmic radiation is that of a sea of rapidly moving nuclei, stripped of their electrons and converging incessantly on the earth homogeneously from each direction in space. Protons are must abundant, while the frequency of particles diminishes with increasing atomic number. Neutrons, electrons and gamma rays are largely absent; at least they are not found in the primary component near the top of the atmosphere.

The observed intensity and energy distribution of the rays at ground level and high altitude is not necessarily a true relection of what one might find in space away from the earth, since the particles at the low energy end

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of the spectrum are deflected by the earth's magnetic field and by magnetic fields external to the earth. An observed spectrum of heavy primaries, as measured by Danielson et al. (48) is given in Figure 1. Data are not given near the North Pole, where measurements in different years have very different results. Ellis et al. (3) have shown that the cutoff in low energy particles is caused by a magnetic field not due to that of the sun or the earth, and in the last 20 years it has become increasingly clear that low energy nucleon components of the primary cosmic rays show great variations.

From the isotropic distribution of the primary rays, it seems clear that the majority of them must originate outside of the solar system, and in order to explain their presence one must propose a satisfactory injection and acceleration mechanism, as well as one for elimination of some of the particles. We know several types of stellar events that involve emission of ionized matter into space. Fermi (4) (7) suggested that collisions of particles with ionized magnetic clouds can cause their acceleration. From general considerations of energy density in space, it is now believed that most of the cosmic rays within our galaxy originate here and are contained within it (5) by virtue of the magnetic fields at the edge of the galaxy. The particles may have a mean life of perhaps 10^6 years before they escape into intergalactic space. The strongest sources of cosmic rays in our galaxy are believed to be the radio stars, many of which are located near the center of the galaxy (6).

The level of cosmic radiation is governed by the equilibrium between the generating process and the escape process and locally on the presence of magnetic activity resulting from cosmic clouds. The above outlined principles predict an energy distribution for the primaries in agreement with the experimentally found distribution at high energies per nucleon (above several Bev/nucleon). If N(E) be the number of particles in energy range dE

$$\frac{dN}{dE} = -E^a \qquad \text{where } a = -1.8$$

This relationship is followed up to the highest primary events: $E \sim 10^{16}$ ev. Knowing the distribution of cosmic ray primaries over the surface of the earth and their dependence on energy, Rossi (8) states that the energy flux of cosmic radiation in the neighborhood of the earth is

$$3.5 \times 10^{-3} \text{ erg cm}^{-2} \text{ sec}^{-1} \text{ ster}^{-1}$$

and that cosmic ray energy density in space is

$$1.4 \times 10^{-12} \text{ erg cm}^{-3} \sim 1 \text{ ev cm}^{-3}$$

These figures correspond to about

$$7.2 \text{ primary particles cm}^{-2} \text{ sec}^{-1}$$

and to a dose level of about 25 millirad per day.*

This latter figure is about twice the dose one receives at geomagnetic latitude of the United States near the top of the atmosphere (1). There are so many uncertainties in the calculation that the figure may be off by a factor of two.

Variation in the Cosmic Radiation.

Over the last twenty years important spatial and temporal variations in cosmic ray intensity and energy distribution have been detected. These are important in radiation studies not only because they are necessary for evaluation of the dose, but also because they should be correlated to results of balloon and rocket flight tests of biological specimens.

Solar Flares.

The most spectacular changes in the primary component of cosmic radiation are those associated with solar flares. The events briefly accounted are as follows: a region of the solar chromosphere having an area of a few ten-thousands of the solar surface starts intense light emission. The luminosity of the flare increases greatly for a period of 2-3 minutes, then gradually decays with a mean life of about one half hour. Radio waves are received with slight delay. Primary cosmic rays rise to a maximum about one hour after the light flash and decrease to normal within a day. The flare is followed 1-2 days later by an intense magnetic storm and frequently a concomitant decrease in cosmic ray intensity.

Five important solar flares have been recorded during the past 15 years (9).† During the last important solar flare (10) there was an increase of as much as 30 fold in neutron intensity (11) within 15 minutes,

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*1 rad = 100 ergs g^{-1}; 24 hour day

†February 28, 1942; March 7, 1942; July 25, 1946; November 19, 1949; and February 23, 1956.

reflecting similar increases in the primary particles (at 54°N, 71°W) whereas mesons only increased 58% (10). The increase in the primary low energy component, up to 4 Bev/nucleon, was much greater than that in the high energy part of the spectrum. One of the most interesting aspects of cosmic ray increases after solar flares is that the rays strike the earth in very uneven distribution. Firor (12) calculated the probable zones of impact of cosmic rays on the earth in the energy range of 1 to 10 Bev and found that if the particles come from the sun, then due to deflecting influences of the earth's magnetic field some zones receive more dose than others. Geomagnetic latitudes between 25° and 60° exhibit an increase, while equatorial and polar zones should remain relatively free of change. A good part of the North American continent falls in the heaviest irradiated zone. Existing data on the geographical distribution of the flare-type increases bear out the theoretical predictions, and thus we are now quite certain that the particles arriving associated with the solar flares do originate in the sun and are accelerated in a reasonably direct manner. When man has learned to fly at a distance of one or more earth diameters away, he should experience the full, undeflected intensity of the solar-flare particles in each direction, in some locations reinforced by the albedo (reflections) from the earth's magnetic field. It also seems reasonable that should one attempt to fly closer to the sun than we are at present, the cosmic rays of solar origin should increase in intensity at least as fast as the inverse square distance law would predict. Now a high primary radiation intensity in prolonged flight or in residence on one of the planets may make serious limitations on life span and evolutionary processes. Thus, solar cosmic rays should be considered in the definition and limitations of Strughold's Helioecosphere (13). Contributions of solar-flare doses of cosmic rays to the average dose level at ground level or at high altitude are not significant. The quantitative observations have been too recent, however, to predict what variation in the size of solar flares we may expect in times to come.

Cosmic Ray Increases with Small Solar Flares.

Simpson *et al.* (14) found that numerous small solar flares correlate with increases in the primary cosmic radiation as observed by neutron changes. Again the increases are attributed to generation of rays by the sun.

Direct measurements on the time variation of the primary nucleon component of cosmic rays near the top of the atmosphere are difficult to perform, and ever since the detection of the heavy nuclei there have been doubts as to the nature and magnitude of some variations. In an ingenious experiment, Koshiba and Schein (15) investigated the time variations of $Z > 10$ nuclei at an altitude of 100,000 feet. They found an amplitude variation of about 35% within a few hours elapsed time. Their experiments give good indication of the difficulties of correlating biological changes in balloon flights to cosmic ray spectrum and intensity. It seems imperative that the physical and biological measurements be done simultaneously.

The increases of cosmic radiation which correlate to solar flares are the only ones which seem to be due to direct production of the rays by the sun. For all other sun-correlated intensity changes Morrison (16) suggested a common cause: time and energy modulation of the incoming galactic cosmic ray beam by random diffusion and deflection of the particles through turbulent clouds of ionized plasma emitted by the sun. Among such events are the sporadic decreases of overall intensity of cosmic rays arriving at the terrestrial surface. These were discovered by Forbush (17) during intense magnetic storms. Other such variations are the 27 day recurrent minima in the cosmic ray intensity and eleven year variation of the primary particle spectrum and intensity.

Magnetic Storms.

Intense magnetic storms usually follow solar flares by about a day. Since 1936, 33 violent solar flares have been seen, 23 of which resulted in definite decreases in cosmic ray intensity of about 5% in the ground level meson component and approximately 25% in the primary nucleon component. All this change is in the energy interval 0-5 Bev/nucleon. It usually takes 5-10 days for the intensity to return to normal. The magnetic storms may signify passage across the earth of a turbulent ion cloud which originated in the solar flare. Such a cloud disturbs and sweeps out many of the electrons from the Heaviside layer and can cause the well-known northern lights. The abundance of very low-energy particles in these clouds is not known; neither do we have sufficient information about whether or not they significantly contribute to dose.

27-Day Cycle of Variation.

Another type of solar cosmic ray variation is correlated with the sun's rotation period of 27 days (18). This effect amounts only to approximately 3% for the low energy nucleon component and 0.5% for the meson component. It is not regular and its study is made difficult by the superimposed fluctuations and different kinds of variations. There is some evidence that cosmic ray maxima occur within about a day after the central meridian passage of a magnetic monopole region (sunspot) in the chromosphere of the sun, and Morrison assumed that this region of the sun initiates a magnetic region in space into which low energy cosmic rays diffuse with ease.

Eleven Year Variation.

The most interesting glimpse into the energy spectrum and intensity of primary cosmic radiation is given by the eleven year solar cycle. This latter is usually interpreted in terms of overall sunspot activity reflected by numerosity and intensity of terrestrial magnetic storms. Forbush (17) demonstrated that low sunspot activity is accompanied by high cosmic ray intensity and high sunspot activity by low intensity. Examples of these variations were given by Neher (19) who compared measurements of ionization of primary particles in the years of 1937, 1951 and 1954. Figure 2 indicates measurements near the magnetic north pole on the three occasions. In 1937 the sunspot activity was maximum, and the ionization minimum; in 1954 the sunspot activity was minimum and the cosmic ray ionization above the geomagnetic north pole more than doubled. In 1951, a year of medium sunspot activity, the cosmic rays were at a level considerably higher than in 1937.

In years of high sunspot activity, primaries of low energy are not admitted, but in years of low activity these can arrive at the surface of the earth in regions where the earth's own geomagnetic field permits (near the poles). In 1951 the increase over the minimum was mainly due to particles between 1.5 and 4 Bev/nucleon; in 1954 the protons of lower than 1.5 Bev and perhaps other particles of similar magnetic rigidity increased significantly. From the solar maximum to the minimum, the energy being brought to the earth by cosmic rays increased by 14%. The number of incoming particles increased by a factor of more than 2.4. The dose increased by even a greater factor than 2.4.

The presence of low-energy particles near the north pole does not materially affect the safety considerations for flying for temporary periods in the temperate and warm zones up to 200,000 feet. We should be prepared, however, to find in true space flights a higher dose rate, such as one finds at high altitudes over the magnetic poles in years of low sunspot activity. Much more exploration is needed in the low-energy region to know the exact dose rate, and great variations are expected from magnetic clouds and solar eruptions.

Looking back to the history of the universe, Teller (20) makes the suggestion that the overall intensity of the galactic component of cosmic rays may have significantly altered at times in the past. If by explosion of a nova or some other process a new radio star were to be formed on the same bundle of magnetic lines of force which pass through the solar system at a distance of perhaps 1,000 light years or less from our own location, then a great increase of cosmic ray intensity could be expected. We know that such events do occur and by watching the sky we may have advance notice of them. An increase of cosmic ray levels by a factor of 1000 might lead to increased mutation rate and enhanced multiple mutation frequency. It is well known that in the course of evolution of the species, as yet unexplained gaps exist where intermediate living forms are missing. The cosmic increases mentioned may account for the apparently anomalously rapid evolutionary epochs. One must admit, however, that at the present time we do not attribute more than 10-15% of natural mutation rate to radiation, and temperature increases or changes in chemical environment can also lead to increased mutation rates. From radiocarbon dating it appears as though during the last 20,000 years there has been no very important increase in cosmic ray intensity.

II. Methods of Obtaining Knowledge of Biological Effects due to Primary Cosmic Rays.

During the last few years, successful development of balloon techniques has made possible the limited exposure of biological materials to cosmic radiation. This development, pioneered by Simons and associates (21)(22)(23)(24), has resulted in the demonstration of observable biological effects and culminated in making it feasible for man to spend several hours time at altitudes near 100,000.

The qualitative evidence, briefly summarized as obtained from balloon flights and studies in cyclotrons and reactors, is as follows: Single cells and unicellular organisms may be killed and their cell division or proliferation inhibited by single heavily ionizing cosmic ray primaries. The sensitivity of various cells is very different in this respect. We know from the work of Conger and Giles (25) that a single alpha particle can cause profound shattering of chromosomes in *Tradescantia* microspores. Zirkle and Bloom (26) have shown that protons are much more effective on the nucleus of newt heart cells in tissue culture than on the cytoplasm. Birge and Sayeg (27) have shown that six-times ionized carbon ions can kill individual yeast cells, but will not do so in each instance when they pass through the cell. They obtained some evidence that killing effectiveness of the carbon nuclei is actually diminishing in the most ionizing portions of the track. Eugster (28) has demonstrated in balloon experiments that eggs of artemia salina, a salt crab, can be occasionally killed by a single cosmic ray event. Reverse biochemical mutations can be apparently accelerated by primary cosmic rays as indicated by preliminary work carried out by Stone *et al.* on *Neurospora* (29). None of these studies has as yet shown conclusively an unexpectedly great efficiency of heavy nuclei to affect cells as compared to quantitative studies with other, better-known radiations. The relative biological effectiveness values (RBE) previously estimated (1) still appear to give conservatively low estimates from the point of view of health protection.

For a number of years there has been an interest on the part of meteorobiologists to correlate variations in biological systems with mateorologic phenomena, solar and lunar cycle, etc. The possible influence of cosmic ray showers at ground level with chemical reducing power of bacteria was recently investigated by Tzchaschel et al. (49). After prolonged careful observations, some correlation between mean cosmic ray level and reducing ability was found.

Tissues

The function of organized multicellular units may be knocked out by single heavily ionizing events. This was first clearly demonstrated by Chase and Post (30). They have flown an inbred strain of mice with black hair to high altitude and observed that the hair color has changed to white in single, isolated hair follicles exposed to heavy nuclei. Eugster (28) designed another technique where an excised piece of skin is flown and then regrafted to the animal for further study.

Analysis of the data by Chase has so far failed to give a definite clue to the nature of the particle needed to cause the hair-color change. Assuming that all particles that ionize heavier than a threshold value can cause the affect, while those ionizing lighter cannot, then the flights in 1954 suggest that a linear energy transfer of at least 7×10^8 ev g^{-1} cm^2 is needed. The 1955 flights show effect for particles of greater than 3.5×10^9 ev g^{-1} cm^2 LET. These figures were derived by using particle frequency tables prepared by Schaefer (31)(32). One source of possible interpretational error is in the continuing variation of primary intensity and energy distribution near cutoff discussed earlier in this report. This was not directly taken into account. One should apparently monitor the distribution of primary events in each flight. Nevertheless, cosmic ray intensity variations do not seem large enough to explain the discrepancy of the results a year apart, and biological variations of sensitivity dependent on environmental factors (temperature, state of anoxia, state of stress) may well have been involved. The interpretation is also complicated by the fact that obliquely incident particles may cross the skin twice, thus producing greater effect.

Some interesting events were found that allow one to calculate the cross section for hair-color change for certain particles. In a few cases a streak of white hairs resulted, pointing to the passage of a particle (or a narrow bundle of particles) along the surface of the skin. One such streak was 2.9 mm long, and 13 white hairs were found along it.

Now assume that the number of white hairs along a finite segment of Δx of the track is Δn; the number of hair follicles originating in the skin per mm^3 N_h and the "cross section" for producing a white hair σ, then

$$\Delta n = \sigma \cdot N_h \cdot \Delta x$$

or

$$\sigma = \frac{\Delta n}{\Delta x} \frac{1}{N_h}$$

for the above track assuming an average spacing of 120μ between hairs,* we get $\sigma \approx 750\ \mu^2$; this corresponds to a "target" area of about 30 μ in diameter. The diameter of the hair bulb is about 40 μ, and the target area seems somewhat larger than the area occupied by the matrix cells which store the basic pigment granules. Previous work by Chase (51) tends to show that active follicles have 6-12 dendrite cells which are sources of the melanine granules. Thus it would appear as though it is sufficient for a heavy primary to cross the matrix of pigmented cells any place, not necessarily passing through each individual cell, and inactivate the pigmentary role of 6-12 melanogenic cells and more than 30 matrix cells. It is possible that the particle making the particular track was very heavy, and if it was also a very fast particle, the delta rays might have penetrated as far as 100 micra from the track. We know, however, that high energy delta rays are not efficient in causing a change of hair color. Calculations were also made regarding the distribution of secondary x-rays around the track, originating from rearrangement of the primary ionization, but these are absorbed within 10 μ from the track, and in fact, the high dose portion of the track is only 1-2 μ wide. It appears, therefore, that some very heavy particles can cause biological effects in tissue at a distance from their ionizing core. Further studies are required to clarify the reason. It is possible that the trauma caused by a particle in the vicinity of the hair follicle will affect the pigment cells, or that the change in hair color results from temporary or permanent impairment of capillary circulation supplying the follicle.

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*Chase, private communication.

Two additional events were found in the balloon experiments on mouse skin. In one case, a cluster of perhaps 30-40 hair follicles was affected, and these gave rise to white hair; in another animal many scattered white hairs resulted over the entire animal. The first event seems to be too big for a single particle to have originated it and the second would necessitate a shower of many heavily ionizing particles. If each follicle were individually irradiated, it would have taken hundreds of electrons to produce this event. Both events may have been caused by very rate cosmic ray phenomena; further studies would be needed to obtain their frequency. The highest energy events in cosmic ray physics are known as Auger showers, which may have as much as 10^{16} ev in their primary. These events are usually observed at ground level, since they cause large showers of particles and x-rays, sometimes over a square mile area. The Auger showers may originate as single particles; they produce a narrow beam of many secondaries when they hit the atmosphere. These in turn produce cascades and eventually end up as large showers. Statistically, these events are so rare that a person flying at high altitude may be exposed to only one per year. It is interesting to speculate that the two unusual events observed by Chase are actually expressions of unusual cosmic ray phenomena. It is, of course, also possible that the unusual patterns of hair-color changes are expressions of biological chain reactions, or variations of sensitivity accentuated by the special environment conditions, or that by chance a high frequency of heavy primaries arrived.

In the field of tissue responses, again a certain amount of work is reported based on ground level observations. In the past, various unsubstantiated claims have been made regarding tissue effects (carcinogenic effect, effect on embryonic state, etc.). Recently Brown *et al.* (50) purport to show an effect of lead-induced showers on the pigmentary effector system of the Fiddler crab. These authors did not attempt to measure the cosmic ray intensity in their experiments and neglected to duplicate the results by exposing their animals to x-rays.

Progress in heavy ion work with accelerators.

Up until recently, the only sources of fast heavy ions were cyclotrons that utilized multiply-charged ions formed close to their ion cources for acceleration (33)(34)(35), and the only place where biological work was carried out with them was in Berkeley (36).

On April 11, 1957, the first full energy nitrogen beam was obtained from the new Heavy Ion Linear Accelerator (HILAC) at the Radiation Laboratory (37). This machine was designed for accelerating multiply-charged ions to an energy of 10 Mev per nucleon and it is one of two similar accelerators (38)(39) (the second one is being built at Yale University). An ion source provides milliampere beams of ions with charge-to-mass ratio, $e/m = 0.15$; these are accelerated in a Cockroft-Walton machine to 0.07 Mev per nucleon and enter a short linear accelerator. Here their energy reaches 1 Mev per nucleon and the beam is passed through a very thin layer of gaseous matter where the ions lose electrons so that their charge-to-mass ratio becomes $e/m \approx 0.35$. The rest of the acceleration is carried out in a cavity 108 inches in diameter and 50 feet long that is provided with 68 drift tubes. A photograph of the internal aspect of this cavity is given in Figure 3. So far, strong beams of carbon, nitrogen, oxygen and neon particles have been obtained and there is some hope for acceleration of other ions up to heavily ionized argon. The machine delivers particles with very uniform energy traveling in a nearly parallel stream. Figure 4 shows two oxygen nuclei coming to rest in nuclear emulsion and a third oxygen particle which makes a nuclear disintegration. Figure 5 shows similar events in an electron sensitive nuclear emulsion. These are reproduced by courtesy of Harry H. Heckman. The intensity of the beam is more than ample for biological experimentation--the dose is limited only by efficient cooling of the target and it seems feasible to give as much as 10^9 Rad. The beam is pulsed and a single pulse is 2 millisec in duration, 5 pulses per second. A sizeable dose can be delivered by a single pulse.

Biophysical experimentation is beginning in 1957, and after initial dose calibrations it will be possible to do both fundamental and applied radiobiological studies. A biological exposure device was designed by Fluke and Birge. A schematic view of such a device is shown in Figure 6.

It is shown that the beam is first deflected by an "analyzer" magnet, which will assure uniformity in particle momenta, then is passed through a vacuum tube, several feet long, before striking the biological exposure device. At the left end of the tube a scattering foil may be employed to spread the narrow beam of the HILAC to a uniform field of approximately 2 cm diameter.

For biological exposures it is desirable to provide a method of selecting the energy of particles; this is taken care of by an absorber wheel. The radiation exposure may be done in vacuum, as would be the case for dried enzymes, viruses, or cells; a thin layer of exposed animal tissue may be irradiated in air through a window. The dose may be measured by measurement of the beam current or in a foil chamber that collects delta rays knocked out from a thin foil.

Table I shows the LET values and the approximate depth of penetration of different particles available, as given by Fluke.*

Ion	Energy Mev	Initial LET Kev/μ	Total Range mg/cm^2	Useful Range mg/cm^2
$C^{(6+)}$	120	165	57	28
$N^{(7+)}$	140	225	49	25
$O^{(8+)}$	160	295	43	22
$Ne^{(10+)}$	200	460	34	17

The machine is thus suitable for study of surface events in small animals, eg. on skin, cornea, mesentery or brain surface. A small bundle of nerve fibers could also be penetrated by any of the available beams.

The successful operation of the HILAC at the sample intensities obtained makes it profitable to think of further extensions of the method. Controlled stripping of electrons from atoms should make it feasible to accelerate nuclei with any atomic number, along principles similar to those used at present. Also, acceleration of the ions to much higher energies should be possible. Doubling of the present energy may be reached by adding another section of linear acceleration. Energies of several Bev per nucleon can be reached when one uses a HILAC type machine for injection of particles in a synchrocyclotron. One method for injection has been described (40).

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*Private communication.

Biological work with high energy cyclotron beams.

It has been pointed out repeatedly (1)(30) that the hazard of heavily-ionizing cosmic rays might lie in part in damage to body cells and tissues, which have essential function, low redundancy and low rate of replacement or recovery from radiation. It is assumed that nerve cells fall in this category, and speculations have been made concerning the existence of foci in the brain which depend on very few cells to function. We do know that large parts of the brain lobes can be destroyed or invaded by tumor without great apparent damage to life itself. However, the hypothalamus has small centers that have essential roles in homeostatic regulation; destruction of a single pair of such centers should be considered.

For several years now,.the Berkeley group has applied narrow beams of protons and deuterons to the brain and hypothalmus of the rat (41), and the effects of pituitary irradiation have been explored in detail (42)(43). The beam diameter can be made as small as about 500 microns. Lesions were only observed, however, when beam diameters larger than 1 or 2 mm here were used. The brain has slight movements reflecting the heartbeat and respiration, and these movements tend to increase the irradiated area when exposure is not instantaneous. It is possible to obtain a fairly well defined hypothalamic lesion, like the one shown in Figure 7, where there is complete liquefaction of cellular material inside and no visible damage outside the region. Most of the time, however, the lesions are irregular and their spread follows pathways of circulatory supply. With elapsed time, nerve trunks that leave the irradiated lesion also show progressive degeneration. Physiological malfunction is often present as a result of irradiation, even before histological damage becomes evident. In acute experiments (3 months), lesions were obtained only if 8000 rad or more were given, although with refinement of observational techniques one should be able to detect damage at smaller doses. Symptoms observed included diabetes insipidus, impairment of growth and appetite, lowered thyroid iodine uptake, regression of gonads, hyperexcitation, rage, abdominal bleeding, failure of body temperature control. The damage is in part secondary to radiation damage to the capillary bed. The inner core of heavy primary cosmic ray particles is sufficiently ionizing to produce permanent nerve damage. At present it is believed that many particles have to strike in the same vicinity before the lesion produced becomes large enough to produce permanent observable changes in homeostatic balance.

After only 945 rad to the pituitary region, obesity resulted in the animals over a span of two years. When chronic effects are under study, one obtains changes with relatively small doses (43).

Doses of over 1000 Rad seem to result in permanent destruction of capillaries and sclerosis of larger blood vessels. The microscopic lesions from heavy primaries, though very small in number, would undoubtedly add to this kind of "aging process" in the brain.

Studies with high energy protons on animals and humans are being continued in Berkeley. Recently the 200-Mev proton cyclotron of Svedberg in Uppsala, Sweden, was also adapted to localized irradiation studies. Borje Larsson, in collaboration with Leksell, Redsed and Sourander, are making significant contributions to the problem of radiosensitivity of neural tissue and the localization of instinctive behaviour centers in animals.*

Radiation safety in flying.

Since the previous paper (1) new recommendations have been issued by the National Bureau of Standards for permissible exposures (44). These new standards do not change the validity of the previous calculations. Thus flying activities up to the top of the atmosphere remain within the permissible limit. Only high above the poles, in certain years, should one expect to observe a higher dose.

A new estimate is presented here for travel conditions in a space ship traveling for long periods of time unshielded by the magnetic field of the earth (for practical reasons higher up than one earth radius). In the first part of this paper, the 24-hour daily mean dose is quoted as 25 m rad. Variations may exceed 100%. If one assumes a relative effectiveness of 7 for primary cosmic rays (1), an aviator might be exposed to 1.2 Rem per week. This is four times the weekly permissible dose, but an individual may spend up to $\frac{1}{2}$ year or 12 weeks in flight per year if he has no other significant exposure during the year.

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*The last problem on a USAF contract.

It seems likely that long flights into space will cause exposures in excess to our presently accepted permissible doses. The possible effects of radiation, expressed as average, would still be small for the individual. For considerations to eventual individual or population damage, one might well take the statistical view suggested more than 100 years ago by Compers and recently considered in detail by Jones (45). Briefly, the physiologic age of the individual is characterized by certain figures representing his chance to die, or his chance to get some disease. The probability to die is a function increasing exponentially through most of a man's lifetime with a doubling time of about 8 years, but populations from different countries, or exposed to different environmental conditions, are represented by different death probability regression lines.

Two individuals of different actual age have identical physiological age if they belong to populations that have the same rate of death. Assessment of animal data and analysis of Hiroshima survivors led Jones to postulate that the effect of a dose of radiation is to cause immediate aging; one roentgen is supposed to increase physiological age by about 5-10 days. A single dose is not supposed to change the doubling time of death rate, but the probability of various diseases, particularly cancer and leukemia, increase in step with the aging. Leukemia incidence and mutation rate are supposed to double after a dose of 25-50 r, but our ignorance in these fields is so great that we have no reliable measurements at all at doses below 50r; it is possible that some recovery mechanism exists which makes man more resistant to low dose rates. Blair (46) found recovery in animals exposed to x-ray, but claims much less recovery for fast neutrons, and we do not know whether the effect of very heavy nuclei is prone to recovery or the damage is permanent.

Because of the large variety of cosmic ray events, the statistical approach should prevail for consideration of the hazard. Thus, if 1000 people fly simultaneously on a given day, three of these may have an Auger shower passed through their body, while the others would not be exposed to this event at all.

A statistical approach would be of value in determining the physiological age of aviators, since this method would bring out the areas of greatest hazard. One environmental factor that actually is responsible for definite physiological changes is reduced oxygen tension. Not only professional pilots, but a large segment of the population is exposed to this from time to time. Yet the author cannot find any data on physiological age measurements in animals during continuous or intermittent anoxia. Even this factor interferes with radiation effect, since x-ray irradiated animals live longer if they are anoxic at the time of exposure.

In balloon flights of the near future, men plan to ascend to 100,000 feet elevation, and will be exposed to some heavy primaries. The effects should be so minute that they may escape detection. However, if our knowledge of x-rays can be carried to this field (47), then it would seem that a dark adapted person should be able to "see" very heavily ionizing single tracks as a small light flash, since they would pass through several retinal receptors, enough to correspond to a visual object of greater than 1' angular aperture. If a track travels within the plane of the retina, several rods and cones may be inactivated, producing a microscopic retinal lesion that may be detectable by visual field measurements. The statistics of the situation are comparable to Chase's skin experiments, except that the rods are smaller (3 μ diameter) and are closer than hair follicles (a few microns apart).

CONCLUSIONS

1. Cosmic ray intensity near the earth, but away from its magnetic field, averages 3.5×10^{-3} erg cm^{-2} sec^{-1} $ster^{-1}$ corresponding to a dose of about 25 millirad per 24-hour day. These figures are uncertain by about 100%.
2. Most primary cosmic rays originate in our galaxy and reach the earth isotropically. About 10% of the primary rays originate from the sun.
3. Long term changes in cosmic ray intensity depend on galactic events. The birth of radio stars may considerably modify cosmic ray intensity.
4. Short term changes in cosmic ray intensity correlate with solar activity. In part, the ionized magnetic clouds originating from the sun modulate the intensity of galactic rays arriving on the earth; in part, solar primaries are accelerated and add to cosmic ray intensity.
5. The most spectacular variations in the primaries follow large solar flares by about an hour. The primary component may increase by as much as 30 fold. Smaller sunspots are followed by minor increases.
6. Following solar flares by a day, there is a few percent decrease in cosmic ray intensity correlated with atmospheric radio and magnetic disturbances.
7. There is an important variation in primary, particularly low energy cosmic rays over an 11-year cycle. The variation in space (away from earth) is at least 2.4 fold and is high when sunspot activity is low.
8. Smaller variations also exist. Direct high altitude measurement of primary particles show over 20% variation of intensity within a few hours.
9. Due to the variations in time and space in cosmic ray spectrum and intensity, it is difficult to obtain quantitative measurements of biological effects of cosmic rays correlated with their energy spectrum. At present, such tests have chiefly qualitative significance.
10. It is established that single primaries near the top of the atmosphere can kill single cells and unicellular organisms, but do not always do so. They also cause mutations.

11. Significant effects of primary cosmic ray particles have been shown on hair follicles. Some of these effects seem to appear as much as 15 microns away from the track of the particles; others are much too large to be caused by direct ionizing interaction with single primaries. The cause may be unusually large cosmic ray events or biological chain reactions.
12. A new Heavy Ion Linear Accelerator has been completed in Berkeley, yielding accelerated nuclei from C^{6+} to Ne^{10+} with 10 Mev energy per nucleon.
13. Biophysical experiments have been initiated to provide quantitative information of radiation effects over a 200-fold range in linear energy transfer on single cells and thin layers of tissues.
14. There are no theoretical obstacles to accelerating heavy nuclei to energies of several Bev per nucleon.
15. Flights near the top of the atmosphere may be carried out frequently without obtaining more dose than the permissible weekly limit suggested by the National Bureau of Standards.
16. In space, away from the earth's shielding magnetic field, a yearly permissible dose may be obtained in about 12 weeks of flying. Direct measurements of spatial cosmic ray intensity are needed.
17. Proton and deuteron irradiation of essential hypothalamic centers indicates that several thousand Rad dose over a cubic millimeter area is needed to produce lesions with significant deleterious effect. Obesity and permanent sclerotic impairment of circulation may result from smaller doses or more localized rays.
18. For full evaluation of radiation effects on aging in pilots, more corollary information is needed. We do not as yet know the effect of partial anoxia on aging or the effect of other stress that involves the pituitary-adrenal axis.
19. Dark adapted flyers at very high altitude may be able to observe a small light flash when a heavy primary crosses their retina, and some slight permanent damage to their visual field might result.

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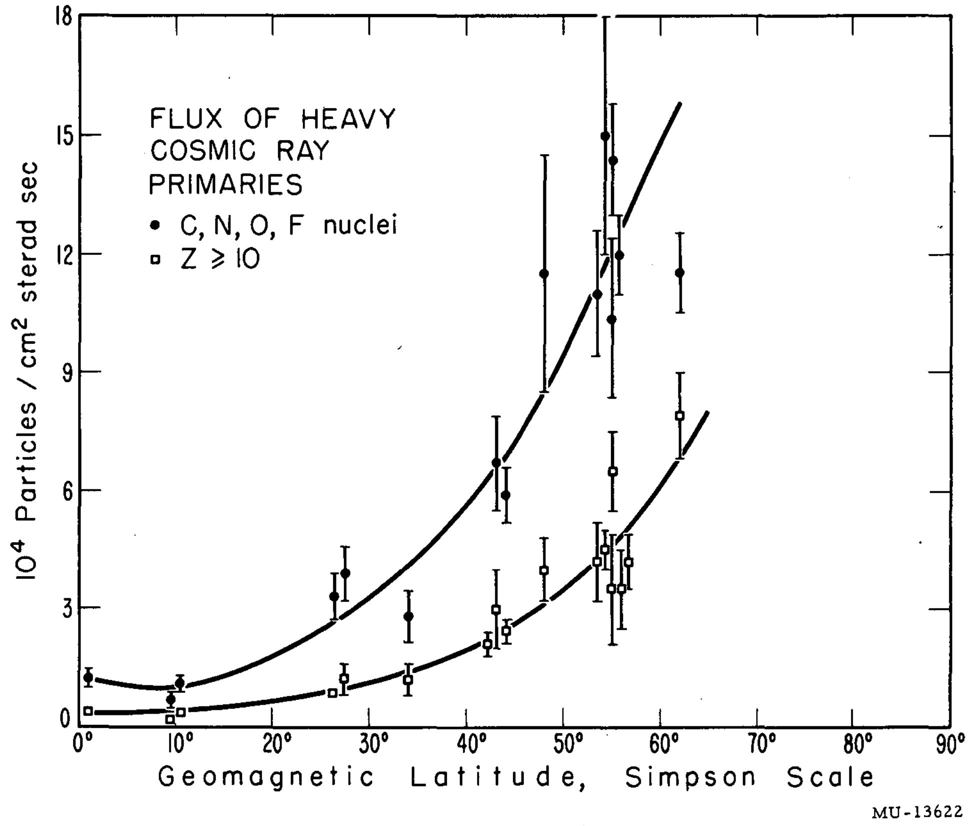


Fig. 1. Flux of heavy cosmic ray primaries as function of geomagnetic latitude corrected according to a method proposed by Simpson. Data by Danielson, Freier, Naugle and Ney (48).

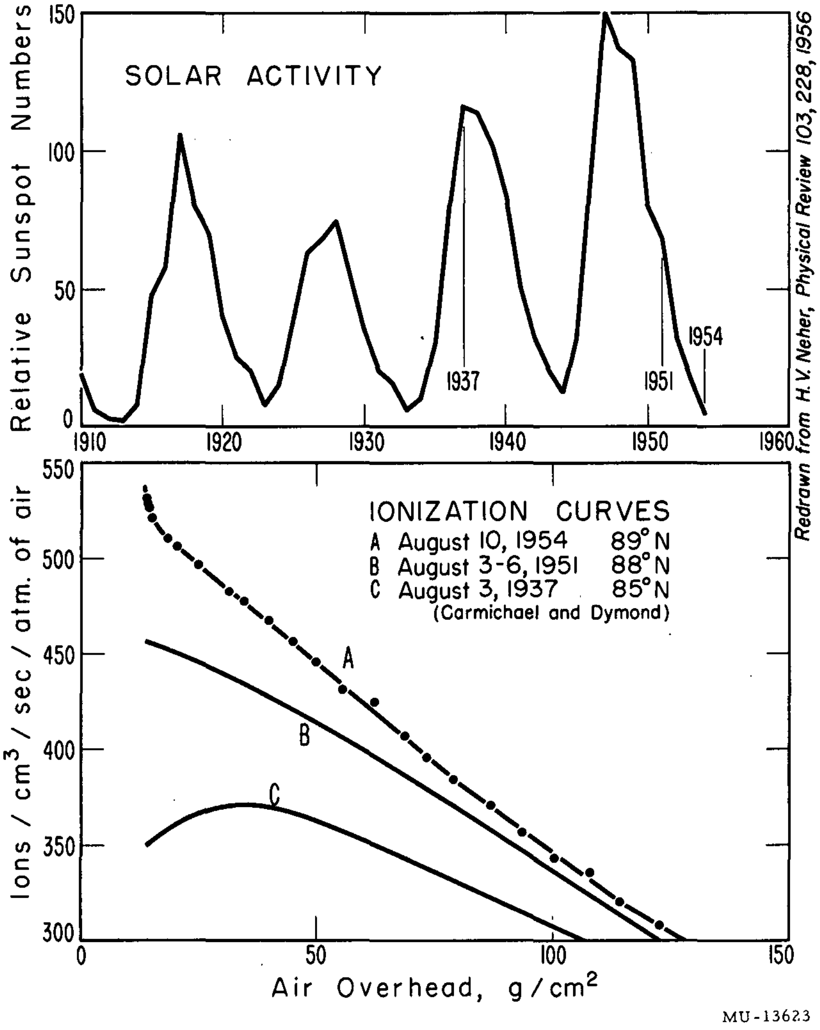
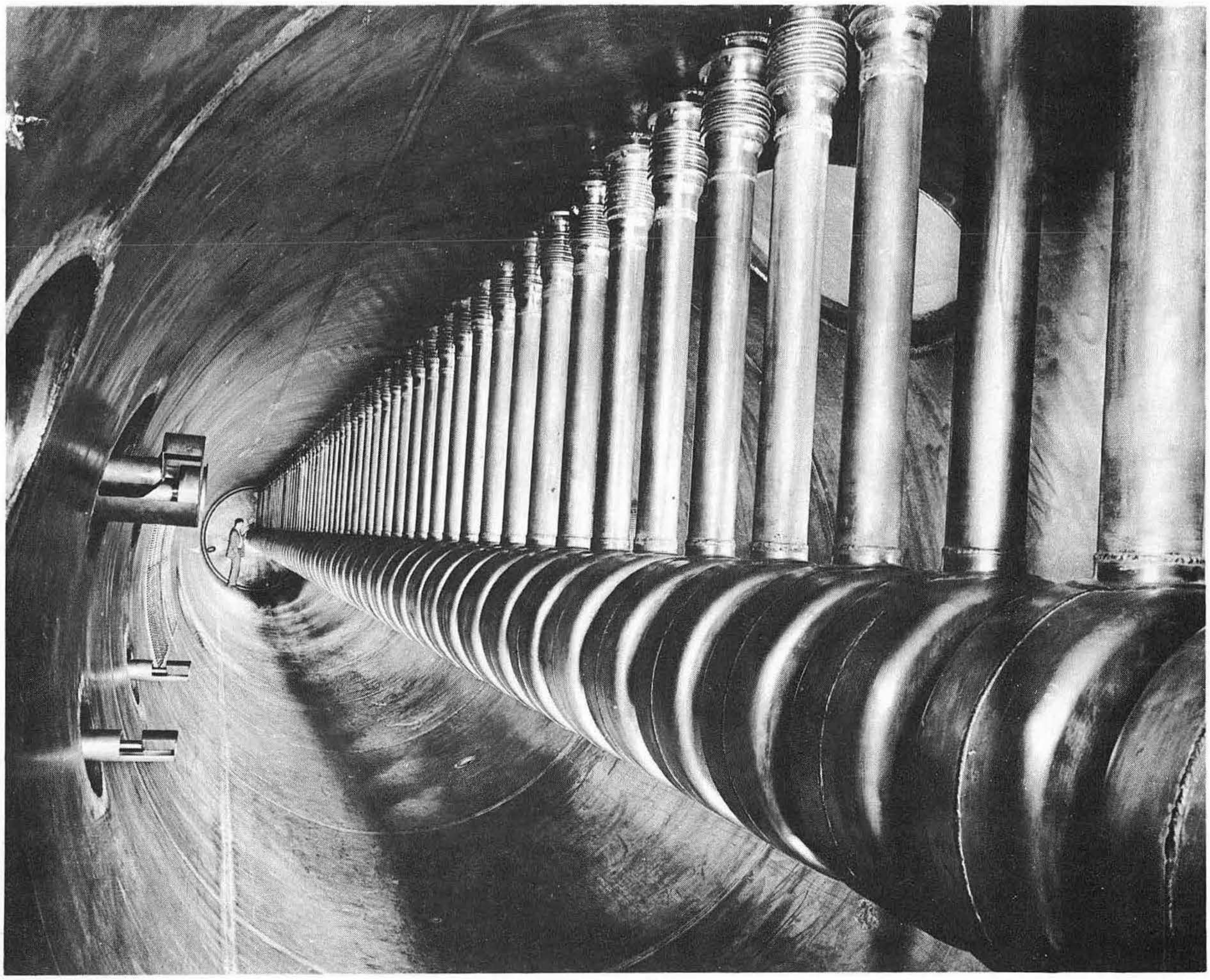


Fig. 2. Upper graph: Solar activity as measured by the relative sunspot numbers.

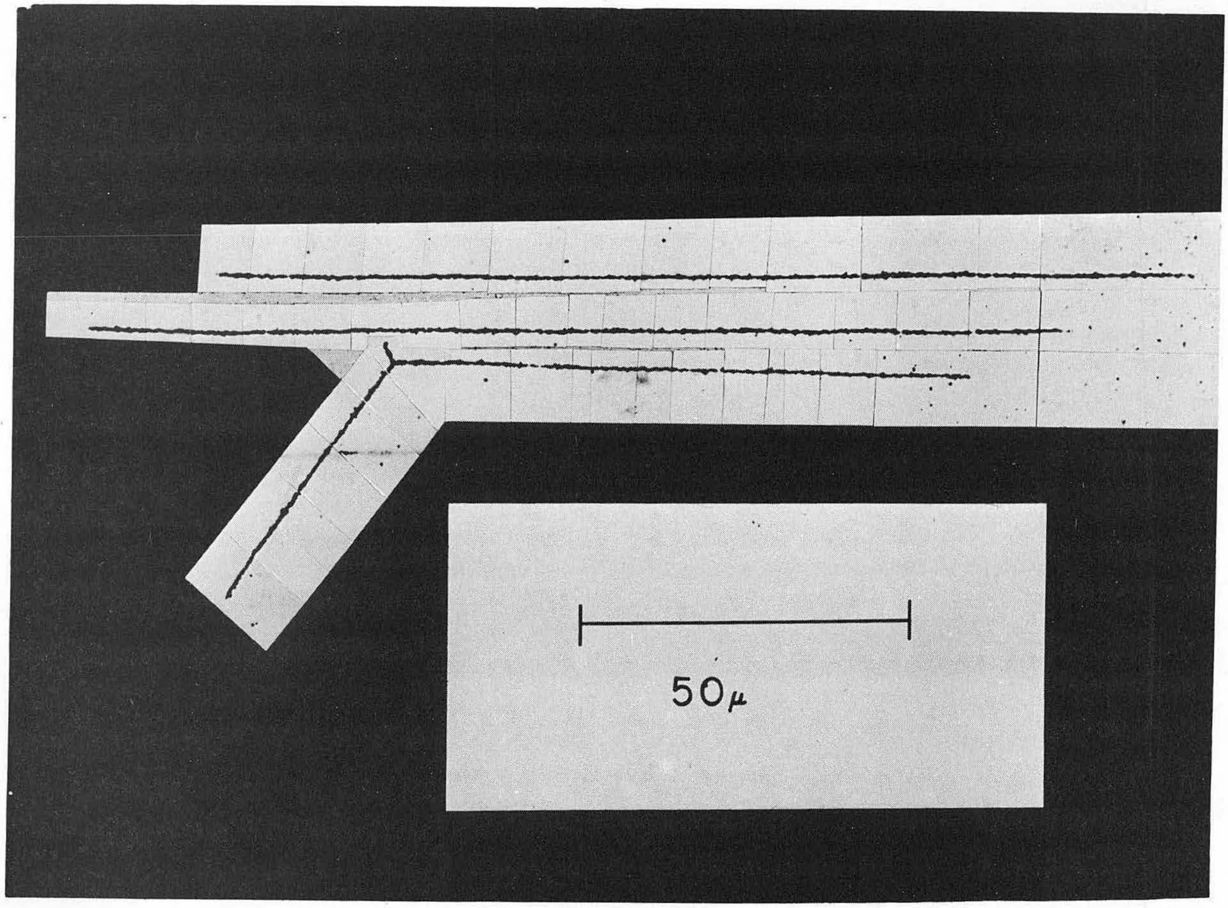
Lower graph: Ionization curve near the top of the atmosphere near the geomagnetic north pole for three different years. (1954, sunspot minimum; 1937, sunspot maximum, 1951 medium activity).

Based on H. V. Neher (Phys. Rev. 103, 228 (1956).



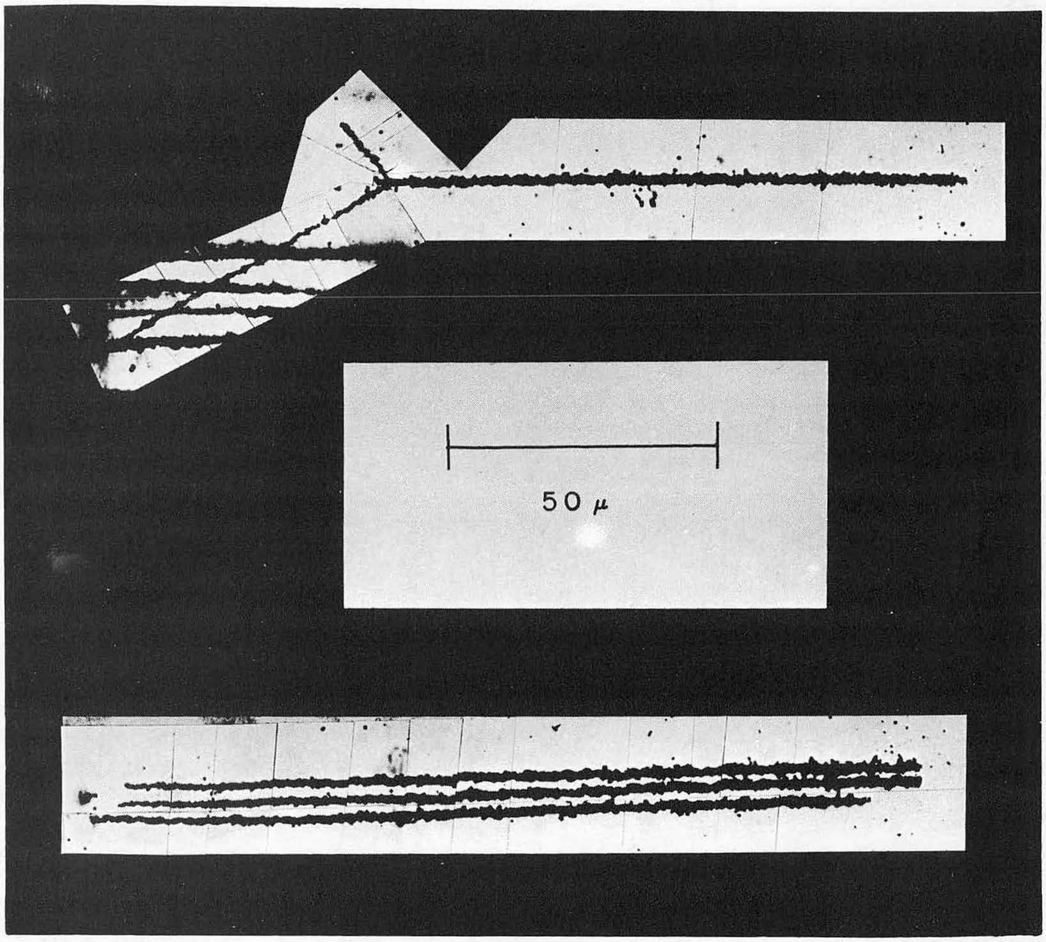
ZN-1852

Fig. 3. Interior of the main tank of the Berkeley Heavy Ion Linear Accelerator, showing the precise array of drift tubes. For size comparison, note person at opposite end of tank.



ZN-1851

Fig. 4. Two fast oxygen nuclei coming to rest in nuclear emulsion, and a third one involved in nuclear collision. The particles move from right to left. Reproduced by courtesy of Harry H. Heckman.



ZN-1850

Fig. 5. Oxygen tracks in electron sensitive emulsion, which shows the ionization due to delta rays. Reproduced by courtesy of Harry H. Heckman.

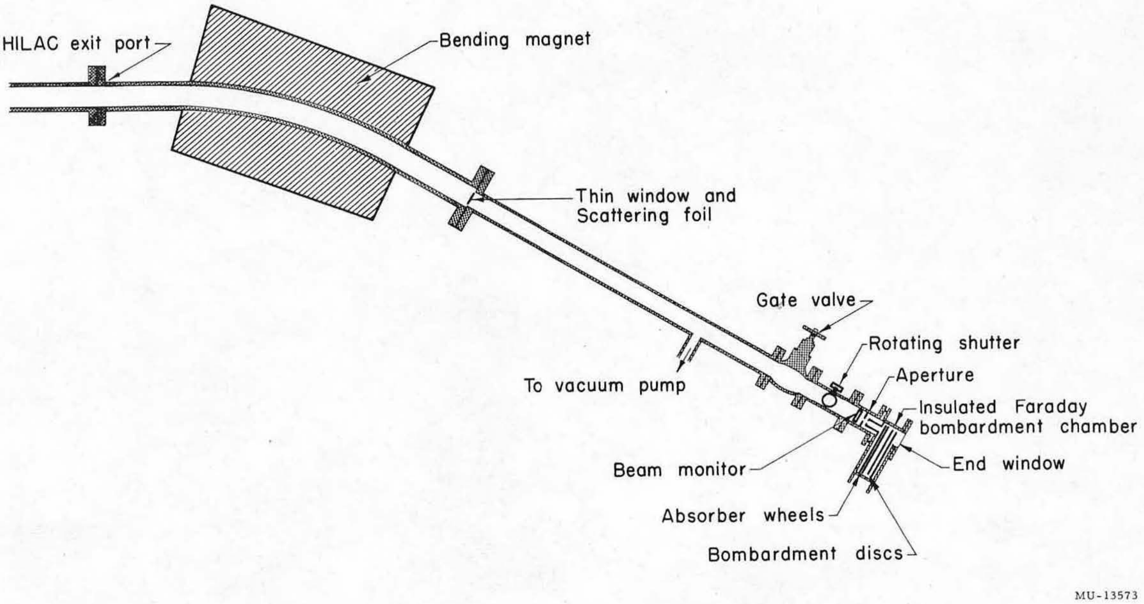


Fig. 6. General arrangement for biological exposures with multiply-charged ions from the HILAC.

ZN-1849

Fig. 7. Sagittal section of rat hypothalamus in the region of the median eminence, showing contours of a deuteron-induced lesion. Dose 16,000 Rad. The edge of the lesion, rich in glial cells, follows the contour of the beam, which was 2.4 mm in diameter. Rat sacrificed 135 days after irradiation. Asur Eosin strain. From unpublished data of the Donner Laboratory group.