Leighton that the Mankato drift of southern Minnesota is probably correlative with the Port Huron moraine of Michigan, and, pending further field studies and radiocarbon dates of pertinent deposits, will yield to Leighton's proposal that the term *Mankato* be retained as a substage of the Wisconsin, in its new pre-Two Creeks position.

Leighton's suggestion that the Valders border of the Des Moines lobe lies at the Big Stone moraine represents a modification of a much earlier suggestion of Leverett (Fig. 1), who at one time designated this moraine as marking the fifth substage of the Wisconsin (*3*, Fig. 5). The suggestion has renewed appeal as one casts about for a Valders terminus north of the Mankato region.

The Big Stone moraine across the Minnesota River valley sharply truncates elongate ridges that Leverett implied were lateral moraines of the shrunken Des Moines lobe of the fourth substage. Leighton interprets these ridges instead as crevasse fillings; he likens the relations to the transection of the Lake Border interlobate moraine (Cary) in Michigan by the Port Huron moraine (Mankato), and considers that in both areas the intervening retreat should be of interstadial rank. Retreat of Mankato ice into the Red River valley during the Two Creeks interstadial, in this view, would allow the formation of Lake Agassiz I, with a broad southern outlet via River Warren I (Minnesota Valley). Valders readvance to the Big Stone moraine would be followed in turn by final retreat and the formation of Lake Agassiz II.

The elongate ridges in question are composed of clay till (*4*, p. 105). Aerial photographs suggest that they are neither lateral moraines nor crevasse fillings, but are erosional remnants of the Mankato till plain separated from one another by multiple drainageways funneling broadly from the Big Stone moraine into the center of the Minnesota Valley. The moraine was later cut by the River Warren drainage of Lake Agassiz.

With this interpretation, the necessity for inferring a distant withdrawal of the Des Moines lobe before readvance to the Big Stone moraine is reduced. The only reports of overridden lake beds in the Agassiz area refer to a much earlier lake (C^{14} dated as $>$ 36,000 years old, Bronson, samples W-102 and W-468). At any rate, correlation of the Big Stone moraine with the Valders does not help with the problem in question because the C^{14} dates for undisturbed Lake Agassiz beds in Minnesota and southern Manitoba are mostly of Two Creeks age or older (*9*), and the Valders drift border must therefore be north of the radiocarbon sites.

Elson (*15*) postulated a Valders ice front extending from the Lake Winnipeg region eastward to Lake Superior and thence south to the Michigan Upper Peninsula and the Valders type area. This line circumvents Minnesota completely and denies the identification of Valders drift of the Superior lobe in northeastern Minnesota, which I (*16*) had made on the basis of lithologic and stratigraphic similarity to the Valders of northeastern Wisconsin. My Superior-lobe Valders in Minnesota had met with some radiocarbon difficulties, however: on the basis of interbedding it was considered to have formed contemporaneously with drift of the St. Louis sublobe (of the Des Moines lobe), which had its origin in the Red River valley in the very area where undisturbed Lake Agassiz sediments gave pre-Valders C^{14} dates. A new date (*17*) pertinent to this specific problem comes from glacial Lake Aitkin, a feature formed during the retreat of this St. Louis lobe and the presumed Valders Superior lobe. This date of 11,710 ± 325 years before the present (sample W-502) seems to be too old for late Valders, and fits the pattern of Two Creeks or "late Mankato" dates for the Anoka sand plain (Grantsburg sublobe of Des Moines lobe) and Lake Agassiz. If Elson's or some other northern Valders line is confirmed by additional work, the red clay till of northeastern Minnesota must reflect some pre-Two Creeks readvance of the Superior lobe. Two earlier Superior-lobe advances have been described (*13*), one as far as the St. Croix moraine (Cary maximum), a later one to the Mille Lacs and Highland moraines (Mankato?).

Despite the uncertainties of the correlations from lobe to lobe, the evidence from Lake Huron to the Dakotas, however, seems today to support the view that an important readvance of several ice lobes occurred just prior to the Two Creeks interstadial. Although I have previously suggested that this readvance be included as a late phase of the Cary, following Bretz, I am willing to apply to it the term *Mankato,* following Leighton, with the hope that correlation of the Mankato drift of the Des Moines lobe with the Port Huron of the Lake Michigan and Huron lobes will be more strongly confirmed.

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References and Notes

1. I am obliged to my coauthors of earlier discussions of this problem, Meyer Rubin of the U.S. Geological Survey and J. H. Zumberge of the University of Michigan, for reading this further discussion. I also appreciate the many keen comments offered by Leighton and many other participants in the 1956 Glacial Field Trip of the Geological Society of America, during which much of the field evidence bearing on the Cary-Mankato-Valders problem in eastern Minnesota was reviewed.
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4 April 1957

Dependence of Acute Radiosensitivity on Age in Adult Female Mouse

The literature on radiation sensitivity of animals at advanced ages is not extensive. Zirkle *et al.* (*1*) determined the LD_{50} for x-rays in the mouse as a function of age for ages ranging from 1.5 to 12 months. Hursh and Casarett (*2*) reported LD_{50}'s for rats at ages of 6 and 16 months. Kohn and Kallman (*3*) made a careful determination of the LD_{50} for single doses of x-rays for ages ranging from 40 to 640 days. Several studies have been made of age changes in sensitivity during the period of postnatal growth (*4*).

The paucity of information about acute lethality at advanced ages may be the result, in part, of the cost of such measurements when the conventional method of plotting a dosage-survival curve is employed. An effort was therefore made to develop a more efficient and less costly method of measuring the acute lethal action of ionizing radiation (*5*).

It was found, previously, that the mean accumulated dose that is required to determine a mean survival time of about 30 days (MAD/30 days) under a regime of daily exposure is correlated with the $LD_{50}/30$ days (*6*). This observation was based on interspecies comparison, but a high correlation has since been observed between these two measures for several mouse genotypes (*7*). A pilot study of age-dependence in acute radiosensitivity was therefore carried on, by use of the mean accumulated dose procedure.

Carworth female mice received at this laboratory at from 5 to 6 weeks of age were caged in groups of ten (11 in one

case), in 8- by 8- by 8-inch wire-mesh cages (*8*). The cage groups were maintained in the animal colony until they had reached assigned test ages, when they were exposed to 100 r of x-radiation per day, 5 days per week, for the duration of life. The cages were transported to the x-ray cubicle and were irradiated; the mice that they contained were in a vertical x-ray beam that delivered about 15 r/min 0.5 inch above the cage floor. Dose rates were measured with Victoreen condenser chambers. Radiation factors were: 200 kvp (peak) at 15 ma from a half-wave generator; 0.5 mm Cu and 1.0 mm Al added filtration; half-valve layer, 0.9 mm Cu.

The distributions of survival times after the beginning of treatment are given in Table 1. Mean after survivals (MAS), their standard error (SE), the standard deviations of the survival curves (SD), and the mean accumulated doses (MAD) are also given.

In the period from 100 to 600 days of age, the mean accumulated dose shows comparatively little dependence on age, but in the period from 600 to 800 days of age, it decreases rapidly.

The results found here are in fairly good accord with those of two LD_{50} studies that covered the same age ranges. Zirkle *et al.* (*1*) and Kohn and Kallman (*3*) found little change in LD_{50} in the first year, and Hursh and Casarett (*2*) found LD_{50}'s of 715 r for 6-month-old, and 600 r for 16-month-old, rats. Studies currently under way indicate that in mice there is a small but significant increase in LD_{50}/30 days and MAD/30 days during the period from 100 to 400 days of age (*9*). All of these data are consistent in indicating that the change of radiosensitivity with age is small during the first half of the adult life span.

The dependence of radiosensitivity on age in the later part of the life span has not been reported previously. The data presented here indicate that sensitivity

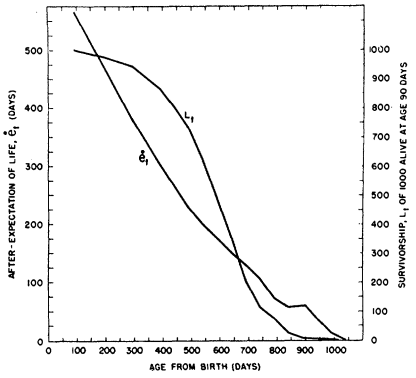

Fig. 1. Survivorship and after-expectation curves for untreated CF No. 1 female mice that were maintained in the same laboratory environment as the mice that were tested for radiosensitivity.

increases rapidly with age in this period. Although the samples available for test at advanced ages were small, the downward trend observed at ages greater than 600 days is highly significant. This is confirmed by current studies (*9*).

The survivorship curve and the after-expectation of life curve for untreated CF No. 1 female mice is given in Fig. 1. These curves are based on a large sample of mice that were maintained in the same laboratory environment contemporaneously with the mice that were tested for radiosensitivity.

One of the reasons for making this study on the age-dependence of radiosensitivity was to test the adequacy of a set of postulates about the lethal action of ionizing radiations. In brief, the postulates specified that injury is proportional to dose, that recovery is proportional to amount of injury, that all kinds of radiation injury sum with the effects of age, and that injury due to aging accumulates as a linear function of age. These postulates had been enunciated by me (*8*) and, in a basically similar form, by Blair (*10*). An important deduction was that the curve of LD_{50} versus age should have approximately the form of the curve of after-expectation of life; that is, it should be approximately linear during the first half of life and concave upward throughout adult life. The curve of mean accumulated dose versus age (Table 1) departs markedly from this form. In view of the available data on LD_{50} versus age, and of the form of the radiosensitivity curve found in this study, it is concluded that one or more of the postulates referred to in the first part of this paragraph must be revised (*11*).

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Table 1. Survival times of CF No. 1 female mice exposed to 100 r 5 days per week, mean after-survival times (MAS), standard errors of means (SE), standard deviations of survival times (SD), and mean accumulated dose (MAD). Day 0 was the day of first exposure.

Age at exposure (day)	Survival time (day)											*n*	MAS	SE	SD	MAD
95	16	18	21	21	23	25	26	28	29	30	36	11	24.8	1.8	5.8	1827
151	24	31	32	35	36	36	37	38	39	41		10	34.9	1.6	4.9	2560
263	13	21	27	28	36	37	38	38	38	41		10	31.7	2.9	9.1	2320
375	14	25	32	36	38	44	44	49				8	35.3	4.1	11.5	2562
375	18	31	33	36	36	36	38	39	42	48		10	35.7	2.5	7.8	2620
487	18	32	32	34								4	29.0	3.7	7.4	2175
543	24	28	29	30	32	35	46					7	32.0	2.5	6.6	2329
599	15	16	23	32	35	41						6	27.0	4.3	10.6	1983
599	27	32	33									3	30.7	1.9	3.2	2300
711	4	18	28									3	16.7	6.9	12.0	1267
711	16											1	16.0			1200
823	3	6										2	4.5			400

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18 February 1957

Oxidation of Chlorpromazine by Peroxidase and Catalase

The *in vivo* and *in vitro* conversions of chlorpromazine to its sulfoxide have been observed (*1, 2*). The mechanism of oxidation has not been described. This report is concerned with the oxidation of the drug by hydrogen peroxide in the presence of the enzymes peroxidase and catalase. Peroxide oxidation of phenothiazines generally has long been known (*3*); however, under the conditions prevailing in biological systems, the uncatalyzed peroxidation is sluggish.

It was found that in the range *p*H 3 to 6.3 chlorpromazine was readily converted to a deep red substance by hydrogen peroxide and peroxidase. A similar result was obtained with catalase over a more restricted *p*H range, no color appearing above *p*H 4.5. In both cases, the solutions bleached at rates dependent on the relative concentrations of the reagents. Both the extent of color production and the rate of bleaching