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Normal Mouse and Rat Strains as Models for Age-related Cataract and the Effect of Caloric Restriction on its Development

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The purpose of this study was to determine: (1) which of the commonly used strains of laboratory rats and mice provide good models for human age-related cataract, and (2) whether long term caloric restriction, a regimen that prolongs both median and maximum life span in rodents, would also delay the time of appearance of this age-related pathology.

Three strains of mice and two rat strains commonly used in laboratory work and maintained on either ad libitum (AL) or calorically restricted (CR) diets in the National Institutes of Aging and Diet Restriction colony were examined by slit lamp for age-related cataracts at four or more time points during their life spans. These strains were Brown Norway and Fischer 344 rats, and C57BL/6, (C57BL6 × DBA/2)F1 and (C57BL/6 × C3H)F1 mice. None of these strains develop congenital cataracts. Various stages of cataract were found in the great majority of these animals in old age. In both rat strains and one mouse strain the cataracts occurred after mid-life, were most advanced late in life, and were similar in locations and appearance to those in humans. In the two mouse strains in which some cataracts appeared as early as 10–14 months of age, previously identified genetic defects affecting the eye were probably involved in the early appearances. CR extended life spain in all five rat and mouse strains and also delayed both the time of first appearances and the subsequent increase in cataract severity over time in the four dark-eyed strains. CR did not delay cataract formation in the single albino rat strain studied. In summation: (1) commonly used strains of laboratory rats and mice that are free of congenital or early appearing cataracts due to genetic defects would appear to serve as appropriate models for human age-related cataract, (2) caloric restriction (CR) provides a protective effect, delaying development of cataracts in the dark-eyed mouse and rat strains, while also extending their life spans, (3) CR did not delay the development of lens damage in the nonpigmented eye of the single albino strain studied, although it extended life span.

Key words: age-related cataract; life span; caloric restriction; mouse; rat; model; eye pigment.

1. Introduction

It is highly desirable to have a naturally occurring, easily available animal model of human age-related cataract for studies of cataract development, causation and related biochemical and molecular genetic events. At present, a number of non-induced rodent models for cataract are available. However, most of these differ from the human age-related cataract, in that the time of cataract appearance or the initiation of the pre-cataractous changes take place early in post-natal life, or even in utero (Hosokawa et al., 1988; Kruk, 1990; Zigler, 1990; Tripathi et al., 1991; Phelps Brown and Bron, 1996a; Smith, Sundberg and Linder, 1997). Other possible models develop cataracts late in life but all of these in the reports we accessed were found to be pink-eyed albino animals that have been shown to be susceptible to both light-induced cataract and retinitis (Coleman et al., 1977; Gorthy, 1977; Anver and Cohen, 1979; Rao, 1991; Toyoda et al., 1992). It is important that an animal model parallel human cataracts in time of appearance, lens regions involved, and the occurrence and progression of the lesion during late life span, as well as its development in a pigmented eye. We present here a comparative cross-sectional study over the life spans of three strains of mice and two of rats, all commonly used in research, that were maintained on ad libitum (AL) or calorically restricted (CR) diets in the aging and caloric restriction colony of the National Institute of Aging (NIA) at the National Center for Toxicological Research (NCTR) in Jefferson, AR, U.S.A. Four of the strains were dark eyed, the fifth was albino, as detailed in the Materials and Methods section. The animals were studied by slit lamp at four or more age points during the life span of each strain, allowing comparison times of cataract occurrence and progression with median and maximum strain life span under both AL and CR diet conditions.

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2. Materials and Methods

Animals, Diets and Procedures

The strains examined were as follows: Mice: C57BL/6/NIAA (acronym B6); (C57BL/6NIAA × DBA/

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2NIAA)F1 (acr. B6D2F1); (C57BL/6NIAA × C3H/NIAA(F1 (acr. B6C3F1). Rats: Brown Norway/NIAA (acr. BN); Fischer 344/NIAA (acr. F344) (an albino strain). All animals were members of the NIA aging and caloric restriction colony, housed and examined in the facilities of the NCTR with a portable slit lamp. A smaller number of B6D2F1 and B6C3F1 animals from the same origin were shipped to the University of Washington and their lenses examined and photographed with a photography-equipped slit lamp, kindly furnished by Dr John I. Clark. Males only were used in all groups with the following exceptions due to animal availability: in the F344 AL rats at 28 months, six males and nine females; in the BN AL at 34 months, five males and three females; in the B6 CR at 25 months, seven males and five females; in the B6D2F1 at 19 months, 11 males and four females; and at 30 months, all females in AL and three males and 13 females in CR. In the above listed groups comparison of the females with appropriate males did not indicate either statistical or trend differences by sex for occurrence time or grade of cataracts. In this study the right eye only was examined in rats and the left eye only in mice for reasons of positioning in hand-held restraint and because of the large number of animals examined (500) in a limited time period. All animals were restrained by hand without anesthesia.

In most instances 15 animals in each age and diet group were examined at each life span time point. Four or more age points were included for each diet group in each strain in this cross-sectional study. Because this colony ships out older animals, it was necessary to take the number available at the time of the study. When less than 15 animals were available at the oldest time point this may be determined by observing Panels A in Figs 7, 9, 11, 13 and 15, where each symbol indicates an individual animal.

Institutional Animal Care and Use Committee regulations for both NCTR and the University of Washington and NIH guidelines for the humane use of animals were followed. All animals were caged singly from 14 weeks of age onward and were fed the same NIH 131 diet, corresponding to Purina diet 5022-3-C2N, with supplementation of vitamin levels in the pellets for the CR diet to bring those levels to equivalence with the AL diet. Caloric intake for the CR mice and rats was reduced gradually between 14 and 16 weeks of life to 60 % of the mean intake established for similar aged AL animals of the same strain, and maintained as such throughout life span. The cages were of clear plastic with wire grid tops and without bonnets. The room lighting was cool white fluorescent. Foot candle intensity within the cages varied from 15–60 (average 41) at top shelf levels in the cage racks. The highest level listed above is about half that found in the offices of the investigators. No effort was made to systematically rotate the cages.

Equipment and Agents Used

A Kowa SL-14 portable slit lamp (Kowa Optimed Inc., Torrence, CA, U.S.A.) was used to examine the eyes of all of the strains on site at NCTR, with the exception of ages 20, 24, 30 and 42 months in the B6D2F1 mouse strain and a small number of 4, 18 and 30 months old B6C3F1 mice. These latter animals were shipped by air from NCTR to the laboratory of NSW at the University of Washington where, after a 5–7 day acclimatization period, their eyes were examined and several photographed with a Nikon FS-2 slit lamp with camera attachment (Nikon Co., Kogaku, Japan), kindly made available by Dr John I. Clark. The slit lamp positioning for both instruments was first frontal view, followed by 30° angle viewing. The animals' pupils were dilated with 1 % tropicamide (Mydriacyl, Alcon Inc., Humacao, Puerto Rico) which produced full dilation.

Cataract Scoring

The scoring for rats was based on a progressive 5 point staging basis. Class 1 cataract indicated a mild clouding or opalescence and corresponded to the classification of decreased nuclear lucency previously described as 'late senile lens change' (Leibowitz et al., 1980). Classes 2 and 3 represented progressive stages of opacity, with class 3 commonly showing regional localization of the cataract as nuclear, posterior cortical or subcapsular. Class 4 constituted a progression in which the cataract was easily visible to the viewer's eye without need for the slit lamp, usually occupying most or all of the lens. With the slit lamp the lens presented complete opacity. Class 5 represented hypermature cataract with a completely opaque white marble-like appearance and often, irregular outline. Although classes 4 and 5 were viewable without the slit lamp, it was used on all animals to determine cataract classification. In mice, classes 4 and 5 were merged to a 4 only, due to the limits imposed by the smaller eye of this species. The examiner was without knowledge of the age or diet group of the animals presented to him.

Life Span Calculations

The strain survival curves were furnished by NCTR from studies completed between 1988 and 1992, using approximately 50 animals for each diet cohort in each strain. Median life span is reported here as the time point at which 50 % of the animals in the group under study had died and maximum life span is reported as the time point at which only 10 % of the group studied remained alive. The animals used in the cataract studies reported in this paper were not those used to establish the NCTR survival curves but were from the same production colonies.

Statistical Tests

Comparisons were made at multiple age points in each strain for AL vs CR animals for the presence and degree of severity of cataracts using the non-parametric Mann–Whitney rank test for comparison of means. The Bonferroni adjustment was used, reducing the possibility of chance event producing error at the age points where significance was noted. The *P* values are reported in the figure legends. Parametric *t*-test values were also computed on the several age points, were found to be significant at the same ages as the Mann–Whitney comparisons and are, therefore, not reported. The computer statistics package used was SPSS 61.1S for Power Mac.

3. Results

Types of Cataract

The method of classification of the cataracts has been given in the Methods section. When regionalization was seen in class 3 cataracts these were most commonly nuclear or posterior cortical, but posterior subcapsular and anterior cortical cataracts were also observed. Combinations of nuclear cataract with other regions were also common. In the mature cataracts of both species apparent water clefts were common and occasional brunescence was observed in the rats. Several spoke cataracts were seen in both rats and mice. Slit lamp photographs of cataracts in B6D2F1 and BC3F1 mice that were shipped to our laboratory at the University of Washington are shown in Figs 1–6.

Age-related Cataract Incidence (Number of Occurrences at Each Time Period) Regardless of Diet

In the two rat strains and in the B6C3F1 mouse strain the cataracts appeared late in life span, with the greatest advancement of the condition usually near the time point for median life span for the strain and diet group examined (see cataract numbers and degree of severity in relation to the median life span indicator arrows in Figs 7, 9 and 11). In the B6 mouse strain the cataracts appeared earlier, although the majority appeared in the latter half of the median life span of this most short-lived of the three mouse strains examined (Figs 13 and 14). However, in the B6D2F1 hybrid mice 13/32 mice had some degree of cataract by 14 months (Fig. 15). In this long-lived hybrid mouse strain this represents many occurrences at a time less than halfway to the point of median life span for either diet group. The putative genetic and cellular causes for early cataract incidence (number of occurrences at a time point) in the B6 and the B6D2F1 strains are detailed in the Discussion section.

The Effect of Diet

All of the dark eyed strains of mice and rats benefited from CR by a delay in cataract appearances. In Figs 7, 11, 13 and 15 this is apparent by comparing the relative numbers and degree of severity of cataracts for the CR animals to those of the AL animals in the A (upper) panels. Panels B (lower) present the means $\pm$ S.E. of the degrees of cataract development, expressed as classes 1–4 or 5 at each age point shown on the abscissa. The median life span of each diet group is indicated by arrows on the abscissa in the lower panels. Non-parametric statistical analyses (Mann–Whitney rank test with BonFerroni adjustment) indicated strong statistical differences for cataract numbers and stage of development (severity) between AL and CR animals at the time points of greatest divergence in all diet comparisons. The *P* values are noted in the individual figure legends. An adequate spread of age points was available to determine both the approximate time of earliest cataract appearances and a curve for their increasing severity with increasing animal age in the five strains examined. Among these five strains the BN rats (Fig. 7) and the B6C3F1 mice (Fig. 11) best followed a time course of late life appearance and subsequent progression in severity expected in age-related cataract, as well as demonstrating the partial protection afforded by CR.

However, the albino F344 rat strain received no benefit from CR insofar as the time course of cataract occurrence and progression was concerned, (Fig. 9), even though CR extended life span in this strain as it did in others (Fig. 10). The effect of light on the lens and retina of albino rodents is referred to in the Discussion section. Regardless of the non-effect of CR, the time of appearance of the more severe cataracts in the F344 was primarily confined to later life span in both AL and CR cohorts, as noted by comparing the cataract numbers and degrees of progression to the markers indicating median life span in Fig. 9 (B). The cataract incidence in CR was significantly greater than that in AL at 28 months, a time well beyond the median life span for AL animals in this strain.

4. Discussion

Our intent was to study five different rodent strains available from the NIA aging and diet restriction colony at age intervals in order to establish the cataract incidences, peak of occurrences and the progression of severity, and to establish the most fitting models among these strains for the human condition. We also wished to determine the effect of CR on the time of development of cataracts in these same strains. On the basis of the present findings it is suggested that the long-lived B6C3F1 mouse strain and the long-lived BN rat strain constitute excellent

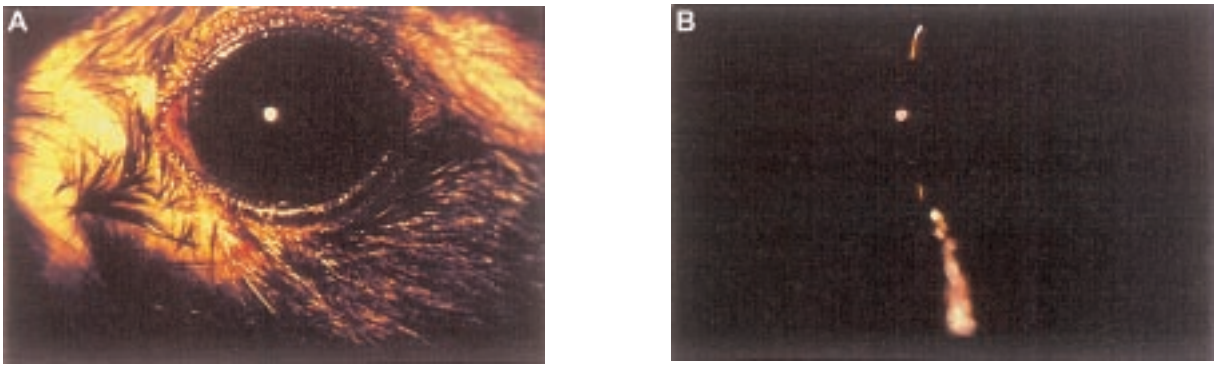

FIG. 1. (A) A non-cataractous eye in 8 month old B6D2F1 mouse, frontal view. (B) Same non-cataractous eye shown in (A), viewed here by slit lamp at 30° angle.

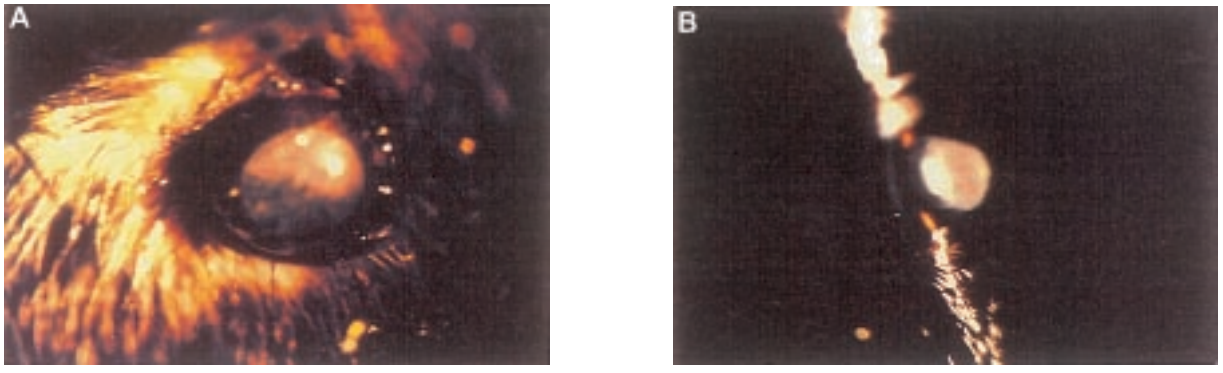

FIG. 2. (A) Class 4 apparent hypermature cataract present in 25 month old B6D2F1 AL mouse. (B) Same class 4 cataract shown in (A), viewed by slit-lamp at 30° angle.

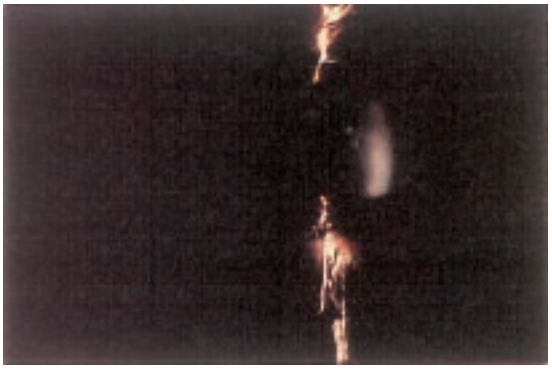

FIG. 3. Twenty-nine month old B6D2F1 AL mouse with class 3 posterior cortical cataract, viewed by slit lamp at 30° angle.

FIG. 4. Twenty-nine month old B6D2F1 CR mouse with class 3 posterior subcapsular cataract, viewed by slit lamp at 30°.

FIG. 5. Twenty-eight month old B6C3F1 AL mouse with class 3 diffuse cataract, viewed by slit lamp at 30°.

FIG. 6. Twenty-eight month old B6C3F1 CR mouse with class 2 posterior subcapsular/subcortical cataract, viewed by slit lamp at 30°.

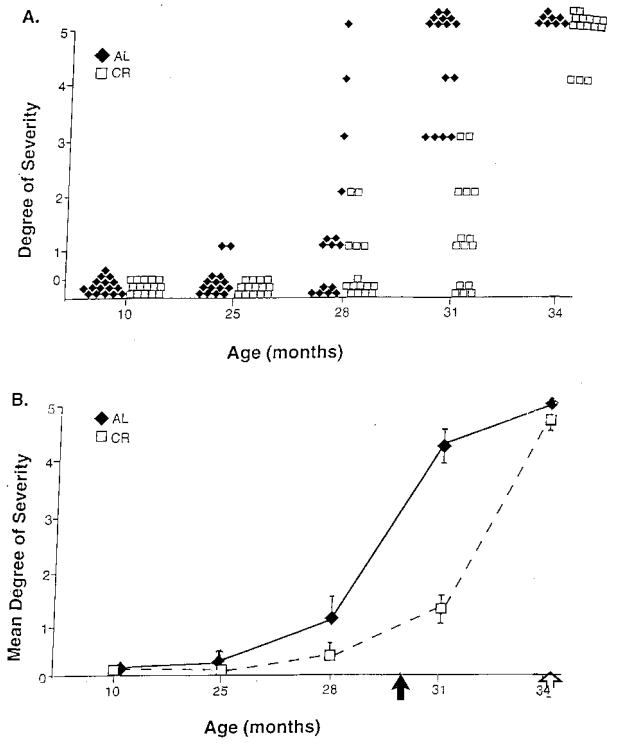

FIG. 7. Chronological incidence of cataracts in BN rats. (◆) AL rats. (□) CR rats. Ordinate numbers indicate classifications of cataract progression as described in Materials and Methods. The abscissas show the animal ages at which data for each age point were collected. AL and CR animals were the same age at each time point. In (A) each symbol indicates an individual rat. In (B) the mean degree of cataract severity (± S.E.) is shown for each age and diet group at each age point. When S.E. bar is missing either the mean was zero or all animals were clustered at the same mean. A dark filled arrow for the AL animals and an open arrow for the CR animals under the abscissa indicates their respective median life spans. $P < 0{\cdot}0001$. for CR vs AL comparison at 31 months.

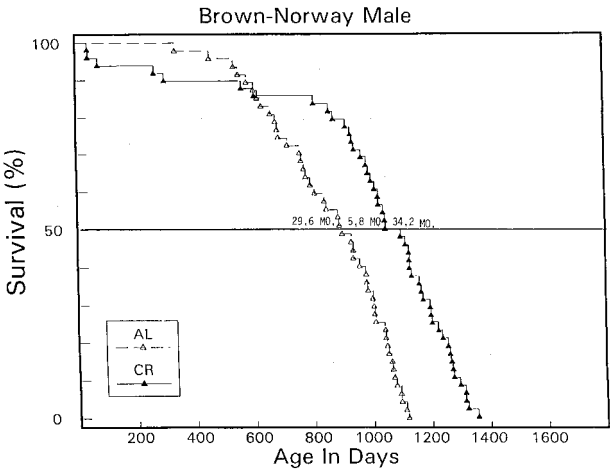

FIG. 8. Life span data for BN rats as furnished by the National Center for Toxicological Research and established for the NIA aging and caloric restriction colonies, from which the (nonidentical) animals in this study were drawn. Symbol identities are indicated on the figure and each symbol indicates an individual animal. Ordinate represents percentage survival, abscissa represents time in days. To facilitate comparisons, median life span data for the two diet groups are also shown in months on the 50 % survival line, reading from left to right as AL median life span, difference between AL and CR median life spans, and CR median life span, respectively.

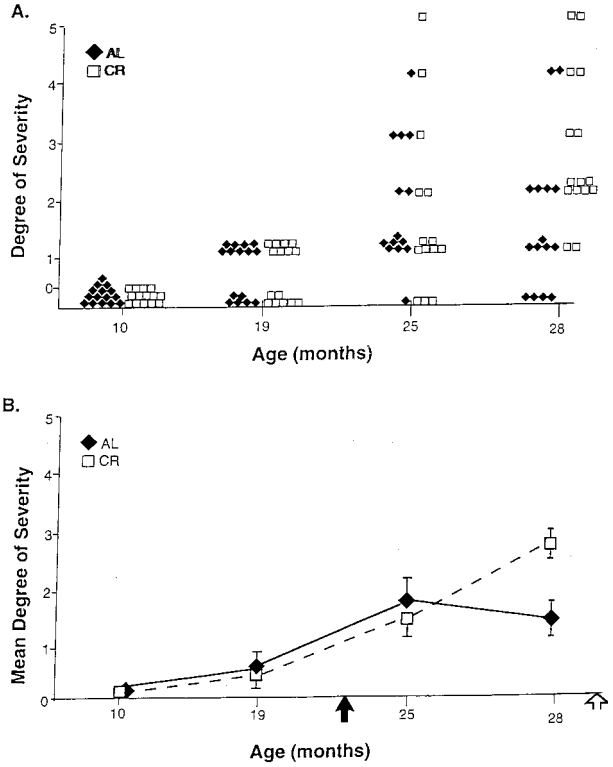

FIG. 9. Chronological incidence of cataracts in F344 rats. Data arranged as in Fig. 7. Statistical significance at 28 months, $P < 0{\cdot}001$ for AL vs CR.

models for studies on the development of age-related cataract, since both develop cataracts late in life span in a very high proportion of the individuals examined, and the positioning of the cataracts resembles that in humans. The determination that CR significantly delayed cataract formation in all four of the dark eyed rodent strains, adds cataract to the list of pathologies favourably affected by CR (Weindruch and Walford, 1988a,b). We are not the first to report the development of cataracts in mice and rats. However, in all previous studies that we have been able to access the animals were from strains predisposed to develop congenital or early cataracts (Hosakawa et al., 1988; Kruk, 1990; Zigler, 1990; Taylor et al., 1995; Phelps Brown and Bron, 1996a; Smith et al., 1997) or, if of otherwise normal genetic eye inheritance, were albinos, which have been shown to develop light-induced retinal damage and cataracts (LaVail, Sidman and Gerhardt, 1975; Gorthy, 1977; Rao, 1991; Toyoda et al., 1992). Light-induced cataracts in albino F344 rats were reported in studies by Rao (1991) and by Toyoda et al. (1992), in which the percentage of animals developing cataracts over a 24 month period was related to fluorescent light intensity in the cages. In both studies

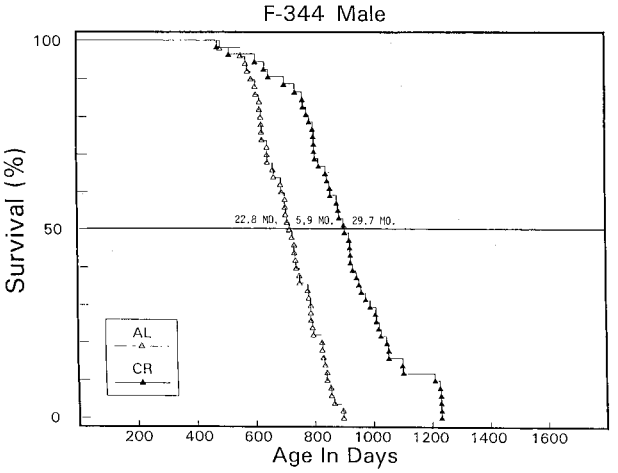

FIG. 10. Life span data for F344 rats. Data arranged as in Fig. 8.

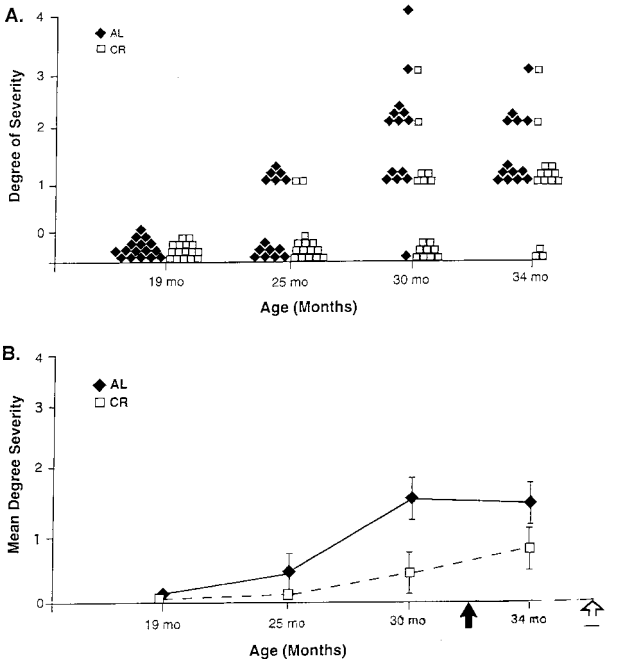

FIG. 11. Chronological incidence of cataracts in B6C3F1 mice. Data arranged as in Fig. 7. $P < 0{\cdot}01$ at 30 months for CR vs AL.

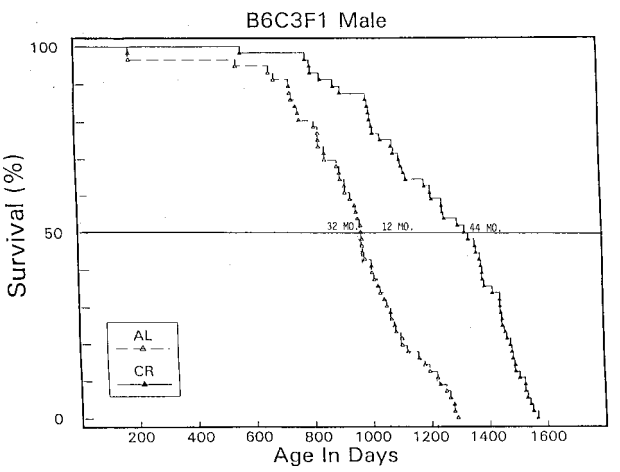

FIG. 12. Life span data for B6C3F1 mice. Data arranged as in Fig. 8.

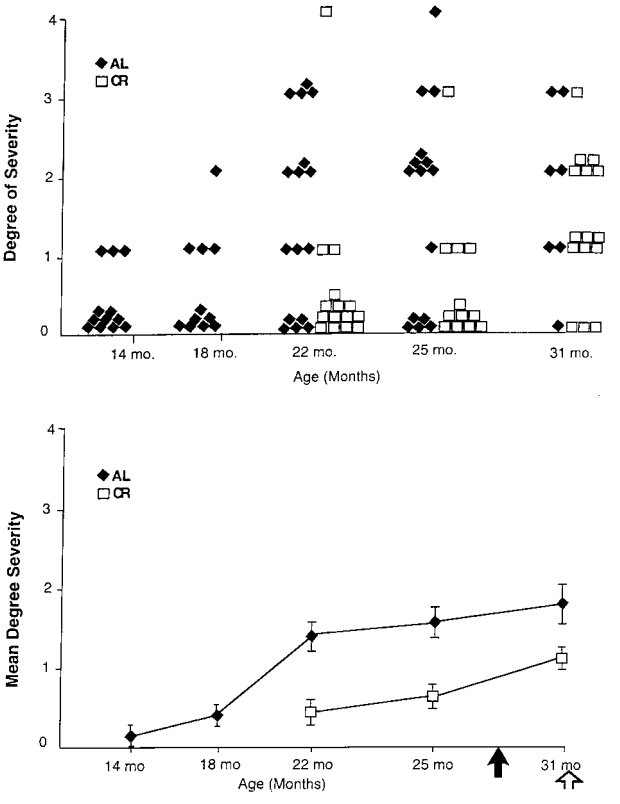

FIG. 13. Chronological incidence of cataracts in B6 mice. Data arranged as in Fig. 7. $P < 0{\cdot}001$ at 2 and 25 months, $P < 0{\cdot}01$ at 31 months for CR vs AL.

cataract presence was determined by gross inspection and varied from 1 to 68% in the first study and from 3 to 47% in the second, as related to degree of light exposure. Unfortunately, both reports were complicated by the fact that the animals examined were on carcinogenicity studies. However, no relationships between the treatment groups and the incidence of cataracts were observed. Gorthy (1977) reported a 66% incidence of advanced posterior subcapsular and/or supranuclear cataracts in albino Wistar rats with 'a normal life expectancy of 32 months' by 29–30 months of age, with lighting conditions not reported. A study in otherwise untreated young albino A/J mice found lens opacities developing by 50–60 weeks, correlated with a decrease in the development of lens epithelial cells (LECs) into fiber cells, when the mice were exposed to near UV light 12 hr per day (Zigman, Yulo and Schultz, 1974). Studies on cataract occurrences in Royal College of Surgeons (RCS) rats with inherited retinal dystrophy and a tendency to develop early cataracts were carried out by LaVail et al. (1975) and, also, by Hess et al. (1985). In the first named study a dark-eyed variant of the RCS was mated with congenic pink-eyed RCS, both with inherited retinal dystrophy. The F2 matings

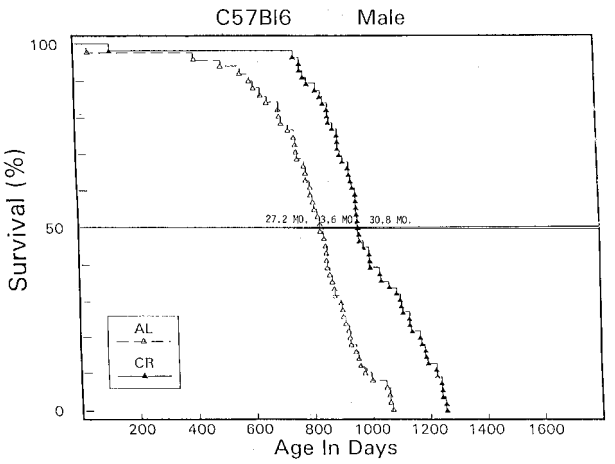

FIG. 14. Life span data for B6 mice. Data arranged as in Fig. 8.

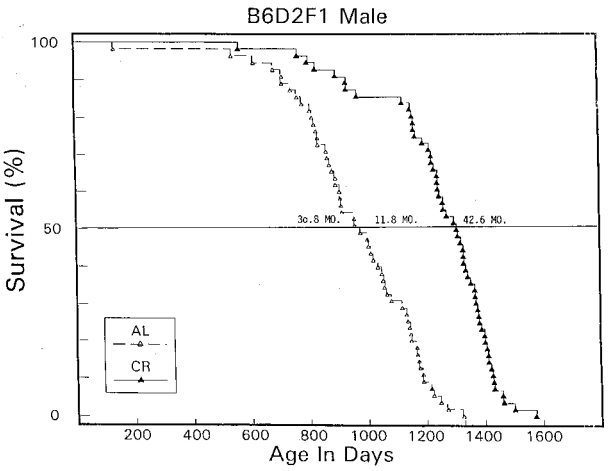

FIG. 16. Life span data for B6D2F1 mice. Data arranged as in Fig. 8.

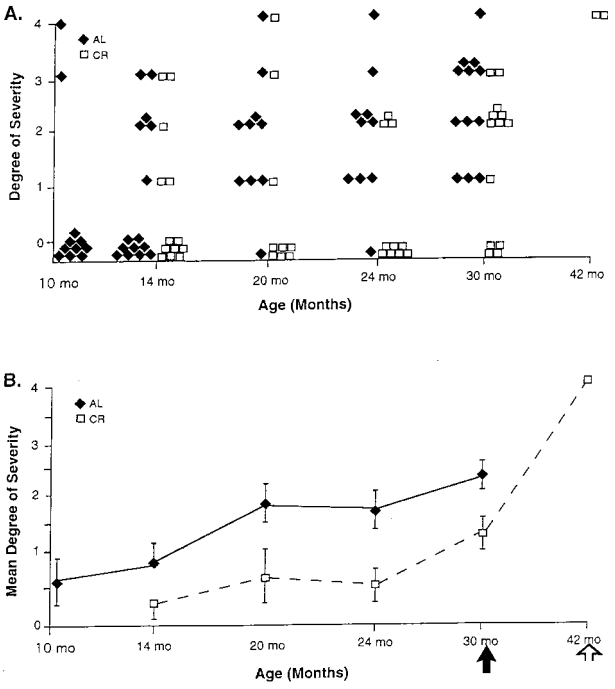

FIG. 15. Chronological incidence of cataracts for B6D2F1 mice. Data arranged as in Fig. 7. $P < 0{\cdot}01$ at 14, 20, 24 and 30 months for CR vs AL.

resulted in both pink-eyed and dark-eyed offspring, among which the dark-eyed animals developed eight-fold less cataracts than the pink-eyed animals. In the Hess study it was shown that a purified ingredient diet reduced the number of mature cataracts detected by gross observation by ten-fold when compared to diets with similar but non-purified ingredients. However, the possibility of a less appetizing diet producing a self-induced CR effect among the animals was not considered. Also, the small number of slit lamp observations carried out detected the occurrence of less advanced cataracts in the purified diet group.

Long term CR is a well-studied condition and is the only regimen that extends both median and maximum life span in both mammals and lower life forms (Weindruch and Walford, 1988a,b; Sohal and Weindruch, 1996, and Figs 8, 10, 12, 14 and 16). Evidence has been provided that at least a part of its effect is due to limiting the amount of oxidative damage that develops in several tissues (Sohal et al., 1994; Sohal and Weindruch, 1996), including H_2O_2 exposed LECs (Li et al., 1998). In our presently reported study all four of the dark-eyed mouse and rat strains examined developed cataracts later in life span in CR animals than in AL fed controls. When AL and CR groups were compared for degree of cataract severity there were strong statically significant differences at one or more time points in all four strains (Figs 7, 11, 13 and 15). It is notable in the BN rats, in particular, that the advantage for CR at 31 months was highly significant, but was essentially lost by 34 months (nevertheless, this is equivalent to a 7 year delay if extrapolated to the human lifespan). Thus, the time for appearances and advancement in severity of the cataracts in this dark eyed strain was delayed by CR, but not prevented. In the mouse strains this catch-up phenomenon was not so obvious. It is noted that Taylor et al. (1995) have previously reported a reduction in cataracts that accompanied CR in the cataract-prone Emory mouse. Given the antioxidant protection afforded by CR (Leveille et al., 1984; Sohal et al., 1994; Sohal and Weindruch, 1996; Li et al., 1998), and the evidence for the encouragement of cataracts in albino rats and mice under brighter lighting conditions (LaVail et al., 1975; Rao, 1991; Toyoda, 1992), the CR delay of cataract development in dark-eyed animals in the present study appears to further strengthen the case for photo-oxidation participating in the causation of cataract (Varma, Devamancharan and Morris, 1991; Green, 1995; Spector, 1995). It is of interest that CR also was found to decelerate the progressive reduction in the relative

proportion of lens gamma crystallins with increasing animal age in the B6C3F1 strain (Leveille et al., 1984). Our results add age-related cataract to the list of age-related pathologies protected against by CR (Weindruch and Walford, 1988a,b; Sohal and Weindruch, 1996).

In the albino F344 strain rat CR did not delay the time of appearance nor the progression of cataracts with advancing age. The incidence in the CR group significantly exceeded that of the AL at an age point when very few AL animals remained alive (28 months, Figs 9 and 10), suggesting the possibility of a last surviving subpopulation effect. Given the tendency of pink-eyed rats and mice to develop both light-induced retinal degeneration, and cataract (LaVail et al., 1975; Rao, 1991; Toyoda et al., 1992), it seems possible that the photo-oxidant effect of moderate light exposure in the nonpigmented F344 eye overwhelmed an antioxidant effect provided by CR. It is important to note, however, that both diet groups of F344 rats developed their earliest mild cataracts between 10 and 19 months of age. Further, they developed the more severe forms near the age of median life span for their strain, as did the dark-eyed BN strain. This relatively late appearance of advanced cataracts in the F344 is difficult to explain in relation to expected greater photo-oxidative damage in the non-pigmented eye and the non-effect of CR on time of cataract development in this strain. However, it could be related to resident antioxidant enzyme levels or enzymatic DNA repair systems that become inadequate only late in life. The light levels, reported above under Materials and Methods and to which all five strains were exposed, were relatively low when compared to usual indoor lighting levels.

The conditions imposed by genetic background must be considered in choosing a strain for a model of age-related cataract. Even apparently normal strains, such as the B6 and the DBA/2 may carry a genetic predisposition leading to somewhat earlier cataract formation. Thus, the B6 and, especially, the hybrid B6D2F1, developed cataract earlier than the other strains examined, with some cataracts appearing relatively early in life span (Figs 13 and 15). The B6 has been shown to have a diminished LEC replication rate, as determined both in vivo (Robinson, Holmgren and Dewey, 1993) and in vitro (Lipman and Muggleton-Harris, 1982–83). Approximately 15% of the animals in this strain and in its hybrid, B6D2F1 at the NCTR had a previously recorded condition in these strains known as 'small eye' (Robinson et al., 1993), in which the eye is noticeably smaller than normal, with a correspondingly small lens. Small eye animals were eliminated from our study group, but this condition may be only the extreme manifestation of cellular replicative insufficiency in the eyes of the two strains named above. The earlier occurrence of cataract seen here in the hybrid B6D2F1 strain may also be due in part to a heritable secondary angle glaucoma-like condition that has been reported for the DBA/2 parent (Sheldon et al., 1995; Smith et al., 1996; Chang et al., 1999). Relatedly, we had previously found a reduced space for the aqueous collecting channel in aged B6D2F1 mice, and protection against this age-related change by CR (Li and Wolf, 1997). It is likely that this DBA/2 condition was inherited in the hybrid B6D2F1 and may have provided cataractogenic conditions that compounded the replication defect inherited from the B6 parent (Phelps Brown and Bron, 1996a, c). Apparently, the C3H parentage in the B6C3F1 hybrid strain not only avoided this problem inheritable from the DBA/2, but also negated any effects from the B6 parent, since the B6C3F1 developed cataracts only late in life span.

Several retrospective studies of large groups of nondiabetic humans have reported a statistically significant relationship between relatively early development of age-related cataract and a shorter life span for the subpopulations with such cataracts (Hirsch and Schwartz, 1983; Podgor, Cassel and Kannel, 1985; Benson, Farber and Caplan, 1988; Street and Jafitt, 1992; Minassian, Mehra and Johnson, 1992; Thompson et al., 1993). It would be of interest, therefore, to determine the relationship of times of cataract occurrences to life span in several rodent strains not affected by albinism or genetic eye defects. While the two rat strains assayed in this study do appear to develop most cataracts at a time relative to their individual life span expectancies, their eye pigmentation differs and they represent only a single comparison.

In conclusion, we report here that in three commonly used laboratory mouse strains and two commonly used laboratory rat strains, age-related cataracts of various degrees of severity had developed in the great majority of animals that were alive at the time point of the individual strain's median life span. In particular, the BN rat and the B6C3F1 mouse developed the initial stages of cataract only late in life with progressive severity to or beyond the time of median life span of the respective strains. To our knowledge, this is the first complete report of age-related cataract in genetically normal, dark-eyed mice and rats and these strains may be useful as models for human age-related cataract and related experimentation. CR significantly delayed the cataract occurrences in all strains examined except the albino rat strain, suggesting that it may provide protection against moderate photo-oxidative damage that accrues in LECs, as it does for oxidative damage at other sites. Genetically determined defects in lens growth plus a glaucoma-like condition were thought to be involved in the earlier appearances of cataracts in two of the mouse strains, the B6 and the B6D2F1, respectively.

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