Blindness: Its Relation to Age of Menarche

Abstract. *Blindness in human females is associated with an age of menarche which is earlier than normal. When blindness is accompanied by a total loss of light perception, menarche is even earlier.*

There is considerable evidence of a relationship between light exposure and gonad function in certain birds and mammals (*1*); there are also widely-quoted anecdotes which connect the advent of springtime with *furor sexualis* in Eskimos (*2*). But so far as we have been able to find, there is no direct published evidence that the maturation or subsequent functioning of the human gonad is influenced by photic stimuli. Since it is not practical to expose human subjects to altered light conditions for long enough periods to perform planned experiments, we have attempted to investigate the effects of light on the human ovary by comparing the age of menarche in girls with and without visual function and light perception. The data for this study were obtained by direct questioning or examination of medical records of the girls in the following four groups (*3*). (i) One hundred and eighty-one prematurely born girls who were made blind by retrolental fibroplasia (RLF) during the first few months of life. Of these, one hundred and one girls had light perception; the remaining eighty had none (*4*). (ii) Ninety-nine prematurely born girls with normal vision (*5*). (iii) Fifty-four girls born at full term, who were blind at birth or became blind during the first year of life (hereinafter referred to as "full-term blind") (*6*). (iv) Two hundred and thirty-six girls born at full term with normal vision (*7*).

Blindness, for our purpose, is defined as visual acuity of 20/200 or less, in both eyes. Retrolental fibroplasia (*8*) is a disorder of the retina and vitreous which occurs almost exclusively in premature infants of low birth weight; it has been demonstrated that the incidence of the disease is positively associated with the length of exposure of the premature infant to supplementary oxygen. In the study reported here, possible special effects of this disease (or of prematurity) on sexual maturation were ruled out by including full-term blind, as well as prematurely born blind girls. Again, it was necessary to exclude the possibility that the process which produced blindness might also affect sexual development. We therefore retained in the study only those girls whose cause of blindness is known and whose pathology is believed to be limited to the orbit and unrelated to neuroendocrine disorders. For the same reason, any of the following associated diagnoses caused exclusion from all four groups: nonorbital or multiple developmental abnormalities, blindness of a hereditary or familial nature, albinism, neurological disorders, deafness, migraine, neonatal trauma or hemorrhage, neoplasms, toxoplasmosis, chorioretinitis of unknown etiology, orbital infection, subnormal intelligence, emotional problems which required hospitalization, and specific medical entities such as tuberculosis, rheumatic fever, diabetes, and Stein-Leventhal syndrome. In this way, it was felt that any effect of blindness on sexual development could be attributed to the absence of responses to photic stimuli and not to the agent which caused the blindness.

No girl of less than 110 months of age was admitted to the study.

The prematurely born girls with normal vision, born during approximately the same years as the girls with retrolental fibroplasia, served as controls for the RLF group. The student nurses, born between 1940 and 1946, were controls for the full-term blind girls, whose birth years range from 1938 to 1954. There were no differences in age of onset of menarche among the nonblind groups admitted to the study, nor, within any population among sets of girls from different geographical regions.

This study was, of necessity, retrospective. The data were collected from the records of resident blind schools (35 percent) or from questionnaires answered by the girls themselves (65 percent). The questionnaire requested that, if the exact age at menarche could not be recalled, the uncertainty be indicated. In about 60 percent of the answers in each group, age at menarche was given to the nearest month; in the remaining 40 percent, where age at menarche was given in years only, 6 months were added in each instance, in an effort to distribute the possible error.

Retrolental fibroplasia was first encountered in the late 1930's, reached its peak of incidence in 1952 and 1953, and declined thereafter, so that since then, cases have occurred only sporadically (*8*). For this reason, the mean age of the group of girls with RLF is low, and a certain fraction of them has not yet reached menarche. If, in analyzing our data, we had used the mean age of those girls who had attained menarche, the findings would have been biased in favor of an earlier age of menarche in the younger groups. To give a realistic representation of the age of menarche of a group which contains some members who have not yet reached menarche, a life-table analysis (*9*) was applied to the data. By using this method, all the observations could be used, including those made on girls who had not yet attained menarche.

It was found that, among prematurely born girls, blindness is associated with an earlier onset of menarche than that observed in girls with normal vision. This effect is increased when light perception as well as vision is absent (Fig. 1). In girls born at full term, blindness due to a variety of causes also produces an earlier age of menarche (Fig. 2). (In this group, the number of subjects with documented early loss of light perception was not large enough to permit a separate analysis of the combined effects of blindness and loss of light perception.)

Among polyestrous mammals, the relation between light and gonadal function has been well studied in the rat (*10*). In this species, exposure of immature animals to extra illumination leads to an earlier onset of sexual maturation, as indicated by earlier spontaneous vaginal opening (*11*). Subsequently, such animals are longer in vaginal estrus than normal, and for several months at least, their ovaries are larger than normal. Conversely, rats kept in constant darkness show

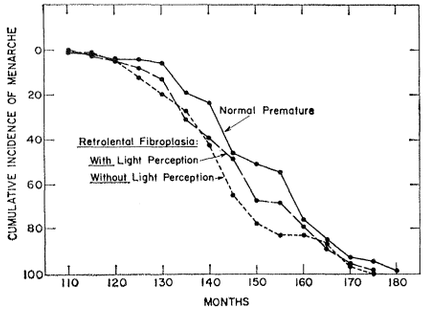

Fig. 1. Cumulative incidence of menarche (expressed as percentage of total) of premature groups: nonblind, and RLF with and without light perception.

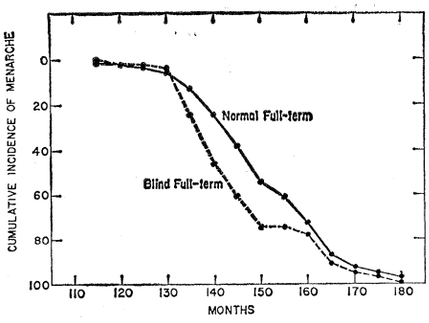

Fig. 2. Cumulative incidence of menarche (expressed as percentage of total) of full-term groups: blind and normal.

a delay in sexual maturation, and then a decrease in the proportion of time spent in vaginal estrus. For several weeks after bilateral orbital enucleation, rats show a marked decrease in vaginal estrus (that is, decrease in the incidence of estrous phases as observed in daily vaginal smears); after 3 or 4 weeks, when normal cycling starts again, the cycles are not affected by environmental illumination (*12*).

In view of the results of these experiments with animals, it is surprising that in this preliminary study early blindness in humans appears to accelerate sexual maturation. Moreover, the magnitude of the effect appears to be related to the severity of the visual loss.

One might postulate either that light affects rat and human gonads differently, or that loss of visual function, even when it includes loss of light perception, does not produce the same neuroendocrine effects as the actual absence of light. (This consideration arises in our study, in which we have substituted blindness for absence of light.) It has recently been shown that environmental light can penetrate the mammalian skull in sufficient amount to activate photoelectric cells imbedded in the brain tissue (*13*). It is therefore a possibility that light, acting on the neuroendocrine axis of the blind human (even one who is totally without light perception) in the absence of retinal responses to light, produces an imbalance which results in earlier menarche. However, at least one effect of light on the human endocrine apparatus seems to require receptors which are located solely in the retina, since the ability of light to induce a rapid eosinopenia (presumably through the release of adrenal steroids) is lost in the presence of macular degeneration (*14*).

It is well known that emotional factors can influence ovulation in humans, and that a wide variety of diseases, ranging from simple malnutrition (*15*) to specific endocrinopathies, depress ovarian function. It might be conjectured that the relation between blindness and human ovary function is nonspecific, and a consequence of the emotional stress and behavioral adaptations associated with blindness. This hypothesis seems unlikely: although there are many instances of nonspecific inhibition or delay of human gonad function, few if any are known in which acceleration occurs without some specific disturbance in neuroendocrine function [for example, hypothalamic and pineal tumors (*16*)]. It seems more probable that stimulation of the retina by environmental light produces a specific effect on the human ovary.

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3. We thank the following institutions for their cooperation: the Boston Lying-in Hospital; the Schools of Nursing of the Beth Israel Hospital, Boston, the Children's Hospital Medical Center, Boston, and the Massachusetts General Hospital, Boston; the Arizona State School for the Deaf and Blind, the Arkansas School for the Blind, the California School for the Blind, the Colorado School for the Deaf and Blind, the Diamond Head School, Honolulu, the Iowa Braille and Sight-Saving School, the Kansas School for the Blind, the Nebraska School for the Blind, the New York State School for the Blind, the Ohio State School for the Blind, the Oregon State School for the Blind, the Tennessee School for the Blind, and the Virginia State School.
4. This group of 181 females was composed of 22 girls born between 1938 and 1949 at the Boston Lying-in Hospital, 14 girls in M. J. Kings RLF series [*Arch. Ophthalmol.* **43**, 694 (1950)] born for the most part in New England between 1938 and 1949, and 145 girls born between 1939 and 1954, who were or had been pupils in the various schools for the blind listed in reference (*3*).
5. Girls who were born at the Boston Lying-in Hospital between 1938 and 1949.
6. Girls who were or had been pupils at the schools for the blind mentioned in reference (*3*) born between 1938 and 1954. Of more than 150 girls whose records were examined, only 54 were judged admissible to the study, by criteria already given.
7. Girls born between 1940 and 1946 who were, at the time of the study, students in the nursing schools of three Boston hospitals: 63 at the Massachusetts General Hospital, 75 at the Beth Israel Hospital, and 98 at the Children's Hospital.
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Calcium Absorption in Man: Based on Large Volume Liquid Scintillation Counter Studies

Abstract. *A technique has been developed for the in vivo measurement of absorption of calcium in man after oral administration of 1 to 5 microcuries of calcium-47 and continuous counting of the radiation in the subject's arm with a large volume liquid scintillation counter. The maximum value for the arm counting technique is proportional to the absorption of tracer as measured by direct stool analysis. The rate of uptake by the arm is lower in subjects with either the malabsorption syndrome or hypoparathyroidism. The administration of vitamin D increases both the absorption rate and the maximum amount of calcium absorbed.*

Recent studies have shown that two significant physiologic mechanisms underlying the development of osteoporosis are (i) increased bone resorption (*1, 2*) and (ii) relative calcium deficiency (*1, 3*). Calcium deficiency may be a result of inadequate dietary intake or defective absorption of calcium. Among the techniques for the study of calcium absorption in man are meta-