Why can't we explain refractive error?

J.C. Bear*

This essay is respectfully dedicated to the memory of Monroe J. Hirsh, O.D., Ph.D., 1917-1982, whose research and scholarship have been an inspiration for my own efforts.

Abstract:

Refractive error is a quantitative trait, and its variation is readily considered from the point of view of quantitative genetics, or genetic epidemiology. This article reviews the development of refractive error in childhood, and its epidemiology and genetics. There is considerable epidemiological evidence that the development of refractive error is influenced by vision activity. Possible influences of other environmental factors such as nutrition have not been sufficiently investigated. Observed familial resemblances in refractive error are consistent with a considerable additive genetic contribution to variation in the range of low to moderate error; higher errors may be more strongly inherited. Recent investigations suggest vision activity, as a feature of common familial environment, can inflate measures of genetic resemblance if not taken into account. The significance of refractive error as an indicator of liability to serious ocular disorders is outlined, and suggestions made of advice to offer persons concerned about the occurrence or recurrence of refractive error in their families.

Abrégé

Un defaut de réfraction est une caractérisque quantitative et ses variantes se décrivent en termes de génétique quantitative. Ce travail discute du développement des erreurs de réfraction dans l'enfance ainsi que de leur epidemiologie et de leur herédité. Il y a suffisamment de preuves pour supporter que le développement d'un vice de réfraction est influencé par l'activité visuelle. Jusqu'à date la récherche n'est pas concluante que d'autres facteurs, comme la diète, influence le developpement. Les ressemblances familiales de la réfraction supporte l'idée d'un effect cumulatif de l'héridité dans la variante des faibles et moyennes erreurs de réfraction. Les grandes erreurs subiraient une influence heriditaire plus forte. Des études récentes suggèrent que l'activité visuelle, manifestie dans un environment familiale commun, veut fausser les données de ressemblance génétique si on l'ignore. On fait allusion à la possibilité de prédire si une erreur de réfraction puisse devenir une affection oculaire serieuse. Enfin on suggère des moyens de conseiller des personnes ou des parents inquiets de l'existence d'un vice de réfraction chez leurs enfants ou autre membre de la famille.

*Ph.D.
Division of Community Medicine
Memorial University of Newfoundland
St. John's
Newfoundland A1B 3V6

Introduction

When your editor asked me at the Biennial Congress in St. John's to write this note for CJO, he suggested I refer to Dr. Hirsch's (1) article "What you always wanted to know about myopia, but never dared to ask." The first of many perceptive observations in that article is, that if you want something to be read, you must give it a provocative title. "A review and synthesis of recent studies in the biology, epidemiology and genetics of ocular refraction" won't do, even though this was more or less what I understood was wanted, along with some suggestions of information patients and parents of children with refractive errors might find useful in understanding these conditions. Like Hirsch, having got you to start reading, I now admit my duplicity. Unlike Hirsch, who wrote from long and extensive experience, I must however admit that my presumptuousness is great, because I have no experience in the measurement of refractive error, and became seriously interested in this attribute only recently, as a result of being drafted onto the committee supervising Avrum Richler's Ph.D. research (2). In short, my acquaintance with the topic is general, not specific. On the other hand, considering a topic in a rather general context sometimes improves insight.

The viewpoint of this article is that of quantitative genetics. As the name suggests this is the genetics of quantitative traits, of attributes like height and refractive error, which are measured, as opposed to for instance ABO blood group antigens, which are counted. Quantitative genetics is also an approach which makes allowance for environmental influences in trait variation. In fact, the quantitative genetics of man is coming to be thought of as genetic epidemiology (3). Using a variety of statistical analyses, quantitative geneticists attempt to evaluate the resemblances of various sorts of relatives for a quantitative trait, such as refractive error (hereafter RE), and from these resemblances to assess the proportions of total population variation in the trait attributable to genetic factors, environmental variation, and interactions of genotype and environment. The genetic factors have traditionally been treated as if they were numerous and acting in an additive manner, with effectively

An Original Article

A Study of 250 Varilux 2 Prescriptions

André Bétournay, O.D.

Various characteristics of the patients are studied in relation to successful fit of Varilux 2® lenses.

This study summarizes the re
obtained by Varilux 2® lens we
and defines a policy for correctio
presbyopia in future patients. A metho
presenting the Varilux 2 lenses to pati
and a clinical procedure were develop
The cases were chosen randomly fr
from each month of the ye
the patient's age, sex, occu
of glasses (if any), type
or, power of the Varilux 2 c
to obtained, and the type
rection needed.
cases studied, 10 patients
not able to successfully we

Reprinted from OPTICAL INDEX, (Volume 56, Number 2, February 1981), and copyright by The Professional Press, 101 East Ontario Street, Chicago, Illinois 60611.

PREFERRED PROGRESSIVE ADDITION LENSES

Harry O. House, OD

Although progressive addition lenses have been popular in Europe for years, they are new in the United States. This article reports a clinical study of 20 patients that was conducted to learn more about the effectiveness and patient reception of these new multifocal lenses.

out the sample population. Ea
scription had to be compatib
manufacturer's limitations in al
of the progressive lenses.
Patients were told that after
had tried each pair of lenses,
could either retain the type of le
they preferred for regular wear o
turn all three sets in exchange fo
standard bifocal or reading presc
tion.

PATIENT INFORMATION—Th
study population was comprised of 2
patients with the following distribution
14 women, 6 men, 14 professional
workers, six nonprofessional workers.
Their previous prescription type was
as follows: six emmetropic, one myop-
ic, seven hyperopic and six were al-
ready wearing reading glasses. Pre-
scription types dispensed were as fol-
lows: five emmetropic prescriptions,
six hyperopic prescriptions, seven low
myopic (0 to −3.00) and two high
myopic (above −3.00) prescriptions.
The following prescription add powers
were noted (Note: No previous bifo-
cals): Seven, +1.00 add; five, +1.25
add; five, +1.50 add; three, +2.00
add.

This patient cross-section also in-
cluded five patients who were receiv-
ing hormone therapy, four who had
hypertension and were taking medica-
tions and three who had glycemic
problems. In addition, one patient had
chronic open angle glaucoma and was
taking Valium® and another had ar-
thritis on the clinical level.

FITTING PROCEDURE
were allowed to se
long as the le
enough
of the

Reprinted from OPTICAL INDEX, Volume 56, Number 11, November 1981. Published and copyright by The Professional Press, 101 East Ontario Street, Chicago, Illinois 60611. Printed in U.S.A.

The Varifocal Extension of Ben Franklin's Genius

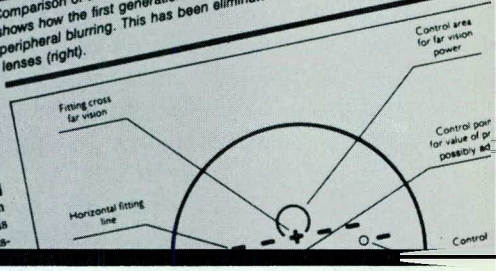
By Philip Mullins

Benjamin Franklin gained a place in optical history by applying his practical genius to the problems encountered by those in middle age experiencing difficulty focusing their eyes on near objects. By combining in one lens the two halves of a lens designed to correct vision at distance and a lens to correct vision at near, he is widely acknowledged as the inventor of the bifocal.

Ametropes of middle age and over have universally come to rely on bifocal, trifocal or varifocal corrections for their everyday visual needs.

ACCOMMODATION IS THE KEY

Comparison of the optical aberration caused by progressive power lenses. Left shows how the first generation of progressive power lenses suffered from peripheral blurring. This has been eliminated in the second generation of such lenses (right).



Editor's REVIEW of optometry

CHANGING A 'HAPPY' TRIFOCAL WEARER TO PROGRESSIVE ADDITION LENSES

R. Michael Daley, F.N.A.O.

Many practitioners hesitate to prescribe progressive addition lenses for patients who have been wearing bifocals or trifocals without complaint. They don't want to press satisfied wearers too closely for details because they worry that the patient will express some dissatisfaction with his prescription. The fact is that many patients aren't truly satisfied with their multifocal glasses. While progressive

copy to the typewriter to check what she had written. Finally, she said large areas of her vision were blurred because of the lines separating the segments.

Margaret said
to these p
she had lea
new bifocals
dividing line
ments. She wo
might try wear

DIAGNOSTI
The patient's tri
was −4.50 −1.50
eye and −4.50 −1
left. There was a

was about two inches hi
intermediate
it was

Fitting Varilux 2 into your practice

It's new, it's different. And patients will want the lens if they know you have it.

Richard S. Hubler, O.D

With any new product, knowledgeable people make our work easier. Our recall message by telephone or mail includes, "... and we want to show you something new." To make it easier for about Varilux 2.

equal influences on trait variation, but allowance can be made for the possibility that particular genes have large effects on trait variation. Generally, environmental factors are not individually specified, though they can be. This approach is not very specific, compared to what can be said about gene action and environmental influence in an ever-increasing number of instances; quantitative genetic analysis should supplement and guide more specific investigations, rather than supplant them. When, however, influences on trait variation seem numerous, and none seems of overwhelming importance, as I shall argue is the case for RE, such analyses may provide useful insight and guidance in suggesting more specific investigations that should be undertaken. I shall not attempt to review quantitative genetics here; the standard text is by Falconer (4), and an excellent article by Spivey (5) is available in the vision literature. A good starting point for review of the recent human genetic literature is the comprehensive text by Vogel and Motulsky (6).

The Variable

At the outset, it is worth stating clearly, for present purposes, what RE is taken to mean. Following Hirsch's (1) lead, discussion is here confined to errors resulting from underlying variation in axial length, which make up the bulk of RE in the general population. To anticipate conclusions, but in an attempt to avoid prejudicing them, high RE, arbitrarily those outside ± 6D, are excluded from consideration; this will be explained shortly. An emphasis on myopic errors is unavoidable, as these have been studied much more extensively than hyperopia or emmetropia. In short, as the *usual* answer to the question "Why is my child myopic?" it can be said "The child's eyes have grown too large or long for images to be focussed sharply on the retina." As to why the eyes are too large or long, there are no simple answers.

In quantitative terms, RE shows a continuous, unimodal population frequency distribution, like height or weight or blood pressure, with values for most persons clustering around the population mean, in emmetropia, and progressively fewer values toward the hyperopic and myopic extremes. The population distribution of RE is also unusually peaked, or tightly clustered about the mean (leptokurtotic, in statistical terms). The extreme values of this population frequency distribution are "pathological", requiring therapeutic amelioration. A quantitative geneticist or epidemiologist would wonder whether these extremes are perhaps qualitatively as well as quantitatively different from errors in the middle of the distribution, those accepted as more of less "normal". Most investigators share this outlook — it characterizes the work of Hirsch (1) and many others. An understanding of total population variation in RE is thus a pre-requisite to explaining its extreme values. These may be simply the "tails" of the population variation, or they may result from more specific causes, such as generalized clinical disorder, environmental factors or genes of large effect relative to other influences on variation, or pathological interactions of constitution with environmental insult; all of these possibilities are known to occur in high RE (7).

Identification of the factors influencing population variation in RE, as well as any specific factors associated with extreme values, might be expected to yield ideas as to how the occurrence of extreme errors as well as moderate RE might be lessened or prevented. At the end of this paper, I will outline the importance of identifying such factors.

Changes with Age

In populations of children followed over time, it has been amply demonstrated that the population distribution of RE shifts toward myopia as the children grow older (8-10). This shift parallels increases with age in the population mean of length of the optic axis (10). Axial length and RE are strongly correlated throughout the normal range of refraction, as well as in high myopia and hyperopia (11).

As a group, myopes show a higher rate of axial elongation and of refraction change than do emmetropes and hyperopes. It is not correct, however, to think of myopes as a group distinct from the rest of the population by virtue of a higher rate of axial growth. Relatively great axial elongation is observed in a proportion of children with hyperopic and emmetropic initial refractions as well, and seems as often to decrease hyperopia as to increase myopia (12, 13). Presumably high hyperopia reflects a short axis that elongates little (12). "Rapid growth" appears to be simply one end of a roughly balanced, normal distribution of ocular growth (12), and though most myopic eyes are probably in part too large or long as a result of ocular growth in childhood and adolescence, it is more productive to think in terms of a distribution of axial elongation influencing a distinct distribution of initial RE, pushing, as far as myopia is concerned, some emmetropes to myopia and most myopes to more extreme myopic values. Consistent with this is the variable rate of progress, from none to considerable, observed in uncomplicated (14) and in high (15) myopia.

In relating growth of the eye to RE, it is important to remember that the anatomical deviation underlying even large RE is relatively slight. A departure of one millimeter from the average axial length of 24 mm implies 3D of RE, other things being equal. This 4% deviation in an anatomical dimension causes considerable inconvenience, whereas a similar difference in height, say from a mean value of 173 cm. to a 4% greater value of 180 cm., would excite little comment or difficulty. Moreover, this 1 mm is the order of normal increase in axial length from age 3 to age 13 years, an interval during which height increases on the order of 60%, but refraction usually changes even less than the 1 mm elongation would imply, because decreases in lens and cornea power

usually compensate for the axial elongation (10). This is the source of the leptokurtosis of the population distribution of RE, that is of the relative excess of low RE values over what would be expected were the association of components of refraction random (1). These relationships, and the very complexity of the eye, indicate elaborate genetic control of ocular growth and development must be assumed *a priori*. But, considering the other side of the coin, RE must be exquisitely sensitive to genetic and environmental perturbations influencing the size and shape of the eyeball.

Some Genetics

From this biological background, consideration of the population genetics and epidemiology of RE can commence. Any factor influencing the growth of the eye must be suspected to influence RE also. Several such influences have been postulated on logical and sometimes laboratory data, but the convincing demonstration of their actions and interactions in individuals and populations may be very difficult.

As just indicated, genetic control of RE is likely but is unlikely to be absolute. Genetic variation must be suspected to account for some of the population variation in RE for two reasons. First, numerous single gene conditions are known which include unusual RE among their manifestations (16), establishing that genetic variation in RE is possible. Second, RE depends upon ocular dimensions, and correlations between related individuals are generally found both for anatomical dimensions (4, 17) and for growth in these dimensions (18). Indeed, modest correlations among relatives — offspring with parents and sibs with one another — are generally observed for RE (19-23) and for ocular dimensions (20-23). The RE correlations run on the order of 0.2-0.3, values less than those usually found for anthropometrics such as stature, but indicating that, if the simplest assumptions of quantitative genetics are made (see Introduction), as much as 40-60% of total population variation in RE might be attributable to genes of small effect acting additively. Qualifications are, however, necessary.

What applies for the general population may not be a good description of the situation in individual families. High RE probably results, in many instances, from the transmission in families of genes of large effect. Such families are properly excluded in making genetic estimates for the bulk of the population, since they are genetically distinct, their frequency is unknown, and the high RE is sometimes only one part of a more general ocular disorder. Setting aside such cases, the genetic component in variation in the general population cannot be thought of simply as something which, added to variation attributable to environmental factors, gives total population variation in RE, even though the calculations imply this. Individuals may respond to environmental influences in different ways, and genetic differences between the individuals may underlie these differences in response. Moreover, close relatives share a common environment as well as common heredity, and factors of familial environment relevant to variation in RE may be inflating the correlations of relatives compared to those that would be observed were these factors of common environment not operating. These points will be taken up again after reviewing the epidemiology of RE. The observed familial correlations may be taken to suggest heredity accounts for a substantial proportion of population variation in RE, but they may not give a very accurate impression of the size of this.

Some Epidemiology

Knowledge regarding the epidemiology of RE is not extensive. Its salient features are these:

a. The distribution of RE is nonliterate peoples with hunting and gathering economies is shifted toward hyperopia by comparison with that found in urbanized literate populations (24-26). Incidentally (for purposes of present discussion) extremes of RE and poor visual acuity from whatever cause are relatively rare among hunter/gatherers, consistent with the reasonable suggestion that reduced visual acuity confers a severe selective disadvantage in such modes of life (27).

b. Among Alaskan Eskimo and Canadian Eskimo and Amerind peoples myopia is uncommon among older persons, but myopia (predominantly of mild degree) is common among persons born since World War II. These are the first among these people to be substantially exposed in childhood to aspects of standard North American culture such as compulsory schooling and processed foods (23, 28, 29).

c. In Denmark, on the other hand, the association of RE with level of education, as evaluated in representative samples of male conscripts, remained constant for 80 years from 1882 to 1964. More educated groups showed considerably more myopic distributions than did less educated groups, the proportion with myopia greater than 1.5D showing a graded decrease from 30% of men academically qualified to enter University to 3% of unskilled workers. The total proportion of men with mild or moderate myopia was little changed in the 80 year interval (30).

d. Recent investigations in a rural Newfoundland population (31) found a general, fairly consistent and graded association of RE with nearwork activity as reported by the subjects of the investigation, myopic errors being correlated with higher levels of nearwork, intermediate errors with intermediate levels, and hyperopia with lower levels. This association was found to persist in persons aged 5-60 years despite age trends in RE toward myopia below and hyperopia above the age of 20 years, and despite much better formal education being available to persons aged 30 years and under than to older persons. It seems improbable that the members of this population were subtly adjusting their nearwork activity to their RE,

and much more likely that nearwork was influencing RE. The regression coefficients relating RE to nearwork were on the order of -.2 to -.4 D/hr of nearwork/day, depending on age, after adjustment by linear regression for age, sex and education. This suggests the potential for nearwork to influence refractive error is considerable, since the levels of education and nearwork activity reported in this population were not high. It is obviously desirable that a similar investigation be carried out elsewhere to assess the generality or not of these findings.

e. There is rather more myopia in the United States than in Europe. Some 14.5% of Danish males aged 18-20 (30) and some 10.7% of British males aged 18-22 (32) were found to have minus RE of any degree in 1964 and 1960 respectively, but some 25-30% of males of those ages, in a representative survey sample of the U.S. population studied in 1971-72, wore corrective lenses indicating minus RE (33).

Nearwork is the only environmental factor which must clearly be suspected on the basis of accumulated epidemiological evidence to influence RE. Plausible mechanisms for this influence have been suggested: the accommodative effort which accompanies nearwork increases intraocular (vitreous chamber) pressure, and might cause the globe to increase in size and the RE to become more myopic (34, 35). The accommodative capacity of myopic 18-year olds is superior to that of emmetropes and hyperopes, sometimes greatly so, and change in RE between the ages of 10 and 18 years has been found to be correlated with accommodative power at age 18 (36). That this mechanism in fact operates, or is this simple, is however by no means proven, primarily because young myopes, by virtue of their myopia, do not need to accommodate to see clearly in doing nearwork (36). Studies of the amount of accommodative effort children actually make would be of value and are being undertaken in Denmark (Dr. E. Goldschmidt, personal communication). As an alternative hypothetical mechanism by which nearwork might lead to an increase in axial length, it seems possible that the tensions exerted by the extraocular muscles in effecting convergence to view near objects is sufficient to increase intraocular pressure greatly for short periods, and irreversibly deform the sclera at the posterior pole of the globe, where it is weaker (37, 38).

The association observed of RE with nearwork must not preclude consideration of other possibilities for environmental influence. An influence of nearwork on refraction was suggested by Kepler in 1611, a few years after he correctly described the optics of the eye, and has thus been suspected for almost as long as ocular refraction has been correctly understood (7, 30). Such an association has been vigorously sought without much regard for other environmental factors which might be varying along with nearwork and confounding observations.

The most important of these is nutrition. Diet can clearly influence growth rate, and its composition tends to change as a result of the same social forces that change the nearwork regime. Thus, a hunting and gathering population is often introduced to schooling and radical diet changes, such as a sudden abundance of refined carbohydrates, at about the same time. Suspicion of confounding of such simultaneous effects must be entertained in evaluating the changing myopia incidence in the Canadian North, for instance (23). It is very difficult to evaluate diet composition, particularly in retrospect, so this point may well remain moot for some time. Reports to date (39-41) associating specific dietary excesses or deficiencies with RE are difficult to interpret, since it is not clear what allowance they make for nearwork and social class variation. Available data suggest the eye is to a remarkable extent spared from otherwise general growth retardation in man and animals (42). Indeed, while grossly malnourished (marasmic) infants are less hyperopic than adequately nourished infants, this difference seems reversible with correction of the malnutrition (43).

Since rate of change of RE seems related to rate of growth of the eye, it is reasonable to attempt to relate refractive error directly to growth. Most attempts have been aimed at finding an association of RE with stature, and have found none once the associations of both RE and stature with social class are taken into account (44). Sorsby et al. (12), in relating changes in axial length and changes in RE to changes in height and weight in children followed longitudinally, found no indication that rate of overall growth was related to rate of change in RE or axial length. These workers were able to study relatively few subjects and though not easy to collect, more data on these relationships would be valuable, since the association sought is probably weak. In this context, it is noteworthy that the mean stature of Danish conscripts increased 10 cm. from 1860-1960 (44), consistent with the secular trend in stature observed very generally in Europe which seems at least partially attributable to improvements in nutrition (45), whereas in this time interval no change could be detected in the general distribution of RE in these men (30).

Taking together what data are available on the association of RE with diet, growth and stature, it seems fair to conclude that if variation within usual North American and European diets does indeed influence RE, this influence is either small, or is a function of composition rather than quantity. The growth of the eye in early childhood deserves much more study (10, 12), but in broad terms growth of the eye parallels that of the head as a whole, being largely complete well before adolescence, and shows no adolescent growth spurt (45). It is thus probably inappropriate and possibly misleading to seek a relationship between ocular growth and total body growth during adolescence, when the two patterns of growth are quite different (46).

Some Interactions

At this point, it is perhaps becoming apparent why we can't as yet explain RE. The questions involved and relationships sought are subtle. Family studies indicate the genetic control of RE is substantial, but not complete. Epidemiological studies implicate nearwork as *one* environmental factor influencing RE, but are not nearly extensive enough to allow specification of the extent of this influence in individual cases. More basic biological considerations suggest that any influence on growth and development could influence RE, but, ambiguously, available data are consistent with ocular growth being well protected from such perturbations. To make matters more difficult, there is little data on the progressive changes in RE with age in representative groups of children followed through adolescence, which would give population standards against which RE changes in individual children could be judged. There are as yet few data on RE and nearwork, let alone other environmental factors, collected for the same series of individuals. There are almost no data on RE and nearwork in persons related to one another, which would allow investigation of familial resemblances in RE with allowance for environmental effects. Thus, evaluation of genotype/environment interactions underlying the population distribution of RE is also hampered by the limited data available.

Our own investigations in Newfoundland (see reference 19 for details) emphasize the probable complexity of the situation without doing much to resolve it. As stated, in investigating RE variation in a rural Newfoundland population, ample reason was found to suspect nearwork influenced RE. Data were available on the relationships of population members to one another, and with this data it seemed appropriate to investigate whether nearwork, as an aspect of common familial environment, could inflate measures of the resemblance of close relatives to one another and thus lead to a falsely high impression of the genetic contribution to RE variation. The resemblances among sibs and the resemblances of offspring to their parents were measured using correlation and regression techniques. First, measured RE values were adjusted for the associations found of RE with age and sex, then the RE measurements were adjusted for education and nearwork levels as well. The data were treated as describing the total population rather than as a representative sample, since about 80% of the residents of the communities studied had been included in the investigation. A consistent picture emerged: the further adjustment substantially *reduced* the measures of resemblances of relatives to one another, though resemblances after further adjustment were comparable to those found in family studies elsewhere, indicating that nearwork, as an aspect of common familial environment, was inflating the resemblances.

Closer examination of the results raised further questions about the nearwork-refraction relationship, however; there were indications that the analysis did not completely separate out the influence of nearwork on refraction. This was not surprising for three reasons. First, adjustment of RE for age, sex, education and nearwork was purely by linear regression. That is, in the absence of evidence sufficient to postulate a more complicated relationship, individual RE values were adjusted for the influences of the associated variables by simply measuring their deviations from straight lines plotted through the data so as to best indicate the association of RE with each variable. Second, data were cross-sectional. That is, each subject was evaluated once only, giving only a static impression of the long term, dynamic relationships between the variables. Third, the measure of nearwork influence on RE was completely *ad hoc*, being simply the combined statistical effects of usual nearwork at the time of the investigation, as reported by the subject, and the formal education of the subject in years, which provided the only measure available of nearwork in earlier life. In summary, adjustment was statistical, not biological, and suspicions of its biological imperfections seem justified.

As an interesting sidelight, in this study persons aged less than 30 years were found to resemble their parents of like sex in RE more than they resembled their parents of opposite sex. This pattern is not explicable on any simple genetic hypothesis, but would be expected on the plausible suppositions that boys tended to acquire their nearwork habits preferentially from their fathers rather than their mothers, girls on the other hand copied their mothers, and nearwork influenced RE.

The overall implication of these findings is that not only must the interaction of heredity and environment be considered in describing population variation in RE; but moreover the variation of environmental factors among families is relevant.

It is important to realize that the observed pattern of interaction of genetic and environmental influences on RE is expected to vary among and within populations, depending on relative exposures to environmental influences. Assuming for instance that nearwork influences the RE of all persons toward myopia, RE might appear to be a strongly inherited attribute in groups doing relatively little nearwork, and probably also in groups doing generally high levels of nearwork, because the influence of nearwork on RE would in both cases be roughly equivalent on each population member. If exposure to nearwork *varied*, however, RE would appear less strongly inherited, as a result of this additional contribution to its variation in the population. If exposure to nearwork *changed*, as for example if educational opportunity improved over time, relatives of similar ages might appear more similar in RE

than relatives of different ages. This is in fact the case for RE. Sibs are generally found to resemble one another in RE to a greater degree than offspring resemble their parents (see reference 19), as would be expected since educational opportunities, and presumably nearwork activity, of sibs are usually relatively similar, while educational opportunities for children have in this century generally improved substantially over those of their parents. This increased resemblance results from environmental change, not genetic factors. (The tentative nature of comparisons of RE of persons of markedly different ages must however be borne in mind in this context). If family members had similar nearwork patterns, familial resemblances would again be increased, as suspected in the Newfoundland investigations already described (19), and further complications of genotype/environment interaction can readily be imagined.

It is assumed in the preceding discussion that individuals vary little in their response to environmental influences on RE. It is not known whether this assumption is valid, but its validity is a particularly interesting question. Available data (47, see also Epidemiology section, above) are compatible with a general shift in RE distribution in the population with exposure to environmental influences. In the Newfoundland study (31), association of nearwork with RE involved not only higher levels in myopes, but also lower than average levels of nearwork in hyperopes. More specific investigations are necessary, however, before the existence of persons whose eyes are particularly sensitive to usual environmental influences can be ruled out. It is of course such specifically susceptible persons for whom environmental modification might prove most valuable in keeping RE within acceptable limits.

Presumably such susceptibility would take the form of inappropriate axial elongation, since RE is in general a result of inappropriate axial length. Even assuming these influences are general and responses uniform, persons inheriting long eyes would form a group particularly susceptible to myopia (23), while persons of intermediate axial length would be less susceptible and persons inheriting short axes might have their hyperopia environmentally reduced.

Some Advice

What advice can be given to parents concerned about the occurrence of a RE in their children sufficient to require correction, or to parents concerned that their children will have an extreme RE? Uncomplicated mild or moderate errors must be considered separately from higher errors.

For moderate or mild RE, general reassurance seems in order. Everyone has a refractive error, just as everyone is a particular height. As this review emphasizes, the background to population and familial variation in RE seems complex, and heredity and environment interact in determining a particular RE, but only general statements about this are possible at present. Variation in the range of mild to moderate RE should occasion no surprise. Children should resemble their parents in RE to some degree only, common familial environment as well as heredity may be relevant, and a substantial proportion of variation may be "random" in the sense of being unattributable statistically to any specific influence. "Therapy" in the form of corrective lenses is adequate.

Low and moderate myopes are at higher risk than are emmetropes and hyperopes to retinal detachment and glaucoma; their contribution to the prevalence of these disorders is thus disproportionately large (48). These complications are almost always of adult onset and therefore primarily the concern of the individual rather than the parent. Inappropriate anxiety must not be generated; these conditions are uncommon compared to other serious morbidities of adult onset, but they imply severe visual handicap or blindness if not vigorously treated. Everyone should be aware of the warning signs of these disorders, and the intraocular pressure of older adults routinely checked, since the overall population incidence of glaucoma is about 1/100. This is particularly so for myopes whose risk of glaucoma is about 1/35, and of glaucoma before age 50 about 1/23 (48).

The genetic and epidemiological data are primarily concerned with myopia; even less is known about hyperopia and astigmatism. Reports that these are strongly familial, based on limited and selected family data (16, 21), are difficult to interpret. A strong genetic basis would not be surprising, since the environmental factors which may influence refraction in European and North American populations would promote a shift toward myopia, and highlight familial transmission at the other end of the refraction scale. There are indications in longitudinal data that axial elongation during childhood is in some cases very slight, or does not occur. Whether the resulting hyperopic individuals form a distinct group, or the low end of a distribution of axial elongation (see Changes with age, above) is not known (10, 12). Similarly, whether this lack of ocular growth is familial is not known. Persons with high hyperopia and astigmatism should be particularly encouraged to make sure their children undergo early vision screening, since this is simple and inexpensive, and errors predisposing to amblyopia can be particularly sought out. (Vision practitioners are encouraged to collect and carefully analyse data from such families to improve genetic estimates and prognosis prediction.)

Despite the strong suspicion that nearwork may substantially influence RE, reducing hyperopia and increasing myopia, the extent of this influence is not yet known. The plausible suggestion that diet can influence RE remains at present insufficiently explored. Drastic manipulations of these or other environmental factors, aimed at "preventing" or reducing RE are unjustifiable at

this time (49). This is not meant to rule out the possibility of specific intervention being developed in the future, particularly for higher errors, but such intervention should be proportionate to the problem; myopia is much less a handicap than malnutrition or illiteracy.

High myopia has serious implications. It is a common cause of blindness, particularly blindness of onset below old age. About 14% of cases of registered blindness are attributable to high myopia, a proportion almost equal to that attributable to diabetic retinopathy or to congenital defects (primarily retinitis pigmentosa). The usual causes of blindness in high myopia are chorioretinal atrophy and hemorrhage, and less often retinal detachment (48). Risk of retinal detachment rises dramatically with degree of myopia (48). These complications appear to be mechanical failures resulting from the inordinate axial length (50, 51). High myopia is clearly familial; some cases presumably represent extremes of the population distribution of refractive error and axial length, but in addition many pedigrees have been collected suggesting the action of genes of large effect, and inheritance of high myopia with other ocular defects (7, 16). Genetic counselling should be based on any familial pattern apparent, but often none will be and empiric risks of a child being affected must then be given (52). Referral of concerned patients to a genetic counsellor is appropriate.

The risk of blindness in high myopia, and the disproportionate association of significant ocular morbidity with lower degrees of myopia, provide ample justification for continuing to investigate refractive error at the population level. Further stimuli to research include the association of vision handicap with high hyperopia, the considerable aggregate expenditure for correction of mild and moderate RE, and the indications that high errors are in a sense "diseases of civilization" which are particularly common, for unknown reasons, in North America. In reviewing myopia research ten years ago, Hirsch (1) emphasized as much what he didn't know as what he did know. Over the intervening decade, some progress is apparent in our knowledge of refractive error, but ignorance still overshadows knowledge, while the reasons for dispelling that ignorance have become much more sharply defined.

Acknowledgements

Discussions with many people have helped me both directly and indirectly in developing the ideas outlined here. In the specific context of this article, I must acknowledge my particular indebtedness and gratitude to Drs. Avrum Richler, Ernst Goldschmidt, Gordon Johnson and Maurice Belanger. M. Fennessey and D. Williams carefully prepared the manuscript.

References

1. Hirsch M.J. What you always wanted to know about myopia, but never dared to ask. *Canadian Journal of Optometry* 34: 54-66 (1972).
2. Richler A. Thesis: A study of ocular refraction in western Newfoundland. St. John's, Memorial University of Newfoundland (1979).
3. Morton N.E., Outline of Genetic Epidemiology. S. Karger, Basel (1982).
4. Falconer D.S. Introduction to Quantitative Genetics. Oliver and Boyd, Edinburgh (1960).
5. Spivey B.E. Quantitative genetics and clinical medicine. *Transactions of the American Ophthalmological Society* 74: 661-707 (1976).
6. Vogel F., Motulsky A.G. Human Genetics. New York: Springer-Verlag (1979).
7. Duke-Elder S., Abrams D. Ophthalmic Optics and Refraction. Vol. V *in* Duke-Elder, S. (ed) System of Ophthalmology. St. Louis: C.V. Mosby Co. (1970).
8. Hirsch M.J. The refraction of children. Chapter 5 *in* Hirsch M.J., Wick R.E. (eds) Vision of Children. Philadelphia: Chilton Books (1963).
9. Young F.A., Beattie R.J., Newby F.J., Swindal M.T. The Pullman study — a visual survey of Pullman school children, Part II. *American Journal of Optometry and Archives of the American Academy of Optometry* 31: 192-203 (1954).
10. Sorsby A., Benjamin B., Sheridan M., Stone J., Leary G.A. Refraction and its components during the growth of the eye from the age of three. Medical Research Council Special Report Series No. 301. London: Her Majesty's Stationery Office (1961).
11. Gernet H. Oculometric findings in myopia. *Doc. Ophthal. Proc.* Series 28: 71-77 (1981).
12. Sorsby A., Leary G.A. A longitudinal study of refraction and its components during growth. Medical Research Council Special Report Series No. 309. London: Her Majesty's Stationery Office (1970).
13. Fledelius H.C. Changes in refraction and eye size during adolescence. *Doc. Ophthal. Proc.* Series 28: 63-69 (1981).
14. Rosenberg T., Goldschmidt E. The onset and progression of myopia in Danish school children. *Doc. Ophthal. Proc.* Series 28: 33-39 (1981).
15. Goldschmidt E., Fledelius H.C., Erlin Larsen F. Clinical features in high myopia. *Doc. Ophthal. Proc.* Series 28: 233-244 (1981).
16. Sorsby A. Ophthalmic Genetics. New York: Appleton-Century-Crofts (1970).
17. Roberts D.F., Billewicz W.Z., McGregor I.A. Heritability of stature in a West African population. *Annals of Human Genetics* 42: 15-24 (1978).
18. Roberts D.F. Genetics of growth. *British Medical Bulletin* 37: 239-246 (1981).
19. Bear J.C., Richler A., Burke G. Near-work and familial resemblances in ocular refraction: a population study in Newfoundland. *Clinical Genetics* 19: 462-472 (1981).
20. Sorsby A., Leary G.A., Fraser G.R. Family studies on ocular refraction and its components. *Journal of Medical Genetics* 3: 269-273 (1966).
21. Young F.A., Leary G.A. The inheritance of ocular components. *American Journal of Optometry and Archives of the American Academy of Optometry* 49: 546-555 (1972).
22. Alsbirk P.H. Refraction in adult West Greenland Eskimos. *Acta Ophthalmologica* 57: 84-95 (1979).
23. Johnson G.J., Matthews A., Perkins E.S. Survey of ophthalmic conditions in a Labrador community. I. Refractive errors. *British Journal of Ophthalmology* 63: 440-448 (1979).
24. Holm S. Les états de la réfraction oculare chez les palénégrides au Gabon, Afrique Équatoriale Française. *Acta Ophthalmologica Supplementum* 13 (1937).
25. Skeller E. Anthropological and ophthalmological studies on the Angmagssalik Eskimos. *Meddelelser om Grønland* 107: 4 (1954).

26. Taylor H.R. Racial variations in vision. *American Journal of Epidemiology* 113: 62-80 (1981).
27. Post R.H. Possible cases of relaxed selection in civilized populations. *Humangenetik* 13: 253-284 (1971).
28. Young F.A., Leary G.A., Baldwin W.R., West D.C., Box R.A., Harris E., Johnson C. The transmission of refractive errors within Eskimo families. *American Journal of Optometry and Archives of American Academy of Optometry* 46: 676-685 (1969).
29. Woodruff M.E., Samek M.J. A study of the prevalence of spherical equivalent refractive states and anisometropia in Amerind populations in Ontario. *Canadian Journal of Public Health* 68: 414-424 (1977).
30. Goldschmidt E. On the etiology of myopia. *Acta Ophthalmologica* Supplementum 98 (1968).
31. Richler A., Bear J.C. Refraction, nearwork and education: a population study in Newfoundland. *Acta Ophthalmologica* 58: 468-478 (1980).
32. Sorsby A., Sheridan M., Leary G.A. Vision, visual acuity, and ocular refraction of young men. *British Medical Journal* i: 1394-1398 (1960).
33. Roberts J., Rowland M. Refraction status and motility defects of persons 4-74 years, United States, 1971-1972. DHEW Publication No. (PHS) 78-1654. National Center for Health Statistics, Hyattsville MD. (1978).
34. Young F.A. The development and control of myopia in human and subhuman primates. *Contacto* 19: 16-31 (1975).
35. Young F.A. Intraocular pressure dynamics associated with accommodation. *Doc. Ophthal. Proc.* Series 28: 171-176 (1981).
36. Fledelius H.C. Accommodation and juvenile myopia. *Doc. Ophthal. Proc.* Series 28: 103-108 (1981).
37. Greene P.R. Mechanical considerations in myopia: relative effects of accommodation, convergence, intraocular pressure, and the extraocular muscles. *American Journal of Optometry and Physiological Optics* 57: 902-914 (1980).
38. Ku D.N., Greene P.R. Scleral creep in vitro resulting from cyclic pressure pulses: applications to myopia. *American Journal of Optometry and Physiological Optics* 58: 528-535 (1981).
39. Gardiner P.A. Dietary treatment of myopia in children. *Lancet* i: 1152-1155 (1958).
40. Lane B.C. Calcium, chromium, protein, sugar and accommodation in myopia. *Doc. Ophthal. Proc.* Series 28: 141-148 (1981).
41. Lane B.C. Elevation of intraocular pressure with daily sustained closework stimulus to accommodation, lowered tissue chromium and dietary deficiency of ascorbic acid (vitamin C). *Doc. Ophthal. Proc.* Series 28: 149-155 (1981).
42. Young F.A., Leary G.A., Zimmerman R.R., Strobel D.A. Diet and refractive characteristics. *American Journal of Optometry and Archives of the American Academy of Optometry* 50: 226-233 (1973).
43. Halasa A.H., McLaren D.S. The refractive state of malnourished children. *Archives of Ophthalmology* 71: 827-831 (1964).
44. Goldschmidt E. Myopia and height. *Acta Ophthalmologica* 44: 751-761 (1966).
45. Tanner J.M. Human growth and constitution *in*: Harrison G.A., Weiner J.S., Tanner J.M., and Barnicot N.A. (eds.) Human Biology 2nd ed. Oxford: Oxford University Press (1977).
46. Sorsby A. Biology of the eye as an optical system. Chapter 34 *in* Duane TD (Ed) Clinical Ophthalmology, revised edition. Hagerstown MD: Harper and Row (1980).
47. Richler A., Bear J.C. The distribution of refraction in three isolated communities in western Newfoundland. *American Journal of Optometry and Physiological Optics* 57: 861-871 (1980).
48. Perkins E.S. Morbidity from myopia. *The Sightsaving Review* 49: 11-19 (1979).
49. Belanger G.M. Controlling the refractive state of the human eye. *Canadian Journal of Optometry* 43: 116-118 (1981).
50. Curtin B.J., Karlin D.B. Axial length measurements and fundus changes in the myopic eye. *American Journal of Ophthalmology* 71: 42-53 (1971).
51. Karlin D.B., Curtin B.J. Myopia and chorioretinal lesions. *American Journal of Ophthalmology* 81: 625-635 (1976).
52. Bergsma D. (ed.) Birth Defects Atlas and Compendium 2nd ed. New York, Alan R. Liss (1979).