possibility that one of the parents carries the defective gene, but it
did not manifest itself. This would once again mean a 40% risk for
all future children. But, and this is to be expected, experience shows
that this possibility is very remote indeed. According to Kaelin
(1955) see Vogel (1967), among 959 siblings of sporadic cases only
13 were affected (1.36%). The objection that it was a selected series
and, therefore, resulted in very optimistic figures, has been raised
against Kaelin’s statistics, but a more recent random series, under­taken in Holland, arrived at more or less the same results. Of 887
junior siblings of sporadic cases only 10 (1.13%) were affected,
figures which correspond to Kaelin’s estimate. Therefore, this risk
is virtually negligible and no reason to advise against more children.
As a reasonable precaution, however, later children should have
regular eye examinations.

It is generally advisable to consider separately the risk for later
siblings of unilateral and bilateral cases. Risk figures are somewhat
(not much) higher for siblings of bilateral sporadic cases.

3. As a final situation, let us consider the problem of the normal
brother or sister of a sporadic R case, who wishes to know the risk
involved for his or her future children.

In such a case, there is a high degree of probability that both the
inquirer and his children will be free of the R gene. The possibility
that the gene is present but did not manifest itself either in him or
his parents and can therefore affect his children, is again very remote;
no reason to advise against children. A group that examined 90
children of the siblings of 42 sporadic cases (28 unilateral, 14 bi­lateral) in respect to this possibility, discovered only one affected
child.

Although there is no reason to advise against children, regular eye
examinations for them should be strongly recommended.

Chapter V

The Autosomal Recessive Mode of Inheritance and
Tests for the Detection of Heterozygotes

Compared to the problems presented by the autosomal recessive
mode of inheritance, the autosomal dominant mode seems simple.
Apart from very rare new mutations, the autosomal recessive mode
presents one with the progeny of ostensibly normal parents who are heterozygous for the gene in question; i.e. they carry only one defective gene and the normal allele with its “healthy” information prevents the defect from manifesting itself. Fig. 11 is a diagram of the typical situation.

Fig. 11. The most typical mating pattern in the autosomal recessive mode of inheritance

It follows logically that every child from such a union has a 25% chance of inheriting two defective genes and therefore being homozygous and sick. \(2 \times 25\% = 50\%)\ is the probability that the children will be, like the parents, heterozygous gene bearers. There remains the 25% chance that a child will inherit two normal genes and be homozygous for the normal allele; it will then be unable to pass on the defect. On the average, the ratio of normal to defective in such families is 1:3. Once again, in this discussion the pattern of heredity and the manifestation probability are independent of sex.

Among the relatives of affected individuals, further sufferers are to be expected primarily among their siblings who are also subject to the 25% homozygosity risk.

The size of the family unit has steadily decreased in the industrial society. Because each family has comparatively few children, it often seems as if the sufferers of an autosomal recessive defect were sporadic cases. They tend to be the only affected member in their own family, and sometimes in the entire kinship; yet their disease is definitely hereditary. Therefore, with this mode of inheritance it is an error to conclude that the anomaly is not hereditary simply because there are no other cases in the family.