The presence of HbS and HPFH in the *cis* form has not been reported, but is entirely feasible from our knowledge of the genetics and arrangement of the complex of β, γ, and δ genes[2]. A type of HPFH which has only about 5% HbF has been described[3]. We have recently examined a family in which, in contrast to other HPFH classes, β^A chains are produced in *cis* to HPFH (ref. 4) and have speculated that a type of HPFH with production of β^S chains in *cis* is possible. Martinez and Colombo may have detected this combination. They report, however, a heterogeneous intracellular distribution of HbF in I_1 and III_1, whereas a homogeneous distribution is one of the criteria of HPFH. Consequently, it is more probable that I_1 and III_1 merely have sickle cell trait with somewhat elevated HbF.

In summary, we believe that Martinez and Colombo have misjudged the genetic aspects of several members of this family and have made unwarranted interpretations. In all probability, I_1 and III_1 have sickle cell trait, I_2 and III_2 have β^{thal} trait, and II_1 has S-β^o-thal.

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1 Martinez, G., and Colombo, B., *Nature*, **252**, 735 (1974).
2 Huisman, T. H. J., *et al., Ann. N.Y. Acad. Sci.*, **232**, 107 (1974).
3 Sukumaran, P. K., *et al., Br. J. Haemat.*, **23**, 403 (1972).
4 Huisman, T. H. J., Miller, A., and Schroeder, W. A., *Am. J. Human Genet.* (in the press).

DRS MARTINEZ AND COLOMBO REPLY—The argument put forward by Schroeder and Huisman[1] in their criticism to our paper[2] rests entirely on the sentence: "it is more probable that I_1 and III_1 merely have sickle cell trait with somewhat elevated HbF (foetal haemoglobin)", as confirmed by the last sentence of their letter. With this statement they want to imply that the elevation of HbF is determined by some nongenetical factor(s). This means that to interpret the elevated percentages of HbF in I_1, III_1 and III_2 the following assumptions must be made. A subject and his grandmother, both showing HbS trait only, have exceptionally elevated percentages of HbF which are exactly the same (and by definition are not genetically determined); and a simple β^{thal} carrier is doubly exceptional because this subject not only shows HbF levels exceptionally high for this condition[3], but also these levels do not show the intrafamilial segregation reported by many authors (see, for example, refs 3 and 4). We consider that it must be very exceptional as only the opposite situation has been reported in the literature.

Being somewhat reluctant to postulate so many unwarranted hypotheses, we preferred to propose just one, that is, that in our family there was a segregation of a type of hereditary persistence of foetal haemoglobin (HPFH).

If we are in the presence of a type of HPFH the hypothesis that this HPFH is in *cis* to β^S (as mentioned and rejected also by Schroeder and Huisman) cannot be accepted for the following reasons: the ratio β^S/β^A was normal in I_1 and III_1; the gamete transmitted from II_1 to III_2 should be a recombinant between HPFH and β^S.

Thus the fact that the gene for this HPFH could not be in *cis* to β^S nor to β^A (see pedigree) enabled us to claim that we were in the presence of a "new type of HPFH".

It is evident then that the objection raised by Schroeder and Huisman concerning the intracellular distribution of HbF becomes completely irrelevant.

In summary, we believe that Schroeder and Huisman have misjudged the genotypes of all the members of this family showing elevated percentages of HbF. In fact trying to reject the most logical interpretation of our findings, they were forced to discard *tout-court* the possibility that this persistence of HbF was hereditary, thus creating for each member of the family the unwarranted, although unexpressed, number of necessary hypotheses.

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1 Schroeder, W. A., and Huisman, T. H. J., *Nature*, **257**, 70–71 (1975).
2 Martinez, G., and Colombo, B., *Nature*, **252**, 735 (1974).
3 Weatherhall, D. J., and Clegg, J. B., *The thalassaemia Syndromes* (Blackwell, Oxford, 1972).
4 Friedman, S., Hamilton, R. W., and Schwartz, E., *J. clin. Invest.*, **52**, 1453 (1973).

Ultraviolet light and human cataract

WEITER and Finch[1] could find no difference in paramagnetic species between normal and cataractous human lenses but demonstrated that prolonged ultraviolet irradiation of normal human lens produced free radical species, which they presumed were derived from tryptophan. They suggest that the production of free radicals by ultraviolet light might be a mechanism for photoinduced lens damage.

The theory that the ultraviolet radiation of sunlight (or from other sources) can cause brown nuclear cataract has been the subject of prolonged discussion, but there are two major arguments against such a theory[2]: (1) The proteins of the brown cataractous nucleus do not show a loss of tryptophan compared with the normal human lens[2], whereas a substantial loss of tryptophan is found in the products of *in vitro* photo-oxidation of lens proteins[3]; and, (2) in brown nuclear cataract, only the lens nucleus is pigmented and it is difficult to see how ultraviolet light could act on proteins of the lens nucleus alone, rather than those of the cortex, which are very similar; especially as absorption of ultraviolet by the cornea and outer layers of the lens would ensure that little harmful radiation could reach the centre of the lens.

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1 Weiter, J. J., and Finch, E. D., *Nature*, **254**, 536–537 (1975).
2 Dilley, K. J., and Pirie, A., *Expl Eye Res.*, **19**, 59–72 (1974).
3 Buckingham, R. H., and Pirie, A., *Expl Eye Res*, **14**, 297–299 (1972).

WEITER AND FINCH REPLY—The invariance of tryptophan content in normal and cataractous lenses as opposed to the loss of tryptophan in the *in vitro* photooxidation of lens proteins may result from the likelihood that the tryptophan in the lens proteins *in vivo* may absorb the radiation and transmit the energy to some other species (for example, lipids) to produce the radical, which may in turn cause damage to the lens. If this is so, the tryptophan would remain essentially unaffected. Steen[1] has shown that tryptophan in an ethylene glycol–water glass at 77 K absorbs ultraviolet light to produce the radical in the solvent, and tryptophan itself may not form the radical. The growth of radical, however, in both Steen's and our own (unpublished) experiments with lens material is not linear with respect to exposure time, thereby indicating the possibility of some degradation of tryptophan and its consequent unavailability for excitation. It is likely that this could be the result of a mechanistic detail rather than tryptophan degradation. Production of a radical through tryptophan excitation may involve several steps and this may diminish the efficiency of radical production.

The second point we would make is that Steen[1] has pointed out that the formation of free radicals by ultraviolet light on tryptophan in ethylene glycol–water glass is accompanied by significant coloration of the sample and this was attributed to trapped electrons. The trapping was most efficient in the presence of a substantial concentration of H^+ ions, which are known to scavenge electrons very well. If we assume that the cataract coloration results from trapped electrons, a differential cationic concentration between the cortex and the nucleus could explain this nuclear pigmentation through a colour

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