globin have been discovered. One of them, haemoglobin *E*, was found in the Veddas of Ceylon³, and while the presence of sickling was confirmed in those Veddoid populations of India in whom it had been originally described, several other Veddoid populations⁴—including the Veddas themselves⁵—were found to be free from sickling. We decided, therefore, to examine once more Australian aborigines, this time for the presence of haemoglobin *E*.

We collected blood from a hundred and sixty-six aborigines in Queensland; a hundred and forty-eight were of unmixed Australian ancestry according to their own accounts and also to their appearances. Of the others, seventeen had some European, one some Indian, and one some Chinese forbears. The bloods of fifty-five were collected on a visit to the Mona-Mona Mission, of fifty-five from a mission near Daintree, and of fifty-six from one near Yarrabah. The blood was taken under sterile conditions and arrangements were made for speedy transport with cooling on the way, so that the specimens were examined in London less than ten days after they had been obtained in Australia. All bloods were submitted to filter-paper electrophoresis. A barbitone buffer of pH 8.6 and of ionic strength 0.05 was used. All haemoglobins moved as a single band in the position of normal adult haemoglobin controls. Hence not only did these Australian aborigines not carry haemoglobin *E*, but also the presence of all other known abnormal variants of adult haemoglobin could be excluded as well.

It is still too early to assess the extent to which the distribution of sickle cell haemoglobin and of malarial infection are related⁶. It would be even more premature to speculate on the correlation of the distribution of malaria with that of other haemoglobins such as *E*. Nevertheless, it is noteworthy that malaria is thought to be a recent importation into the Australian mainland, and that its aborigines, unlike most of the older populations of tropical Africa and Asia, do not seem to possess multiple haemoglobins.

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Stability of Iso-alleles

THE high stability of most genes when kept under natural conditions is deduced from the relative rarity of spontaneous mutations which produce striking deviations from normality. The existence of wild-type iso-alleles, that is, of different alleles usually causing the same normal phenotype although distinguishable by their effects under special conditions, raises the question whether mutations from one iso-allele to another are more frequent than mutations with more obvious new effects.

In order to obtain relevant data, males of a wild-type ('Canton-S') stock of *Drosophila melanogaster*, which had been made isogenic some time before the experiments, were crossed to homozygous *ci ey^R* females (*ci* = cubitus interruptus, *ey^R* = eyeless-Russian; both located in chromosome 4). The resulting *F*₁ *ci ey^R/++* individuals were expected to have uninterrupted fourth veins in their wings, since the Canton wild-type allele, *+^C*, is dominant over the *ci* allele. In case a mutation had occurred, from *+^C* to an iso-allele of the type of *+^s* which has reduced dominance¹, the appearance of interruptions on the wings would have been expected, the frequency of this event being dependent on the penetrance of the new '*ci/+^s*' genotype. Similarly, iso-alleles of *ci* might have been expected which would give vein interruptions in a new genotype '*ci^u/+^C*'.

More than 31,000 *F*₁ flies were raised, partly at 26° C. and partly at 18° C., the lower temperature providing a more sensitive environment in view of the known increasing penetrance and expressivity of the *ci* phenotype with decreasing temperature. Most of the *F*₁ flies had normal venation, but five females and fifteen males had the very weak *ci* or *ci*-like phenotype of class I², characterized by localized thinning of the cubital vein (Table 1).

Table 1. *F*₁ FROM *ci ey^R/ci ey^R* × CANTON ♂♂

Temp.	Normal		<i>ci</i> -like	
	♀♀	♂♂	♀♀	♂♂
26°	9,745	9,236	2	8
18°	6,669	5,392	3	7

Seventeen of these twenty possibly mutant flies were individually tested in crosses to flies homozygous or heterozygous for *ci ey^R*. (The other three individuals left no progeny.) Sixteen of the seventeen flies did not produce any further non-eyeless *ci*-type offspring. The deviant parents had apparently unchanged *ci ey^R/+^C* genotypes, and their *ci* or *ci*-like phenotype was simply an expression of rare penetrance of *ci* in *ci/+^C* heterozygotes. The seventeenth individual, a female, proved to have been heterozygous for a new recessive mutant allele similar to the *ci* mutant employed in these crosses but with peculiarities in expression of its own, notably frequent interruptions in the inter-crossvein section of the fourth vein. This new *ci* mutant had arisen from the *+^C* allele.

There is thus no evidence among some 31,000 tested gametes for mutation from *+^C* to a recognizable wild-type iso-allele, or from *ci* to a recognizable mutant iso-allele, in contrast to the finding of a typically deviant *ci* mutant from *+^C*. It must be added, however, that at the temperatures used, incomplete penetrance could have kept a considerable fraction of wild-type iso-alleles from phenotypic expression.

A priori, no close relation between type of effect and frequency of mutation should exist. The limited experiments reported here agree with this expectation.

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