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Mydriasis and heredity*

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Routine ophthalmoscopy and fundoscopy of 673 individuals revealed 42 whose irides failed to dilate to a clinically useful degree within 25 to 30 min after the administration of drops of 1 % mydracil. These individuals occurred with different frequency among the Aymara, Mestizo, and non-Aymara groups which made up the sample of examinees. The phenomenon was most common among the Aymara, less common among the Mestizos, and least common among the non-Aymara. Distribution of affected individuals within the three groups suggests that the trait is inherited.

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Application of drops of a mydriatic to the conjunctival sacs produces dilation of the pupils in most human beings; the rapidity with which this occurs varies, however, with the specific drop and the person. The failure to dilate promptly is not a chance phenomenon; indeed substantial experimental evidence supports the common clinical impression that mydriasis takes place more slowly in individuals with dark irides (Barbee & Smith 1957, Obianwu & Rand 1965, Haddad et al. 1970). Since the frequency of the latter persons clearly differs among ethnic groups, it is reasonable to presume that the proportion of individuals whose pupils do not dilate under common dosage and in the customary time will differ among different ethnic and racial groups as, indeed, they do (Howard & Lee 1927, Chen & Poth 1927, 1929, Emiru 1971). It is, of course, a simple step from this conclusion to the conjecture that this "aberrant" behavior is inherited. This presumption is strengthened by the known hyper-reactivity of individuals with Down syndrome to at least one mydriatic, atropine (Harris & Goodman 1968), and Bertler & Smith's (1971) evidence of the concordance in pupillary responses seen in monovular but not binovular twins. Still further support is to be found in observations on rabbits where the failure of the irides to respond to the mydriatic, atropine, is hereditary and reflects the presence or absence of the enzyme atropinesterase (Sawin & Glich 1943); for a recent review see Szorady (1973).

Given these observations, it is reasonable to assume that the failure of human irides to dilate in a specified interval of time may reflect either qualitative or quantitative in-

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herited biochemical differences. Rarely, however, have families been studied in their responses to a mydriatic or cyclopegic administered in a standardized manner. The data we report here are exceptional in two respects. First, in the populations involved high proportions of "non-dilators" are to be expected because of the generally dark coloration of the iris. Second, these data embrace village-wide observations conducted as a matter of routine in support of an epidemiological study of the effects of the hypoxia of altitude on cardiovascular disease. These populations were not intentionally selected, therefore, because of their possible responses to mydriatics, but rather as a consequence of their presumed adaptation to the hypoxia of altitude. While it is conceivable that the two responses may be interrelated, they do not appear so because highland-adjusted families currently living in the lowlands of Chile have the same rate of "failures" to dilate as characterize their highland kinsmen and kinswomen.

Materials and Methods

In 1972, an investigation termed the "Multinational Andean Genetic and Health Program" was initiated in the Departamento de Arica, the most northerly region of Chile, adjacent to Peru and Bolivia. While this program (which continues) has many objectives, that which is relevant here is the evaluation of the burden of ophthalmic disease and disability among the indigenes, the Aymara, of the interior of Arica and their kinsfolk of the coast.

In 1973 and 1974, during the months of October and November, 2,096 individuals ranging in age from 15 days to 90 years were examined. The nature of this examination has been described elsewhere (Schull & Rothhammer 1977); two separate ophthalmic examinations were made – one by the physician who performed the general physical examination, and the second by an ophthalmologist certified by the American Board of Ophthalmology. The former examination was made in every instance where a physical examination took place; the latter appraisal, which gave rise to the data reported here, involved slightly more than a third of all persons examined. These individuals were all residents of three communities (Lluta, Putre, and Visviri) and within these communities they were not preferentially selected, except that no effort was made to examine routinely children less than 6 years of age. The examination entailed direct ophthalmoscopy as well as slit-lamp microscopy. A mydriatic (1 % mydracil; tropicamide, i. e., N-ethyl-2-phenyl-N-(4-pyridlmethyl)-hydracrylamide) was routinely used, except where medically contraindicated, to enhance visualization of the posterior chamber, fundus, and retina. Two drops were placed in the inferior cul-de-sac of each eye by a trained medical technician; pressure was then applied with cotton pledgets over the lacrimal puncta for 10 s. In all cases, the drops were instilled by one of two technicians, both medically trained, and the techniques were identical in both eyes. Nano et al. (1960) have shown that mydracil produces dilation quickly, generally within 10 to 15 min after its administration. Maximum pupillary diameter is achieved, on average, within 20 min of instillation of the drops, and the pupillary diameter remains unchanged for approximately 2 h, after which the pupil slowly returns to its original diameter, reaching the latter 8 or 9 h after the instillation. Mydracil is effective in all age groups (Nano et al. 1960, also see Smith 1971).

At the time of examination, the pupils of each individual into whose eyes mydriatics were instilled were "scored" by the ophthalmologist as to whether clinically satisfactory dilation had or had not occurred. The assessment was based upon two factors:

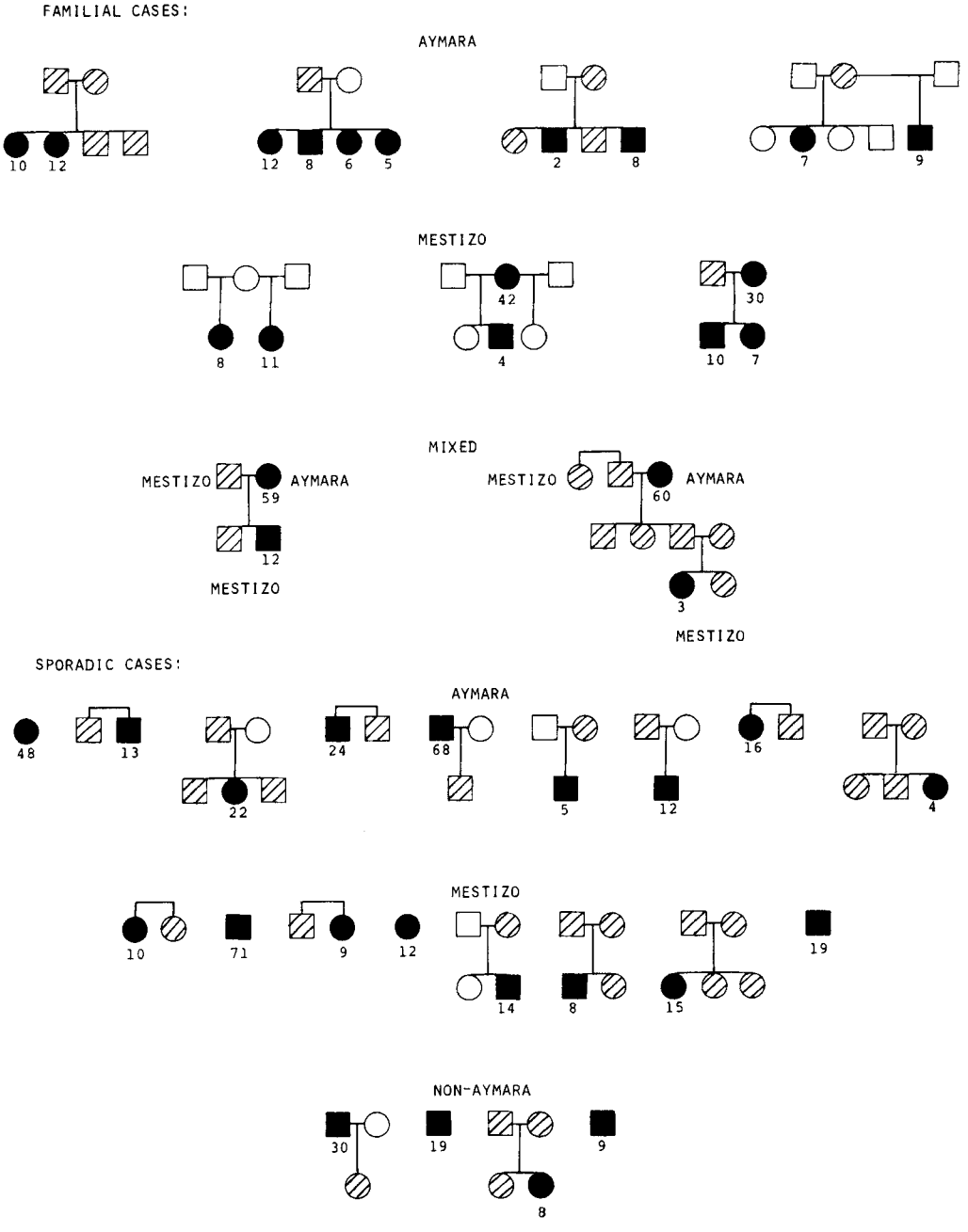

Fig. 1. Simple pedigrees of the individuals who failed to respond to mydracil. Solid squares or circles denote individuals whose eyes failed to dilate in the standard time (20–25 min) upon the instillation of two drops of mydriatic; hatched squares (males) or circles (females) denote "normal responders"; empty squares or circles are untested individuals. The ages in years of the "affected" individuals are indicated.

Table 1

A summary of the characteristics of the individuals who failed to respond to mydracil

	Aymara	Mestizo	Non-Aymara
Incidence	21/238	17/292	4/143
Sex ratio (M:F)	9:12	7:10	3:1
Mean age	19.5 ± 4.5*	16.8 ± 4.1	16.5 ± 5.1
Age range	2–68	4–71	8–30
"Sporadic cases"	9	8	4
Males	5	4	3
Females	4	4	1
"Familial cases"	12	9	0

* Standard error of the mean

1) whether or not the pupils constricted under the influence of the light of the biomicroscope, and 2) whether the pupil was adequately dilated so that the ophthalmologist could examine the peripheral retinal structures. The reason for recording the adequacy of dilation was in order to interpret whether an adequate fundoscopic examination could be carried out and relied upon in each patient.

The algorithm by which an individual is designated to be an Aymara, Mestizo or non-Aymara has been described *in extenso* elsewhere (Schull & Rothhammer 1977).

Results and Discussion

Figure 1 sets out our observations as a series of brief pedigrees. None of the 42 individuals indicated here as being "affected" gave evidence of any ocular or systemic disease which might account for his or her inability to respond to the mydriatic drug. Inspection of the pedigrees readily reveals that failure to dilate occurs as frequently among females as males, and therefore it is highly improbable, if many loci are involved, that a substantial number are associated with the sex chromosomes. Support for this contention follows from an examination of Table 1 where the data are briefly summarized. Transmission does not accord with the supposition that one important locus or a number of loci of lesser importance which determine this response are associated with the X chromosome.

Our data are too limited to warrant an elaborate segregation analysis; however, superficially at least they are consistent with the hypothesis that "failure to dilate promptly" represents the homozygous state for an autosomal gene with appreciable frequency among Aymara. Generations are skipped, no predilection for one or the other sex is apparent, and the proportion of "affecteds" is at least superficially consonant with this thesis. No one of the "affected" individuals is, however, known to be the product of a consanguineous marriage. Finally, segregation within families cannot here be viewed as a phenomenon secondary to the segregation of eye color, for the Aymara and Mestizos have, almost without exception, dark brown irides.

It is note-worthy that coca-chewing is widely practised by the Aymara, particularly those who reside in Bolivia and Peru. While the Chilean government has attempted to discourage the practice, it is used cryptically throughout the year by some individuals and more openly by many at the time of traditional festivals, such as the ritual planting of the new potatoes. Cocaine itself is a mydriatic, and is known to produce unequal effects on light and dark irides of human subjects (Chen & Poth 1927, 1929, Patil 1972). Whether persistent use of coca would ultimately impinge upon its effects as a mydriatic, or the effect of similarly acting drugs is not known. However, it seems an unlikely explanation for the present data because many of the nonresponders are children who are not normally coca-chewers.

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