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Affected Parent and Age of Onset in Huntington's Chorea

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In a recent report, Merritt *et al.* (1969) searched the literature and their own material for cases of Huntington's chorea with onset before the age of 21. They found that when the disease began in childhood or adolescence the history was generally on the father's side. In 89 out of 113 cases in which descent could be determined, the father or his relatives were affected. The sex ratio among the affected young people was essentially 1:1. In discussing their results Merritt *et al.* suggest, referring to Bell (1934), that female choreics have fewer children than male choreics; hence, in a representative sample of choreics, including juvenile cases, we should find that paternal predominates over maternal descent. However, in Bell's work roughly the same percentages of male and female choreics failed to marry, and among those who did marry males and females had approximately the same average number of children. More recent work (Reed and Neel, 1959) finds that fertility is sharply reduced in male but not in female choreics. Reed and Neel report that the average male choreic has 1·8 and the average female choreic 2·8 children, the principal source of the difference being a larger proportion of male choreics who do not marry. It appears, therefore, that in the adult form of the disease, which accounts for all but 1 or 2% of the cases (Myrianthopoulos, 1966), females have more children and maternal descent predominates. Hence, the predominance of paternal descent in the juvenile cases is an exception to the rule in Huntington's chorea.

As an alternative explanation, Merritt *et al.* (1969) suggest that 'affected male parents may induce a shift to a younger age of onset in their offspring', i.e. paternal cases *in general* have an earlier onset than maternal cases. The purpose of this study is to examine this alternative explanation for the predominance of paternal descent in the juvenile form of Huntington's chorea.

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Material and Methods

Between March 1964 and March 1965, one of us (C.R.P.) searched the records of all state mental hospitals in Pennsylvania for cases of Huntington's chorea. The search resulted in 243 hospital-diagnosed cases. For the purposes of this study two additional criteria were used. (1) The record had to show a definite date for onset of the disorder; in two cases where onset was very early, i.e. less than 20 years, hospital admission was used as the date of onset; otherwise a case was not included unless the date of onset was given independently of hospital admission. (2) There had to be good evidence in the record as to which parent was choreic; most cases were unambiguous, one side of the family or the other including a hospital-diagnosed choreic. Many cases, however, were located as maternal or paternal on the strength of a note in the record to the effect that 'mother had same trouble', or something similar.

Imposition of these two criteria reduced the material to 130 cases, 84 maternal and 46 paternal cases. The difference in numbers of cases is what would be expected from the fertility figures quoted by Reed and Neel.

Results

The Figure presents age of onset in cumulated percentages for paternal and maternal cases. In agreement with Merritt *et al.* (1969) we found five cases with onset before 21 years of age, all of them paternal cases. However, the rest of the Figure does not bear out the hypothesis of a general shift towards earlier onset in cases of paternal descent. After the age of 20 the two curves run together, intersecting at three points. The means are 37·5 and 40·2 for the paternal and maternal distributions; the corresponding medians are 38·0 and 39·2. Neither difference approaches significance. If the five cases of early onset are deleted, paternal mean onset becomes 40·1 or virtually the same value as in the maternal cases.

Discussion

The results show no general shift towards earlier onset in the paternal cases. Hence, the predomi-

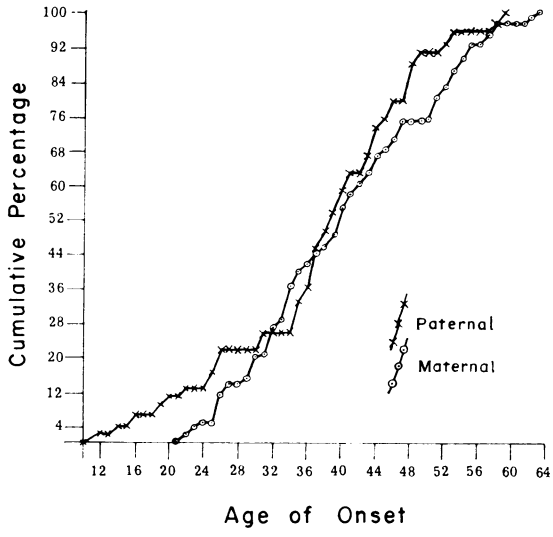

FIG. Age of onset in cumulative percentages for 84 maternal and 46 paternal cases of Huntington's chorea.

nance of paternal descent in the juvenile form of Huntington's chorea remains to be explained. One possibility is that male choreics, though less fertile than female choreics in general, may be more fertile in families which tend towards early onset. Penrose (1948) reported a correlation between age of onset in parent and child of 0·59; Bell (1934) reported a value of 0·50 for the same relation. We would expect, therefore, that the onset in the affected parent of a juvenile case would be fairly early. However, Reed and Neel (1959) found that the relative fertility of male and female choreics was a function of the age at which they died, hence, by implication, age of onset. Among choreics who died at the age of 40 or older the females had somewhat less than twice as many children on the average as the males. But among choreics who died before 40 the males had a slightly higher mean fertility, 1·25 to 1·00. If age of onset in the affected parents of juvenile choreics is early, the fact may interfere directly with successful conception and pregnancy in the women and reduce their fertility disproportionately.

Though they did not draw attention to the result, Merritt *et al.* found 12 juvenile cases among the sibs of their 89 paternal cases and no juvenile cases among the sibs of their 24 maternal index cases. The difference is significant at the 0·05 level (Fisher's exact test). One explanation is that the sibships are larger in families of paternal descent.

The possibility that male fertility, while lower in general, is higher in families with early onset needs to be examined. If it fails to stand, more speculative explanations will have to be considered.

Summary

Though maternal descent predominates in Huntington's chorea generally, paternal descent is more common in cases which begin in childhood or adolescence. The hypothesis of a general shift towards earlier onset in cases of paternal descent was examined. A survey of the records of all state mental hospitals in Pennsylvania resulted in 130 cases in which age of onset and descent from the father's or the mother's side could be determined. In agreement with previous findings, five cases with onset before 21 were of paternal descent. However, after the age of 20 the cumulative distributions for age of onset in paternal and maternal cases were essentially the same. Hence, the data gave no support to a general tendency for onset to be earlier in paternal cases. The suggestion is made that while male choreics are less fertile than females in general, they may be more fertile in families which tend towards the juvenile form of the disease.

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