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Brief Reports

Prevalence of Huntington's Disease among UK Immigrants from the Indian Subcontinent

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Using the records of Churchill Hospital, Oxford, and those of genetics centres and other national institutions, the minimum prevalence of HD among immigrants from the Indian subcontinent was found to be almost half that found in the indigenous UK population. However, this observed prevalence was probably depressed, and therefore may not differ greatly from that estimated for European populations. All the identified cases were immigrants from Pakistan, the Punjab and Gujerat; none were from Bangladesh.

Huntington's disease (HD) has been reported worldwide (Hayden, 1981). Prevalence in white Caucasian populations is between 16 and 92 affected individuals per million. Low prevalence has been reported in Finns (5 per million; Palo *et al*, 1987), in Japanese subjects (3.8 million; Kishimoto *et al*, 1957), and in South African blacks (0.6 per million; Hayden, 1981). There have been isolated reports of HD from India, the diagnosis being based on clinical findings and, in most cases, a family history compatible with autosomal dominant transmission (Singh *et al*, 1959; Khosla & Arora, 1973). Chhuttani (1957) identified 38 affected persons among five families from north India. However, there has been no survey of the prevalence of HD in the Indian subcontinent. Indeed, many clinicians may not be aware that this disease does occur in UK immigrants from that subcontinent; such an awareness is indispensable if the families are to be given proper counselling and access to the latest techniques of molecular genetics – pre-symptom diagnosis and pregnancy diagnosis.

Method

Cases of HD were ascertained from our own records and, by telephone and written contact, from all regional and subregional genetics centres in the UK as well as from the National Hospital for Nervous Diseases and the Association to Combat Huntington's Chorea (Combat); all contacted centres responded. In addition, one of us (RSS) checked the records of the Maudsley and Bethlem Royal Hospitals. Cases were positively identified from our own records, from four of the regional genetics centres (Birmingham, Leeds, Manchester and Nottingham), and from Combat. The diagnosis in all the cases was based on clinical findings and family history.

Results

We identified 17 immigrants (14 families) from the Indian subcontinent (Pakistan, the Punjab, and Gujerat) who were affected with HD and living in this country in 1988, and a further three affected who had died in the UK during 1985–87. In this group, the age at onset of symptoms ranged from 19 years to the late 50s (median age 44 years), and clinical signs and symptoms resembled those found in English families. One patient was initially diagnosed as schizophrenic, the diagnosis later being revised to HD; one patient committed suicide.

Discussion

Studies of HD prevalence within the UK, published during the last 20 years, give rates ranging from 52–92 per million (Hayden, 1981), and the same source quotes rates of 16–70 per million for other European countries (publications since 1970), and 22–84 per million for populations of predominantly European origin overseas (USA, Canada, Australia, whites in South Africa). Lower prevalence rates were reported by earlier studies in Europe and America, perhaps because of an emphasis on studying hospital populations rather than the whole community (Hayden, 1981).

Within the UK, there are 1.26 million persons from the Indian subcontinent (Haskey, 1988). With a minimum of 17 identified HD cases, a crude estimate of prevalence within this subpopulation is therefore 13.5 per million, or 15.9 per million if the three additional cases dying between 1985 and 1987 are included.

The UK Indian population is predominantly a young one, with only 37.4% (471 000) aged over 30 years (Haskey, 1988) compared with 58% of the indigenous UK population (Shaw, 1988). We attempted a simple age-related correction as follows. In populations of European origin, 12% of HD cases present before their 30th birthday (Hayden, 1981), but the actual prevalence of HD in the population aged below 30 years will be considerably less than this. A check on HD cases known to our department, and alive in June 1988, showed eight of 104 (7.7%) to

be aged under 30 years. Assuming an overall prevalence rate in the UK population of 50 cases per million, we calculated age-related prevalence rates for HD as follows: for the UK population aged below 30 years, $50 \times 7.7/100 \times 1/0.42 = 9.2$ cases per million, and for those over 30 years of age, $50 \times 92.3/100 \times 1/0.58 = 79.6$ cases per million. Applying the age-corrected prevalence rates to the Indian population in the UK, we would expect to find 7.3 cases $((1.26–0.471) \times 9.2)$ under 30 years old and 37.5 cases (0.471×79.6) over 30 years old, a total of 44.8. We actually found 17 (20) cases in this population, almost half as many as would be expected with an overall UK prevalence of 50 per million.

Emigration and immigration policies might act as selective factors in our population. Moreover, within the UK, some cases will not be diagnosed, the family history being concealed or unknown or not available (in India many die too young to manifest the disease). Furthermore, our method of ascertainment is incomplete, since a small proportion of cases will not be known to clinical geneticists, the National Hospital, or Combat. All these factors will depress the observed prevalence, and thus the gene frequency of HD at birth within the Indian immigrant population may not differ greatly from that estimated for European population groups.

Most immigrants to the UK originate either from Pakistan, Punjab and Gujerat in India, or from Bangladesh; these areas are linguistically close (Indo-European tongues), but not necessarily genetically akin. We ascertained no cases from Bangladesh, although Bangladeshis constitute 10% of the UK Indian population (Haskey, 1988). South Indians, who are linguistically distinct (Dravidian), form a very small part of the present UK population, but we do not know whether HD is rare or common in that group (Hayden, 1981). All reports of HD in India (Chhuttani, 1957; Singh *et al*, 1959; Khosla & Arora, 1973) have been from the northern states of India and from western Pakistan (now Pakistan). The ascertained UK cases also originate from this region and the adjoining area of Gujerat.

If the mutation rate in HD is very low then, depending on the place and point in time that the original mutations occurred, HD will be spread very unevenly through the populations of the world. Higher rates of mutation for HD would result in a more homogeneous distribution among different population groups. The HD gene may have been in India for a long time. Chhuttani (1957) claimed to have traced back a family pedigree from Punjab (273 members, 27 affected) for over 200 years.

No UK Indian family was large enough for a linkage study, but colleagues are storing DNA. Identification of the specific mutations in apparently unrelated families, UK and Indian, would allow resolution of the prevailing controversy regarding a single v. multiple geographical origins. Studies of haplotypes in HD (Snell *et al*, 1989; Theilmann *et al*, 1989) have detected linkage disequilibrium for two close DNA markers on chromosome 4; Theilmann *et al* (1989) found that haplotype distributions were not markedly different for UK and non-UK families (the non-UK group included two families from India, but those results were not reported separately).

Since submitting this paper we have identified a further six cases of HD among immigrants from the Indian subcontinent.

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