# HUNTINGTON'S CHOREA IN SOUTH AFRICA

## A PRELIMINARY COMMUNICATION DRAWING ATTENTION TO ITS FREQUENT OCCURRENCE

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Studies in human heredity are impeded by difficulties which do not face those who investigate the genetics of laboratory breeding stocks. Among these are the relatively small size of most human families and the fact that a single investigator can personally study not more than about three or four generations.

In South Africa genetically determined illnesses are common, and unique opportunities are available for their study. The segregation of the ethnic groups in South Africa results in relatively pure races. The White population remains largely distinct from the Bantu, the Indians and other such peoples. A small number of individuals have broken the racial barrier and this has resulted in the formation of the Coloured peoples, among whom the genetic diseases of both the White and Black races are encountered. The differences in the racial incidence of diseases can readily be established in a multiracial country like South Africa, and the occurrence of similar hereditary conditions in different 'pure-bred' races is presumptive evidence that a separate gene mutation must have taken place.

In South Africa the families which can be studied are often large, since it is not uncommon for individuals to marry at an early age and for the number of their offspring to reach double figures.

### GENEALOGICAL STUDIES

Genealogical studies of Afrikaner families are assisted in a number of ways. A Bible containing the family tree is passed down the generations as an heirloom by some families. Its value is self-evident in a family having an inherited disease. The manner in which the Afrikaner families name their children is also of immense help in the tracing of the pedigree. Until recently many families christened their offspring according to an accepted convention. The eldest son was always named after the father's father, the second eldest son after the mother's father, and the third eldest after the father. The first three daughters were baptized in a similar fashion. The eldest daughter was given the name of the mother's mother, the second the name of the father's mother, and the third the name of the mother (Fig. 1). Even today there are some Afrikaner families that use this method of naming their children.

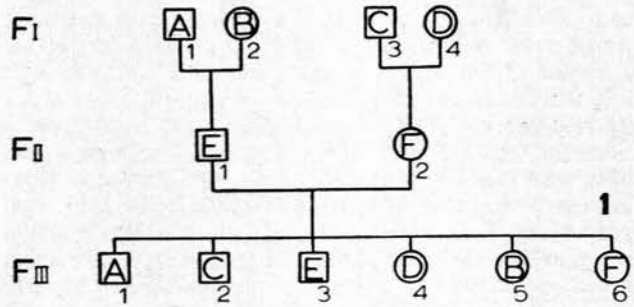


*Fig. 1.* Naming of children (see text).

From the above it is apparent that if the name of the eldest uncle is known, one also knows the name of the paternal great-grandfather ('oupa grootjie'). Likewise, if the birth order of the father's and mother's siblings is known, it is possible to give the names of other ancestors.

Probably the most valuable aid to human genetics in South Africa is the *magnum opus* which De Villiers published in 1894.[1] This author compiled a register which contains the names and dates of baptism of descendants of all the original Cape settlers. By making use of this invaluable masterpiece it is possible to trace the ancestry of many South Africans through three centuries, back to the original immigrants. By talking to the oldest living members of a family and studying family Bibles it is often possible to trace families back to the register of De Villiers. The Afrikaner method of naming children sometimes assists when details about one generation are lacking.

### HUNTINGTON'S CHOREA

Because of the favourable conditions in South Africa for studies in human genetics, an attempt was made to investigate Huntington's chorea in this country. The families of all diagnosed patients were traced whenever possible. Doctors who were likely to meet the condition were contacted, either personally or by letter. The diagnosis was accepted when it fulfilled the clinical triad of: (*a*) choreiform movements, (*b*) progressive mental deterioration coming on after a period of apparent normality, and

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(*c*) a positive family history of a similar condition that was inherited as a Mendelian dominant. All other patients diagnosed by members of the medical profession were noted, but they were viewed equivocally unless they were subsequently found to belong to a family in which established cases of the disease were known to be present.

*Presentation*

It should be emphasized that Huntington's chorea can first manifest itself in a large variety of ways. Individuals may present with involuntary movements or psychiatric disturbances. Some of the South African patients tend to have generalized abnormal movements from the onset. The involuntary movements may begin in the face, trunk, or upper or lower extremities. Particularly in the early phases of the condition, the movements are not necessarily choreiform. The initial movements may be in the form of a twitch or spasm. As the disease progresses, choreiform movements become more apparent and the association with athetosis is not uncommon. A disturbance in walking may be the first apparent manifestation of the condition, and the gait may be bizarre and apparently hysterical.

Many South African patients present with a disturbance in the personality, and it is often the immediate family who detect the early mental signs. Later the individual may become aggressive and paranoid. Mental deficiency is fairly common and may be the original manifestation of Huntington's chorea in some cases. Involuntary movements may begin years later. However, it would appear that mental deficiency may be the sole manifestation of the mutant gene.

*Diagnosis*

During the investigation it was found that a detailed knowledge of affected families often assisted in the diagnosis of Huntington's chorea. In atypical cases the diagnosis was often unsuspected by clinicians if the family history was lacking. Occasionally relatives of affected individuals were genuinely unaware that the condition was present in the family. This was not uncommon in those instances where the families were large and where contacts with numerous relations were lost owing to migration.

However, on rare occasions, individuals falsely deny the presence of the disease. The father of one patient emphatically denied that other members of the family were of unsound mind, mentally defective or mentally abnormal in any way, although his wife had been admitted to a mental hospital because of Huntington's chorea and not one of his children was psychiatrically normal. Sometimes the diagnosis is suspected clinically in the absence of a positive family history, and frequently in such instances the diagnosis is subsequently confirmed by examining the relatives.

Individuals with mental retardation or dementia may be cast out by their families. When such patients are institutionalized under the Mental Disorders Act no family history is obtainable and the diagnosis must depend totally on the clinical findings. One such patient was sent to a mental hospital, having been deserted by his own family. His name was known, but a family history was unobtainable. This patient has the same Christian and surname as other members of a large Afrikaner choreic family.

A further difficulty in the diagnosis of Huntington's chorea arises out of adoption of children. This most commonly occurs when an unmarried woman has given birth to illegitimate offspring before the onset of manifest disease in herself. At least two women whose children were adopted have subsequently developed the clinical features of Huntington's chorea. When such children develop Huntington's chorea in later life, the disease might be mistakenly termed 'sporadic' in the absence of an attainable family history.

*Attitude of Families with the Disease*

Members of South African choreic families were found to show a marked diversity in their attitude towards the condition. Some knew that the disease was a family illness, but believed that since their ancestors had had it there was nothing to fear. Such persons did not believe there was any necessity to limit the number of their offspring and it was not uncommon for them to have large families. Members of another family, being aware that the disease was inherited, believed that they should limit their children to small numbers (2 - 4). Others considered complete birth control to be necessary. Many laymen are ignorant of genetics, and it was not uncommon to encounter patients' relatives who failed to believe that the condition was inherited. This view was sometimes held even when they were aware of numerous affected relatives. Such individuals would offer fanciful theories as to why each person became affected.

In at least three families spouses of affected individuals knew that the disease was inherited, but maintained that they would not inform their children 'because it may upset them unnecessarily'. Such an attitude may account for the fact that many individuals appear to be genuinely unaware of the disease, though it is in their family. Some members of affected families have dissociated themselves from the family when they discovered that Huntington's chorea was present among their blood relations. Fortunately some of them have refused marriage, but in one family known to me an individual changed his name legally, but still married and had offspring.

A number of individuals have committed suicide on discovering the condition in their family. This tendency to self-destruction was commented upon by George Huntington in his famous publication of 1872,[2] and he considered suicide to be a feature of the disease which became named after him. Suicide has been encountered fairly often in the South African families, but it is not altogether clear whether it is a psychological reaction to the discovery of the condition in the family, or whether it is a complication of the depression that is sometimes present in the early stages of the disease. Perhaps both occur.

One would expect that sterility would be welcomed when it occurred. Sterility is in fact present in certain members of South African choreic families, but a few of them wish that they could have children of their own in spite of being aware that the children may become affected in later life.

*Occurrence in Various Races*

Huntington's chorea occurs in the English, German, Austrian, Jewish and Afrikaner sections of the White races

in South Africa. The disease is, however, most prevalent among the Afrikaner section. Coloured families having the condition are known. There is at least one Bantu family

TABLE I. DATA ON KNOWN SOUTH AFRICAN FAMILIES WITH HUNTINGTON'S CHOREA

| *Family* | *Race* | *Origin* | *Patients* | | *Known members of family* |
|---|---|---|---|---|---|
| | | | *Known living* | *Deceased* | |
| WI | Afrikaner | SA | 1 | 22 | 131 |
| TU | English | England | 5 | 10 | 73 |
| BA | Austrian | Austria | 1 | 6 | 49 |
| SO | Jewish | SA | 2 | 1 | 10 |
| DB | Afrikaner | Holland | 18 | 21 | 611 |
| TH | Coloured | SA | 3 | 1 | 31 |
| DA | Jewish | Russia | 2 | 6 | 30 |
| GO | Coloured | SA | — | 2 | 2 |
| HO | Afrikaner | Holland | 6 | 14 | 158 |
| SC | German | Germany | 2 | 1 | 13 |
| TY | English | England | 3 | 2 | 28 |
| RO | Afrikaner | Holland | 9 | 7 | 97 |
| ED | English | England | 1 | 3 | 12 |
| VE | English | SA | 1 | 1 | 17 |
| DL | Zulu | SA | 1 | 7 | 20 |
| JA | English | SA | 1 | 1 | 7 |
| | | Total | 56 | 105 | 1,289 |

that has what can clinically be called Huntington's chorea. It has been possible to trace 16 different South African families with Huntington's chorea (Table I).

It should be emphasized that details concerning many members of the choreic families are lacking, and the actual size of some families is considerably larger than is shown in Table I.

A challenging problem in any genetic study is whether it is possible to trace family heritages to a common ancestor. This has been attempted in the present investigation. Three Afrikaner families (DB, HO and RO) can be traced to a common ancestral family (Fig. 2). If this is more than a coincidence it would seem that Huntington's chorea was first introduced into this country from Holland in the middle of the 17th century. When Jan van Riebeeck set sail from Amsterdam on 24 December 1651 to found a Dutch settlement in South Africa, he took with him a married couple ($F_i^1$ and $F_i^2$) who subsequently had a daughter ($F_{ii}^2$) who married a young Hollander ($F_{ii}^1$) who emigrated to South Africa in 1660. It is from this mating that three Afrikaner choreic families can be traced.

## CONCLUSION

There is a large hiatus in the available information concerning the South African choreic families, and details about many of their relatives are lacking. There can be no doubt, however, that the incidence of Huntington's chorea in this country is considerably greater than is reflected in Table I. If the disease was in fact introduced into South Africa in the 17th century, it seems likely that there is a potential at present for a very large number of persons to have the disease. Many patients have perhaps not been diagnosed because of the absence of a positive family history, and others may have gone undetected or undiagnosed because of failure to think of the condition.

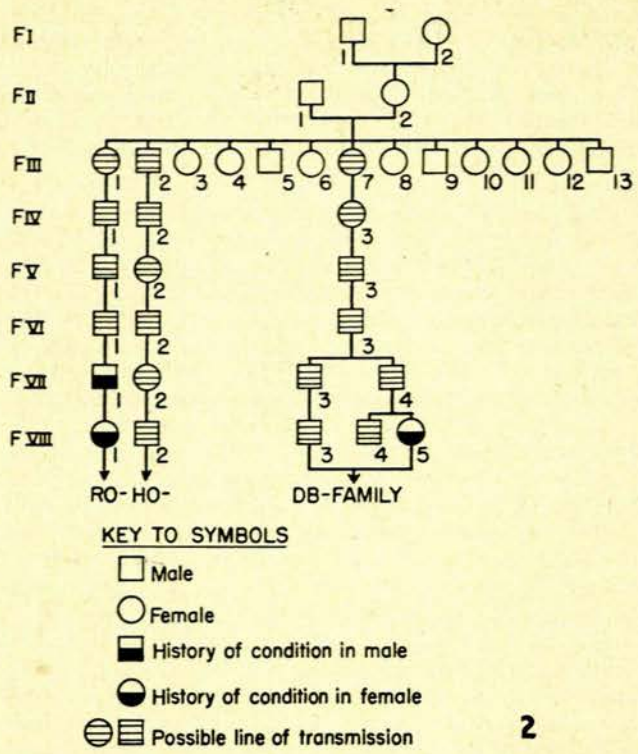


*Fig. 2.* Linkage of Afrikaner families to Holland (before 1660).

Undoubtedly many patients are not institutionalized. Huntington's chorea should be considered in the differential diagnosis of all cases of involuntary movement, dementia, mental deficiency, and hereditary mental disease.

## SUMMARY

The factors favourable to the study of hereditary disease in South Africa are presented. Some of the early clinical manifestations of Huntington's chorea are discussed and the difficulties in making the diagnosis are mentioned. The attitudes of members of affected families to the disease are considered. The South African families are summarized in tabular form, giving the race, country of origin, known cases, and known members of the families. Of the 16 known choreic families, 9 have been traced to their foreign ancestral origin. Three of the Afrikaner families descended from a family that came from Holland in the middle of the 17th century. It is felt that Huntington's chorea in South Africa is commoner than is generally appreciated.

I wish to thank the many members of the medical profession who cooperated in this study. The expenses in this investigation were partly covered by a research grant from the Council for Scientific and Industrial Research. Figs. 1 and 2 were kindly photographed by the photographic unit of the Department of Medicine, University of the Witwatersrand, Johannesburg.

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