# HUNTINGTON'S CHOREA, WITH SPECIAL REFERENCE TO ITS INCIDENCE IN MALTA

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The epidemiology of mental disorder is at the moment assuming a role of increasing importance. This aspect of psychiatry, however, still awaits study in Malta. It was, therefore, considered that a review of my experience of the morbidity and prevalence of such a disabling disease as Huntington's Chorea in Malta over the past twenty years might be of interest.

Huntington's Chorea is known to be a hereditary degenerative disease of the basal ganglia and of the cortex of the brain. It commonly manifests itself clinically at middle age in the form of choreiform movements or of muscular rigidity, which are often accompanied by mental deterioration.

The case material on which this study is based was either seen personally, the observations being complemented by information obtained from normal relatives of affected individuals, or else gathered from past records at the Attard Mental Hospital since 1861 and at the St. Vincent De Paule Hospital since 1892. The records from these two hospitals were found useful in tracing present cases back to their ancestors and in constructing family pedigrees but were otherwise of limited value for two reasons: (a) they were indicative only of a part of the prevalence of the disease since only the more severe mental cases found their way into hospital; and (b) the entries of the older records are not so detailed and exhaustive as to satisfy the clinical research worker though they may have served their purpose for the routine hospital work of the time.

I have been able to collect 22 Huntington's Chorea families in Malta comprising 125 cases. Of these 72 were men and 53 women; 100 are dead and 25 alive. The number of cases personally observed is 26. This number has been limited by two factors: (a) Huntington's Chorea is an uncommon disease and, therefore, no large series of cases may be expected to be found in a small population as that of the Maltese Islands (317,739 in May 1966); and (b) there are no means, such as notification whereby all existing cases can be traced and examined. It is, therefore, realized that the statistical data of the present study though approximate are not final and are likely to be an underestimate of the actual prevalence of the disease amongst us.

## Historical

A form of chorea called St. Vitus's Dance or Dancing Mania occurred in Europe from the tenth century onwards. The malady sometimes took epidemic proportions in the Middle Ages and was characterised by gesticulations and excitement. The reference to St. Vitus is due to the fact that patients suffering from the disease went processionally in search of a cure to the chapel dedicated to this saint in Zabern (Alsace) in 1418 (1). In Italy it was ascribed to the bite of a venomous spider, the tarantula, and was therefore called tarantism. In later years the disease was considered to be of an hysterical nature (2). It is not possible to say what is the relationship of St. Vitus's Dance and tarantism to the conditions which we today identify as Huntington's Chorea. This form of chorea was first described in the U.S.A., the earliest report of a case going

back to 1816. Other descriptions followed in 1834, 1841, 1848 and 1863, the disease being variously referred to as Chorea Major, Pandemic Chorea, Hereditary Chorea, Chronic Hereditary Chorea and Chronic Chorea.

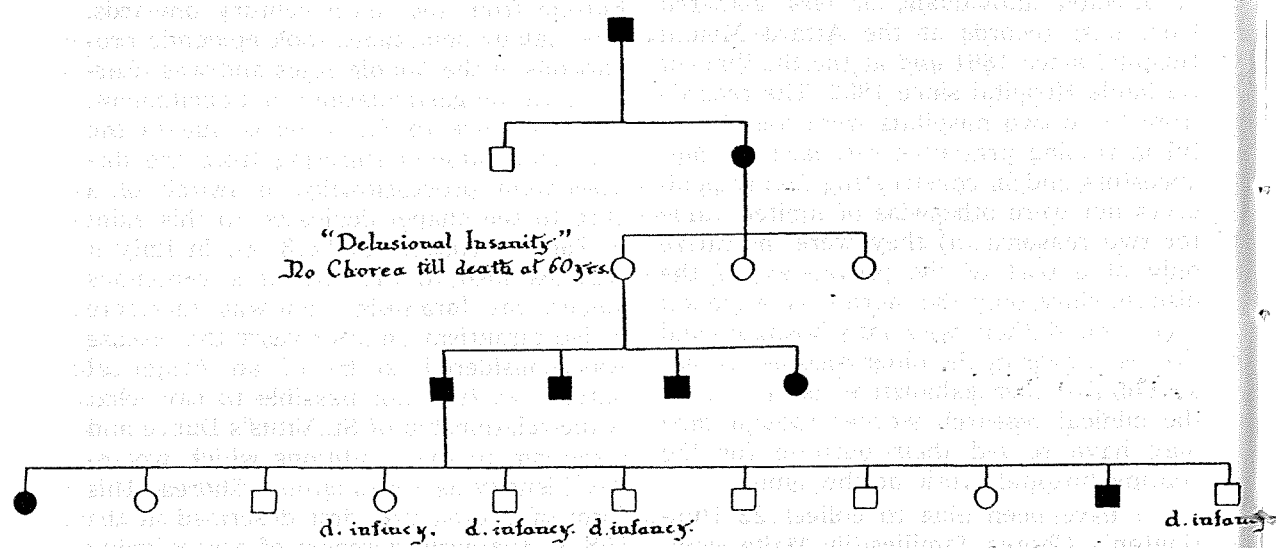
The most detailed and comprehensive description of the disease was that of George Sumner Huntington (1850-1916) who read a paper "On Chorea" before a medical society on the 15th February 1872. This American physician had the opportunity of studying cases observed since 1797 by his grandfather and by his father (Abel and George respectively) in one of the American foci of the disease in Long Island (3). He emphasised the hereditary character of the disease, its appearance in adult life and the tendency of affected persons to become psychotic.

It has been established that the cases observed in the U.S.A. were descended from two brothers who emigrated from Bures in Essex, England, to Boston Bay in 1630. Sufferers from the disease were tried for witchcraft in the Colonial Courts of America and others were persecuted as it was traditionally believed that a remote ancestor of the affected families was cursed with the disease because he had mocked Christ on the Cross (4). During the succeeding three centuries about one thousand descendants of the original pair have suffered from the disease up to 1932 (5).

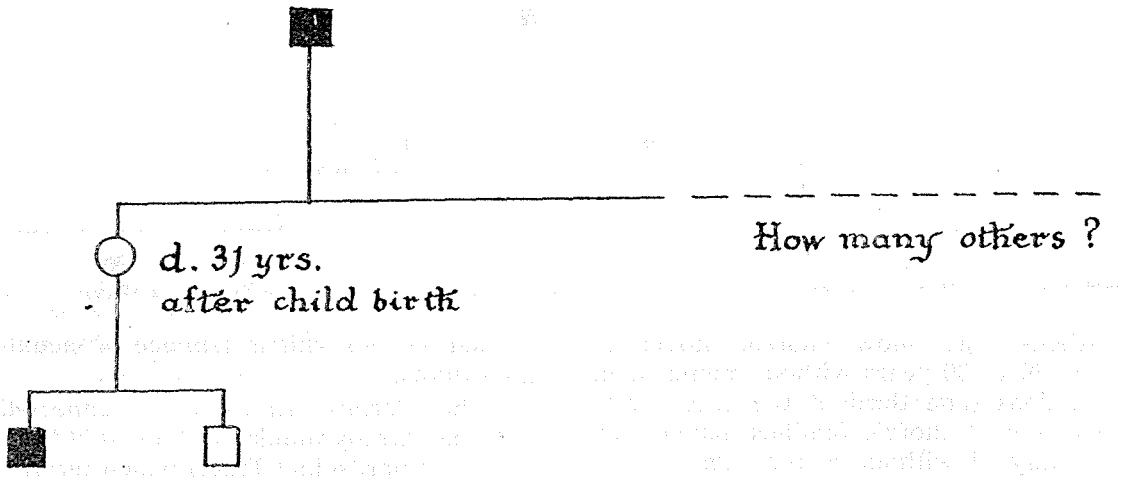
Since 1872 the disease has been reported from dierent parts of the world. In Britain the first case was recorded in 1887 (6). In Malta the earliest documented instance of Huntington's Chorea that I have been able to trace dates from January 1872. The patient was a man of 70 years from Żurrieq who was admitted to the Ospizio at Floriana and diagnosed as suffering from St. Vitus's Dance. It is of interest to note that some of the early cases seen in the late 19th century in Australia (Victoria) were similarly labelled (7). There is no doubt that the Malta case diagnosed as St. Vitus's Dance was one of Huntington's Chorea for I have succeeded in tracing the subsequent history of his pedigree up to the present day *(Ped. 1)*. Needless to say this patient could not have been labelled as Huntington's Chorea in January 1872 because, as already stated, it was exactly in February of that year, that is a month later, that George Sumner Huntington read his paper on this malady in America.

**Oldest known family with Huntington's Korea**
**1872—1966**

**Pedigree I**



**Pedigree II**




A further case to be diagnosed in Malta, this time as Chronic Chorea, was a woman of 64 years from Mosta who was admitted to the Mental Hospital in 1888. The first patient to be labelled as Huntington's Chorea was a man from Hal Għarghur who was admitted to the same hospital in May 1916.

## Heredity

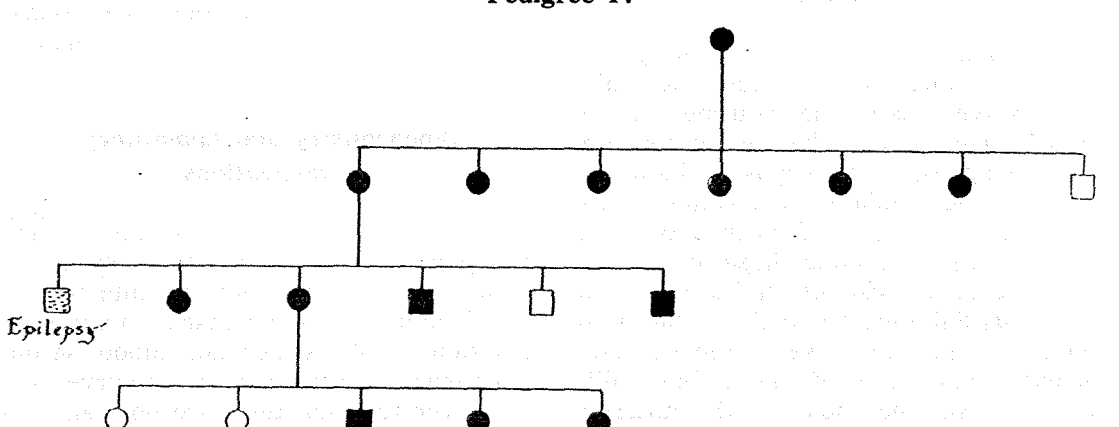
Huntington's Chorea affects both sexes. It is transmitted as a single autosomal dominant gene directly to the children from either parent. Instances of three monozygotic twins have been recorded where both of each pair developed the ilness (8). Theoretically one expects 50% of the offspring to develop the disease but in actual practice the incidence is in the region of 30% although instances of higher percentage are met with (9) *(See Peds. 1 and 4).*

It has been said that Huntington's Chorea never skips a generation (10) but instances have been described, though infrequently, where the disease does not appear in one or two generations but manifests itself in a later one (11) *(See Peds. 1, 2 and 3).*

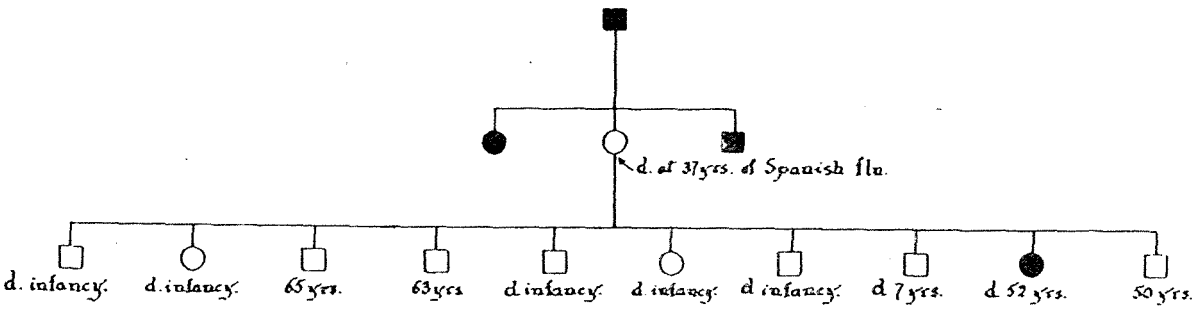
Members of the affected families who escape the disease do not transmit it to their offspring (12).

It seems that the mental and motor traits are inherited separately and more or less independently of one another. Thus

**Pedigree IV**



**Pedigree III**




patients may show choreic movements from 20 to 30 years without mental manifestations (one third of the cases) while members of choreic families may become mentally ill without motor signs, the so-called cases of "Huntington's Chorea without chorea" (13).

Sometimes there is a negative family history. In such a case the appearance of the disease is due to a spontaneous new mutation in a germ cell of one or other normal parent (14). This is a very rare occurence, the estimated rate of mutation for Huntington's Chorea being 5 per million per generation. However, the appearance of a case with a negative family history may also be an instance of a "skip" where the disease does not appear in previous generations which, therefore, appear normal; or else the patient may be an illegitimate offspring whose real father is not the normal one shown in the pedigree but another one suffering from chorea.

## Pathology

Although the lesions of Huntington's Chorea are diffused throughout the brain, they involve mostly the neurones of the frontal cortex and of the corpus striatum (basal ganglia). The corpus striatum is formed of the Caudate Nucleus and of the Lentiform Nucleus. The former is made up of small cells resembling those of the cortex; the latter consists of the Putamen and the Globus Pallidus. The cells of the Putamen are small like those of the Caudate Nucleus, while those of the Globus Pallidus are large like those of the anterior horns of the spinal column. They are marked by two whitish laminae of medullated fibres.

The Corpus Striatum is connected with the extrapyramidal system (Red Nucleus and Rubrospinal Tract) which terminates round the motor cells of the anterior horns of the spinal cord from which rises the motor fibres to the muscles. The extrapyramidal system exercises a coordinating and inhibitory control over the motor cells and fibres just mentioned.

The lesion of Huntington's Chorea consists of a degeneration and atrophy of the small cells of the Caudate Nucleus and Putamen (which are really one nucleus) and of the neurones of the cortex of the brain especially of the frontal region. As a result there is a general shrinking of the brain (white and grey matter) and secondary dilatation of the internal ventricles and hydrocephalus. These lesions give rise to the hyperkinetic and hypotonic form of the disease. When, in addition to the damage of the above-named structures, there is also loss of the large cells of the Globus Pallidus, the disease assumes the akinetic and Parkinsonian or rigid form (15).

## Biochemistry and Laboratory Investigations

Brain: the only consistent finding is copper reduction in all parts of the brain, except in the central white matter and thalamus, and increased amounts of strontium. CSF is normal. Blood serum coper levels are normal, sugar curve normal. Liver function tests are normal. Urinary copper excretion is normal. Other

routine laboratory investigations are normal. EEG is normal or may show evidence of cortical degeneration but no specific changes (16).

## Aetiology

It is not known what produces the degenerative changes of Huntington's Chorea but it is thought that they are due to some inherited metabolic defect as has been shown, for instance, to be the case in Wilson's Hepato-Lenticular Degeneration which appears to be due to an abnormal copper metabolism and is characterised by the deposition of excessive amounts of copper in the brain and liver and by increased excretion of copper and aminoacids in the urine (17).

## Age of onset

The majority of cases begin between the ages of 30 and 50 the average being about 42 years. The onset is slightly earlier in women than in men. However, variations, both individual and familial, occur in the age of onset. In fact cases have been recorded with an onset ranging from such extremes as 3 to 60 and even 70 years of age.

The clinical picture tends to vary with the age of onset. In cases starting in the twenties or earlier, rigidity and slowness are the main signs; in the forties choreic movements are the characteristic features; and in the sixties, intention tremor is the chief manifestation (18).

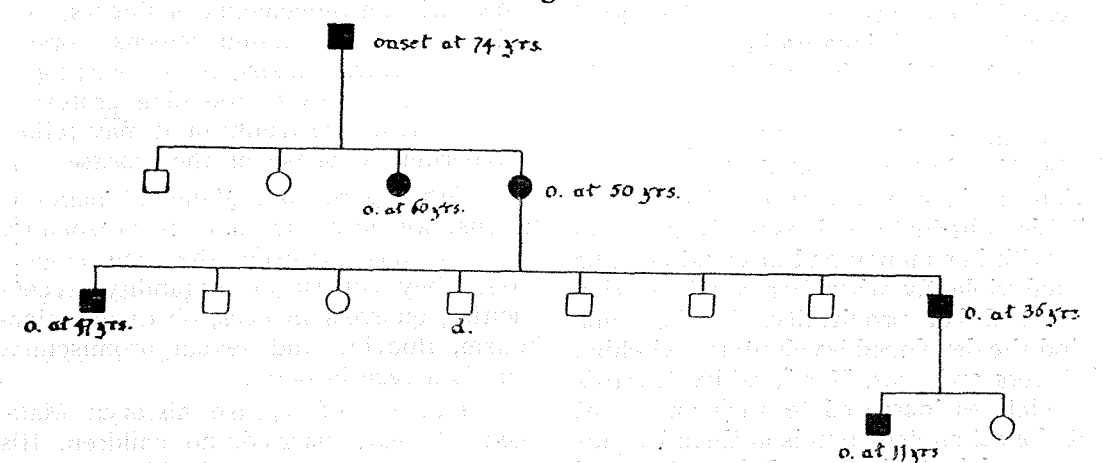
According to some investigators the disease tends to appear at earlier ages in succeeding generations (19) but other workers do not uphold this so-called Anticipation Theory (20). I have, however, come across a few cases in Malta which lend support to it. *(Ped. 5).*

## Clinical Picture

The clinical picture is the result of the combined pathological involvement of the basal ganglia and cortex. It, therefore, consists of neurological and mental manifestations with or without the presence of some other associated disease. The features presented by our cases are identical with the descriptions given by other authors who studied the disease abroad. The neurological changes are either of the hyperkinetic and hypnotic type or of the akinetic and rigid type. This akinetic form may be found by itself or superimposed on the hyperkinetic type or following it. The mental changes consist of personality alterations, psychoses or dementia. The associated diseases are usually mental deficiency and epilepsy.

The neurological signs usually appear before the mental ones but there are instances in which the psychic disturbances precede the neurological changes by many years; or else the neurological and psychotic manifestations appear simultaneously.

**Pedigree V**



The hyperkinetic type of the disease begins insidiously with involuntary movements of a jerky and irregular character. They are abrupt and coarse. They may start in any part of the body but the face, neck and upper limbs are usually the first to be affected. In the face they take the form of grimacing, twitchings of the corners of the mouth, pursing of the lips and raising of the eyebrows. Speech is indistinct and explosive with grunting noises. There is difficulty in swallowing, with choking during meals.

In the upper limbs the movements consist in fiddling and clumsiness of the fingers which progress to abrupt extension-flexion movements of the digits and wrists causing the patient to drop objects from his hands and rendering him unable to dress himself and do housework. In the end he may be so incapacitated that he has to be fed, dressed and attended to with regard to his personal hygiene and other needs.

Owing to the involvement of the lower limbs the gait is unsteady, curtsying and staggering, the patient walking on a wide base to offset his ataxia. The movement may ultimately become so severe that he falls to the ground and has to be nursed in bed.

The choreic movements are increased on voluntary effort but disappear during sleep. Apart from these disturbances there may also be twisting and athetoid movements of the limbs and trunk.

On neurological examination we find increased deep muscle reflexes, decreased muscle tone and inco-ordination (finger-nose test, etc). The plantars remain flexors.

Summary of a case history: Female, single. She first manifested abnormal behaviour at the age of 39 years. She became irritable, obstinate and excessively generous with her money and possessions. She reacted violently when her relatives tried to control her prodigality. At the same period she developed involuntary twitching of fingers and toes. Her hostility towards her relatives increased to such an extent that she attempted to poison them by putting cresol in their soup. When thwarted in her desires she threatened to commit suicide. By the age of 41 years she had become very erotic, claimed to be engaged to a high ranking personage, exposed herself at home and appeared indecently dressed in public. The choreic movements became more pronounced involving the head, trunk and all four limbs. Her gait became so unsteady that she sometimes lost her balance and fell to the ground. Owing to the ataxia she had to be confined to bed during the last two years before her death.

The akinetic and rigid variety occurs at an earlier age — some thirteen or fourteen years — than the typical choreic form but is much less frequent (21). There is rigidity and stiffness of the body, a bending forward of the trunk, adduction or slight abduction of the arms and flexion of the elbows, wrist and finger joints. The facies is expressionless and immobile with staring eyes and infrequent blinking of the eyelids; the speech is slurred and drawling. The patient moves slowly and walks in small quick steps but running is easier than walking. On neurological examination there is cog-wheel rigidity on passive movements of the elbow; poor co-ordination and increased deep reflexes with ankle clonus and extensor plantar reflexes if the pyramidal system is involved (22).

The akinetic and rigid variety may occur by itself; or it may be superimposed on the hyperkinetic form when the choreic movements may change into athetosis (slow twisting movements of fingers, face and tongue) and torsion spasms (torsion dystonia) which consist in the twisting of the spine and pelvis producing grotesque contortions of the trunk; or it may follow a hyperkinetic phase of the disease (23).

With regard to the mental manifestations, we may find that the personality changes may precede the neurological ones. They consist of irritability, eccentricities, quarrelsomeness, obstinacy, alcoholism, thieving and sexual promiscuity. Here is a case in point.

Summary of a case history:: Male, aged 40 year, married, no children. His wife observed a change in his character

at the age of 37 years. Previously docile and efficient at his job, he started complaining of a feeling of being unsettled, of tiredness and insomnia. He became progressively irritable, stubborn, quarrelsome and aggressive, swearing on the least provocation and inclined to drink excessively. Because of his hostile tendencies he has come in contact with the police on a few occasions and has been sent away from at least two jobs so that he remains unemployed to the present day.

At times he feels mildly depressed for short periods. Occasionally he is seized by intense fear, almost amounting to panic, or by a feeling of being on the verge of losing consciousness. Since about six months his fingers "keep moving against his will". He tries to control them by flexing them in his palm as if forming a fist. His grip on objects is so unsustained on account of these movements that he spills liquids from glasses held in his hand. There are also sharp "kicking" jerks in his legs.

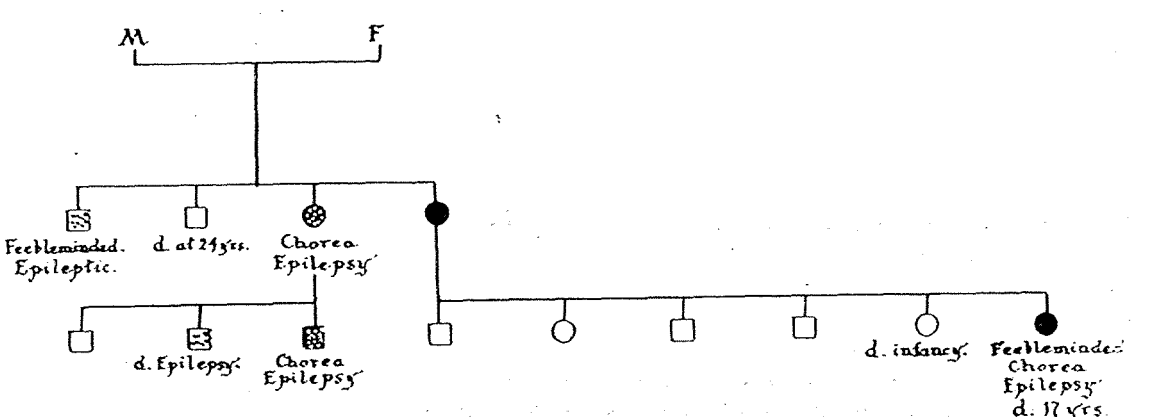
His mother had chorea; two brothers also suffer from the same condition. He was first seen six months ago when he was placed on phenotiazines. He is now less irritable, is sleeping well and his movements are less frequent and pronounced but his behaviour remains unchanged.

The psychoses may occur before the appearance of the chorea or may arise during its course. They take the form of mood disorders, ranging from apathy to depression with suicide or mania; paranoid or schizophrenic reactions; and confusional states (24).

The dementia may have a delayed onset or may never appear in some cases. When it occurs it is progressive and consists in the usual features of defects of memory, impaired judgment, disorientation, emotional lability, restlesseness and self-neglect (25).

The following case-history illustrates these features. Female, aged 61 years, widow, no children. Onset of her illness dates since three-and-a-half years ago with involuntary movements of the limbs which have grown steadily worse. Concurently with the developments of these limb movements, her relatives noticed that she started to become neglectful of her personal appearance and of her home. She often stayed naked at home. When she went out she was a cause of embarrassment to motor-drivers because of her unsteady gait. On one occasion she was hit by a motor-bike but suffered no serious injury. She has become obstinate, ignoring advice and refusing the help of others. She has been telling people that she wants to get married again and actually came across a paralytic who accepted to marry her if she gave him £100. She is forgetful; for instance she would go to the grocer but would not recall what she went there for; or would forget to pay for goods or else would go to a flower-shop and ask to buy a stove. Though she is oriented to place, she is only partly so to time and

**Pedigree VI**



person. She has no insight into her condition.

Mental deficiency and epilepsy may be found not only in patients affected with chorea but also in other non-choreic members of the family *(Ped. 6)*. The genetic relationship of these associated diseases with Huntington's Chorea is not clear (26).

### Duration of the disease

The average duration of the disease is 11 to 16 years for both the choreic and the rigid/akinetic forms, the shortest duration on record being two years from the appearance of symptoms and the longest 50 years (27). The illness persists until the patient dies but there may be periods when it becomes stationary (28).

Death is from exhaustion or intercurrent disease (29) or choking while eating. These patients have a voracious appetite and they tend to gulp their food; hence the importance of giving them nourishment in a semi-solid form to avoid choking.

### Differential Diagnosis

Huntington's chorea must be distinguished from other conditions manifesting choreic movements or rigidity. The main conditions that must be considered in the differential diagnosis are:

1. Sydenham's chorea which is associated with infectious diseases (such as puerperal and rheumatic fevers) and carditis. The family history is negative.
2. Hemichorea due to embolic brain disease.
3. Post-encephalitic parkinsonism. Here one may encounter serious difficulties as, apart from the rigidity, choreiform and athetoid movements may be found in parkinsonism. A past history of an acute feverish illness with headache and lethargy points to post-encephalitic parkinsonism. There is an absence of a family history of Huntington's chorea.
4. Senile chorea. This is not hereditary and is not necessarily accompanied by dementia.
5. Psychoses. When Huntington's chorea starts with a psychosis such as depression, paranoid state or dementia, the only feature that clinches the diagnosis, until the appearance of choreiform movements, is the family history.

### Prevalence

Reliable statistics of the prevalence of Huntington's Chorea are not available. Estimates vary widely from about 4 cases per 100,000 population in Michigan, U.S.A.; 5.5 in the Duchy of Cornwall and 7.2 in the county of Northamptonshire, England (30).

Basing ourselves on the number of living cases of Huntington's chorea known to us (25), the prevalence in Malta (population 317,739 in May 1966) works out at 7.8 per 100,000; but the actual figure is likely to be higher than this for the reasons already stated at the beginning of this paper. The number of cases is likely to rise as more patients will come to light with a heightened awareness of the disease among medical practitioners. The emigration of thousands of healthy individuals each year will also lead to an apparent increase in the prevalence of the disease as the affected members are left behind in Malta. Apart from these two factors, we may expect a real increase in the number of persons at risk owing to the diminished infantile mortality rate as more gene-carrying babies are destined to survive and reach adult age to develop the disease and transmit it to their offspring.

### Distribution of the Disease in Malta

The main focus of the disease is Hal Għargħur with six families; then follow Sliema with five and Qormi with three families. Naxxar, Mosta, Valletta and Senglea have two families each. Żebbuġ, Floriana, Marsa, Tarxien, Balzan, Luqa, Mqabba and Gżira possess one family each. These foci are in no way fixed for affected members of one family sometimes move to another town or village thus giving rise to a new focus in a different place. For example the descendants of the first case known to us have moved from Żurrieq to Valletta, Floriana and Marsa. The

least mobile have been the cases from Hal Għargħur perhaps because, being agriculturalists, they were tied down to the soil and because their village remained somewhat isolated from the rest of the Island until quite recent times owing to the lack of adequate transport in the past. On account of these factors Hal Għargħur remained a relatively closed community and this explains why this locality shows the biggest concentration of families. It must, however, be admitted that it has not yet been possible to find a common origin for the various affected families in this village. This may be due to the fact that owing to inadequate and incomplete information about their ancestry, the pedigrees cannot be traced as far back as the generation where linkage by marriage may have initially started.

No cases have so far been met with from Gozo.

Although there is one particular surname that occurs more frequently than any other among patients with Huntington's Chorea I have counted forty-seven other surnames of individuals that have suffered or are suffering from the disease. Five of these surnames are British but in only one instance is there the possibility that the bearer may have been responsible for importing the disease into Malta. The other British surnames are of Maltese choreic wives of normal British husbands.

**Prevention and Treatment**

There is no cure for Huntington's Chorea. Surgical treatment is ineffective and we can only hope to alleviate, by means of drugs, the hyperkinesis of the choreic variety. We have, however, no means of preventing, arresting or reversing the mental deterioration.

Among the drugs that are employed, reserpine and the phenothiazines (such as trifluoperazine and dartalan) have been found most useful in reducing the choreic movements (31).

As there is no doubt that the disease is of a hereditary nature, the only logical and effective measure to combat its spread is to prevent its propagation by carriers (i.e. eugenic control). Theoretically the only sure way of dealing with this disease and of safeguarding future generations is the sterilization of all persons vulnerable to the illness and not only of those who are already suffering from chorea. The reasons for casting this wide net are:

a) although certain personality traits, physical characters and EEG findings have been observed to herald the development of the disease, there are actually no reliable means of identifying at an early age those who harbour the gene from the non-carriers of it (32) as can be done in other genetically determined conditions such as thalassaemia minor and phenylketonuria (33);

b) although it is true that Huntington's Chorea is produced by a lethal gene, i.e. a gene that kills its own carrier, the clinical manifestations appear so late in life in the majority of cases (34) that those carrying the gene are already married and with offspring before the malady declares itself.

In practice, however, there are psychological, ethical and religious objections to sterilization which present unsurmountable obstacles to the adoption of eugenic control. On the psychological side the strongest barrier one has to face is the parental instinct, i.e. the desire of married couples of having children either because of an innate fondness for them or because of the desire to have descendants for the retention of one's own property in one's own family.

The ethical factor and the religious convictions of the patient are equally formidable hurdles to overcome and must be respected. It is needless to remind you that for Catholics direct sterilization is unlawful and immoral. But these difficulties should not breed an attitude of fatalism and nihilism. In fact affected individuals and their children should be advised against marriage and infertile couples should not be encouraged to seek treatment for their sterility.

Thanks to the outlook of the Catholic Church with regard to family limitation it is now possible to help vulnerable parents to reduce the potential number of their offspring and thus diminish the inci-

dence of the disease. The Church does not oppose the spacing of births on medical and eugenic grounds but makes it lawful from the moral angle to use the safe period for this purpose not only "for a considerable period of time" but "even for the entire duration of the marriage" (35). Today we have appropriate facilities, such as the Cana Clinics, where advice and instruction on birth regulation are available (36).

Finally a few words about the need for notification of the disease. In the past the scope of notification was the quick detection of infectious illnesses so that prompt measures could be taken to stem their advance in time. Nowadays the aim of notification has been extended to obtain information about the prevalence of non-infectious diseases such as cancer and coronary thrombosis. It is only through a similar statutory notification of Huntington's Chorea to the Public Health Authorities that we can arrive at a reasonably accurate epidemiological picture of the pattern of morbidity of this disease in the Maltese Islands. I, therefore, suggest that Huntington's Chorea be made a notifiable disease.

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*In the pedigree plans a* square *stands for a male and a* circle *for a female;* black *stands for a sufferer from the illness.*


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