

# Chorea- Diagnosis and Management

**Definition:** a continuous flow of irregular, jerky, and explosive movements, that flit from one portion of the body to another in random sequence. Each muscle contraction is brief, often appearing as a fragment of what might have been a normal movement, and quite unpredictable in timing or site. Sometimes it can occur with other movement disorders so that it is not uncommon in HD, for example, to see patients in which the chorea and dystonia merge to give the appearance of "hanging chorea". The best way to detect chorea is often to ask patients to do something and look at the limbs carefully – thus one can see finger flicking with walking and irregular movements in the arms and legs with rhythmical hand tapping tasks.

Chorea is seen in a large number of conditions (see Table), but the commonest cause outside the L-dopa treatment of PD is Huntington's disease. However there are a number of non-inherited conditions in which chorea can occur and it is important to screen for these as they may be treatable. A figure summarising the approach to chorea by age and cause is given in figure 1, with the more common causes summarised below.

**HUNTINGTON'S DISEASE (HD)** is a rare, dominantly inherited, relentlessly progressive disease, usually of middle life, characterised by chorea, cognitive decline leading to dementia and psychiatric disorders. It affects about 1 in 10,000 and is the result of an abnormal CAG triplet repeat in the gene coding for huntingtin on chromosome 4. The abnormal expansion of the CAG repeat in HD (>36 repeats) causes a new gain of function in the mutant huntingtin which leads to neuronal dysfunction and death, although the pathogenic pathway underlying this is still not fully understood. The brain is generally atrophic, with conspicuous damage to the cerebral cortex and corpus striatum, where there is loss of nerve cells and reactive gliosis without inflammatory changes associated with extensive neurotransmitter changes.

The onset is typically insidious in middle life, usually between the ages of 30 and 50 years and can be with motor, cognitive and/or psychiatric symptoms and signs. The initial symptoms are frequently those of a change in personality and behaviour, but chorea may be the first sign of the illness. At this stage the patient often retains insight, fully aware of what is in store based on their experiences with affected relatives. Serious depression is common and suicide is a risk and erratic behaviour at work or in society may lead to psychiatric referral. As the disease progresses, cognitive deficits become more pronounced and chorea more severe with walking, speech, and the use of the hands all becoming impaired. As the disease progresses, many patients develop increasing rigidity and akinesia, with reduction of the chorea. Finally the patient becomes bed-ridden with marked weight loss and death occurs on average about 15-20 years from the onset. In younger patients with juvenile HD (defined as disease onset before the age of 21 years) the patient more often presents with behavioural and cognitive problems and an akinetic-rigid parkinsonian syndrome (the Westphal variant), with epileptic fits and little in the way of chorea.

Despite the wide spectrum of clinical manifestations of Huntington's disease, the diagnosis is now straightforward with genetic testing - although this needs to be undertaken sensitively and with the help of trained geneticists.

However in some cases the characteristics of the disease are not overtly manifest and a history is not available, which can mean that the diagnosis is overlooked (see Table). This is especially the case if the family history appears negative because of the early death of the parents.

There is currently no cure for HD but drugs that target the dopaminergic striatal network can be used to treat the movement disorder, and this includes tetrabenazine and sulpiride as well as the newer atypical neuroleptic drugs such as risperidone and olanzepine. However careful consideration needs to be given as to the need to use anti-choreiform drugs as they produce side-effects and the patient is often not especially troubled by the movement disorder. In some cases though these drugs may be as useful in treating some of the psychiatric symptoms of HD as much as the movement disorder. Other drugs may also be required for their psychiatric symptoms including selective serotonin/noradrenergic reuptake inhibitors for depression and carbamazepine, lamotrigine and sodium valproate as mood stabilisers. In younger akinetic patients there may be some value in trying levo-dopa for their parkinsonian syndrome, although the benefits are often slight and poorly sustained. In all cases HD patients benefit from regular follow-up with close attention being paid to their drug therapies along with their support in the community.

More recent experimental therapies for HD have included the use of neurotrophic factors, such as ciliary neurotrophic factor (CNTF); non-specific neuroprotective therapies (e.g. co-enzyme Q) and fetal striatal neural allotransplantation. As yet the efficacy of any of these therapies remains unproven.

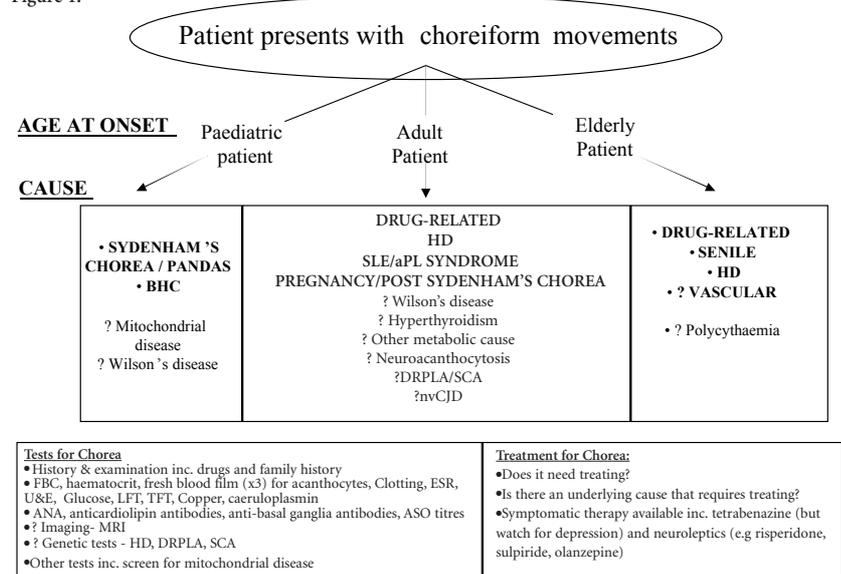
Predictive testing programmes are now available for at risk individuals, provided by a multi-disciplinary team specialised in this condition.

**SYDENHAM'S CHOREA** (St. Vitus dance) is seen as a consequence of streptococcal infection, but nowadays is part of the controversial PANDAS (Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection) which is associated with obsessive-compulsive disorders and anti basal ganglia antibodies.



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Figure 1.



Most cases of Sydenham's chorea occur between the ages of 7 and 15 years of age and are usually gradual in onset, but may be abrupt. The initial symptoms are often psychological, with irritability, agitation, disobedience, and inattentiveness with a confusional state occurring in about 10 per cent of patients. Generalised chorea then appears and may worsen for a few weeks with speech involvement although in about a fifth of cases the chorea may be predominantly unilateral, and in severe cases is accompanied by flaccidity and subjective weakness (chorea mollis). Although cardiac disease may be found, the child usually has no fever or other manifestations of rheumatic fever.

The chorea and psychological disturbance slowly recover over 1 to 3 months, rarely up to 6 months, but can recur. Those who have suffered one or more attacks of Sydenham's chorea are at particular risk of developing chorea in adult life during pregnancy (CHOREA GRAVIDARUM), or when exposed to drugs such as oral contraceptives, digoxin, or phenytoin.

Treatment is for the chorea in HD, but it is normal for the child to be given a course of antibiotics (typically penicillin) for the underlying streptococcal infection. The efficacy of immunosuppressive therapies in this and PANDAS is not known.

ANTI-CARDIOLIPIN ANTIBODIES as part of the phospholipid syndrome or SLE are also associated with chorea and are worth looking for, because if present the patient responds to anti-coagulants and immunosuppressant therapies. Other treatable causes such as THYROTOXICOSIS and POLYCYTHAEMIA are said to cause chorea and worth excluding along with other metabolic causes (see table 1). In elderly patients there is the disputed entity of SENILE CHOREA which can look like the chorea of HD, but it is not associated with other symptoms or signs and the genetic defect of HD.

Finally there are a host of other rare conditions that are worth considering, although most of these causes cannot be treated and one is left treating the chorea symptomatically.

HEMIBALLISM refers to wild flinging or throwing movements of one arm and leg and like those of chorea, are irregular in timing and force, but predominantly involve the large proximal muscles of the shoulder and pelvic girdle. They can be seen in Sydenham's chorea but more typically occur in the elderly hypertensive and/or diabetic patients as a result of a stroke involving the subthalamic nucleus, although lesions at other anatomical sites can cause this movement disorder. It may appear as the hemiplegic weakness improves with thalamic pain, although in other patients the hemiballism appears abruptly without weakness or sensory deficit and its intensity varies from mild to such a severity as to cause injury and to require treatment.

Hemiballism due to stroke usually gradually remits spontaneously over 3 to 6 months, but when treatment is needed it is typically with haloperidol or tetrabenazine although occasionally interventional neurosurgery for this condition is required and may be of benefit.

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**Table: Commonest and/or most important causes of chorea**

- Hereditary -**
  - Autosomal dominant**  
Huntington's disease  
Spinocerebellar ataxias inc. SCA3 and DPRLA
  - Autosomal recessive**  
Neuroacanthocytosis: Genetic disorder with mutations in CHAC gene on 9q21 presents typically in early adulthood with a movement disorder typically chorea and orofacial dyskinesias along with a motor neuropathy, epileptic fits, cognitive decline and psychiatric symptoms.  
Wilson's disease
  - Other**  
Mitochondrial disease  
Benign hereditary chorea (BHC); a rare condition that presents before the age of 10, gets worse over the next decade then improves and stabilises without any other neurological problems developing.
- Drug induced**  
Neuroleptics  
Anti-convulsants  
Anti-PD medication  
Oral contraceptive (often with a history of previous Sydenham's chorea)
- Toxins**  
Carbon monoxide poisoning
- Metabolic**  
Hyperthyroidism  
Pregnancy  
Hyper/Hypoglycaemia  
Electrolyte disturbances
- Infection**  
Sydenham's chorea/PANDAS  
nvCJD
- Immunological**  
Systemic Lupus Erythematosus/  
Anti-phos pholipid syndrome  
? PANDAS
- Vascular**  
Infarction  
Polycythaemia  
Post pump chorea in children: seen in children who have undergone bypass surgery with hypothermia. It normally resolves spontaneously but can persist in some cases.
- Tumours**
- Trauma**  
Cerebral palsy  
Acquired
- Age related**  
Senile chorea
- Paroxysmal**
- Psychogenic**

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