TABLE 114-7 DIFFERENTIAL DIAGNOSIS OF CHOREA

GENETIC DISORDERS	**Autosomal dominant**	Huntington's disease
		Spinocerebellar ataxia (SCA 17 >1-3)
		DRPLA
		Neuroferritinopathy
		Benign hereditary chorea
	Autosomal recessive	Neuroacanthocytosis
		Wilson's disease
		Ataxia (Friedreich's, ataxia-telangiectasia, ataxia with oculomotor apraxia)
		Disorders associated with brain iron accumulation (PKAN)
	X-linked	McLeod's syndrome
		Lesch-Nyan's syndrome
ACQUIRED/SPORADIC	**Medications**	Direct side effects
		Tardive dyskinesia
	Immune mediated	Sydenham's chorea
		Systemic lupus erythematosus
		Anti-phospholipid antibody syndrome
		Vasculitis
		Paraneoplastic (*CRMP5* gene, anti-Hu)
	Infectious	HIV/AIDS
		Variant CJD
		Neurosyphilis
	Endocrine	Hyperthyroidism
		Chorea gravidarum
	Metabolic	Hyperglycemia
		Electrolyte disturbances
		Acquired hepatocerebral degeneration
	Vascular	Basal ganglia infarcts/hemorrhage
	Miscellaneous	Polycythemia vera
		Post-cardiac bypass pump
		Multiple sclerosis
		Sporadic neurodegenerative disorders

CJD, Creutzfeld-Jakob disease; DRPLA, dentatorubropallidoluysian atrophy; PKAN, pantothenate-kinase-associated neurodegeneration; SCA, spinocerebellar ataxia.

The neuropathology of HD is characterized by selective neuronal vulnerability, particularly involving the caudate and putamen of the corpus striatum. Microscopically, the pathological hallmark of the disease is the preferential loss of medium-sized spiny neurons projecting from the striatum to the external pallidum. While HD is associated with a variety of motoric phenotypes, it remains the prototypical choreiform disorder and the most common cause of inherited adult onset chorea. In addition, HD represents one of the most important genetic disorders of adulthood. HD was the first disease recognized to arise from a trinucleotide expansion and serves as a model for the experimental therapeutics of adult-onset neurodegenerative diseases.

Huntington's Disease Phenocopies

Approximately 10% of individuals with an autosomal dominant HD-like disorder will not carry the causative mutation for HD. Among these "phenocopies," only a small minority will have an identifiable genetic mutation. The most common genetic causes in the Caucasian population include spinocerebellar ataxia (SCA) 17, Friedreich's ataxia, HD-like 2, and familial prion disease (HD-like 1). Alternative diagnoses include dentatorubropallidoluysian atrophy (DRPLA), SCA 1-3, and neuroferritonopathy. A benign form of an autosomal dominant chorea, benign familial chorea, without significant behavioral or cognitive impairment can occur.

Wilson's Disease

Wilson's disease is a rare, autosomal recessive disorder of impaired copper metabolism with copper accumulation and neurological and hepatic dysfunction. It causes heterogenous movement disorder including chorea, dystonia, Parkinsonism, and tremor; dystonia and tremor tend to predominate. Onset with movement disorder occurs in about 50% of individuals, the others presenting with liver disease. The mean age of onset is 20; it rarely occurs after the age of 40. Untreated it is invariably fatal; early treatment is associated with better clinical outcomes; therefore, a high level of suspicion should be maintained. Diagnosis is confirmed by the presence of Kayser-Fleischer corneal rings in the setting of increased urinary copper excretion or elevated copper on liver biopsy. Although ceruloplasmin is usually low in symptomatic patients, it is not definitive, and confirmatory testing with ophthalmologic screen, 24-hour urinary copper or liver biopsy is necessary. Treatment consists of drugs that facilitate copper excretion, such as zinc, trientine, tetrathiomolybdate, penicillamine (the latter falling from favor because of its toxicities).

Sydenham's Chorea

Sydenham's chorea is one of the most common causes of childhood onset chorea and is an immune complication of group A streptococcal infection. It presents acutely months after the streptococcal infection, is frequently asymmetric, and may cause behavioral symptoms in addition to chorea. Other features of rheumatic fever may also be present and echocardiography should be performed on any child with suspected Sydenham's. Treatment of the underlying infection, management of complications of rheumatic fever, and supportive care are generally sufficient with the majority of patients having resolution of symptoms by 1 year. A history of Sydenham's may predispose a female patient to adult onset chorea during pregnancy (chorea gravidarum) or in response to estrogen treatment.