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<p>The etiology of Parkinson disease (PD) is multifactorial and is likely to involve different causes in different patients. Several different genes have been identified as causes of familial PD, including <i>alpha-synuclein</i> gene mutations and multiplications, and mutations of <i>parkin</i>, <i>PINK1</i>, <i>DJ1</i>, and <i>LRKK2</i>. The biochemical consequences of these mutations have served to reinforce the relevance of the pathways to pathogenesis previously characterized, for example, mitochondrial dysfunction, oxidative stress, and protein misfolding and aggregation. The recognition that glucocerebrosidase mutations represent a significant risk factor for PD has focused attention on lysosomal function and autophagy as relevant to PD. Several environmental factors have also been shown to influence the risk for PD, although odds ratios remain relatively modest. Specific toxins can cause dopaminergic cell death in man and animals, but they probably have limited relevance to the etiology of PD.</p>	
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<p>The cardinal characteristics of Parkinson disease (PD) include resting tremor, rigidity, and bradykinesia. Patients may also develop autonomic dysfunction, cognitive changes, psychiatric symptoms, sensory complaints, and sleep disturbances. The treatment of motor and non-motor symptoms of Parkinson disease is addressed in this article.</p>	
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<p>Surgical approaches are an important consideration in the management of many movement disorders, particularly for patients refractory to medications. In this article, we review the history, pathophysiology, risks and indications for surgical treatment. Summaries of case studies, case series and clinical trials performed using deep brain stimulation are provided for Parkinson's disease, dystonia, essential tremor and other movement disorders.</p>	
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<p>Tremor is not understood completely, and pharmacotherapy for all tremor disorders is inadequate. Fortunately, deep brain stimulation is effective for</p>	

the most common and disabling tremor disorders. Our understanding of pathologic tremors has increased at an accelerating pace during the past 30 years, and this will hopefully lead to improved pharmacotherapy in the near future.

Genetics and Treatment of Dystonia

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Cordelia S. Schwarz and Susan B. Bressman

The torsion dystonias encompass a broad collection of etiologic subtypes, often divided into primary and secondary classes. Tremendous advances have been made in uncovering the genetic basis of dystonia, including discovery of a gene causing early onset primary torsion dystonia—a GAG deletion in exon 5 of the DYT1 gene that encodes torsinA. Although the exact function of torsinA remains elusive, evidence suggests aberrant localization and interaction of mutated protein; this may result in an abnormal response to stress or interference with cytoskeletal events and the development of neuronal brain pathways. Breakthroughs include the discovery of a genetic modifier that protects against clinical expression in DYT1 dystonia and the identification of the gene causing DYT6, THAP1. The authors review genetic etiologies and discuss phenotypes as well as counseling of patients regarding prognosis and progression of the disease. They also address pharmacologic and surgical treatment options for various forms of dystonia.

Huntington Disease and Other Choreas

719

Francisco Cardoso

Chorea is defined as a syndrome characterized by brief, abrupt involuntary movements resulting from a continuous flow of random muscle contractions. There are genetic and non-genetic causes of chorea. The most common genetic cause of chorea is Huntington's disease (HD). Non-genetic forms of chorea include vascular choreas, auto-immune choreas, metabolic and toxic choreas, and drug-induced choreas. This chapter provides an overview of clinical features, pathogenesis and management of HD, other important genetic causes of chorea, Sydenham's chorea, other autoimmune choreas and vascular choreas.

Tourette Syndrome

737

Joohi Jimenez-Shahed

Tourette syndrome (TS) is a neuro-developmental disorder of childhood that is often associated with various psychiatric morbidities. Timely diagnosis and appropriate management can significantly impact psychosocial functioning. Morbidities may be a major source of disability, and may determine ultimate prognosis, although most children will experience significant improvement or resolution of symptoms by adulthood. Additional management considerations must be made in those with TS symptoms persisting into adulthood. The mainstay of therapy remains dopamine receptor blocking drugs, but new therapies are emerging.

Pathophysiology and Treatment of Myoclonus 757

John N. Caviness

Myoclonus is defined as sudden, brief, shock-like, involuntary movements caused by muscular contractions or inhibitions. Etiologic classification organizes the myoclonus disorders and provides major categories of clinical presentation. However, classifying myoclonus according to its source provides insight about its pathophysiology. The best strategy for symptomatic treatment is derived from defining the pathophysiology by way of source physiologic classification.

Restless Legs Syndrome 779

William G. Ondo

Restless legs syndrome (RLS) affects many people. General population prevalence surveys usually range from 1% to 12%, but most European ancestry studies suggest 10%. The development of validated rating scales and standardized diagnostic criteria have vastly improved the quality of RLS treatment trials. Although multiple medications have shown outstanding efficacy, all of them are felt to provide only symptomatic relief, rather than any “curative” effect. Dopamine agonists are clearly the best investigated and probably the most effective treatments for RLS.

Psychogenic Movement Disorders 801

Elizabeth L. Peckham and Mark Hallett

Psychogenic movement disorders (PMDs) represent a challenging dilemma for the treating neurologist. The terminology to classify this disorder is confusing and making the diagnosis is difficult. Once the diagnosis has been established, treatment options are limited, and the patient generally does not accept the diagnosis.

Peripherally Induced Movement Disorders 821

Joseph Jankovic

Peripherally induced movement disorders may be defined as involuntary or abnormal movements triggered by trauma to the cranial or peripheral nerves or roots. Although patients often recall some history of trauma before the onset of a movement disorder, determining the true relationship of the disorder to the earlier trauma is often difficult. The pathophysiology of these disorders is reviewed.

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