Chorea may also occur in association with vascular diseases, hypo- and hyperglycemia, and a variety of infections and degenerative disorders. Systemic lupus erythematosus is the most common systemic disorder that causes chorea, which can last for days to years. Chorea can also be seen with hyperthyroidism, autoimmune disorders including Sjögren's syndrome, infectious disorders including HIV disease, metabolic alterations, and polycythemia rubra vera; following open-heart surgery in the pediatric population; and in association with many medications (especially anticonvulsants, cocaine, CNS stimulants, estrogens, and lithium). Chorea is commonly seen in association with chronic levodopa treatment (discussed in the section on PD above). Chorea can also be seen in paraneoplastic syndromes associated with anti-CRMP-5 or anti-Hu antibodies (Chap. 122).

HEMIBALLISMUS

Hemiballismus is a violent form of chorea comprised of wild, flinging, large-amplitude movements on one side of the body. Proximal limb muscles tend to be predominantly affected. These movements may affect just one limb (monoballism) or, more exceptionally, both upper or lower limbs (paraballism). The movements may be so severe as to cause exhaustion, dehydration, local injury, and, in extreme cases, death. Fortunately, dopamine-blocking drugs can be very helpful, and importantly, hemiballismus is usually self-limiting and tends to resolve spontaneously after weeks or months. The most common cause is a partial lesion (infarct or hemorrhage) in the STN, but cases can also be seen with lesions in the putamen, thalamus, and parietal cortex. In extreme cases, pallidotomy can be very effective. Interestingly, surgically induced lesions and DBS of the STN in PD patients are usually not associated with hemiballismus.

TICS

A *tic* is a brief, rapid, recurrent, and seemingly purposeless stereotyped motor contraction. Motor tics can be simple, with movement only affecting an individual muscle group (e.g., blinking, twitching of the nose, jerking of the neck), or complex, with coordinated involvement of multiple muscle groups (e.g., jumping, sniffing, head banging, and echopraxia [mimicking movements]). Phonic (or vocal) tics can also be simple (e.g., grunting) or complex (e.g., echolalia [repeating other people's words], palilalia [repeating one's own words], and coprolalia [expression of obscene words]). Patients may also experience sensory tics, composed of unpleasant focal sensations in the face, head, or neck. These can be mild and of little clinical consequence or severe and disabling to the patient.

TOURETTE'S SYNDROME (TS)

TS is a neurobehavioral disorder named after the French neurologist Georges Gilles de la Tourette. It predominantly affects males, and the prevalence is estimated to be 0.03–1.6%, but it is likely that many mild cases do not come to medical attention. TS is characterized by multiple motor tics often accompanied by vocalizations (phonic tics). Patients characteristically can voluntarily suppress tics for short periods of time, but then experience an irresistible urge to express them. Tics vary in intensity and may be absent for days or weeks only to recur, occasionally in a different pattern. Tics tend to present between ages 2 and 15 years (mean 7 years) and often lessen or even disappear in adulthood. Associated behavioral disturbances include anxiety, depression, attention deficit hyperactivity disorder, and obsessive-compulsive disorder. Patients may experience personality disorders, self-destructive behaviors, difficulties in school, and impaired interpersonal relationships. Tics may present in adulthood and can also be seen in association with a variety of other disorders, including PD, HD, trauma, dystonia, drugs (e.g., levodopa, neuroleptics), and toxins.

Etiology and Pathophysiology TS is thought to be a genetic disorder, but no specific gene mutation has been identified. Current evidence supports a complex inheritance pattern, with one or more major genes, multiple loci, low penetrance, and environmental influences. The risk of a family with one affected child having a second is about 25%. The pathophysiology of TS is not known, but alterations in dopamine neurotransmission, opioids, and second-messenger systems have been proposed. Some cases of TS may be the consequence of an autoimmune response to β-hemolytic streptococcal infection (pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection [PANDAS]); however, this entity remains controversial.

TREATMENT TOURETTE'S SYNDROME

Patients with mild disease often only require education and counseling (for themselves and family members). Drug treatment is indicated when the tics are disabling and interfere with quality of life. Therapy is individualized, and there is no singular treatment regimen that has been properly evaluated in double-blind trials. Some physicians use the α-agonist clonidine, starting at low doses and gradually increasing the dose and frequency until satisfactory control is achieved. Guanfacine (0.5–2 mg/d) is an α-agonist that is preferred by some because it only requires once-a-day dosing. Other physicians prefer to use neuroleptics. Atypical neuroleptics are usually used initially (risperidone, olanzapine, ziprasidone) because they are thought to be associated with a reduced risk of tardive dyskinesia. If they are not effective, low doses of classical neuroleptics such as haloperidol, fluphenazine, pimozide, or tiapride can be tried because the risk of tardive dyskinesia in young people is relatively low. Botulinum toxin injections can be effective in controlling focal tics that involve small muscle groups. Behavioral features, and particularly anxiety and compulsions, can be a disabling feature of TS and should be treated. The potential value of DBS targeting the anterior portion of the internal capsule, the GPi, or the thalamus is currently being explored.

MYOCLONUS

Myoclonus is a brief, rapid (<100 ms), shock-like, jerky movement consisting of single or repetitive muscle discharges. Myoclonic jerks can be focal, multifocal, segmental, or generalized and can occur spontaneously, in association with voluntary movement (action myoclonus) or in response to an external stimulus (reflex or startle myoclonus). Negative myoclonus consists of a brief loss of muscle activity (e.g., asterixis in hepatic failure). Myoclonic jerks can be severe and interfere with normal movement or benign and of no clinical consequence as is commonly observed in normal people when waking up or falling asleep (hypnogogic jerks).

Myoclonic jerks differ from tics in that they are not typically repetitive, can interfere with normal voluntary movement, and are not suppressible. They can arise in association with abnormal neuronal discharges in cortical, subcortical, brainstem, or spinal cord regions and can be associated with lesions in each of these regions, particularly in association with hypoxemia (especially following cardiac arrest), encephalopathy, and neurodegeneration. Reversible myoclonus can be seen with metabolic disturbances (renal failure, electrolyte imbalance, hypocalcemia), toxins, and many medications. Essential myoclonus is a relatively benign familial condition characterized by multifocal, very brief, lightning-like movements that are frequently alcohol sensitive. A mutation in the epsilon-sarcoglycan gene has been associated with a variety of myoclonus seen in association with dystonia (myoclonic dystonia).

TREATMENT MYOCLONUS

Treatment primarily consists of managing the underlying condition or removing an offending agent. Pharmacologic therapy involves one or a combination of GABAergic agents such as valproic acid (800–3000 mg/d), piracetam (8–20 g/d), clonazepam (2–15 mg/d), levetiracetam (1000–3000 mg/d), or primidone (500–1000 mg/d) and may be associated with striking clinical improvement in chronic cases (e.g., postanoxic myoclonus, progressive myoclonic epilepsy). The serotonin precursor 5-hydroxitriptophan (plus carbidopa) may be useful in some cases of postanoxic myoclonus.