within the medulla of the brainstem (Fig. 42-5). From the NTS, neurons then project to a division of the ventroposteromedial thalamic nucleus (VPM) via the medial lemniscus. From here, projections are made to the rostral part of the frontal operculum and adjoining insula, a brain region considered the *primary taste cortex* (PTC). Projections from the PTC then go to the *secondary taste cortex*, namely the caudolateral OFC. This brain region is involved in the conscious recognition of taste qualities. Moreover, because it contains cells that are activated by several sensory modalities, it is likely a center for establishing "flavor."

DISORDERS OF OLFACTION

The ability to smell is influenced, in everyday life, by such factors as age, gender, general health, nutrition, smoking, and reproductive state. Women typically outperform men on tests of olfactory function and retain normal smell function to a later age than do men. Significant decrements in the ability to smell are present in over 50% of the population between 65 and 80 years of age and in 75% of those 80 years of age and older (Fig. 42-6). Such presbyosmia helps to explain why many elderly report that food has little flavor, a problem that can result in nutritional disturbances. This also helps to explain why a disproportionate number of elderly die in accidental gas poisonings. A relatively complete listing of conditions and disorders that have been associated with olfactory dysfunction is presented in Table 42-1.

Aside from aging, the three most common identifiable causes of long-lasting or permanent smell loss seen in the clinic are, in order of frequency, severe upper respiratory infections, head trauma, and chronic rhinosinusitis. The physiologic basis for most head trauma–related losses is the shearing and subsequent scarring of the olfactory fila as they pass from the nasal cavity into the brain cavity. The cribriform plate does not have to be fractured or show pathology for smell loss to be present. Severity of trauma, as indexed by a poor Glasgow Coma Scale score on presentation and the length of posttraumatic amnesia, is associated with higher risk of olfactory impairment. Less than 10% of posttraumatic anosmic patients will recover age-related normal function over time. This increases to nearly 25% of those with less-than-total loss. Upper respiratory infections, such as those associated with the common cold, influenza, pneumonia, or HIV, can directly and permanently harm the olfactory epithelium by decreasing receptor cell number, damaging cilia on remaining receptor cells, and inducing the replacement of sensory epithelium with respiratory epithelium. The smell loss associated with chronic rhinosinusitis is related to disease severity, with most loss occurring in cases where rhinosinusitis and polyposis are both present. Although systemic glucocorticoid therapy can usually induce short-term functional improvement, it does not, on average, return smell test scores to normal, implying that chronic permanent neural loss is present and/or that short-term administration of systemic glucocorticoids does not completely mitigate the inflammation. It is well established that microinflammation in an otherwise seemingly normal epithelium can influence smell function.

A number of neurodegenerative diseases are accompanied by olfactory impairment, including PD, AD, Huntington's disease, Down's syndrome, parkinsonism-dementia complex of Guam, dementia with Lewy bodies (DLB), multiple system atrophy, corticobasal degeneration, and frontotemporal dementia; smell loss can also occur in multiple sclerosis (MS) and idiopathic rapid eye movement (REM) behavioral sleep disorder (iRBD). Olfactory impairment in PD often predates the clinical diagnosis by at least 4 years. In staged cases, studies of the sequence of formation of abnormal α-synuclein aggregates and Lewy bodies suggest that the olfactory bulbs may be, along with the dorsomotor nucleus of the vagus, the first site of neural damage

TABLE 42-1 DISORDERS AND CONDITIONS ASSOCIATED WITH COMPROMISED OLFACTORY FUNCTION, AS MEASURED BY OLFACTORY TESTING

22q11 deletion syndrome	Liver disease
AIDS/HIV infection	Lubag disease
Adenoid hypertrophy	Medications
Adrenal cortical insufficiency	Migraine
Age	Multiple sclerosis
Alcoholism	Multi-infarct dementia
Allergies	Myasthenia gravis
Alzheimer's disease	Narcolepsy with cataplexy
Amyotrophic lateral sclerosis (ALS)	Neoplasms, cranial/nasal
Anorexia nervosa	Nutritional deficiencies
Asperger's syndrome	Obstructive pulmonary disease
Ataxias	Obesity
Attention deficit/hyperactivity disorder	Obsessive compulsive disorder
Bardet-Biedl syndrome	Orthostatic tremor
Chagas' disease	Panic disorder
Chemical exposure	Parkinson's disease (PD)
Chronic obstructive pulmonary disease	Pick's disease
Congenital	Posttraumatic stress disorder
Cushing's syndrome	Pregnancy
Cystic fibrosis	Pseudohypoparathyroidism
Degenerative ataxias	Psychopathy
Diabetes	Radiation (therapeutic, cranial)
Down's syndrome	REM behavior disorder
Epilepsy	Refsum's disease
Facial paralysis	Renal failure/end-stage kidney disease
Frontotemporal lobe degeneration	Restless leg syndrome
Gonadal dysgenesis (Turner's syndrome)	Rhinosinusitis/polyposis
Guamanian ALS/PD/dementia syndrome	Schizophrenia
Head trauma	Seasonal affective disorder
Herpes simplex encephalitis	Sjögren's syndrome
Hypothyroidism	Stroke
Huntington's disease	Tobacco smoking
Iatrogenesis	Toxic chemical exposure
Kallmann's syndrome	Upper respiratory infections
Korsakoff's psychosis	Usher syndrome
Leprosy	Vitamin B_{12} deficiency

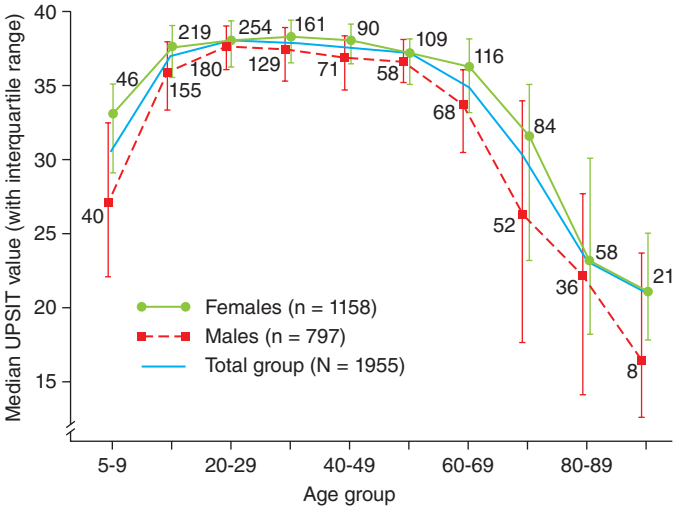

FIGURE 42-6 Scores on the University of Pennsylvania Smell Identification Test (UPSIT) as a function of subject age and sex. Numbers by each data point indicate sample sizes. Note that women identify odorants better than men at all ages. *(From RL Doty et al: Science 226:1421, 1984. Copyright © 1984 American Association for the Advancement of Science.)*