Autonomic Nervous system

The autonomic nervous system (ANS) regulates physiologic processes. Regulation occurs without conscious control, ie, autonomously. The 2 major divisions are the sympathetic and parasympathetic systems.

Disorders of the ANS can affect any system of the body. They can originate in the peripheral or central nervous system and may be primary or secondary to other disorders.

Anatomy

The sympathetic and parasympathetic systems each consist of 2 sets of nerve bodies: one set (called preganglionic) in the CNS, with connections to another set in ganglia outside the CNS. Efferent fibers from the ganglia (postganglionic fibers) lead to effector organs.

The preganglionic cell bodies of the sympathetic system are located in the intermediolateral horn of the spinal cord between T1 and L2 or L3. The sympathetic ganglia are adjacent to the spine and consist of the vertebral (sympathetic chain) and prevertebral ganglia, including the superior cervical, celiac, superior mesenteric, and aorticorenal ganglia. Long fibers run from these ganglia to effector organs, including the smooth muscle of blood vessels, viscera, lungs, scalp (piloerector muscles), and pupils; the heart; and glands (sweat, salivary, and digestive).

The preganglionic cell bodies of the parasympathetic system are located in the brain stem and sacral portion of the spinal cord. Preganglionic fibers exit the brain stem with the 3rd, 7th, 9th, and 10th (vagus) cranial nerves; the vagus nerve contains about 75% of all parasympathetic fibers. Parasympathetic ganglia are located within the effector organs, and postganglionic fibers are only 1 or 2 mm long. Thus, the parasympathetic system can produce specific, localized responses in effector organs, including blood vessels of the head, neck, and thoracoabdominal viscera; lacrimal and salivary glands; smooth muscle of viscera and glands (eg, liver, spleen, colon, kidneys, bladder, genitals); and ocular muscles.

The ANS receives input from parts of the CNS that process and integrate stimuli from the body and external environment. These parts include the hypothalamus, nucleus of the solitary tract, reticular formation, amygdala, hippocampus, and olfactory cortex.

Physiology

The ANS controls BP, heart rate, body temperature, weight, digestion, metabolism, fluid and electrolyte balance, sweating, urination, defecation, sexual response, and other processes. Many organs are controlled primarily by either the sympathetic or parasympathetic system, although they may receive input from both; occasionally, functions are reciprocal (eg, sympathetic input increases heart rate; parasympathetic decreases it).

The sympathetic nervous system is catabolic and activates fight-or-flight responses. Thus, sympathetic output increases heart rate and contractility, bronchodilation, hepatic glycogenolysis and glucose release, BMR, and muscular strength; it also causes sweaty palms. Less immediately life-preserving functions (eg, digestion, renal filtration) are decreased. Ejaculation is a sympathetic function.

The parasympathetic nervous system is anabolic; it conserves and restores. GI secretions and motility (including evacuation) are stimulated, heart rate is slowed, and BP decreases. Erection is a parasympathetic function.

Two major neurotransmitters in the ANS are acetylcholine and norepinephrine. Fibers that secrete acetylcholine are termed cholinergic; they include all preganglionic fibers and all postganglionic

parasympathetic fibers. Fibers that secrete norepinephrine are termed adrenergic; they include most postganglionic sympathetic fibers, except for those that innervate piloerectors, sweat glands, and blood vessels, which are cholinergic. However, sweat glands on the palms and soles also respond to adrenergic stimulation to some degree. There are different subtypes of adrenergic (and cholinergic receptors, varying by location.

Evaluation

History

Symptoms suggesting autonomic dysfunction include orthostatic hypotension, heat intolerance, and loss of bladder and bowel control. Erectile dysfunction is an early symptom. Other possible symptoms include dry eyes and dry mouth, but they are nonspecific.

Physical examination

In a normally hydrated patient, a sustained decrease of > 20 mm Hg in systolic BP or a decrease of > 10 mm Hg in diastolic BP with standing suggests autonomic dysfunction. Heart rate change with respiration and standing should be noted; absence of physiologic sinus arrhythmia and failure of heart rate to increase with standing indicate autonomic dysfunction.

Miosis and mild ptosis (Horner's syndrome) suggest a sympathetic lesion. A dilated, unreactive pupil (Adie's pupil) suggests a parasympathetic lesion.

Abnormal GU and rectal reflexes may indicate ANS deficits. Testing includes the cremasteric reflex (normally, stroking the thigh results in retraction of the testes), anal wink reflex (normally, stroking perianal skin results in contraction of the anal sphincter), and bulbocavernosus reflex (normally, squeezing the glans penis or clitoris results in contraction of the anal sphincter).

Laboratory testing

If patients have symptoms and signs suggesting autonomic dysfunction, sudomotor, cardiovagal, and adrenergic tests are usually done to help determine severity and distribution of the dysfunction.

The quantitative sudomotor axon-reflex test evaluates integrity of postganglionic neurons using iontophoresis; electrodes filled with acetylcholine are placed on the legs and wrist to stimulate sweat glands, and the volume of sweat is then measured. The test can detect decreased, absent, or persistent (after stimulus discontinuation) sweat production. The thermoregulatory sweat test evaluates both preganglionic and postganglionic pathways. After a dye is applied to the skin, patients enter a closed compartment that is heated to cause maximal sweating. Sweating causes the dye to change color, so that areas of anhidrosis and hypohidrosis are apparent and can be calculated as a percentage of BSA.

Cardiovagal testing evaluates heart rate response (via ECG rhythm strip) to deep breathing and to the Valsalva maneuver. If the ANS is intact, heart rate varies with these maneuvers; the ratio of longest to shortest R-R interval (Valsalva ratio) should be ≥ 1.4.

Adrenergic testing evaluates response of beat-to-beat BP to the head-up tilt and Valsalva maneuver. The head-up tilt shifts blood to dependent parts, causing reflex responses. The Valsalva maneuver increases intrathoracic pressure and reduces venous return, causing BP changes and reflex vasoconstriction. In both tests, the pattern of responses is an index of adrenergic function.

Horner's Syndrome

Horner's syndrome is ptosis, miosis, and anhidrosis due to dysfunction of cervical sympathetic output.

Horner's syndrome results when the cervical sympathetic pathway running from the hypothalamus to the eye is disrupted. The syndrome may be central, preganglionic, or postganglionic in origin; it may

be primary or secondary to another disorder. Central lesions include brain stem ischemia, syringomyelia, and brain tumor; peripheral lesions include Pancoast tumor, cervical adenopathy, neck and skull injuries, aortic or carotid dissection, and thoracic aortic aneurysm. A congenital form exists.

Symptoms include ptosis, miosis, anhidrosis, and hyperemia of the affected side. In the congenital form, the iris does not become pigmented and remains blue-gray. Liquid cocaine 10% can be applied to the affected eye; poor pupillary dilation after 30 min indicates Horner's syndrome. If results are positive, 1% hydroxyamphetamine solution or 5% n-methyl hydroxyamphetamine can be applied to the eye 48 h later to determine whether the lesion is preganglionic (if the pupil dilates) or postganglionic (if the pupil does not dilate). Patients with Horner's syndrome require MRI or CT of the brain, spinal cord, chest, or neck, depending on clinical suspicion.

Any identifiable causes are treated; there is no treatment for primary Horner's syndrome.

Migraine

Migraine is a chronic, episodic primary headache. Symptoms typically last 4 to 72 h and may be severe. Pain is often but not always unilateral, throbbing, worse with exertion, and accompanied by autonomic symptoms (eg, nausea; sensitivity to light, sound, or odors). Fortification spectra and other transient focal neurologic deficits occur in a few patients, usually just before the headache. Diagnosis is clinical. Treatment is with serotonin 1B,1D receptor agonists, antiemetics, and analgesics. Preventive regimens include lifestyle modifications (eg, of sleeping habits or diet) and drugs (eg, β-blockers, amitriptyline, valproate, topiramate).

Epidemiology and Pathophysiology

Migraine is the most common cause of recurrent moderate to severe headache; lifetime prevalence is 18% for women and 6% for men in the US. It most commonly begins during puberty or young adulthood, waxing and waning in frequency and severity over the ensuing years and usually diminishing after age 50. Studies show familial aggregation of migraine.

Migraine is thought to be a neurovascular pain syndrome with altered central neuronal processing (activation of brain stem nuclei, cortical hyperexcitability, and spreading cortical depression) and involvement of the trigeminovascular system (triggering neuropeptide release, which produces painful inflammation in cranial vessels and the dura mater).

The triggering mechanism for specific attacks is often unclear. However, many potential migraine triggers have been identified; they include drinking red wine, skipping meals, excessive afferent stimuli (eg, flashing lights, strong odors), weather changes, sleep deprivation, stress, and hormonal factors. Head trauma, neck pain, or temporomandibular joint dysfunction sometimes triggers or exacerbates migraine.

Fluctuating estrogen levels are a potent migraine trigger. Many women have onset of migraine at menarche, severe attacks during menstruation (menstrual migraine), and worsening during menopause. For most women, migraines remit during pregnancy (but sometimes there is an exacerbation during the 1st or 2nd trimester). Oral contraceptives and other hormone therapy occasionally trigger or worsen migraine and have been associated with stroke in women who have migraine with aura.

Symptoms and Signs

In some patients, some migraine attacks are preceded or accompanied by a neurologic aura (prodrome) lasting minutes to an hour (migraine with aura). Most commonly, auras involve visual symptoms

(fortification spectra—eg, binocular flashes, arcs of scintillating lights, bright zigzags, scotomata). Paresthesias and numbness (typically starting in one hand and marching to the ipsilateral arm and face), speech disturbances, and transient brain stem–thalamic dysfunction are less common than visual auras. Some patients have attacks of migraine aura with little or no headache.

Pain varies from moderate to severe, and attacks last from hours to days, typically resolving with sleep. The pain can be bilateral or unilateral, most often in a frontotemporal distribution, and is described as aching, squeezing, or sometimes throbbing.

Migraine is more than a headache. Autonomic symptoms such as nausea (and occasionally vomiting), photophobia, sonophobia, and osmophobia are prominent. Patients report difficulty concentrating during attacks. Routine physical activity usually aggravates migraine headache; this effect, plus the photophobia and sonophobia, encourages most patients to lie in a dark, quiet room during attacks. Severe attacks can be incapacitating, disrupting family and work life.

Attacks vary significantly in frequency and severity. Many patients have several types of headache, including milder attacks without nausea or photophobia; these attacks may resemble tension headache.

Rare forms of migraine include basilar artery migraine, with combinations of vertigo, ataxia, visual field loss, sensory disturbances, focal weakness, and altered level of consciousness. Abdominal migraine (periodic syndrome), which affects children with a family history of migraine, is characterized by 2-h bouts of abdominal pain, flushing or pallor, nausea, and vomiting. These children often develop typical migraines later in life.

Diagnosis

Diagnosis is based on characteristic symptoms and a normal physical (including neurologic) examination. Typical cases without worrisome findings do not require CNS imaging.

Common diagnostic errors include not realizing that migraine often causes bilateral pain and is not always described as throbbing. Autonomic and visual symptoms of migraine often lead to a misdiagnosis of sinus headache or eyestrain. A dangerous error is to assume that any headache in patients known to have migraine represents another migraine attack. A thunderclap headache or change in the previous headache pattern may indicate a new, potentially serious disorder.

In older patients, migraine with aura can be mistaken for a transient ischemic attack, especially when the aura occurs without headache. In younger patients, several unusual disorders can mimic migraine with aura: dissection of the carotid or vertebral artery, antiphospholipid antibody syndrome, cerebral vasculitis, moyamoya disease, CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), and MELAS (mitochondrial encephalopathy, lactic acidosis, and strokelike episodes) syndrome.

Prognosis and Treatment

For some patients, migraine is an infrequent, tolerable inconvenience. For others, it is a devastating malady resulting in frequent periods of incapacity, loss of productivity, and severely impaired quality of life. Consequently, treatment is stratified based on frequency, duration, and severity of attacks. A thorough explanation of the disorder helps patients understand that although migraine cannot be cured, it can be controlled, enabling them to better participate in treatment.

Patients are urged to keep a written headache diary to document the number and timing of attacks, possible triggers, and response to treatment. Identified triggers are eliminated when possible (see also

the practice guideline for patient education concerning treatment of primary headache from the National Headache Foundation). Behavioral interventions (biofeedback, stress management, psychotherapy) are used when stress is a major trigger or when analgesics are being overused.

Acute migraine headache

(See also the practice guideline for the treatment of acute migraine headache from the National Headache Foundation.) Mild to moderate attacks are treated with NSAIDs or acetaminophen. Analgesics containing opioids, caffeine, or butalbital are helpful for infrequent, mild attacks but are prone to being overused, sometimes leading to rebound headache and daily headache syndrome.

In patients whose mild attacks often evolve into incapacitating migraine or whose attacks are severe from the onset, triptans are used. Triptans are selective serotonin 1B,1D receptor agonists. They are not analgesic per se but specifically block the release of vasoactive neuropeptides that trigger migraine pain. Triptans are most effective when taken at the onset of attacks. They are available in oral, intranasal, and sc forms ; sc forms are more effective but have more adverse effects. Combining a triptan with an antiemetic at the onset of attacks is effective when nausea is prominent.

IV dihydroergotamine with a dopamine antagonist antiemetic (eg, metoclopramide 10 mg IV, prochlorperazine 5 to 10 mg IV) is helpful for aborting very severe, persistent attacks. The antiemetic alone may relieve mild attacks.

Triptans and dihydroergotamine can cause coronary artery constriction and are thus contraindicated in patients with coronary artery disease or uncontrolled hypertension; they must be used with caution in older patients and in patients with vascular risk factors.

A good response to dihydroergotamine or a triptan should not be interpreted as diagnostic for migraine because these drugs may relieve headache due to subarachnoid hemorrhage and other structural abnormalities.

Opioids should be a last resort (rescue drug) for severe headache when other measures are ineffective.

Prevention

(See also the practice guideline for the preventive treatment of migraine headache from the National Headache Foundation.) Daily preventive therapy is warranted when frequent migraines interfere with activity despite acute treatment. For patients who use analgesics frequently, particularly those with rebound headache, preventive drugs should be combined with a program for stopping overused analgesics. Choice of drug can be guided by coexisting disorders: eg, a small bedtime dose of amitriptyline for patients with depression or insomnia; a β-blocker for patients with hypertension or coronary artery disease; or topiramate, which can induce weight loss, for obese patients.

Periodic injections of small doses of botulinum toxin into the scalp reduces the number and severity of migraine attacks in some patients unresponsive to other preventive treatments.