Paparella: Volume I: Basic Sciences and Related Principles

Section 9: Otolaryngologic Manifestations of Systemic Diseases and Pain

Chapter 40: Otolaryngologic Manifestations of Systemic Disease

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Of significant concern to otolaryngologists are those patients who present with complaints referable to lesions of the head and neck and in whom these lesions represent the first or the most obvious manifestation of systemic disease. This chapter will discuss various groups of illnesses and describe representative specific entities for each group.

Dermatologic Disorders

Dermatologic disorders with otolaryngologic components include pemphigus, pemphigoid, systemic lupus erythematosus, lichen planus, and Behçet's syndrome. These dermatologic disorders can present initially and primarily in the head and neck. Each could also be classed as an autoimmune disease in accord with current pathophysiologic information.

Pemphigus and pemphigoid are vesiculobullous disorders. Because of nonkeratinized epithelium and chronic masticatory forces, oral vesicles and bullae are likely to rupture before a physician ever sees them. In both disorders the epithelium consistently separates and fluid accumulates in a certain plane, leading to reliable diagnosis by biopsy. In pemphigus the epithelium displays a suprabasal cleft, but in pemphigoid the bullae are subepithelial.

Pemphigus can be divided into four types - vulgaris, vegetans, foliaceus, and erythematosus. All are characterized by intraepithelial bullae with autoantibodies to the intercellular cement substance of stratified squamous epithelium. Acantholysis is prominent and diagnostic. Most commonly the vulgaris type involves the head and neck.

Pemphigus vulgaris occurs in those between 30 and 70 years of age. The incidence is equal between sexes, but there is a predominance in those of Jewish, southern European, and Mediterranean extraction. There is an association with lupus erythematosus, myasthenia gravis, both Hodgkin's and non-Hodgkin's lymphoma, leukemia, and penicillamine treatment.

Onset is insidious, occurring in the mouth in more than 50 per cent of patients. The eruption might be confined to the mouth for months and cause pain, especially with chewing or swallowing. Lesions most commonly develop on the lips but can also be found over the buccal mucosa and gingiva, and even extend into the esophagus. They occur without an erythematous base and rapidly become erosions that bleed easily. Salivation is copious.

Skin lesions are painful and crusted, appearing in areas of friction or trauma. Bullae are ordinarily thin, tense, and round, enlarging at the edges. Rupture leaves a hemorrhagic crust with epidermal tags. Healing is slow. Nikolsky's sign can be elicited on normal skin adjacent to a lesion by pushing sideways. A flaccid bulla without fluid then appears.

Without treatment the course is fatal as a result of dehydration and sepsis. Treatment involves high-dose prednisone, more than 100 mg/day, and is adjusted according to response. In refractory cases chemotherapy might be required.

Pemphigoid is usually classed either as bullous or cicatricial. Bullous pemphigoid is a disease in those over the age of 70. There is an association with pemphigus, lupus erythematosus, pernicious anemia, nonlymphogenic malignancies, and ultraviolet light, and with the administration of penicillin, 5-fluorouracil, benzyl benzoate, Lasix, or oral hypoglycemics. The onset is generally rapid, beginning as a localized asymmetric lesion, initially on the forearm, wrists, or inner thighs, spreading in several weeks to buccal mucosa in 30 to 50 per cent of patients. The extensive labial involvement seen in pemphigus is not present. The bullae are subepithelial, and treatment is with steroids and local hygiene. The duration and dosage of steroids are lower for pemphigoid than for pemphigus.

Cicatricial pemphigoid affects mucosa more severely than the bullous form of the disease. The mouth is the most common site, with the gingiva first affected, often as a desquamative gingivitis. Some of the bullae rupture, leaving tender, bright red, slow-healing erosions over the gingiva, buccal mucosa, palate, tongue, and floor of mouth. With healing comes scarring and adhesions, occasionally so severe as to cause oral stenosis or a pharyngeal web. Laryngeal stenosis can also occur, requiring tracheotomy.

Systemic lupus erythematosus can present with the characteristic bimalar, or butterfly, rash. The typical rash extends across the nose from cheek to cheek, but can be restricted to the nasal dorsum; it erupts after sunlight exposure and is seen in 50 per cent of patients. The affected nose is dry and crusted, and might have an anterior septal perforation. Oral lesions can occur on the buccal mucosa and lateral tongue. Diagnosis is made by biopsy and associated symptoms. Blood studies should include tests for antinuclear and antidouble-stranded DNA antibodies.

Lichen planus presents as a fine, white, reticular pattern, characteristically on the lateral border of the tongue. It can be accompanied by burning pain, which prompts the patient to seek medical assistance. The lesions are distinguished from those of moniliasis by the lack of confluent white patches. Buccal lesions mimic those of Fordyce's condition (ie punctate pale yellow to white discoloration of the posterior buccal mucosa produced by the sebaceous glands, a common finding). Atypical lesions should be biopsied to exclude squamous cell carcinoma or premalignant epithelial conditions.

Behçet's disease is diagnosed by the clinical findings of aphthous ulcers of the mouth, genitals, and conjunctiva. Steroids have been tried, with varying degrees of success.

Immunologic and Granulomatous Disorders

Immunologic and granulomatous conditions with otolaryngologic features include AIDS, rheumatoid arthritis, sarcoidosis, dermatomyositis, relapsing polychondritis, Cogan's syndrome, polyarteritis nodosa, Churg-Strauss syndrome, polymorphic reticulosis, and Wegener's granulomatosis.

Acquired immunodeficiency syndrome (AIDS) is covered in depth elsewhere in this book. The finding of oral or esophageal candidiasis in an otherwise healthy young adult who has not been taking antibiotics and is not known to be immunosuppressed, either by medication or systemic malignancy, strongly suggests AIDS. AIDS also should be suspected in the patient with a viral sore throat that persists, with persistent unexplained cervical adenopathy, and with purple lesions of the palate, which might be Kaposi's sarcoma. It can occur in children, manifesting as recurrently infected sinuses or ears. Laboratory tests including white blood, differential, and platelet counts can uncover uncommon disorders, such as Wiskott-Aldrich syndrome or ataxia-telangiectasia.

Rheumatoid arthritis can involve any synovial joint of the head and neck. Cricoarytenoid arthritis produces hoarseness, and affected arytenoid cartilages appear cherry red in color. This disorder ultimately progresses to ankylosis of the arytenoids. These patients can be intubation hazards, either during acute inflammation or chronic ankylosis. Rheumatoid disruption of the cervical spine threatens atlanto-occipital subluxation during neck extension. Rheumatoid arthritis and amyloidosis both produce subepithelial hyaline deposits that are identifiable by biopsy.

Sarcoidosis is an autoimmune disorder of unknown cause that produces noncaseating granulomas, hypercalcemia, and elevated angiotensin converting enzyme levels. It is a multiorgan disease; above the clavicles it affects the larynx, midface, skin, eyes, and salivary and lacrimal glands. Laryngeal sarcoidosis distorts the epiglottis into a pale, turban shape. Biopsy reveals Schaumann's bodies and asteroids. Heerfordt's syndrome is uveitis with parotid enlargement caused by sarcoidosis. Sarcoidosis of the eye can produce bilateral lacrimal gland enlargement, ultimately leading to dry eyes. In addition, granulomatous uveitis from sarcoidosis is occasionally associated with disequilibrium suggestive of inner ear involvement. Sarcoidosis of the nose and paranasal sinuses results in nasal obstruction and possibly sinusitis. The turbinates appear cobblestoned and enlarged. A distinctive feature of this disease is the failure of the turbinates to decrease in size following application of topical cocaine. One way that a sarcoid patient encounters the otolaryngologist is by referral from the pulmonologist who requests a turbinate biopsy. It is generally believed that two anatomically separate biopsy sites, both showing noncaseating granulomas, are needed to secure the diagnosis. Gallium scanning is diffusely and characteristically positive in involved organs.

Dermatomyositis manifests as a heliotrope-colored facial rash. Dysphagia occurs in at least 50 per cent of patients with this disorder, which affects striated muscle. Laryngeal disease results in aspiration and dysphonia. The true vocal cords are bowed, the arytenoids tip anteriorly, and the vocal processes project into the glottis, creating a keyhole configuration of the glottis. There

is potential for underlying occult malignancy in both dermatomyositis and polymyositis. Scleroderma and systemic lupus erythematosus affect smooth muscle preferentially and produce dysphagia, in this case resulting from dysmotility of the lower esophagus.

Relapsing polychondritis is an autoimmune disorder affecting any cartilage, but most prominently that of the nose and auricle of the external ear. Notably, the ear lobule is spared because it lacks cartilage. Other head and neck sites include the trachea, larynx, and eustachian tubes. Aspirin, steroids, cancer chemotherapy, and dapsone have been used with varying degrees of success. Relapsing polychondritis, sarcoidosis, and Wegener's granulomatosis are three potential sources of subglottic stenosis in an adult with no other demonstrable cause.

Cogan's syndrome is a vasculitis that produces deafness and dizziness, nonsyphilitic interstitial keratitis, and aortic valvular disease in the unfortunate minority of patients.

Sjögren's syndrome is the triad of dry eyes, dry mouth, and an autoimmune disease, which frequently is rheumatoid arthritis. Patients can have recurrent epistaxis and anterior nasal perforation. Diagnosis is by excisional biopsy of a minor salivary gland from the lower lip, which shows lymphocytic infiltration. Patients need chronic moisturizing of the nose, eyes, and mouth. The disease is associated with an increased incidence of lymphoma.

Polyarteritis nodosa is a necrotizing vasculitis that results in widespread systemic illness. Patients can have renal failure, skin lesions resembling extensive third-degree burns, and sudden deafness.

Churg-Strauss syndrome consists of asthma, systemic vasculitis, peripheral eosinophilia, and nasal polyps.

Polymorphic reticulosis, a precursor of lymphoma, causes pansinusitis. Perivascular cuffing by inflammatory cells, without vasculitis, is the histologic feature that distinguishes this disease from Wegener's granulomatosis, a granulomatous vasculitis in which blood vessel walls are destroyed by inflammatory cells. It causes lung cavitation, proteinuria resulting from granulomatous renal vasculitis, pansinusitis, and otitis media with effusion; such a patient is acutely ill. Taken together these two entities replace the older diagnosis of lethal midline granuloma. Polymorphic reticulosis is treated by irradiation and Wegener's granulomatosis by chemotherapy.

The differential diagnosis of granulomatous diseases of the larynx includes tuberculosis, syphilis, sarcoidosis, Wegener's granulomatosis, polymorphic reticulosis, blastomycosis, coccidioidomycosis, and cancer. Sarcoidosis, Wegener's granulomatosis, and relapsing polychondritis are associated with subglottic stenosis. Tuberculosis and leprosy can produce glottic and supraglottic stenosis.

Vertigo can result from autoimmune disorders such as Cogan's syndrome, polymyalgia rheumatica, lupus erythematosus, or rheumatoid arthritis. The erythrocyte sedimentation rate

should be elevated in all cases.

Hematologic Disorders

Hematologic disorders with otolaryngologic manifestations include Osler-Weber-Rendu syndrome and acute leukemia.

Although not a bone marrow dysfunction, Osler-Weber-Rendu syndrome is of considerable importance to those who treat epistaxis. This disease, also called hereditary hemorrhagic telangiectasia, is transmitted as an autosomal dominant trait. In affected individuals the bleeding episodes are chronic, recurrent, and often severe. Patients are anemic as a result of blood loss, predominantly from the nose and gut. The digestive tract contains telangiectatic vessels that lack muscle and elastic tissue in their vessel walls. The lungs and liver contain arteriovenous malformations. Septal perforation is common and arises from repeated cautery. The lips, tongue, nasal mucosa, and sometimes nail beds are spotted with multiple, small. bluish telangiectasie. In severe cases of epistaxis, nasal septal dermoplasty can be effective. This consists of removal of the nasal mucosa affected by telangiectasias and of grafting with skin from a separate donor site.

The acute leukemias often produce epistaxis by two mechanisms. Generalized bone marrow infiltration diminishes the production of platelets and liver involvement reduces the synthesis of coagulation proteins. Hemorrhage from the nose and gut exacerbates the anemia that is part of the primary disease. Leukemic infiltration of the middle or inner ear can produce deafness.

Infectious Disorders

Infectious disorders with otolaryngologic features can be caused by bacteria, fungi, viruses, or parasites.

Mycobacterium tuberculosis infection of the head and neck can produce cervical scrofula, otitis media, and laryngeal and nasal tuberculosis. Tuberculous otitis media typically appears as a clear, odorless otorrhea with multiple tympanic membrane perforations and abundant, pale, small granulation polyps in the middle ear and medial portion of the ear canal. There is a severe conductive hearing loss and sometimes the multiple perforations coalesce to denude the malleus handle completely. Laryngeal tuberculosis begins with nodular interarytenoid lesions that progress to ulcers, perichondritis, and finally cicatricial scarring. Pain is prominent. Leprosy, another mycobacterial disease, presents in the larynx in a similar fashion, except for the absence of pain. Leprosy can also induce septal perforation and vestibular scarring.

Classic laryngeal tuberculosis was rarely seen to occur in the absence of active pulmonary infection, and was said to be the single most contagious form possible. Laryngeal infection is generally believed to result from clumps of the bacilli being coughed up from the lungs, lodging in the interarytenoid area, and colonizing. Laryngeal tuberculosis, however, is no longer reliably

correlated with pulmonary tuberculosis. Laryngeal lesions are found to vary from mucosal hyperemia to granulation tissue, and can be located on any portion of the glottic or supraglottic larynx.

Lupus vulgaris is tuberculosis of the nose. It is characterized by brown, intranasal, gelatinous nodules, with discoloration of the skin of the nose and midface by similar raised, brown lesions. Intranasal ulceration eventually leads to perforation of the nasal septum, usually at the bone-cartilage junction.

Scrofula classically is bilateral marked cervical adenopathy, usually but not always accompanied by active pulmonary tuberculosis. In most cases, cervical node biopsy reveals caseating necrosis. In the absence of caseation, differentiation from sarcoidosis can be difficult. In the United States, 80 to 90 per cent of all tuberculous neck nodes are atypical, signifying that the causative organism is a *Mycobacterium* species other than *M. tuberculosis* - usually *M. avium-intracellulare, M. Kansasii*, or *M. bovis.* Atypical tuberculosis - scrofula - is unilateral and located in the submandibular region, and does not accompany active pulmonary infection. The skin overlying nodes resulting from *M. tuberculosis* infection is never pink, and can be blue or brown; the skin over atypical tuberculosis nodes might start pink and turn pale violet. These organisms are atypical in that they are relatively noncontagious and are resistant to usual antituberculosis medical therapy. *Mycobacterium avium-intracellulare* and lymphoma can produce enlarging cervical nodes in those with AIDS.

It is said that any hearing loss can be characteristic of syphilis infection by *Treponema pallidum.* The finding of a positive fluorescein treponemal antibody absorption test (FTA-ABS) in a vertiginous patient is probably grounds for penicillin treatment of presumed temporal bone lues. Congenital syphilis, acquired in utero from the infected mother, is rarely seen in the United States. The affected infant might have as the only sign a mucoid rhinorrhea, called snuffles. Perioral scarring can occur by the time of birth. These furrows, which radiate outward from the vermilion lips, resemble the perioral wrinkles of the aging face, and are known as rhagades. A saddle nose can develop following extensive perforation of the nasal septum. Dental abnormalities include Hutchinson's teeth, in which the incisors are pointed and notched, and mulberry molars, which are multicusped molars highly susceptible to decay because of faulty enamel encasement. In the absence of any detectable anatomic abnormality, Hennebert's sign (a positive fistula test) can be elicited by insufflation of the sealed external ear canal. Interstitial keratitis is an ocular finding that is highly correlated with congenital lues and is considered historically to the sine qua non of the syndrome. Tertiary syphilitic gummas frequently are found on the bony nasal septum, where they can perforate through the septum or into the hard or soft palate, creating an oronasal fistula.

Lyme disease is caused by the spirocheta *Borrelia burgdorferi*, which has a zoologic reservoir in the tick *Ixodes dammini.* Within 3 to 20 days following a tick bite, a red papule (erythema chronicum migrans) appears at the site of the bite. It expands to a large annular red lesion that can be as large as 16 cm in diameter. Constitutional symptoms associated with the skin lesion include malaise, stiff neck, fever, and backache. There can be generalized

lymphadenopathy. Oligoarticular arthritis (most often in the knees) develops in 45 per cent of patients, cardiac conduction abnormalities (complete heart block) are found in 8 per cent, and neurologic abnormalities occur in 11 per cent. The neurologic abnormalities consist of encephalitis, radiculoneuritis, and cranial neuropathies. Cranial nerve disorders include bilateral or unilateral seventh nerve palsies, and various palsies of cranial nerves III, V, and VIII. These neuropathies resolve within 6 months. Treatment with tetracycline and possibly with prednisone can shorten the duration of symptoms.

Cat scratch disease begins as a pustule 3 days after exposure and rapidly progresses to local and regional adenopathy. Excisional biopsy is curative, but merely suggests rather than confirms the diagnosis. Histologically the nodes contain noncaseating granulomas, which also are found in sarcoidosis, tularemia, and brucellosis. Primary ocular infection produces Parinaud's syndrome of unilateral conjunctivitis and ipsilateral preauricular and cervical adenopathy.

Bubonic plague is caused by *Yersinia pestis,* a gram-negative bacillus transmitted by fleas. A bubo - an enlarged lymph node - can occur anywhere. Diagnosis is by specific antibody titer. Treatment is with streptomycin and chloramphenicol.

Tularemia, a disease transmitted by arthropods and caused by *Franciscella tularensis,* is associated with rabbit and possibly reindeer exposure. It can cause an exudative tonsillitis. Diagnosis is established by a serologic agglutination titer of at least 1:16.

Brucellosis is caused by *Brucella abortus,* which forces spontaneous abortion in cattle and is known for the peculiar leathery placenta that is delivered by the unfortunate cow. Infection in humans is associated with exposure to cattle. Diagnosis is confirmed by a serologic agglutination titer greater than 1:16.

Rhinoscleroma, caused by *Klebsiella rhinoscleromatis,* is a destructive rhinopathy found in eastern Europe and Africa, occasionally in the United States. Differential diagnosis must include carcinoma, leprosy, and the destructive nonsyphilitic treponematoses bejel, yaws, and pinta. Three stages characterize the disease. Infection begins as a chronic rhinitis, progresses to a disfiguring granulomatous mass in the anterior nose that involves the vestibules and upper lip, and finally results in scarring with nasal airway obliteration. This disease can involve the larynx, with similar scarring and airway encroachment. Treatment is somewhat controversial, but administration of tetracycline or streptomycin, or both, is generally recommended. Success can be expected in those with primary or secondary disease but, once the nose has been scarred, only surgery with splinting can salvage the airway.

Actinomycosis is caused by the microaerophilic gram-positive organism *Actinomyces israelii,* which is classed between bacteria and fungi. It can produce suppurative granulomatous cervical adenitis or a cervicofacial infection laced with multiple, draining sinus tracts. Overlying soft tissues are indurated and boardlike. The organism is a normal oral inhabitant but infection seems to be promoted by dental caries and periodontal disease, with which it is usually associated. Sulfur granules representing tangles of filaments of tissue cells and lipid-laden

macrophages (which impart the color yellow) are seen. Microscopically, these granules have a characteristic "sunburst" appearance. Treatment is with penicillin or tetracycline given for up to 1 year. There is a prominent sex predilection, with men being affected two to five times as often as women. Most cases occur in those between 15 to 35 years of age. Differential diagnosis includes other granulomatous diseases, cancer, syphilis, and fungal, mycobacterial, and nocardial infections.

Aspergillosis is now recognized as an increasingly common pathogen in otolaryngologic infections. Three levels of infection exist, reflecting different host-fungus interactions, and require different treatment. Allergic aspergillus sinusitis appears to be an analogue to allergic bronchopulmonary aspergillosis, which both accompanies and exacerbates asthma. In both cases the epithelium is spared. The offending fungus thrives in the blanket of mucus and is sustained by a mechanism that can be therapeutically disrupted by steroids. Invasive aspergillosis, on the other hand, destroys the sinus epithelium and might require both surgical debridement and intravenous antifungals for cure. A third form of host-fungus interaction, in which the host ignores the fungus, is the fungus ball. This dense object is white on computed tomography, and appears as a sphere within the maxillary antrum. The patient might be able to feel it roll around within the sinus. Surgical removal is curative. Staining shows branching septate hyphae of uniform width.

Mucormycosis is an opportunistic mycotic infection produced by a number of molds of the order Mucorales of the subclass *Zygomycetes.* The usual causative organisms include *Rhizopus, Absidia,* and *Mucor* spp, which are ubiquitous in the environment. Patients at risk are those with acidosis, leukemia, or immunodeficiency. This universally fatal infection often involves the central face and is seen in immunocompromised hosts, such as poorly controlled diabetics. The involved nasal mucosa is black and necrotic, with a bloody exudate. Fungal stain shows nonseptate hyphae with right-angle branching. Death usually follows within 1 week of onset. The patient develops fifth and seventh nerve palsies, orbital cellulitis, and exophthalmos.

A general review of the cervical adenopathy produced by these infections shows that well-localized neck disease, not bilateral or diffuse, suggests atypical tuberculosis, cat scratch disease, or toxoplasmosis. Diffuse cervical disease is more likely Epstein-Barr virus (see below) or typical tuberculosis.

Histoplasmosis is caused by the intracellular dimorphic yeast-fungus *Histoplasma capsulatum.* It causes pain and nodular laryngeal lesions similar to those of tuberculosis. In addition, painful ulcers are scattered on the tongue and oral mucosa. The disease is endemic on the Ohio River valley, where almost everyone becomes infected at some point. Head and neck complaints rarely emerge without active pulmonary infection evidenced by cough and chest pain. Treatment of symptomatic cases is with amphotericin B.

Blastomycosis can produce a friable, verrucous, laryngeal mass that so resembles carcinoma that laryngectomy has been mistakenly performed. Ulcerations in the mouth tend to be crusted. Mandibular invasion can produce lytic lesions. Laryngeal and oral lesions occur with

disseminated disease. The causative organism is a dimorphic yeast-fungus, *Blastomyces dermatitidis,* which is endemic to the southeastern United States. It enters its human host through the lungs and from there can infect any organ system. Most commonly the skin of the nose is marked by a verrucous, raised lesion that ultimately scars, even with treatment. Diagnosis is by sputum culture. On biopsy, budding, thick-walled yeast are seen within the Langhans-type giant cells associated with microabscesses. Treatment is with amphotericin B or ketoconazole.

Coccidiomycosis is endemic to the San Joaquin Valley of California. This primary fungal lung disease can involve the skin, lymph nodes, and mucous membranes. It causes laryngeal erythema and edema. Oral lesions are nodular and ulcerated and can be distinguished from blastomycosis only by biopsy, which reveals *Coccidioides immitis,* the causative organism.

Sporotrichosis, caused by *Sporotrix schenckii,* is rose grower's disease. This self-limiting disorder is most commonly seen on the extremities following a relatively minor skin prick from a rose. The disease spreads proximally along the lymphatics, with epitrochlear and axillary adenopathy. Suppurative cervical nodes and nodular intranasal lesions occur. Biopsy reveals the causative organism. The vasculitic response to this infection can closely resemble that seen with Wegener's granulomatosis.

Rhinosporidiosis is a fungal infection caused by *Rhinosporidium seeberi* that is usually found in Asia and Africa. The patient becomes infected by swimming in contaminated water. The nasal lesion is a large, painless, polypoid growth that can fill the nose. Treatment is surgical excision.

Measles and mumps are RNA paramyxoviruses. Measles (rubeola) begins with a fever, followed in 1 to 2 days by the appearance of Koplik's spots. These bright red spots on the buccal mucosa facing the second molar tooth precede the generalized cutaneous rash by 2 to 3 days. Bilateral sensorineural deafness and subacute sclerosing panencephalitis are long-term severe effects.

Mumps can cause parotitis, orchitis, encephalitis, and unilateral sensorineural deafness.

Herpesvirus family members that infect the head and neck include herpes simplex type I, varicella-zoster, Epstein-Barr, and cytomegalovirus. All are DNA viruses. Herpes simplex type I produces the common cold sore (herpes labialis), a self-limiting but painful lesion. Primary infection occurs early in life, with a 60 per cent seroconversion rate observed by 7 years of age and 90 per cent by adulthood. A severe gingivostomatitis can occur. There is variable association with facial nerve paralysis.

The varicella-zoster virus can produce vesicles in the upper respiratory mucous membranes in children and pneumonia in children or adults. The cutaneous rash appears as a single crop of macules, which rapidly progress to vesicles of uniform size. (This distinction is of historical importance, in that smallpox lesions were seen to appear in waves.) The patient has simultaneous skin lesions in various stages, from new eruptions to crusted vesicles.

Ramsay Hunt syndrome is otitic zoster (shingles), a rare but extremely painful reactivation of latent varicella-zoster. The syndrome most likely stems from infection of the geniculate ganglion, and as such is often associated with seventh nerve palsy and sensorineural hearing loss. Vesicles appear on the auricle, ear canal, and tympanic membrane.

The most common nerves involved in zoster are the C3, T5, L1, and L2 nerves. In addition, approximately 20 per cent of cases involve the cranial nerves, usually the first division of the fifth cranial nerve. Vesicles erupt on the face after 1 to 3 days of shooting pains and can also present intraorally. Lesions are almost invariably unilateral. Treatment is symptomatic; prednisone and possibly acyclovir might reduce symptoms. Postherpetic neuralgia remains a problem.

Epstein-Barr virus infection produces the typical mononucleosis, with sore throat, malaise, and posterior cervical adenopathy identical to that seen in toxoplasmosis. Lymph nodes can contain Reed-Sternberg cells. The peripheral blood smear shows atypical lymphocytes, which are also seen in cytomegalovirus, viral hepatitis, toxoplasmosis, rubella, mumps, and roseola infections. The heterophile antibody can remain negative in up to 20% of patients. Most patients complain of a severe sore throat, and the tonsils are enlarged, tender, and covered with a shaggy exudate not clinically distinguishable from that seen with streptococcal infection. Splenomegaly can occur; as long as it is present, there is a risk of splenic rupture with considerably less abdominal trauma than would normally be required to produce this catastrophe.

Cytomegalovirus, like toxoplasmosis (see below), is ubiquitous. Infection usually presents as a mild viral pharyngitis, but it can produce "CMV mono", with violent exudative tonsillitis. Diagnosis is confirmed by a negative heterophile antibody with rising cytomegalovirus titers.

Toxoplasma gondii, the etiologic agent of toxoplasmosis, is an obligate intracellular parasite that usually lives in cats. Human infection often is asymptomatic, but can result in chills and fever and firm, slightly tender, posterior cervical nodes that never suppurate. It is estimated that 70 million Americans have been exposed to this parasite. Diagnosis is supported by a serologic titer greater than 1:1000 or by a lower initial titer, which subsequently doubles over the following 3 weeks. Lymph node biopsy is also helpful.

A histologic finding of pseudoepitheliomatous hyperplasia can suggest blastomycosis, syphilis, tuberculosis, granular cell myeloblastoma, coccidioidomycosis, paracoccidioidomycosis, rhinosporidiosis, or candidiasis. Causes of cervical node caseating necrosis include tularemia, brucellosis, tuberculosis, fungal infection, and atypical tuberculosis infection. Laryngeal membrane can be a feature of diphtheria, candidiasis, mononucleosis, and streptococcal and cytomegalovirus infections.

Nutritional Disorders

Nutritional disorders with otolaryngologic manifestations include marasmus and kwashiorkor and deficiencies of vitamin A, thiamine, niacin, riboflavin, vitamin C, vitamin B_{12},

folic acid, vitamin D, and zinc.

Marasmus and kwashiorkor are the two extremes of pediatric protein and calorie malnutrition. In kwashiorkor the diet might contain adequate calories, but is profoundly deficient in protein. As a consequence of protein depletion, the plasma oncocitic pressure decreases and tissues become edematous. Generalized edema, especially the swollen belly, is a hallmark of the disease.

In marasmus, patients exhibit extreme muscle wasting and failure to gain weight, and generally resemble World War II concentration camp victims. The diet is profoundly deficient in both calories and protein. Marasmus patients are mentally alert and very hungry. Many kwashiorkor victims are anorexic.

Various vitamin deficiencies often accompany protein and calorie malnutrition. Xerophthalmia is the clinical manifestation of vitamin A deficiency. Dryness of the eye spreads from the conjunctiva to the cornea, which can disintegrate and allow extrusion of the lens. Survivors of this severe illness are blind - an earlier clinical sign is night blindness. Burning and dryness of the mouth are common. Excessive intake of vitamin A during pregnancy is associated with cleft palate.

Thiamine (vitamin B1) deficiency causes beriberi and Wernicke-Korsakoff syndrome. These two syndromes can occur when the intake of thiamine is inadequate relative to a largely carbohydrate diet. Beriberi has a wet or dry form according to the presence of edema (including congestive heart failure). Only the dry form is discussed here because patients with this type can present with dizziness and gait instability. The disease is essentially a peripheral neuropathy, marked by anesthesia and paresthesias of the distal extremities. Affected individuals have great difficulty arising unassisted from a squatting position and experience progressive gait instability. Beriberi occurs primarily in the rice-eating peoples of the world because of their ingestion of thiamine-deficient polished rice.

Wernicke-Korsakoff syndrome mainly occurs in alcoholics, and is the most prevalent manifestation of thiamine deficiency in the United States. It is characterized by loss of memory for the immediate past, often concealed by elaborate and quite amusing confabulation. Nystagmus, diplopia, and lateral rectus paralysis are also present.

Niacin deficiency causes pellagra, and occurs in those whose diet consists mainly of corn. Its features are known as the "four Ds" - dermatitis, diarrhea, dementia, and death. The findings of angular stomatitis, cheilosis, and glossitis are of particular interest to otolaryngologists. Burning tongue pain is said to be the earliest clinical sign. Edema pushes the tongue so firmly onto the teeth that dental indentations occur around the tongue margin. A peculiar scaling brown dermatitis appears on sun-exposed skin, known as Casal's necklace on the neck.

Riboflavin deficiency is also known for its oral manifestations, including angular stomatitis and glossitis. Angular stomatitis consists of painful cracks radiating outward from the

oral commissures. Cheilosis is painful cracking on the upper and lower lips at the line of closure. In addition, riboflavin deficiency causes an intensely pruritic and desquamating scrotal or vulvar dermatitis. Glossitis leads to a distinctive magenta tongue.

Scurvy, a disease mainly of historic interest, is a consequence of a diet totally lacking in vitamin C. Capillary walls become fragile and connective tissues lack strength. Teeth loosen, gums swell and bleed, and hemorrhages occur that vary in severity from subungual splinter hemorrhages and cutaneous petechiae to severe epistaxis. The rare infant with scurvy has severe muscle pains and mainly hurts too much to move.

Pernicious anaemia, an apparent deficiency of vitamin B12, can first appear as an intermittently pale, shiny, burning tongue. The lingual papillae atrophy, but partial reversal can occur with vitamin B12 injections. The disorder is usually a genetic problem involving lack of intrinsic factor rather than a dietary deficiency. The other cause of megaloblastic anemia, folic acid deficiency, also results in glossitis and dermatitis.

Rickets, a deficiency of vitamin D, results in the familiar bowlegs found in the toddler. The earliest signs are craniotabes (skull softening), with delayed closure of the fontanelles and excessive sweating on the forehead. Deficiency of vitamin C or D can result in a "rosary", an enlargement of the costochondral junctions.

Zinc deficiency can be associated with hypogonadism, growth retardation, impaired wound healing, and anosmia.

Metabolic Disorders

Metabolic disorders that can be accompanied by otolaryngologic problems include hypothyroidism, diabetes mellitus, Graves' disease, gout, and Addison's disease.

Hypothyroidism from all causes has a similar spectrum of clinical findings. The presence (or absence) and severity of various features depend on the duration and degree of thyroid gland hypofunction. In the United States the addition of iodine to table salt has almost eliminated endemic goiter caused by chronic iodine deficiency. Otolaryngologic symptoms of hypothyroidism include (1) hoarseness (from vocal cord myxedema), (2) nasal airway obstruction (from edema of nasal mucosa), (3) alopecia, ranging from loss of hair from the lateral third of the eyebrows to total body hair loss, (4) dysequilibrium, and (5) cardiac dysrhythmias. Diagnosis is readily confirmed by thyroid function studies. An issue frequently encountered by the head-and-neck oncologic surgeon is the necessity for thyroid supplementation for patients whose thyroid glands have been functionally devascularized because of cancer surgery and irradiation to the neck.

Diabetes mellitus is an occasional cause of dizziness that resolves with blood glucose level regulation. Diabetics can also be treated by otolaryngologists because of immunologic problems resulting from diabetes. Of great notoriety is acute necrotizing otitis externa (malignant

otitis externa). This infection produces severe otalgia, often following insignificant or undetectable trauma to the external ear canal. The causative organism is *Pseudomonas aeruginosa.* Diagnosis is by clinical examination, which detects necrotic ear canal cartilage and exposed bone with granulation tissue at the bony-cartilaginous junction in addition to purulent otorrhea and edematous ear canal skin. Diagnosis is supported by a positive gallium bone scan, indicating osteomyelitis. Treatment requires 1 or more months with anti-pseudomonal antibiotics.

Graves' disease (exophthalmic goiter) causes hyperreflexia, moist hands, heat intolerance, a psychological sense of urgency, cardiac dysrhythmias, vertigo, and bulging eyes. Traction on the optic nerve resulting from extreme exophthalmos might require decompression of the orbital contents by the Caldwell-Luc operation, with removal of the floor and medial and lateral walls of the orbit.

Gout produces tophi on the ears, and occasionally on the midface, which mimic the xanthelasma of hyperlipidemia.

Addison's disease can cause hyperosmia, as can cystic fibrosis.

Neurologic Disorders

Neurologic disorders with otolaryngologic features include multiple sclerosis, diabetic neuropathy, and Guillain-Barré syndrome.

Multiple sclerosis is an idiopathic demyelinating disease of the central nervous system. It is one cause of dizziness. Early signs include internuclear ophthalmoplegia manifested as diplopia with extreme gaze in one horizontal direction, but not in the other. This is attributed to demyelination of the medial longitudinal fasciculus (MLF), which disconnects the neural circuitry necessary to coordinate the paired firing of the contralateral lateral rectus (cranial nerve VI) and medial rectus (cranial nerve III) muscles necessary to attain conjugate gaze. This degenerative disease also produces upper motor neuron denervation and consequent lower motor neuron spasticity, which is often asymmetric.

The neuropathy accompanying severe diabetes mellitus can produce cervical dysphagia. Dizziness is characterized by duration (often weeks) without compensation, and nystagmus and vertigo without nausea.

Guillain-Barré syndrome consists of acute ascending motor paralysis with variable disturbance of sensory function. Facial diplegia occurs in 50 per cent of patients, usually after the legs are quite flaccid and the arms have begun to weaken. There might be pain and tingling of affected neurologic fields. The cerebrospinal fluid is characteristically acellular, with an elevated protein level. Differential diagnosis includes, among many others, polyneuropathy associated with diphtheria, mononucleosis, and hepatitis, lupus erythematosus, other vasculitides, porphyria, poliomyelitis, and botulism.

Causes of tonic laryngeal spasm include tertiary lues (tabes dorsalis), syringomyelia, multiple sclerosis, bulbar palsy, tetanus, rabies, aortic aneurysm, pleural adhesions, and thoracic neoplasms. The last three affect the larynx by irritating the recurrent nerve.

Drugs and Other Toxicities

Drugs and other substances can have harmful effects with otolaryngologic features.

Vertigo can result from drug toxicities, including those caused by aspirin, Tegretol, quinine, Dilantin, erythromycin, the phenothiazines, and ethyl alcohol. Vertigo can also result from exposure to environmental toxins such as the heavy metals. Zinc or lead intoxication can produce anosmia.

Anticonvulsant pseudolymphoma, mainly a Dilantin phenomenon, is accompanied by eosinophilia, hepatosplenomegaly, and cleft lymphocytes resembling those of Hodgkin's disease. Cervical nodes exhibit medullary hypercellularity. The lymph node medulla is rich in plasma cells, so hypercellularity in this zone suggests antibody production.