VOLUME TWO

ANDERSON'S PATHOLOGY

Edited by

JOHN M. KISSANE, M.D.

W.A.D. ANDERSON,

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JOHN M. KISSANE, M.D.

Professor of Pathology and of Pathology in Pediatrics,
Washington University School of Medicine;
Pathologist, Barnes and Affiliated Hospitals,
St. Louis Children's Hospital, St. Louis, Missouri

Former editions edited by

W.A.D. ANDERSON,
M.A., M.D., F.A.C.P., F.C.A.P., F.R.C.P.A. (Hon.)

Emeritus Professor of Pathology and Formerly Chairman
of the Department of Pathology,
University of Miami School of Medicine,
Miami, Florida

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Contributors

ARTHUR C. ALLEN, M.D.

Professor of Pathology, State University of New York, Downstate Medical Center; Director of Laboratories, Jewish Hospital and Medical Center (currently Interfaith Medical Center), Brooklyn, New York

ROBERT E. ANDERSON, M.D.

Professor and Chairman, Department of Pathology, The University of New Mexico, Albuquerque, New Mexico

FREDERIC B. ASKIN, M.D.

Professor of Pathology, University of North Carolina School of Medicine; Director of Surgical Pathology, North Carolina Memorial Hospital, Chapel Hill, North Carolina

SAROJA BHARATI, M.D.

Chairperson, Department of Pathology, Deborah Heart and Lung Center, Browns Mills, New Jersey; Clinical Professor of Pathology, Temple University Medical School, Philadelphia, Pennsylvania; Clinical Professor of Pathology, The Pennsylvania State University, The Milton S. Hershey Medical Center, Hershey, Pennsylvania; Research Professor of Medicine, University of Illinois, Abraham Lincoln School of Medicine, Chicago, Illinois

CHAPMAN H. BINFORD, M.D.

Consultant to the Leprosy Registry, American Registry of Pathology; Formerly Chief, Special Mycobacterial Diseases Branch, Geographic Pathology Division, Armed Forces Institute of Pathology, Washington, D.C.

FRANCIS W. CHANDLER, D.V.M., Ph.D.

Chief, Experimental Pathology Branch, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Georgia

JACOB L. CHASON, M.D.

Neuropathologist, Department of Pathology, Henry Ford Hospital; Clinical Professor of Pathology (Neuropathology), Wayne State University School of Medicine, Detroit, Michigan

MASAHIRO CHIGA, M.D.

Professor of Pathology, Departments of Pathology and Oncology, University of Kansas College of Health Sciences and Hospital, School of Medicine, Kansas City, Kansas

A.R.W. CLIMIE, M.D.

Chief of Pathology, Harper-Grace Hospitals; Associate Professor of Pathology, Wayne State University School of Medicine, Detroit, Michigan

JOSE COSTA, M.D.

Professor of Pathology, University of Lausanne, Lausanne, Switzerland; Formerly Chief, Pathologic Anatomy Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

CHARLES J. DAVIS, JR., M.D.

Associate Chairman, Department of Genitourinary Pathology, Armed Forces Institute of Pathology; Professor of Pathology, Uniformed Services, University of Health Sciences, Washington, D.C.

KATHERINE DeSCHRYVER-KECSKEMETI, M.D.

Associate Professor, Division of Surgical Pathology, Washington University School of Medicine, St. Louis, Missouri

GEORGE Th. DIAMANDOPOULOS, M.D.

Professor of Pathology, Department of Pathology, Harvard Medical School, Boston, Massachusetts

HUGH A. EDMONDSON, M.D.

Professor of Pathology, University of Southern California, School of Medicine, Los Angeles, California

ROBERT E. FECHNER, M.D.

Royster Professor of Pathology and Director, Division of Surgical Pathology, University of Virginia Medical Center, Charlottesville, Virginia

GERALD FINE, M.D.

Chief, Division of Anatomic Pathology, Department of Pathology, Henry Ford Hospital, Detroit, Michigan

KAARLE O. FRANSSILA, M.D., Ph.D.

Chief of Pathology Laboratory, Department of Radiotherapy and Oncology, Helsinki University Central Hospital, Helsinki, Finland

ROBERT J. GORLIN, D.D.S., M.S.

Regents' Professor and Chairman, Department of Oral Pathology and Genetics, and Professor, Departments of Pathology, Dermatology, Pediatrics, Obstetrics-Gynecology, and Otolaryngology, Schools of Dentistry and Medicine, University of Minnesota, Minneapolis, Minnesota

ROGERS C. GRIFFITH, M.D.

Assistant Professor of Pathology and Surgical Pathology, Washington University School of Medicine; Assistant Pathologist, Barnes and Affiliated Hospitals, St. Louis Children's Hospital, and The Jewish Hospital of St. Louis, St. Louis, Missouri

JOE W. GRISHAM, M.D.

Professor and Chairman, Department of Pathology, University of North Carolina, School of Medicine, Chapel Hill, North Carolina

PAUL GROSS, M.D.

Adjunct Professor, Department of Pathology, Medical University of South Carolina, Charleston, South Carolina

DONALD B. HACKEL, M.D.

Professor of Pathology, Department of Pathology, Duke University Medical School, Durham, North Carolina

GORDON R. HENNIGAR, M.D.

Professor and Chairman, Department of Pathology, Medical University of South Carolina, Charleston, South Carolina

CHARLES S. HIRSCH, M.D.

Director of Forensic Pathology, Hamilton County Coroner's Office; Professor of Pathology, University of Cincinnati College of Medicine, Cincinnati, Ohio

DAVID B. JONES, M.D.

Professor of Pathology, Department of Pathology, State University of New York, Upstate Medical Center, Syracuse, New York

HAN-SEOB KIM, M.D.

Associate Professor of Pathology, Baylor College of Medicine; Attending Pathologist, The Methodist Hospital; Attending Pathologist, Harris County Hospital District, Houston, Texas

JOHN M. KISSANE, M.D.

Professor of Pathology and of Pathology in Pediatrics, Washington University School of Medicine; Pathologist, Barnes and Affiliated Hospitals, St. Louis Children's Hospital, St. Louis, Missouri

FREDERICK T. KRAUS, M.D.

Director of Laboratory Medicine, St. John's Mercy Medical Center; Professor of Pathology (Visiting Staff), Washington University School of Medicine, St. Louis, Missouri

CHARLES KUHN III, M.D.

Professor of Pathology, Washington University School of Medicine, St. Louis, Missouri

MICHAEL L. KYRIAKOS, M.D.

Professor of Pathology, Washington University School of Medicine; Surgical Pathologist, Barnes Hospital; Consultant to St. Louis Children's Hospital and Shriner's Hospital for Crippled Children, St. Louis, Missouri

PAUL E. LACY, M.D.

Mallinkrodt Professor and Chairman, Department of Pathology, Washington University School of Medicine, St. Louis, Missouri

MAURICE LEV, M.D.

Director, Department of Pathology, Deborah Heart and Lung Center, Browns Mills, New Jersey; Clinical Professor of Pathology, Temple University Medical School, Philadelphia, Pennsylvania; Clinical Professor of Pathology, The Pennsylvania State University, The Milton S. Hershey Medical Center, Hershey, Pennsylvania

CHAN K. MA, M.D.

Staff Pathologist, Department of Pathology, Henry Ford Hospital, Detroit, Michigan

VINCENT T. MARCHESI, M.D.

Professor and Chairman, Department of Pathology, Yale University, School of Medicine, New Haven, Connecticut

MANUEL A. MARCIAL, M.D.

Research Fellow in Pathology, Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

RAÚL A. MARCIAL-ROJAS, M.D., J.D., M.P.H., M.P.A.

Professor of Pathology and Dean, School of Medicine, Universidad Central del Caribe, Cayey, Puerto Rico; Formerly Chairman, Department of Pathology, University of Puerto Rico, School of Medicine, San Juan, Puerto Rico

ROBERT W. McDIVITT, M.D.

Professor of Pathology, Washington University School of Medicine; Director of Anatomic Pathology, Jewish Hospital of St. Louis; Associate Pathologist, Barnes Hospital; Consultant, Children's Hospital of St. Louis, St. Louis, Missouri

WILLIAM A. MEISSNER, M.D.

Emeritus Professor of Pathology, New England Deaconess Hospital, Harvard Medical School, Boston, Massachusetts

F. KASH MOSTOFI, M.D.

Chairman, Department of Genitourinary Pathology, Armed Forces Institute of Pathology, Washington, D.C.; Professor of Pathology, Uniformed Services University of Health Sciences, Washington, D.C.; Associate Professor of Pathology, Johns Hopkins University, School of Medicine; Clinical Professor of Pathology, University of Maryland Medical School, Baltimore, Maryland; Clinical Professor of Pathology, Georgetown University School of Medicine, Washington, D.C.

WAYKIN NOPANITAYA, Ph.D.

Professor, Department of Pathology, Prince of Songkla University, Songkla, Head-Yai, Thailand

JAMES E. OERTEL, M.D.

Chairman, Department of Endocrine Pathology, Armed Forces Institute of Pathology, Washington, D.C.

ROBERT L. PETERS, M.D.

Professor of Pathology, University of Southern California, School of Medicine, Los Angeles, California; Chief Pathologist, Rancho Los Amigos Hospital, Downey, California

R.C.B. PUGH, M.D., F.R.C.S., F.R.C. Path.

Consulting Pathologist, St. Peter's Hospitals and Institute of Urology, London, England

ALAN S. RABSON, M.D.

Director, Division of Cancer Biology and Diagnosis, National Cancer Institute, Bethesda, Maryland

JUAN ROSAI, M.D.

Professor of Laboratory Medicine and Pathology and Director of Anatomic Pathology, University of Minnesota Medical School, Minneapolis, Minnesota

ARKADI M. RYWLIN, M.D.

Director, Department of Pathology and Laboratory Medicine, Mount Sinai Medical Center; Professor of Pathology, University of Miami School of Medicine, Miami, Florida

DANTE G. SCARPELLI, M.D., Ph.D.

Ernest J. and Hattie H. Magerstadt Professor and Chairman, Department of Pathology, Northwestern University Medical School; Chief of Service, Northwestern Memorial Hospital, Chicago, Illinois

THOMAS M. SCOTTI, M.D.

Formerly Professor of Pathology, University of Miami School of Medicine, Miami, Florida

STEWART SELL, M.D.

Professor and Chairman, Department of Pathology and Laboratory Medicine, University of Texas Health Science Center at Houston, Houston, Texas

HERSCHEL SIDRANSKY, M.D.

Professor and Chairman, Department of Pathology, The George Washington University Medical Center, Washington, D.C.

RUTH SILBERBERG, M.D.

Visiting Scientist, Department of Pathology, Hadassah Hebrew University School of Medicine, Jerusalem, Israel

MORTON E. SMITH, M.D.

Professor of Ophthalmology and Pathology, Washington University School of Medicine, St. Louis, Missouri

SHELDON C. SOMMERS, M.D.

Clinical Professor of Pathology, Columbia University College of Physicians and Surgeons, New York, New York; Clinical Professor of Pathology, University of Southern California, School of Medicine, Los Angeles, California

STEVEN L. TEITELBAUM, M.D.

Professor of Pathology, Washington University School of Medicine and The Jewish Hospital of St. Louis, St. Louis, Missouri

JACK L. TITUS, M.D., Ph.D.

Professor and The Moody Chairman, Department of Pathology, Baylor College of Medicine; Chief, Pathology Service, The Methodist Hospital; Pathologist-in-Chief, Harris County Hospital District, Houston, Texas

DAVID H. WALKER, M.D.

Associate Professor, Department of Pathology, University of North Carolina, School of Medicine; Associate Attending Pathologist, North Carolina Memorial Hospital, Chapel Hill, North Carolina

NANCY E. WARNER, M.D.

Hastings Professor of Pathology, University of Southern California, School of Medicine, Los Angeles, California

JOHN C. WATTS, M.D.

Attending Pathologist, Department of Anatomic Pathology, William Beaumont Hospital, Royal Oak, Michigan; Clinical Assistant Professor of Pathology, Wayne State University School of Medicine, Detroit, Michigan

ROSS E. ZUMWALT, M.D.

Associate Professor of Pathology, University of Cincinnati College of Medicine; Associate Pathologist, Hamilton County Coroner's Office, Cincinnati, Ohio

Preface to eighth edition

Readers and followers of this book will have noticed that this is the first edition in which Dr. W.A.D. Anderson ("Wad" to his innumerable friends) has not actively participated. He remains vigorous and active, however, and has offered welcome encouragement and advice. We all wish him well.

Since the preparation of the seventh edition, spectacular advances have occurred in the basic sciences and in clinical medicine, on which pathology depends and to which it contributes. Advances in immunopathology and hematopathology, to mention only two general areas, and in diseases of the breast and of somatic soft tissues, to mention only two organ systems, have compelled revision of the text.

My first responsibility as editor was to examine the organization of the book to see if major structural revision was in order. I have retained the initial presentation of mechanisms both as a didactically effective transition between the basic sciences and pathology and as a review for readers whose exposure to the basic sciences has not been recent. This section of the book is followed by considerations of diseases of the various organ systems. The emphasis throughout is on the mechanisms whereby normal phenomena and processes become disturbed, giving rise to diseases and lesions.

The seventh edition introduced a chapter on geographic pathology. Even by that time, however, the Jet Age had made geographic pathology an authentic subspecialty with a language and information base of its own. It deserves separate consideration without the duplication of language and concepts that its introduction in a primary pathology text would impose. Thus, with some regret, I decided to remove the chapter on geographic pathology and rely on contributors of organ-system chapters to include geographic factors in their discussions of the epidemiology of various disorders. This effort I believe has been effectively addressed in this edition.

I chose also not to include a separate chapter on venereal diseases. Such a chapter has, over several decades, come to include sociologic and public health considerations that transcend the mechanisms and morphologic expressions of the venereal diseases. These aspects are more appropriately dealt with in works directed to public health or preventive medicine than in a work on pathology. In this edition venereally transmitted diseases are considered along with other agent-mediated diseases.

In the preparation of this edition I have been fortunate in being able to recruit several new contributors. I welcome their contributions and at the same time express my appreciation to previous contributors.

Finally, I would like to express my gratitude to the generation of supporters of *Anderson's Pathology*. I hope the eighth edition continues to merit their support.

John M. Kissane

Preface to first edition

Pathology should form the basis of every physician's thinking about his patients. The study of the nature of disease, which constitutes pathology in the broad sense, has many facets. Any science or technique which contributes to our knowledge of the nature and constitution of disease belongs in the broad realm of pathology. Different aspects of a disease may be stressed by the geneticist, the cytologist, the biochemist, the clinical diagnostician, etc., and it is the difficult function of the pathologist to attempt to bring about a synthesis, and to present disease in as whole or as true an aspect as can be done with present knowledge. Pathologists often have been accused, and sometimes justly, of stressing the morphologic changes in disease to the neglect of functional effects. Nevertheless, pathologic anatomy and histology remain as an essential foundation of knowledge about disease, without which basis the concepts of many diseases are easily distorted.

In this volume is brought together the specialized knowledge of a number of pathologists in particular aspects or fields of pathology. A time-tested order of presentation is maintained, both because it has been found logical and effective in teaching medical students and because it facilitates study and reference by graduates. Although presented in an order and form to serve as a textbook, it is intended also to have sufficient comprehensiveness and completeness to be useful to the practicing or graduate physician. It is hoped that this book will be both a foundation and a useful tool for those who deal with the problems of disease.

For obvious reasons, the nature and effects of radiation have been given unusual relative prominence. The changing order of things, with increase of rapid, worldwide travel and communication, necessitates increased attention to certain viral, protozoal, parasitic, and other conditions often dismissed as "tropical," to bring them nearer their true relative importance. Also, given more than usual attention are diseases of the skin, of the organs of special senses, of the nervous system, and of the skeletal system. These are fields which often have not been given sufficient consideration in accordance with their true relative importance among diseases.

The Editor is highly appreciative of the spirit of the various contributors to this book. They are busy people, who, at the sacrifice of other duties and of leisure, freely cooperated in its production, uncomplainingly tolerated delays and difficulties, and were understanding in their willingness to work together for the good of the book as a whole. Particular thanks are due the directors of the Army Institute of Pathology and the American Registry of Pathology, for making available many illustrations. Dr. G.L. Duff, Strathcona Professor of Pathology, McGill University, Dr. H.A. Edmondson, Department of Pathology of the University of Southern California School of Medicine, Dr. J.S. Hirschboeck, Dean, and Dr. Harry Beckman, Professor of Pharmacology, Marquette University School of Medicine, all generously gave advice and assistance with certain parts.

To the members of the Department of Pathology and Bacteriology at Marquette University, the Editor wishes to express gratitude, both for tolerance and for assistance. Especially valuable has been the help of Dr. R.S. Haukohl, Dr. J.F. Kuzma, Dr. S.B. Pessin, and Dr. H. Everett. A large burden was assumed by the Editor's secretaries, Miss Charlotte Skadel and Miss Ann Cassady. Miss Patricia Blakeslee also assisted at various stages and with the index. To all of these the Editor's thanks, and also to the many others who at some time assisted by helpful and kindly acts, or by words of encouragement or interest.

W.A.D. Anderson

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CHAPTER 24

Upper Respiratory Tract and Ear

ROBERT E. FECHNER

The upper respiratory tract comprises the nose, paranasal sinuses, nasopharynx, larynx, and middle ear with its adjacent mastoid air cells. These structures encounter innumerable airborne agents that are potentially infectious, allergenic, or carcinogenic. Many of the reactive processes and neoplasms provoked by these agents are unique to the upper airway. In addition, diseases that involve multiple systems, such as Wegener's granulomatosis or malignant lymphoma, sometimes have their initial manifestation in the upper respiratory tract. The upper airway may also be secondarily affected by systemic diseases of diverse pathogeneses. Rheumatoid arthritis can damage the small joints in the larynx; tuberculosis or fungal infections can involve the upper airway by hematogenous spread from the lungs; hypothyroidism can produce laryngeal myxedema with resultant alterations in the voice.

This chapter is divided according to the anatomic areas of the upper respiratory tract just listed. A concluding section includes diseases that involve multiple parts of the upper airway.

NOSE

Malformations

Choanal atresia or choanal stenosis results from a membrane, which may contain bone or cartilage, that completely or partially occludes the nose at its junction with the nasopharynx. The defect is probably a persistence of the bucconasal membrane that ordinarily disappears at the seventh week of fetal development. Newborn infants with choanal malformations experience respiratory distress because they instinctively breathe through the nose, and they can be asphyxiated while nursing. The condition occurs in about 1 of 7000 births; there is a familial tendency.[12] About one half of infants with choanal atresia have other anomalies.[5]

Absence of the external nose can occur in association with choanal atresia.[6] Partial or complete duplication of the nose may be accompanied by duplications of foregut structures or may occur as an isolated malformation.[10]

Brain tissue can be located in the subcutaneous tissue of the glabella, with or without an intranasal component. In some patients the brain tissue connects with the cranial cavity through a defect in the skull—a meningoencephalocele. In others there is no communication, and the inaccurate term "nasal glioma" is applied to this heterotopic tissue. Nasal gliomas are not neoplasms, and any growth is commensurate with the growth of the child. Glial tissue dominates, and ganglion cells are rare. Irregular bands of vascular fibrous tissue are intermixed.[7] Heterotopic brain tissue has also been found in the pharynx.[4]

Cysts of the nose are of two major types: dermoid and fissural. Dermoid cysts are developmental anomalies.[8] They are located beneath the skin at any point between the glabella and columella and are usually detected in childhood.[11] In addition to a cutaneous fistula, they can extend deep into the nasal septum or superiorly into the epidural space. The cysts are lined by squamous epithelium associated with hair follicles, sweat glands, and sebaceous glands in any combination.

Fissural cysts arise along the closure lines of the embryonic maxillary and globular processes and are often called nasolabial (nasoalveolar) or globulomaxillary, depending on the location. The cysts are lined mainly by squamous epithelium or columnar epithelium that may or may not be ciliated. Goblet cells are interspersed. Despite their presumed origin from entrapped embryonic epithelium, most do not appear until adulthood. Blacks have a predilection for these cysts.[9]

Skin

The skin of the nose is especially susceptible to solar damage and to inflammatory lesions that are centered in the sebaceous glands, for example, acne vulgaris. *Rhinophyma* is a term used for the hyperplastic glandular type of acne rosacea. Sebaceous glands are increased in number and size, the ducts are distended with keratinous

debris, and dilated capillaries populate the dermis. This histologic complex is seen as an enlarged, lumpy, red nose. Although a variety of neoplasms have been reported in rhinophyma, there is no convincing evidence to indicate more than a chance association.[3]

NASAL CAVITY AND PARANASAL SINUSES

Infectious, allergic, and inflammatory processes

Acute rhinitis and sinusitis

The two most common causes of acute rhinitis are viral infections and allergic reactions. Mucosa reacting to an allergic insult is edematous and hyperemic with an inflammatory infiltrate rich in eosinophils.[58] In viral infections the virus replicates in the epithelial cells and the degenerating epithelial cells are exfoliated.[19] The stroma becomes hyperemic, edematous, and infiltrated with neutrophils, lymphocytes, and plasma cells. Serous or mucinous fluid exudes through the epithelium. Clinically, these changes are manifest as nasal stuffiness and rhinorrhea. If a bacterial infection is superimposed, neutrophils dominate the inflammatory infiltrate and are evident clinically as a thick, purulent discharge.

Similar reactions to allergens or infectious agents occur in the mucosa of the paranasal sinuses, thus readily occluding the ostia. Retention of the exudate adds a sensation of facial fullness or pain to the nasal symptoms.

Bacterial infections of the sinuses can lead to serious complications. Infection of the ethmoid air cells may spread into the orbital soft tissues and the meninges. Sphenoiditis can lead to retrobulbar neuritis. Frontal sinusitis can be followed by meningitis or osteomyelitis of the frontal bone.

Nasal polyps

Nasal polyps are enormous, localized enlargements of the lamina propria mucosa caused by edema, inflammation, and the proliferation of fibroblasts (Fig. 24-1). Abnormal mucous glands are formed in about half of the polyps. These glands are often distended with mucus and form cysts, which contribute further to the mass.[72] Polyps are covered with ciliated epithelium that may be slightly thickened and sometimes undergoes squamous metaplasia. A thick, subepithelial basal lamina is often conspicuous. Ulceration of the surface or infarction of the polyp can occur.

Nasal polyps are often called allergic polyps in patients with atopy. In the absence of atopy the polyps are usually attributed to infection. There are no constant histologic findings that permit this etiologic distinction. Eosinophils, traditionally viewed as a manifestation of allergic response, can be seen in polyps when no allergic basis can be identified clinically.

The pathogenesis of nasal polyps is not clearly understood. Polyps are uncommon before 20 years of age and are seen more frequently in asthmatics than in the general population.[66] It is likely that more than one mechanism exists, depending on different inciting factors and variables in the host's response. In some patients immunoglobulins have been found in polyps at a concentration higher than can be explained by passive diffusion.[21] Eosinophils are especially prominent in these polyps.

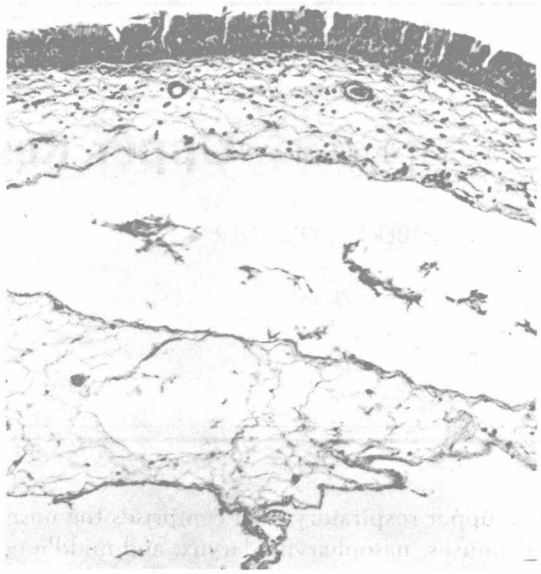

Fig. 24-1. Nasal polyp is edematous stroma with a few subepithelial inflammatory cells. It is covered with normal ciliated epithelium.

A nasal polyp in a person younger than 20 years of age signals the likelihood of cystic fibrosis. Polyps from these patients differ from typical nasal polyps in lacking basement membrane thickening and tissue eosinophilia. The mucus is also histochemically abnormal.[61]

Antrochoanal polyps arise from the mucosa of the maxillary sinus and enter the nasal cavity through a large accessory ostium near the middle meatus. Approximately 10% of normal individuals have an accessory ostium, which appears necessary for the development of the polyp. Within the nasal cavity the polyp protrudes posteriorly through the choana into the nasopharynx. In contrast to typical nasal polyps, approximately one third of the patients with antrochoanal polyps are younger than 20 years of age.[67] The lesions are almost always unilateral and are uncommonly associated with typical nasal polyps. Histologically, however, antrochoanal polyps are similar to nasal polyps except that basement membrane thickening and eosinophilia are less pronounced. Stromal cells with marked nuclear abnormalities may be seen in antrochoanal polyps, as well as in typical nasal polyps. They must not be mistaken for malignant cells.[25]

Mucocele and cholesterol granuloma

The epithelium of the paranasal sinuses secretes 1 to 2 liters of fluid daily as it humidifies the air. If the ostium of a sinus is blocked by inflamed mucosa, trauma, or an osteoma, the secretions accumulate. Two thirds of muco-

celes are in the frontal sinus, and most of the remainder affect the anterior ethmoid sinus. The mucosal lining consists of normal or compressed ciliated epithelium that sometimes has squamous metaplasia. Mucus accumulates not only in the lumen but also in the lamina propria, where it can be phagocytosed by histiocytes (mucophages). The surrounding bone may be eroded.[60]

Hemorrhage into an obstructed sinus results in the accumulation of cholesterol from the breakdown of erythrocytes. The engulfment of cholesterol by histiocytes is termed cholesterol granuloma.[43]

Rhinosporidiosis

Rhinosporidium seeberi is presumably a fungus, but it has not been cultured on artificial media. The various forms of the organism include thick-walled sporangia that contain several thousand spores. The spores mature into trophocytes that have clear cytoplasm, possess a distinct outer membrane, and measure up to about 30 μm wide.[52] Rhinosporidiosis is typically manifested as a friable, nasal polyp, but the nasopharynx, larynx, and conjunctiva are sometimes affected. The organisms elicit a nonspecific inflammatory response of neutrophils, lymphocytes, and plasma cells. The disease is most common in India and Sri Lanka, but rare cases have occurred in lifelong urban residents of the United States.[55]

Rhinoscleroma

A gram-negative diplobacillus, *Klebsiella rhinoscleromatis*, induces a chronic inflammatory response that usually includes plasma cells and foamy histiocytes. The histiocytes, referred to as Mikulicz cells, contain organisms as well as undigested mucopolysaccharides.[46] The inflammation produces deforming, nodular mucosal masses that obstruct the nose, nasopharynx, middle ear, larynx, or lower respiratory tract. Rhinoscleroma is endemic in well-demarcated areas of Africa, Central and South America, Southern Asia, and Eastern Europe. Sporadic cases occur elsewhere, including the United States.[15]

Mucormycosis (phycomycosis)

Mucormycosis is an opportunistic infection by organisms of the order *Mucorales*. Nonseptate hyphae spread along nerves, across tissue planes, and into blood vessels.[71] The last results in thrombosis and infarction. There may be a neutrophilic infiltrate, or inflammation may be negligible. Complications include meningoencephalitis and cerebral infarction.[16]

Aspergillosis

Infections of the paranasal sinuses by *Aspergillus* can take several forms. Septate hyphae can grow within the sinus and form a mass (aspergilloma) that elicits little reaction. At other times there is an indolent inflammatory reaction. Finally, in an immunosuppressed patient the clinical course can be fulminant with spread into the orbit and cranial fossa in a manner identical to mucormycosis.[56]

Atrophic rhinitis

The nasal mucosa of a patient with atrophic rhinitis is dry, appears crusted, and emits a fetid odor. A loss of vascularity and seromucous glands contributes to the atrophy. The normal ciliated epithelium and mucous cells are replaced by squamous epithelium. In some patients there is a history of repeated infections that could explain the condition. Other patients yield no clues regarding the cause.[59]

Myospherulosis

Myospherulosis is an inflammatory and fibrous reaction that occurs after a surgical procedure on the nose or paranasal sinuses. If a hemostatic packing impregnated with antibiotic ointment is used postoperatively, the oil-based vehicle can produce a foreign body reaction. This is accompanied by a peculiar encystment of degenerating erythrocytes. The recrudescence of symptoms that necessitates reoperation may be caused, at least in part, by the foreign body reaction.[73]

Destructive midline processes and Wegener's granulomatosis

The often-used rubric "lethal midline granuloma" is not an acceptable pathologic diagnosis. It is a clinical designation referring to a patient with a destructive lesion of unknown etiology that involves the upper aerodigestive tract. Batsakis[14] has listed no fewer than 35 specific entities that can cause so-called lethal midline granuloma, including unusual infections, Wegener's granulomatosis, and neoplasms that are difficult to diagnosis such as lymphoma, lymphoepithelioma, or midline malignant reticulosis. To be sure, there is the rare patient with a destructive midline lesion that cannot be specifically diagnosed, even after exhaustive study. The term "lethal midline granuloma" can be applied clinically, but only as an admission of diagnostic failure. Some patients in this category have responded to radiation therapy.[31]

Wegener's granulomatosis is characterized by vasculitis and, usually, granulomatous inflammation (Fig. 24-2). Although the changes may be an immune response, the inciting agent(s) is unknown. Patients have nonspecific symptoms interpreted as "chronic sinusitis" or "chronic otitis media." Eventually there is ulceration of the mucosa, discharge, and destruction of subjacent structures such as nasal cartilage. At its fullest expression, Wegener's granulomatosis can attack virtually every organ, but the upper and lower respiratory tract and the kidneys are usually the most severely affected. Most patients respond to cyclophosphamide therapy.[53] Localized forms occasionally occur in either the upper respiratory tract or the lung.[30]

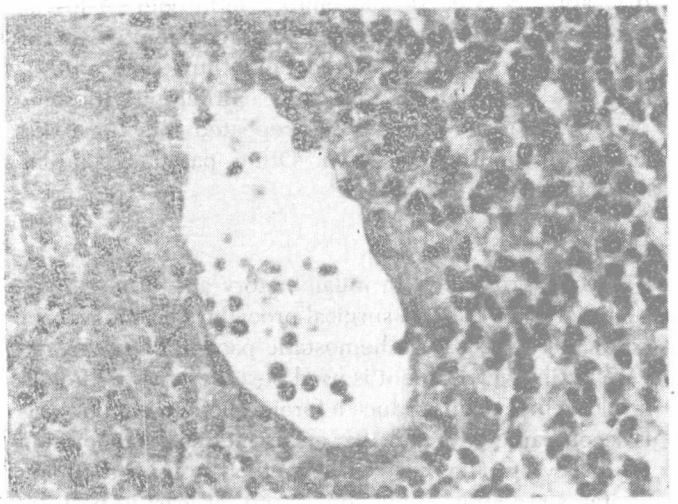

Fig. 24-2. Major alteration in Wegener's granulomatosis is acute inflammation and necrosis of vessel walls. Histiocytes are also seen (*right*).

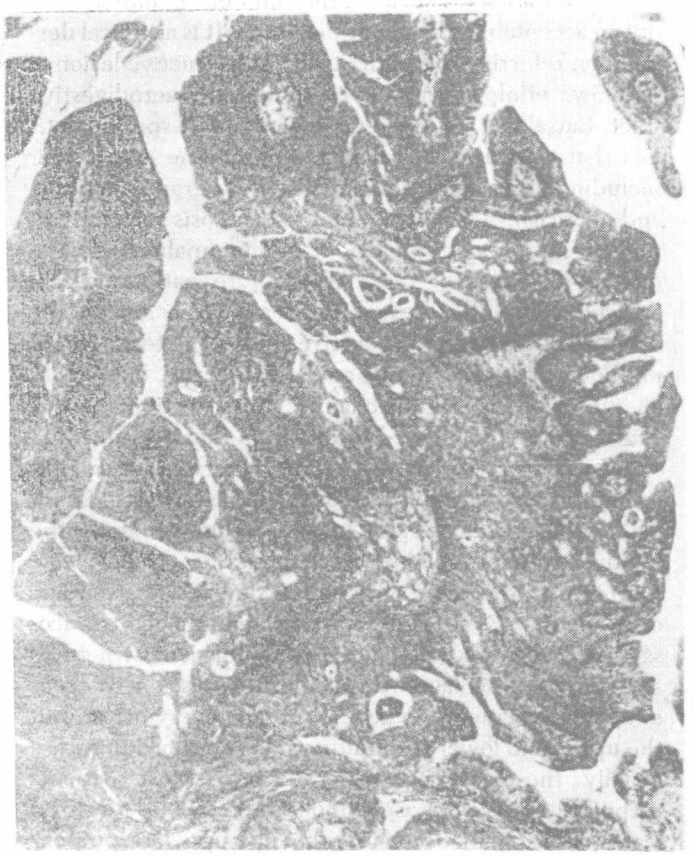

Fig. 24-3. Fungiform papilloma of nasal septum is lined predominantly by intermediate epithelium.

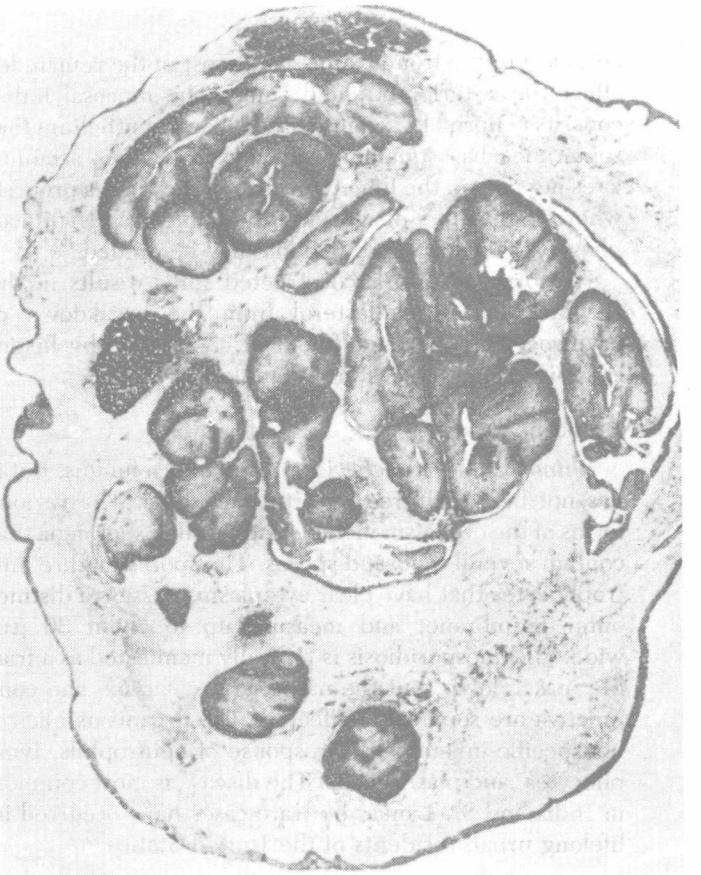

Fig. 24-4. Inverted papilloma has invaginations of intermediate epithelium into stroma. Lesion shown has normal ciliated epithelium on surface.

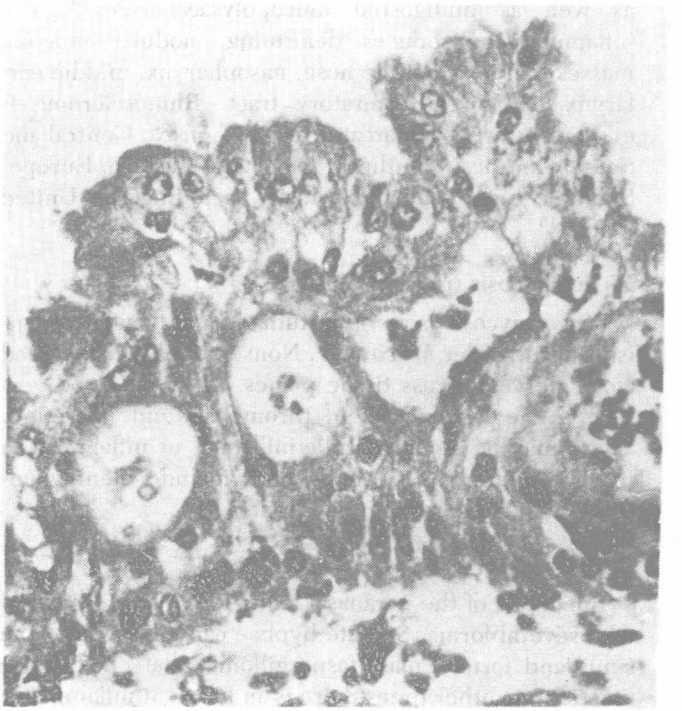

Fig. 24-5. Cylindrical cell papilloma has eosinophilic cells and spherical accumulations of mucus.

Vasculitis is a prerequisite for the diagnosis, whereas granulomas are of secondary importance and need not be present. Vascular changes range from a transmural inflammation of an otherwise intact vessel to necrosis of either a sector or a segment of a vessel. Thrombosis and luminal fibrous obliteration also occur. The granulomas, when present, are composed of mononuclear or multinucleated histiocytes. They may or may not be partly necrotic. Sometimes the only evidences of granuloma formation are small, poorly circumscribed collections of histiocytes.

Papillomas

Papillomas lined by normal or hyperkeratotic epidermis arise in the hair-bearing skin of the nasal vestibule. They are solitary and have no malignant potential.

Papillomas of the nasal cavity and paranasal sinuses have been given a bewildering number of names. The terms most widely employed are inverted papilloma, fungiform papilloma, and cylindrical cell papilloma. Sometimes they are collectively referred to as schneiderian papillomas. Although their cause is not known, they can be viewed as hyperplastic, reactive processes characterized by a proliferation of various epithelial types. Papillomas may erode bone but do not metastasize. They occur mainly in adults, especially middle-aged men. At least half recur locally unless major resections are performed to remove microscopic foci that extend beyond the grossly visible lesion.[20] Patients with fungiform papilloma are not at increased risk for malignancy, but about 5% of patients with inverted papilloma or cylindrical cell papilloma have synchronous or metachronous carcinoma, usually squamous. The carcinomas may be located in the papilloma per se or may arise at the site of a previous papilloma.[68]

The pattern seen with low-power microscopy distinguishes fungiform from inverted papillomas. Fungiform papilloma has an everted or exophytic configuration (Fig. 24-3); the inverted papilloma has invaginations or inversions of the epithelium into the underlying stroma (Fig. 24-4). Fungiform papillomas are nearly always located on the nasal septum. Inverted papillomas involve the lateral nasal wall, and often there is a paranasal sinus component. Both types of papillomas are lined with various combinations of normal ciliated epithelium, hyperplastic ciliated epithelium, mucous cells, squamous epithelium, or intermediate epithelium. The last derives its name because it is morphologically intermediate between normal columnar and normal squamous epithelium. It has also been called transitional epithelium, but this implies an unjustified relationship to transitional epithelium of the urinary bladder.[62]

Cylindrical cell papilloma has columnar or slightly polygonal cells with eosinophilic granular cytoplasm. Mucous cells are interspersed, and they may mimic fungal yeast forms when the mucus is inspissated (Fig. 24-5). The epithelium is arranged serpiginously over an edematous or loosely fibrous stroma.[48]

Benign lesions

Lobular capillary hemangioma (pyogenic granuloma)

Lobular capillary hemangioma has a distinctive lobular arrangement of capillaries in an edematous, fibroblastic stroma (Fig. 24-6).[57] The surface may be ulcerated and have an inflammatory cell infiltrate as well as superimposed reactive granulation tissue. The term "pyogenic granuloma" is often used for the ulcerated lesions. This is a misnomer because they are neither pyogenic infections

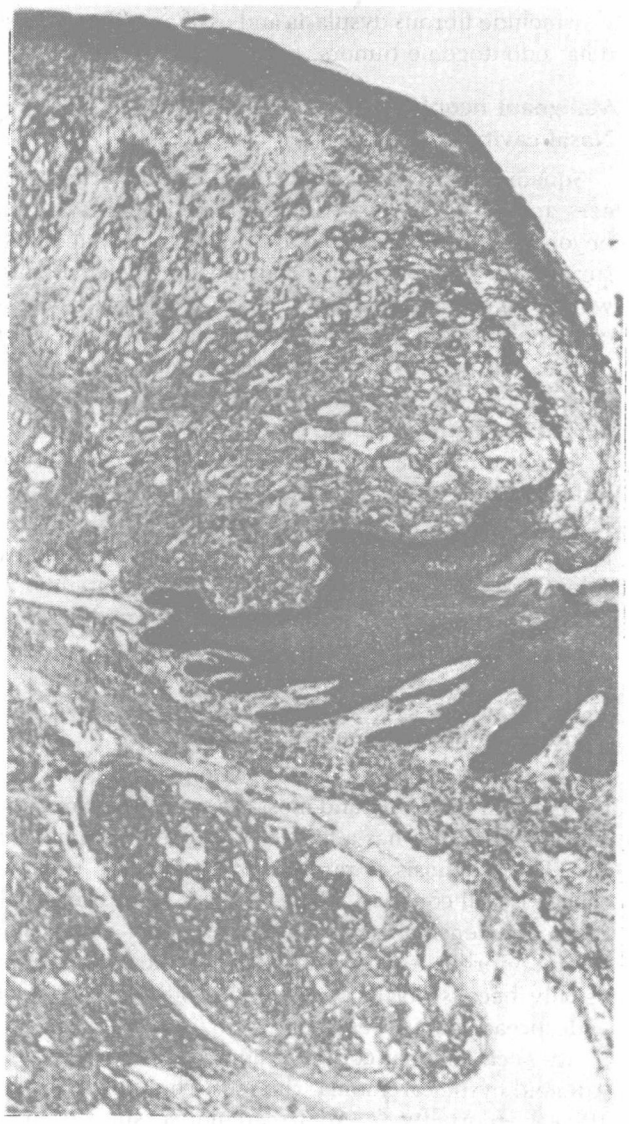

Fig. 24-6. Lobular capillary hemangioma (so-called pyogenic granuloma) has lobular pattern beneath epithelium. Lobular arrangement is lost in superficial, ulcerated portion. (From Fechner, R.E., Cooper, P.H., and Mills, S.E.: Arch. Otolaryngol. **107**:30, 1981. Copyright 1981, American Medical Association.)

nor granulomas. Patients range from 8 to 80 years of age. The lesions are rarely associated with trauma. Some have developed in pregnant women, which explains the appellation "pregnancy epulis' or "pregnancy tumor." Other types of hemangiomas, hemangiopericytoma and angiosarcoma, occur rarely in the nose.[24,34]

Miscellaneous lesions

Necrotizing sialometaplasia can be found in the glands of the nose or paranasal sinuses after surgery.[50] Any tumor arising in the mucosal glands or connective tissue eventually produces obstruction. Lesions include mixed tumors,[26] neural tumors,[63] and fibromatosis.[38] Meningiomas without intracranial connections arise in the nose and sinuses.[45] Osseous lesions that encroach on the airway include fibrous dysplasia and ossifying fibroma, osteoma, odontogenic tumors, and myxoma.[35,39]

Malignant neoplasms

Nasal cavity carcinoma

Squamous carcinomas constitute the majority of cancers arising in the nasal cavity. Most patients are men beyond 50 years of age who are smokers; only about 25% survive.[17] Occupational exposure in nickel refinery workers has been clearly related to nasal squamous cancer. Their neoplasms are concentrated on the anterior tip of the middle turbinate where the maximum air flow takes place.[13] Woodworkers are also at an increased risk for nasal squamous cancer.[44]

Adenocarcinoma is a rare tumor of the nasal mucosa but makes up a disproportionate number of carcinomas in woodworkers.[18,44] Specific carcinogens have not been identified. The tumors seldom metastasize but grow relentlessly and kill more than half of the patients. The microscopic pattern of the neoplasms in woodworkers as well as patients with other occupations often resembles that of colonic carcinoma.[49,65]

Paranasal sinus carcinoma

About 80% of cancers of the paranasal sinuses arise in the maxillary antrum, and most are squamous carcinoma. The patient often has a history of severe, chronic sinusitis. The diagnosis is rarely made when the squamous cancer is still confined to the mucosa. Almost invariably there is extension into surrounding bone, cheek, nose, palate, or orbit. About 75% of patients die of their tumor, usually because of local extension, although 10% have widespread metastases.[23]

Adenocarcinomas comprise about 5% of sinus cancers. Adenoid cystic carcinoma, the most common, has a 90% 10-year mortality.[70] Adenocarcinoma similar to the colonic-like cancer of the nasal fossa occurs in any sinus,[42] but it is especially frequent in the ethmoid sinuses of woodworkers.[44] Mucoepidermoid carcinomas and small cell ("oat cell") carcinomas also arise in the glands of the sinonasal region.[54] Approximately 8% of sinus malignancies are lymphomas, usually of histiocytic type.[69] Following radiation therapy, about 50% of patients survive.

Esthesioneuroblastoma (olfactory neuroblastoma)

The olfactory mucosa covers the superior one third of the nasal septum, the cribriform plate, and the superior turbinate. It has a mitotically active reserve cell layer from which esthesioneuroblastoma is probably derived. Clinically, there is a polypoid mass that may invade the paranasal sinuses or cranial vault. The tumors have diverse histologic patterns resulting from variable amounts of intercellular neurofibrillary material. Rosettes are formed in about 10%. If the tumor lacks these features, it is difficult to distinguish from other small cell malignancies such as rhabdomyosarcoma, undifferentiated carcinoma, or lymphoma. Ultrastructural examination is helpful if neuritic cell processes, neurofilaments, and neurotubules in association with dense core (neurosecretory) vesicles are found.[22]

Esthesioneuroblastoma occurs in all decades, with a peak incidence between the ages of 10 and 30 years. The course of the disease is capricious. Some patients die quickly with widespread metastases, whereas others live for several years before metastases or local recurrence develops. Occasionally, a patient may live with symptomatic disease for many years.[47] Approximately 50% of patients survive the disease, especially young patients with tumor confined to the nasal cavity. Small cell malignancies of the paranasal sinuses may secrete such peptides as calcitonin, ACTH, and MSH. Their relation, if any, to esthesioneuroblastomas remains to be determined.[51]

Malignant lymphoma and midline malignant reticulosis (polymorphic reticulosis)

Malignant lymphomas of conventional histologic types may appear initially in the nasal fossa, paranasal sinuses, or nasopharynx. Most patients subsequently manifest evidence of disseminated disease, although a few are cured by irradiation of the upper respiratory tract.[40]

Midline malignant reticulosis is a histologically distinctive lymphoproliferative disorder. The affected mucosa is thickened and ulcerated. Granulation tissue and inflammation may overlie the neoplastic component, and a deep biopsy is often necessary to reach the lesion. The lymphocytes are variable in size, and the nuclei are often hyperchromatic and convoluted, with prominent nucleoli. Many cells have abundant clear cytoplasm and sharply defined cell membranes (Fig. 24-7). Some cells have features of immunoblasts. The tumor often has a perivascular distribution with infiltration of vessel walls. This vas-