SEVENTH EDITION

PATHOLOGY

EDITED BY **W.A.D. Anderson**
John M. Kissane

VOLUME TWO

VOLUME TWO

PATHOLOGY

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

JOHN M. KISSANE, M.D.

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

SEVENTH EDITION

with 1728 figures and 6 color plates

THE C. V. MOSBY COMPANY

Saint Louis 1977

SEVENTH EDITION (two volumes)

Printed in the United States of America

The C. V. Mosby Company
11830 Westline Industrial Drive, St. Louis, Missouri 63141

Library of Congress Cataloging in Publication Data

Anderson, William Arnold Douglas, 1910- ed.
Pathology.

Includes bibliographies and index.
1. Pathology. I. Kissane, John M. II. Title.
[DNLM: 1. Pathology. QZ4 P2985]
RB111.A49 1977 616.07 77-1052
ISBN 0-8016-0186-X

CB/CB/B 9 8 7 6 5 4 3 2

VOLUME TWO

PATHOLOGY

CONTRIBUTORS

LESTER ADELSON, M.D.

Professor of Forensic Pathology, Department of Pathology, Case Western Reserve University School of Medicine, Cleveland; Chief Pathologist and Chief Deputy Coroner, Cuyahoga County Coroner's Office, Cleveland, Ohio

ARTHUR C. ALLEN, M.D.

Director of Laboratories, The Jewish Hospital and Medical Center of Brooklyn; Clinical Professor of Pathology, State University of New York Downstate Medical Center, Brooklyn, New York; Consultant, Hunterdon Medical Center, Flemington, New Jersey; Consultant, Fort Hamilton Veterans Administration Hospital, Brooklyn, New York

ROBERT E. ANDERSON, M.D.

Professor and Chairman, Department of Pathology, The University of New Mexico, Albuquerque; Consultant, Albuquerque Veterans Administration Hospital, Albuquerque; Consultant, Meson Physics Facility Policy Board, Los Alamos Scientific Laboratories, University of California, Los Alamos, New Mexico; Visiting Research Scientist, Radiation Effects Research Foundation, Hiroshima, Japan

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

ROGER DENIO BAKER, M.D.

Professorial Lecturer, George Washington University School of Medicine and Health Sciences, Washington, D.C.

SAROJA BHARATI

Associate Director, Congenital Heart Disease Research and Training Center, Hektoen Institute for Medical Research; Research Associate Professor of Medicine, Abraham Lincoln School of Medicine, University of Illinois; Associate Professor of Pathology, Rush Medical School, Chicago, Illinois

CHAPMAN H. BINFORD, A.D., M.D.

Chief, Special Mycobacterial Diseases Branch, Geographic Pathology Division, Armed Forces Institute of Pathology, Washington, D.C.

JACOB L. CHASON, M.D.

Professor of Pathology (Neuropathology) and Chairman of the Department of Pathology, Wayne State University School of Medicine, Detroit, Michigan

MASAHIRO CHIGA, M.D.

Professor of Pathology, Department of Pathology and Oncology, University of Kansas Medical Center, Kansas City, Kansas

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

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

SIR THEO CRAWFORD, B.Sc., M.D., F.R.C.P., F.R.C.Path.

Professor of Pathology, St. George's Hospital Medical School, University of London, London, England

GEORGE Th. DIAMANDOPOULOS, M.D.

Associate Professor 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

GERALD FINE, M.D.

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

L. M. FRANKS, M.D., F.C.A.P., F.R.C.Path.

Imperial Cancer Research Fund Laboratories, London, England

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

Professor and Chairman of the Division of Oral Pathology, University of Minnesota School of Dentistry, Minneapolis, Minnesota

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.

Distinguished Research Professor, Department of Pathology, Medical University of South Carolina, Charleston, South Carolina

EMMERICH VON HAAM, M.D.

Professor Emeritus of Pathology, The Ohio State University College of Medicine, Columbus, Ohio

BÉLA HALPERT, M.D.

Emeritus Professor of Pathology, Baylor College of Medicine, Houston, Texas

GORDON R. HENNIGAR, M.D.

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

CHARLES S. HIRSCH, M.D.

Associate Professor of Forensic Pathology, Department of Pathology, Case Western Reserve University School of Medicine, Cleveland; Associate Pathologist and Deputy Coroner, Cuyahoga County Coroner's Office, Cleveland, Ohio

HOWARD C. HOPPS, M.D., Ph.D.

Curators' Professor, Department of Pathology, University of Missouri Medical Center, Columbia, Missouri

†ROBERT C. HORN, Jr., M.D.

Late Chairman, Department of Pathology, Henry Ford Hospital, Detroit, Michigan

DAVID B. JONES, M.D.

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

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

†Deceased.

FREDERICK T. KRAUS, M.D.

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

JOSEPH F. KUZMA, B.S., M.D., M.S.

Clinical Professor of Pathology, Medical College of Wisconsin, Milwaukee, Wisconsin

PAUL E. LACY, M.D.

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

MAURICE LEV, M.D.

Director, Congenital Heart Disease Research and Training Center, Hektoen Institute for Medical Research; Professor of Pathology, Northwestern University Medical School; Professor of Pathology, Rush Medical School; Professorial Lecturer, Pritzker School of Medicine of the University of Chicago; Lecturer in the Department of Pathology, Abraham Lincoln School of Medicine, University of Illinois; Lecturer in the Department of Pathology, the Chicago Medical School, University of Health Sciences; Lecturer in the Department of Pathology, Loyola University, Stritch School of Medicine; Distinguished Professor in the Department of Pediatrics, Rush Medical College; and Career Investigator and Educator, Chicago Heart Association, Chicago, Illinois

VINCENT T. MARCHESI, M.D., Ph.D.

Anthony N. Brady Professor of Pathology and Chairman, Department of Pathology, Yale University School of Medicine, New Haven, Connecticut

RAÚL A. MARCIAL-ROJAS, M.D.

Professor of Pathology and Legal Medicine, University of Puerto Rico School of Medicine; Director, Institute of Legal Medicine, San Juan, Puerto Rico

WILLIAM A. MEISSNER, M.D.

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

JOHN B. MIALE, M.D.

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

MAX MILLARD, M.A., M.B. (Dublin), F.R.C.P. (Ireland), F.R.C.Path. (England), D.C.P. (London)

Director of Pathology Laboratories, South Miami Hospital, Miami, Florida

FATHOLLAH K. MOSTOFI, A.B., B.Sc., M.D.

Associate Chairman, Center for Advanced Pathology; Chairman, Department of Genitourinary Pathology; Registrar, Urologic Registries; Head, World Health Organization International Reference Center on Tumors of Male Genitourinary Tract; Veterans Administration Special Reference Laboratory for Pathology at the Armed Forces Institute of Pathology; Clinical Professor of Pathology, Georgetown University Medical Center, Washington, D.C.; Professor of Pathology, University of Maryland School of Medicine; Associate Professor of Pathology, Johns Hopkins University Medical School, Baltimore, Maryland

WAYKIN NOPANITAYA, Ph.D.

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

JAMES E. OERTEL, M.D.

Chief 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; Director of Pathology and Laboratories, University of Southern California Liver Unit at Rancho Los Amigos Hospital, Downey, California

HENRY PINKERTON, B.S., M.D.

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

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

Department of Pathology, St. Paul's Hospital, London, England

JUAN ROSAI, M.D.

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

ARKADI M. RYWLIN, M.D.

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

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

Professor and Chairman, Department of Pathology, Northwestern University Medical School, Chicago, Illinois

THOMAS M. SCOTTI, A.B., M.D.

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

STEWART SELL, M.D.

Professor of Pathology, School of Medicine, University of California at San Diego, La Jolla, California

†RICHARD SHUMAN, B.S., M.D.

Late Professor of Pathology, Medical College of Pennsylvania; Consultant in Pathology, Veterans Administration Hospital, Philadelphia, Pennsylvania; formerly Chief of Soft Tissue Section, Pathology Division, Armed Forces Institute of Pathology; formerly Head of International Center for Soft Tissue Tumors, World Health Organization, Washington, D.C.

RUTH SILBERBERG, M.D.

Professor of Pathology, Departments of Anatomy and Orthopedic Surgery, Hadassah Hebrew University, School of Medicine, Kiryat Hadassah, Jerusalem, Israel

STANLEY B. SMITH, M.D.

Pathologist, Variety Children's Hospital, Miami, Florida

SHELDON C. SOMMERS, M.D.

Director of Laboratories, Lenox Hill Hospital; 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.

Associate Professor of Pathology, Washington University School of Medicine; Associate Professor of Oral Biology, Washington University School of Dental Medicine; Associate Pathologist, The Jewish Hospital of St. Louis; Pathologist, Shriners Hospital for Crippled Children, St. Louis, Missouri

ROBERT A. VICKERS, D.D.S., M.S.D.

Professor of Oral Pathology, University of Minnesota School of Dentistry, Minneapolis, Minnesota

NANCY E. WARNER, M.D.

Chairman, Department of Pathology, University of Southern California School of Medicine, Los Angeles, California

D. L. WILHELM, M.D., Ph.D.

Professor and Head of School of Pathology, University of New South Wales; Director of Pathology, The Prince Henry Hospital and The Prince of Wales Hospital, Sydney, Australia

LORENZ E. ZIMMERMAN, M.D.

Chief, Ophthalmic Pathology Branch, Armed Forces Institute of Pathology, and Clinical Professor of Ophthalmic Pathology, The George Washington University School of Medicine, Washington, D.C.

†Deceased.

PREFACE to seventh edition

The preface to the sixth edition of *Pathology* mentioned a merging between pathology and other so-called basic sciences that compelled a certain arbitrariness relating to inclusion or exclusion of many subjects in which recent advances had been made. In the preparation of this seventh edition, we have taken cognizance of some of those points of merging to which highly specific, not merely arbitrary, consideration must be given, that is, consideration regarding inclusion in the undergraduate medical curriculum. In planning for and executing this seventh edition, we recognized the fact that many schools now introduce pathology in the first year of the undergraduate medical curriculum. This fact compels teachers of pathology to place their contributions even more specifically in contextual relationship with the so-called "basic sciences" while maintaining relevant contemporariness in their applications to clinical medicine.

To these ends, several chapters have been rewritten by new contributors. We welcome them to this, our joint effort, at the same time that we thank those colleagues whom they have succeeded.

We hope that this revision will continue to entitle this work to the acceptance that preceding editions have enjoyed as a source for consideration by students during their preclinical years, no less than during their clinical years. A conscious effort has been made to continue the emphasis upon clinicopathologic correlations to the end that the work would continue to merit the confidence enjoyed by previous editions as a reliable, up-to-date source of information related to pathologic anatomy, important in the practice of the many defined areas of clinical medicine, including that of pathology itself.

W. A. D. Anderson

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, world-wide 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 Char-

lotte Skacel 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

COLOR PLATES

1 Syphilis, 438

2 Congenital aganglionic megacolon; multifocal epidermoid carcinoma of esophagus; familial multiple polyposis of colon; multiple chronic gastric (peptic) ulcers; carcinomatous ulcer of stomach; carcinoma of stomach, linitis plastica type; multiple carcinoid tumors of ileum, 1278

3 Needle biopsy in epidemic hepatitis; centrilobular bile stasis in patient taking oral contraceptive; acute pericholangitis and cholestasis in needle biopsy; hyaline necrosis in alcoholic, 1340

4 Submassive hepatic necrosis from viral hepatitis; large, deep yellow fatty liver, etiology unknown; granular to nodular liver of advanced Laennec's cirrhosis; small liver with bulging nodules in patient with postnecrotic cirrhosis; suppurative cholangitis with multiple abscesses secondary to carcinomatous obstruction of common duct, 1340

5 Hepatic cirrhosis; arteriovenous fistulas in diabetic cirrhosis; Kayser-Fleischer ring in Wilson's disease; jaundice and biliary cirrhosis after ligation of common bile duct, 1376

6 Ochronosis of knee joint and of intervertebral discs; purulent arthritis developing in course of staphylococcic osteomyelitis, with purulent exudate in both joint capsule and bone marrow; osteoarthrosis of femoral head, with ulceration of articular cartilage and marginal lipping, 2018

CONTENTS

VOLUME ONE

VOLUME TWO

25/Testes, scrotum, and penis

FATHOLLAH K. MOSTOFI

TESTES

Anomalies

Excluding malposition of the testicle, other anomalies are very rare. Anorchidism (congenital absence) and monorchidism (one testicle) have been reported. Synorchidism (fusion of testicles) occurs intra-abdominally. Polyorchidism has been found at operation and necropsy.

Ectopic testis. Ectopic testis is a congenital malposition of the testicle outside of the normal channel of descent. This ectopia, according to its location, is classified as interstitial, pubopenile, femoral, crural, transverse, and perineal.

Cryptorchidism. When the congenital malposition results in retention of the testicle anywhere along the route of descent, it is known as cryptorchidism. The cause of cryptorchidism is not always evident. The various apparent causes are short spermatic vessels or vas deferens, adhesions to the peritoneum, poorly developed inguinal canal or superficial abdominal ring, maldevelopment of the scrotum or cremaster muscles, and hormonal influences. Incomplete descent is found quite frequently during the first few months of infancy. The incidence is about 4% in boys under 15 years of age and about 0.2% in adults. Histologically, the cryptorchid testis before puberty does not differ from the normally descended organ. After puberty, however, it is always smaller than normal. The capsule is somewhat thickened and wrinkled. The epididymis is separated from the mesorchium. There is progressive loss of germ cell elements. The tubules may be lined only with spermatogonia and spermatids, but occasionally there is spermatogenesis. In fact, foci of spermatogenesis are found in 10% of undescended testes. This condition has also been reported in abdominal testis. It is estimated that 10% of men with untreated cryptorchidism remain fertile. The basement membrane of the tubules thicken and hyalinize. In later stages spermatogenesis is rare or absent and the tubules are lined only with Sertoli cells. Tubules with completely occluded lumens are not uncommon. The collecting tubules and rete may be quite prominent, a condition that suggests hyperplasia and even adenoma. The intertubular tissue is sparsely cellular and becomes more dense with age. The interstitial cells of Leydig are conspicuous and vary in number. In some cases the Leydig cells are decreased in number, and in other cases they are increased both in size and in number. They are found singly, in small groups, and occasionally in large masses. In some cryptorchid testicles, most of the atrophied organ is composed of large groups of polyhedral Leydig cells between which may be found scanty fibrous tissue and a few fibrosed tubules. In rare instances, very few cellular elements are encountered and the entire testes become completely fibrosed.

The cause of atrophy of undescended and ectopic testes is not known. There is convincing evidence that an optimum temperature is necessary for spermatogenesis and that temperatures higher than that within the scrotum suppress spermatogenesis. When aspermia or hypospermia exists, the testicle atrophies. The chief function of the scrotum is to regulate the temperature for the testes. Ischemia caused by pressure, stressed by some authors, is definitely a minor factor in causing suppression of spermatogenesis in cryptorchidism. There is a high incidence of tumors of the testes in cryptorchidism.

Intersexuality. A *true hermaphrodite* or *ambisexual* is one who possesses an ovary and a testicle or two ovotestes with or without external genitalia of both sexes. A *pseudohermaphrodite* possesses gonads of one sex and genitalia of either both or opposite sexes. In the *male pseudohermaphrodite,* the testes are present, but the internal genitalia are of both

sexes, and the penis and scrotum are poorly developed. In the *female pseudohermaphrodite,* the ovaries are present, usually in their normal position, the vagina is rudimentary and opens into the urethra, and the clitoris is hypertrophied.

Status of the testis in male infertility

About 15 out of every 100 marriages in the United States are barren, and male infertility accounts for about half of the cases. In all such patients quantitative determination of urinary 17-ketosteroids, estrogens, and gonadotropins; karyotyping; and testicular biopsy are essential to determine the specific cause of the male infertility and whether it is curable. Wong and his co-workers have proposed a simple classification of male infertility: pretesticular, testicular, and posttesticular.

Pretesticular causes of infertility are mainly hypopituitarism, endogenous or exogenous estrogen or androgen excess, hypothyroidism, diabetes mellitus, and glucocorticoid excess.

Hypopituitarism may be prepubertal or postpubertal. Prepubertal causes include lesions in or adjacent to the pituitary (e.g., craniopharyngiomas, trauma, and cysts). Such patients eventually manifest sexual infantilism, failure of somatic growth, and varying degrees of adrenal and thyroid hypofunction. Testicular biopsy shows small immature seminiferous tubules and immature Leydig cells similar to prepubertal testis.

Postpubertal hypopituitarism results from tumors, trauma, or infarction. Testicular biopsy shows maturation arrest, loss of germ cells, reduced diameter of tubules, and progressive thickening and hyalinization of tunica propria. The Leydig cells are small and shriveled.

Hypopituitarism may be the result of genetic defects in gonadotropin secretion. There are no demonstrable lesions of the pituitary and deficiencies of adrenal and thyroid function or growth. The patients may show deficiency of both follicle stimulating (FSH) and luteinizing hormones (LH), or the FSH may be normal but LH deficient. The patients are generally tall and eunuchoid. Testicular biopsy in the former shows small and immature seminiferous tubules resembling prepubertal testis. In the latter the seminiferous tubules show a greater degree of development than do the Leydig cells.

Estrogen excess may be endogenous (hepatic cirrhosis, adrenal tumor, Sertoli or Leydig cell tumor) or exogenous (administered to patients with cancer of prostate). Initially, the biopsy shows failure of maturation, progressive decrease of germinal elements, diminished diameter of seminiferous tubules, and thickening and hyalinization of tunica propria. Eventually there is complete sclerosis of tubules and atrophy of Leydig cells. The findings are identical to those of postpubertal hypopituitarism.

Androgen excess may be endogenous (adrenogenital syndrome, androgen-producing adrenal cortical or testicular tumors) or exogenous (oral administartion). Pathologic findings depend on whether the condition developed before or after puberty. If prepubertal, the result is virilism and failure of the testis to mature. If postpubertal, there is progressive loss of germ cells and, unless recognized and remedied, tubular sclerosis.

Glucocorticoid excess, whether endogenous (Cushing's syndrome) or exogenous (administered for treatment of ulcerative colitis, rheumatoid arthritis, or bronchial asthma) can result in oligospermia and maturation arrest or hypospermatogenesis.

Hypothyroidism and diabetes mellitus may result in decreased fertility. Hypospermatogenesis is followed by thickening of tunica propria. In uncontrolled diabetes autonomic neuropathy may result in impotence.

Testicular causes of infertility are agonadism, cryptorchidism, maturation arrest, hypospermatogenesis, absence of germ cells (Sertoli cell–only syndrome), Klinefelter's syndrome, mumps orchitis, and irradiation damage.

Agonadism

Congenital agonadism is extremely rare and consists of total absence of the testes. If this occurs in early embryonic life, the infant will be female. Occasionally in cryptorchid boys the epididymis ends blindly, but careful search fails to show any gonadal tissue (the "vanishing testis syndrome"). The chromosomal pattern is XY. Since testes must have been present in fetal life to initiate male development, they must have been resorbed after that period.

Bilateral anorchia may be associated with incomplete differentiation of male genitalia. The gonads and the internal genital structures may be absent or rudimentary. These findings suggest that the testes must have been present to initiate male sex development but vanished before maturity.

Jost showed that fetal testis played an important role in the early development of the wolffian structures and regression of müllerian

elements. The development of wolffian structures was related to the local androgen production, whereas regression of müllerian elements seemed to be influenced by additional nonandrogenic factors. Federman's excellent discussion of the situation may be summarized as follows: If the male fetus begins life with dysgenetic testis, varying degrees of pseudohermaphroditism may ensue; if gonadal failure occurs before organization of the genital tract, female external genitalia will result; if gonadal failure occurs during the period of male sexual differentiation, ambiguous genitalia may result; if, however, testicular failure occurs after the sixteenth week of gestation, the male structures are established and the patient would develop as a male but without testes.

Cryptorchidism

The histology of cryptorchidism is described on p. 1013.

Maturation arrest

Maturation arrest is manifested in a testicular biopsy by the failure of normal spermatogenesis at some stage. Most commonly this is at the stage of primary spermatocytes. No secondary spermatocytes, spermatids, or spermatozoa are present. It may also be at the spermatid stage with few or no spermatozoa.

The Sertoli cells, testicular tunica propria, and Leydig cells are normal as is the diameter of the seminiferous tubules. There is oligospermia, or azoospermia. The urinary FSH, LH, and 7-ketosteroids are normal.

Hypospermatogenesis

Hypospermatogenesis is more difficult to detect. All cells of spermatogenic series are present in the same proportions as normal, but the number of each variety is decreased. The seminiferous tubules are of normal size. Sertoli and Leydig cells and the tunica of the tubules are normal. Patients have oligospermia with normal urinary FSH, LH, and 17-ketosteroids.

Absence of germ cells (Sertoli cell–only syndrome)

The characteristic feature of this group is the absence of germ cells with the seminiferous tubules lined solely by exuberant Sertoli cells. In a few tubules germ cells may persist. The diameter of seminiferous tubules is decreased; the tunica propria of the tubules is not thickened and the Leydig cells are normal. The secondary sex characteristics are well developed; the patients are potent but infertile. The urinary 17-ketosteroids are normal, but urinary FSH and LH are invariably high.

Klinefelter's syndrome

About 3% of male sterility is attributable to primary hypogonadism. This syndrome is characterized by testicular hypoplasia, azoospermia, gynecomastia, eunuchoid build, increase of urinary gonadotropin, and, not infrequently, subnormal intelligence. The diagnosis is seldom made before puberty. Chromosome studies reveal an XXY intersexuality caused by fertilization of an ovum whose divided X chromosome failed to separate. Such individuals have a sex-chromatin pattern similar to genetic females. However, other individuals with a similar or nearly similar syndrome are genetically males.

There is increased urinary excretion of pituitary gonadotropic hormones, but the reason is not that there are any abnormalities of the pituitary gland but is attributed to the absence of the controlling influence of some testicular hormones.

The tests are usually small (1.5×0.5 cm). The histology of the biopsy varies widely. It has been reported that the tubules are sclerosed and hyalinized and there is an apparent increase in the number of interstitial cells. Tubular fibrosis is progressive and is associated with retardation of spermatogenesis. Spermatogenic activity varies greatly. Careful examination of a biopsy may fail to show any activity whatsoever, but it may be found only on examination of the entire testis. Maturation as far as primary spermatogenesis, even to the stage of secondary spermatocytes and spermatids and, in rare instances, spermatozoa, has been reported. The release of sperm from the testis to the ejaculate is uncommon, but a few have been observed.

Mumps orchitis

The histology of mumps orchitis is described on p. 1017. Ten to 20 years after the initial infection, depending on the extent of testicular involvement, there may be oligospermia or azoospermia. The 17-ketosteroids and LH are normal, and the level of FSH is elevated.

Irradiation damage

Permanent germ cell destruction results from exposure to radiation so that in time the tubules are lined by Sertoli cells only. The diameter of seminiferous tubules is progres-

sively smaller and the tunica is thicker, terminating in sclerosis. Leydig cells are preserved. The patient is azoospermic or oligospermic. Urinary FSH is elevated, but the 17-ketosteroids and LH are normal.

Posttesticular causes of infertility consist mainly of block, which may be congenital (absence or atresia of vas deferens or epididymis) or acquired. Acquired is more frequent and may be either on the basis of infection (gonorrhea, etc.) or surgical intervention (voluntary or iatrogenic). The clinical manifestation is azoospermia. The testicular biopsy in such patients shows active spermatogenesis. The seminiferous tubules may be dilated, and there may be hypospermatogenesis or cellular sloughing, or both.

Another cause of posttesticular infertility is impaired sperm mobility. Wong and his coworkers reserve this term specifically to those cases in which the sperm counts are adequate and the testicular biopsy specimens are normal, yet the mobility of spermatozoa in the semen is either greatly impaired or absent.

In all men with infertility, testicular biopsy is necessary for proper categorization and for prognosis.

Acquired atrophy

Excluding undescended testicles, acquired atrophy occurs in senility, prolonged hyperpyrexia, debility, avitaminosis, cirrhosis of the liver, hypothyroidism, schizophrenia, estrogen medication for carcinoma of the prostate, and diseases of the pituitary gland and hypothalamus. Faulty or suppressed spermatogenesis without other changes may questionably be considered as mild atrophy. The early findings in atrophy are degenerative changes of the spermatogonia cells. As atrophy progresses, the germinal epithelial cells disappear, leaving only Sertoli cells resting on a thickened basement membrane. The seminiferous tubules become small and farther apart, and the interstitial cells of Leydig appear prominent (Fig. 25-1).

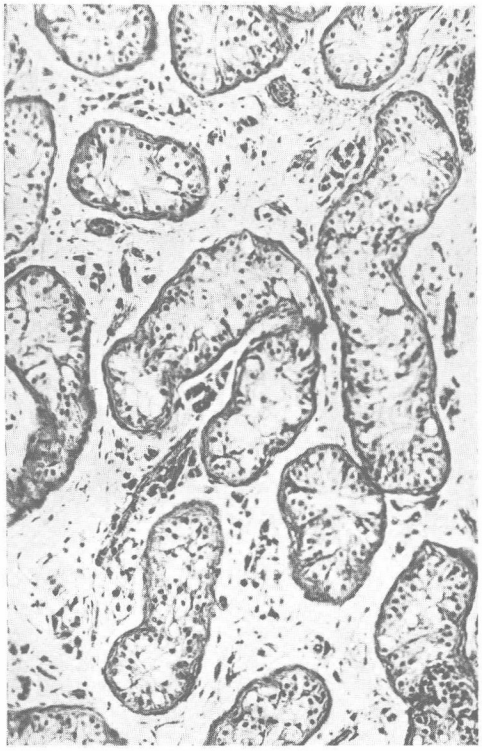

Fig. 25-1. Atrophy of testicle. Thickened tubular basement membranes lined with degenerated spermatogonia and Sertoli cells. Prominent Leydig cells in interstitial tissue.

Thrombosis and infarction

Hemorrhage, thrombosis, and infarction of the testicle occur in trauma, torsion, leukemias, bacterial endocarditis, and periarteritis nodosa (Fig. 25-2). Birth trauma may cause hemorrhage of the testicle. Many such hemorrhages are small hematomas that rapidly resorb.

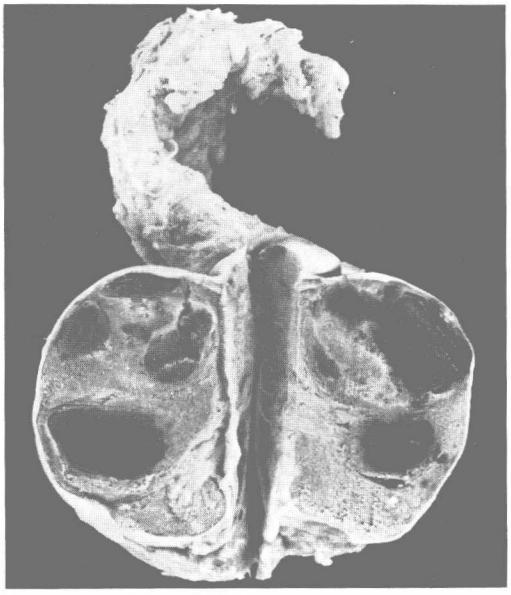

Fig. 25-2. Multiple infarcts of testicle in periarteritis nodosa.

Torsion

A sudden twisting of the spermatic cord results in strangulation of the blood vessels