Principles and Management of Urologic Cancer

edited by
Nasser Javadpour, M.D., F.A.C.S.

Principles and Management of Urologic Cancer

edited by
Nasser Javadpour, M.D., F.A.C.S.

Urologist in Charge and Senior Investigator,
National Cancer Institute and Consultant,
National Naval and Walter Reed Army Hospitals
Bethesda, Maryland

THE WILLIAMS & WILKINS COMPANY
Baltimore

Made in the United States of America

Library of Congress Cataloging in Publication Data

Main entry under title:

Principles and management of urologic cancer.

Includes bibliographies and index.
1. Urinary organs—Cancer. 2. Generative organs, Male—Cancer. I. Javadpour, Nasser. [DNLM: 1. Urologic neoplasms. WJ160 P957]
RC280.U74 616.9'94'6 78-18211
ISBN 0-683-04463-X

Composed and printed at the
Waverly Press, Inc.
Mt. Royal and Guilford Aves.
Baltimore, Md. 21202, U.S.A.

Foreword

Cancers of the urinary tract in women and of the urogenital tract in men are common, accounting for 25% of all new malignancies in men and 4% of new tumors in women. Fortunately, during the last decade the field of urologic oncology has blossomed providing new hope for patients with these malignancies. These advances have been distributed throughout the field, providing new insight into etiology, diagnosis, and treatment.

Refined diagnostic procedures utilizing improved noninvasive techniques have led to earlier diagnosis and more accurate staging. In patients with renal masses, the use of sonography or computed tomography in combination with percutaneous needle aspiration and cytology has rendered operative exploration of most cystic renal masses obsolete. Years ago, the field of urology provided one of the first tumor markers, acid phosphatase. Today the use of radioimmunoassay techniques to measure acid phosphatase, alpha-fetoprotein, chorionic gonodotropin, and other markers has enabled the clinician to detect the presence of tumors that are not otherwise demonstrable. In the future, the use of other immunobiological markers, such as ABO blood group antigens, may provide further insight into the biological activity of these malignancies.

Over the past decade, many institutions have reported their experience in the surgical management of urological tumors. These reports form a basis for defining the limitations of surgery alone in the management of these malignancies. Based on these findings, clinical and pathological criteria for staging have been refined and the indications for adjunctive therapy with irradiation or chemotherapy have been better appreciated. In the management of patients with invasive carcinoma of the bladder, the combination of radiation and surgery has resulted in improved survival, and the development of effective chemotherapeutic protocols has revolutionized the management of patients with disseminated testicular tumors.

The rapid developments in the field of urological oncology have outpaced the ability of many clinicians to assimilate and apply these advances. This book provides a much needed authoritative and comprehensive compendium in which the field of urological oncology is analyzed in cross-section. First,

the basic principles of etiology, epidemiology, and pathogenesis and principles of various treatment modalities are discussed. Following this approach, each individual neoplasm is analyzed separately. The authors have admirably covered all aspects of this rapidly developing field, leaving the reader with an understanding of the broad scope of oncology and a detailed understanding of each separate malignancy. This book should be part of the library of every practicing urologist, oncologist, and clinician who deals with problems in urological cancer.

Patrick C. Walsh, M.D.
Professor and Director
Department of Urology
The Johns Hopkins Medical School

Preface

The objectives of this book are to provide the practicing urologist, oncologist and student with the principles of diagnosis and management of urologic cancer.

Although the molecular biology and clinical problems of cancer are complex there have been encouraging advances in the past several years. The majority of these advances have been in the areas of tumor markers, new chemotherapeutic regimens, improved surgical and radiation techniques and the recognition of efficacious combinations of treatment modalities. The improved survival of patients with Wilms' tumors, testicular cancer and embryonal rhabdomyosarcoma reflects these improvements.

This book has been designed to cover first the general topics of epidemiology, carcinogenesis, pathogenesis, the design of clinical trials and the principles of immunobiology, chemotherapy, radiation therapy, and nuclear medicine as they apply to urologic cancer. The remaining portion is directed at cancer of specific organs including adrenal, kidney, bladder and the male genital system in children and adults.

Although each topic is covered in depth, I would like to cite two areas of advancement which I feel have been particularly significant. First, although the fields of immunobiology and immunotherapy of cancer are in their infancy, it is from investigation in this area that the technique of radioimmunoassay has been made available. This technique has allowed sensitive and specific measurement of tumor markers, which in turn has given us the ability to stage and monitor certain tumors with near complete accuracy. Second, in the past several years it has been recognized that in a complicated clinical setting such as cancer, the superiority of one treatment over another should be solved by utilizing a prospective randomized clinical trial. It is also clear that retrospective studies have biases against which large sample size is no protection. The recognition that prospective randomized clinical trials are superior has lead to the scientific evaluation of treatment modalities in answering specific questions in the treatment of some cancers.

Attempts have been made in compiling the bibliographies to provide the reader with selected references rather than an encyclopedic review of the literature.

In keeping with the recent unprecedented progress in cancer and cancer research, contributors of recognized au-

thority have been chosen for each section. The great contributions of time and talent by the participating authors I humbly appreciate. Finally, I am grateful to Williams & Wilkins for their cooperation at all stages of preparation.

Nasser Javadpour, MD
National Cancer Institute

Contributors

Tom Anderson, M.D., Senior Investigator and Attending Physician, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

George T. Bryan, M.D., Ph.D., Professor, Human Oncology, Wisconsin Clinical Cancer Center, University of Wisconsin, Madison, Wisconsin

Willian L. Caldwell, M.D., Director, Division of Radiation Oncology, Department of Human Oncology, Wisconsin Clinical Cancer, University of Wisconsin, Madison, Wisconsin

Philip Cole, M.D., Dr. P. H., Unit of Epidemiology and Biostatistics, International Agency for Research on Cancer, Lyon, France. Present address: Professor, Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts

C. J. Davis, Jr., M.D., Armed Forces Institute of Pathology, Washington, D.C.

N. Reed Dunnick, M.D., Staff Radiologist, Clinical Center, National Institutes of Health, Bethesda, Maryland

R. Cameron Emmott, M.D., Guest Worker, Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

Patrick Guinon, M.D., Chief of Division of Urology, Abraham Lincoln School of Medicine, University of Illinois, Chicago, Illinois

Nasser Javadpour, M.D., FACS, Urologist in Charge and Senior Investigator, National Cancer Institute and Consultant, National Naval and Walter Reed Army Hospitals, Bethesda, Maryland

Gerald S. Johnston, M.D., Chief, Department of Nuclear Medicine, Clinical Center, National Institutes of Health, Bethesda, Maryland; Professor of Medicine and Director of Nuclear Medicine, University of Maryland School of Medicine, Baltimore, Maryland

Gerald M. Lower, Jr., Ph.D., Assistant Professor, Human Oncology, Wisconsin Clinical Center, University of Wisconsin, Madison, Wisconsin

Edwin M. Meares, Jr., M.D., Whitney Professor of Urology, Chairman, Division of Urology, Tufts University School of Medicine; Chairman, Department of Urology, New England Medical Center Hospital, Boston, Massachusetts

Claude E. Merrin, M.D., Chief, Department of Urologic Oncology, Roswell Park Memorial Institute, Buffalo, New York

Alan S. Morrison, M.D., Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts

F. K. Mostofi, M.D., Chief, Genitourinary Pathology Department, Armed Forces Institute of Pathology, Washington, D.C.

Gerald P. Murphy, M.D., D.Sc., Director, Roswell Park Memorial Institute, Buffalo, New York

Carl A. Olsson, M.D., Professor and Chairman, Department of Urology, University Hospital, Boston University School of Medicine, Boston, Massachusetts

Biswamay Ray, M.D., Assistant Professor, Division of Urology, University of Illinois Hospital, Chicago, Illinois

Richard Simon, Ph.D., Chief, Biometric Branch, Clinical Oncology Program, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

Joseph Spaulding, M.D., Assistant Clinical Professor, Department of Urology, University of California School of Medicine at San Francisco; and Acting Chairman, Veterans' Administration Hospital, San Francisco, California

Ralph W. deVere White, M.D., Assistant Professor of Urology, University Hospital, Boston University School of Medicine, Boston, Massachusetts.

Contents

Chapter 1

Epidemiology of Urologic Cancers

ALAN S. MORRISON, M.D.
PHILIP COLE, M.D.

Introduction

Urologic cancers include malignancies of the genital and urinary organs of men and urinary organs of women. In the United States, urologic cancers account for about one-quarter of all new cases of cancer among men and about 15% of male cancer deaths. For women, cancer of the urinary organs accounts for 4% of new cases of cancer, and 3% of cancer deaths. By site, the cancers to be discussed here are those of the prostate, urinary tract (urinary bladder, renal pelvis, ureter, urethra), kidney (including nephroblastoma), testis and penis.

Even by itself, cancer of the prostate can rightly be considered a serious public health problem. Among White men, the prostate is the second most frequent site of cancer development. Among Black men, cancer of the prostate is now the most commonly occurring malignancy. Important questions in the etiology of prostate cancer concern its relationship to sexual factors and to benign prostatic hypertrophy. Of urologic cancers, bladder cancer has been the most intensively studied epidemiologically. Cigarette smoking and employment in certain occupations appear to cause most cases that occur in industrialized areas. Undescended testis has been well documented as a risk factor for testicular cancer, but little else is known of the etiology of this tumor. Cancer of the kidney has been related to cigarette smoking. The little that is known of cancer of the penis suggests that this disease is related in some way to poverty, poor penile hygiene or a genital virus.

Basic Methods

Epidemiology is the science which deals with the occurrence of human illness. The statistics most commonly used to measure the occurrence of illness are the incidence rate and the mortality rate. These rates sometimes are expressed, respectively, as the number of new cases, or of deaths, occurring in a population of 100,000 in a year. In the present

review these rates are expressed as cases, or deaths, per 100,000 person-years. Ratios of incidence or mortality rates often are used to compare these rates for different groups of people. The "relative risk" or "relative incidence" is taken to be the ratio of the incidence rate of a disease in a group that has been exposed to a particular factor, to the incidence rate of a group that has not been exposed. Another disease measure related to incidence and mortality rates is the *proportional* incidence or mortality. This statistic gives the number of cases or deaths for a particular disease as a proportion of all cases or deaths. Where incidence or mortality rates are not available, proportional data can provide useful information. However, proportional incidence and mortality figures have the major limitation that such figures reflect not only the rates of the disease of interest, but also the rates of all other conditions in the groups being studied.

A statistic of particular value to clinicians is the "relative survival." The relative survival is the probability that a patient with a disease will not die from that disease for a given period of time. The time periods most often used are the 3, 5 and 10 year periods following diagnosis. The word "relative" indicates that the effects of causes of death other than the disease in question have been removed from the total mortality experience that is observed.

Disease rates may vary greatly with age, sex and race. As a result, statistics often are presented separately for individual age, sex or race groups. Such statistics are then referred to as "specific" for these characteristics, for example, "age-specific incidence rates," and "age-sex specific 5 year relative survival." For purposes of comparison or presentation, sets of specific rates or survival probabilities may be summarized with a single figure by adjustment, that is, by taking a weighted average of the specific data using a "standard" set of weights. The summary statistic is referred to as "standardized," for example, the "age-standardized incidence rate."

In the next section, a number of sources of broadly based data on disease rates are described. If these routinely available sources do not provide desired information on disease rates in relation to specific factors of interest, then *ad hoc* studies may be done. The most frequently used designs are the follow-up or cohort study, and the case-control study. In a follow-up study, incidence or mortality rates are observed for groups defined by exposure. For example, incidence rates of bladder cancer might be determined for a group of smokers and for a group of nonsmokers, and these rates then would be compared. In a case-control study, groups are defined, instead, on the basis of the development of disease, and the exposure patterns of the groups are measured. For example, the proportion of smokers could be determined for patients with newly diagnosed bladder cancer (the "cases") and for a group of unaffected people (the "controls"). Despite the "retrospective" nature of case-control studies, these studies do allow for valid measurement of relative risk of developing a disease according to exposure status.

Sources of Data

The following sources contain detailed information on cancer incidence, mortality and survival.

1. Third National Cancer Survey: Incidence Data.[9] This volume provides crude incidence rates for cancer of every site, as well as data specific for age, sex and race. The source of the data is a survey done in nine areas of the United States in 1969–71.
2. Cancer Incidence in Five Continents, Volume III.[45] This volume provides information similar to that described above but includes data on populations all over the world. A discussion of cancer registration is also presented.
3. Vital Statistics of the United States.[38] Each year the Division of Vital Statistics of the United States publishes numbers of deaths and death rates for most cancer sites according to age, sex and race.
4. Atlases of cancer mortality.[28, 29] These volumes pictorialize cancer mortality rates by county for most cancer sites. One volume pertains to Whites and one to non-Whites.
5. Ca—A Cancer Journal for Clinicians.[7] Each year the January-February number of this journal includes detailed estimates of number of cases and of deaths for cancers of most sites. This issue serves well for the purpose of keeping up with the evolving picture of cancer in the United States. (This journal is available without cost from state or national headquarters of the American Cancer Society.
6. Cancer Patient Survival, Report Number 5.[4] These reports are prepared periodically by the SEER (Surveillance, Epidemiology and End Results) program of the National Cancer Institute. They provide both overviews and detailed data on survival, by site, according to age, sex, race and other factors.

Epidemiology by Site

Sites will be considered in decreasing order of incidence rate in the United States, that is, prostate, urinary tract, kidney, testis and penis. Each section will begin with a presentation of rates according to age, sex, race and so on—the "descriptive" features of the disease. This information is summarized in Tables 1.1–1.4 and Figs. 1.1–1.5.

Table 1.1 presents U.S. incidence rates for each site by age and race (and sex, when appropriate).[9] Time trends of U.S. incidence and mortality rates[10] for the three most frequently occurring urologic sites are summarized in Table 1.2. Age-standardized incidence rates of urologic cancers for various countries[45] are given in Table 1.3, and data on relative survival for the five sites[4] are presented in Table 1.4. Figs. 1.1 to 1.5 present graphically the incidence rates in Table 1.1.

The descriptive data provide a background for the discussion of the effects of specific risk factors that follows. For

TABLE 1.1. Age-specific and Age-standardized Incidence Rates* for Cancers of Urologic Sites in the United States†

Age	Prostate		Bladder				Kidney				Testis		Penis	
			Male		Female		Male		Female					
	White	Black	White	Black	White	Black	White	Black	White	Black	White	Black	White	Black
<5			0.2		0.1		1.9	2.5	1.7	1.7	0.5			
5–9	0.1		0.0				0.6	0.5	0.7	0.3	0.0			
10–14			0.1		0.0		0.3	0.5	0.1		0.2			
15–19			0.2		0.2	0.3	0.0	0.3	0.1	0.8	2.3	0.3		
20–24			0.9	0.8	0.1		0.2	1.2	0.3	1.3	7.0			
25–29	0.1		1.0		0.4	0.4	0.4		0.3	0.8	6.3	1.4	0.1	
30–34	0.1		1.9	1.2	0.7	0.5	0.9	1.2	0.5	1.5	7.9	1.2	0.1	
35–39	0.2	0.6	3.0	2.4	1.3		2.3	0.6	1.5	1.0	7.7	1.2	0.3	
40–44	1.4	2.9	7.0	3.5	2.0		4.0	5.3	2.9	3.4	5.5	1.8	0.5	1.2
45–49	4.6	7.1	13.5	12.5	3.4	3.7	10.5	11.9	3.5	2.6	4.8	2.4	0.7	3.0
50–54	16.6	36.2	24.5	10.9	7.7	6.6	14.6	15.7	7.1	9.7	3.0	1.4	1.3	1.4
55–59	52.2	116.6	40.2	25.8	13.2	3.5	18.9	18.8	10.0	9.2	3.2	0.8	2.4	5.5
60–64	126.8	269.5	69.1	38.4	16.4	10.4	28.3	28.5	11.5	8.6	1.9		2.9	8.9
65–69	254.2	462.6	113.3	52.6	25.3	20.4	38.8	22.0	16.5	16.3	1.5	1.2	5.0	9.8
70–74	429.5	785.3	152.3	74.6	36.0	33.7	39.9	37.3	19.8	10.7	3.4	3.7	4.9	16.8
75–79	655.9	922.6	192.3	98.4	48.3	30.6	52.0	44.1	19.5	17.8	2.6	3.4	4.8	6.8
80–84	825.6	1274.6	223.8	113.4	64.0	46.2	52.5	26.7	24.4	27.7	2.6		8.1	13.3
85+	882.4	865.8	198.9	77.9	61.0	43.6	53.5	17.3	22.3	5.5	1.4		7.1	17.3
All ages‡	45.9	78.1	20.3	10.7	5.3	3.6	7.8	7.1	3.7	3.6	3.7	0.9	0.8	1.9
All ages §	57.7	94.9	23.5	12.2	6.2	4.3	8.6	7.6	4.0	3.8	3.4	0.8	0.9	2.2

* Cases per 100,000 person-years in nine registration areas.
† Data from reference 9.
‡ Standardized to the 1950 U.S. standard population.
§ Standardized to the 1970 U.S. standard population.

TABLE 1.2. Time Trends* of Incidence and Mortality Rates† for Cancer of Prostate, Bladder and Kidney in the United States

	Incidence Rate‡			Mortality Rate		
	1937–39	1947–48	1969–71	1940	1950	1969–71
Prostate						
Male						
White	32.0	37.4	45.2	16.7	15.7	14.8
Black	26.9	43.8	68.6	13.0	19.6	27.2
Bladder						
Male						
White	14.1	17.2	21.3	6.2	6.1	5.9
Black	3.8	4.8	9.8	3.5	4.3	5.0
Female						
White	6.6	7.1	5.6	3.1	2.6	1.8
Black	3.9	5.6	3.5	2.3	3.0	2.5
Kidney						
Male						
White	4.3	5.2	8.2	2.5	3.2	4.1
Black	3.0	4.8	6.9	1.3	1.9	3.0
Female						
White	2.8	2.9	3.8	1.6	1.8	1.8
Black	0.8	2.5	3.3	0.8	1.3	1.5

* Data from reference 10.
† Respectively, cases and deaths per 100,000 person-years adjusted to the 1950 U.S. standard population.
‡ Incidence rates based on seven common registration areas of the first, second and third national cancer surveys.

TABLE 1.3. Age-standardized Incidence Rates* for Cancers of Urologic Sites in Several Populations†

Country	Prostate	Bladder		Kidney		Testis	Penis
		Male	Female	Male	Female		
Denmark	21.8	16.1	4.2	7.2	5.1	4.9	1.0
Finland	22.7	8.7	1.8	6.3	3.9	1.1	0.6
England and Wales‡	18.0	16.8	4.0	4.4	2.0	2.6	0.9
Yugoslavia	16.8	7.0	1.4	3.5	1.8	1.9	0.5
Hawaii							
Caucasian	42.3	18.7	5.2	4.7	4.6	3.3	0.2
Japanese	24.6	11.1	3.2	4.0	1.5	0.3	0.5
Alameda (California)							
White	40.4	19.2	5.1	7.1	3.6	4.4	0.6
Black	75.0	8.6	3.9	6.0	2.5	0.5	1.2
Israel							
Jews born in Israel	9.7	16.9	4.6	3.7	2.8	1.3	0.0
Jews born in U.S. and Europe	12.6	14.6	3.3	7.2	4.3	2.6	0.1
Japan (Miyagi)	2.7	3.7	1.3	1.5	1.2	0.8	0.4

* Cases per 100,000 person-years adjusted to the World Standard Population.
† Data from reference 45.
‡ Mean of seven registries.

TABLE 1.4. Five-Year Relative Survival (Percentage) after Diagnosis of Cancer of Urologic Sites in the U.S. by Extent of Disease, and Time Period*

	Extent of Disease and Time Period							
	Local		Regional		Distant		All	
	1950–54	1965–69	1950–54	1965–69	1950–54	1965–69	1950–54	1965–69
Prostate								
White	60	70	40	61	14	20	43	57
Black	56	65	(19)	(51)	12	16	37	50
Bladder								
Male								
White	67	71	17	23	7	4	54	62
Black		(42)	(6)	(12)	(0)	(0)	(25)	29
Female								
White	60	76	22	16	(3)	5	51	62
Black		(64)		(7)			(20)	(31)
Kidney								
Male								
White	60	70	(26)	39	2	5	33	41
Black					(0)	(0)	(43)	(28)
Female								
White	53	66	(31)	(40)	7	6	34	43
Black		(77)				(5)	(21)	(52)
Testis								
White	77	89	(55)	68	(12)	24	57	68
Black								
Penis								
White	(83)	(74)					(71)	(64)
Black								

* Data from reference 4. Lacunae indicate that too few observations were made to permit estimation. Figures in parentheses are based on few observations and are somewhat unreliable.

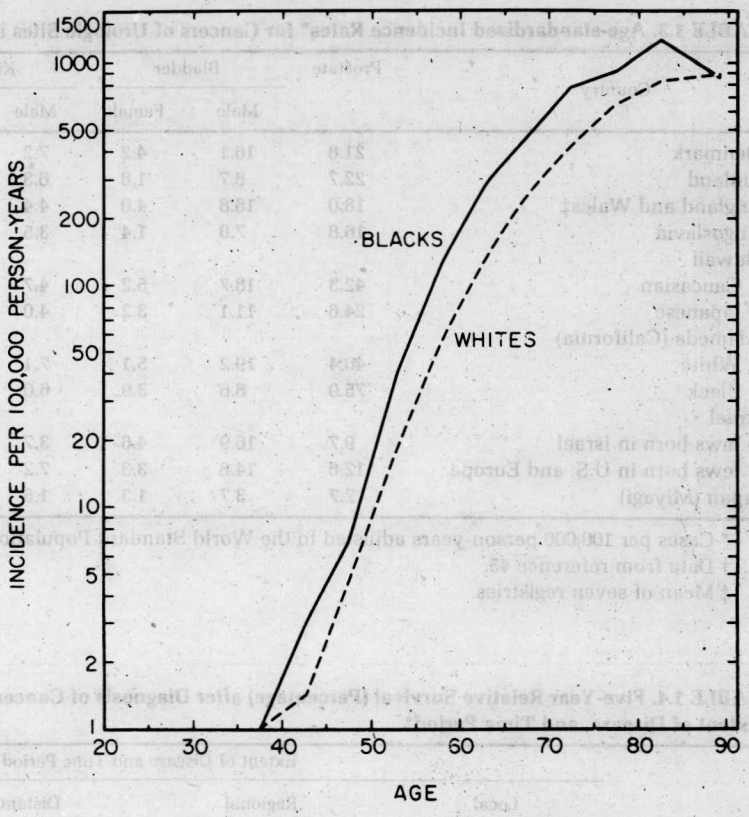

Fig. 1.1. Incidence rate of cancer of the prostate in the United States, 1969–71, by age and race.[9]

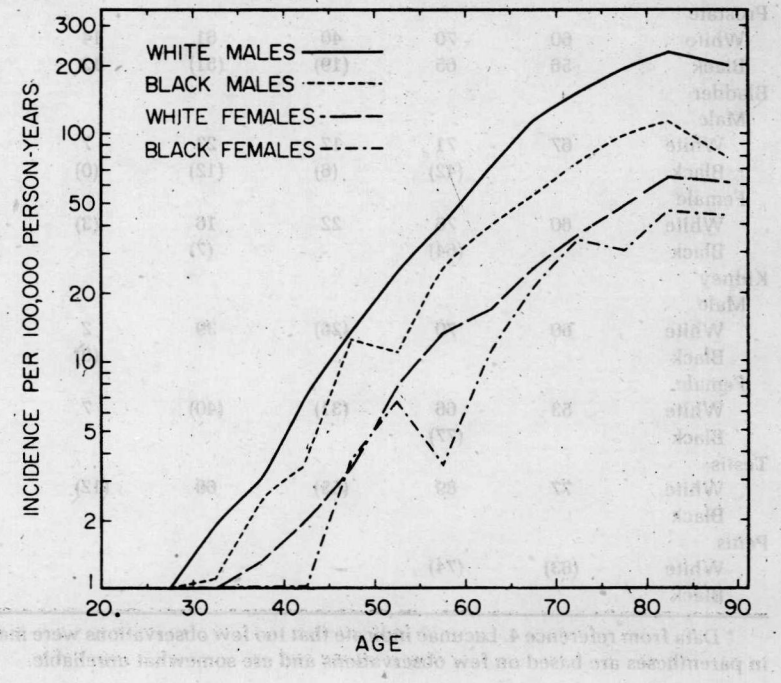

Fig. 1.2. Incidence rate of cancer of the bladder in the United States, 1969–71, by age, sex and race.[9]