

CONTEMPORARY ISSUES IN
SURGICAL PATHOLOGY

**PATHOLOGY
OF THE TESTIS
AND ITS ADNEXA**

Edited by
**Aleksander Talerman
Lawrence M. Roth**

CHURCHILL LIVINGSTONE

PATHOLOGY OF THE TESTIS AND ITS ADNEXA

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Dedicated to our wives
Margaretha and Ann-Katrin

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Preface

In this volume we have endeavored to present an up-to-date review of the disease processes affecting the testis and its adnexa that are most commonly encountered by the pathologist, urologist, and medical oncologist. As testicular tumors and tumorlike conditions represent the most important aspect of testicular and paratesticular diseases encountered by this audience, and because of the remarkable progress in this field during the last decade, a considerable part of this volume is devoted to various aspects of testicular neoplasms.

Although we have attempted to present a complete review of the pathology of testicular and paratesticular neoplasms, we have tried to place emphasis on new developments in the field. In this regard, new or incompletely understood entities, recently developed diagnostic techniques, such as immunocytochemistry, analysis of intermediate filaments, measurement and application of tumor markers, and new trends in therapy are covered in depth. Tumorlike lesions and non-neoplastic diseases affecting the testis and its adnexa are also discussed in some detail.

It has been the intention of the editors to allow the contributors a free forum for their opinions. Thus the views of some contributors may differ from those expressed by others. As many aspects of this subject are still controversial, such differences are inevitable in a multiauthored book and provide a forum for discussion.

This volume is not intended to compete with standard textbooks on the subject. Instead we have attempted to discuss some aspects which perhaps have not received sufficient coverage elsewhere, and to emphasize the multidisciplinary approach to testicular disease which is so important at the present time. For these reasons this book may be of interest to investigators dealing with various aspects of the cancer problem in general, in addition to those concerned specifically with testicular neoplasms.

Although testicular disease is usually only encountered by the pathologist, urologist, and medical oncologist of large medical centers with a special interest and experience in this field, the great advances in treatment make it imperative to provide the exact diagnosis and to use the correct therapeutic approach when one encounters such patients. It is hoped that this volume will provide some guidance and help to achieve this goal as well as contribute in some measure toward a better understanding of testicular and paratesticular disease.

Finally we wish to thank all our colleagues for their excellent contributions. We also wish to thank Mrs. Cathy Regovic for her competent secretarial assistance, and Ms. Kim Loretucci and Ms. Kamely Dahir of Churchill Livingstone, our publishers, for their help and cooperation.

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Epidemiology of Testicular Neoplasms

Lyly Teppo

Testicular tumors form an interesting group of malignant neoplasms with many exceptional and even unique epidemiologic features.¹ They occur mainly in young and middle-aged adults, and this suggests that their risk factors are different from those relevant to most other epithelial cancers. Moreover, it is believed that the origin of the great majority of testicular tumors is the germ cell. This may be of great importance because possible environmental risk factors in testicular cancer are liable to influence future generations.

The epidemiologic features of testicular cancer are outlined here. Special emphasis is placed upon germ cell tumors; other types of cancer will be mentioned only briefly.

INCIDENCE

There is substantial variation in the incidence of testicular cancer in different parts of the world. Table 1-1 lists the rates in selected countries.² High rates (4 to 6/100,000) are found in Denmark, Norway, and New Zealand, whereas Finland and some countries of eastern and southern Europe have low rates (1 to 2/100,000). Black populations in Africa seem to experience an extremely low risk of testicular cancer.³ Similarly, the rate among blacks in the United States is much lower than that observed among whites.⁴ Cancer of the testis is also rare in Asia.

Table 1-1. Age-Adjusted Incidence Rates ("World Standard Population") of Testis Cancer in Selected Countries and Areas in the mid 1970s

Country, Area	Incidence (/10 ⁵)
Denmark	6.7
New Zealand (non-Maori)	4.5
Norway	4.4
German Democratic Republic	4.0
United States, Bay Area (white)	4.0
Canada, Alberta	3.8
United States, Connecticut	3.6
United States, Los Angeles (white)	3.6
Canada, British Columbia	3.3
Sweden	3.0
United Kingdom, Birmingham	2.9
Israel (Jews)	1.9
Finland	1.7
Canada, Quebec	1.6
Colombia, Cali	1.5
Brazil, Sao Paolo	1.4
Hong Kong	1.4
United States, Bay Area (black)	1.4
China, Shanghai	0.9
India, Bombay	0.9
United States, Los Angeles (black)	0.9
Japan, Miyagi	0.8
Puerto Rico	0.8

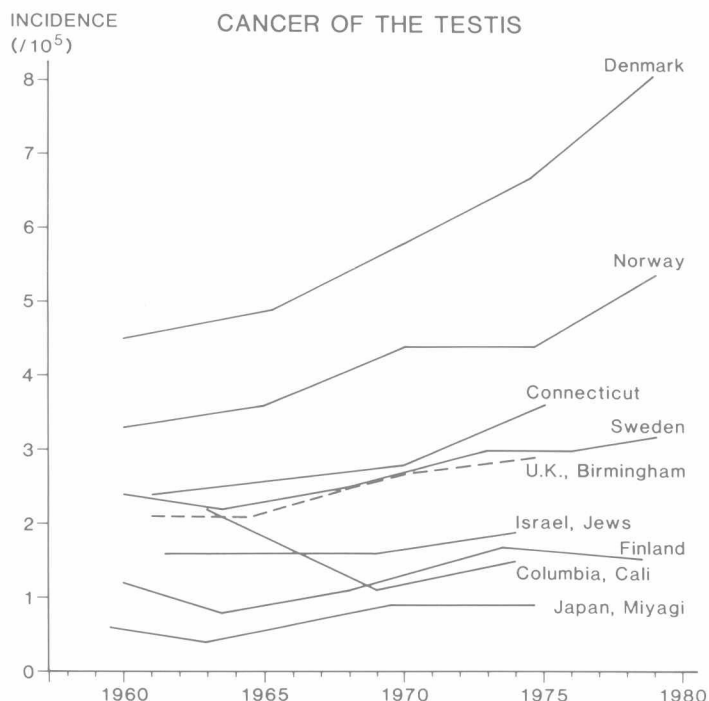


Fig. 1-1. Trends in the age-adjusted ("world standard population") incidence rate of testis cancer in selected countries. (Based on data in Waterhouse J, Muir C, Shanmugaratnam K, Powell J (eds): *Cancer Incidence in Five Continents*. Vol. IV. IARC Scientific Publications No. 42. International Agency for Research on Cancer, Lyon, 1982; *Cancer Incidence in Denmark 1978, 1979 and 1980: Danish Cancer Registry, Copenhagen, 1983*; *Incidence of Cancer in Norway 1978, 1979, 1980, 1981. The Cancer Registry of Norway, Oslo, 1981, 1982, 1983*; *Cancer Incidence in Sweden 1976, 1977, 1978, 1979, 1980. National Board of Health and Welfare, The Cancer Registry, Stockholm, 1980, 1981, 1982, 1983.*)

TRENDS

There has been a slight increase in the incidence of cancer of the testis in many areas (Fig. 1-1). The Danish Cancer Registry has reported a steady increase since the mid 1940s. The observed trends may be partly attributable to random variation of low rates or to more accurate reporting to cancer registries.

AGE DISTRIBUTION

The great majority of testicular cancers occur in young and middle-aged adults aged between 20 and 45 years of age. In addition, in many parts of the world there are peaks in young children (0 to 4 years) and in old age. This unique distribution reflects the variation in the incidence of different histologic types. Yolk sac tumors and mature teratomas occur in young children, while seminoma and

various other types of malignant germ cell tumors predominate in adults. In older persons, most of the tumors are lymphomas or sarcomas.

Figure 1-2 gives the age-specific incidence rates of testicular cancer in a high-risk, moderate-risk, and low-risk area (Denmark, Connecticut, and Finland, respectively).² The peak incidence in Denmark occurs 10 years later than that observed in Connecticut or Finland. In all these areas, prepubertal boys experience a very low risk of testicular cancer. It appears that the differences in the general risk are largely due to differences in the risks among young adults and middle-aged men. The variations in incidence among boys less than 5 years of age are not similar to those observed in adults. Similarly, the risks among elderly men show inconstant variation, which is at least partly due to differences in various cancer registries' coding of testicular lymphomas, namely, whether they are coded as testicular tumors or as malignant lymphomas.

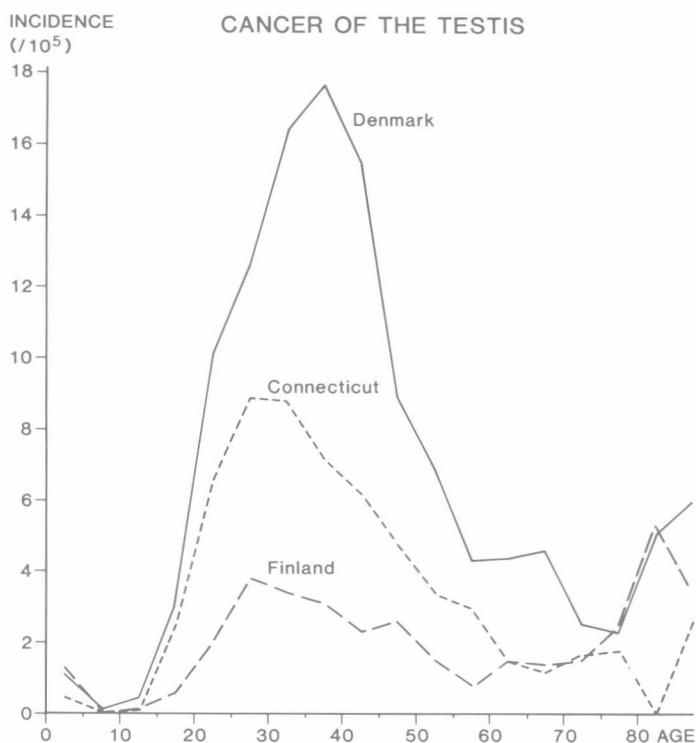


Fig. 1-2. Age-specific incidence rates of testis cancer in Denmark 1973 to 1976 (high-risk area), Connecticut 1973 to 1977 (moderate-risk area), and Finland 1971 to 1976 (low-risk area). (Based on data in Waterhouse J, Muir C, Shanmugaratnam K, Powell J (eds): *Cancer Incidence in Five Continents, Vol. IV*. IARC Scientific Publications No. 42. International Agency for Research on Cancer, Lyon, 1982.)

URBAN-RURAL DISTRIBUTION

In Finland, seminoma has a distinct urban preponderance (urban-rural ratio of the age-adjusted incidence rates is 1.5), whereas no difference between the urban and rural populations is found in the risk of other germ cell tumors (i.e., embryonal carcinoma, teratocarcinoma, choriocarcinoma and their different combinations, urban-rural ratio 1.1⁵). In this analysis the classification of the municipalities into "urban" and "rural" was based on the official definitions which do not always describe the municipalities' real character. A

more detailed picture of the situation was obtained in an analysis in which the 464 municipalities in Finland were divided into four or five categories according to the numerical value of different background variables describing the degree of urbanization and industrialization.⁶ Within each of these groups the age-specific numbers of cases (and populations) of each municipality were added together, and age-adjusted incidence rates were calculated (Fig. 1-3). The increase in the total risk of testicular cancer coincided with an increasing percentage of the population living in urban-type centers and each inhabitant hav-

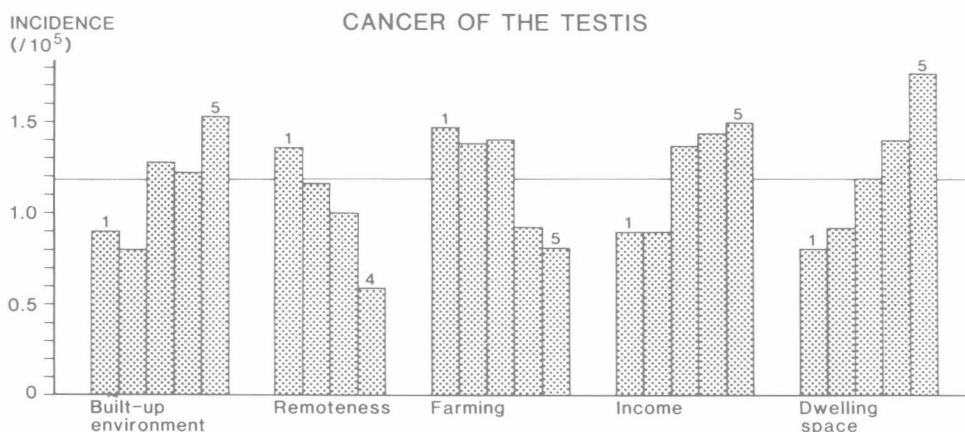


Fig. 1-3. Testicular cancer in Finland, 1955 to 1974: incidence rates (adjusted for age to the mean population of Finland) in classes of municipalities defined by the values of background variables referring to the degree of urbanization and standard of living. The horizontal line indicates the rate for the whole population. Definitions of the variables and their classes: Built-up environment; percentage of population living in urbanlike centers in 1970, 1, lowest, 5, highest; Remoteness; distance between the center of the municipality and the town center of the local economic area, 1, shortest, 4, longest; Farming; percentage of population in farming and forestry 1950, 1, lowest, 5, highest; Income; average monthly income per inhabitant in 1968, 1, lowest, 5, highest; Dwelling space; mean dwelling space per inhabitant in 1970, 1, lowest, 5, highest (Based on data in Teppo L, Pukkala E, Hakama M et al: Way of life and cancer incidence in Finland. A municipality-based ecological analysis. *Scand J Soc Med Suppl* 19:1, 1980.)

ing a higher mean income and larger dwelling space. A decrease in the total risk coincided with an increasing percentage of the population engaged in farming and forestry, and residing further from the center of the local economic area ("remoteness"). This shows that in the low risk area of Finland the association between the developed, urbanized environment and higher risk of testicular cancer is demonstrable even after an individual categorization of the living area. In Denmark both seminomatous and nonseminomatous tumors occur more frequently in persons living in towns.⁷ No urban-rural difference in the risk of testicular cancer (all types) has been found in Norway.²

Talerman et al.⁸ have reported an urban-rural ratio of 0.6 for seminoma and 0.5 for teratoma in the Netherlands, that is, a clear rural preponderance. A high risk of developing testicular cancer was also associated with

rural residence in the United States: the relative risk (rural vs. urban) was 2.3 for seminoma, 1.4 for other histologic types.⁹ In England and Wales a slight rural preponderance has been found for seminoma (U-R ratio of the rates, 0.8), although no difference was recorded for nonseminomatous tumors.¹⁰ In the area covered by the Birmingham Cancer Registry, the urban-rural ratio of the incidence rates of all testicular cancers taken together was 1.13 in 1964 to 1968, and 0.73 in 1969 to 1973. This change was due to a marked increase in the rural rate.

Consequently, no consistent risk pattern in urban-rural distribution is seen among the various types of testicular cancer. This can at least partly be attributable to differences in the character of the "urban" and "rural" environments between sparsely populated countries (such as Finland) and highly industrialized areas.

Table 1-2. Standardized Incidence Ratios (SIR) of Testis Cancer at Ages 35–69 Years in Finland in 1971–1975 in the Main Occupational Categories

<i>Occupational Category</i>	<i>Observed</i>	<i>Expected</i>	<i>SIR</i>
Technical, scientific, humanistic, and artistic	21	8.3	2.55 ^a
Legal	2	0.2	10.98 ^b
Teaching	7	1.9	3.66 ^c
Technical	10	3.9	2.56 ^b
Administration, managerial, and clerical	9	4.5	2.01
Administration	7	2.6	2.69 ^b
Sales	5	4.1	1.21
Services	3	2.8	1.06
Transport, communication	7	8.0	0.88
Industry, manufacturing	18	28.4	0.63
Farming, forestry	11	18.3	0.60
Other or unspecified	10	9.6	1.04

From unpublished data of the Finnish Cancer Registry.

^a $p < 0.001$ ^b $p < 0.05$ ^c $p < 0.01$

SOCIOECONOMIC STATUS, OCCUPATION, RELIGION

Several investigators have reported an association between the high risk of testicular cancer and high socioeconomic status, which is itself defined differently. Record linkage between the files of the Finnish Cancer Registry from 1971 to 1975 and the National Census records of Finland in 1970 revealed a clear association between social class defined by main occupational categories and the risk of testicular cancer (Table 1-2). A significantly elevated standardized incidence ratio (SIR) was found among “academic professions” and in those employed in administrative, managerial, and clerical work. On the other hand, low SIRs were encountered in persons working in manufacturing and in farming and forestry.

Davies¹¹ studied death rates specific to social groups in England and Wales and found high rates of testicular cancer among profes-

sionals and administrative and clerical workers. The differences between the social classes had already persisted for some 50 years. Ross et al.¹² in Los Angeles used census tract information in their analysis, and also showed that high risk was associated with high social class.

In the case-control analysis of Graham et al.,⁹ based on testicular cancers reported to the New York State Tumor Registry, high risk was associated with professional occupations, rural residence, being native-born, having been married at some time, and being a Protestant. Each of these factors carried a higher risk, even when considered in the context of other traits. The risk was highest among those with several of the above-mentioned characteristics. The results were similar for both seminomas and nonseminomatous tumors. The authors concluded that part of the low rate of testicular cancer among the American black population may be attributable to difference in the socioeconomic status of whites and blacks.