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Gonadal and extragonadal germ cell tumors in the United States, 1973–2007

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Abstract

Germ cell tumors (GCTs) most often arise in the gonads but some develop extragonadally. The aim of this study was to examine sex- and race-specific trends in incidence and survival of gonadal (GGCTs) and extragonadal GCTs (EGCTs) in the US from 1973 to 2007. We also examined the topographic distribution of EGCTs by race and sex.

We estimated age-specific and age-standardized incidence rates and 5-year relative survival rates (RSR) of GCTs using the Surveillance, Epidemiology, and End Results (SEER) Program (SEER 9 registries). GCTs and their topographic sites were identified using ICD-O morphology and topography codes.

Of 21,170 GCTs among males, 5.7% were extragonadal (whites 5.5%; blacks 16.3%). Of 2,093 GCTs among females, 39.3% were extragonadal (whites, 36.9%; blacks 51.0%). The incidence of GGCT was much higher among white (56.3/1,000,000) than black males (10.0/1,000,000) while there was no difference in incidence between white and black females (3.2/1,000,000). The rates of EGCT among men and women of both races were similar (range:1.9 – 3.4/1,000,000). The most frequent extragonadal sites were mediastinum among males and placenta among females. The 5-year RSR of testicular GCT was higher among whites (97%) than blacks (90%), as was the 5-year RSR of ovarian GCT (whites, 92%; blacks 85%). In general, the 5-year RSRs of EGCTs were lower than the 5-year RSRs of GGCTs.

The different incidence trends of GGCTs and EGCTs and distinct age-specific incidence patterns by anatomic site of EGCTs suggests that GGCTs and EGCTs may have different etiologies.

Keywords

testicular neoplasms; ovarian neoplasms; incidence; time trends; germ cell tumors; extragonadal germ cell tumors

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Introduction

Germ cell tumors (GCTs) most frequently arise in the gonads, but some develop extragonadally (Schmoll 2002) (Ebi et al. 2003) (Bokemeyer et al. 2002) (Bokemeyer et al. 2003). Extragonadal germ cell tumors (EGCTs) have similar morphology as gonadal germ cell tumors (GGCT) and most often occur in the midline of the body, e.g. anterior mediastinum, retroperitoneum, pineal gland etc. Gain of isochromosome 12p is an important chromosomal marker of both GGCTs and EGCTs (Chaganti et al. 1994) (Schneider et al. 2006) (Cossu-Rocca et al. 2006) (Poulos et al. 2006).

A widely accepted hypothesis suggests an embryonic genesis of GCTs (Schmoll 2002) (Hainsworth & Greco 1992) (Oosterhuis et al. 2007). Primordial germ cells (PGCs) originate from the proximal epiblast and migrate along the midline of the body through the hindgut to the genital ridge. Once at the genital ridge, PGCs are referred to as gonocytes. Depending on the sex-chromosomal constitution and corresponding microenvironment in the gonadal ridge, gonocytes differentiate into either oocytes or pre-spermatogonia (Oosterhuis & Looijenga 2005). A disturbed migration of PGCs results in misplacement at different sites in the body's midline. EGCTs are believed to develop after malignant transformation of these residual PGCs. Different stages of development of the precursor cells and microenvironmental conditions may determine the final histology of the tumors at different sites. This hypothesis might explain the occurrence of GCTs at various sites especially in the sagittal midline of the brain, mediastinum, and retroperitoneum (Fossa et al. 2003). Another hypothesis suggests that metastases of GGCTs in the retroperitoneal space and the posterior mediastinum of adolescent and young adult males are misdiagnosed as primary EGCT because the primary GGCT regressed ("burned out") (Hainsworth & Greco 1992). Histologic studies of the testes of EGCT patients have revealed that some have testicular scars, i.e., fibrous tissue and microlithiasis that may reflect burned-out testicular GCTs. This misdiagnosis may be especially relevant for retroperitoneal EGCT, given the relatively high risk of metastasis to this area (Bokemeyer et al. 2002) (Bokemeyer et al. 2003) (Fossa et al. 2003) (Daugaard et al. 1987).

Recently, Oosterhuis and Looijenga proposed the classification of GCTs into five types based on the maturation stage and imprinting status of the originating germ cell (Oosterhuis & Looijenga 2005). All Type II GCTs are thought to originate through reprogramming of neoplastic primordial germ cells/gonocytes. In the testis, nonseminomatous components originate from reprogrammed intratubular germ cell neoplasia unclassified (ITGCNU, also known as testicular carcinoma in situ) lesions or seminoma cells (Mostofi et al. 1987); while in the ovary, GCTs originate from dysgerminoma cells and in the dysplastic gonad from the neoplastic primordial germ cells of gonadoblastoma. The precursor lesions in the anterior mediastinum and midline of the brain have not yet been identified. However, the fact that the tumors in these sites may be composed of germinoma (counterpart of testicular seminoma and ovarian dysgerminoma) or of germinoma combined with nongerminomatous components, is in keeping with the hypothesis that these tumors are the result of reprogramming of a neoplastic PCG. The type I tumors, not characterized by isochromosome 12p, lack a seminomatous/dysgerminomatous/germinomatous component. This suggests they originate from primitive germ cells that are immediately reprogrammed to pluripotency, without prior neoplastic proliferation of the PCGs.

Descriptive epidemiologic features such as age patterns, incidence trends, and survival could improve our understanding of EGCTs and may provide clues to differences in EGCT etiology. The aim of this study was to compare epidemiologic features including incidence trends and survival of GGCTs and EGCTs among U.S. males and females from 1973 through 2007.

Material and Methods

We extracted incidence rates, by sex and race, of gonadal and extragonadal GCTs from the Surveillance, Epidemiology, and End Results (SEER) Program original 9 registries for the years 1973–2007 (National Cancer Institutes 2009). Before incidence estimation, we restricted the cases to primary malignant GCTs among white or black persons. Other racial/ethnic groups were not included due to small numbers.

We used ICD-O-3 (International Classification of Disease for Oncology) topography and morphology codes to classify the tumors (2002). Topograpy code C62 identified testicular tumors while code C56 identified ovarian tumors. All other topographic sites were considered extragonadal. Among males, morphology codes 9060-9062, 9064 identified seminomas, while codes 9065-9102 identified nonseminomas. Among females, morphology codes 9060-9064 identified dysgerminomas, the histologic equivalent of seminomas, while other GCTs were identified by histologic type: embryonal carcinoma (9070), yolk sac tumor (9071), teratoma (9080-9084), mixed germ cell tumor (9085), and choriocarcinoma (9100-9101). For simplicity we collectively refer to this grouping as non-dysgerminomas (Nogales et al. 2003).

We analysed the incidence of EGCTs by sex and race using two digit ICD-O topography codes (C00, C01, C02, …, C80). Herein, we report topography-specific incidence rates by sex and race if the absolute number of cases for the incidence rates were 16 or more for the overall registration period 1973–2007. In addition, certain extragonadal sites mentioned in prior studies were analyzed in detail, including pineal gland (C75.3), pituitary gland (C75.1), brain (C71.0–71.9), thymus (C37.9), mediastinum (C38.1–3), retroperitoneum (C48.0), pelvis (C49.5, 76.3), placenta (C58), and uterus (C54–55). Details of the inclusion/exclusion criteria and the corresponding counts are presented in Figure 1.

Statistical methods

We calculated crude, age-specific and age-standardized incidence rates of GCTs stratified by sex, race, and histologic group. To study the incidence among children, we calculated age-specific rates for age groups 0–14 years. Incidence estimates based on less than 16 cases were not reported.

We used a median/average smoothing process to model age-specific incidence rates (1-year age groups) to increase clarity of the underlying pattern. We first calculated the median incidence for every three contiguous 1-year age groups and then calculated weighted means (0.25 for age group x−1, 0.50 for age group x, and 0.25 for age group x+1) (Selvin 2001).

We estimated 5-year relative survival rates (RSR) by dividing observed survival rates by the expected survival rates of persons of the same age and sex. The expected survival rates were obtained from population life tables of the SEER program. We chose 1990–2007 as the years of diagnoses and follow-up period. We excluded cases identified solely by death certificate or autopsy. Relative survival estimates are presented only for sites that had at least 60 registered cases in at least one of the strata of sex and race.

Results

Between 1973 and 2007, 23,263 GCTs were diagnosed among white and black persons in the SEER-9 registries (Figure 1). Among white and black men, 5.5% and 16.3% of all GCTs were EGCTs, respectively, while among white and black women, these proportions were 36.9% and 51.0%, respectively.

The overall incidence of GGCT was, as anticipated, much higher among white males (56.3/1 million) than black males (10.0/1 million) (Table 1). In contrast there was no difference in incidence of GGCT between white and black females (3.2/1 million). The rates of EGCT among men and women of both races were on par with the rate of GGCTs among women, ranging from 1.8 – 3.4/1 million (Table 1). Among white males, the incidence of seminoma was higher than that of nonseminoma. In contrast, among white females, the incidence of dysgerminoma was lower than that of non-dysgerminoma (Table 2). The findings by histology were similar among black persons (results not shown).

Trends in incidence of GCTs by race and sex are provided in Figure 2. The incidence of GGCTs among white males continuously increased from 1973 through 2007 (average annual percent change (APC) in incidence = 1.7%, 95% confidence interval (95%CI): 1.4% to 1.9%). In contrast, the incidence of EGCTs among white males remained fairly constant over the entire time period (APC = 0.6%, 95%CI: −0.2% to 1.4%). Among black males, the incidence of GGCTs increased (APC = 1.5%, 95%CI: 0.3% to 2.7%), with the largest increase between 1988 and 2002. The incidence of EGCTs among black males increased from 1973 until 1992, then plateaued before declining in the latest time period; however, these rates are based on small numbers making calculation of the difficult. Among white and black females, the incidence rates for GGCT and EGCTs had similar trends with small decreases over time (APCs: GGCT white = −0.2%, 95%CI: −0.9% to 0.4%, GGCT black = −1.2%, 95%CI: −3.1% to 0.6%, EGCT white = −0.7%, 95%CI: −1.4% to 0.2%, EGCT black = −0.8%, 95%CI: −2.4% to 0.8%). The fluctuation of rates among black females was large, likely due to small numbers.

As shown in Table 3, the most frequent extragonadal sites were mediastinum, pineal gland, retroperitoneum, and brain among males and placenta, pelvis, uterus, and brain among females. Although there was a tendency toward higher rates of EGCTs among white than black females, rates of placental GCTs were higher among black females (white: 0.9 per 1 million; black: 1.7 per 1 million).

Histology-specific analyses among white persons revealed that EGCTs of the brain, pineal gland and pituitary gland were predominantly seminomas/dysgerminomas (67%, 74%, 78%, respectively). In contrast, EGCTs of the pelvis were predominately nonseminomas/ nondysgerminomas (96%) (Table 3). The frequencies of EGCTs by site were similar among black persons, although based on small numbers (results not shown).

The age-specific incidence patterns of testicular GCTs had an early peak at ages 0–1 years and a steep increase starting at puberty. In contrast, ovarian GCTs had a steep increase starting at age 5 years (Figure 3). Among EGCTs, brain tumors had an early peak (0–1 year) and a second peak starting at puberty while pineal tumors had a steep increase starting at age 5 years. Mediastinal and retroperitoneal GCTs showed steep increases starting at puberty, while pelvic GCTs had only one age peak, at 0–1 years (Figure 4).

The 5-year RSRs of testicular GCTs were higher among white (97%) than black males (90%) (Table 4) Stratification by histologic group revealed that seminoma RSRs among white (98%) and black males (96%) were very similar (results not shown). The RSRs of nonseminomas, however, were considerably lower among black (78%) than white males (94%) (results not shown). Among females, the 5-year RSR of ovarian GCTs was higher among white (92%) than black females (85%). Among white females, the RSR was higher for dysgerminoma (96%) than non-dysgerminoma (90%) (results not shown). There were too few cases among black females to stratify by histology.

Overall, the 5-year RSRs of EGCTs were generally lower than those of GGCTs (Table 4). Among white males, the highest 5-year RSR among EGCTs was that of the pineal gland

(90%), followed by the brain (83%), retroperitoneum (81%) and mediastinum (58%). Among women, placental GCTs had similar 5-year RSRs to those of gonadal GCTs. A comparison of 5-year RSRs of EGCTs of the brain among white persons found better survival among males (83%) than females (65%). Small numbers precluded comparison of other sites by sex and race.

Discussion

Our study provides evidence that incidence trends and age patterns of GGCTs and EGCTs differ. While the incidence of testicular GCT increased from 1973 through 2007, the incidence of EGCTs among men remained virtually constant. Among females, the incidence of all GCTs showed a small decrease over time.

The different time trends of GGCTs and EGCTs suggest that the etiology may differ, although it is believed that GCTs originate from primitive germ cells of which the developmental potential differs according to its stage of maturation and pattern of genomic imprinting (Oosterhuis & Looijenga 2005). The considerably lower incidence of GCTs among females than males is likely related to the lower number of germ cells in the ovaries than the testes (Moller & Evans 2003) (Giambartolomei et al. 2009). Further, in contrast to testicular germ cells, ovarian germ cells do not proliferate after puberty. Finally, sex differences in etiologic factors or mechanisms might explain observed incidence differences by sex.

In the current study, GCTs of the pelvis had a distinctive feature: they occurred, almost exclusively, among newborns or young infants and were predominantly nonseminomas/nondysgerminomas. Sacrococcygeal teratoma is one of the most common congenital tumors. Its estimated prevalence is 1/27,000 live births with a female-to-male ratio of 4:1. About 10% of congenital sacrococcygeal teratomas are malignant (Lakhoo 2010) (Swamy et al. 2008). According to a Kiel Pediatric Tumor Registry report, the majority of GCTs of the abdomen, retroperitoneum and sacrococcyx in infants are teratomas (Harms et al. 1989). Sacrococcygeal tumors develop totally or partially in front of the sacrum. Sacrococcygeal tumors that develop totally in front of the sacrum should be included with retro- and intraperitoneal tumors (Harms et al. 1989). Similar to Harms et al. (Harms et al. 1989), we observed higher incidence rates of pelvic GCTs among females than males. The peak in incidence of pelvic GCTs at early ages most likely reflects that many are congenital sacrococcygeal GCTs.

Mediastinal GCTs occurred overwhelmingly among males. Among males, the steep increases in incidence of mediastinal and retroperitoneal EGCTs at onset of puberty may reflect a hormone-related promotion of neoplastically transformed cells that arose during embryogenesis. Among white males, the age-specific incidence pattern of mediastinal GCTs was similar to the pattern of testicular GCTs. Evidence based on case series and case reports suggests that mediastinal nonseminomatous GCTs are associated with Klinefelter syndrome (McKenney et al. 2007) (Oosterhuis et al. 2007). These tumors are known to have a poor prognosis (IGCCCG 1997), which has been explained by resistance to cisplatin-based chemotherapy (Bokemeyer et al. 2002). Also similar to testicular GCT, the estimated 5-year RSR of mediastinal nonseminoma was considerably lower than that of mediastinal seminoma.

In their review of EGCTs, McKenney et al. (McKenney et al. 2007) recently stated that "*most purely retroperitoneal GCTs in adults represent metastases from an undiscovered or occult primary in the testicle, or, rarely, ovary*". If retroperitoneal EGCTs are metastases of GGCTs, this would imply that these tumors are more aggressive than localized GGCTs and

that these tumors are more frequently associated with metachronous GGCTs. Accordingly, one would expect lower survival rates for retroperitoneal GCTs than GGCTs and a greater likelihood of metachronous GGCTs among patients with retroperitoneal than mediastinal GCTs. Our findings among white males corroborate these hypotheses. Although we were not able to adjust the RSRs for stage at diagnosis, the 5-year RSR was lower for retroperitoneal GCTs than for testicular GCTs. Interestingly, if retroperitoneal EGCTs were mainly metastases from occult cancer of the testis, one might also expect an increase of the incidence of these metastases if the stage distribution at diagnosis of testicular cancer had remained constant over time. Previous analyses of the SEER data by our group, however, found that testicular cancers have been diagnosed at increasingly earlier stages over time. Thus, it is conceivable that the decrease in retroperitoneal EGCT incidence may be due to fewer later stage testicular cancers being diagnosed (McGlynn et al. 2005).

Bokemeyer et al. noted the inferior prognosis of retroperitoneal GCTs in contrast with gonadal GCTs (Bokemeyer et al. 2002). Among 635 EGCT patients, the authors observed metachronous testicular tumors among 4.2% of men with retroperitoneal GCTs and only 1.1% of men with mediastinal GCTs (Bokemeyer et al. 2002). Similarly, Fossa et al. reported that 18 of 53 (34%) men with retroperitoneal GCT and 3 of 15 (20%) men with mediastinal GCT presented with testicular carcinoma in situ (Fossa et al. 2003). Although these observations are in line with a multi-site development of GCTs, they could also indicate that some retroperitoneal GCTs are metastases from burned-out testicular GCTs.

The vast majority of GCTs of the brain and pineal gland (predominantly seminoma/dysgerminoma) among white males occur during the second and third decades of life. In contrast to pineal gland GCTs, EGCTs of the brain had an early age peak at ages 0–1 years. The incidence of EGCTs of the placenta (predominantly choriocarcinoma) was higher among black than white females and may be due to higher birth rates among black (19/1000) than white (14/1000) women (Martin et al. 2010).

Our study had several notable strengths, including a large sample size (23,263). The data were drawn from an extensive population-based collection of registries with considerable time-depth covering almost four decades. In addition, the SEER registries are known to have well-validated, comprehensive histologic and topographic data. Nevertheless, several factors may limit our results. A substantial number of EGCTs were registered as having an unknown primary site, complicating the interpretation of the topographical distribution. Even with large numbers overall, several subsite- and histology-specific analyses could not be conducted as the numbers of cases were too small to allow a meaningful analysis. In addition, genetic analyses of poorly differentiated carcinomas involving primarily midline structures report that several of these tumors are actually EGCTs (Motzer et al. 1991) thus the incidence of EGCTs may be underestimated (Hainsworth & Greco 1992). Finally, the estimation of RSR of GCTs did not account for tumor stage and treatment modalities.

In conclusion, we provide detailed incidence and survival analysis of gonadal and extragonadal GCTs among black and white persons in the US from 1973 to 2007. The different incidence trends of GGCTs and EGCTs and distinct age-specific incidence patterns by anatomic site of EGCTs suggests that GGCTs and EGCTs may have different etiologies. In general, the prognosis of EGCTs was poorer than the prognosis of GGCTs.

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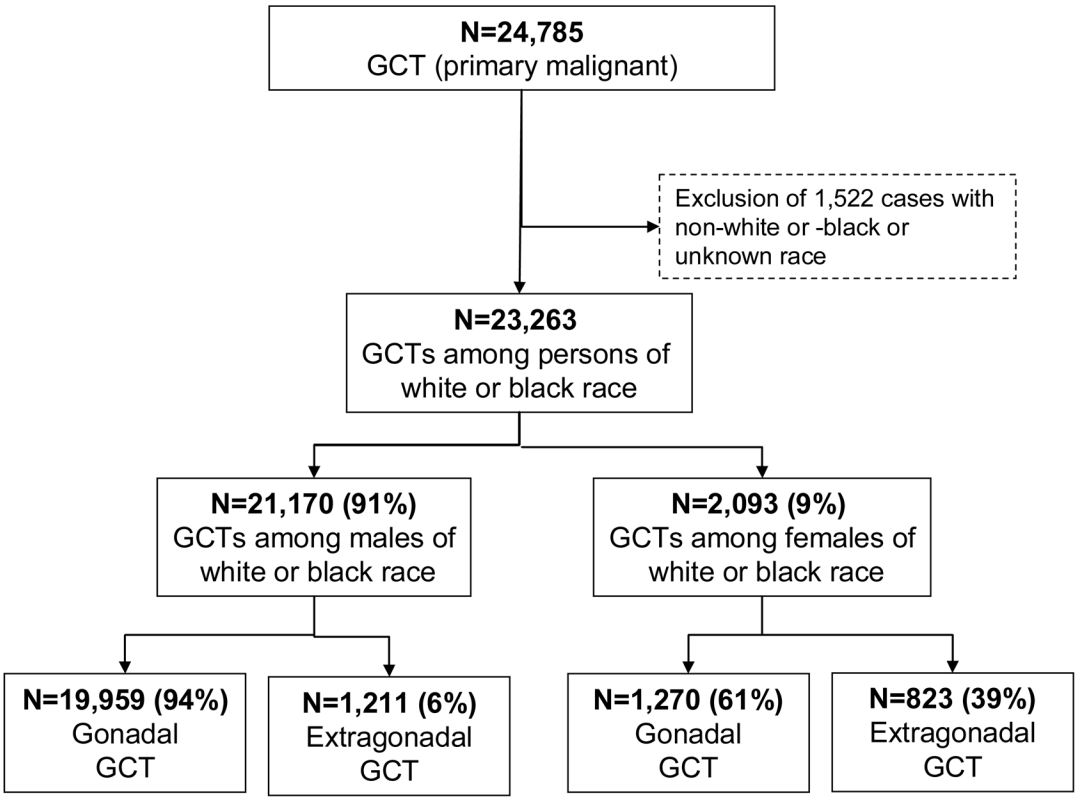


Figure 1.
Gonadal and extragonadal germ cell tumors among whites and blacks, SEER-9, 1973–2007

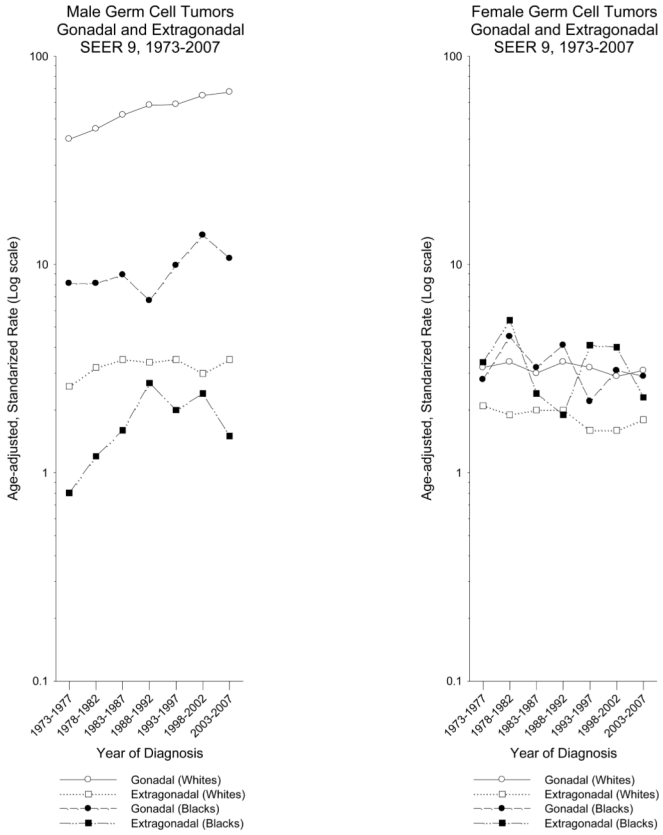


Figure 2.
Incidence time trends of gonadal and extragonadal germ cell tumors among males and females, US SEER-9, 1973–2007 (Cases per 100,000)

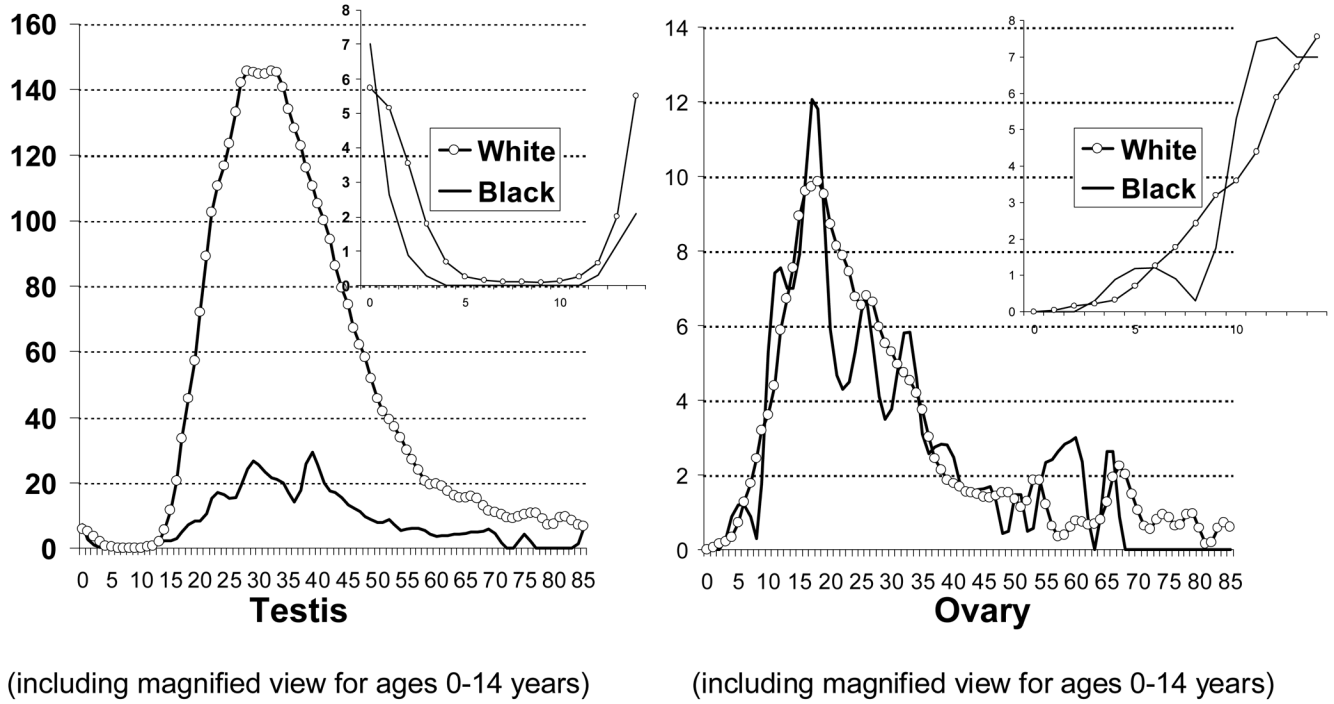
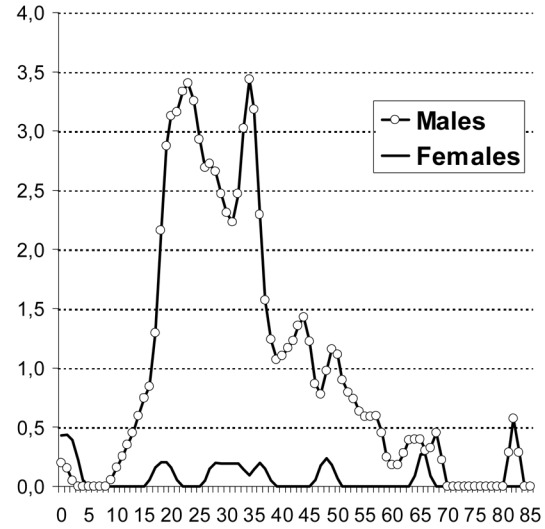
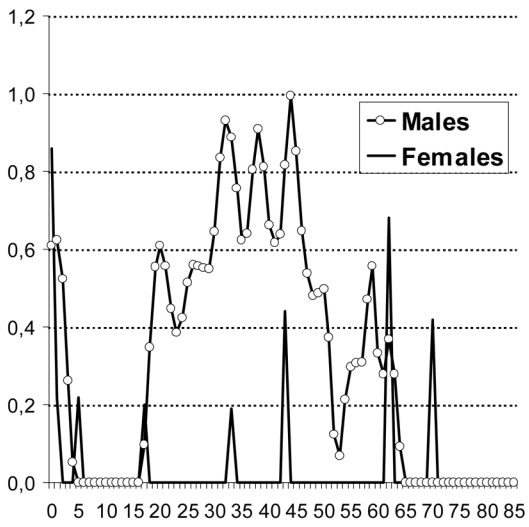


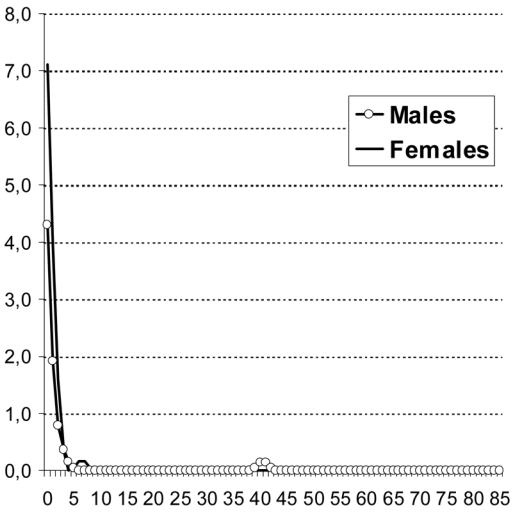
Figure 3.
Age-specific incidence rates of gonadal germ cell tumors among by race, US SEER-9, 1973–2007(Cases per 1 million)



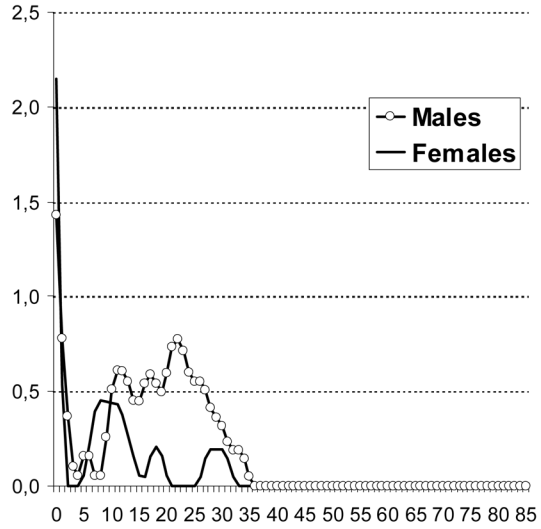
Mediastinum



Retroperitoneum



Pelvis



Brain

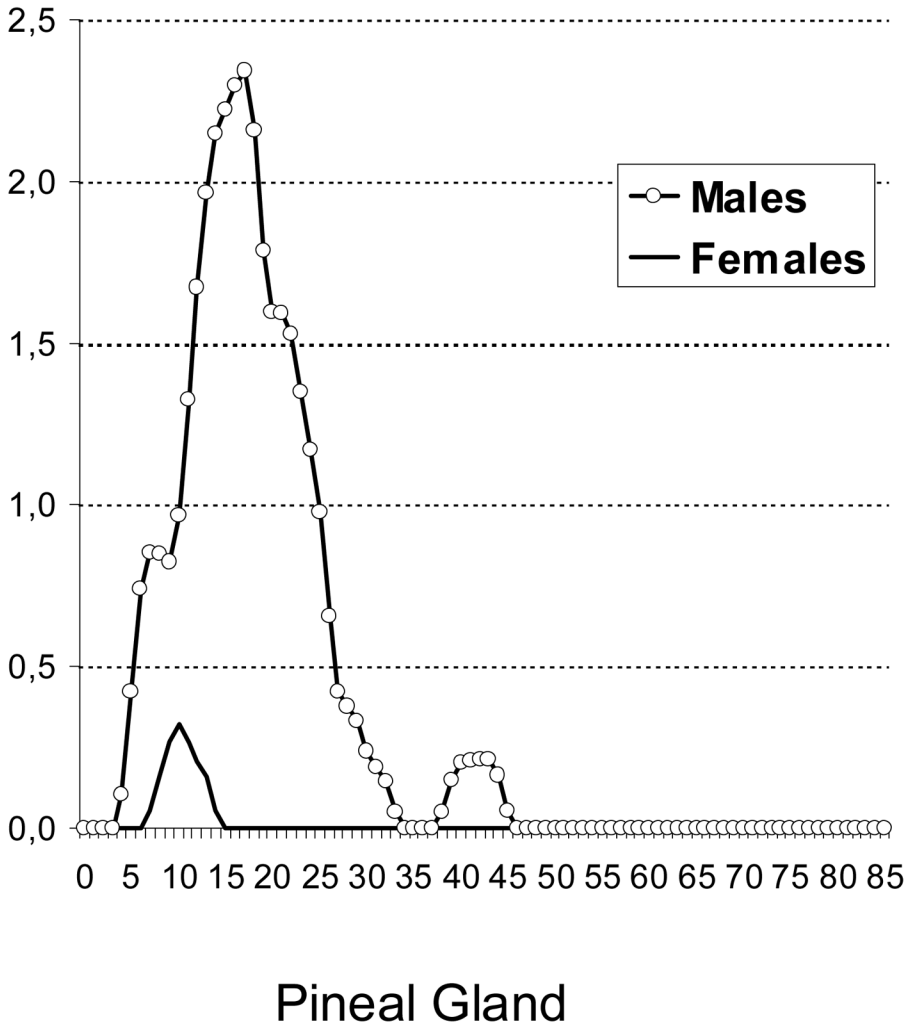


Figure 4.
Sex- and age-specific incidence rates of extragonadal germ cell tumors among whites, US SEER-9, 1973–2007 (Cases per 1 million)

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Table 1

Age-standardized incidence rates (cases per 1 million, US 2000 population standard), gonadal and extragonadal germ cell tumors among white and black males and females in the US (SEER-9, 1973–2007)

		Overall	By Calendar Period		
			1973–1984	1985–1996	1997–2007
White Males	Population size	328,840,919	102,224,234	112,934,860	113,681,825
Gonadal germ cell tumors					
	Count	19,517	4688	7130	7699
	ASR	56.3	44.0	57.0	65.6
	SE	0.4	0.7	0.7	0.7
Extragonadal germ cell tumors					
	Count	1125	318	423	384
	ASR	3.3	3.0	3.5	3.3
	SE	0.1	0.2	0.2	0.2
Black Males	Population size	44,167,482	11,496,501	15,095,037	17,575,944
Gonadal germ cell tumors					
	Count	442	92	135	215
	ASR	10.0	8.3	8.5	11.9
	SE	0.5	1.0	0.8	0.8
Extragonadal germ cell tumors					
	Count	86	15	36	35
	ASR	1.8		2.3	1.8
	SE	0.2		0.4	0.3
White Females	Population size	337,913,118	106,268,059	116,539,442	115,105,617
Gonadal germ cell tumors					
	Count	1095	387	387	321
	ASR	3.2	3.3	3.3	2.9
	SE	0.1	2.1	0.2	0.2
Extragonadal germ cell tumors					
	Count	641	239	217	185
	ASR	1.9	2.1	1.8	1.7
	SE	0.1	0.1	0.1	0.1

		Overall	By Calendar Period		
			1973–1984	1985–1996	1997–2007
Black Females	Population size	48,568,799	12,576,823	16,672,993	19,318,983
Gonadal germ cell tumors					
	Count	175	51	65	59
	ASR	3.2	3.4	3.4	2.9
	SE	0.2	0.5	0.4	0.4
Extragonadal germ cell tumors					
	Count	182	58	56	68
	ASR	3.4	4.0	2.9	3.3
	SE	0.3	0.6	0.4	0.4

ASR: age-standardized rate; SE: standard error of ASR

Table 2

Age-standardized incidence rates (cases per 1 million) of extragonadal germ cell tumors by primary site, sex and histologic group (whites only); SEER-9, 1973–2007

	White Males						White Females					
	Seminoma			Nonseminoma			Dysgerminoma			Non-Dysgerminoma		
Topography (ICD-O)	**N**	**ASR**	**SE**	**N**	**ASR**	**SE**	**N**	**ASR**	**SE**	**N**	**ASR**	**SE**
Gonadal germ cell tumors												
Testis (C62.0–C62.9)	10,994	32.7	0.33	8,398	23.1	0.25						
Ovary (C56)							393	1.1	0.06	701	2.0	0.08
Primary sites of extragonadal germ cell tumors												
Thymus (C37.9)	9			9			1			1		
Mediastinum (C38.1–C38.3)	194	0.6	0.04	212	0.6	0.04	12			26	0.1	0.02
Retroperitoneum (C48.0)	73	0.2	0.03	81	0.2	0.03	1			12		
Pelvis (C49.5, C76.3)	4			35	0.1	0.02	0			60	0.2	0.02
Uterus (C54–C55)							1			45	0.1	0.02
Female genital tract (C57)							3			20	0.1	0.01
Placenta (C58)							0			312	0.9	0.05
Brain, NOS (C71.0–C71.9)	59	0.2	0.02	24	0.1	0.01	26	0.1	0.02	15		
Pineal gland (C75.3)	127	0.4	0.03	48	0.1	0.02	7			3		
Pituitary gland (C75.1)	17	0.0	0.01	3			11			5		
Malignant neoplasm of other and ill-defined sites (C76excl. C76.3)	2			6			0			2		
Other sites*	16	0.0	0.01	44	0.1	0.02	6			46	0.1	0.02
Unknown primary site (C80.9)	57	0.2	0.02	105	0.3	0.03	6			21	0.1	0.01
All extragonadal germ cell tumors	558	1.6	0.07	567	1.6	0.07	74	0.2	0.03	567	1.6	0.07

*all other sites had less than 16 registered cases in each sex-race stratum of the registration period 1973–2007

Table 3

Age-standardized incidence rates (cases per 1 million) of gonadal and extragonadal germ cell tumors by primary site, sex and race; SEER-9, 1973–2007

	Males						Females					
	White			Black			White			Black		
Topography (ICD-O)	**N**	**ASR**	**SE**	**N**	**ASR**	**SE**	**N**	**ASR**	**SE**	**N**	**ASR**	**SE**
Gonadal germ cell tumors												
Testis (C62.0–C62.9)	19,517	56.3	0.41	442	10.0	0.49						
Ovary (C56)							1,095	3.2	0.10	175	1.9	0.1
Primary sites of extragonadal germ cell tumors												
Thymus (C37.9)	18	0.1	0.01	0			2			0		
Mediastinum (C38.1–C38.3)	406	1.2	0.06	25	0.5	0.11	38	0.1	0.02	3		
Retroperitoneum (C48.0)	154	0.5	0.04	7			13			6		
Pelvis (C49.5, C76.3)	39	0.1	0.02	4			60	0.2	0.02	18	0.3	0.17
Uterus (C54–C55)							46	0.1	0.02	23	0.3	0.09
Female genital tract (C57)							23	0.1	0.01	2		
Placenta (C58)							312	0.9	0.05	92	1.7	0.17
Brain, NOS (C71.0–C71.9)	83	0.2	0.03	8			41	0.1	0.02	11		
Pineal gland (C75.3)	175	0.5	0.04	23	0.4	0.09	10			0		
Pituitary gland (C75.1)	20	0.1	0.01	0			16	0.0	0.01	1		
Malignant neoplasm of other and ill-defined sites (C76excl. C76.3)	8			1			2			0		
Other sites*	60	0.2	0.02	9			52	0.2	0.02	19	0.4	0.09
Unknown primary site (C80.9)	162	0.5	0.04	9			27	0.1	0.02	7		
All extragonadal germ cell tumors	1,125	3.3	0.10	86	1.8	0.20	641	1.9	0.07	182	3.4	0.25

*all other sites had less than 16 registered cases in each sex-race stratum of the registration period 1973–2007; ASR: age-standardized rate; SE: standard error of ASR

Table 4

5-year relative survival (RSR in %) of gonadal and extragonadal germ cell tumors by primary site, sex and race; SEER-9, 1990–2007

	Males						Females					
	White			Black			White			Black		
Topography (ICD-O)	**N**	**RSR (%)**	**SE**	**N**	**RSR(%)**	**SE**	**N**	**RSR(%)**	**SE**	**N**	**RSR(%)**	**SE**
Gonadal germ cell tumors												
Testis (C62.0–C62.9)	11,468	97	0.2	292	90	2.1	-	-	-	-	-	-
Ovary (C56) *	-	-	-	-	-	-	545	92	1.3	87	# 85	#4.1
Primary sites of extragonadal germ cell tumors												
Mediastinum (C38.1–C38.3) *	209	58	3.6	15	-	-	14	-	-	1	-	-
Retroperitoneum (C48.0)	65	81	5.4	2	-	-	7	-	-	5	-	-
Placenta (C58) *	-	-	-	-	-	-	122	94	2.4	40	88	5.3
Brain, NOS (C71.0–C71.9) *	61	83	5.4	7	-	-	29	*65	*9.1	9	-	-
Pineal gland (C75.3) *	112	90	3.1	17	-	-	2	-	-	0	-	-
All extragonadal germ cell tumors *	608	68	2.1	57	71	6.4	308	82	2.3	103	78	4.3

Persons with multiple primaries were included;

* The relative cumulative survival increased from a prior interval and has been adjusted;

SE: estimated standard error of the RSR