

AYHAN O. ÇAVDAR, TEZER KUTLUK

BACKGROUND

There are marked differences between childhood and adult cancer. First, cancer is generally a rare disease among children. Annual incidence of all cancer in children under 5 years of age in developed countries is only 0.5%, according to a new report [1]. In European countries, 1% of all malignant neoplasms occur in patients younger than 20 years of age [2-4]. Second, childhood cancers are histologically variable, and embryonic tumors are the most common, while the majority of adult cancers are carcinomas [1,5,6]. Twelve types of malignant childhood tumors have been classified according to the International Classification of Childhood Cancer (ICCC) [1,7-10]; however, pediatric cancers can also be divided into 3 subgroups [6]:

1. Embryonal tumors, which show early age peaks. Retinoblastoma, neuroblastoma, and hepatoblastoma have the highest incidence rate in the first year of life.
2. Juvenile neoplasms, which are unique to younger age groups.
3. Adult-type tumors, which are rarely seen in children.

Prenatal factors are considered to affect the incidence of tumors in children under the age of 5 years [11]. It is generally accepted that cancer results from genetic changes [1,12]. The carcinogenic process in children is much shorter than in adults. Infancy is the age when cancer incidence rates are the highest during childhood; therefore, it is reasonable to assume that many pediatric cancers result from aberrations in early developmental stages and in utero. An increased risk of childhood cancers has been described to be associated with certain genetic conditions or syndromes such as chromosomal abnormalities, DNA repair disorders, congenital

anomalies, hereditary immune deficiency states, and other hereditary syndromes [1,6].

Racial differences have been observed in childhood tumors, even within Western countries [2,12]. A peak incidence in acute lymphocytic leukemia (ALL) usually occurs between the ages of 2 and 3 years in White American children and 1 to 4 years in European children, but not among African Americans [1,2]. Ewing sarcoma is another well-established example of racial differences, with the lowest incidence rate in Black children (African or American) [1,6]. Furthermore, there are marked variations between populations in the incidence of specific types of childhood cancers. Nearly one-third of all childhood neoplasms are leukemias, with an age-standardized incidence rate (ASR) of 35-50 per million [1,7]. International variation occurs in the rate of ALL, and the higher incidence of ALL in early childhood has usually been associated with higher levels of socioeconomic status. This suggests that environmental factors play a role [1,9,13]. Although a considerable number of environmental or exogenous factors have been suggested as risk factors for childhood cancers, only a few have been proven, and they are mostly infectious agents, including Epstein-Barr virus, hepatitis B virus, human immunodeficiency virus, and human herpesvirus 8. These infections are probably responsible for the international variation in the incidence of some childhood cancers, such as lymphoma, nasopharyngeal carcinoma, hepatic cancer, and Kaposi sarcoma [1,6,13,14]. In addition, some parasitic infections have been implicated, particularly malaria in tropical Africa, acting as a co-factor for Burkitt's lymphoma, and schistosomiasis in Egypt, causing bladder cancer [1,11,15].

RESULTS

The total number of childhood cancers registered under 15 years of age varies greatly among the Middle East Cancer Consortium (MECC) registries, ranging from 102 in Cyprus to 1,339 in Jordan (Table 15.1). This is due both to different periods of registration in these countries and to variations in the size of their respective populations.

Table 15.2 shows the ASRs of all cancers and the main types of cancer, and Figure 15.1 shows the ASRs of all cancers, by sex, in children under 15 years of age in MECC countries. The most striking finding is that the highest incidence of childhood cancer occurred among female children in Cyprus (179.5). This rate was even higher than that found among females in the SEER data (146.3). Males had a higher incidence rate than females in all other MECC countries (ranging from 130.6 to 150.3). The lowest overall incidence was in Jordan (114.8).

In terms of the type of malignancy, leukemia was the most common neoplasm in males in all MECC countries, with the exception

of Egypt, where lymphoma in males exceeded the incidence of leukemia (56.7 vs. 33.6) (Table 15.2; Figures 15.2 and 15.3). The second highest lymphoma rate was in Israeli Arabs, with an ASR of 32.6 in males (Table 15.2 and Figure 15.3). The incidence rate of ALL was 38.2, 21.4, 15.9, 24.3, 27.8, and 39.7 in Cypriots, Israeli Jews, Israeli Arabs, Egyptians, Jordanians, and US SEER, respectively, whereas it was 12.7, 5.5, 6.4, 3.1, 5.7, and 7.3 for acute myeloid leukemia in the same countries. Interestingly, the rate of central nervous system (CNS) tumors was found to be the highest in females (55.6) in Cyprus (Table 15.2 and Figure 15.4). Although lymphomas were more common than CNS tumors in male Israeli Jews, male and female Israeli Arabs, male Egyptians, and male Jordanians, the opposite was true for the rest of the registries. Sympathetic nervous system tumors were also higher in Cyprus than in the other MECC countries and the US SEER population, particularly in males (28.4). Jordan had the lowest incidence of sympathetic nervous system tumors. It is of interest that no retinoblastoma was diagnosed in Cyprus, even in the under-5-years age group. As far as renal tumors were concerned, incidence rates were again the highest in Cypriot children, particularly in females (14.6), compared with the other MECC countries (Table 15.2).

Table 15.1. Childhood Cancer: Number of Cases for All International Classification of Childhood Cancer Sites, by Age and Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001

Age Group	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER* 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
<5 y	41	19	22	404	220	184	170	98	72	157	86	71	557	336	221	1,699	898	801
5-9 y	27	14	13	291	183	108	93	60	33	156	100	56	404	229	175	1,013	583	430
10-14 y	34	17	17	303	175	128	74	41	33	168	99	69	378	217	161	1,096	553	543
15-19 y	47	18	29	554	287	267	106	54	52	185	104	81	462	244	218	1,644	882	762
<15 y	102	50	52	998	578	420	337	199	138	481	285	196	1,339	782	557	3,808	2,034	1,774
<20 y	149	68	81	1,552	865	687	443	253	190	666	389	277	1,801	1,026	775	5,452	2,916	2,536

*SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

The total incidence of hepatic tumors ranged from 2.5 in Israeli Arabs to 1.1 in Jordanians (Table 15.2).

The incidence of malignant bone tumors was slightly higher in Cypriot males (10.2) and Israeli Jewish males (9.5) as well as in female Egyptians (9.3), compared with other MECC countries.

Interestingly, these tumors had the lowest ASR in Israeli Arabs, although it was found to be high (8.6) among Egyptian children (Table 15.2).

Soft tissue sarcomas showed a slightly higher ASR among Israeli Arabs, particularly in females (14.7) and in male Israeli Jews (12.8) (Table 15.2).

Table 15.2. Childhood Cancer: Age-Standardized Incidence Rates* for International Classification of Childhood Cancer (ICCC) Sites, by Sex, in Children under Age 15 Years in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001†

ICCC Site	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER‡ 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
All cancers	170.0	161.0	179.5	133.3	150.0	115.8	119.9	137.8	100.9	130.9	150.3	110.7	114.8	130.6	98.1	153.3	159.9	146.3
Leukemia	53.0	52.8	53.2	31.8	34.7	28.7	29.4	33.8	24.8	31.9	33.6	30.2	39.2	46.5	31.4	50.4	54.0	46.6
Lymphomas and reticuloendothelial neoplasms	15.7	20.1	11.2	20.0	26.5	13.1	24.2	32.6	15.4	37.7	56.7	17.7	19.0	23.8	13.9	13.5	16.3	10.5
Central nervous system and miscellaneous intracranial and intraspinal neoplasms	40.1	25.3	55.6	24.2	25.9	22.4	16.5	22.7	10.1	16.9	15.7	18.1	18.9	21.5	16.2	32.5	34.6	30.3
Sympathetic nervous system tumors	22.3	28.4	15.8	15.8	16	15.5	12.0	12.4	11.7	9.5	11.8	7.0	6.1	7.0	5.2	11.2	10.3	12.1
Retinoblastoma	0.0	0.0	0.0	2.8	2.3	3.3	2.1	2.0	2.2	2.4	-	3.5	4.6	4.4	4.9	5.6	6.6	4.6
Renal tumors	11.3	-	14.6	6.9	8.4	5.3	5.7	4.1	7.3	5.4	4.4	6.4	5.1	4.4	5.8	9.2	8.0	10.3
Hepatic tumors	-	-	0.0	1.3	2.2	-	2.5	2.1	2.9	1.9	1.9	2.0	1.1	1.2	0.9	2.9	2.5	3.3
Malignant bone tumors	7.9	10.2	-	8.1	9.5	6.7	3.3	4.3	2.3	8.6	8.0	9.3	6.0	7.3	4.7	5.2	5.3	5.1
Soft tissue sarcomas	9.8	12.1	-	11.0	12.8	9.1	13.6	12.5	14.7	7.9	9.0	6.7	6.3	7.3	5.2	10.8	11.7	9.9
Germ cell, trophoblastic, and other gonadal neoplasms	-	0.0	-	3.1	1.5	4.7	3.6	2.8	4.4	2.2	1.8	2.6	3.4	2.7	4.3	5.3	5.4	5.2
Carcinomas and other malignant epithelial neoplasms	3.9	0.0	8.1	5.6	6.7	4.4	4.3	5.7	2.9	2.4	2.5	2.2	4.3	3.9	4.6	5.7	4.4	7.0
Other and unspecified malignant neoplasms	0.0	0.0	0.0	1.9	2.1	1.6	2.2	2.1	2.2	3.9	3.3	4.5	0.7	0.7	0.8	0.5	0.3	0.6
Not classified by ICCC	-	0.0	-	1.0	1.3	-	-	-	0.0	-	0.0	-	-	0.0	-	0.7	0.5	0.8

*Rates are per 1,000,000 and are age-standardized to the World Standard Million.

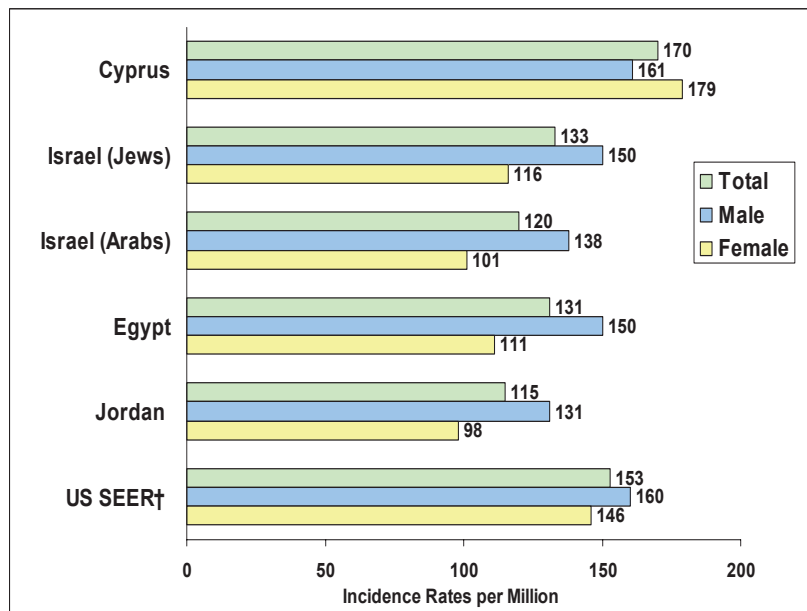
†The symbols "-" = 1-2 cases; and "*numeral*" (italic) = 0 or 3-15 cases.

‡SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

The incidence of germ cell tumors was slightly lower in all MECC countries than in US SEER data, with the lowest total ASR of 2.2 noted in Egypt versus 5.3 in US SEER. In Cyprus, there were only 2 cases, so the ASR could not be properly estimated.

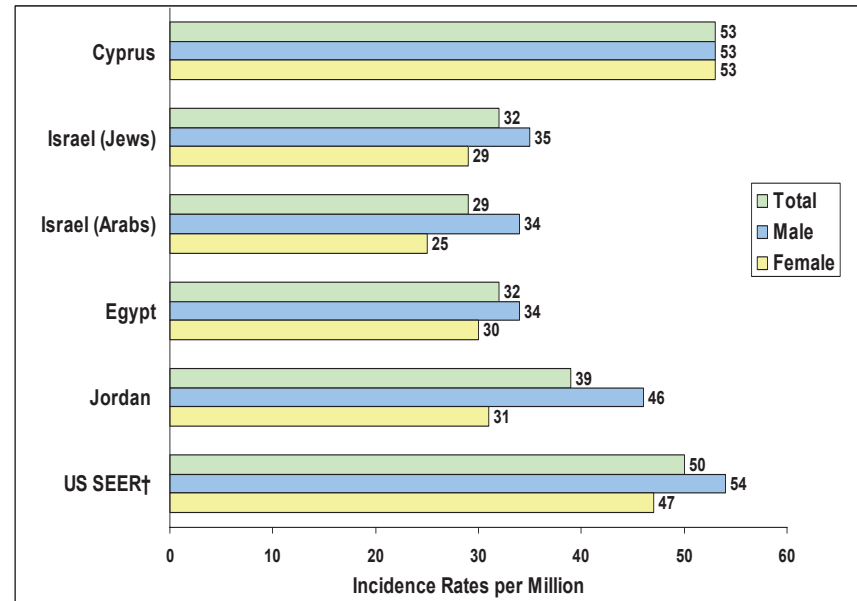
The incidence rate of carcinomas and other malignant epithelial neoplasms was low in all MECC countries. Interestingly, no cases were registered in male Cypriots, whereas female Cypriots (8.1) and male Israeli Jews (6.7) had slightly higher rates (Table 15.2).

Figure 15.1. Childhood Cancer: Age-Standardized Incidence Rates* of All Cancers for Children under Age 15 Years, by Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001



*Rates are per 1,000,000 and are age-standardized to the World Standard Million.
 †SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

Figure 15.2. Childhood Cancer: Age-Standardized Incidence Rates* of Leukemia for Children under Age 15 Years, by Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan and US SEER – 1996-2001



*Rates are per 1,000,000 and are age-standardized to the World Standard Million.

Other and unspecified malignant neoplasms were generally low in MECC countries. No such cases were reported from Cyprus (Table 15.2).

Table 15.3 shows the incidence rates according to the ICCC site for children under 20 years of age. The total ASR of malignant tumors was again highest in Cyprus (178.6), and was also relatively high among Israeli Jews (154.2).

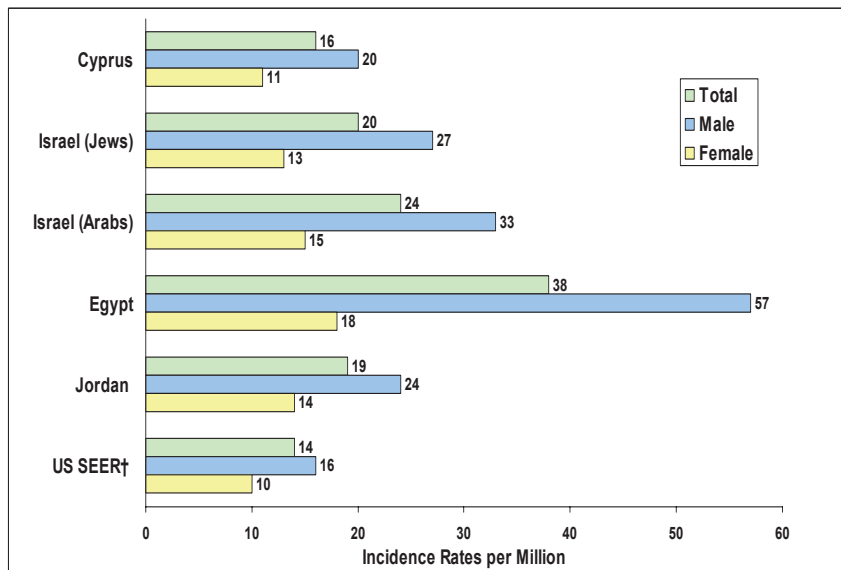
Table 15.4 shows the ASRs of all malignant neoplasms in 5-year age groups for males and females. In Cyprus, the incidence

rates of cancers under 5 years (199.2 in males; 241.8 in females) seemed again higher than in the other MECC countries and similar to the US SEER rates (210.4 and 196.9, respectively). The highest incidence rates in adolescents were in female Cypriots (262.0) and male and female Israeli Jews (226.2) (Table 15.4).

Comparing Other Childhood Cancer Registries with MECC

Comparison of the rates reported by cancer registries in some European countries [2-4] with those of MECC countries is shown in Table 15.5. Analysis of the total ASRs of childhood cancer in MECC and European countries revealed the highest rates in Cyprus (170.0) and Italy (158.0). These 2 countries had almost the

Figure 15.3. Childhood Cancer: Age-Standardized Incidence Rates* of Lymphoma and Reticuloendothelial Neoplasms for Children under Age 15 Years, by Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001

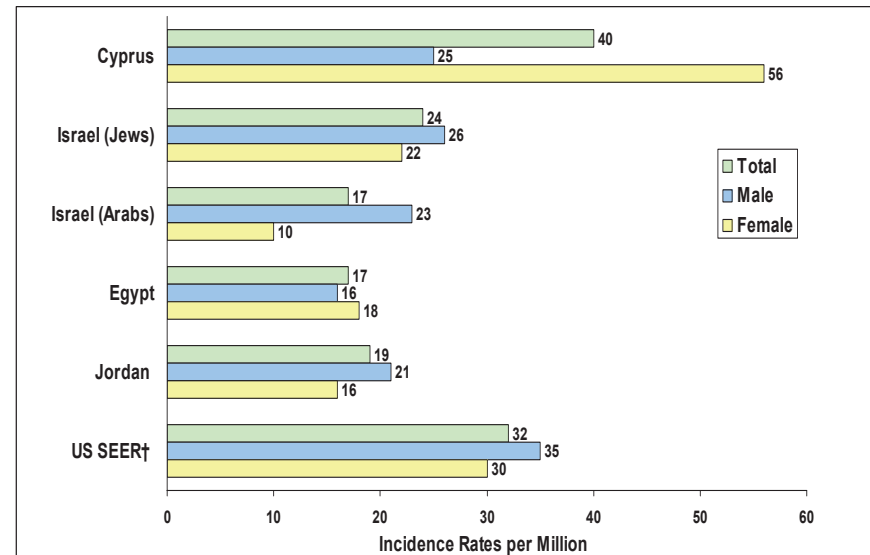


*Rates are per 1,000,000 and are age-standardized to the World Standard Million.
 †SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

same incidence rate of leukemia (53.0 and 53.9, respectively). With the exception of Cyprus (53.0), MECC registries in general tended to have a lower incidence rate of leukemia (29.4 to 39.2) than in the European countries, where incidence of leukemia varied from 41.0 to 53.9 [3]. In a previous study, the frequency of T-cell ALL was found to be high in Egypt [16]. Childhood leukemia rates were found to be higher in Jordanians than in Israeli Jews, according to a recent report [17].

According to Table 15.5, the incidence of lymphoma tended to be higher in the MECC countries than in Europe, but Spain and Italy had a relatively high rate of this malignancy (19.3 and 18.6, respectively). The highest rate of lymphoma within MECC

Figure 15.4. Childhood Cancer: Age-Standardized Incidence Rates* of Malignant Central Nervous System and Miscellaneous Intracranial and Intraspinal Neoplasms for Children under Age 15 Years, by Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001



*Rates are per 1,000,000 and are age-standardized to the World Standard Million.
 †SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

Table 15.3. Childhood Cancer: Age-Standardized Incidence Rates* for International Classification of Childhood Cancer (ICCC) Sites, by Sex, in Children under Age 20 Years in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001†

ICCC Site	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER‡ 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
All cancers	178.6	160.0	198.1	154.2	167.6	140.1	126.9	140.7	112.4	134.8	153.1	115.6	119.7	132.4	106.4	164.0	171.0	156.5
Leukemia	49.1	46.8	51.4	30.2	34.1	26.2	27.3	30.6	23.8	32.1	35.2	28.9	36.5	43.1	29.5	45.4	48.5	42.2
Lymphomas and reticuloendothelial neoplasms	26.2	23.4	29.0	33.7	37.7	29.4	29.7	37.8	21.1	37.3	54.5	19.3	23.1	26.0	20.1	20.3	22.5	18.0
Central nervous system and miscellaneous intracranial and intraspinal neoplasms	34.1	25.5	43.1	21.5	22.4	20.6	17.0	22.0	11.8	15.2	15.0	15.5	18.7	21.6	15.6	29.3	32.0	26.3
Sympathetic nervous system tumors	17.2	22.0	12.3	12.6	12.6	12.6	9.7	10.2	9.1	7.5	9.2	5.8	5.0	5.6	4.3	8.8	8.2	9.5
Retinoblastoma	0.0	0.0	0.0	2.2	1.8	2.6	1.6	1.6	1.7	1.9	-	2.7	3.6	3.4	3.8	4.4	5.1	3.6
Renal tumors	8.7	-	11.3	5.4	6.7	4.1	4.4	3.2	5.6	4.2	3.4	5.0	4.1	3.5	4.7	7.4	6.6	8.2
Hepatic tumors	-	-	0.0	1.1	1.7	-	2.2	1.6	2.9	1.9	1.8	1.9	0.9	1.1	0.7	2.5	2.2	2.9
Malignant bone tumors	14.1	19.7	8.3	10.6	13.8	7.3	5.2	5.9	4.4	10.6	11.1	10.1	8.7	10.0	7.2	6.9	8.1	5.6
Soft tissue sarcomas	8.6	11.3	-	12.8	13.7	11.9	14.7	13.5	16.0	9.7	9.1	10.4	6.1	6.7	5.5	12.4	13.6	11.0
Germ cell, trophoblastic, and other gonadal neoplasms	5.0	-	8.3	6.6	7.6	5.6	3.4	2.8	4.1	2.6	1.8	3.5	4.5	3.5	5.5	11.2	13.6	8.6
Carcinomas and other malignant epithelial neoplasms	13.0	0.0	26.6	14.3	12.4	16.3	8.8	8.1	9.5	6.9	6.5	7.3	7.9	7.4	8.5	14.2	9.7	18.9
Other and unspecified malignant neoplasms	0.0	0.0	0.0	2.2	2.0	2.3	2.6	2.9	2.4	4.6	4.3	5.0	0.6	0.5	0.7	0.6	0.4	0.8
Not classified by ICCC	-	0.0	-	1.0	1.2	0.9	-	-	0.0	-	0.0	-	-	-	-	0.6	0.5	0.7

*Rates are per 1,000,000 and are age-standardized to the World Standard Million.

†The symbols "-" = 1-2 cases; and "*numeral*" (italic) = 0 or 3-15 cases.

‡SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

countries was in Egyptians (37.7), followed by Israeli Arabs (24.2). The recently established cancer registry in Turkey has also revealed a high incidence rate of lymphomas (19.6) among Turkish children [18,19].

CNS tumor rates were somewhat low in MECC countries (with the exception of 40.1 in Cyprus) as compared with European countries, where the highest rate of 42.8 was found in Sweden [19].

Table 15.5 shows that within MECC countries, the highest rate of neuroblastoma occurred in Cypriots (22.3); the rate was also high in Israeli Jews (15.8). In Europe, France and Italy showed high rates of this tumor (13.5 and 13.4, respectively). The incidence of retinoblastoma was low in general within MECC countries.

Slightly higher incidence rates, ranging from 3.4 to 4.8, were found in Europe. Renal tumors again had the highest rate in Cyprus (11.3) within MECC countries, an ASR similar to that found in Sweden (10.2). The incidence of hepatic tumors in MECC registries was not grossly different from that in European countries; both showed low rates. The incidence rates of bone tumors were the highest in Egyptians (8.6), followed by Israeli Jews (8.1) and Cypriots (7.9). Among European countries, Spain (7.6) and Italy (7.5) had the highest rates.

Soft tissue sarcoma was most common in Israeli Arabs (13.6), whereas Sweden had the highest rate (10.5) among European countries. Germ cell tumors were lowest in Egypt and Cyprus within the MECC countries (Table 15.5).

Table 15.4. Childhood Cancer: Age-Standardized Incidence Rates* for all International Classification of Childhood Cancer Sites, by Age and Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001

Age Group	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER† 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
<5 y	220.0	199.2	241.8	155.9	165.3	145.9	155.3	174.4	135.1	145.9	156.2	135.1	132.2	155.0	108.0	203.8	210.4	196.9
5-9 y	124.4	125.3	123.3	117.5	144.3	89.5	99.1	124.7	72.2	122.6	153.7	90.1	102.9	113.5	91.8	115.1	129.4	100.1
10-14 y	154.1	149.6	158.9	120.8	136.0	104.9	95.7	103.7	87.3	120.2	138.6	100.9	104.8	116.9	92.0	128.3	126.4	130.3
15-19 y	208.3	156.7	262.0	226.2	228.3	224.0	151.1	150.5	151.8	148.1	162.6	132.8	136.8	138.6	134.8	200.8	209.3	191.8
<15 y	170.0	161.0	179.5	133.3	150.0	115.8	119.9	137.8	100.9	130.9	150.3	110.7	114.8	130.6	98.1	153.3	159.9	146.3
<20 y	178.6	160.0	198.1	154.2	167.6	140.1	126.9	140.7	112.4	134.8	153.1	115.6	119.7	132.4	106.4	164.0	171.0	156.5

*Rates are per 1,000,000, and rates for the broad age groups are age-standardized to the World Standard Million.

†SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

Interestingly, the total ASR of childhood tumors in Turkey (Izmir registry), 115.6, was quite low and similar to the rate (114.8) in Jordan (Table 15.5).

SUMMARY AND CONCLUSIONS

The results of this analysis of MECC registries may be summarized as follows:

1. Among MECC countries, the total incidence of childhood tumors was highest in Cyprus (170.0).

2. Leukemia was the most common childhood malignancy in all MECC countries, with the exception of Egypt. However, the MECC ASR of leukemia was somewhat low compared with the European countries. The incidence of ALL was highest in Cyprus.

3. The total ASR of lymphoma in Egypt (37.7) exceeded leukemia (31.9), with a very high rate among male children (56.7). Male Israeli Arabs also had a high rate of lymphoma. The incidence of lymphoma in MECC countries was generally high, compared with Europe (14.3) and the US SEER population (13.5).

Table 15.5. Childhood Cancer: Comparison of Age-Standardized Incidence Rates* in MECC Countries, Some European Countries, and US SEER**

Country/Registry	Total Rate	Leukemia	Lymphoma	CNS [§] Tumors	Neuro-blastoma	Retino-blastoma	Renal Tumors	Hepatic Tumors	Bone Tumors	Soft Tissue Sarcomas	Germ Cell Tumors
Europe	130.9	42.4	14.3	28.1	9.8	3.8	8.6	1.4	5.4	8.3	4.0
France	135.6	41.3	15.7	28.2	13.5	4.2	9.3	1.3	6.6	7.4	4.0
Italy	158.0	53.9	18.6	32.7	13.4	3.9	8.6	1.8	7.5	9.2	3.8
United Kingdom	121.0	41.0	11.1	27.6	8.6	4.0	7.7	1.1	4.9	8.0	3.7
Sweden	154.3	41.7	13.8	42.8	4.9	4.8	10.2	2.2	5.6	10.5	3.5
Turkey	115.6	41.4	19.6	16.8	7.6	3.3	6.7	1.1	3.9	7.6	4.1
Cyprus	170.0	53.0	15.7	40.1	22.3	0.0	11.3	-	7.9	9.8	-
Israel (Jews)	133.3	31.8	20.0	24.2	15.8	2.8	6.9	1.3	8.1	11.0	3.1
Israel (Arabs)	119.9	29.4	24.2	16.5	12.0	2.1	5.7	2.5	3.3	13.6	3.6
Egypt	130.9	31.9	37.7	16.9	9.5	2.4	5.4	1.9	8.6	7.9	2.2
Jordan	114.8	39.2	19.0	18.9	6.1	4.6	5.1	1.1	6.0	6.3	3.4
Germany	128.7	44.8	14.5	24.3	11.6	3.4	8.9	1.3	5.6	8.5	4.5
Spain	137.9	41.1	19.3	27.6	12.6	3.6	7.6	1.8	7.6	9.0	3.8
US SEER	153.3	50.4	13.5	32.5	11.2	5.6	9.2	2.9	5.2	10.8	5.3

*Rates are per 1,000,000 and are age-standardized to the World Standard Million.

†The symbols "-" = 1-2 cases; and "*numeral*" (italic) = 0 or 3-15 cases.

‡The period covered is different for each population and ranges from 1968-99. See <http://www-dep.iarc.fr/accis.htm> for details.

Sources: Data on Cyprus, Egypt, Israel, and Jordan are from the MECC data set, and US SEER data are from the SEER Program, National Cancer Institute. Data from other countries are from the Automated Childhood Cancer Information System (ACCIS), <http://www-dep.iarc.fr/accis.htm>.

§CNS refers to central nervous system.

4. CNS tumors were the second most common neoplasms after leukemia in Cyprus, particularly in females (55.6), with a total ASR of 40.1.

Within the MECC registries, the pattern of rates in Cyprus showed a similarity to the Western world and somewhat differed from other MECC countries. This may be due to genetic differences between the Cypriots and Arabs and Jews, or to differences in environmental factors in these populations, and needs further investigation. The situation is similar to that in Uruguay, where the incidence and types of childhood tumors were found to be closer to those in North America and Western Europe than in Latin America [20].

5. The rates of other types of childhood tumors in MECC countries were not substantially different from those in the Western world. It is interesting to note the similar ASRs of total childhood tumors in Turkey (115.6) and Jordan (114.8).

The MECC registration system has provided useful information about the incidence of childhood cancers in Middle Eastern countries and should be continued. The higher incidence rate of lymphoma in Egyptians and Israeli Arabs requires further studies from the environmental point of view, including viral (EBV) and nutritional factors. EBV infection has been found to be strongly associated with malignant lymphomas (Hodgkin and Burkitt's lymphoma) serologically and at molecular levels in Turkish children [14,15], so should be investigated further. An important future addition to the registration program would be the collection of survival data for children with malignant disease.

REFERENCES

- [1] Stiller CA. Epidemiology and genetics of childhood cancer. *Oncogene* 2004;23:6429-44.
- [2] Steliarova-Foucher E, Stiller C, Kaatsch P, Berrino F, Coebergh JW, Lacour B, et al. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCIS project): an epidemiological study. *Lancet* 2004;364:2097-105.
- [3] International Agency for Research on Cancer. ACCIS: automated childhood cancer information system. 2006. Available at: <http://www-dep.iarc.fr/accis.htm>. [Last Accessed: 1/06].
- [4] Gatta G, Corazzari I, Magnani C, Peris-Bonet R, Roazzi P, Stiller C. Childhood cancer survival in Europe. *Ann Oncol* 2003;14:v119-v127.
- [5] Gurney JG, Bondy ML. Epidemiologic research methods and childhood cancer. In: Pizzo P, Poplack DG, editors. *Principles and practice of pediatric oncology*, fourth edition. Philadelphia (PA): Williams & Wilkins; 2001. p. 13-20.
- [6] Pinkerton CR, Cushing P, Sepion B. Epidemiology and aetiology of childhood cancer. In: *Childhood cancer management: a practical handbook*. London (UK): Arnold; 1994. p. 28-41.
- [7] Parkin DM, Kramarova E, Draper GJ, Masuyer E, Michaelis J, Neglia J, et al. International incidence of childhood cancer. IARC publication no. 144. Lyon (France): International Agency for Research on Cancer; 1998.
- [8] Kramarova E, Stiller CA, Ferlay J, Parkin DM, Draper GJ, Michaelis J, et al. The international classification of childhood cancer. IARC technical report no. 29. Lyon (France): International Agency for Research on Cancer; 1997.
- [9] Parkin DM, Stiller CA, Draper GJ, Bieber CA, Terracini B, Young JL, et al. International incidence of childhood cancer. IARC scientific publications no. 87. Lyon (France): International Agency for Research on Cancer; 1988.
- [10] Parkin DM, Stiller CA, Draper GJ, Bieber CA. The international incidence of childhood cancer. *Int J Cancer* 1988;42:511-20.
- [11] Pratt CB. Some aspects of childhood cancer epidemiology. *Pediatr Clin North Am* 1985;32:541-56.
- [12] Stiller CA, Bunch KJ, Lewis IJ. Ethnic group and survival from childhood cancer: report from the UK Children's Cancer Study Group. *Br J Cancer* 2000;82:1339-43.
- [13] Parkin DM, Stiller CA. Childhood cancer in developing countries: environmental factors. *Int J Ped Hemat Oncol* 1995;2:411-7.

- [14] Cavdar AO, Pamir A, Gozdasoglu S. Hodgkin's disease in children: clinico-epidemiologic and viral (Epstein-Barr virus) analyses. *Med Pediatr Oncol* 1999;32:18-23.
- [15] Cavdar AO, Yavuz G, Babacan E, Gozdasoglu S, Unal E, Ertem U, et al. Burkitt's lymphoma in Turkish children: clinical, viral [EBV] and molecular studies. *Leuk Lymphoma* 1994;14:323-30.
- [16] Kamel AM, Ghaleb FM, Assem MM, Hindawy DS, Jaffe ES, Magrath IT. Phenotypic analysis of T-cell acute lymphoblastic leukemia in Egypt. *Leuk Res* 1990;14:601-9.
- [17] Freedman LS, Barchana M, Al Kayed S, Qasem MB, Young JL, Edwards BK, et al. A comparison of population-based cancer incidence rates in Israel and Jordan. *Eur J Cancer Prev* 2003;12:359-65.
- [18] Kutluk T. First national pediatric cancer registry in Turkey: a Turkish pediatric oncology group study (abstract). *Ped Blood & Cancer* 2004;43:452.
- [19] Fidaner C, Eser SY, Parkin DM. Incidence in Izmir in 1993-1994: first results from Izmir Cancer Registry. *Eur J Cancer* 2001;37:83-92.
- [20] Castillo L, Fluchel M, Dabezies A, Pieri D, Brockhorst N, Barr R. Childhood cancer in Uruguay: 1992-1994. Incidence and mortality. *Med Pediatr Oncol* 2001;37:400-4.