

# International Classification of Childhood Cancer, Third Edition

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**BACKGROUND.** The third edition of the International Classification of Diseases for Oncology (ICD-O-3), which was published in 2000, introduced major changes in coding and classification of neoplasms, notably for leukemias and lymphomas, which are important groups of cancer types that occur in childhood. This necessitated a third revision of the 1996 International Classification of Childhood Cancer (ICCC-3).

**METHODS.** The tumor categories for the ICCC-3 were designed to respect several principles: agreement with current international standards, integration of the entities defined by newly developed diagnostic techniques, continuity with previous childhood classifications, and exhaustiveness.

**RESULTS.** The ICCC-3 classifies tumors coded according to the ICD-O-3 into 12 main groups, which are split further into 47 subgroups. These 2 levels of the ICCC-3 allow standardized comparisons of the broad categories of childhood neoplasms in continuity with the previous classifications. The 16 most heterogeneous subgroups are broken down further into 2–11 divisions to allow study of important entities or homogeneous collections of tumors characterized at the cytogenetic or molecular level. Some divisions may be combined across the higher-level categories, such as the B-cell neoplasms within leukemias and lymphomas.

**CONCLUSIONS.** The ICCC-3 respects currently existing international standards and was designed for use in international, population-based, epidemiological studies and cancer registries. The use of an international classification system is especially important in the field of pediatric oncology, in which the low frequency of cases requires rigorous procedures to ensure data comparability. *Cancer* 2005;103:1457–67. © 2005 American Cancer Society.

**KEYWORDS:** childhood cancer, classification, cancer registries, epidemiology.

It has been established firmly that, for children, classification of tumors should be based on morphology rather than, as in adults, the primary site of origin. The first internationally accepted classification of Birch and Marsden,<sup>1</sup> which classified the tumors coded according to the International Classification of Diseases for Oncology (ICD-O),<sup>2</sup> was used for the presentation of the comparative

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tables of incidence in International Incidence of Childhood Cancer, volume 1.<sup>3</sup>

The publication of the second edition of the ICD-O<sup>4</sup> and the 10th revision of the International Classification of Diseases<sup>5</sup> necessitated an update of the childhood classification to allow for the new and expanded coding of cancer which these have introduced. The resulting International Classification of Childhood Cancer<sup>6</sup> became the standard for presentation of international data on childhood cancer incidence and survival.<sup>7-9</sup>

Ever-improving diagnostic methods, based increasingly on genetic studies and pathologic studies, have prompted a third edition of the ICD-O (ICD-O-3),<sup>10</sup> which introduced numerous new morphology codes, in particular, for leukemias and lymphomas. To accommodate the acquired knowledge reflected in changes to the coding of neoplasms, we propose here the third edition of International Classification of Childhood Cancer (ICCC-3), based on the ICD-O-3.

To ensure that the ICC-3 is adopted as the standard in cancer registries and also is accepted by oncologists for meaningful, population-based comparisons, the draft proposal was reviewed by experts from the fields of pathology, clinical pediatric oncology, and cancer registration. Their valuable comments contributed to the final version.

### Rules Governing the ICC-3

A standard classification of tumors is essential for comparing incidence and survival across regions and time periods. The ICC-3 is designed to facilitate presentation and comparison of population-based data on childhood cancer. The principles applied can be summarized as follows:

1) The ICC-3 applies the rules, nomenclature, and codes (morphology, topography, and behavior) of the ICD-O-3.<sup>10</sup>

2) ICC-3 categories are defined in conformity with international classifications of the pathology and genetics of neoplasms, notably, the series *The World Health Organization Classification of Tumors*.<sup>11-14</sup>

3) Although it accommodates new concepts of tumor histogenesis, the ICC-3 provides continuity with previous classifications.

4) Three levels of hierarchical classification are developed: Level 1 (12 main diagnostic groups) and Level 2 (47 diagnostic subgroups) comprise the main classification table. Level 3 is an optional "extended classification" and comprises 2-11 divisions of selected diagnostic subgroups. This division of some diagnostic subgroups reflects the availability of detailed information that permits homogeneous groups of tumors to be distinguished within them and, thus,

allows their separate study. However, it is preferable to keep these divisions optional and distinct from the main table, because their use will not always be possible (due to inadequate diagnostic methods) or of interest (due to small number of cases).

5) The "matrix" concept (Rule F) of the ICD-O-3<sup>10</sup> is respected, which means that, in theory, all morphology codes may occur in combination with any behavior code. Although all morphology codes listed in the ICD-O-3 are included in the conversion table, only the tumors with malignant behavior are classified in the ICC-3, with the exception described in point 6:

6) Nonmalignant intracranial and intraspinal tumors are included in the ICC-3, as in its predecessors.<sup>1,6</sup> Finally,

7) tumors that are known to occur only rarely in young patients also are included in the ICC-3, because they may be encountered in a population-based cancer registry.

### The Classification

Table 1 assigns the combinations of morphology and topography codes of ICD-O-3<sup>10</sup> to ICC-3 main diagnostic groups and subgroups. In Table 2, selected subgroups are classified further into divisions. The considerations for grouping the tumors are given below.

#### *I. Leukemias, myeloproliferative diseases, and myelodysplastic diseases.*

Leukemias are divided into subgroups to distinguish lymphoid leukemias (Ia); acute myeloid leukemias (Ib); chronic myeloproliferative diseases, including chronic myeloid leukemias (Ic); and the unspecified or combined types (Ie). The subgroup of lymphoid leukemias (Ia) is subdivided further in Table 2, which permits reporting of statistics for different cell lineages. Chronic lymphocytic leukemia (M-9823) also is included in Ia, because it is exceedingly rare in children<sup>15</sup> and, thus, will not affect the rates of acute lymphoid leukemia, the predominant childhood leukemia type. A separate subgroup (Id) is created for refractory anemia, myelodysplastic syndrome, and other myeloproliferative diseases, representing 3-9% of the hematologic malignancies in children.<sup>16</sup> These entities were considered non-malignant in ICD-O-2<sup>4</sup> and, thus, were excluded from previous classifications.

#### *II. Lymphomas and reticuloendothelial neoplasms.*

The ICC-3 maintains the division of lymphomas into the 2 major groups, Hodgkin lymphomas (IIa) and non-Hodgkin lymphomas (IIb). One particular type of non-Hodgkin lymphoma, Burkitt lymphoma, constitutes a separate subgroup due to huge differences

**TABLE 1**  
**International Classification of Childhood Cancer, Third Edition: Main Classification Table**

Diagnostic group	ICD-O-3 code(s) <sup>10</sup>	
	Morphology	Topography
I. Leukemias, myeloproliferative diseases, and myelodysplastic diseases		
a. Lymphoid leukemias	9820, 9823, 9826, 9827, 9831–9837, 9940, 9948	
b. Acute myeloid leukemias	9840, 9861, 9866, 9867, 9870–9874, 9891, 9895–9897, 9910, 9920, 9931	
c. Chronic myeloproliferative diseases	9863, 9875, 9876, 9950, 9960–9964	
d. Myelodysplastic syndrome and other myeloproliferative diseases	9945, 9946, 9975, 9980, 9982–9987, 9989	
e. Unspecified and other specified leukemias	9800, 9801, 9805, 9860, 9930	
II. Lymphomas and reticuloendothelial neoplasms		
a. Hodgkin lymphomas	9650–9655, 9659, 9661–9665, 9667	
b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	9591, 9670, 9671, 9673, 9675, 9678–9680, 9684, 9689–9691, 9695, 9698–9702, 9705, 9708, 9709, 9714, 9716–9719, 9727–9729, 9731–9734, 9760–9762, 9764–9769, 9970	
c. Burkitt lymphoma	9687	
d. Miscellaneous lymphoreticular neoplasms	9740–9742, 9750, 9754–9758	
e. Unspecified lymphomas	9590, 9596	
III. CNS and miscellaneous intracranial and intraspinal neoplasms		
a. Ependymomas and choroid plexus tumor	9383, 9390–9394 <sup>a</sup>	
b. Astrocytomas	9380 <sup>a</sup>	C72.3
	9384, 9400–9411, 9420, 9421–9424, 9440–9442 <sup>a</sup>	
c. Intracranial and intraspinal embryonal tumors	9470–9474, 9480, 9508 <sup>a</sup>	
	9501–9504 <sup>a</sup>	C70.0–C72.9
d. Other gliomas	9380 <sup>a</sup>	C70.0–C72.2, C72.4–C72.9, C75.1, C75.3
	9381, 9382, 9430, 9444, 9450, 9451, 9460 <sup>a</sup>	
e. Other specified intracranial and intraspinal neoplasms	8270–8281, 8300, 9350–9352, 9360–9362, 9412, 9413, 9492, 9493, 9505–9507, 9530–9539, 9582 <sup>a</sup>	
f. Unspecified intracranial and intraspinal neoplasms	8000–8005 <sup>a</sup>	C70.0–C72.9, C75.1–C75.3
IV. Neuroblastoma and other peripheral nervous cell tumors		
a. Neuroblastoma and ganglioneuroblastoma	9490, 9500	
b. Other peripheral nervous cell tumors	8680–8683, 8690–8693, 8700, 9520–9523, 9501–9504	C00.0–C69.9, C73.9–C76.8, C80.9
V. Retinoblastoma	9510–9514	
VI. Renal tumors		
a. Nephroblastoma and other nonepithelial renal tumors	8959, 8960, 8964–8967, 8963, 9364	C64.9
b. Renal carcinomas	8010–8041, 8050–8075, 8082, 8120–8122, 8130–8141, 8143, 8155, 8190–8201, 8210, 8211, 8221–8231, 8240, 8241, 8244–8246, 8260–8263, 8290, 8310, 8320, 8323, 8401, 8430, 8440, 8480–8490, 8504, 8510, 8550, 8560–8576, 8311, 8312, 8316–8319, 8361	C64.9
c. Unspecified malignant renal tumors	8000–8005	C64.9
VII. Hepatic tumors		
a. Hepatoblastoma	8970	
b. Hepatic carcinomas	8010–8041, 8050–8075, 8082, 8120–8122, 8140, 8141, 8143, 8155, 8190–8201, 8210, 8211, 8230, 8231, 8240, 8241, 8244–8246, 8260–8264, 8310, 8320, 8323, 8401, 8430, 8440, 8480–8490, 8504, 8510, 8550, 8560–8576, 8160–8180	C22.0, C22.1
c. Unspecified malignant hepatic tumors	8000–8005	C22.0, C22.1

(continued)

**TABLE 1**  
(continued)

Diagnostic group	ICD-O-3 code(s) <sup>10</sup>	
	Morphology	Topography
VIII. Malignant bone tumors		
a. Osteosarcomas	9180-9187, 9191-9195, 9200	C40.0-C41.9, C76.0-C76.8, C80.9
b. Chondrosarcomas	9210, 9220, 9240	C40.0-C41.9, C76.0-C76.8, C80.9
c. Ewing tumor and related sarcomas of bone	9221, 9230, 9241-9243 9260	C40.0-C41.9, C76.0-C76.8, C80.9
d. Other specified malignant bone tumors	9363-9365 8810, 8811, 8823, 8830 8812, 9250, 9261, 9262, 9270-9275, 9280-9282, 9290, 9300-9302, 9310-9312, 9320-9322, 9330, 9340-9342, 9370-9372	C40.0-C41.9 C40.0-C41.9
e. Unspecified malignant bone tumors	8000-8005, 8800, 8801, 8803-8805	C40.0-C41.9
IX. Soft tissue and other extraosseous sarcomas		
a. Rhabdomyosarcomas	8900-8905, 8910, 8912, 8920, 8991	
b. Fibrosarcomas, peripheral nerve sheath tumors, and other fibrous neoplasms	8810, 8811, 8813-8815, 8821, 8823, 8834-8835	C00.0-C39.9, C44.0-C76.8, C80.9
c. Kaposi sarcoma	8820, 8822, 8824-8827, 9150, 9160, 9491, 9540-9571, 9580 9140	
d. Other specified soft tissue sarcomas	8587, 8710-8713, 8806, 8831-8833, 8836, 8840-8842, 8850-8858, 8860-8862, 8870, 8880, 8881, 8890-8898, 8921, 8982, 8990, 9040-9044, 9120-9125, 9130-9133, 9135, 9136, 9141, 9142, 9161, 9170-9175, 9231, 9251, 9252, 9373, 9581 8830	C00.0-C39.9, C44.0-C76.8, C80.9
e. Unspecified soft tissue sarcomas	8963	C00.0-C63.9, C65.9-C69.9, C73.9-C76.8, C80.9
X. Germ cell tumors, trophoblastic tumors, and neoplasms of gonads		
a. Intracranial and intraspinal germ cell tumors	9180, 9210, 9220, 9240 9260	C49.0-C49.9 C00.0-C39.9, C47.0-C75.9
b. Malignant extracranial and extragonadal germ cell tumors	9364	C00.0-C39.9, C47.0-C63.9, C65.9-C69.9, C73.9-C76.8, C80.9
c. Malignant gonadal germ cell tumors	9365	C00.0-C39.9, C47.0-C63.9, C65.9-C76.8, C80.9
d. Gonadal carcinomas	8800-8805	C00.0-C39.9, C44.0-C76.8, C56.9, C62.0-C62.9
e. Other and unspecified malignant gonadal tumors	8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8143, 8190- 8201, 8210, 8211, 8221-8241, 8244-8246, 8260-8263, 8290, 8310, 8313, 8320, 8323, 8380-8384, 8430, 8440, 8480-8490, 8504, 8510, 8550, 8560-8573, 9000, 9014, 9015 8441-8444, 8450, 8451, 8460-8473 8590-8671 8000-8005	C56.9, C62.0-C62.9 C56.9, C62.0-C62.9 C56.9, C62.0-C62.9
XI. Other malignant epithelial neoplasms and malignant melanomas		
a. Adrenocortical carcinomas	8370-8375	
b. Thyroid carcinomas	8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8190, 8200, 8201, 8211, 8230, 8231, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8430, 8440, 8480, 8481, 8510, 8560-8573 8330-8337, 8340-8347, 8350	C73.9

(continued)

TABLE 1  
(continued)

Diagnostic group	ICD-O-3 code(s) <sup>10</sup>	
	Morphology	Topography
c. Nasopharyngeal carcinomas	8010–8041, 8050–8075, 8082, 8083, 8120–8122, 8130–8141, 8190, 8200, 8201, 8211, 8230, 8231, 8244–8246, 8260–8263, 8290, 8310, 8320, 8323, 8430, 8440, 8480, 8481, 8500–8576	C11.0–C11.9
d. Malignant melanomas	8720–8780, 8790	
e. Skin carcinomas	8010–8041, 8050–8075, 8078, 8082, 8090–8110, 8140, 8143, 8147, 8190, 8200, 8240, 8246, 8247, 8260, 8310, 8320, 8323, 8390–8420, 8430, 8480, 8542, 8560, 8570–8573, 8940, 8941	C44.0–C44.9
f. Other and unspecified carcinomas	8010–8084, 8120–8157, 8190–8264, 8290, 8310, 8313–8315, 8320–8325, 8360, 8380–8384, 8430–8440, 8452–8454, 8480–8586, 8588–8589, 8940, 8941, 8983, 9000, 9010–9016, 9020, 9030	C00.0–C10.9, C12.9–C21.8, C23.9–C39.9, C48.0–C48.8, C50.0–C55.9, C57.0–C61.9, C63.0–C63.9, C65.9–C72.9, C75.0–C76.8, C80.9
XII. Other and unspecified malignant neoplasms		
a. Other specified malignant tumors	8930–8936, 8950, 8951, 8971–8981, 9050–9055, 9110 9363	C00.0–C39.9, C47.0–C75.9
b. Other unspecified malignant tumors	8000–8005	C00.0–C21.8, C23.9–C39.9, C42.0–C55.9, C57.0–C61.9, C63.0–C63.9, C65.9–C69.9, C73.9–C75.0, C75.4–C80.9

ICD-O-3: International Classification of Diseases for Oncology, third edition; CNS: central nervous system.

<sup>a</sup> Tumors with nonmalignant behavior are included for all morphology codes on the line.

across the world in incidence rates of this tumor.<sup>7</sup> Burkitt lymphoma (IIc) may be pooled with the division for overall presentation of mature B-cell lymphomas (IIb2). The miscellaneous lymphoreticular neoplasms include mast cell tumors, malignant histiocytosis, and histiocytic and dendritic cell neoplasms (IIId). In the extended classification of non-Hodgkin lymphomas, the first three divisions correspond to those existing within the subgroup of lymphoid leukemias and may be combined with them for analyses by cell lineage.

It should be noted that the definition of the code M-9702 in ICD-O-3 is ambiguous for the purposes of ICC-3: It is used both for “mature T-cell lymphoma, not otherwise specified” and “T-cell lymphoma, not otherwise specified.” This ambiguity may not be important for T-cell lymphomas overall, because the majority of unspecified T-cell lymphomas in adults are mature types. However, in children, most T-cell lymphomas are known to be of the precursor cell type.<sup>17</sup> Coders should be aware of this problem and should use the code M-9729 (precursor T-cell lymphoblastic lymphoma) for an apparently unspecified T-cell lymphoma in a child.

### III. Central nervous system and miscellaneous intracranial and intraspinal neoplasms.

Ependymomas and choroid plexus tumors represent a single group (IIIa), but the two tumor types may be distinguished by the extended classification. Astrocytomas are grouped with glioblastoma and optic nerve glioma (IIIb). The intracranial and intraspinal embryonal tumors (IIIc) are divided further into the principal groups of embryonal central nervous system (CNS) tumors in Table 2. Other gliomas (IIId) and other specified intracranial and intraspinal neoplasms (IIIe) also are subdivided into relatively homogeneous divisions in the extended classification. Intracranial and intraspinal germ cell tumors constitute a subgroup within the germ cell tumors, trophoblastic tumors, and neoplasms of gonads (Xa). Cerebral neuroblastoma, which is considered a synonym for supratentorial primitive neuroectodermal tumor (PNET) (M-9473),<sup>18</sup> belongs in subgroup IIIc and division IIIc2. This arrangement reflects the general opinion that neuroblastoma in CNS is related more closely to PNET than to neuroblastoma elsewhere in the body, and it stipulates verification of coding for each case of neuroblastoma in brain.

**TABLE 2**  
**International Classification of Childhood Cancer, Third Edition: Extended Classification Table**

ICCC-3 division	ICD-O-3 code(s) <sup>10</sup>	
	Morphology	Topography
Ia. Lymphoid leukemias		
1. Precursor cell leukemias	9835, 9836, 9837	
2. Mature B-cell leukemias	9823, 9826, 9832, 9833, 9940	
3. Mature T-cell and NK cell leukemias	9827, 9831, 9834, 9948	
4. Lymphoid leukemia, NOS	9820	
Iib. Non-Hodgkin lymphomas		
1. Precursor cell lymphomas	9727, 9728, 9729	
2. Mature B-cell lymphomas (except Burkitt lymphoma) <sup>a</sup>	9670, 9671, 9673, 9675, 9678-9680, 9684, 9689-9691, 9695, 9698, 9699, 9731-9734, 9761, 9762, 9764-9766, 9769, 9970	
3. Mature T-cell and NK-cell lymphomas	9700-9702, <sup>b</sup> 9705, 9708, 9709, 9714, 9716-9719, 9767, 9768	
4. Non-Hodgkin lymphomas, NOS	9591, 9760	
IIia. Ependymomas and choroid plexus tumor		
1. Ependymomas	9383, 9391-9394 <sup>c</sup>	
2. Choroid plexus tumor	9390 <sup>c</sup>	
IIic. Intracranial and intraspinal embryonal tumors		
1. Medulloblastomas	9470-9472, 9474, 9480 <sup>c</sup>	
2. PNET	9473 <sup>c</sup>	
3. Medulloepithelioma	9501-9504 <sup>c</sup>	C70.0-C72.9
4. Atypical teratoid/rhabdoid tumor	9508 <sup>c</sup>	
IIId. Other gliomas		
1. Oligodendrogliomas	9450, 9451, 9460 <sup>c</sup>	
2. Mixed and unspecified gliomas	9380 <sup>c</sup> 9382 <sup>c</sup>	C70.0-C72.2, C72.4-C72.9, C75.1, C75.3
3. Neuroepithelial glial tumors of uncertain origin	9381, 9430, 9444 <sup>c</sup>	
IIie. Other specified intracranial and intraspinal neoplasms		
1. Pituitary adenomas and carcinomas	8270-8281, 8300 <sup>c</sup>	
2. Tumors of the sellar region (craniopharyngiomas)	9350-9352, 9582 <sup>c</sup>	
3. Pineal parenchymal tumors	9360-9362 <sup>c</sup>	
4. Neuronal and mixed neuronal-glial tumors	9412, 9413, 9492, 9493, 9505-9507 <sup>c</sup>	
5. Meningiomas	9530-9539 <sup>c</sup>	
VIa. Nephroblastoma and other nonepithelial renal tumors		
1. Nephroblastoma	8959, 8960	
2. Rhabdoid renal tumor	8963	C64.9
3. Kidney sarcomas	8964-8967	
4. pPNET of kidney	9364	C64.9
VIIIc. Ewing tumor and related sarcomas of bone		
1. Ewing tumor and Askin tumor of bone	9260 9365	C40.0-C41.9, C76.0-C76.8, C80.9 C40.0-C41.9
2. pPNET of bone	9363, 9364	C40.0-C41.9
VIIIId. Other specified malignant bone tumors		
1. Malignant fibrous neoplasms of bone	8810, 8811, 8823, 8830 8812, 9262	C40.0-C41.9
2. Malignant chordomas	9370-9372	
3. Odontogenic malignant tumors	9270-9275, 9280-9282, 9290, 9300-9302, 9310-9312, 9320-9322, 9330, 9340-9342	
4. Miscellaneous malignant bone tumors	9250, 9261	
IXb. Fibrosarcomas, peripheral nerve sheath tumors, and other fibromatous neoplasms		
1. Fibroblastic and myofibroblastic tumors	8810, 8811, 8813-8815, 8821, 8823, 8834-8835 8820, 8822, 8824-8827, 9150, 9160	C00.0-C39.9, C44.0-C76.8, C80.9
2. Nerve sheath tumors	9540-9571	
3. Other fibromatous neoplasms	9491, 9580	
IXd. Other specified soft tissue sarcomas		
1. Ewing tumor and Askin tumor of soft tissue	9260 9365	C00.0-C39.9, C47.0-C75.9 C00.0-C39.9, C47.0-C63.9, C65.9-C76.8, C80.9

(continued)



TABLE 2  
(continued)

ICCC-3 division	ICD-O-3 code(s) <sup>10</sup>	
	Morphology	Topography
2. pPNET of soft tissue	9364	C00.0–C39.9, C47.0–C63.9, C65.9–C69.9, C73.9–C76.8, C80.9
3. Extrarenal rhabdoid tumor	8963	C00.0–C63.9, C65.9–C69.9, C73.9–C76.8, C80.9
4. Liposarcomas	8850–8858, 8860–8862, 8870, 8880, 8881	
5. Fibrohistiocytic tumors	8830 8831–8833, 8836, 9251, 9252	C00.0–C39.9, C44.0–C76.8, C80.9
6. Leiomyosarcomas	8890–8898	
7. Synovial sarcomas	9040–9044	
8. Blood vessel tumors	9120–9125, 9130–9133, 9135, 9136, 9141, 9142, 9161, 9170–9175	
9. Osseous and chondromatous neoplasms of soft tissue	9180, 9210, 9220, 9240 9231	C49.0–C49.9
10. Alveolar soft parts sarcoma	9581	
11. Miscellaneous soft tissue sarcomas	8587, 8710–8713, 8806, 8840–8842, 8921, 8982, 8990, 9373	
Xa. Intracranial and intraspinal germ cell tumors		
1. Intracranial and intraspinal germinomas	9060–9065 <sup>c</sup>	C70.0–C72.9, C75.1–C75.3
2. Intracranial and intraspinal teratomas	9080–9084 <sup>c</sup>	C70.0–C72.9, C75.1–C75.3
3. Intracranial and intraspinal embryonal carcinomas	9070, 9072 <sup>c</sup>	C70.0–C72.9, C75.1–C75.3
4. Intracranial and intraspinal yolk sac tumor	9071 <sup>c</sup>	C70.0–C72.9, C75.1–C75.3
5. Intracranial and intraspinal choriocarcinoma	9100 <sup>c</sup>	C70.0–C72.9, C75.1–C75.3
6. Intracranial and intraspinal tumors of mixed forms	9085, 9101 <sup>c</sup>	C70.0–C72.9, C75.1–C75.3
Xb. Malignant extracranial and extragonadal germ cell tumors		
1. Malignant germinomas of extracranial and extragonadal sites	9060–9065	C00.0–C55.9, C57.0–C61.9, C63.0–C69.9, C73.9–C75.0, C75.4–C76.8, C80.9
2. Malignant teratomas of extracranial and extragonadal sites	9080–9084	C00.0–C55.9, C57.0–C61.9, C63.0–C69.9, C73.9–C75.0, C75.4–C76.8, C80.9
3. Embryonal carcinomas of extracranial and extragonadal sites	9070, 9072	C00.0–C55.9, C57.0–C61.9, C63.0–C69.9, C73.9–C75.0, C75.4–C76.8, C80.9
4. Yolk sac tumor of extracranial and extragonadal sites	9071	C00.0–C55.9, C57.0–C61.9, C63.0–C69.9, C73.9–C75.0, C75.4–C76.8, C80.9
5. Choriocarcinomas of extracranial and extragonadal sites	9100, 9103, 9104	C00.0–C55.9, C57.0–C61.9, C63.0–C69.9, C73.9–C75.0, C75.4–C76.8, C80.9
6. Other and unspecified malignant mixed germ cell tumors of extracranial and extragonadal sites	9085, 9101, 9102, 9105	C00.0–C55.9, C57.0–C61.9, C63.0–C69.9, C73.9–C75.0, C75.4–C76.8, C80.9
Xc. Malignant gonadal germ cell tumors		
1. Malignant gonadal germinomas	9060–9065	C56.9, C62.0–C62.9
2. Malignant gonadal teratomas	9080–9084, 9090, 9091	C56.9, C62.0–C62.9
3. Gonadal embryonal carcinomas	9070, 9072	C56.9, C62.0–C62.9
4. Gonadal yolk sac tumor	9071	C56.9, C62.0–C62.9
5. Gonadal choriocarcinoma	9100	C56.9, C62.0–C62.9
6. Malignant gonadal tumors of mixed forms	9085, 9101	C56.9, C62.0–C62.9
7. Malignant gonadal gonadoblastoma	9073	C56.9, C62.0–C62.9
Xif. Other and unspecified carcinomas		
1. Carcinomas of salivary glands	8010–8084, 8120–8157, 8190–8264, 8290, 8310,	C07.9–C08.9
2. Carcinomas of colon and rectum	8313–8315, 8320–8325, 8360, 8380–8384,	C18.0, C18.2–C18.9, C19.9, C20.9, C21.0–C21.8
3. Carcinomas of appendix	8430–8440, 8452–8454, 8480–8586,	C18.1
4. Carcinomas of lung	8588–8589, 8940, 8941, 8983, 9000, 9010–	C34.0–C34.9
5. Carcinomas of thymus	9016, 9020, 9030	C37.9
6. Carcinomas of breast		C50.0–C50.9
7. Carcinomas of cervix uteri		C53.0–C53.9
8. Carcinomas of bladder		C67.0–C67.9
9. Carcinomas of eye		C69.0–C69.9
10. Carcinomas of other specified sites		C00.0–C06.9, C09.0–C10.9, C12.9–C17.9, C23.9–C33.9, C38.0–C39.9, C48.0–C48.8, C51.0–C52.9, C54.0–C54.9, C55.9, C57.0–C61.9, C63.0–C63.9, C65.9–C66.9, C68.0–C68.9, C70.0–C72.9, C75.0–C75.9
11. Carcinomas of unspecified site		C76.0–C76.8, C80.9

(continued)

**TABLE 2**  
(continued)

ICCC-3 division	ICD-O-3 code(s) <sup>10</sup>	
	Morphology	Topography
XIIa. Other specified malignant tumors		
1. Gastrointestinal stromal tumor	8936	
2. Pancreatoblastoma	8971	
3. Pulmonary blastoma and pleuropulmonary blastoma	8972, 8973	
4. Other complex mixed and stromal neoplasms	8930-8935, 8950, 8951, 8974-8981	
5. Mesothelioma	9050-9055	
6. Other specified malignant tumors	9110	
	9363	C00.0-C39.9, C47.0-C75.9

ICCC-3: International Classification of Childhood Cancer ICD-O-3: International Classification of Diseases for Oncology, third edition; NOS: not otherwise specified; NK cell: natural killer cell; PNET: primitive neuroectodermal tumor; pPNET: peripheral PNET.

<sup>a</sup> Burkitt lymphoma (IIc), as a mature B-cell non-Hodgkin lymphoma, may be pooled with IIb2 for overall presentation of B-cell lymphomas.

<sup>b</sup> 9702 "T-cell lymphoma, NOS" in a child almost always corresponds to code M9729.

<sup>c</sup> Tumors with nonmalignant behavior are included for all morphology codes on the line.

#### **IV. Neuroblastoma and other peripheral nervous cell tumors.**

Most tumors of this group fall within the subgroup IVa, neuroblastoma and ganglioneuroblastoma, the typical tumors of young children. Subgroup IVb contains rare peripheral nervous cell tumors, olfactory tumors, and some neuroepitheliomatous neoplasms of extracranial and extraspinal sites.

#### **V. Retinoblastoma.**

All retinoblastoma morphology types are included in this uniquely homogeneous group of tumors, which occur almost exclusively in children age < 5 years.

#### **VI. Renal tumors.**

The largest subgroup of renal tumors (VIa) comprises > 90% of renal tumors that occur in children.<sup>7</sup> They are nonepithelial tumors, which form four divisions in the extended classification: nephroblastoma, rhabdoid renal tumor, kidney sarcomas, and peripheral PNET (pPNET) of the kidney. Renal carcinomas constitute the subgroup VIb, and unspecified malignant renal tumors constitute the subgroup VIc. Other tumors of the kidney, such as some rare sarcomas (e.g., ectomesenchymoma<sup>19</sup>) and teratomas, are classified into groups IX and X, respectively.

#### **VII. Hepatic tumors.**

Hepatoblastoma, which is a rare malignant embryonal tumor with divergent patterns of differentiation, constitutes a separate subgroup (VIIa) within the hepatic tumors due to its almost exclusive occurrence in childhood.<sup>20</sup> Two other subgroups comprise hepatic carcinomas (VIIb) and unspecified malignant hepatic tu-

mors (VIIc). Other tumors of the liver (various sarcomas, rhabdoid tumor, teratomas, yolk sac tumor, and carcinosarcoma) are to be reported within the corresponding morphology groups of the ICC-3.

#### **VIII. Malignant bone tumors.**

Osteogenic malignant tumors are the largest subgroup of malignant bone tumors in children (VIIIa), closely followed by the subgroup of Ewing and related sarcomas (VIIIc). The latter includes the histogenetically related tumors:<sup>21</sup> Ewing tumor of bone, ill defined and unspecified sites, Askin tumor of bone,<sup>22</sup> pPNET of bone, and melanotic neuroectodermal tumor of bone. The pPNETs are distinguished from the other two histologies in the extended classification (Table 2).

The remaining malignant tumors of bone in children are represented almost equally by cartilage tumors (VIIIb) and other specified (VIIId) and unspecified (VIIIe) malignant bone tumors. The subgroup of other specified tumors (VIIId) includes a range of tumors, some of which are extremely rare, especially in children. Divisions are provided for chordomas and for fibrous, odontogenic, and miscellaneous tumors; the latter include giant cell tumor of bone and adamantinoma of long bones.

#### **IX. Soft tissue and other extraosseous sarcomas.**

There are five subgroups in group IX. The first subgroup (IXa) comprises all histologic types of rhabdomyosarcomas defined in the ICD-O-3, except rhabdomyosarcoma with ganglionic differentiation or ectomesenchymoma (M-8921/M-8923), which exhibits both neuroectodermal and mesenchymal elements<sup>23</sup> and, thus, is classified in subgroup IXd. Sub-



group IXb, which is composed of fibrosarcomas, peripheral nerve sheath tumors, and other fibromatous neoplasms, is less homogeneous and, thus, is divided further in the extended classification. Kaposi sarcoma (IXc) is distinguished from other vascular tumors because of the large international variation in incidence in children across the world, largely the consequence of the epidemic of human immunodeficiency-acquired immunodeficiency syndrome (AIDS) in many African countries.<sup>7,24</sup> Other specified soft tissue sarcomas are split into 11 divisions. The last of these is comprised of various rare sarcomas together with mesenchymoma, which is not now considered a clinicopathologic entity.<sup>25</sup>

#### ***X. Germ cell tumors, trophoblastic tumors, and neoplasms of gonads***

This group of tumors includes all malignant tumors of gonads (in children, represented mainly by germ cell tumors) as well as germ cell tumors of all other sites. The subgroup of intracranial and intraspinal germ cell tumors includes, like other CNS tumors, those with nonmalignant behavior. The extended classification for three subgroups of germ cell tumors (Xa, Xb, and Xc) reflects the categories that are used extensively by pediatric oncologists<sup>26</sup> and permits grouping of all germinomas, teratomas, embryonal carcinomas, etc., irrespective of the site of tumor.

#### ***XI. Other malignant epithelial neoplasms and malignant melanomas.***

The first 5 distinct subgroups reflect specific epidemiologic interests in different parts of the world: adrenocortical carcinomas (XIa), thyroid carcinomas (XIb), nasopharyngeal carcinomas (XIc), malignant melanoma (XIId), and skin carcinomas (XIe).<sup>7,27-30</sup> The last subgroup of other and unspecified carcinomas (XIff) comprises 11 divisions (Table 2), according to the site of origin. Such categorization may be useful especially for comparisons in older children or adolescents, in whom these types of tumors are more common. A specific division for carcinomas of the appendix allows malignant carcinoid of the appendix to be distinguished. This is usually a nonmalignant tumor,<sup>31</sup> and coding practices differ between cancer registries, so that it may be convenient to exclude epithelial tumors of the appendix from geographic comparisons. The separation of carcinoma of the eye permits international differences in incidence of carcinoma of the conjunctiva to be discerned, especially in relation to the AIDS epidemic in Africa,<sup>32</sup> as well as possible errors in coding retinoblastoma.

#### ***XII. Other and unspecified malignant neoplasms.***

All of the neoplasms not mentioned above are included in the group XII. The tumors grouped in subgroup XIIa are very rare (0.1%), distinct, specified entities that are not classified elsewhere. The most numerous or interesting groups were assigned to separate divisions (Table 2).

Subgroup XIIb includes unspecified tumors that occur in the digestive system (except the liver), respiratory system, skin (integument), genitourinary system (except gonads and kidney), and tumors that occur at ill defined and unknown primary sites that were not considered in the "unspecified" subgroups of the groups III, VI, VII, VIII, and X. Unspecified morphologies of leukemias and lymphomas are classified most appropriately into subgroups Ie and Iie, respectively.

## **DISCUSSION**

The 3-level structure of the ICCC-3 provides the classification with both simplicity and flexibility. Although the definition of the main groups and most of the subgroups preserves the continuity with the previous classification schemes, the divisions of the extended classification allow categories of tumors of similar origin to be pooled across the higher level groups. This is true for the different cell lineages of lymphoid neoplasms; rhabdoid tumors of the CNS, kidney, and soft tissues; Ewing sarcomas of bone and soft tissues; and PNET of the peripheral nervous system, kidney, bone, and soft tissue.

Leukemias and lymphomas are the groups of neoplasms for which most extensive revision was introduced in the ICD-O-3<sup>10</sup> based on a combination of morphology, immunophenotype, genetic abnormalities, and clinical criteria of the World Health Organization classification of tumors of hematopoietic and lymphatic tissues.<sup>13</sup> The ICD-O-3 codes reflect the concept of eliminating the largely artificial distinction between lymphoid leukemias and lymphomas by sharing leukemia/lymphoma nomenclature. To allow historic comparison, however, the ICD-O-3 provides synonymous codes for such neoplasms.<sup>10</sup> A similar approach was chosen for the ICCC-3: Leukemias constitute a separate diagnostic group from lymphomas to secure continuity in reporting of data. At the same time, distinct cell lineages of hematopoietic and lymphoid neoplasms may be pooled across subgroups Ia and Iib, irrespective of leukemic or lymphomatous presentation of the disease, if immunophenotyping for these neoplasms is available.

The inclusion of intracranial and intraspinal tumors with nonmalignant behavior in the ICCC-3 promotes systematic collection of data on these tumors

and their inclusion in routine statistics, which still is not the rule in all cancer registries. This is even more important now than before, because the ICD-O-3 assigns a nonmalignant behavior code to pilocytic astrocytoma, which is one of the most common childhood CNS tumors.<sup>33</sup> Unlike tumors located elsewhere in the body, intracranial and intraspinal neoplasms present with similar clinical symptoms, prognosis, and late effects, whether or not the tumor is malignant. In addition, the nonmalignant intracranial and intraspinal tumors have different patterns of occurrence (by site, histology, gender, and age); thus, it is of interest to register these tumors irrespective of behavior.<sup>34</sup> Tumors classified as nonmalignant in the ICD-O-2 may represent up to one-third of intracranial and intraspinal tumors in children, and this proportion varies between registries<sup>7,34</sup>; the classification of pilocytic astrocytoma as nonmalignant would increase this proportion to more than one-half. With the progressive use of noninvasive diagnostic techniques, incidence rates of intracranial and intraspinal nonmalignant tumors may increase faster than the rates for malignant tumors.

The “unspecified” categories defined by the ICC-3 express a measure of the potentially misclassified tumors. A large proportion of tumors classified as unspecified, therefore, reduces the comparability of different data sets. In such cases, it is preferable to compare only the main diagnostic groups.

The ICC-3 is a classification system applied to ICD-O-3 morphology and topography codes, and it is assumed that the codes are assigned correctly. Because the ICC-3 conversion table does not guard against errors of coding, careful data quality checks must be exercised before classification of the tumors. An automatic conversion program that incorporates a number of verification procedures (including the concerns stated above) is in preparation.

In 2000, Birch and Kelsey proposed a classification scheme for childhood cancer within the framework of the United Kingdom’s epidemiologic study of childhood cancer,<sup>35</sup> which was based on the ICD-O-2.<sup>4</sup> The major structural difference concerns Ewing tumors and pNETs, which are grouped into a single category with peripheral nervous cell tumors in the Birch and Kelsey classification, in contrast to the ICC-3. The remainder of bone and soft tissue sarcomas are then combined into one group, apart from a few rare histologies that are classified elsewhere. The “other specified malignancies” (equivalent to the ICC-3 subgroup IIIa) belong to the group named “other carcinoma/melanoma,” corresponding largely to group XI of the ICC-3. Langerhans cell histiocytosis constitutes a group apart from lymphopoietic neo-

plasms. Two epidemiologically important diagnoses, Burkitt lymphoma and Kaposi sarcoma, do not have their own subgroups, which limits the value of the Birch and Kelsey classification scheme outside populations of European descent. There are some other minor differences between the classifications. Furthermore, the Birch and Kelsey classification, in addition to ICD-O-2 codes, includes some codes from ICD-O-3 and SNOMED. This can lead to ambiguity in the case of numeric codes appearing in more than one system with different meanings.

From a clinical perspective, Birch and Kelsey sometimes may appear to be the more appropriate classification scheme. However, because the ICC-3 is based on the most recent international standards, it complies with valid international systems of data collection, coding, and classification, which are essential prerequisites for advancing the quality and comparability of international population-based data on childhood cancer.

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