Malignant Germ Cell Tumors

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Frederick J. Rescorla

Introduction

Germ cell tumors are a relatively uncommon group of neoplasms which can have a variety of presentations affecting the fetus, infant, child, and adolescent. They are interesting for several reasons: in children the extragonadal site predominates compared with gonadal locations; the most common malignant histology is yolk sac tumor which has alpha fetoprotein as a sensitive marker; the survival has been excellent in the era of cooperative group trials utilizing cisplatin, etoposide and bleomycin; and, based on the effectiveness of chemotherapy, neoadjuvant therapy followed by surgery is indicated to avoid excision of normal structures in unresectable cases.

The location of the tumor often determines the timing of presentation. For instance, with vaginal lesions, bleeding often occurs relatively early in the disease progression and these tumors rarely have metastases at diagnosis [53]. In comparison, sacrococcygeal and retroperitoneal abdominal tumors often achieve a large size prior to the onset of symptoms and the rate of metastases in these tumors is over 50 % [11, 52]. Ovarian tumors can achieve a large size before presentation due to the size of the pelvis whereas testes tumors are usually diagnosed at a much smaller size. The histologic variants also differ by site and age. Among the extragonadal sites, yolk sac histology predominates in the younger children which include all of the sacrococcygeal and genital tumors. In mediastinal tumors a significant proportion are older children and the histology is more varied including germinoma, choriocarcinoma and mixed tumors with either benign and malignant or multiple malignant components. In the prepubertal testes tumors yolk sac predominates whereas in puberty there is wide histologic variation.

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Embryology and Classification

Germ cell tumors are thought to arise from arrested or aberrant migration of common progenitor cells. These primordial cells originate near the allantois of the embryonic yolk sac endoderm and migrate to the genital ridge at 4–5 weeks gestation. Germ cell migration is thought to be mediated by c-KIT receptors and stem cell factors [38, 64] and arrest of this process is thought to lead to germ cells at nongonadal sites like the retroperitoneum. Aberrant migration can lead to germ cells at sites such as the sacrococcygeal region, neck, and mediastinum.

The totipotential nature of these cells allows a wide variety of tumors (Fig. 19.1) [65]. Seminoma or dysgerminoma is rare before puberty but occurs at gonadal sites in adolescence. Embryonal carcinoma can further differentiate into embryonic tumors such as mature and immature teratomas or the more malignant extra-embryonic tumors such as a yolk sac or choriocarcinoma. Most childhood germ cell tumors are benign, comprising mature and immature teratomas. Teratomas contain elements from one or more of the embryonic germ layers and contain tissue foreign to the site of origin [20, 41]. Immature teratomas contain primitive neuroepithelium and are graded between I and III [48]. The Pediatric Oncology Group (POG)/Children's Cancer Group (COG) intergroup studies have confirmed the role of complete surgical excision alone as treatment for pediatric immature teratoma regardless of histologic grade [18, 45]. These studies have however noted an association between grade III immature teratoma and microscopic foci of yolk sac tumor emphasizing the need for thorough histologic evaluation of all germ cell tumors.

Yolk sac tumor (also called endodermal sinus tumor) is the most common malignant histologic variant in infancy and childhood and can develop metastases to lymph nodes or lungs. Other malignant histologic types include choriocarcinoma and embryonal carcinoma. Malignant elements coexist in approximately 25 % of pediatric germ cell tumors [29] and benign elements (teratoma) are often present with

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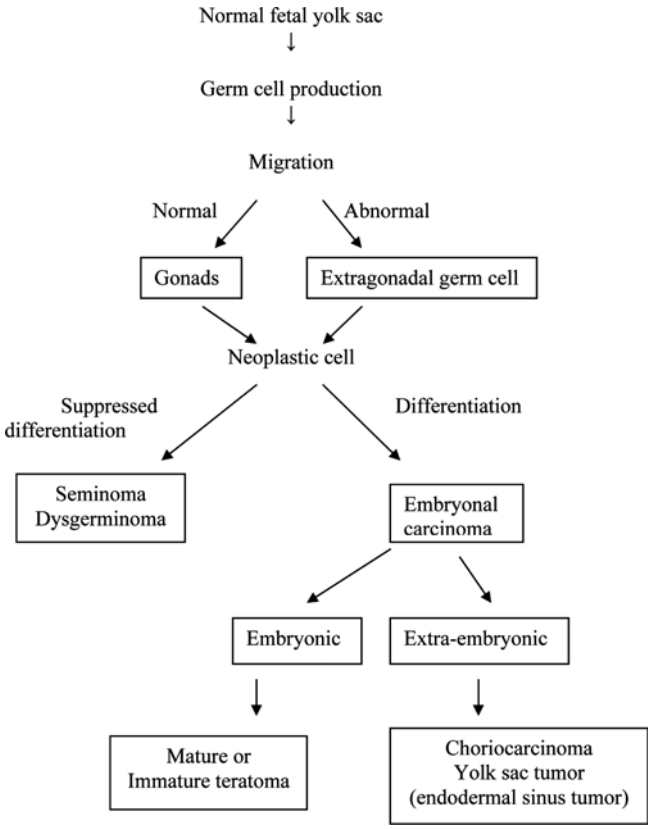

Fig. 19.1 Classification system for development of germ cell tumors

malignant tumors particularly in the mediastinum [10] and ovary [12].

Genetics and Risk Factors

Children with intersex disorders, undescended testes, and Klinefelter's syndrome associated with thoracic teratoma have an increased risk of germ cell tumors. Children with intersex disorders have an increased risk of developing gonadoblastoma, an in situ lesion with the capability of transforming into dysgerminoma, yolk sac tumor, immature teratoma, or choriocarcinoma [56]. The presence of a Y chromosome is thought to be the risk factor and thus includes male pseudohermaphrodites (under-androgenized males) with testosterone deficiency, androgen insensitivity syndrome, or 5α reductase deficiency as well as mixed gonadal dysgenesis [56]. The risk of malignancy in complete androgen insensitivity is approximately 3.6 % at age 20 and 22 % at age 30 [44]. Gonadectomy is recommended in these children.

The occurrence of testicular cancer is also increased in boys with undescended testes. Approximately 0.4 % of the general population has undescended testes; however, the incidence among males with testicular cancer is 3.5–12 % [26]. In addition, the risk appears even higher with intra-abdominal testes as Campbell [14] notes that this site accounts for only 14.3 % of undescended testes but 48.5 % of the tumors in undescended testes. In addition, the contralateral testes are also at increased risk as 20 % of tumors in patients with undescended testes occur in the contralateral scrotal testes [35]. Seminomas occur with an increased frequency in the undescended testes compared with descended testes [63]. Although some have noted a decreased rate of seminoma after orchiopexy [36], the effect of orchiopexy on the rate of testicular cancer is not known.

Tumor Markers

Yolk sac tumors are the most common histologic type of malignant germ cell tumor in childhood and serum alpha-fetoprotein (AFP) levels should be obtained at the time of presentation. Persistently elevated levels after surgery are suggestive of residual disease whereas elevations after an initial drop can indicate progressive or recurrent disease.

AFP is normally elevated in fetal life and as synthesis does not stop completely at birth, the half-life, which is usually considered to be 5 days, may vary during the first few months of life [67]. AFP levels should drop to normal by 9 months of age [66]. Choriocarcinoma, although less common, has human chorionic gonadotropin (hCG) as an easily identifiable marker. The half-life of hCG is 16 h. Lactate dehydrogenase is elevated in many germ cell tumors; however, is a nonspecific marker.

Extragonadal Germ Cell Tumors

Extragonadal tumors account for approximately two-thirds of pediatric germ cell tumors compared to only 5–10 % in adults [50]. The sacrococcygeal site is the most common, followed by the anterior mediastinum, pineal, retroperitoneum, and less commonly the neck, stomach and vagina. The current staging system utilized by the Children's Oncology Group (COG) for extragonadal tumors is listed in Table 19.1. The overall risk-based treatment scheme is listed in Table 19.2.

Sacrococcygeal Tumors

Sacrococcygeal tumors are relatively rare, affecting approximately 1:35,000 live births [57]. They occur more commonly in girls (70–80 %) and they usually present in one of two clinical patterns: neonates with large predominately benign tumors (mature and immature teratomas) (Fig. 19.2); or, infants and children between birth and 4 years of age with primarily pelvic, malignant (yolk sac) tumors (Fig. 19.3).

Table 19.1 Children's Oncology Group staging system for malignant extragonadal tumors in childhood

Stage I	Complete resection at any site, coccygectomy for sacrococcygeal site, negative tumor margins
Stage II	Microscopic residual; lymph nodes negative
Stage III	Lymph node involvement with metastatic disease. Gross residual or biopsy only; retroperitoneal nodes negative or positive
Stage IV	Distant metastases, including liver

Table 19.2 COG Study AGCT 0132 (2003–2011)

Low risk		
Stage I	Testes	Surgery
Stage I	Ovary	Alone
All immature	Teratomas	
Intermediate risk		
Stage II–III	Ovary	PEB × 3
Stage II–IV	Testes	
Stage I–II	Extragonadal	
High risk (off study)		
Stage III–IV	Extragonadal	PEB × 4
Stage IV	Ovary	

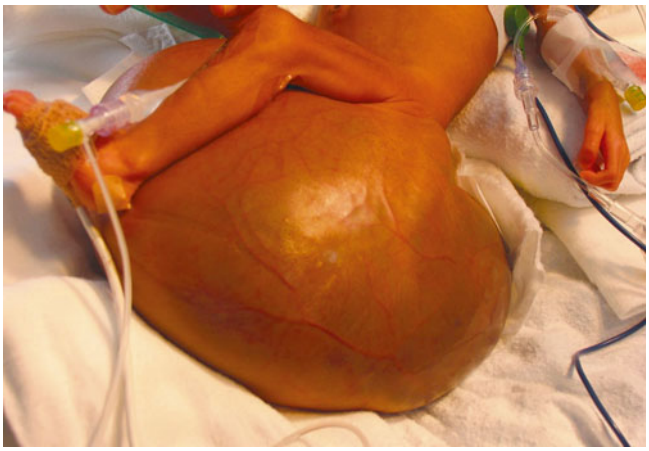

Fig. 19.2 A large Type I sacrococcygeal teratoma

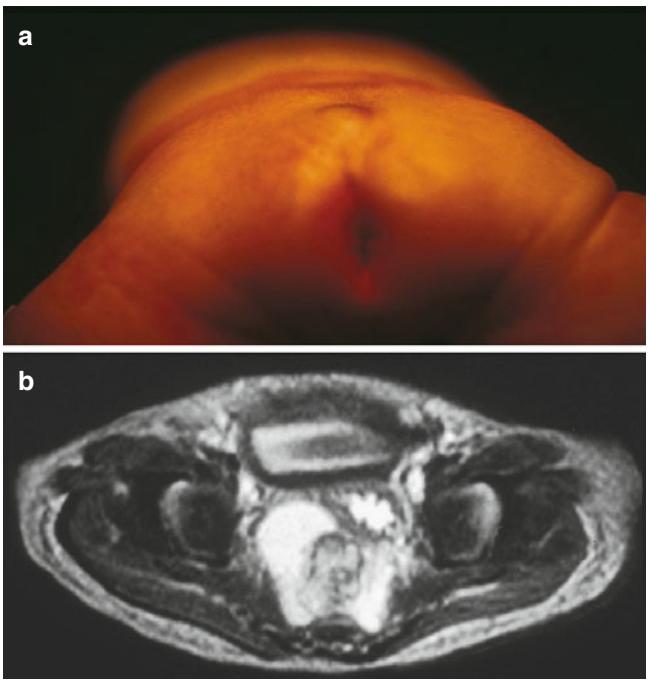

Fig. 19.3 A 2 month old boy with a malignant sacrococcygeal tumor. (**a**) Photograph of small external portion. (**b**) MRI scan demonstrating a pelvic tumor

Sacrococcygeal teratomas can also be noted in utero and if the lesion is greater than 5 cm in size abdominal delivery should be considered in order to avoid dystocia and tumor rupture [25]. High output cardiac failure can also occur due to shunting leading to fetal hydrops [13]. Detection early in gestation and hydrops are ominous and properly selected fetuses may benefit from fetal resection or intervention. Adzick et al. [1] reported the first successful fetal resection. Makin et al. [40] reported 41 antenatally diagnosed SCTs and performed fetal intervention in 12, including cyst drainage to facilitate delivery or relieve bladder obstruction and laser ablation or alcohol sclerosis for hydrops. Although the overall survival for antenatally diagnosed lesions was 77 %, the survival for fetal intervention was 50 % and only 14 % for fetal intervention for hydrops. One recent study noted that the survival for prenatally detected lesions was highest for small lesions (<10 cm) or larger predominantly cystic tumors (100 %), whereas the survival was lowest (48 %) in the large (>10 cm) lesions with increased vascularity, vascular steal syndrome, or rapid growth [7]. Adzick and colleagues currently recommend fetal resection for high-output failure less than 28 weeks gestation and consideration of ex utero intrapartum therapy (EXIT) in those between 28 and 36 weeks [55].

Altman et al. (in a survey of the Surgical Section of the American Academy of Pediatrics) developed a classification system which is widely utilized today (Fig. 19.4) [2]. In this survey the rate of malignancy was higher in older infants (<2 months, 7 % girls and 10 % boys malignant; >2 months, 48 % girls and 67 % boys malignant). Malignancy rates in children presenting after the newborn period in many series is as high as 90 % [22,

51]. The higher malignancy rate with the less apparent lesions may be due to an error in the initial diagnosis which is most commonly confused with a neural defect. In addition, many older infants may have no external mass and symptoms may develop later as the mass enlarges, frequently leading to constipation and urinary tract dysfunction.

An interesting group of children, first reported by Ashcraft and Holder, present with an autosomal dominant condition consisting of the triad of presacral teratomas, anal stenosis,

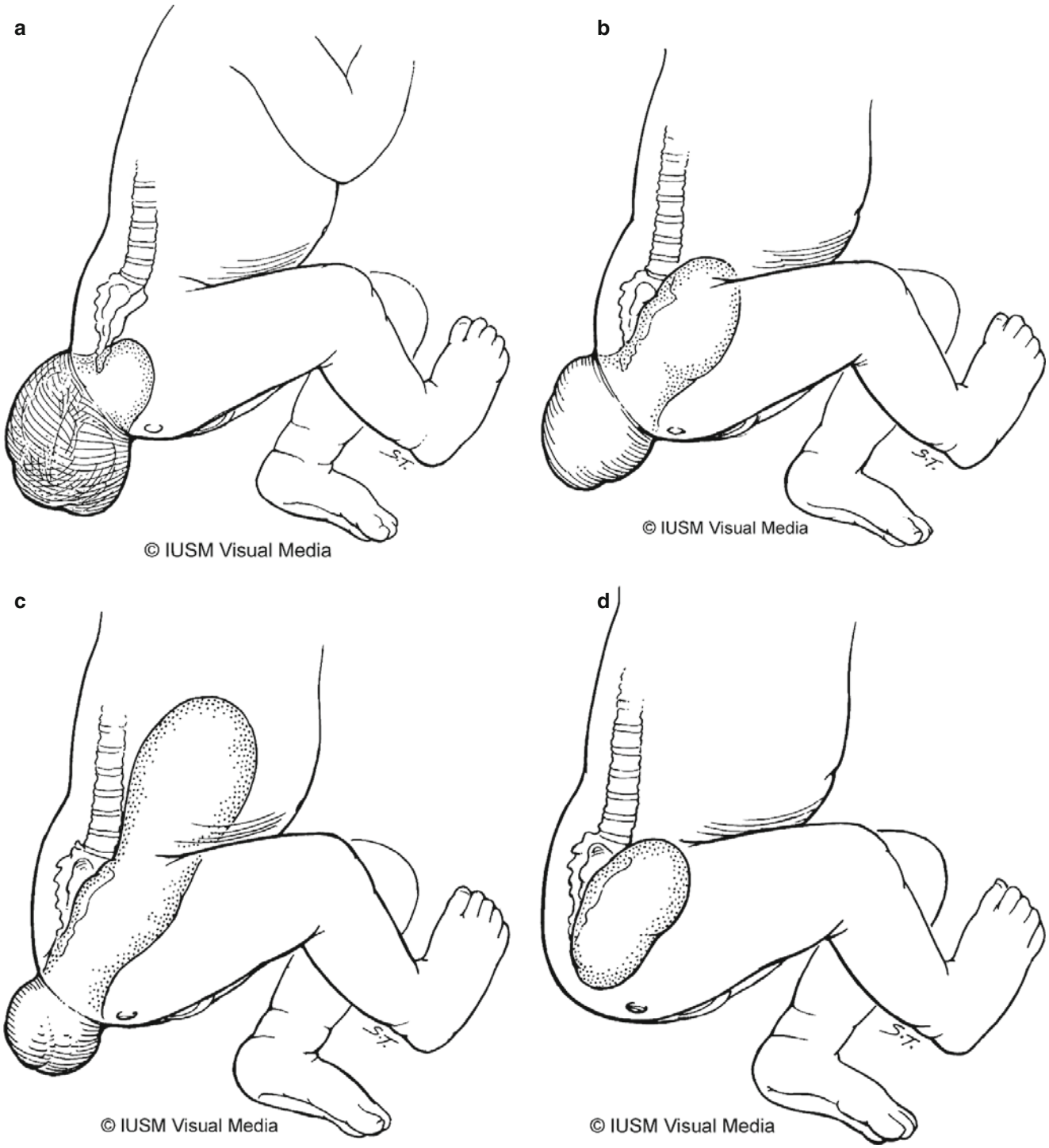

Fig. 19.4 Classification of sacrococcygeal teratomas based on Altman's study. (**a**) Type I (46.7 %) is predominantly external. (**b**) Type II (34.7 %) is external with intrapelvic extension. (**c**) Type III (8.8 %) is visible externally but predominantly pelvic and abdominal. (**d**) Type IV (9.8 %) is entirely presacral

and sacral defects [3]. Currarino et al. [17] suggested that adhesions between endoderm and neural ectoderm form, causing a split notochord resulting in this association of defects.

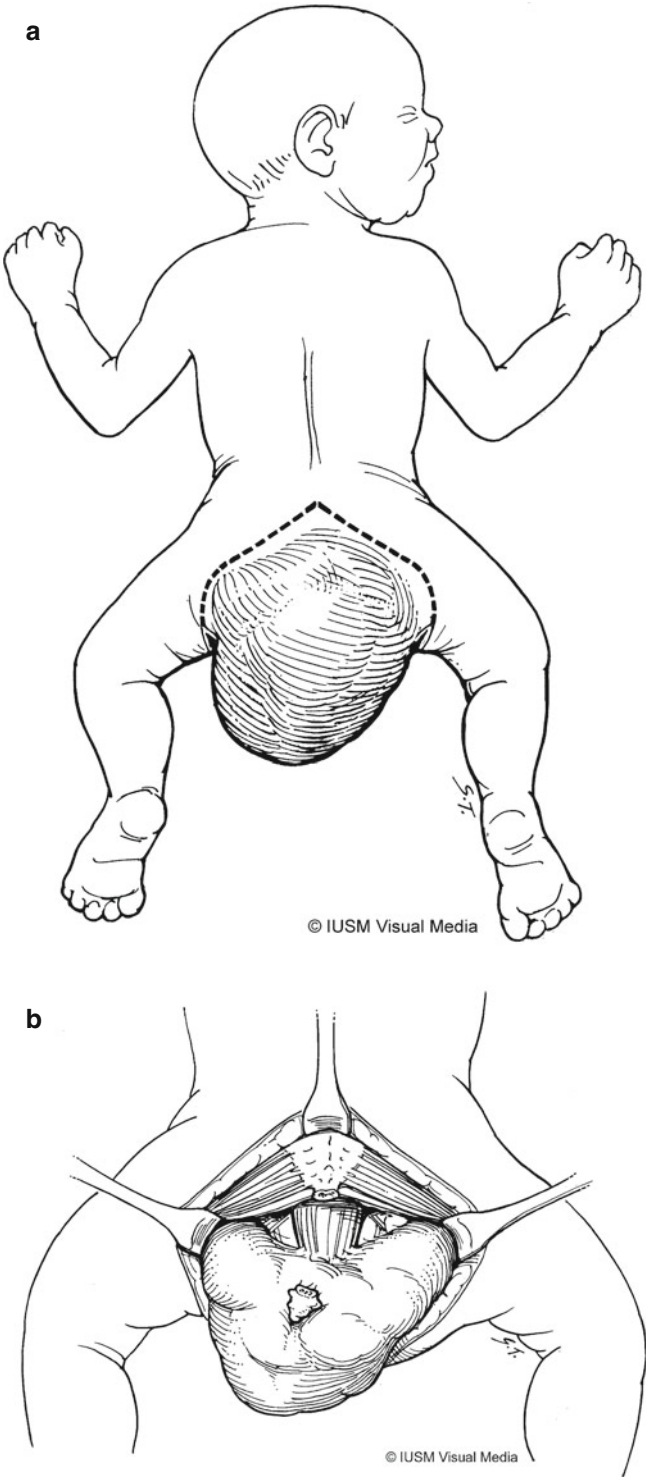

Fig. 19.5 Operative excision of (**a**): Sacrococcygeal teratoma in a neonate with an inverted "V" incision. (**b**) The tumor along with the coccyx is excised, taking care to avoid injury to the rectum

Prior to surgical resection of a neonatal tumor, the degree of pelvic and abdominal extension should be determined by ultrasound, CT, or MRI. In cases with significant pelvic extension, an abdominal approach (open or laparoscopic) may be needed to mobilize the pelvic component and divide the middle sacral artery. In addition, in high vascular flow lesions it may be useful to gain control of the distal aorta in order to allow temporary vascular occlusion if bleeding is encountered [37]. The lesion can be excised with the child in the prone position (Fig. 19.5). Excision of the coccyx is an essential part of the procedure as Gross et al. [31] initially reported a 37 % recurrence rate when the coccyx was not removed. Closure of the wound can be accomplished by bringing the apex of the anterior inverted "V" incision to the open of the posterior portion as demonstrated in Fig. 19.6. This brings the rectum back to a more posterior location from its original displaced position. Sometimes this closure leaves unsightly protruding tissue laterally, and on alternative closure reported by Fishman et al. [24] involved closure bringing the ventral portion of the lateral flaps to a more central posterior.

Most neonates have mature or immature teratomas and are managed with observation during the first few days of life. Operative resection is usually carried out in the first week of life. Recurrent tumors are noted in 4–21 % of these cases [8, 51] and 50 % of these are malignant. The development of malignancy may be the result of a pathologic sampling error which missed an initial malignancy or incomplete resection that leaves a small malignant focus. Follow-up should include serial serum AFP levels to ensure return to normal by 9 months of age as well as follow-up serum AFP levels and rectal examination every 3 months to 3 years of age.

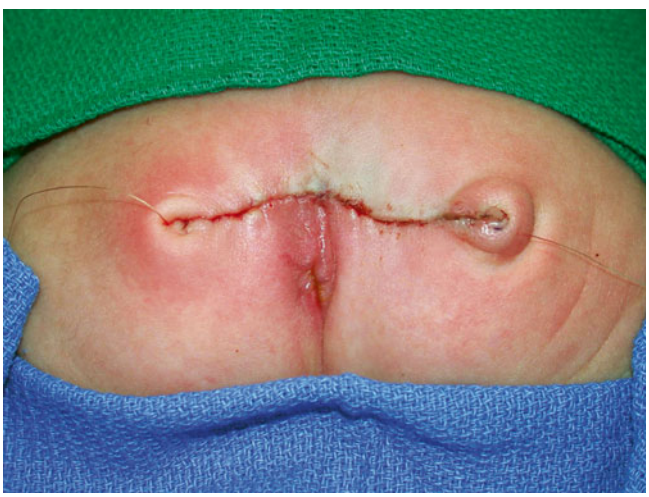

Fig. 19.6 Transverse closure (**a**) and (**b**) use of closure which brings excessive ventral tissue to a more central location leaving two right angled buttock scars

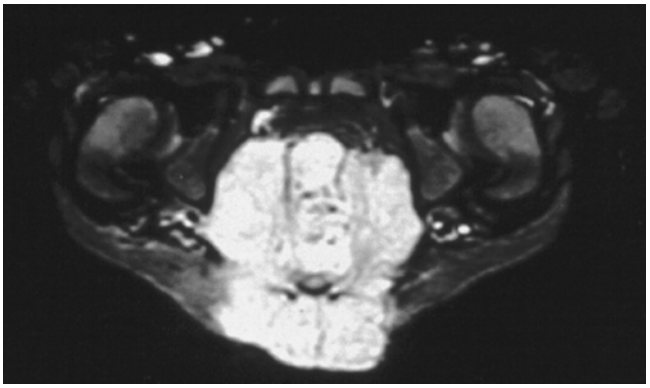

Fig. 19.7 Appearance of a large unresectable sacrococcygeal yolk sac tumor treated successfully with biopsy, neoadjuvant chemotherapy and subsequent excision

Older infants and children with primarily malignant presacral tumors can be approached in a similar fashion; however, due to extensive abdominal extension, initial resection is often not possible and biopsy and neoadjuvant chemotherapy with cisplatin, etoposide, and bleomycin are utilized (Fig. 19.7). The introduction of platinum-based therapy in the late 1970s has significantly improved the survival of these malignant tumors. Schropp et al. [57] noted an 11 % survival prior to 1978 and 86 % after 1978 with the use of platinum-containing therapy.

The POG/CCG intergroup study of 74 infants with malignant sacrococcygeal tumors comprised 62 girls and 12 boys with a median age of 21 months [52]. Fifty-nine percent had metastatic disease at diagnosis and the initial procedure was biopsy in 45 and resection in 29. All patients received chemotherapy with etoposide, bleomycin, and either standard or high-dose cisplatin. The overall 4-year event-free survival (EFS) and survival were 84 ± 6 % and 90 ± 4 %, respectively. There was no difference in survival based on presence or absence of metastases, initial or delayed resection, or dose of cisplatin. This study confirmed the effective role of neoadjuvant chemotherapy in initially unresectable cases. Long-term follow-up of the newborn and older children is necessary as neuropathic bladder or bowel abnormalities have been reported in 11–41 % of patients [28, 42, 43]. A recent long-term study observed that 9 % of the patients had involuntary bowel movements, 13 % soiling, 16 % constipation, and that 30 % lacked urinary control, all factors correlating adversely with quality of life [21].

Abdominal/Retroperitoneal

Abdominal and retroperitoneal sites account for approximately 4 % of pediatric germ cell tumors [11]. Most tumors at these sites are benign with malignancy occurring in 15 % of cases. The POG/CCG study included 25 children with 80 % less than 5 years of age [11]. The most common symptoms were abdominal or back pain followed by fever, weight loss, constipation, or an acute abdomen. Elevated AFP was the most common marker abnormality as yolk sac tumor was identified in 19, and in four with components of choriocarcinoma, beta HCG was elevated. Most had advanced unresectable disease and 17 had metastatic disease at diagnosis.

Although the majority of patients could only undergo debulking or biopsy, the postchemotherapy outcome was excellent. Four with initial biopsy only had no tumor residual tumor after chemotherapy and 13, with subsequent surgery, had complete resection. The 6-year EFS was 82.8 ± 10.9 % and overall survival 87.6 ± 9.3 %. This is compared to a mortality of over 80 % prior to the advent of cisplatin-based chemotherapy [30]. Based on this study primary excision should be performed if a complete resection can be accomplished without removing normal structures. Otherwise, initial biopsy with neoadjuvant chemotherapy will usually allow a secondary resection.

An interesting subgroup of these tumors is the infantile choriocarcinoma syndrome in which infants present in the first 7 months of life with anemia and hepatomegaly. Tumor production of ß-HCG in these infants can lead to precocious puberty. These tumors are thought to arise as primary placental tumors with metastasis to the fetal liver. The mother must also be followed as metastatic disease has occurred in the mother [11].

Growing Teratoma

A rare but important clinical scenario involves the enlargement of benign elements of a tumor, mature or immature teratomas referred to as the "growing treatoma syndrome" [39]. The child in Fig. 19.8a had a extensive tumor and biopsy demonstrated immature teratoma and the serum AFP was normal for the age of the child. The child received chemotherapy for a presumed germ cell malignancy and unfortunately the benign elements continued to grow (Fig. 19.8b) making subsequent resection more difficult than at initial presentation. Initial resection and avoidance of chemotherapy in lack of definite malignancy is important in the management of germ cell tumors.

Mediastinal

The mediastinal site for germ cell tumors accounts for approximately 6–18 % of all pediatric mediastinal tumors

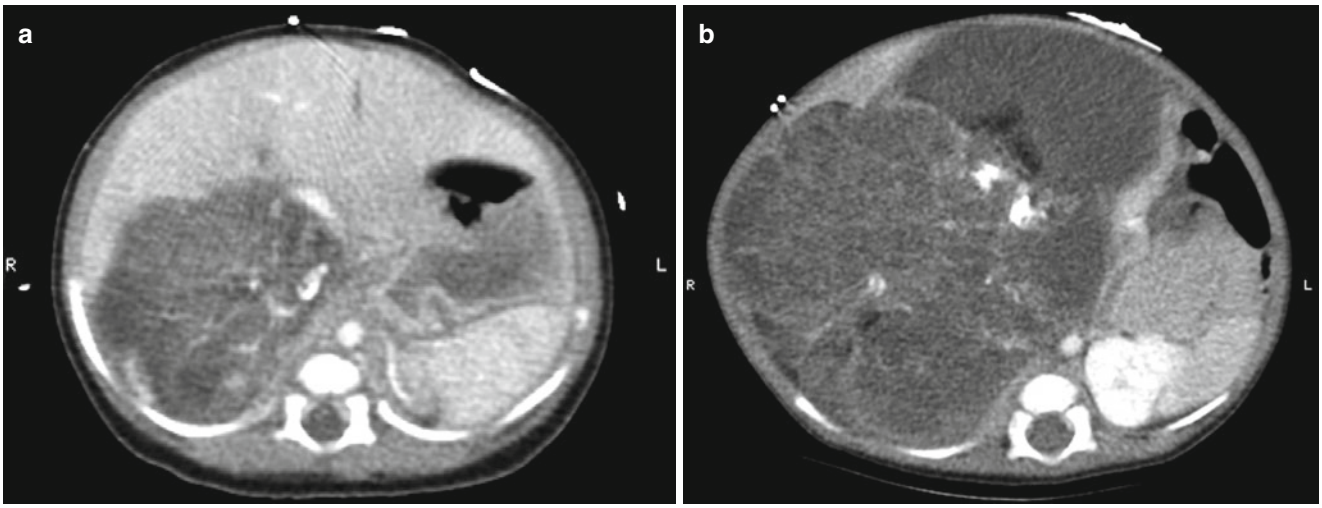

Fig. 19.8 Growing Teratoma. (**a**) A 4-weeks old child with a large tumor. Biopsy demonstrated immature teratoma. (**b**) Three months later, significant tumor growth

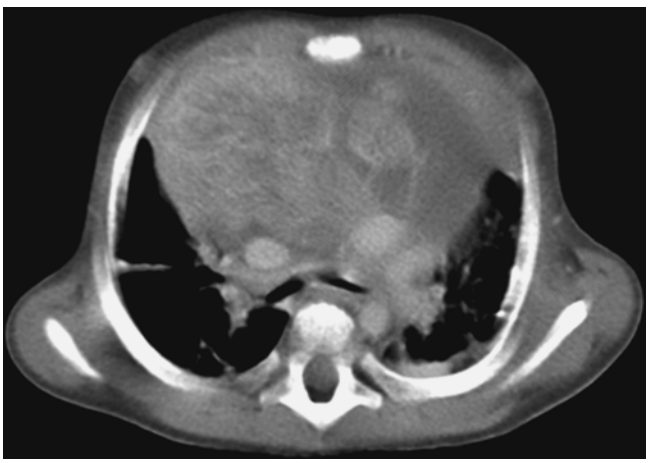

Fig. 19.9 CT scan of a large mediastinal germ cell tumor with airway compromise

and of these 86 % are benign [9, 30]. Many of these tumors achieve a large size prior to detection probably due to the lack of confining boundaries (Fig. 19.9). The clinical presentation is usually respiratory distress in younger children whereas older patients present with chest pain, precocious puberty or facial fullness reflective of venous obstruction. Malignant mediastinal germ cell tumors are more commonly in males and an association with Klinefelter's syndrome has been noted. The presence of hypogonadism, relative increase in leg length compared with overall stature and mild developmental delay should lead to the consideration of Klinefelter's syndrome [10, 39]. Mediastinal germ cell tumors are also associated with hematologic malignancies including leukemia and erythrophagocytic syndrome.

There were 36 patients in the POG/CCG study [10]. Tumor marker elevations included 29 with increased serum AFP and 16 with elevated serum ß-hCG. The histology was more heterogeneous than other extragonadal sites with yolk sac tumor found among the children less than 5 years whereas older patients had yolk sac tumors as well as germinoma, choriocarcinoma, and mixed tumors.

Fourteen children underwent resection at diagnosis followed by chemotherapy with 12 survivors. Eighteen children underwent biopsy followed by neoadjuvant chemotherapy and subsequent resection with 13 survivors.

Biopsy technique options include image-guided or open technique using the Chamberlain anterior approach or standard thoracotomy. Eight of ten image-guided biopsies in the POG/CCG study were successful. In this study both resection at diagnosis and post chemotherapy was frequently difficult due to adherence to the thymus, pericardium, superior vena cava, innominate vein, subclavian artery, aorta, vagus and phrenic nerves, as well as lung. Occasional sacrifice of these structures is needed to accomplish a complete resection. Resections were accomplished most frequently (20/31) by median sternotomy followed by thoracotomy (11/31).

Anterior mediastinal tumors pose unique anesthetic risks and careful preoperative assessment should be performed to determine the form of anesthetic. There is a risk for cardiopulmonary arrest with induction of anesthesia due to tracheal compression [32, 49]. Greater than 35–50 % tracheal compression is associated with increased morbidity [4, 60]. If significant airway compression is present, a percutaneous image-guided biopsy with local anesthesia with or without sedation may allow confirmation of malignancy and administration of neoad-

juvant chemotherapy to decrease tumor size prior to resection.

The survival on the POG/CCG study was 71 ± 10 %, which is lower than the other extragonadal sites, with all deaths occurring in boys over 15 years of age. Interestingly, no death occurred in patients with yolk sac tumors. In some patients with mixed tumors, the benign elements (teratoma) may persist or enlarge as the malignant elements shrink with chemotherapy, the "Growing Teratoma Syndrome." In the POG/CCG study over half of the postchemotherapy specimens contained mature and immature teratoma [10]. In view of the high rate of viable germ cell tumors, complete resection of any residual tumor present after completion of chemotherapy should be performed.

Genital

Primary germ cell tumors of the genital region are rare, primarily occurring in girls less than 3 years of age [16, 47]. Presenting signs and symptoms include most commonly vaginal bleeding followed by a pelvic mass or urinary obstruction (Fig. 19.10) [53]. This lesion can be confused with the botryoides type of embryonal rhabdomyosarcoma. Older reports utilizing surgery and VAC (vincristine, dactinomycin, and cyclophosphamide) reported 67 % survival [16] whereas the POG/CCG report of 13 children (12 vaginal, 1 penile) utilizing a neoadjuvant approach with etoposide, bleomycin and either standard or high-dose cisplatin reported a 4-year survival of 91.7 % [53]. Genital preservation was possible in 11 of 12 survivors. In view of this data, initial biopsy, neoadjuvant therapy and postchemotherapy evaluation usually demonstrates significant shrinkage. In the POG/CCG study, 9 of 11 treated with neoadjuvant therapy had residual masses including one with progression, one had residual yolk sac tumor, and seven with necrotic nonviable residual [53].

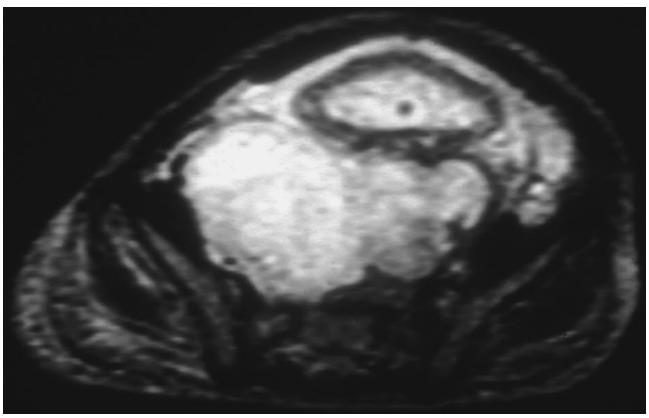

Fig. 19.10 CT scan demonstrating a pelvic mass associated with a vaginal germ cell tumor

Cervicofacial Teratoma

Nearly all of these lesions present in the neonatal period, one-third with airway obstruction, and most are benign mature or immature teratomas [5]. Large fetal tumors can cause hydrops and fetal demise whereas some have been salvaged with fetal resection. Fetal resection should be considered if hydrops develops prior to 28 weeks gestation [33]. An EXIT procedure with the potential for intubation, tracheostomy or resection while on placental support should be considered for those without hydrops.

Testes

Most boys present with a testicular mass allowing preoperative evaluation; however, some present with an acute scrotum with signs and symptoms of torsion, hydrocele, or hernia leading to intraoperative diagnosis and evaluation. A scrotal ultrasound may demonstrate a solitary mass in a child presenting with a testicular swelling or mass. If a discrete mass is noted along with normal-appearing testes, this may represent a testicular teratoma and enucleation is considered adequate therapy. Although the incidence of malignancy in prepubertal testes masses is not known, one report observed that 74 % were benign with 48 % teratomas and only 5 % yolk sac tumors [59]. These benign lesions would not be associated with an elevated serum AFP level. Diagnostic work-up should include determination of serum markers and an abdominal and chest CT. The initial diagnostic procedure is a transinguinal exploration with occlusion of the spermatic vessels at the internal ring prior to mobilization of the testes. If a solitary mass is noted, it should be excised with ligation of the entire spermatic cord at the level of the internal ring. Children with no other evidence of disease are followed with serum AFP levels and if these decline to normal appropriately, are considered Stage I (Table 19.3). The role of observation alone in the management of Stage I testes was confirmed in the CCG/POG study of 63 Stage I tumors [58]. This study excluded boys older than 10 years and therefore consisted entirely of patients with yolk sac tumors. The 6-year survival rate was 100 % and EFS 78.5 % ± 7.0 %. Most recurrences occurred within 6 months and all were salvaged with chemotherapy. Of interest, transcrotal violation was associated with a significantly increased rate of recurrence. Most (85 %) of children will present with Stage I disease compared to only 35 % of adults [23, 34]. The predominant histology in these prepubertal children is yolk sac tumor and thus serum AFP levels are elevated.

Table 19.3 Children's Oncology Group staging system for testes tumors

Stage I	Limited to testis (testes), completely resected by high inguinal orchiectomy; no clinical, radiographic, or histologic evidence of disease beyond testes. Patients with normal or unknown tumor markers at diagnosis must have a negative ipsilateral retroperitoneal node sampling to confirm Stage I disease if radiographic studies demonstrate lymph nodes >2 cm
Stage II	Transscrotal orchiectomy; microscopic disease in scrotum or high in spermatic cord (≤5 cm from proximal end)
Stage III	Retroperitoneal lymph node involvement, but no visceral or extra-abdominal involvement. Lymph nodes >4 cm by CT or >2 cm and <4 cm with biopsy proof
Stage IV	Distant metastases, including liver

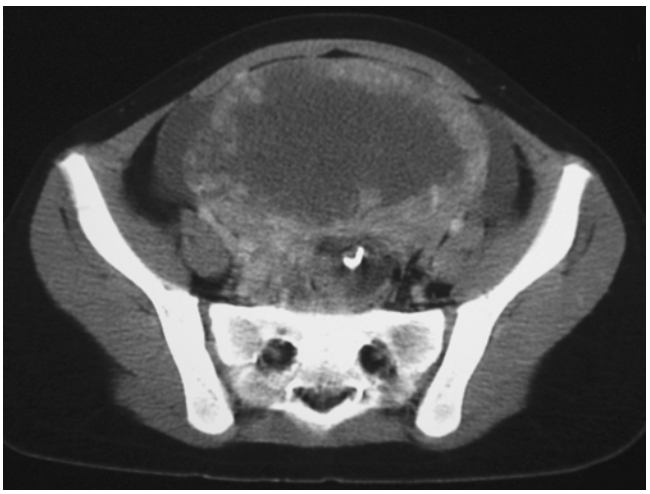

Fig. 19.11 CT scan of a large malignant ovarian mixed yolk sac tumor and teratoma with solid and cystic components

If preoperative evaluation reveals retroperitoneal disease (Stage III) or pulmonary metastases (Stage IV), an initial inguinal orchiectomy is still performed followed by chemotherapy (Table 19.2). Residual disease should be excised and if viable tumor is present, additional chemotherapy administered. The survival of Stage II tumors treated with postoperative chemotherapy although small (n = 17) was 100 % [54]. The survival of Stage III and IV patients treated with chemotherapy was still very high with a 6-year overall survival and EFS of 100 and 94.1 % for Stage III and 90.6 and 88.3 % for Stage IV [19].

Ovary

Ovarian tumors are one of the more common germ cell tumors in female children and adolescents. Of all ovarian masses, most (80 %) are benign (epithelial cysts, teratomas, immature teratomas) often with predominantly cystic components (Fig. 19.11). Symptoms include pain, distention, or the presence of a mass. Less common presentations include acute abdomen secondary to torsion or tumor rupture and precocious puberty.

Although a low risk of malignancy (2 %) is quoted in adult series [15, 46, 62], caution must be taken as many

Table 19.4 Children's Oncology Group operative guideline for ovary tumors

1. Collect ascites or peritoneal washings for cytology
2. Examine entire peritoneal surface and liver; excise suspicious lesions
3. Unilateral oophorectomy
4. Wedge biopsy of contralateral ovary, only if suspicious
5. Omental inspection and excision if adherent or contains nodules
6. Biopsy of suspicious or enlarged retoperitoneal or pelvic lymph nodes

tumors have solid and cystic components. Billmire et al. [12] reported the CCG/POG experience with 131 children and adolescent girls which is the largest series in the era of modern chemotherapy. In this report 57 % of the tumors had cystic components, thus highlighting the difficulty of determining malignancy preoperatively. The mean age was 11.9 years. In addition, the histology showed mixed tumors in most, with teratoma coexisting with malignant elements in 60 girls.

The 6-year EFS and survival by Stage in the POG/CCG study were: Stage I 95, 95.1 %; Stage II 87.5, 93.8 %; Stage III 96.6, 97.3 %; and Stage IV 86.7, 93.3 %. In view of the excellent survival of Stage I tumors, the excellent survival of Stage I girls with microscopic yolk sac tumors treated with surgery alone [18] as well as two series of Stage I girls treated with surgery alone with a 67 % EFS and 97.4 % OS [6, 29], the recently completed COG study treated Stage I ovarian tumors with observation. Unfortunately the low risk arm was closed early due to a greater than anticipated rate of recurrence for Stage I ovarian tumors (<70 % EFS) [27]. The OS was still 95 % due to successful salvage with chemotherapy in most of the girls. The current staging procedure is listed in Table 19.4 and the staging system in Table 19.5. The current recommended therapy is surgery alone for Stage I ovarian tumors.

Tumors with extensive involvement of other structures may be initially managed with biopsy and postchemotherapy excision. Radical removal of the uterus is not recommended. The current recommendation for bilateral tumors is to attempt ovarian preservation if possible on the least involved side, particularly if a plane of demarcation exists between the tumor and normal ovarian tissue. These findings and conclusions are consistent with other germ cell tumors

Table 19.5 Children's Oncology Group staging system for ovary tumors

Stage I	Limited to ovary (peritoneal evaluation should be negative). No clinical, radiographic, or histologic evidence of disease beyond the ovaries
Stage II	Microscopic residual; peritoneal evaluation negative
Stage III	Lymph node involvement; gross residual or biopsy only; contiguous visceral involvement (omentum, instestine, bladder); peritoneal evaluation positive for malignancy
Stage IV	Distant metastases, including liver

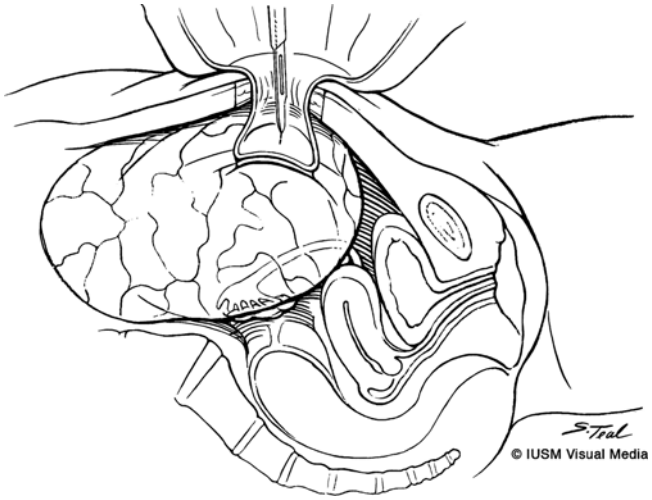

Fig. 19.12 Illustration of technique involving fixation of a plastic sheet to a large benign cystic ovarian tumor with decompression without spill

reflective of effective chemotherapy to increase the success of conservative surgery.

Many adolescents present with primarily cystic lesions and most of these are benign. Laparoscopy has been widely utilized in the management of ovarian lesions in childhood, adolescents, and adults. The main controversy surrounds the ability to perform a cancer type procedure in cases where the exact tumor histology (benign vs. malignant) cannot be determined preoperatively. If the lesion is primarily solid or if the serum markers are elevated, an open procedure is indicated. If the serum markers are normal and the lesion is primarily cystic, particularly if there is a very large cystic component, a less invasive technique may be considered; however, avoidance of tumor spill must be assured. One minimal access procedure involves laparoscopic excision of the tumor from its attachments, placement in a retrieval bag, and delivering the neck of the bag outside of the abdominal cavity through the umbilical opening. The cyst is then punctured, the fluid removed and the cystic lesion, contained within the bag removed without spill and sent for pathologic examination. In the second technique, useful for giant cysts, the cyst is exposed through an approximate 5-cm incision, a bag glued to the cyst with cyanoacrylate adhesive as described by Shozu et al. [61]. The cyst is then incised by cutting through the center of the bag-cyst interface, the fluid removed without spill, and the decompressed cyst then removed from the abdominal cavity (Fig. 19.12). The remainder of the standard procedure, peritoneal/ascitic fluid sampling, omental inspection, and excision and evaluation of the peritoneal surface can be performed laparoscopically. The only aspect which cannot be accomplished is palpation of retroperitoneal nodes, although depending on the size and habitus of the child or adolescent, a small incision may allow this to be accomplished.

Conclusion

The survival for pediatric germ cell tumors has dramatically improved since the introduction of platinum-based therapy in the 1970s. The survival for Stage I gonadal tumors and all immature teratomas at any site is excellent and these are managed by surgical excision and subsequent observation. The survival for intermediate-risk tumors including Stage II-IV testes, Stage II-III ovarian and Stage I-II extragonadal is also very high and reductions in therapy have been possible based on cooperative pediatric trials conducted in the 1990s. The survival for high-risk tumors, Stage III-IV extragonadal and Stage IV ovarian is lower and these have been managed with longer courses of chemotherapy. The current treatment as outlined in Table 19.2 is reflective of a risk based approach.

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