Diagnosis	CTR 1954-1968	
	Male	Female
Leukaemia	252	212
Lymphoma		
(Hodgkin's and non-Hodgkin's)	66	30
Medulloblastoma	56	21
Neuroblastoma	67	35
Connective tissue	108	79
Presacral teratoma	3	11

Table II

Childhood cancer forms a relatively small part of the total picture of human neoplasia but studies in this field may throw light on a number of problems in oncology.

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Teratomas and yolk-sac tumours

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A teratoma may be defined as a tumour composed of multiple tissues foreign to the part of the body in which the tumour arises. Over the years many theories have been put forward to explain the origin of these neoplasms. It was customary at one time to regard them as representing the frustrated development of a conjoined twin. Willis (1967), following Askenazy (1907), concluded that they arise from totipotential cells which become scattered throughout the various parts of the body during embryonic life, normally remaining dormant but capable of further growth and differentiation if suitably stimulated. The theory commended in this paper is that arising largely from the work of Pierce and Abell (1970) and Teilum (1971) and accepted as a working hypothesis by the British Testicular Tumour Panel (Pugh, 1976), namely, that teratomas arise from germ cells, these being the only truly totipotential cells in the body.

The germ cells first appear in the embryo in the wall of the yolk sac whence they migrate (fig 1) around the hinder end of the primitive gut to the genital ridge on the posterior abdominal wall. Here they congregate and are absorbed into the developing gonad which later descends to the pelvis or scrotum. It is suggested that during this migration some germ cells may get left behind on the journey or may stray too far and come to rest at various sites along the dorsal wall of the embryo near the mid-line (fig 2). If these cells do not degenerate but remain viable they may give rise to tumours in precisely these situations, that is, the retroperitoneum, sacral region, mediastinum, and pineal region.

If one accepts Teilum's contention (fig 3) that seminoma, dysgerminoma, teratoma, yolk-sac tumour, and choriocarcinoma are all tumours derived from germ cells then it follows that any of these tumours, alone or in combination, could arise not only in the gonads but also at any of the sites mentioned above where stray germ cells may come to rest. This accords well with observation and experience as the examples given in this paper will help to show.

Teratoma of the testis

The Testicular Tumour Panel classified teratomas of

3 mm EMBRYO

Fig 1 Diagrammatic representation of the origin and migration of the germ cells.

Fig 2 Aberrant migration of germ cells could account for the occurrence of tumours of germ-cell origin in extragonadal situations.

Fig 3 Tumours of germ-cell origin (modified from Teilmann).

the testis into four types: differentiated (TD) when all the constituent tissues are fully differentiated and organoid; malignant undifferentiated (MTU) when no organoid differentiation can be found; malignant

intermediate (MTI) when there is a mixture of undifferentiated and organoid tissue; and malignant trophoblastic (MTT) when a substantial amount of undoubted trophoblastic tissue is present.

Of 28 testicular teratomas in boys up to the age of 15 submitted to the Panel, three-quarters (21) were of the fully differentiated type (TD) and behaved in an entirely benign manner (Brown, 1976). To the naked eye these were circumscribed solid or cystic tumours in the body of the testis, often with fibrous and cartilaginous areas. Histologically they are composed of miscellaneous types of epithelium mixed with mesodermal tissues, especially cartilage, and sometimes nervous tissue and other elements, all of fully differentiated and mature appearance. Such completely differentiated teratomas of the testis occur almost exclusively in children, being extremely rare in adults.

Six of the teratomas were classified as of intermediate type on the basis of areas of poor differentiation of either epithelial or mesodermal tissues. In this connection it should be appreciated that, in young patients, lack of full differentiation of the tissues does not always indicate malignancy but may be merely a manifestation of immaturity. It is often very difficult to distinguish between immature and malignant tissue, especially where neural or regenerative elements are concerned, but it is important to attempt to do so before expressing a view on the probable behaviour of the tumour. Of these boys with teratomas of intermediate type, two, both aged 14 years, died with metastases within a year of operation despite radiotherapy, while three others remain alive and well 10 years, 11 years, and one year after simple orchidectomy. One teratoma was classified as undifferentiated (MTU), but this patient was aged 15, on the verge of adulthood. All the patients with differentiated teratoma were 14 years of age or less at the time of orchidectomy and it would appear probable that up to about the age of 14 most testicular teratomas are cured by orchidectomy alone but that after this age the more malignant tumours begin to appear and need more drastic treatment. No trophoblastic testicular teratoma was encountered in children by the Panel and its occurrence in young patients must be extremely rare. None of the teratomas in children was associated with seminoma, but one contained large amounts of yolk-sac tumour; this tumour proved fatal after a year but it could well be that the bad outcome was a feature of yolk-sac tumour rather than teratoma.

Teratoma of the ovary

Ovarian teratomas in children may be either solid or cystic. Virtually all the cystic ones are benign.

(Langley, 1968). The solid teratoma may be either benign or malignant and sometimes it grows to a very large size. The histological structure is similar to that of teratoma of the testis and it can be classified on the same basis. In examining solid teratomas it is essential to take numerous blocks from all parts of the tumour to search for malignant areas, and the same problems arise as in the testis of distinguishing between malignant and immature tissue. Malignant ovarian teratoma can prove fatal in a few months. The teratoma may on occasions be combined with dysgerminoma or yolk-sac tumour in the same tumour mass.

Sacroccocygeal teratoma

This tumour is usually congenital and presents at birth as a large skin-covered solid and cystic pendulous tumour projecting from the lower part of the back of the infant. It may ulcerate, give rise to severe haemorrhage or even interfere with delivery. The tumour often extends through or around the sacrum up into the retroperitoneal region and may obstruct the ureters or displace or surround other pelvic structures. Histologically it shows the usual teratomatous structure with or without evidence of malignancy and sometimes contains foci of yolk-sac tumour. It is rarely susceptible to surgical removal owing to the involvement of neighbouring structures, and the infant usually dies in a short time.

Teratomas may also arise in the sacral region in older children but these tumours tend to be presacral in position, presenting as pelvic tumours. Any such tumours removed by the surgeon should be subjected to a very careful search for malignant tissues or areas of yolk-sac tumour.

Other extragonadal teratomas

Teratoma, benign or malignant, can arise in a number of other situations, most of which are in or near the mid-line of the body and near the spinal axis. It may be retroperitoneal, mediastinal, cervical or even intracranial. It is preferable to describe it in these regional terms rather than as 'teratoma of the bladder' or 'teratoma of the thymus' and so on, since, although an individual organ may be involved, it is improbable that the tumour actually arises in it.

Diagnosis of teratoma

In summary, the histological diagnosis of teratoma is usually easy. Distinction from a hamartoma should not present a problem since a hamartoma does not contain tissues foreign to the part of the body in

which it arises. The decision as to whether or not a given teratoma shows evidence of malignancy may, however, be exceedingly difficult.

Yolk-sac tumour

In recent years it has gradually become clear that the tumour of the testis of boys, previously known as orchioblastoma, infantile adenocarcinoma or juvenile embryonal carcinoma, has the same histological structure as the ovarian tumour of young girls which Teilum (1971) had named endodermal sinus tumour and as other tumours of the mediastinal region which had been called mesoblastoma vitellinum. If the histogenetic theory outlined at the beginning of this paper (fig 3) is accepted and these tumours are regarded as originating in germ cells with differentiation towards extra-embryonic (yolk-sac) structures rather than embryonic ones, then it would seem logical to discard most or all of the above synonyms and refer to the tumour wherever it occurs as 'yolk-sac tumour'.

The histological appearance (figs 4 and 5) of yolk-sac tumours from all sites is that of an adenocarcinoma with papillary, solid, and cystic areas and usually mucus-secreting. The cells mostly show a clear cytoplasm and, in acinar or cystic areas, the part of the cell containing the nucleus often tends to bulge inwards towards the lumen. Prominent perivascular formations or 'mantles' of cells are often seen around blood vessels. These glomeruloid structures or Schiller-Duval bodies are very characteristic when present but may be hard to find, especially in yolk-sac tumours of the testis. The tumour cells may contain hyaline eosinophilic cytoplasmic globules. The stroma is relatively scanty and in the papillary areas consists of delicate fibrovascular stalks.

Yolk-sac tumour of the testis

Synonyms: Orchioblastoma, embryonal carcinoma of infantile or juvenile type, adenocarcinoma of infant testis, endodermal sinus tumour.

Yolk-sac tumour of the testis usually occurs in very young boys and may be present at birth. In the 53 cases referred to the Testicular Tumour Panel, the age of the patient ranged from less than 1 year to 5 years with a mean age of presentation of 17 months. The tumour presents as a rapidly growing painless testicular swelling and, when removed, presents as an unencapsulated, firm or soft yellow or white mass, sometimes with cystic areas, replacing most or all of the testis. The histological structure is as described above. In all but one of the Panel's examples from children the tumour existed in pure form unassociated with seminoma or teratoma; the exception was

Fig 4 Yolk-sac tumour of testis. Adenocarcinomatous pattern with microcystic areas. Mucus-secreting.

Fig 5 Yolk-sac tumour of ovary. Solid and acinar patterns. Note typical sleeve or 'mantle' of cells around a blood vessel.

the one forming part of a teratoma mentioned above. Testicular yolk-sac tumours in this pure form are exceedingly rarely encountered outside childhood. When they occur in adults they almost always are combined with teratoma. Although the tumour grows rapidly and tends to metastasize to lymph nodes and distant sites, the prognosis is not as bad as might be expected. About half the Panel's cases were apparently cured by simple orchidectomy, and a three-year survival rate of about 60% can be expected. It is possible that more intensive treatment might lead to better results. The histological appearances are of little help in predicting the outcome of a case which seems to depend much more on age and length of history. The younger the patient and the shorter the history, the better is the prognosis.

Yolk-sac tumour of the ovary

Synonym: Endodermal sinus tumour.

Yolk-sac tumours of the ovary are much more malignant than those of the testis, and in the recorded cases almost all the children have died. This may be due at least partly to the tumour not being discovered in the ovary until a relatively late stage, whereas a testicular swelling soon becomes obvious.

An exception to this was the case of a girl aged 9 with six weeks' history of an abdominal mass. Laparotomy revealed a solid tumour, 13 × 10 × 8 cm, in the left ovary with metastatic nodules on the colon and bladder. All the tumour was excised and proved histologically (fig 5) to be yolk-sac (endodermal sinus) tumour. Aggressive therapy was begun and she remains well and apparently free from tumour three years later.

Yolk-sac tumours of the ovary may occur in pure form or may be combined with dysgerminoma or teratoma.

Extragenital yolk-sac tumour

Yolk-sac tumour in pure form or combined with teratoma occurs in all the sites already listed where tumours of germ-cell origin can arise. Two personal examples are:

(1) a girl aged 2 years with a few months' history of a pelvic mass and constipation. Laparotomy

revealed an inoperable tumour mass filling the pelvis and surrounding the rectum. Biopsy showed yolk-sac tumour combined with teratomatous elements. Intensive therapy has been started but it is too early to assess the outcome;

(2) a girl aged 7 years with a cough of a few weeks' duration. A chest x-ray showed a mass at the hilum of the lung which thoracotomy revealed to be a vascular inoperable mass. Biopsy showed yolk-sac tumour in pure form, presumably having arisen in the mediastinum.

Diagnosis of yolk-sac tumour

The histological diagnosis of yolk-sac tumour, like that of many rare neoplasms, depends very much on the pathologist having heard of the tumour, being aware of the various sites in which it may arise, and thinking of it when presented with the section. Since it is predominantly a tumour of childhood the thought should occur not only in relation to gonadal tumours and teratomas but whenever an unexpected adenocarcinomatous tumour presents itself for diagnosis from an unusual site in a young person.

There is no problem in predicting the behaviour of the tumour as all yolk-sac tumours should be regarded as malignant and capable of metastasizing.

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