



# TERATOMAS

Rupert A. Willis, D.Sc., M.D., F.R.C.P.

ARMED FORCES INSTITUTE OF PATHOLOGY

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# ATLAS OF TUMOR PATHOLOGY

Section III—Fascicle 9

## TERATOMAS

by

Rupert A. Willis  
D.Sc., M.D., F.R.C.P.

Professor of Pathology, University of Leeds Medical School  
Leeds, England

Formerly Pathologist to the Alfred Hospital, Consultant Pathologist to the Austin Hospital for Chronic Diseases, and Lecturer on the Pathology of Tumours in the University of Melbourne, Australia; Sir William H. Collins Professor of Human and Comparative Pathology, Royal College of Surgeons, London; and Pathologist to the Royal Cancer Hospital, London.

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# ATLAS OF TUMOR PATHOLOGY

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**Rupert A. Willis**

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## TERATOMAS

### NOMENCLATURE

**SYNONYMS AND RELATED TERMS:** Teratoma (Gr. and Lat.); bidermoma; cholesteatoma of ovary; compound ovarian tumor; dermoid; dermoid cyst; dysembryoma; embryoma; epignathus; "fetus in fetu"; hairy cyst; mixed cyst; "mixed teratoid tumor"; monodermoma; "parasitic fetus"; teratoblastoma; teratoid tumor; tridermoma. A teratoma may mistakenly be called a tumor of the tissue that predominates in its structure (for example, ovarian goiter for a teratoma of the ovary). For the synonyms of Malignant Teratomas see that section.

A teratoma is a true tumor or neoplasm composed of multiple tissues foreign to the part in which it arises. Teratoma is the most suitable name for this class of tumor; its literal meaning—"a malformation which is also a true tumor"—is very appropriate. Particular tumors can then be designated benign teratoma or malignant teratoma according to their structure or behavior. This is the simplest terminology and is all that is necessary.

The names teratoblastoma and teratoid tumor have no advantages over teratoma and are clumsier. Teratocarcinoma, now a prevalent substitute for "malignant teratoma containing epithelial elements," is an unnecessary and unsatisfactory term: it may be supposed to imply carcinomatous change in the epithelial components of the teratoma, whereas in most teratomas malignancy is not restricted to any particular component but is a property of the whole tumor (see the discussion of Malignant Teratomas).

Dermoid cyst is a frequently used synonym for benign cystic teratomas of the ovary or other sites. It is an unfortunate term for three reasons: (a) the same name (or epidermoid cyst) is applied—and correctly so—to sequestration skin-lined cysts of the skin, cranial cavity, and other parts, and these cysts are quite unrelated to teratomas; (b) the simplest benign teratoma usually contains several or many other tissues besides skin; and (c) in some so-called "dermoid cysts," the main cyst is lined wholly or mainly, not by skin, but by nervous, respiratory, or alimentary tissue, or by mixtures of these.

Embryoma is a particularly bad name; it affirms that a teratoma represents an embryo, a hypothesis which, though still widely held, is certainly erroneous (see the section on Hypotheses of the Origin of Teratomas).

### DEFINITION

A teratoma is a true tumor; i.e., unlike a simple malformation, it has powers of progressive growth in both benign and malignant forms. Teratomas can and should be distinguished from non-neoplastic malformations of all kinds, whether relatively simple heterotopias of particular tissues or complex malformations such as double monsters or imperfect twins, which lack neoplastic attributes. This distinction needs to be specially emphasized, for many kinds of malformations have been confused with teratomas by one writer or



another. Sequestration dermoid cysts of the skin or cranial cavity, branchial cysts, enterogenous cysts, and many other developmentally misplaced and supernumerary parts and tissues (Albrecht's "hamartomas")—all of these constitute masses of multiple kinds of tissues in the wrong places; but they are non-neoplastic masses, quite unrelated to teratomas, and they will not be considered further here.

Teratomas contain multiple tissues of kinds foreign to the part. In this they differ from mixed tumors peculiar to particular regions. A mammary fibroadenoma, even when its fibromatous component undergoes cartilaginous or bony change, is not a teratoma, because its components are clearly derived from indigenous mammary tissue. A nephroblastoma of the kidney, even when some of its cells become rhabdomyoblastic, is not a teratoma, because it is derived from and composed of embryonic tissue which is specifically renal in nature. This and other mixed embryonic tumors of viscera may show aberrant differentiation of their young plastic tissues, but they do not contain completely exotic tissues, such as respiratory, alimentary, dental, or central nervous tissues, all of which are common in teratomas. So also, the mixed tumors of the endometrium are not teratomas because, although they may develop such tissues as cartilage and muscle, these are not truly exotic, but are derivable by metaplasia from the endometrium itself. The same applies to tumors of other mesenchymal tissues, in which aberrant differentiation has taken place, e.g., bone or cartilage in soft tissue growths; such tumors have sometimes been referred to as "mesenchymomas."

## CLASSIFICATION

Teratomas form a single class of tumors, within which, however, there is a wide range of structure and behavior.

Structural subdivision into cystic and solid types, or into monodermal, bidermal, and tridermal forms, according to the number of "germ-layers" represented in their component tissues, is quite artificial and serves no useful purpose.

Behavioristic subdivision into benign and malignant teratomas is of value and can usually be made on structural grounds; benign teratomas are composed wholly of mature, fully differentiated tissues, while malignant ones almost always contain in addition embryonic tissues of variable degrees of immaturity. However, even this distinction is not clear-cut; a few borderline tumors occur in which, although the tissues appear "benign" and fully differentiated, they are not completely quiescent but are multiplying and may later show accelerated growth and malignant behavior.

## INCIDENCE

**Age.**—Teratomas of various sites are discovered at ages which show plainly that most, if not all, of these growths take origin early in embryonic development. Most sacrococcygeal, retroperitoneal, cervical, intrapericardial, and intracranial teratomas are known to have been present at birth or are discovered in early childhood. Ovarian, testicular, and mediastinal teratomas are discovered at rather later average ages, but still in early adult life, the average ages for these three sites being about 33, 30, and 27 years respectively. Since many of these growths are very large and clearly of long duration when first discovered, and since many cases of congenital teratomas in these situations have been observed, there is little doubt that the gonadal and mediastinal teratomas also arise at an early period of development. The delay in the discovery of the ovarian and mediastinal tumors is readily understood; they are usually benign and slow growing and are so situated that they are unlikely to cause symptoms until they attain considerable size.

The group of malignant testicular teratomas is an apparent exception to the rule that teratomas arise during early development; although situated in an organ where they are likely to be discovered before they have attained great sizes, most of them do not make their clinical appearance until the third decade or later. However, cases do occur in which enlargement of the testis has been noticed since childhood or for many years before the onset of rapid malignant growth; and there is also a well known group of cases in which bulky, highly malignant metastases develop from small unsuspected primary testicular teratomas, the structure of which, at the time they are examined, may appear well differentiated and "benign." It is therefore possible that teratomas of the testis, like those of other sites, take origin during early development, and that, having usually lain dormant during childhood and adolescence, they grow actively as malignant tumors in early adult life. This change of behavior may be connected with the general endocrine or metabolic state of the bearer, or possibly with local injury or inflammation.

**Sex.**—Apart from the genital organs themselves, there are distinct sex differences in the frequency of teratomas of various sites. Retroperitoneal, presacral, and coccygeal teratomas appear to be a little more frequent in females than in males. On the other hand, intracranial teratomas are commoner in males; this applies particularly to pineal teratomas, of which almost all those reported have been in boys. While mediastinal teratomas affect the sexes nearly equally, malignant members of this group are usually in males.

**Site.**—Teratomas arise, in order of frequency, in ovaries, testes, anterior mediastinum, retroperitoneal region, presacral and coccygeal regions, pineal and other intracranial sites, neck, and abdominal viscera other than the

gonads. (See the fascicles corresponding to these anatomic sites.) Ovarian teratomas outnumber all the rest put together. It is a striking fact that, with relatively few exceptions, teratomas occur in tissues which developmentally occupy median, or nearly median, preaxial positions. This fact suggests that their genesis is in some way related to disturbances emanating from the embryonic axis of the body.

Species.—In mammals teratomas have rarely been recorded except in man and the horse. Jackson and Brues described a transplantable ovarian teratoma of the mouse. I have seen two examples of cystic teratomas of the dog's ovary, one of which was benign, and the other, very fully studied by Dr. C. L. Oakley of London, though consisting mainly of well differentiated tissues, produced cellular peritoneal metastases. The Armed Forces Institute of Pathology in Washington has a specimen of malignant ovarian teratoma from a 2-year-old Hereford cow. It is 20 cm. in diameter and weighs 5,700 gm., containing a great variety of both well differentiated and embryonic tissues. Teratomas are quite common in the testes of young horses, in which they may be found unexpectedly following gelding operations (Willis and Rudduck); they are almost all of benign type, composed of fully differentiated tissues, including skin, teeth, respiratory and alimentary epithelia, central nervous tissue, nerves and ganglia, cartilage, bone, adipose tissue, and muscle; and they are sometimes multiple and bilateral (figs. 1, 25).

Avian teratomas have occurred spontaneously in the testes of cocks, and have also been evoked experimentally by injections of zinc or copper salts in these organs (Michalowsky; Falin; Bagg). Further study of this remarkable result is needed before assessing its possible significance for mammalian pathology.

## HYPOTHESES OF THE ORIGIN OF TERATOMAS

This is not the place for a detailed critique of the numerous speculations which have been indulged in regarding the nature and histogenesis of teratomas.\* The most popular of these, expressed in the name "embryoma," has been that these growths represent distorted fetuses, derived either from included twins of the bearers or from parthenogenetic proliferation of the bearers' own germ cells. This view is clearly erroneous for the following reasons: the common sites of teratomas are not the sites of parasitic twins; most teratomas are known to arise during early stages of development when their bearers have no mature germ cells capable of parthenogenesis; proper topographical study of teratomas shows that, unlike most amorphous fetuses,

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\* For other hypotheses on the origin of teratomas, particularly regarding the germ cell and the seminomas, see Fascicle 32, "Tumors of the Male Sex Organs."

they show no signs of a vertebrate axis or of regional relationship of parts, even when they contain highly organized structures, i.e., they are fundamentally non-fetiform; and, finally, the view that they represent embryos completely ignores the important fact that they are true neoplasms, with powers of independent progressive growth which have never been observed in either "amorphi" or parasitic twins.

The genesis of teratomas is still far from understood, but it will be clarified by increasing knowledge of the chemistry of early embryonic growth, the chemistry of the "organizers" or growth hormones which determine the orderly sequences of normal development, and the mutual influences of growing plastic tissues on one another. As has already been suggested, the site distribution of teratomas points to the operation of growth disturbances emanating from the primary axis—the notochord and contiguous structures which are derived by invagination of tissue at Hensen's node in the early embryo and which constitute the primary organizer. Experimental embryologists have shown that the blastulas deprived of their primary organizer regions, or blastomeres removed from pregastrular embryos, can grow and differentiate into a variety of tissues, but do so in a chaotic manner and without forming an axis or defined organs. Perhaps teratomas represent areas of tissue which during early embryonic development escaped from the action of the primary organizer; and perhaps knowledge of the chemistry of this escape may bring with it an understanding also of the neoplastic qualities of teratomas.

## GROSS

Teratomas vary greatly in structure according to the variety of the tissues which they contain and according to whether they are benign or malignant.

Benign teratomas are usually grossly cystic, showing one or more large cysts into which the solid components project in the form of one or more small or large eminences; and, on cutting into them, many of their fully differentiated tissues are easily recognized by the naked eye—skin, hairs, teeth, bone, cartilage, adipose tissue, etc. (pl. I, figs. 2-5, 7-14, 17). The contents of the common skin-lined cysts are sebaceous matter, often associated with shed hairs or flakes of keratin; and in some cases the sebaceous material consists of numerous spherical "butter-balls," formed by mechanical agitation. As much as 10 gallons of sebaceous fluid has been seen in one tumor. In some teratomas, the main cavity is not lined by skin but by alimentary or respiratory mucosal tissue or by central nervous tissue, and therefore contains not sebum, but mucoïd secretions or clear watery cerebrospinal fluid. The grossly cystic character of most benign teratomas is simply a consequence of the continued accumulation of their cutaneous or other secretions.



Figure 1A-B. Multiple bilateral teratomas in a horse's testes. Natural size. A.F.I.P. Acc. Nos. 219005-1 and 219005-2.

Figure 2. Skiagram of a "dermoid cyst," showing several teeth socketed in a mass of bone. (From the Armed Forces Institute of Pathology.) A.F.I.P. Acc. No. 72520.

Figure 3. Photograph of a benign cystic ovarian teratoma, showing an irregular intracystic eminence. Natural size. See figure 8. (From Willis, R. A., "A further study of the structure of teratomata." J. Path. Bact., 45:49-65, 1937.) A.F.I.P. Acc. No. 219005-5.