plasma membranes. But again the septa are about 15 to 17 nm thick, arranged with regular periodicity (Figures 2 and 3). In sections normal to the cell surface, the septa sometimes show two outer lines of higher density, as described in invertebrate septate junctions (Figure 2). In more oblique sections, the septa seem to cross not only the intercellular gap but also the apposed plasma membranes (Figure 3).

The septate junctions most often occur between two areas where the intercellular space is irregularly dilated. The plasma organelles and the nucleus of the involved spermatogonia, however, reveal no pathological phenomena. As the longest junction could be followed only over 500 nm and appeared only in few serial sections, these cell contacts possibly represent macular structures and do not surround the cells completely[22]. Since we failed to obtain tangential sections of these junctions, no conclusions regarding the spacial configuration of the septa can be made.

Discussion. The septate junctions between human spermatogonia differ noticeably from the well defined invertebrate septate junctions: The septa are more than twice as thick, and the periodicity about three-fold greater than in invertebrate septate junctions. Moreover, the contact areas are very short and extremely rare. On the other hand, the periodicity is very regular, and the structural characteristics in the two patients are very similar.

BULGER and TRUMP[23] emphasize that septate junctions in renal tubular epithelium of the rat and the English sole appeared only under certain experimental conditions. Likewise, YAMAMOTO and KONDO[24] interpret the septate junctions observed between adjacent mitochondria of rats and cats as a consequence of exceptional circumstances. Our material is too small to determine whether the septate junctions between human spermatogonia are real structures or artefacts. The often irregularly dilated intercellular space around the contact areas could indicate a certain artificial membrane alteration.

An interesting observation has recently been reported by GORIUS et al.[25] and FLANDRIN et al.[26] who found septate junctions between erythroblasts in a case of refractory anemia. Considering that septate junctions are a common feature between epithelial cells of invertebrates, i.e. between less differentiated cells, one could speculate that in higher organisms undifferentiated cells such as erythroblasts and spermatogonia under certain conditions could retain the potency to form such contact areas.

Zusammenfassung. Kurze, septiert aussehende Zellverbindungen mit regelmässiger Periodizität der Septen konnten vereinzelt zwischen Spermatogonien bei einem Patienten mit Fertilitätsstörung und in normalem Hodengewebe nachgewiesen werden. Die morphologische Struktur dieser Verbindungen wird mit den septierten Zellverbindungen der Invertebraten verglichen, und einige Beziehungen zu septierten Zellverbindungen bei Vertebraten werden diskutiert.

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Cytology of Experimental Teratomas and Teratocarcinomas

Experimental teratomas and teratocarcinomas can easily be produced in mice by transplanting gastrulation embryos to extrauterine sites[1, 2]. Approximately 50% of such grafts give rise to malignant tumors (teratocarcinomas) and the remaining 50% form benign tumors with a limited growth potential (teratomas)[2]. The present study sought to determine whether benigh tumors could be differentiated from malignant tumors in cytologic smears from aspirates obtained with a thin needle.

Material and methods. Teratomas and teratocarcinomas were produced in C3H/H mice by transplanting 7-day-old mouse egg-cylinders under the kidney capsule of adult isogenic hosts[2]. Two months after transplantation 10 tumor-bearing animals were sacrificed and aspiration with a thin needle (0.6 mm in diameter) attached to a syringe with a tight fitting piston was done from solid areas of tumors. The aspirated material was spread on a slide to form a thin film, air dried and stained with May-Grünwald-Giemsa (MGG) or with hemalaun and eosin. Histologic slides were made from all the tumors examined. In addition to the embryo-derived tumors, we biopsied and studied retransplantable neurogenic teratocarcinomas obtained after sequential retransplantation of an embryo-derived teratoma described in detail previously[3].

Results. 5 of the embryo-derived tumors were classified histologically as malignant and 5 as benign. The basis for the distinction was the presence or absence of undifferentiated embryonic stem cells, designated, in accordance with the concept of PIERCE[4], 'embryonal carcinoma cells'. These cells are the only 'malignant', i.e. rapidly proliferating, element in teratocarcinomas and are not found in benign teratomas. Cytologically it was not possible to differentiate malignant from benign tumors. Aspirates of all 10 tumors contained cells in a continuous spectrum from fully differentiated to undifferentiated. It was possible to identify squamous cells, columnar cells with

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or without cilia and mucin droplets, melanin-containing cells, striated muscle cells, fibroblasts and nerve cells. Most cells, however, could not be properly identified and were considered to represent undifferentiated embryonic cells. These cells had round or polyhedral nuclei, with finely dispersed chromatin, an occasional nucleolus and a narrow rim of cytoplasm (Figure 1). It was not possible to recognize the embryonal carcinoma cells on cytological smears, and none of the cells could be classified as 'malignant' according to the standard criteria used in clinical cytology.

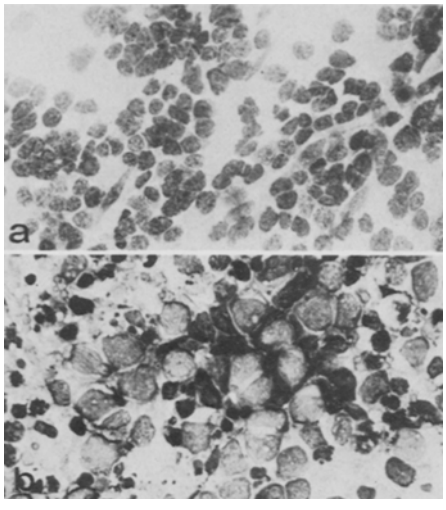

Fig. 1. Primary embryo-derived tumors. a) Undifferentiated cells from a teratocarcinoma. Nuclei have a finely granular, evenly dispersed chromatin pattern. MGG. × 320. b) Undifferentiated cells from a teratoma intermixed with small, darkly nucleated cells. MGG. × 480.

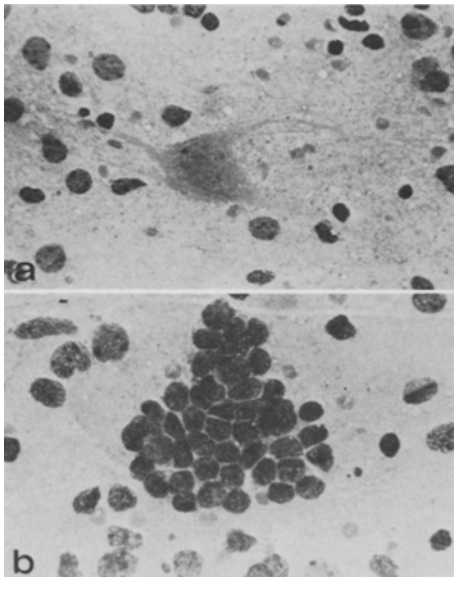

Fig. 2. Neurogenic teratocarcinoma, 30th retransplant generation. a) Nerve cell surrounded with nondescript cells, most probably of glial origin. MGG. × 480. b) Group of atypical cells with darkly stained nuclei. Note multiple nucleoli in the surrounding cells with lightly stained nuclei. MGG. × 480.

The smears of the aspirates from the retransplantable neurogenic teratocarcinoma differed from those obtained from primary embryo-derived tumors. Of the differentiated cells in these smears, one could recognize only neural cells (Figure 2). There were also some smaller cells, presumably glial and/or immature neuroectodermal cells that could not be properly identified. In addition there were groups of small cells with a coarse and dense chromatin pattern, which were considered to represent embryonal carcinoma cells. Prominent, often multiple, nucleoli were found in both darkly and lightly stained nuclei.

Discussion. Cytologically we were unable to distinguish the 'benign' from 'malignant' teratoid tumors obtained by transplanting 7-day-old embryos under the kidney capsule, despite the fact that some of these outgrowths behaved and appeared histologically as either malignant or benign. None of the cells from these tumors displayed the conventional cytologic features of malignancy. This is in keeping with our previous finding that the cells in embryo-derived teratocarcinomas do not differ basically from the embryonic cells from which they were derived[2]. Teratocarcinomas develop from the transplanted embryos not because the cells undergo a 'malignant transformation' but because there is no efficient control to check their proliferation or to direct their differentiation into non-proliferating somatic tissues.

After retransplantation, teratocarcinomas frequently undergo some changes. The neurogenic teratocarcinoma studied developed from a slow growing into a rapidly proliferating tumor and thus became more malignant[3]. In smears, the usual cells from this tumor showed atypia of malignant cells. It was not entirely clear, however, whether this atypia was a reflection of biological malignancy or a mere morphologic expression of the tetraploidy of this tumor (unpublished observation) that developed during retransplantation.

Zusammenfassung. Von bei Mäusen erzeugten Teratomen und Teratocarcinomen entstehen in der Hälfte der Fälle ungefähr gleich häufig bösartige wie gutartige Mischtumoren. Bei der Punktion und der nachfolgenden cytologischen Untersuchung war es jedoch nicht möglich, aus den Abstrichen maligne und benigne Tumoren zu trennen.

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