

47. Role of mesenchyme in the early cytodifferentiation of human prostate, P. KELLO-KUMPU-LEHTINEN and R. SANTTI, Department of Anatomy, University of Turku, Kiinamyllynkatu 10, 20520 Turku 52, Finland

The electron microscope study of human embryos and fetuses aged 6-15 weeks revealed that the mesenchyme, which is adjacent to the epithelium of the urogenital sinus at the level of the mesonephric duct openings, is the local initiator of the morphological differentiation of the human prostate. The epithelial outgrowths were found to appear after the mesenchymal changes, e.g. the increased cell density and the differentiation of the mesenchymal cells became evident in the ninth week. The mesenchymal differentiation in the homologous portion of the female urethra was shown to lag behind that of the male. The cytodifferentiation of the prostatic mesenchyme correlated with the ultrastructural differentiation of testicular Leydig cells, suggesting that the mesenchymal changes are determined by fetal androgens. By the end of the eleventh week a lumen was seen in the terminal portion of some solid cellular cords completing the acinar structure for the first time. Most of the prostatic epithelial cells were undifferentiated and resembled the basal cells in normal adult prostate. However, some apical cells of the stratified epithelium became polarized and secretion granules appeared in the Golgi area and apical parts of the cells in the thirteenth week. These granules contained acid phosphatase activity demonstrable by electron microscope histochemical techniques. As a sign of the possible inductive role of the mesenchyme in glandular morphogenesis direct epithelio-mesenchymal cell contacts were seen in association with the polarization of the epithelial cells and the appearance of secretory activity. It is possible that epithelio-mesenchymal interactions, and more specifically stromal influences on the proliferation and differentiation of the epithelial cells, continue throughout life and play an important role in the growth of both the normal and the pathological prostate.

48. Prostatic carcinoma: correlation of hormonal pattern in plasma and urine to local extent of tumour, presence of metastases, grade of differentiation and primary response to hormonal treatment, S. RANNIKKO¹, A.-L. KAIRENTO², S.-L. KARONEN² and H. ADLERCREUTZ², ¹III Department of Surgery and ²Department of Clinical Chemistry, University of Helsinki, 00290 Helsinki, Finland

In order to investigate the correlation of hormonal pattern in prostatic cancer with local extent of the tumour (T classification in the TNM classification system), presence of metastases (M classification), grade of differentiation (G classification) and primary response to hormone treatment plasma FSH, LH, prolactin (PRL), testosterone (T), estrone (E1), estradiol (E2), progesterone and cortisol and urinary 17-ketosteroids (17-KS), an-

drosterone (A), etiocholanolone (Et), DHEA, 17-ketogenic steroids (17-KGS), pregnanediol, pregnanetriol, estrone, estradiol and estril were measured in 32 patients with histologically or cytologically verified cancer. 22 patients were treated with orchidectomy, six with orchidectomy and Estradurin® (polyestradiol phosphate = PEP) (Leo, Hälsingborg, Sweden) and 4 with PEP.

The plasma hormonal pattern was the same if the tumour was confined to the gland or extended beyond the capsule, but urinary 17-KS ($P < 0.005$), 11-deoxy-17-ketosteroids ($P < 0.05-0.025$) and 17-KGS ($P < 0.025$) were significantly lower and urinary A/Et ratio ($P < 0.025$) higher in the patients with tumours extending beyond the capsule. Patients with metastases had significantly higher plasma E2 ($P < 0.05$) and lower plasma T/E2 ($P < 0.025$) and T/E1+E2 ($P < 0.05$) ratios than those without metastases. Patients with less differentiated tumours had significantly higher plasma E1+E2 values ($P < 0.025$) and lower plasma T/E1+E2 ratio ($P < 0.025$) than those with well differentiated tumours. Patients with a good primary response to hormonal treatment had significantly higher plasma T ($P < 0.05$), T/E2 ($P < 0.025$) and T/E1+E2 ($P < 0.025$) and T/PRL ($P < 0.025$) ratios than those who primarily responded poorly. Patients with a poor response to treatment (8 subjects) all had ratios of T (nmol/l)/E2 (pg/ml) below 1.0 and T (nmol/l) / PRL (mIU/l) below 0.1 but in the group with a good response (18 subjects) both high and low ratios were found.

It is concluded that a low plasma androgen/estrogen ratio is typical for patients with less differentiated metastasizing prostatic carcinoma and a high T/E2 and T/PRL ratio means a good response to hormonal treatment. However, those with low ratios had a variable response. Of the hormones assayed only plasma T, E2, E1 and PRL seemed to have some association with the prostatic cancer. Assay of urinary hormones is probably of little value in this disease.

OVARIAN FUNCTION AND DISEASE

49. Gap communicating junctions in theca interna cells of developing mouse follicles, G. FAMILIARI and P.M. MOTTA, Department of Anatomy, Faculty of Medicine, University of Rome, Italy

The theca interna has been studied by transmission and scanning electron microscopy as well as by freeze-etching in a variety of developing and atretic follicles with particular reference to the occurrence and development of intercellular junctions.

A) In primordial and primary follicles, the theca interna consists of a few layers of concentrically arranged fibroblasts and small bundles of collagen fibres. Intercellular junctions such as zonulae adherentes (ZA) and gap junctions (GJ) are rarely observed. When present they are very small.

B) In growing follicles the theca interna

layer may show three different cell types: 1. fibroblast-like cells, 2. steroid-secreting cells and 3. transitional elements. The intercellular junctions (ZA and GJ) are relatively more numerous at this time.

C) In graafian and preovulatory follicles the theca interna cells generally assume a clear polyhedral shape and become larger than those observed in previous stages. The cytoplasm of these elements is filled with organelles considered characteristic for steroid cells (smooth endoplasmic reticulum, mitochondria with villiform and/or tubular cristae and lipid droplets). Fibroblast-like cells and intermediary stages are also observed. In this stage of follicular development the GJ increase in number and in length in some cases assuming the typical aspects of annular structures (annular GJ). The other junctions appear rather diminished.

D) In atretic (graafian and preovulatory) follicles the steroidogenic cells of the theca interna survive and appear to be mixed up with a number of fibroblasts. Numerous cells among these show signs of cytoplasmic alteration and are degenerating. GJ and ZA are still present between preserved cells and may be numerous.

In all the follicles studied GJ and ZA are always present not only between two differentiated theca interna (steroidogenic) cells, but also between two immature elements and/or closely related mature and immature cells. Further occasional solitary cilia are observed in the variable population of the above theca interna cells.

GJ (communicating junctions) therefore may have a role in the cellular differentiation of the theca interna and possibly also coordinate the hormonal activity of their cellular population which also seems to persist during follicular atresia. In these cases in fact the theca interna cells, which have already assumed a steroidogenic function, are called "interstitial gland-cells" of thecal origin.

Closely related to the coordination role among theca interna cells (differentiation and hormonal production) is the occurrence of a single cilium in a few of these cells.

The intriguing possibility that this organelle may have an important function should not be completely ruled out if gap junctions are regarded as selective channels for transferring intercellular signals.

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50. Ovulation. A morphological analysis by scanning and transmission electron microscopy. P.M. MOTTA and S. MAKABE, Department of Anatomy, Faculty of Medicine, University of Rome, Italy, and Department of Obstetrics and Gynecology, Toho University, School of Medicine, Tokyo, Japan

A combination of transmission electron microscopy (TEM) freeze etching, high voltage E/M (HiVo) and scanning E/M (SEM) offers the potential of deriving new and fundamental insights into morphological correlates of physiological processes. This combination has proven to be of particular value when applied

to the study of mammalian reproduction. The purpose of this review is to describe the results of such an approach to the morphodynamic processes in the ovary as they relate to the process of ovulation and to the fertilizable stage of the gametes.

The exposed surface of the mammalian ovary is covered by the ("germinal") superficial epithelium which is composed of a single layer of polyhedral cells. The free surface of these elements is populated by numerous microvilli and a single cilium. By SEM the superficial cells display several features likely to be related to the phase of the cell cycle and to other special activities as, for example, endocytosis. These features include: branching evaginations, blebs, ruffles, lamellipodia and a number of pits and small cavities. The demonstration of submicroscopic changes on the surface of the ovarian epithelium indicates that it may undergo a cyclic process similar to that occurring within other structures of the ovary and in other regions of the genital tract during the reproductive cycle. Further it is suggested that the superficial epithelium with its proliferating invaginations into the ovarian cortex might be (also in the mature ovary) a continuous and important source (a real "germinal" layer) of a number of somatic ovarian components.

Preovulatory follicles are blister-like structures protruding from the ovarian surface. In the basal and periapical areas the superficial cells are covered with a decreasing number of microvilli. At the apex the covering cells are very flattened and rare microvilli are noted. In other cases the superficial cells, largely altered, were degenerating and sloughing off. In these areas a fluid was observed infiltrating the subjacent tunica albuginea, accumulating under the basal lamina, penetrating and distending the intercellular spaces of the surface epithelium. At the time of ovulation the oocyte was completely covered with follicle cells. The zone pellucida has a stratified arrangement and this suggests discontinuity in the secretion of its material. The cytoplasm of the granulosa cells in these and in other regions of the preovulatory follicles was filled with contractile microfilaments. Finally small desmosomes and gap (communicating) junctions were noted not only between oocyte and companion cells but also among granulosa cells. These aspects are related to eventual coordinative signals occurring at the time of ovulation between oocyte and granulosa cells. SEM and TEM results suggest that an increase of fluids (edema) probably mediated through a local secretion of steroids (theca interna) might be related to the final dissolution of the weakened apical wall of the preovulatory follicle. Other causes such as contraction of smooth muscle cells of the theca externa mediated through autonomic nerves; action of lytic enzymes produced by cells located in the periapical areas of preovulatory follicles (granulosa, theca and superficial epithelium); and vascular changes are also described in the light of modern submicroscopic analysis.

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