Development of the Early Human Ovary and Role of the Mesonephros in the Differentiation of the Cortex*

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Summary. The morphogenesis of the primary gonadal differentiation, of the sexual differentiation and the growth of the ovarian cortex during its early period have been studied on 10 human embryos between 12 and 95 mm CR-length. Semithin sections of glutaraldehyde-OsO₄-fixed and plastic-embedded material were used to demonstrate the structural events on a cellular level. The primary gonadal blastema within the genital ridge is formed by two types of somatic cells: cells segregated from the mesonephros and cells of the proliferating coelomic epithelium. The two types of cells show a tendency to intermingle and they enclose the immigrating primordial germ cells. In the female gonad the indifferent period terminates between day 40 and 42 of ovulation age (20 to 23 mm CR-length). Between day 40 and 50 the blastemal content of the indifferent gonad is remodelled and an ovarian cortex differentiates. Cellular strands extending from the primary blastema and strands from the superficial blastemal layer contribute to the formation of the cortex. Within the newly formed medulla, remnants of the disintegrating primary blastema differentiate into medullary cords.

Cells of mesonephric origin which invade the growing cortex via the rete blastema interact with cells deriving from the superficial epithelium, and both exert their opposite influence on the germ cells. While female sexual differentiation is characterized by failure of the dark mesonephric cells to completely penetrate the gonadal blastema, the morphogenetic process resulting in the formation of the ovarian cortex shows a strong invasion of the cortex by the dark mesonephric cells. Dark cells advance at the most superficial layer of the cortex and increase in number at the deeper level of the cortex. Onset of oogonial proliferation and meiotic prophase seems to depend on the numerical proportion between the activating dark and the inhibiting light supporting cells.

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* Supported by the Deutsche Forschungsgemeinschaft
**Key word:** Ovary – Organogenesis – Mesonephros – Ovarian cortex – Granulosa cells – Germ cells – Human

**Introduction**

Descriptions of the early ovarian differentiation do not convey a uniform conception regarding this developmental process. Some representations emphasize the outgrowth of a second generation of "sex cords" as being the only significant event of the female organogenesis. Sex cords take shape and are part of the new-formed ovarian cortex, while the blastemal material of the former indifferent gonads becomes dislocated and finally indistinguishable in the medullary compartment. Other descriptions stress the inconspicuousness of the developmental process, during which the indifferent gonad slowly slides into the female state. According to this concept, which has been formulated by Jost et al. (1973), the ovary undergoes a period of continuation of its undifferentiated stage, simply growing until the first primordial follicles are formed. Sexual differentiation proceeds dissymmetrically: While in the male gonad testicular cords differentiate suddenly, in the female counterpart no pronounced morphogenetic event can be ascertained.

Both structural concepts have been discussed at length during the last decades, each of them supported by a functional concept. One of these concepts, which has most influenced the discussion on gonadal development, is Witschi's theory of "cortico-medullary-antagonism" (Witschi 1957, 1962, 1965). While the basic developmental concept proved to be indefensible, some of the structural findings are still accepted and terms like "cortex" and "medulla" are in common use. On the other hand, Jost's idea of a chronologically uneven morphogenetic process led to the postulation of a male determining principle (Jost 1970b, 1971, 1972). According to this conception, the male "gonadal sex" is realized through the influence of a "male organizer" and results in the formation of testicular structures. The female primordium needs no organizer activity, since its undifferentiated state basically remains unchanged. The studies on the male determining function of the HY-antigen conclusively support Jost's idea. (Ohno 1979; Müller 1981; Wachtel 1981; Wolf 1981).

The two concepts, however, inadequately explain the morphogenetic process of early ovarian differentiation. Are there developmental processes which make the early ovary distinguishable from the indifferent gonad? Witschi affirms this point. In the human and other species the growth of the cortex begins after sexual differentiation. But still other species fit better into the concept of Jost: No new cortex is formed and the indifferent gonadal blastema proliferates continuously, developing into the specific female cortex. Since the human ovary belongs to that group which develops a cortex after sexual differentiation, a renewed study using plastic-embedded semithin section might permit a better insight into the structural events during and shortly after sexual differentiation of the ovary. Furthermore,