For many years, understanding placental pathology was thought to demand only a limited knowledge of implantation and early placental development, because disturbances of these early steps of placentation seemed to cause abortion rather than affecting placental structure and function. Increasing experience with assisted fertilization, however, has taught us that a high percentage of these cases show impaired fetal and neonatal outcome such as an increased incidence of intrauterine growth retardation and retroplacental hematoma, as well as increased perinatal mortality (Beck & Heywinkel, 1990). The causal connections are still unknown, although the authors give some arguments that placental causes must be considered. It must be speculated that improper conditions during implantation handicap early development and finally result in the inappropriate functioning of the fetoplacental unit.

Basic information concerning early development may be of increasing importance and thus is presented in this chapter. The pathologically interesting interactions between the site of implantation and the shape of the placenta are considered in Chapter 13.

**Prelacunar Stage**

According to the general definition of the placenta given earlier, the development of the placenta begins as soon as the fetal membranes establish close and stable contacts with the uterine mucosa, that is, as soon as the blastocyst implants. The first step of implantation is called apposition. In the human it takes place around day 6 to 7 postcoitus (p.c.) (day 1 p.c. = the first 24 hours after conception). During this stage, the implanting blastocyst is composed of 107 to 256 cells (Hertig, 1960; Boyd & Hamilton, 1970). It is a flattened vesicle, measuring about 0.1 x 0.3 x 0.3 mm in diameter. Most of the cells make up the outer wall (trophoblast) surrounding the blastocystic cavity (Figure 5.1a). Generally speaking, the trophoblast is the forerunner of the fetal membranes, including the placenta. The inner cell mass, a small group of larger cells that form the embryoblast, is apposed to the inner surface of the trophoblastic vesicle. The embryo, umbilical cord, and amnion are derived from these cells. Moreover, both embryoblast-derived mesenchyme and embryoblast-derived blood vessels contribute to the formation of the placenta.

In most cases, the blastocyst is oriented in such a way that the embryonic pole (that part of the blastocyst bearing the embryoblast at its inner surface) is attached to the endometrium first (Boyd & Hamilton, 1970). Accordingly, this part of the circumference is also called the implantation pole. Rotation of the blastocyst in such a way that the embryonic pole and the implantation pole are not identical results in abnormal cord insertion. Thus, in moderate cases we find an eccentric or marginal insertion of the cord; in severe cases a velamentous cord insertion may be the consequence (see Chapter 12). The usual implantation site is the upper part of the posterior wall of the uterine body, near the midsagittal plane. According to Mossman (1937, 1987), this region is homologous with the antimesometrial wall of a bicornuate uterus, where primary attachment takes place in most mammals.

In all species, implantation is introduced by attachment of the apical plasma membranes of the blastocystic trophoblast to the apical plasma membranes of the uterine epithelium. This phenomenon has been described by Denker (1990) as a cell biological paradox because apical plasma membranes of epithelia are normally known to be nonadhesive. Adhesiveness is a normal quality of basolateral epithelial plasma membranes, which are thus attached both to each other and to their basal laminae.

The blastocyst and the endometrium show this usual epithelial behavior throughout the entire preimplantation phase so long as the blastocyst moves in the fallopian tube and uterine cavity. Apical adhesiveness of both
epithelia, the trophoblast and endometrium, is apparently achieved for only a short, specific phase, which has been called the implantation window (Psychoyos, 1988). This phase is used for attachment of the blastocyst. To find or to generate this window is the most important prerequisite for successful implantation following in vitro fertilization.

With the noninvasive types of implantation, the epithelochoorial placentation (e.g., pig, horse, some ruminants), implantation is arrested at the stage of attachment. Invasion with destruction of either epithelial surface does not follow. In contrast, in most mammals more intimate types of maternal–fetal contacts are established by invasion. In the human, implantation is also an invasive process. Knowledge of structural details, however, is largely lacking, as appropriate human material is rare and is usually poorly preserved when it is available. Numerous studies in animals have revealed the existence of three types of invasive implantation (Schlafke & Enders, 1975; Denker, 1990).