In 1672, Regner de Graaf first published a description of the corpus luteum and recognized that the presence of a corpus luteum is associated with a fetus in utero. The definitive experiments of Corner (1), Allen and Reynolds (2) showed that pregnancy in rabbits is controlled by a product of the corpus luteum -- the ovarian steroid progesterone. Nevertheless, at present there is no unifying concept which would define the major role of progesterone in animal tissues. Furthermore, the biochemical actions of this steroid at the molecular level of cell metabolism have been so elusive that it is difficult even to construct a good hypothetical mechanism of action. The biologic effects of progesterone may be grouped as follows: (1) uterine endometrial cells are transformed in such a way that they may receive the early embryo and facilitate its implantation; (2) myometric activity is suppressed, aiding in retention of the embryo during implantation and growth prior to normal parturition; (3) numerous and varied metabolic parameters may be altered which may have no direct impact on maintenance and termination of pregnancy.

The effects of progesterone on the myometrial cell have been studied and reviewed by Csapo (3). Uterine muscle functions normally only if its spindle-shaped cells possess, as a result of estrogen stimulation, sufficient concentrations of contractile proteins for adequate working capacity. The excitable membrane of the uterine muscle cell must also be capable of undergoing periodic changes between rest and activity. The spontaneous rhythmic activity of the individual cell membrane must be transmitted to the contractile system of the myoplasm through an effective excitation. Progesterone exerts a "blocking effect" so that an excitation wave
cannot spread from one region to another. This steroid has been reported to increase the membrane potential to an extent where spontaneous activity is suppressed (4) and a gradual reduction in spike discharge occurs (5). The molecular mechanism for the inhibitory effect of progesterone on uterine muscle is not clear. Progesterone has been reported to inhibit incorporation of radiolabeled glycine into protein in both control and estrogen treated uteri(6), potassium ion influx and efflux through myometrial cell membranes (7), and mitochondrial respiration (8). The relationship of these inhibiting events to the progesterone "quieting" effect on uterine myometrium can be only speculative.

Although progesterone is needed for alveolar development in breast tissue of some species, the major new capacity which develops in animals in response to progesterone is the ability of the uterine endometrial cells to accept and support the blastocyst. Under the influence of estrogen the endometrium proliferates and becomes dense. Progesterone inhibits further endometrial proliferation and the epithelium becomes secretory. The outline of the endometrial glands becomes irregular and the nuclei become basally prominent. The glycogen content of the epithelium increases, the stroma becomes edematous, and an increase in perivascular alkaline phosphatase occurs. The endometrium is now able to accept, hold, and nourish the fertilized ovum. These cytobiological changes probably reflect earlier intracellular biochemical events.

This cellular "transformation" may require gene activation and transcription of chromosomal information, but few model systems have been available to investigate specific progesterone mediated changes in nucleic acid and protein metabolism. Over the past three years, this laboratory has reported a series of studies on the mechanism of action of progesterone in the chick oviduct, a unique model system for investigation of progesterone regulation of protein synthesis. Estrogenic substances are known to stimulate oviduct growth in newborn and older chicks (9) and we have found that estrogen markedly stimulates synthesis of oviduct DNA and RNA and numerous tissue specific proteins, similar to other model systems presently available (10). However, the administration of a single dose of progesterone to estrogen-stimulated chicks results in the induction of synthesis of a specific oviduct protein, avidin (11,12). Unless otherwise indicated, avidin was determined in all subsequent studies by the method of Korenman and O'Malley (13), an assay utilizing the unique biological affinity of avidin for biotin labeled with $^{14}$C. In addition to the biological assay, the experimental product has been rigorously identified as avidin by two additional criteria. Rabbit antiserum to avidin was utilized to precipitate an avidin-$^{14}$C-biotin complex and to demonstrate an increased rate of incorporation of labeled amino acids into avidin during the incubation (14). The newly synthesized