

Protocols to induce ovulation and “progesterone block” experiments



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Drugs for ovulation induction and exogenous hormones have been used since the 1960s.

Clomiphene citrate (CC) was an emerging area of research in the 1960s. It was first used to treat patients with oligomenorrhea, and later as a treatment for anovulation. The 1966 *Fertility and Sterility* article in which Whitelaw (1) reported its use in 217 women, related the indication of its use, dosage, side effects, and the hormonal changes that follow its administration. This contributed a general agreement on treatment, with CC established as an effective method of inducing ovulation and improving fertility in oligoovulatory patients.

Patients who did not conceive with the use of CC were often treated with human menopausal gonadotrophin (HMG) therapy for ovulation induction with intrauterine insemination (IUI) therapy. Also in 1966, Kistner (2) first reported similar pregnancy rates in women undergoing ovulation induction who received sequential CC/HMG compared to HMG therapy alone. In the following decades, many authors confirmed the same outcomes of ovulation induction with sequential CC/HMG versus HMG protocols, reporting decreased incidence of ovarian hyperstimulation syndrome and multiple gestations, as well as reduced costs.

That same year, Csapo (3) published a paper regarding the effect of massive intramuscular treatment with medroxyprogesterone acetate in 62 patients during labor. This trial was part of a series of experiments that he started 10 years previ-

ously to test the “progesterone block” theory, according to which progesterone serves to block the contraction of muscles in the pregnant uterus. He further found that this blocking action of progesterone shifts from the ovarian corpus luteum to the placenta in the 7th to 8th week of gestation. Indeed, from his experiments performed in rabbits and rats, he proved that in the first 50 days of pregnancy, luteectomy caused a progesterone withdrawal, leading to uterine contractions and abortion. It was shown that this could be avoided before the 9th week of gestation by exogenous progesterone supplementation. This is now commonplace treatment for luteal phase support in assisted reproduction cycles. Thus, Csapo (3) provided the evidence for actions of progesterone as an essential hormone in the process of reproduction, from the implantation to the maintenance of pregnancy and the onset of labor, 50 years ago.

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