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Protect yourself and others from COVID-19.

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Progesterone supplementation for IVF pregnancies and pregnancies at high risk for spontaneous preterm birth.

It will not have gone unnoticed by many of you that IVF patients in particular are being treated with progesterone vaginal pessaries as a means of enhancing the process of implantation.

Progesterone is necessary for successful implantation of the embryo. Luteal phase support is therefore a requirement for optimal outcome following egg collection and embryo transfer in an in-vitro fertilization (IVF) cycle. It has been shown that ovarian stimulation during IVF treatment, particularly in cycles incorporating GnRH α , leads to an impaired luteal phase with progesterone insufficiency. Furthermore the process of harvesting oocytes can strip granulosa cells from the oocyte thus reducing the production of endogenous progesterone.

Both human chorionic gonadotrophin (hCG), which stimulates steroid production in the corpus luteum, and progesterone administration in the luteal phase improve the clinical pregnancy rate. However hCG can increase the risk of Ovarian Hyperstimulation Syndrome and so progesterone pessaries are favoured. Vaginal administration of progesterone has shown to be at least as effective as IM administration, and significantly more effective than oral treatment. Progesterone support of luteinisation has been used from 2 weeks to 12 weeks of gestation.

Administration of progesterone up to the time clinical pregnancy is detected significantly reduces the rate of subclinical miscarriage, whilst continued administration beyond this time produced no apparent benefit.

The normal progesterone pessaries contain 100 mg of the hormone and are administered vaginally 3 x daily until 12 weeks.

Contraindications to Progesterone R

Some patients may be unsuitable for supplementation with progesterone such as those with liver dysfunction, or conditions worsened by fluid retention such as epilepsy, hypertension, asthma, diabetes, cardiac or renal dysfunction or previous history of venous thromboembolism,

Use of Progesterone Pessaries to Prevent Preterm Labour.

Progesterone reduces myometrial sensitivity to oxytocin, blocks adrenergic receptors and prostaglandin synthesis and stimulates lymphocyte-associated synthesis of progesterone induced blocking factor, all of which facilitate uterine quiescence during pregnancy.

Vaginal progesterone therapy is recommended for women who are found to have a short cervix at the time of the routine midtrimester scan. Current evidence suggests that progesterone reduces the risk of preterm birth in these women, with evidence of improved perinatal outcomes. The 2013 Cochrane Review has a general conclusion that vaginal progesterone is of benefit in women with previous history of preterm birth. Currently, vaginal progesterone 100–200 mg daily is recommended from early pregnancy until 36 weeks gestation.

For patients with a singleton pregnancy and a mid trimester cervical length <25 mm and a previous spontaneous preterm delivery the use of progesterone pessaries was shown in a large metaanalysis to significantly reduce the rate of premature birth at 32 and 35 weeks and their effects (RR 0.29-0.68).

Cervical cerclage was equally effective in reducing preterm deliveries at 37,35,32 and 28 weeks.

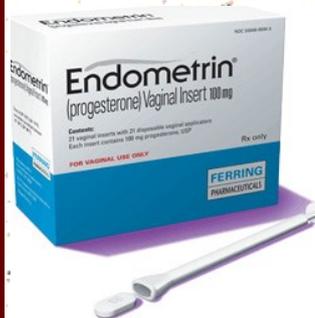


Cervical Length Assessment. The median cervical length at 20 weeks is 42mm, the 1st centile is 23mm. There appears to be value in linking shortened cervical lengths with an increase in the risk of preterm delivery. Cervical lengths of 30mm (10th centile), 27mm (5th centile) and 22mm (2.5th centile) gave relative risks of preterm birth prior to 37 weeks of 3.8, 5.4, and 6.3, respectively, with even greater relative risk at earlier gestations. If a transabdominal ultrasound is undertaken and the cervical length is greater than 35mm then this precludes a transvaginal cervical length below 25mm with over 95% sensitivity.

Progesterone Treatment In 2019 a large meta-analysis demonstrated that progesterone treatment was effective for the prevention of preterm delivery in predisposed women. Vaginal progesterone reduced preterm birth at less than 34 weeks (OR 0.29; 3 studies, moderate-quality evidence), and at less than 37 weeks (OR 0.43, 5 studies, moderate-quality evidence).

Guidelines for Cervical Assessments and Treatment

Current local guidelines include measuring the cervical length at a mid trimester ultrasound scan even in women who are asymptomatic. If the cervix is **<1.5 cm long** and especially if there has been a previous preterm birth prescribe progesterone pessaries 200mg nocte until 34 weeks gestation, delivery or prelabour rupture of membranes. If the patient is asymptomatic but has had a prior preterm birth then the cervix should be measured at the 19 week morphology scan and again at 24 weeks. Those whose cervix is **<2.5 cm in length** should be considered for progesterone pessaries 200 mg nocte until 34 weeks.



Transvaginal Cerclage² ((Shirodkar / McDonald Cervical)

History of one or more second-trimester pregnancy losses with painless cervical dilation

Prior successful indicated cerclage

Second trimester painless cervical dilation

Singleton pregnancy < 24 wks GA with cervical length <25mm.

The practice operates Monday to Friday with early Tuesday morning appointments for antenatal visits

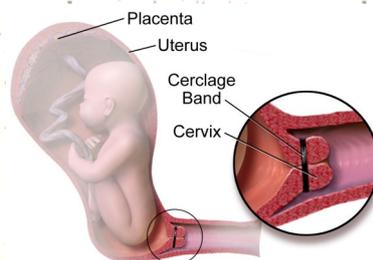
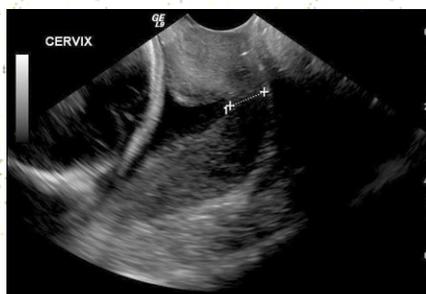
Further Reading:

- Conde-Agudelo A, Romero R, Da Fonseca E, et al. Vaginal progesterone is as effective as cervical cerclage to prevent preterm birth in women with a singleton gestation, previous spontaneous preterm birth, and a short cervix: updated indirect comparison meta-analysis. *Amer J Obstet Gynecol.* 2018;219(1):10-25
- Jarde A, Lutsiv O, Beyene J, McDonald SD. Vaginal progesterone, oral progesterone, 17-OHPC, cerclage, and pessary for preventing preterm birth in at-risk singleton pregnancies: an updated systematic review and network meta-analysis. *BJOG.* 2018; 27 November. doi: 10.1111/1471-0528.15566

The Shirodkar Suture.

The Shirodkar technique was first described by Dr V. N. Shirodkar in Bombay in 1955. The modified Shirodkar technique, adapted from Shirodkar's original described in 1955 involves upward displacement of the bladder to avoid injury. A vertical incision is made over the posterior cervix. A woven Mersilene tape on a large needle is then passed through the submucosal tunnel from anterior to posterior on both sides of the cervix. The suture is normally inserted prophylactically at 14 weeks and removed at 38 weeks.

In 1990 a study of 66 sutures in 46 patients with cervical incompetence was reported by Frieden et al. The term delivery rate was 88% with 100% neonatal survival. A 2014 study by Bonney et al included 139 women who had a Shirodkar suture inserted. 101 were elective procedures, 30 ultrasound-indicated and 8 were performed in the presence of visible membranes. Elective Shirodkar cerclage produced a success rate of 95.9% and conferred a MGA of 38.0 weeks. Ultrasound-indicated cerclage gave a success rate of 93.3% with a MGA of 37.5 weeks. The success rate for rescue Shirodkar cerclage was 75.0% with a MGA of 33.5 weeks.



Cerclage Correction of the Cervix