

# Is progesterone replacement therapy effective in managing heavy and irregular menstrual bleeding and associated severe dysmenorrhoea in the first few years after onset of menstruation in young girls due to physiological progesterone deficiency associated with non-ovulatory menstrual cycles in a still-maturing Hypothalamic-Pituitary-Ovarian axis?

Venables A<sup>2</sup>, Zahir S<sup>3</sup>, O'Brien B<sup>1</sup>, Viswanathan D<sup>1</sup>, Kimble RMN<sup>1</sup>

<sup>1</sup> Royal Brisbane and Women's Hospital & Queensland Children's Hospital, Brisbane, QLD, Australia

<sup>2</sup> University of Queensland Faculty of Medicine, Herston, QLD, Australia

<sup>3</sup> QCIF Facility for Advanced Bioinformatics, Institute for Molecular Bioscience, The University of Queensland, Brisbane, QLD, Australia



Children's Health Queensland  
Hospital and Health Service

## BACKGROUND:

In the first two years following menarche, approximately half of menstrual cycles are anovulatory<sup>1</sup> due to the still-maturing brain and an immature Hypothalamic-Pituitary-Ovarian (HPO) axis.

This results in a physiological progesterone deficiency, manifested by the impact of unopposed estrogen on the endometrium with **heavy menstrual bleeding, irregular cycles and associated pain** from both vaginal egress and retrograde menstruation from an anatomically maturing uterus with a small cervical opening.

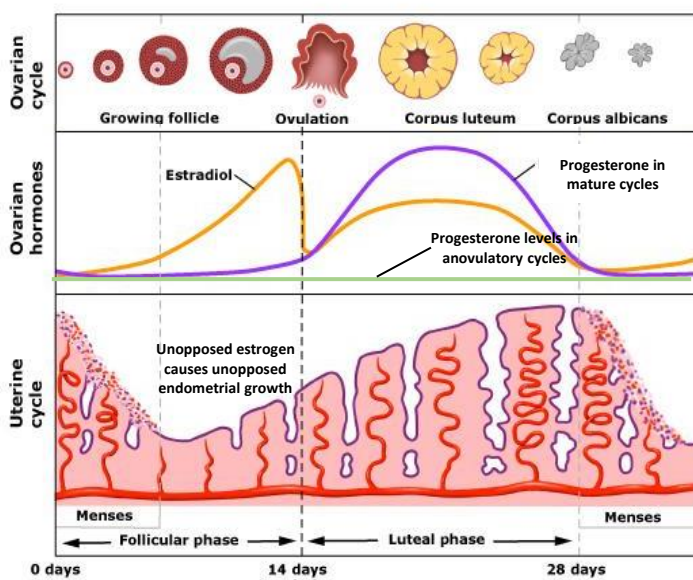


Figure 1: Mature (ovulatory) and Immature (anovulatory) female hormone cycles

## AIM:

Evaluation of the **effectiveness of progesterone replacement therapy** for patients with symptomatic non-ovulatory cycles due to an immature HPO axis.

## METHODS:

Data from the Queensland Children's Hospital Paediatric and Adolescent Gynaecology Service between 2016-2020 were retrospectively analysed. Symptoms of heavy menstrual bleeding, dysmenorrhoea, cycle irregularity and self-reported improvement in quality of life were compared before and after treatment with progesterone. Results were statistically analysed using McNemar's Test.

## RESULTS:

Table 1: Number of patients showing improvement in symptoms with progesterone replacement therapy.

	Oral Progesterone	Depot Progesterone	Depot or Oral Progesterone
Patients with reduction in HMB	65/81 (80.2%) p<0.001	25/26 (96.2%) p<0.001	84/92 (91.3%) p<0.001
Patients with reduction in dysmenorrhoea	53/66 (80.3%) p<0.001	18/20 (90%) p<0.001	67/74 (90.5%) p<0.001
Patients with reduction in cycle irregularity	36/55 (65.4%) p<0.001	19/22 (86.4%) p<0.001	52/64 (81.3%) P<0.001

## DISCUSSION:

**Progesterone replacement therapy, balancing out unopposed estrogen, given orally or via depot is an effective management** for heavy and irregular menstrual bleeding and associated severe dysmenorrhoea in the first few years after onset of menstruation in young girls due to physiological progesterone deficiency associated with non-ovulatory menstrual cycles in a still-maturing Hypothalamic-Pituitary-Ovarian axis. Progesterone replacement therapy is the **most appropriate first-line treatment** for this age group to treat progesterone deficiency with its impact on the endometrial overgrowth contributing to the heavy menstrual bleeding and retrograde menstruation, which is not without longer term consequences such as endometriosis and chronic pelvic pain.

Resorting to the Combined Oral Contraceptive Pill (COCP) should only be considered if there are additional indications, in order to **reduce the possibility of side effects related to the OCP in this age cohort**.

A thorough explanation of this physiological phenomenon to patients and their carers assists with reassurance and compliance with treatment, and allays anxiety about, and unnecessary need for, the OCP.

## REFERENCES:

1. Metcalf MG, Skidmore DS, Lowry GF, Mackenzie JA. Incidence of ovulation in the years after the menarche. Journal of endocrinology. 1983;97(2):213-9.