The role of progesterone levels on the day of human chorionic administration in the context of stimulated cycles co-treated with GnRH analogues has been a matter of intense debate for over two decades. Today, there is convincing evidence that in the general population the presence of an elevated progesterone concentration on the day of hCG is associated with a decreased probability of pregnancy achievement after a fresh in-vitro fertilization cycle.

The potential moderating effect of ovarian response on the latter association seems to be an important parameter when evaluating the clinical implications of progesterone elevation. Several studies have attempted to evaluate the effect of progesterone elevation on the cycle outcome of hyper or hypo responders, thus testing the hypothesis that the effect of progesterone elevation on the probability of pregnancy might be indeed dependent on the type of ovarian response. Although the available evidence is limited, there are strong indications that in hypo responders the effect of progesterone elevation is even more prominent than the general population. At the same time, in hyper-responders, where progesterone elevation is more frequent, a concentration of P>1.5 ng/mL might not be sufficient to cause a clinically significant deterioration in terms of pregnancy rates. In these patients, higher concentrations of progesterone on the day of hCG are required for a decrease in pregnancy rates to be evident.

Overall, available evidence suggests that hypo-responders undergoing fresh IVF cycles are more vulnerable to the negative effects of progesterone elevation, whereas hyper-responders, who are patients of better prognosis, seem to be able to partially compensate for this effect. These interesting findings highlight the complexity of the role progesterone elevation in fresh IVF cycle outcome and also the need for further research in this field.