

**Hormonal Male Contraception
and Mood
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Hormonal Male Contraception and Mood

- AEs reports in uncontrolled studies
 - True incidence, severity and drug-relationship difficult to assess
- Minimal placebo-controlled/experimental data available
- Testosterone
 - Normal sexual function is generally maintained
 - Aggression is unlikely to be a major issue
 - Significant mood disturbance is relatively rare
- Progestins
 - Preliminary signals indicating significant mood-related SAEs
 - Possible behavioural side effects is a key issue in MHC development
 - Mood changes in men - similarities to response to changes in luteal phase progesterone (& ALLO) PMDD in women

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- Monitoring of mood states by validated questionnaires is a requirement for future hormonal contraceptive studies
- Some men may be particularly susceptible to mood changes
 - Information to volunteers
 - Exclude men with previous history of mood (panic) disorders
- Ensure optimal pharmacokinetics of T replacement - replicate physiological levels
- Select progestin not only on suppression of gonadotrophins but also on neuroactivity profile
- Monitor pharmacokinetics of progestins and allopregnanolone levels

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- Low background levels of progesterone in men – more sensitive to acute rise and fall in levels of progestins
- Polymorphisms in neuronal GABAergic receptor subunit regulation and metabolism (by $5\alpha R$ and $3\alpha\text{-HSD}$) of progesterone to pregnanolone may determine individual susceptibility to mood changes in response to exogenous progestin
- Interactions between progestins (and metabolites) and T may modify behavioural response
- Further basic research and placebo-controlled clinical studies on behavioural effects of progestins (with T priming/replacement) in males are indicated