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Progesterone Prophylaxis for Postnatal Depression

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Abstract: The outcome of 255 women, who had previously suffered from postnatal depression (PND), revealed that progesterone prophylactic treatment prevented a recurrence in 92%. The series included 96 women, who wrote letters describing their previous PND, of whom 49 had infanticidal of suicidal fears and 50% had been hospitalised with psychosis. Among these letter writers only 6% suffered a recurrence, suggesting that PPT is as successful in preventing postnatal psychosis as in depression.

Zusammenfassung: *Progesteron-Prophylaxe bei nachgeburtlicher Depression.* Das Untersuchungsergebnis bei 255 Frauen, die an nachgeburtlicher Depression litten, zeigte, daß eine vorbeugende Progesteron-Behandlung in 92% einen Rückfall verhinderte. In der Untersuchtungsreihe waren 96 Frauen, die über ihre letzte Depression schriftlich berichteten, von denen 49 Ideen, ihr Kind zu töten oder Selbstmordgedanken hatten und die Hälfte wegen Psychosen einen Krankenhausaufenthalt hatten. Unter den Frauen, die einen schriftlichen Bericht gaben, wurden nur 6% rückfällig, was zur Annahme führte, daß eine vorbeugende Progesteron-Behandlung sowohl nachgeburtlichen Psychosen als auch Depressionen verhindert.

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In the absence of double blind placebo controlled trials this is yet another survey confirming the beneficial effect of progesterone prophylaxis treatment (PPT) for postnatal depression (PND). But each new survey[1] emphasises previously overlooked facts, as indeed this one does. I intend discussing these new findings, rather than merely show that this new survey gives similar results to previous surveys[2–4] which showed that the expected recurrence rate of 68%[5] can be decreased to between 7 and 10% with PPT.

Throughout the studies the definition of PND has been "the first episode of psychiatric symptoms, severe enough to require treatment, occurring after delivery and before the return of normal menstruation." This definition excludes the blues, but includes puerperal psychosis.

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It is hypothesised that PND represents failure to adapt to changes in hormone levels associated with delivery, lactation and the return of menstruation.

The last decade has seen our understanding of the power of molecular biology. Spiroff et al.[6] mention on their gigantic tome on *Clinical Gynecologic Endocrinology and Infertility*: – "It won't be long before endocrine problems will be explained, diagnosed and treated at a molecular level. Soon the traditional hormone assays will be a medical practice of the past."

This is particularly applicable to PND for the characteristics of progesterone and progesterone receptors are now being appreciated and some of the unique characteristics of progesterone receptors are beginning to be understood[7]. We now know that progesterone is essential for in vitro fertilisation[8]. Also that progesterone molecules need to bind to progesterone receptors before they can be transported to the cell nucleus where they are metabolised[9]. Therefore blood progesterone level estimations do not correlate with progesterone utilisation. Again, it is known that progesterone receptors do not bind to progesterone molecules in the presence of adrenalin[10] or low blood glucose.

The last decade has also increased our understanding of maternal behaviour in vertebrates. Maternal behaviour includes cleaning, feeding, warming and protecting the young immediately after birth. Studies in monkeys, sheep, rabbits, and rodents have shown that maternal behaviour is absent in nulliparus animals, but may be experimentally produced by giving nulliparus females a course of oestrogen and progesterone, such as the placenta would normally have produced[10–14]. More important is the finding that when mice are immunised to produce progesterone antibodies[15] or progesterone receptor antibodies[16] there follows a normal pregnancy and labour, but the mice have lost their maternal behaviour and will reject their newborn or cannibalise them. This suggests that loss of maternal behaviour in animals is similar to PND in humans.

Last year Brian Harris[17] and his team in Cardiff were able to show that women who developed postnatal blues had a salivary progesterone level above normal in late pregnancy, which dropped lower than the norm in the early puerperium. This confirmed a study I did with 14 general practitioners in North London in 1971[18] showing that women who developed PND were those who were very well in late pregnancy. Harris et al.[19] has started a double blind placebo controlled trial of progesterone levls in PND in Cardiff, but results are unlikely to be known for five years.

PPT advises progesterone 100 mg intramuscularly daily for seven days followed by progesterone suppositories 400 mg twice daily for two months or until the return of menstruation. Should there be any suggestion of symptoms returning the dose may be increased to six suppositories 400 mg daily or 100 mg intramuscular daily.

Last year's study[1] covered 281 pregnant women, who had requested information about PPT, and were asked to forward names and addresses of their general practitioners and obstetricians to whom full information was sent. In follow up questionnaires were sent to these women and their medical advisors. Information received covered the outcome of 255 (91%) pregnancies. Eight women aborted. Incomplete PPT was received by 28, and a non-puerperal psychiatric illness had previously occurred in 19. Thus 200 women received full PPT among whom there

Table 1. Letter writers requesting progesterone prophylaxis, n = 96

Suicide attempts	9
Suicidal fears	17
Infanticide	1
Infanticidal fears	12
Hurting	3
Murdering	2
Hitting	2
Shaking	2
Drowning	1
Mutilating	1
Suffocating	1
Violence	10

Table 2. Questionnaires Sent Out

Patients: 255	Missing information	26
	Aborted	8
	Incomplete treatment	28
	Non puerperal illness	19
	No recurrence PND	182

were 17 failures, 14 within three months and 3 later, giving an overall success rate of 92%, within the range of previous studies.

Although women were initially only asked to give the names and addresses of their medical attendants 96 spontaneously included letters giving details of symptoms and 41 of the duration of their previous illness. Hospitalisation for puerperal psychosis may be expected in one in 200 new mothers, and postnatal depression in one in ten. Among these letter writing women an exceptionally high figure of 50% had been hospitalised for psychosis. These women were justifiably apprehensive in asking for help to prevent a recurrence, and were at the severe end of the PND spectrum.

Their previous illness had also been long, with 44% lasting longer than one year.

Most disturbing was the high incidence of fears of infanticide, suicide and violence.

There were vivid descriptions of psychosis with the voices which "must be obeyed", and "the tremendous control needed to overcome the urges" to violence and the fears of infanticide or suicide.

One described sitting in the bath when "my stomach started to churn and felt empty. Suddenly the voices came out of nowhere 'Drown yourself do it, do it.'"

"The voices seemed to be coming constantly telling me to stab myself in the heart."
"I was being told to get a breadknife out of the drawer and stab myself in the heart."
"I wanted to kill myself. All I wanted was to be pregnant again, I felt so empty."

Fortunately among these 96 letter writers there were only six (6%) who experienced a recurrence of their previous illness. This compares with an expected

recurrence rate after hospitalisation for psychosis among 45 women of 84%[5], demonstrating that PPT is even more effective in puerperal psychosis than postnatal depression. This is the message I want you to take home. Progesterone prophylaxis is effective in preventing psychosis.

The memory of homicidal thoughts and fears in a previous pregnancy return when the woman is again pregnant and she makes every effort to prevent a recurrence. Requests for help must be taken seriously. This places on us a responsibility to ensure there is no recurrence of PND or psychosis.

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