*British Journal of Psychiatry* (1989), **154**, 660–667

# The Hormonal Environment of Post-natal Depression

BRIAN HARRIS, SANDRA JOHNS, HEDI FUNG, ROGER THOMAS, RICHARD WALKER, GRAHAM READ AND DIANA RIAD-FAHMY

The incidence of post-natal depression is high, and dramatic changes in steroid hormones and prolactin occur in the post-partum period. In an attempt to correlate these events, 147 mothers, six to eight weeks after delivery of a healthy infant, completed standard psychological tests, including the Edinburgh, Montgomery–Åsberg, and Raskin scales. They also provided matched samples of plasma for assay of cortisol, oestradiol, progesterone and prolactin, and saliva for assay of cortisol and progesterone. All steroid concentrations were within the appropriate normal ranges. Of the mothers, 14.9% were depressed on all three scales. Significant correlations were seen between depression ratings and salivary progesterone and prolactin. In bottle-feeders, salivary progesterone was positively associated with depression, whereas in breast-feeders it was negatively associated. Plasma prolactin levels were inappropriately low in depressed breast-feeders. These data indicate that differing therapies may be appropriate for depression in breast- and bottle-feeders.

All the major population studies of mothers during the year after delivery report a high incidence of post-natal depression. In approximately 300 mothers followed through into the late puerperium after delivery at the London Hospital, the incidence of post-natal depression was 10.8% (Pitt, 1968). Similarly, in a group of 120 mothers screened for depression while attending a routine post-natal clinic six weeks after delivery, Paykel *et al* (1980) found symptoms of mild depression in 20%. The Edinburgh Postnatal Depression Scale (Cox *et al*, 1987) was introduced partly as a screening procedure to aid identification of such patients.

Factors found to be associated with this condition include an increased number of life events during the preceding 12 months, previous psychiatric illness (Paykel *et al*, 1980), marital disharmony (Kumar & Robson, 1984; Watson *et al*, 1984), and a higher level of neurotic symptoms when well (Cox *et al*, 1982).

'Post-partum blues' refers to the minor depressive symptoms which may become more pronounced four days after delivery (Cox *et al*, 1982). This distinctly time-associated phenomenon, which in the study of Paykel *et al* (1980) had an association with subsequent post-natal depression only in the absence of life events, may have an underlying hormonal basis. Certainly, after delivery, major changes occur in circulating concentrations of numerous hormones, including progesterone, oestradiol, cortisol, prolactin, and possibly endorphins. It is conceivable that there may be an association between the fall of progesterone concentrations after delivery and the subsequent onset of depression and anxious mood. Indeed, progesterone therapy has been advocated as a treatment for post-natal depression (Dalton, 1983); but before advocating prophylactic supplementation, it is essential to demonstrate unequivocally that women with post-natal depression have a progesterone deficit. Comparison of progesterone levels in depressed and non-depressed mothers was therefore a major objective of this study.

Attempts to monitor changes in hormone levels before and after delivery have relied almost exclusively on measurement of plasma steroids. Thus the total (protein-bound plus free) progesterone and oestradiol concentrations have been reported (Nott *et al*, 1976) rather than the free, biologically active component of the hormone. When circulating in the blood, progesterone is extensively bound to cortisol-binding globulin (CBG), while oestradiol is bound by sex-hormone-binding globulin (SHBG). Anderson *et al* (1985) have shown that, although total hormone concentrations are greatly increased at the end of pregnancy, plasma 'free' values remain relatively low (progesterone 1.76–2.77%, oestradiol 0.84–2.7%). It is the ratio of free oestradiol to free progesterone that is important as a predictor of labour (Darne *et al*, 1987). Since data relating to changes in 'free' hormone concentrations are sparse, the possibility remains that changes in 'free' biologically active hormone(s) may be of importance in modulating mood.

Saliva is a useful alternative to plasma for the analysis of progesterone and cortisol, particularly since the development of sensitive radioimmunoassays (RIAs), which facilitate precise determination of the low levels of these steroids. It has also been demonstrated that salivary concentrations of most

neutral steroids reflect plasma 'free' levels (Riad-Fahmy *et al*, 1982), and that saliva concentrations reflect those in plasma regardless of the salivary flow rate (Cook *et al*, 1986). In addition, saliva samples are easily collected without causing stress, at home, and thus multiple samples may be obtained in conjunction with assessment of mood (Feksi *et al*, 1984). It appeared worthwhile therefore, to increase the understanding of the possible modulating influence of steroids in post-natal depression by measuring salivary hormone concentrations at a time when some women were depressed, and to compare such data with those derived from a non-depressed group.

## Methods

### Subjects

Over the course of a year (1984–85), 147 mothers were assessed at the Caerphilly District Miners' Hospital, South Wales. The mothers had all had routine bookings for delivery at the hospital: the mean length of gestation was 16 weeks at presentation. The age range of the subjects was 17–40 years (mean 24.6), and parity varied from one to five, with 98 mothers having had children previously. Psychiatric assessment of the mothers was at a routine post-natal follow-up clinic, approximately six to eight weeks after delivery.

The women participating in this study were part of a larger investigation of the role of post-partum thyroid dysfunction (Fung *et al*, 1988). Sixty-five mothers were found to be antibody positive (microsomal and antithyroglobulin), and the remainder were antibody negative. They were otherwise medically unscreened. Application of Pearson correlation matrices to this database failed to demonstrate any association between thyroid-antibody status and non-thyroidal hormone parameters. Of the 147 mothers participating, 138 had vaginal deliveries, and nine had Caesarean sections: no mothers delivered either a stillborn or severely handicapped baby.

#### *Mode of feeding*

At the time of assessment, 29 women stated that they were breast-feeding their babies, whereas 118 were bottle-feeding. In breast-feeders, detailed information regarding the relationship between feeding and sampling time was not requested, since measurement of prolactin, the only hormone known to show gross changes after feeding, was not originally envisaged.

### Psychiatric assessments

Each mother was assessed clinically in the afternoon (13.30–15.00 h) by one experienced psychiatrist (BH). The following questionnaires were also used: the Edinburgh Postnatal Depression Scale (Cox *et al*, 1987), the Raskin 3 Area Scale for Depression (Raskin *et al*, 1970), the Montgomery–Åsberg Depression Rating Scale (Montgomery & Åsberg, 1979), and the Beck Depression Inventory (Beck *et al*, 1961); with cut-off scores of greater than 12 for the Edinburgh scale, greater than 7 for the Raskin scale (Paykel *et al*, 1980), and greater than 11 for the Montgomery–Åsberg scale. A study by Snaith *et al* (1986) indicated that mild depression on the Montgomery–Åsberg scale scored between 7 and 18 (inclusive): thus the cut-off point in the present study represents the mid-point of this range. No cut-off point was used for the Beck Depression Inventory, since it was included only to examine correlations with other scales.

### Sample collection

At the time of psychiatric assessment, six to eight weeks after delivery, a matched blood and saliva sample was collected from each subject. In addition, each mother was provided with a set of plastic tubes (5 ml Z/5, Steralin Ltd, Feltham, England) to be used for collection of a saliva sample at 22.00 h that evening and again at 08.00 h the following morning. These two saliva samples, collected at home, were returned by mail to the laboratory. All samples (plasma and saliva) were stored at −20°C within an hour of receipt. Each mother was sent £2 on receipt of saliva samples and completed questionnaires. To assess the effect of delays in the postal system on steroid concentrations, 20 additional samples of saliva were collected from mothers at 14.00 h. Each sample was divided into two, one half being sent through the post by first-class mail, the other half being deep-frozen within an hour of collection. The matched samples of saliva were subsequently analysed within the same assay, and no significant differences were found for either progesterone or cortisol concentrations.

### Hormone analyses

Plasma progesterone and oestradiol concentrations were determined by direct RIAs using kits supplied by Diagnostic Products Ltd and Steranti Ltd, respectively. However, since plasma progesterone concentrations proved to be at or below the sensitivity of the kit, samples were re-assayed by the more sensitive procedure used for measurement of this steroid in saliva. Measurement of plasma cortisol relied on a direct 'in-house' RIA (Riad-Fahmy *et al*, 1979). Plasma prolactin concentrations were determined at the Supra Regional Assay Service Protein Hormone Laboratory, University of Wales College of Medicine, Cardiff, using an 'in-house' assay.

Salivary progesterone and cortisol were determined using the previously reported procedures of Walker *et al* (1978, 1979).

### Statistical analyses

The data were analysed using the Pearson correlation matrix, and a series of Student's *t*-tests. Since the hormone data showed a skew distribution, logarithmic transformation of the hormonal concentrations was performed,

which resulted in a more normal distribution. Correlations between various parameters were based on slightly differing numbers of subjects, owing to varying rates of compliance.

## Results

All plasma and salivary hormone concentrations were within normal physiological ranges.

### Compliance

Of the 147 women contacted initially at antenatal clinic, 49 failed to keep their post-natal appointment. These women were therefore visited at home, and assessed during the afternoon at approximately the same time as they would have been at the post-natal appointment clinic. Only 20 mothers did not return their saliva samples and home questionnaires, while one other could not be contacted as she had left the area.

### Relationship between plasma and salivary steroid concentrations

Matched plasma and saliva samples were provided by 132 subjects at approximately 15.00 h. Using the Pearson correlation matrix, cortisol concentrations were significantly related ($P<0.001$, $r=0.50$) as were progesterone concentrations ($P<0.001$, $r=0.451$).

### The correlation of psychometric indices

As might be expected, the correlations between the Edinburgh, Raskin, and Montgomery–Åsberg scales were all found to be highly significant: Edinburgh/Raskin ($r=0.80$, $P<0.001$), Raskin/Montgomery–Åsberg ($r=0.92$, $P<0.001$). The Beck scale correlated well with other scales, but the associations were weaker: Beck/Edinburgh ($r=0.68$, $P<0.001$), Beck/Raskin ($r=0.62$, $P<0.001$), and Beck/Montgomery–Åsberg ($r=0.61$, $P<0.001$).

### Categorisation based on cut-off points for psychometric indices

Analysis of the questionnaires showed that 14.9% of patients were depressed on the three questionnaires, an additional 4.9% were depressed on two questionnaires, and a further 9% had depressive symptoms on one questionnaire only. For individual questionnaires the rates were: Edinburgh 22%; Raskin 25%; Montgomery–Åsberg 17%. Moreover, the rates of depression in breast- and bottle-feeders were similar (e.g. Edinburgh scale: 19% and 23% respectively).

There were no discrepancies in the categorisation of patients; those scoring above the cut-off point on all three questionnaires were all judged to be depressed on clinical assessment.

### Hormonal v. psychometric indices

Data derived by measurement of plasma and salivary hormones in the various subgroups of depressed and non-depressed women are summarised in Table I. It is apparent that although hypercortisolaemia has been implicated in depression, this study revealed no consistent differences in either plasma or salivary cortisol concentrations between depressed and non-depressed women. Plasma oestradiol concentrations also showed no consistent differences between depressed and non-depressed women. The higher concentrations of this steroid in bottle-feeding women not taking a contraceptive pill are explicable in terms of their earlier resumption of follicular maturation. In marked contrast to cortisol and oestradiol, progesterone and prolactin concentrations were associated with differences in mood. These associations are detailed in Tables II and III respectively.

#### *Salivary progesterone*

The application of a series of Student's *t*-tests to the salivary progesterone data revealed no consistent differences between the mean concentrations in depressed and non-depressed women. Salivary progesterone concentrations at the three sampling times were most frequently associated on a Pearson correlation matrix with Beck scores. Data presented in Table II indicate that in bottle-feeders there was a positive association of progesterone with depressive symptoms: the reverse was true for breast-feeders.

#### *Plasma prolactin*

In the total population, depression was significantly associated with decreased prolactin concentrations (Table III). In the non-depressed subgroups, the finding of consistently higher prolactin levels in breast-feeders is in keeping with consensus views on the stimulus of suckling. The significantly lower prolactin concentrations in the majority of subgroups of depressed women is noteworthy.

## Discussion

It is reasonable to hypothesise that post-partum mood changes are linked to the changing concentrations of steroid hormones such as progesterone, oestradiol and cortisol, and possibly to variation in prolactin levels. Cortisol concentrations rise during pregnancy and, after delivery, there is a dramatic fall. There is approximately a 100-fold fall in plasma progesterone in the few days after delivery and a tenfold fall in oestradiol in the 24 hours after delivery (Butler & Leonard, 1986). As the menstrual cycle becomes re-established, there is firstly an increase in oestradiol, and then a later increase in progesterone. Prolactin levels rise during pregnancy, rise further after delivery, and thereafter levels are dependent on the mode of feeding, remaining high where breast-feeding is established.

TABLE I
*Hormonal parameters in samples collected at 1500 h by post-partum women*

| | *On contraceptive pill* | | | | | | | | *Not on contraceptive pill* | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Depressed*[1] | | | | *Non-depressed* | | | | *Depressed*[1] | | | | *Non-depressed* | | | |
| | *Mean*[2] | *+s.d.* | *−s.d.* | n | *Mean*[2] | *+s.d.* | *−s.d.* | n | *Mean*[2] | *+s.d.* | *−s.d.* | n | *Mean*[2] | +s.d. | −s.d. | n |
| *Bottle-feeders* | | | | | | | | | | | | | | | | |
| Plasma cortisol: nmol/l | 357 | 531 | 240 | 6 | 236 | 402 | 139 | 18 | 150 | 249 | 90.5 | 9 | 192 | 359 | 103 | 70 |
| Saliva cortisol: nmol/l | 6.83 | 14.2 | 3.27 | 7 | 5.32 | 9.98 | 2.84 | 22 | 3.00 | 6.83 | 1.32 | 10 | 6.09 | 11.8 | 3.15 | 73 |
| Plasma progesterone: nmol/l | 0.923 | 5.11 | 0.167 | 7 | 0.356 | 0.750 | 0.169 | 20 | 1.23 | 7.32 | 0.21 | 9 | 0.94 | 3.75 | 0.23 | 71 |
| Saliva progesterone: pmol/l | 95.2 | 378 | 24.0 | 7 | 57.1 | 132 | 24.7 | 22 | 123 | 358 | 42.2 | 10 | 88.5 | 210 | 37.2 | 71 |
| Plasma oestradiol: pmol/l | 37.2 | 86.7 | 15.9 | 7 | 46.7 | 98.9 | 22.1 | 20 | 199 | 684 | 58 | 10 | 210 | 502 | 88 | 71 |
| *Breast-feeders* | | | | | | | | | | | | | | | | |
| Plasma cortisol: nmol/l | — | — | — | 0 | 159 | 303 | 83.5 | 11 | 129 | 304 | 54.7 | 3 | 225 | 394 | 128 | 14 |
| Saliva cortisol: nmol/l | — | — | — | 0 | 5.51 | 8.01 | 3.79 | 11 | 6.49 | 8.41 | 5.00 | 3 | 5.72 | 15.5 | 2.11 | 14 |
| Plasma progesterone: nmol/l | — | — | — | 0 | 0.484 | 1.04 | 0.226 | 11 | 0.329 | 0.601 | 0.180 | 3 | 0.538 | 1.33 | 0.218 | 14 |
| Saliva progesterone: pmol/l | — | — | — | 0 | 79.4 | 300 | 21.0 | 10 | 55.4 | 139 | 22.2 | 2 | 82.8 | 239 | 28.7 | 13 |
| Plasma oestradiol: pmol/l | — | — | — | 0 | 58.4 | 114 | 29.9 | 11 | 84.3 | 175 | 44.1 | 3 | 75.6 | 138 | 41.3 | 14 |

1. Depressed = women scoring above cut-off points on Edinburgh, Raskin *or* Montgomery–Åsberg scales.
2. Geometric mean.

TABLE II

*Psychometric variables significantly associated with salivary progesterone concentrations (pmol/l) in samples collected at stated times*

| *Population* | *Time* | *Depression variable* | n | r *value*[1] | *Significance (P)* |
|---|---|---|---|---|---|
| Overall | 08.00 | Beck | 126 | 0.24 | 0.05 |
| Bottle-feeders | | | | | |
| (all) | 08.00 | Beck | 99 | 0.36 | 0.001 |
| | 15.00 | Beck | 96 | 0.31 | 0.002 |
| | 22.00 | Beck | 99 | 0.22 | 0.05 |
| Bottle-feeders | | | | | |
| (− pill) | 08.00 | Beck | 72 | 0.28 | 0.05 |
| Bottle-feeders | | | | | |
| (+ pill) | 08.00 | Beck | 26 | 0.56 | 0.003 |
| | | Edinburgh | 20 | 0.45 | 0.04 |
| | | Raskin | 27 | 0.48 | 0.01 |
| | | Montgomery–Åsberg | 27 | 0.55 | 0.003 |
| | 15.00 | Beck | 26 | 0.46 | 0.02 |
| Breast-feeders | | | | | |
| (all) | 08.00 | Edinburgh | 25 | −0.40 | 0.05 |
| | 15.00 | Beck | 26 | −0.54 | 0.01 |
| | 22.00 | Edinburgh | 25 | −0.44 | 0.05 |
| | 22.00 | Raskin | 27 | −0.41 | 0.05 |
| | 22.00 | Montgomery–Åsberg | 27 | −0.57 | 0.01 |
| | 22.00 | Beck | 27 | −0.57 | 0.01 |
| Breast-feeders | | | | | |
| (− pill) | 15.00 | Beck | 16 | −0.63 | 0.01 |
| | 22.00 | Edinburgh | 15 | −0.65 | 0.01 |
| | 22.00 | Raskin | 17 | −0.55 | 0.05 |
| | 22.00 | Montgomery–Åsberg | 17 | −0.68 | 0.01 |
| | 22.00 | Beck | 17 | −0.66 | 0.01 |
| Breast-feeders | | | | | |
| (+ pill) | 08.00 | Raskin | 10 | −0.65 | 0.05 |
| | 08.00 | Montgomery–Åsberg | 10 | −0.74 | 0.05 |
| | 15.00 | Montgomery–Åsberg | 10 | −0.64 | 0.05 |

1. Correlation coefficients were calculated for all psychometric variables v. salivary progesterone at all sampling times. Only correlations significant at $P<0.05$ are shown.

Evidence implicating steroid hormones in behavioural change comes from a number of sources. Animal studies have shown that progesterone has an anxiolytic action in the oestrogen-primed female rat, but not in the androgenised or eunuchoid rat (Rodriguez-Sierra *et al*, 1986). Again, oestrogens in the ovariectomised rat can produce lordosis behaviour, and the rate at which this behaviour is produced can be varied by administration of progesterone (McEwen & Parsons, 1982). These changes in behaviour with changing steroid concentrations are thought to be linked to the central nervous system (CNS) via the hypothalamus (McEwan & Pfaff, 1985).

At the cellular level, oestrogens and progesterone are related to receptor levels on the surfaces of lymphocytes and platelets. The number of lymphocyte $\alpha$-adrenoreceptors falls after childbirth, corresponding to a fall in the circulating levels of oestrogen and progesterone (Metz *et al*, 1983). Although of interest, peripheral models need not necessarily reflect events in the CNS. In rabbits, oestrogen treatment caused a significant decrease in $\alpha$-adrenoreceptor number and function in platelets, but not in brain preparations (Mishra *et al*, 1985). In addition, Biegon *et al* (1983) report that, in the ovariectomised female rat, oestrogen induces a reduction in $5HT_1$ receptors and $\beta$-adrenergic receptors, with a concomitant increase in $5HT_2$ receptors. By contrast, progesterone alone increased $5HT_2$ and decreased $5HT_1$ receptors, but was without significant effect on noradrenergic receptors. When given with oestrogen, progesterone blocked the oestrogen-mediated increase in $5HT_2$ receptors, but did not inhibit the decrease in $5HT_1$ receptors or in $\beta$-adrenergic receptors.

Biegon *et al* (1983) emphasise that $\beta$-adrenergic and $5HT_2$ receptors are implicated in antidepressant action. Thus the modulation of these two receptor

https://doi.org/10.1192/bjp.154.5.660 Published online by Cambridge University Press

TABLE III
*Prolactin concentrations (mU/l) in samples collected at 15.00 h by post-partum women*

| *Population* | *Depressed* | | | | *Non-depressed* | | | | P[1] |
|---|---|---|---|---|---|---|---|---|---|
| | *Mean* | *+s.d.* | *−s.d.* | n | *Mean* | *+s.d.* | *−s.d.* | n | |
| Overall | 232 | 387 | 139 | 32 | 337 | 787 | 145 | 64 | 0.008 |
| Bottle-feeders (all) | 208 | 321 | 135 | 26 | 246 | 410 | 148 | 52 | NS |
| Breast-feeders (all) | 373 | 675 | 206 | 6 | 1322 | 2483 | 704 | 12 | 0.002 |
| Bottle-feeders (+pill) | 256 | 394 | 166 | 7 | 205 | 348 | 121 | 10 | NS |
| Bottle-feeders (−pill) | 189 | 290 | 124 | 18 | 257 | 425 | 156 | 42 | 0.021 |
| Breast-feeders (−pill) | 254 | 376 | 172 | 3 | 1524 | 3234 | 718 | 7 | 0.002 |

[1] Significance of the differences between polactin concentrations in the depressed and non-depressed subgroups.

types by steroid hormones might be relevant to hormone-linked affective changes in the premenstrual and post-partum periods. Data from clinical studies indicating the importance of steroid hormones in affective disorders are, as yet, limited. In an open study, Dalton (1983) claims to have reduced the incidence of post-natal depression by giving daily prophylactic progesterone immediately after delivery for two months or until menstruation returned. Oestrogen has also been used, with some success, for treating persistently depressed women, in double-blind trials with placebo (Klaiber *et al*, 1979). These authors produced evidence that oestrogen therapy is related in such cases to monoamine oxidase activity.

Despite these clinical findings, studies that have assessed steroid levels in the context of post-natal depression have failed to provide major findings. In an early study, Handley *et al* (1980) showed a minor association of puerperally depressed mood with high cortisol at 38 weeks' gestation. However, the same group later found no association between post-natal depression and plasma cortisol, oestrogen, or progesterone levels (Gard *et al*, 1986). Similarly, Nott *et al* (1976) found no association of mood in late pregnancy or the puerperium with plasma oestrogen and progesterone levels. More recently, Butler & Leonard (1986) found no association of plasma progesterone, oestradiol, or cortisol with depressed mood six to eight weeks post-partum.

By contrast, it is known that hypersecretion of cortisol is associated with 'endogenous types' of depression (Carroll *et al*, 1981). It has been hypothesised (Railton, 1961) that withdrawal of cortisol follows delivery, and that this drop in cortisol is a factor in producing post-natal depression. Railton has, in fact, administered prednisolone, and claims to have successfully treated post-natal depression. The present study provided no evidence for an association between plasma cortisol and depression. The only obvious finding was an elevation in plasma cortisol levels in bottle-feeders on the pill compared with those not taking contraceptive preparations. This is in accordance with the induced synthesis of CBG by synthetic oestrogens (Durber & Daly, 1976). Similar differences were neither found nor expected in breast-feeders, since this group would probably be taking a progestin-only preparation.

During the puerperium, major changes occur in circulating concentrations of binding proteins modulated both by changes in endogenous oestradiol, and by administered oestrogen-containing contraceptive preparations. Since the plasma 'free' steroids are generally accepted to be the biologically active moiety, measurement of this fraction is desirable but technically difficult. Salivary-based studies obviate these difficulties. The differing concentrations of binding proteins in puerperal subjects are reflected in the reduction in the coefficient ($r$) seen in correlations between salivary and plasma concentrations of the steroids, progesterone and cortisol. Thus, in the present study, the $r$ values for both steroids were approximately 0.5 compared with $r$ values $>0.9$ observed in studies of non-puerperal subjects (Walker *et al*, 1979; Vining *et al*, 1983).

Although saliva samples were collected at three time points, no consistent differences in salivary cortisol were seen between depressed and non-depressed subjects in any subgroup at any time point; thus only data derived from 15.00 h samples are shown in Table I. Data relating to salivary progesterone are of rather greater interest. In bottle-feeders, salivary progesterone at each time point correlated positively with several indices of depression, whereas in breast-feeders, salivary progesterone correlated negatively with such indices. These data

therefore serve to emphasise the need for a clear distinction to be made in the treatment regimes advocated for women who breast-feed and those who bottle-feed. A deficit of progesterone is suggested in the depressed breast-feeding mothers. This appears to be confirmed by the lower incidence of depression in breast-feeders who take contraceptive preparations and, therefore, receive progestins. Thus there would appear to be some basis for advocating additional progesterone as a prophylactic measure against post-partum depression in breast-feeders. In the group of bottle-feeders, the converse holds true: depression is correlated positively with salivary progesterone. Furthermore, the incidence of depression in bottle-feeders taking the pill (24%), and thus receiving additional progestin, is higher than that in bottle-feeders not taking the pill (12%). These data militate against administering progesterone supplements in bottle-feeders.

These differing associations of progesterone and depression ratings in the two feeding groups prompted retrospective analysis of prolactin levels (Table III). There was also a significant difference in prolactin levels between the breast-feeders who were and were not depressed. In effect, concentrations of prolactin in depressed breast-feeders were at levels more appropriate for bottle-feeders. In breast-feeders there was a negative association between prolactin and depression ratings, but the association achieved significance only for the Edinburgh scale ($r = -0.66$; $P = 0.003$). While it is appreciated that the numbers of depressed breast-feeders are small, and that sampling time in this retrospective study was not controlled with regard to the last breast-feed, the much lower absolute concentrations of prolactin in the depressed mothers suggests it would be worthwhile to confirm these findings in a larger prospective study.

Lack of knowledge regarding the aetiology of post-natal depression makes rational prophalaxis or treatment difficult. Since this condition, like those of post-partum blues and pre-menstrual tension, occurs at times when circulating steroid concentrations are rapidly changing, frequent sampling is required to facilitate understanding of the complex aetiology of these conditions. Salivary-based investigations coupled with the use of simple psychiatric scores appear well suited for resolving such current psychiatric problems.

### Acknowledgements

The authors would like to thank the Tenovus Organisation for its support, and Professor K. Griffiths for advice and encouragement. Their gratitude is expressed to Dr Robert Newcombe (Department of Medical Statistics, UWCM) for his help with the statistical analyses.

### References

ANDERSON, P. J. B., HANCOCK, K. W. & OAKEY, R. E. (1985) Non-protein bound oestradiol and progesterone in human peripheral plasma before labour and delivery. *Journal of Endocrinology*, **104**, 7–15.

BECK, A. T., WARD, C. H., MENDELSON, M., *et al* (1961) An inventory for measuring depression. *Archives of General Psychiatry*, **4**, 561–571.

BIEGON, A., RECHES, A., SNYDER, L., *et al* (1983) Serotonergic and noradrenergic receptors in the rat brain: modulation by chronic exposure to ovarian hormones. *Life Sciences*, **32**, 2015–2021.

BUTLER, J. & LEONARD, B. E. (1986) Postpartum depression and the effect of nomifensine treatment. *International Clinical Psychopharmacology*, **1**, 244–252.

CARROLL, B. J., FEINBERG, M., GREDEN, J. F., *et al* (1981) A specific laboratory test for the diagnosis of melancholia. *Archives of General Psychiatry*, **38**, 15–22.

COOK, N., HARRIS, B., WALKER, R., *et al* (1986) Clinical utility of the dexamethasone suppression test assessed by plasma and salivary cortisol determinations. *Psychiatry Research*, **18**, 143–150.

COX, J. L., CONNOR, Y. & KENDELL, R. E. (1982) Prospective study of the psychiatric disorders of childbirth. *British Journal of Psychiatry*, **140**, 111–117.

——, HOLDEN, J. M. & SAGOVSKY, R. (1987) Detection of postnatal depression – development of the 10 item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry*, **150**, 782–786.

DALTON, K. (1983) Prophylactic progesterone treatment for postnatal depression. *Abstracts of Marce Society Annual Meeting*. London: Marce Society.

DARNE, J., MCGARRIGLE, H. H. G. & LACHELIN, G. C. L. (1987) Increased saliva oestradiol to progesterone before idiopathic pre-term delivery, a possible predictor for pre-term labour. *British Medical Journal*, **294**, 270–272.

DURBER, S. M. & DALY, J. R. (1976) A simple method for the determination of free cortisol in plasma, with normal levels in men and women, incuding women taking low-oestrogen contraceptives. *Clinica Chimica Acta*, **68**, 43–48.

FEKSI, A., HARRIS, B., WALKER, R. F., *et al* (1984) "Maternity blues" and hormone levels in saliva. *Journal of Affective Disorders*, **6**, 351–355.

FUNG, H. Y. M., KOLOGLU, M., COLLISON, K., *et al* (1988) Post partum thyroid dysfunction in Mid Glamorgan. *British Medical Journal*, **296**, 241–244.

GARD, P. R., HANDLEY, S. L., PARSONS, A. D., *et al* (1986) A multivariate investigation of post-partum mood disturbance. *British Journal of Psychiatry*, **148**, 567–575.

HANDLEY, S. L., DUNN, T. L., WALDRON, G., *et al* (1980) Tryptophan, cortisol and puerperal mood. *British Journal of Psychiatry*, **136**, 498–508.

KLAIBER, E. L., BROVERMAN, D. M., VOGEL, W., *et al* (1979) Oestrogen therapy for severe persistent depressions in women. *Archives of General Psychiatry*, **36**, 550–554.

KUMAR, R. & ROBSON, K. M. (1984) A prospective study of emotional disorders in childbearing women. *British Journal of Psychiatry*, **144**, 35–47.

MCEWEN, B. S. & PARSONS, B. (1982) Gonadal steroid action on the brain: neurochemistry and neuropharmacology. *Annual Review of Pharmacology and Toxicology*, **22**, 555–598.

—— & PFAFF, D. W. (1985) Hormone effects on hypothalamic neurons: analysing gene expression and neuromodulator action. *Trends in Neurosciences*, **8**, 105–110.

METZ, A., STUMP, K., COWEN, P. J., *et al* (1983) Changes in platelet alpha 2-adrenoceptor and 2-adrenoceptor binding postpartum. Possible relation to maternity blues. *Lancet*, *i*, 495–498.

MISHRA, N., HAMILTON, C. A., JONES, C. R., *et al* (1985) Adrenoceptor changes after oestrogen treatment in platelets and other tissues in female rabbits. *Clinical Science*, **69**, 235–238.

MONTGOMERY, S. A. & ÅSBERG, M. (1979) A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*, **134**, 382–389.

NOTT, P. N., FRANKLIN, M., ARMITAGE, C., *et al* (1976) Hormonal changes and mood in the puerperium. *British Journal of Psychiatry*, **128**, 379–383.

PAYKEL, E. S., EMMS, E. M., FLETCHER, J., *et al* (1980) Life events and social support in puerperal depression. *British Journal of Psychiatry*, **136**, 339–346.

PITT, B. (1968) Atypical depression following childbirth. *British Journal of Psychiatry*, **114**, 1325–1335.

RAILTON, I. E. (1961) The use of corticoids in post-partum depression. *Journal of the American Medical Women's Association*, **16**, 450–452.

RASKIN, A., SCHULTERBRANDT, J., REATIG, N., *et al* (1970) Differential response to chlorpromazine, imipramine and placebo. A study of sub-groups of hospitalised depressed patients. *Archives of General Psychiatry*, **23**, 164–173.

RIAD-FAHMY, D., READ, G. F., GASKELL, S. J., *et al* (1979) A simple direct radio-immunoassay for plasma cortisol featuring a $^{125}I$ radio-ligand and a solid-phase separation technique. *Clinical Chemistry*, **25**, 665–668.

——, ——, WALKER, R. F., *et al* (1982) Steroids in saliva for assessing endocrine function. *Endocrine Reviews*, **3**, 367–395.

RODRIGUEZ-SIERRA, J. F., HAGLEY, M. T. & HENDRICKS, S. E. (1986) Anxiolytic effects of progesterone are sexually dimorphic. *Life Sciences*, **38**, 1841–1845.

SNAITH, R. P., HARROP, F. M., NEWBY, D. A., *et al* (1986) Grade scores of the Montgomery–Åsberg depression and the clinical anxiety scales. *British Journal of Psychiatry*, **148**, 599–601.

VINING, R. F., MCGINLEY, R. A., MAKSVYTIS, J. J., *et al* (1983) Salivary cortisol: a better measure of adrenal cortical function than serum cortisol. *Annals of Clinical Biochemistry*, **20**, 329–335.

WALKER, R. F., RIAD-FAHMY, D. & READ, G. F. (1978) Adrenal status assessed by direct radioimmunoassay of cortisol in whole saliva or parotid fluid. *Clinical Chemistry*, **24**, 1460–1463.

——, READ, G. F. & RIAD-FAHMY, D. (1979) Radioimmunoassay of progesterone in saliva: application to the assessment of ovarian function. *Clinical Chemistry*, **25**, 2030–2032.

WATSON, J. P., ELLIOTT, S. A., RUGG, A. J., *et al* (1984) Psychiatric disorder in pregnancy and the first postnatal year. *British Journal of Psychiatry*, **144**, 453–462.

*Brian Harris, BSc, MBS, DPM, MRCPsych, *Consultant Psychiatrist, Department of Psychological Medicine, University Hospital of Wales, Cardiff*; Sandra Johns, MB, ChB, MRCPsych, *Consultant Psychiatrist, Cefn Coed Hospital, Swansea*; Hedi Fung, MB, ChB, MD, *Registrar in Obstetrics, King's College Hospital Group, Denmark Hill, London SE5 9RS*; Roger Thomas, MB ChB, MRCPsych, *Consultant Psychiatrist, Whitchurch Hospital, Cardiff*; Richard Walker, PhD, *Senior Biochemist, Tenovus Institute, University of Wales College of Medicine*; Graham Read, PhD, *Senior Biochemist, Tenovus Institute, University of Wales College of Medicine*; Diana Riad-Fahmy, PhD, DSc, *Top Grade Biochemist, Tenovus Institute, University of Wales College of Medicine, Heath Park, Cardiff*

*Correspondence