Acta psychiat. scand. (1979) *60*, 449–464

Department of Psychiatry (Chairman: *Albert J. Silverman*, M.D.), University of Michigan, Ann Arbor, Michigan, U.S.A.

Psychobiology of mental disorders associated with childbearing

AN OVERVIEW

M. STEINER

The diagnostic issues, classification, incidence, genetic factors, and theories of etiology of psychiatric illness associated with childbirth are reviewed. Psychologic influences, psychosocial factors and the concept of biologic maladaptation associated with prospective motherhood are discussed.

Postpartum mental distress is not a unitary phenomenon. The physiology of the puerperium is thus not a cause in itself of any of the symptoms, but rather must be regarded as a contributing or triggering factor acting upon an underlying predisposition.

Clinical research of postpartum psychiatric syndromes (PPS) and animal behavior studies are inconclusive.

It is suggested that major neuroendocrine research strategies currently used in studying affective disorders and schizophrenia should be applied in studying PPS.

Key words: Animal behavior – postpartum psychiatric syndromes (PPS) – psychoneuroendocrinology – psychosocial.

Normal pregnancy, delivery and lactation are associated with major psychological, physiological, anatomical, biochemical and endocrinological changes. To understand the clinical problems related to childbearing, the normal pattern of functional changes, as well as their disturbances, must be examined. In recent years, growing interest and attention have been devoted to neuroendocrine function in mental disorders, especially the hypothalamic-pituitary-adrenal (HPA) and the hypothalamic-pituitary-gonadal (HPG) systems (*Carroll* (1978)). Changes along the HPA axis as well as along the HPG axis are known to occur during the postpartum period (*Hamburg et al.* (1968), *Yalom et al.* (1968), *Dalton* (1971), *Nott et al.* (1976)). The relationship between these changes and psychosocial as well as psychopathological changes occurring concomitantly has not yet been established. This overview will be limited to the current state of clinical and psychoneuroendocrine knowledge in the disorders regarded as postpartum psychiatric syndromes (PPS). I shall deal largely with clinical studies together with some basic investigations.

DIAGNOSTIC ISSUES

The diagnostic criteria and classification of psychiatric illness associated with

0001–690X/79/100449–16$02.50/0

childbirth have been reconsidered many times over the past two decades. Numerous reviews (*Hamilton* (1962), *Huhn & Drenk* (1973), *Pitt* (1975), *Herzog & Detre* (1976)) as well as large scale longitudinal studies (*Jansson* (1964), *Protheroe* (1969)) have addressed themselves to the history and development of the "postpartum" concept in psychiatric nosology. It is generally accepted today that PPS can no longer be viewed as entities *per se*. At one end of the spectrum "maternity blues" are regarded as a "trivial, fleeting phenomenon, so common as to be regarded as normal" (*Pitt* (1973)). The main symptoms are mild depression, anxiety, and minimal clouding of consciousness. The peak incidence is around the third postpartum day, the symptoms lasting from hours to a couple of days, usually disappearing without any treatment or intervention. At the other end of that same spectrum we find different forms of mental illness associated with childbirth that resemble similar illnesses developing at any other period in life. Thus the classification by diagnosis of a severe psychotic PPS, usually requiring hospitalization, will be mainly within the range of the affective disorders and the schizophrenias. This is already reflected in the recent draft of the DSM-III (American Psychiatric Association (1978)). Under the heading of "Psychoses not elsewhere classified" it is suggested that: "Postpartum psychoses" that *do not* meet the criteria for an Organic Mental Disorder, Schizophreniform Disorder, Paranoid Disorder or Affective Disorder should be included under Atypical Psychosis. The non-psychotic "milder" reactions are respectively categorized within the neurotic-personality type disorders. According to this view childbearing may act as a precipitating factor or a trigger mechanism to almost any kind of mental illness.

There seems to be yet another distinct, very much disputed, PPS which is favored in the European literature as a separate entity. This postpartum clinical phenomenon is described very much as resembling a mild acute organic brain syndrome. The symptoms observed are: inability to sustain attention, distractability, poor recent memory, labile mood, confusion, bewilderment and transient delirious states (*Jansson* (1968), *Kane et al.* (1968)). These clinical pictures are sometimes referred to as amential or pseudoamential states. It is claimed that for this group of patients the title "Postpartum psychosis" should be maintained (*Huhn & Drenk* (1973)). For most other cases, standard psychiatric categories are appropriate, the only problem being that "old names die hard".

INCIDENCE

The incidence of "normal" maternity blues was shown to be as high as 50–80 % in some studies (*Pitt* (1973)). The incidence of psychiatric illness associated with childbearing is usually believed to be around 3 % (*Ryle* (1961), *Tod* (1964)), but observations of a much higher incidence up to 10.8 % have also been reported (*Pitt* (1968)). Much of the controversy can be attributed to the time factor and to the heterogeneous diagnostic criteria used in different studies. The differentiation between puerperal reactions (within the first 6 weeks postpartum) and lactational reactions (late onset of the illness – 6 weeks up to 3 or even 6 months postpartum) still causes a diagnostic dilemma. There seems to be a

great confusion as to the time limits for including or excluding patients in the postpartum category. But even if we agree that in some cases at least the onset of a psychiatric disorder (or its recognition) probably simply coincides with the obstetric event rather than results from it, the incidence is high. Mental illness following one in 30 deliveries in a given general population (*Tod* (1964)), let alone one in 10 in a teaching hospital (*Pitt* (1968)), is quite a sizeable incidence. Evidence was also produced to show that endogenous depression was five times more likely in the puerperium than at other times in women of this age-group (*Ryle* (1961)).

GENETIC FACTORS

Heredity seems to play little part in conditions clinically described as postpartum confusion or delirium. A genetic role in the PPS described as schizophreniform or affective in nature is much greater. A frequency of "positive heredity" as high as 32 % was found in one study (*Huhn & Drenk* (1973)). The highest proportion recorded in the literature was 65 % (*Osterman* (1963)). No specific details were given in these studies as to the nature of the psychiatric disorders included nor to the "degree" of the relatives involved.

Melges (1968) reports on 51 % of the women in his study that knew of severe PPS among their relatives (more than half of them for their mothers and sisters). There is only one anecdotal report on PPS in identical twins (*Kane* (1968)). In a recent controlled longitudinal study (*Thuwe* (1974)) the frequency of psychiatric disorders in children of women who have been under treatment for PPS, was found to be 47 %, and 58 % when grandchildren were added. About half of these probands were treated as inpatients in psychiatric hospitals. This work provides some evidence of genetic factors in the general category of PPS. Disregarding this etiologically heterogeneous group it seems to be at least suggestive of a dominant transmission playing some part in the operation of these genetic factors. None of the genetic studies to date seem to be conclusive regarding this question.

PPS and affective disorders. Many investigators point to a close relation between manic-depressive disorders and affective reactions associated with labor. Women suffering from an affective disorder, diagnosed independently of the postpartum period, risk a 10–40 % chance of having an episode of affective disorder during the postpartum period (*Bratfos & Haug* (1966), *Reich & Winokur* (1970)). The rates of risk in the unipolar group seem to be lower than in bipolar patients (*Baker et al.* (1971)). Women with bipolar illness were found to be three and one-half times more likely to have a depressive or manic postpartum episode than at any other time in their lives (*Reich & Winokur* (1970)). In some previously known bipolar women a change in their cycling pattern was noticed, i.e. during the postpartum period they behaved more like rapid cyclers (*Herzog & Detre* (1974)). A prospective study through pregnancy and puerperium revealed an evolution of mood changes in women who later developed puerperal depression which was characterized by anxiety in the first trimester, elation during later

pregnancy and depression in the puerperium. These women also had a higher incidence of premenstrual depression following the puerperal depression (*Dalton* (1971)).

PPS and schizophrenia. The course and prognosis of puerperal schizophrenia seems to follow the same pattern as in non-puerperal schizophrenics. First degree relatives of probands developing puerperal schizophrenia have the same morbidity risk for non-puerperal schizophrenia as expected among relatives of non-puerperal schizophrenics. Nevertheless, the chance for any particular puerperal schizophrenic woman to develop a second schizophrenic episode following further pregnancies is as great as 1 in 5 (*Protheroe* (1969)).

Several reports support the view that the onset, course, and outcome of puerperal schizophrenia are determined by a physiological interaction between mother and fetus (*Shearer et al.* (1967), *Taylor* (1969)). No such causal relationship was found in a replication study which tried to further test this hypothesis (*Schorer* (1972)). The ratio of affective to schizophreniform postpartum illness ranges from 1:1.5 to 1:5 in the American literature (*Brew & Seidenbert* (1950), *Oswald & Regan* (1957)) whereas in the British literature the ratio is closer to 3.3:1 (*Martin* (1958), *Protheroe* (1969)). Similar findings of a higher ratio of postpartum affective to schizophrenic illness were also reported later by *Herzog & Detre* (1974). This study seems to be in better agreement with the incidence of affective versus schizophrenic illness in the general population which has been reported as being at least 4–8:1 (*Fieve* (1973)).

THEORIES OF ETIOLOGY

Psychosocial factors

Sociocultural attitudes toward puerperium. Taboos and superstitions regarding puerperium, although rare, are still represented in various forms in modern society. Cross-cultural studies have shown that society's attitude towards sexuality in general has a direct influence upon beliefs regarding labor and birth. The more positive the attitudes towards sexuality, the easier and more effectively functioning are all the operations and processes of early motherhood (*Gadpaille* (1975)). The husband's psychosocial supportive role and his physical as well as mental involvement in the event of childbearing have already been recognized as critical issues. Concern has also been recently expressed that modern obstetric practice and changes in the provision of maternity services tend to neglect the psychological perinatal needs of mothers (*Bardon* (1973)).

Psychologic influences. The puerperium acts to a greater or lesser degree as a stress which may induce or precipitate any form of psychological disturbance in the predisposed woman (*Ryle* (1961)). Although there seems to be no direct correlation between neuroticism *per se* and PPS (*Meares et al.* (1972)), many psychological determinants are involved. Changes in body image, activation of unconscious intrapsychic conflicts and the emotional reorganization required to become a mother are all part of the normal ego functions and adjustments made during each pregnancy.

Some of the important factors in the dynamics of psychopathology that have been described and studied are: ambivalent identification with the patient's own mother, overidentification with the newborn baby, unresolved sexual identification, hostility towards the infant, fear of object loss, and identity diffusion (*Osterman* (1963)). Additional significant contributing factors are low tolerance to pain and suffering associated with previous deliveries and with dysmenorrhea, marital conflict with lack of feedback from husband, and an ambivalent attitude towards the pregnancy, especially if unplanned (*Nilsson* (1970), *Nilsson & Almgren* (1970)).

Mild anxiety should be accepted as a normal accompaniment of pregnancy and parturition whereas the presence of pathological anxiety during pregnancy appears to be a hallmark for the development of a PPS (*Tod* (1964)). With the development of modern and sophisticated maternity care most of the physical, medical, and gynecological complications around the perinatal period are now less important as contributing factors to the development of PPS.

Observations on human maternal behavior have focused on reciprocal behavior patterns developing very early in the relationship between mother and infant (*Thoman* (1975)). Ethologists claim that human maternal behavior does not differ from the observed pattern of nesting, retrieving, grooming, and exploring as seen in nonhuman mammalian mothers immediately before, during and after delivery. In home births when the mothers are active participants in delivery, they pick up the infant, examine its body with their fingertips and start breastfeeding within the first minutes after delivery (*Klaus et al.* (1975)). It is still common practice on most maternity units to separate infant from mother for at least several hours postpartum. It seems now as if this routine has a rather disruptive effect on normal maternal behavior patterns. Whether this adds just another stressful contributory factor to the development of postpartum psychopathology is still in debate.

It is hypothesized that PPS occur in women whose personality patterns and genetic predisposition render them selectively vulnerable to the prospective mothering task. As stated by *Rosenwald & Stonehill* (1972) postpartum psychoses seem to be a psychologically heterogeneous category held together by a concept of biologic maladaptation.

Physiologic factors

Two concepts must be borne in mind when the physiology of PPS is discussed. In the first place, as has already been mentioned, postpartum mental distress is not a unitary phenomenon. Several different and distinct disorders are included, sharing with each other only the fact that the onset of the disorder coincides with the obstetric event. Secondly it must be remembered that the symptoms observed in PPS do occur at other times in the person's life, do not necessarily occur each time the person is giving birth to a child, do not occur in all women, and do occur in men. The physiology of the puerperium is thus not a cause in itself of any of the symptoms, but rather must be regarded as a contributing or triggering factor acting upon an underlying predisposition.

Theories of hormonal etiology. The fact that severe mental disorders occur postpartum, premenstrually, at menopause, and with the use of some oral contraceptives has been at least suggestive of some relationship between the HPG axis and these reactions (for reviews of these topics see: *Nott et al.* (1976), *Steiner & Carroll* (1977), *Studd et al.* (1977), *Weissman & Slaby* (1973), respectively). The endocrine changes occurring before, at, and immediately after parturition are unique in their magnitude, rapidity, and complexity of regulation. Many hypotheses of hormonal etiology of PPS have been put forward over the years. Most of them focus on postpartum mood changes as related to progesterone (P) and/or estrogens (E). Others suspect relative changes along the thyroid axis, changes in the levels of gonadotrophins, of prolactin (PRL), and of circulating corticosteroids.

Progesterone and estrogens. The "Progesterone Theory" (*Hamburg et al.* (1968), *Yalom et al.* (1968)) attributed the postpartum depression to the sudden fall of P occurring between the first and the second stages of labor. This is the biggest change over time in concentration of this hormone that a woman would experience in her lifetime. *Dalton* (1971) along the same lines suggested an elated mood shift related to the prepartum rise and a subsequent postpartum depression following the sudden loss of the placental steroid output. There is only one published attempt to correlate hormone findings and clinical findings to further test this hypothesis (*Nott et al.* (1976)). This failed to produce any strong evidence (1) that levels of P before delivery are excessively high in women who develop PPS; (2) that the rate of fall is too fast; and (3) that there is an abnormal E/P ratio in these patients.

As to the "Estrogen Withdrawal Theory" it has been suggested that postpartum depression might be related to estriol withdrawal, estriol being the estrogen mainly secreted by the placenta, but this again has not yet been confirmed (*Smith* (1975)). Endogenous E secretion is thought to play a role in the regulation of serum PRL concentrations (*Buckman et al.* (1976)). Some catechol estrogens have recently been identified in various brain and endocrine tissues of the rat in concentrations that exceed those of their parent E (*Paul & Axelrod* (1977)). These catechol estrogens seem to have an important role in neuroendocrine regulation. The enzyme monoamine oxidase (MAO) in plasma has been reported to be inhibited by E (*Klaiber et al.* (1971)). Elevated levels of plasma MAO activity were reported in premenopausal depressed women (*Klaiber et al.* (1972)) later on treated successfully with conjugated E. These studies are somewhat suggestive as to the role of estrogens but to date no correlative measurements of plasma E are available for PPS.

Prolactin. The most important known actions of PRL in the human are related to reproduction. Low physiological concentrations of PRL may be of importance for P production by luteal tissue. During pregnancy PRL serum levels rise progressively until term. This increase is probably related to supra-maximal E stimulation. E seems also to block the action of PRL on the breast, preventing lactation from being initiated during pregnancy. When E levels fall rapidly after

parturition, lactation is initiated. PRL is the critical hormone for the postpartum initiation of lactation. Suckling induces a further significant increase in PRL levels of breast-feeding mothers during the first 2 months postpartum. The physiological hyperprolactinemia in nursing mothers causes disturbances along the HPG axis resulting in anovulation. The hypothalamus normally inhibits prolactin release by a prolactin-inhibiting factor (PIF), which is believed to be dopamine. Various inputs such as stress (*Noel et al.* (1972)) and suckling (*Noel et al.* (1974)) act upon the hypothalamus. In addition, there seems to be a short-loop feedback regulation of PRL secretions (between the pituitary and the hypothalamus) as well as some influence of E from the ovary and placenta which regulate pituitary sensitivity to hypothalamic factors (*Martin et al.* (1977)).

It has been suggested that PRL may be involved in a variety of mental disorders (*Horrobin et al.* (1976)). Elevated baseline plasma PRL levels were reported in only some patients with unipolar as well as bipolar depressive illness (*Sachar et al.* (1973)). No such correlation could be replicated in another study (*Arana et al.* (1977)) where depression, as seen in an outpatient clinic, was not associated with increased PRL release. A PRL deficiency was proposed in schizophrenia (*Horrobin et al.* (1976)) but this highly speculative hypothesis has not so far been confirmed. In fact several studies have reported normal baseline PRL plasma levels in acute and chronic schizophrenia (*Meltzer et al.* (1974), *Brambilla et al.* (1976)).

The evidence for a direct role for PRL in the premenstrual tension syndrome (PMTS) is somewhat better (*Carroll & Steiner* (1978)). We have recently shown that in women suffering from severe PMTS the plasma PRL levels are significantly higher during the luteal-premenstrual phase when compared with the follicular-postmenstrual levels (*Steiner et al.* (1978)). In another study the premenstrual PRL rise was confirmed and it was also shown that women with this syndrome have higher basal PRL levels at other times in their cycle when compared with controls (*Halbreich et al.* (1976)).

Whether PRL has any causative relationship to PPS is still questionable. It seems appropriate to mention here that *Dalton* (1971) suggested that those women who experience difficulties in adjusting to the differing hormone levels of the premenstruum will tend to have even greater difficulty in adjusting to the hormone levels of the puerperium.

Corticosteroids. During the stress of childbirth significant changes occur in the circulating levels of ACTH and cortisol. ACTH increases significantly after the early phase of labor and cortisol increases at a later phase and immediately after delivery, and both decrease significantly within 4 hours postpartum (*Tuimala et al.* (1976)). The rise of corticosteroid levels during pregnancy is attributed to an increase of corticosteroid-binding globulin (CBG) in maternal blood. The additional increase at the time of delivery reflects a change in total cortisol. It seems to represent a combination of a prelabor surge of fetal cortisol production together with a maternal physical and psychological stress response associated with labor (*Talbert et al.* (1977)). Dexamethasone infusion to mothers during labor had no effect on maternal plasma cortisol (*Jolivet et al.* (1974)).

In view of the acknowledged role that the HPA axis plays in certain types of depression (*Carroll et al.* (1976)) and the proposed synergism between PRL and steroid hormones (gonadal as well as adrenal cortical) (*Nicoll* (1973)) further investigation in evaluating these changes in relationship to PPS is required.

Other possible hormonal theories. It is generally agreed that follicle stimulating hormone (FSH), which is suppressed during pregnancy, recovers to levels seen in normally menstruating women 3–4 weeks after delivery. The recovery of luteinizing hormone (LH) responsiveness to the exogenous luteinizing hormone releasing hormone (LHRH) occurs within 4–9 weeks postpartum (*Miyake et al.* (1978)). The cause for the time difference in the response of LH and FSH during the puerperium is still obscure. Thus the recovery of pituitary function is faster for FSH than for LH following delivery and at 2 weeks after delivery a reversal from menstruating women on the FSH/LH secretory responsiveness to LHRH is observed (*Canales et al.* (1974)). Inhibition of PRL secretion leads to a faster recovery of gonadotrophin secretion toward the menstrual type (*Villalobos et al.* (1976)). An increase in the production and secretion of gonadotrophic hormones, especially of FSH but also of LH, has been observed in climacteric women (*Lauritzen* (1977)), but so far direct effects of these hormones on human mood and behavior seem to be very modest (*McAdoo et al.* (1978)).

In contrast to the suppressed pituitary gonadotrophic function it has been demonstrated that pituitary responsiveness to thyrotrophin releasing hormone (TRH) during pregnancy and the puerperium is similar to that of non-pregnant young women (*Vandalem et al.* (1977)). Numerous studies show that patients with endogenomorphic depression have an abnormal pituitary response to intravenous TRH challenge. Most significant is the diminished thyroid-stimulating hormone (TSH) release but changes in growth-hormone (GH) and in PRL release have also been noted (*Loosen et al.* (1976)). Changes in cortisol may account for some of these observations, but again this type of inquiry has not been yet addressed specifically to PPS.

Major neuroendocrine research strategies that seem appropriate in studying PPS have not yet been applied systematically. Clinical features alone are unlikely to resolve the disputes about how postpartum psychiatric syndromes should be classified. One possibility would be to study a group of postpartum depressed women with similar methods that are currently used in research of the affective disorders. Escape from dexamethasone suppression, decreased GH response to insulin, d-amphetamine, and L-dopa, increased GH response to TRH, and decreased TSH response to TRH are all prominent neuroendocrine dysfunctions that have been reported in affective disorders. Such a study would possibly help us in answering the question whether postpartum depression and endogenomorphic depression have a common pathophysiology.

Miscellaneous physiologic theories. During the first decade of the catecholamine hypothesis of affective disorders at least one attempt was made to apply the theory in PPS (*Treadway et al.* (1969)). In this study a significant correlation

was observed between decreased urinary norepinephrine (NE) excretion and the severity of postpartum depression. It was hypothesized that a reduction in NE linked to gonadal hormone changes produces an increased biologic susceptibility to affective disorders in the puerperium. These data today seem very inconclusive. We now know that hypophysiotrophic function is regulated at least by dopamine (DA), NE, and serotonin (5-HT). These are the principal biogenic monoamines accepted to be central nervous system neurotransmitters. Acetylcholine (ACh) also is important although the evidence is less complete. To emphasize the complexity of this issue let us consider the role of these neurotransmitters on PRL secretion. PRL release is inhibited by DA, by L-dopa, the precursor of DA, and by several DA agonists. Administration of drugs that depress hypothalamic DA activity causes an increase in PRL secretion. There are some indications that NE may promote PRL release, and NE synthesis inhibitors seem to reduce PRL release. It is also suggested that the cholinergic system can inhibit PRL release, and that its effects are mediated via the catecholamines. Most of these conflicting data are derived from animal studies (*Meites* (1977)). As stated earlier, PRL seems to have a critical role in the puerperium. Its involvement in the pathophysiology of PPS is still unknown, but regardless of what this role might be proven to be, the various, often conflicting, effects of the different neurotransmitters will have to be accounted for.

It has been suggested that depressive illness may be related to a functional deficiency of 5-HT. The rate of brain 5-HT synthesis depends in part on the free plasma tryptophan concentrations. A significant correlation between this variable and the severity of postpartum affective disturbances was reported by two British workers (*Stein et al.* (1976), *Handley et al.* (1977)). Patients who appeared clinically to have severe postpartum depression had low free plasma tryptophan concentrations similar to those found in depressive illness. An extension of this work to confirm these pilot data is still needed. The mechanism by which this deficiency might cause postpartum mood changes is yet to be determined. Recent advances in our understanding of the physiology and pharmacology of serotonergic neurons have confirmed a modulatory role of these pathways on the sleep-waking cycle. Several years ago some inferential evidence was brought forward as to an excessive decrease in the level of Stage 4 sleep in late pregnancy (*Karacan et al.* (1969)). These investigators suggested a failure or delay in the rebound of this stage in the early postpartum period as a contributory factor to the PPS. To further clarify this issue future integrative studies of sleep-EEG are needed. As with the other "markers" already mentioned, here, too, it remains to be seen whether REM-latency and REM-activity have any bearing on postpartum depression.

RESEARCH IN ANIMAL BEHAVIOR

To reproduce in an animal a syndrome that one is trying to study in man seems to be an utopian goal. Ideally, such an animal model should mirror the physical and/or behavioral disorder, and should respond to treatment in ways comparable to that observed in humans. Psychiatry poses additional problems

in that the diagnostic tools and scales that are used in classifying human behavioral disorders are still in a state of flux. It is thus not surprising that the search for animal models still goes on, PPS not being an exception. Nevertheless PPS have one obvious "advantage" over many other psychiatric disorders, namely, the partal event itself as well as the pre- and postpartum physical and behavioral changes can easily be studied in animals. Basic animal studies which cannot be done with humans have focused on specific responses affecting the perinatal period. Some of these studies will be reviewed in this section. Whether we are ready to try to apply some of these findings to postpartum health care practices remains questionable.

It has been repeatedly emphasized that the crucial psychic conflict common to all PPS centers around the onset of the mother-infant relationship. An attempt to assess qualities of the mother-infant relationship in rhesus monkeys in a quantitative fashion has been described (*Hinde & Simpson* (1975)). Measurements of "maternal warmth", "maternal rejectingness", "maternal control", and "meshing/dissonance" were shown to be predictive of the future mental well being of mother and offspring. In the rat, maternal behavior consists of four principal components: nursing or crouching over the young, retrieving the pups, licking the pups, and nest-building. The onset of maternal behavior occurs around 24 hours prepartum, it is hormonally determined and estradiol seems to play a major role. The extension of the maternal behavior into the immediate postpartum period requires the resolution of tendencies of fear-avoidance of pups (*Rosenblatt* (1975)). In some animals several hours of contact with the pups is required for maternal behavior to be firmly established. There seems to be a period of special vulnerability to disruption of this pattern. This critical period is believed to correspond to the time of transition from hormonal to non-hormonal regulation of maternal behavior shortly after parturition (*Rosenblatt* (1975)). Maternal behavior (e.g. retrieving) appears spontaneously postpartum and can also be induced in virgin rats exposed to pups ("pup-induced maternal virgins"). However, crosstransfusion from spontaneous retrieving females and from pup-induced maternal virgins to a third group of recipient virgins failed to shorten latencies for retrieving. These experiments tend to support the concept of a non-hormonal basis for maternal behavior in the rat (*Terkel & Rosenblatt* (1971)). It was further demonstrated that PRL release is not essential in maintaining general maternal responsivity in the postpartum rat (*Stern* (1977)). This seems to be true but for one specific maternal drive. Part of the "normal" maternal behavior in many lactating female mammals is a high level of aggression. This postpartum maternal aggression seems to be facilitated by high levels of PRL (*Wise* (1974)).

Other observations suggest a role for sex hormone mediated changes in monoamine metabolism in the control of instinctive emotional behavior. Monoamine metabolism was studied in the mouse brain during the immediate postpartum period (*Greengrass & Tonge* (1972)). NE and DA concentrations in the cortex, thalamus, hypothalamus and striatum areas were significantly lower during the 5 days following parturition when compared to diestrus levels. Normetanephrine concentrations were significantly elevated, suggesting an increased NE turnover,

whereas 5-HT levels were low. Assuming that the psychological as well as physiological postpartum states are controlled by the balance between these neurotransmitters and their central hormonal activity, various methods of manipulating the system were proposed. Lesions of the nucleus accumbens were followed by heightened emotionality, impaired lactational performance, and the absence of maternal behavior (*Smith & Holland* (1975)). The administration of sex hormones to mice producing an artificial E/P imbalance caused significant alterations in monoamine metabolism throughout the brain (*Greengrass & Tonge* (1974)). Many more experiments would be necessary before anything could be advanced to explain the effects of E, P, PRL, or any other substance on monoamine metabolism in relation to PPS.

TREATMENT

The classic biological treatments for PPS are essentially the same as for any other reactive, affective, schizophrenic, or organic psychiatric disorder. Indications for specific treatments follow the same rules as for a similar non-puerperal episode. Thus major and minor tranquilizers, antidepressants or electroconvulsive therapy (ECT) are used as indicated. Some studies suggest that the main criteria for preferring ECT should be the severity of the depression and the necessity for an immediate response (Royal College of Psychiatrists (1977)). The sudden and acute onset of a psychotic puerperal depression with suicidal and infanticidal urges is undoubtedly within this category. An additional relatively recent different aspect of treatment procedure is the conjoint mother-and-baby hospitalization and treatment program which has gained worldwide popularity (*Lindsay* (1975)).

Lithium has been reported effective in controlling postpuerperal mania (*Gershon & Yuwiler* (1960)), but most studies evaluating lithium in PPS are uncontrolled, anecdotal reports (*Prien* (1975)). Relatively favorable controlled results are reported with a combination of perphenazine and lithium carbonate in a group of patients suffering from postpartum delirium, i.e. "postpartum psychosis", as described in the European literature (*Silberman et al.* (1975)). *Dalton* (1971), maintaining the common cause hypothesis for premenstrual and puerperal depression, finds that both have an excellent response to high daily dose progesterone given by intramuscular injection. No controlled data are available for this treatment. The beta-adrenergic blocking agent propranolol in high doses was compared with chlorpromazine in puerperal manic and maniform schizophrenic women. Propranolol caused noticeable improvement within the first week of treatment and had a marked advantage over chlorpromazine both with respect to the duration of symptoms and quality factors (*Steiner et al.* (1973)). This uncontrolled open pilot study still needs further confirmation.

Bromocriptine (2-Br-α-ergocryptine), a potent dopaminergic agonist, primarily suppresses PRL secretion. Puerperal lactation is initiated and regulated by PRL. In two double-blind studies bromocriptine was clearly a better and more specific inhibitor of lactation when compared with placebo and with a combined estrogen/androgen compound (*Rolland & Schellekens* (1978)). Evidence has also been

produced that mental symptoms, especially tension and irritability, which are present in the premenstrual tension syndrome, were ameliorated by treatment with bromocriptine (*Andersch et al.* (1975), *Steiner et al.* (1979)). Bromocriptine is already under current investigation in the treatment of severe cases of endogenomorphic depression (*Agnoli et al.* (1978)). Whether the suppression of postpartum lactation with bromocriptine will also be of psychological benefit in any of the PPS remains to be investigated.

PROGNOSIS

The long-term prognosis of postpartum mental illness was found to be correlated with the general psychiatric diagnosis. The short-term prognosis seems to depend on a varity of factors other than diagnosis, including onset of symptoms within 3 weeks of delivery, past history of psychiatric illness, response to treatment within the first 10 days of hospitalization and the presence of physical problems pre-, during and postpartum (*Wilson et al.* (1972)). Exceptions are the so-called organic, confusional, amential states as well as the catatonic clinical picture which usually follow a very short episodic course (*Huhn & Drenk* (1973)).

SUMMARY AND CONCLUSIONS

Hippocrates speculated that suppressed lochial discharge could be carried toward the head and result in "agitation, delirium, and attacks of mania". Half a century ago mankind was still plagued with "Septic Insanity of Labour". We have come a long way since. With modern antiseptic midwifery these problems disappeared. We seem to have now an acceptable classification for the psychiatric disorders associated with childbearing. A considerable amount of work has been done investigating the incidence, the genetic factors involved and the psychologic influences pertaining to PPS. Research into the various possible neuroendocrine and physiologic etiologies of PPS poses similar problems as with any other mental disorder. We do know of some specific hormonal changes occurring at the time of the partal events. Whether these endocrine differences reflect an underlying etiopathogenic alteration in mental puerperal reactions is still unknown. The temporal interaction of these hormones, the possibility of a synergistic effect between prolactin and steroids, and their correlation with certain mental disorders specific to women should be an important aim of further investigation.

There is an old wives' tale that when mental disturbances surface during the puerperal period lactation should be suppressed immediately. Prescientific man has been a careful and often accurate observer. Added to our knowledge about the role of prolactin it seems as if once again an old wives' tale may become a fruitful stimulus for research.

ACKNOWLEDGMENTS

I wish to thank Professor *B. J. Carroll* for his valuable assistance and supervision, Drs. *R. F. Haskett* and *R. J. Katz* for their comments, and Ms. *Ruth Metski* for her expert editorial management.

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Received May 8, 1979

Meir Steiner, M.D.
Dept. of Psychiatry
Mental Health Research Institute
University of Michigan
Ann Arbor, Michigan 48109
U.S.A.