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Point of View

A Hormonal Component to Postnatal Depression

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Disorders of the thyroid gland are associated with disorders of mood (Thomas *et al*, 1970; Van Uitert & Russakoff, 1979; Folks, 1984; Young, 1984; Jadresic, 1990). Both hypothyroid and hyperthyroid states can be associated with depression, which is sometimes accompanied by psychotic features such as delusions and hallucinations (Wilson & Jefferson, 1986). Similarly, primary affective disorders can be accompanied by changes in thyroid function, with low thyroid-stimulating hormone (TSH) levels and elevated thyroxine (T_4) (Kirkegaard & Faber, 1980), and in major depressive illness there is often a blunted TSH response to thyrotrophin releasing hormone (TRH) (Prange *et al*, 1972; Loosen, 1987).

Pregnancy and the post-partum period are sometimes accompanied by pathological changes in thyroid function, which can be properly interpreted only against the background of those changes normally occurring. Thyroid-gland enlargement is common in pregnancy, and uptake of iodide from the blood increases during the first trimester, compensating for increased urinary excretion of iodide. There is also an increase in total triiodothyronine (T_3) and T_4 due to higher levels of thyroxine-binding globulin, but free T_3 and T_4 remain within the normal range. During the post-partum period there is a gradual decrease in thyroid-gland volume but a more rapid reversion of thyroxine-binding globulins to normal (Rodin, 1989; Rasmussen *et al*, 1989).

Over 50 years ago, Sheehan (1939) described a syndrome following delivery where hypopituitarism resulted from anterior pituitary necrosis and was accompanied by resulting hypothyroidism, often with symptoms of depression. This rare condition occurred at a rate of one per 30 000 births. However, Roberton (1948) described mild hypothyroidism as a fairly frequent condition occurring in women over several months after delivery, with no obvious explanation for this. Thirty years later, Amino *et al* (1978) first described a group of postnatal women with positive thyroid antibodies and hypothyroidism presenting with cold extremities, dry skin, and swelling of the front of the neck. In a definitive study (Amino *et al*, 1982), thyroid dysfunction related to autoimmune disorder was shown to occur at a rate of 5.5% in child-bearing Japanese women. Other studies have confirmed this high rate of occurrence (Jansson *et al*, 1984; Fung *et al*, 1988), and a recent survey of the world literature indicates a rate of 3.5–6% reported from most studies (Gerstein, 1990), sometimes a transient thyrotoxicosis preceding the hypothyroidism (Jansson *et al*, 1984). Thyroid microsomal antibody titres characteristically increase between two and five months post-partum, then decrease until the end of the first post-natal year. Jansson *et al* (1987) have shown that this rise in antibody levels occurs as a result of activation of certain immunoglobulin-producing B-cell clones.

Although there is overwhelming evidence that postnatal depression, occurring at a rate of 10–20% (Paykel *et al*, 1980; Cox *et al*, 1982; Kumar & Robson 1984), is associated with background factors such as previous personality, previous psychiatric illness, marital disharmony and life events (Paykel *et al*, 1980; Watson *et al*, 1984), it is possible that a subgroup have a basis for depressed mood in thyroid disorder. Furthermore, it has been shown that there is an association between stressful life events, background factors and onset of thyroid disease. Such an association was frequently hypothesised by earlier writers, but without supporting evidence (Lidz & Whitehorn, 1949; Ham *et al*, 1951). More recently, a controlled study from Scandinavia has shown negative life events to be a risk factor for Graves' disease (Winsa *et al*, 1991), although the methodology used in the study was subsequently subject to much criticism (Harris *et al*, 1992*b*). Even more fascinating is a possible link between stress, the immune system, thyroid disorder and depression, and it is likely that stress and its resultant mental state affects the immune system, with release of lymphokines, which in turn alter mental state (Dantzer & Kelly, 1989; Leonard, 1990). Most hormonal studies have investigated steroids such as progesterone, cortisol and oestradiol (Nott *et al*, 1976; Harris *et al*, 1989*b*; O'Hara *et al*, 1991). However, studies are now emerging which have examined thyroid disorder and depressed mood in the year following delivery. Harris *et al* (1989*a*) examined the rates at which depression occurred in 65 antibody-positive and 82 antibody-negative women at six to eight weeks post-partum: those women with *actual* thyroid dysfunction as determined by abnormal plasma T_3, T_4, and TSH (as opposed to positive-antibody status) showed a modest but significant excess of depression in terms of DSM-III major depression (American Psychiatric

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Association, 1980). However, microsomal and thyroglobulin antibody levels continue to rise in antibody-positive women and reach a mean peak at about four months post-partum (Fung *et al*, 1988). Later studies have therefore assessed women at various points in time in the nine months following delivery. Pop *et al* (1991) looked at an unscreened population of 100 or more women and found an association of major and minor depression (according to Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978)) with disturbed thyroid function in the post-partum period. They did not comment on the antibody status of such women; but further analysis of their data suggests there was an increased risk of depression in thyroid-antibody-positive women. An excess of such depression (i.e. major and minor according to RDC) has been documented in antibody-positive women assessed at 8, 12, 20 and 28 weeks post-partum, but there was no excess of definite major depression, in particular. Interestingly, the excess of depression ('any' RDC depression) in thyroid-antibody-positive women was independent of whether or not the women had *actual* thyroid dysfunction in terms of plasma T_3, T_4 and TSH (Harris *et al*, 1992*a*). This was also true of the same population screened at six weeks post-partum using the General Health Questionnaire (GHQ; Goldberg, 1972), thyroid-antibody-positive women having a highly significant increase in rate of 'caseness'. A possible explanation for this finding may be that, in the 10% of women in the general population who are positive for thyroid antibodies (Prentice *et al*, 1990), development of post-partum thyroiditis produces general malaise which is identified as minor depression. On the other hand there may be a rapid flux of hormones, ranging from hyper- to hypothyroid states, which is not detected by simple plasma sampling, as, for example, carried out at monthly intervals.

Extrapolation of the findings back to the general population shows that 1% of all post-partum women would show major mood disorder associated with autoimmune thyroid disease occurring in the thyroid-antibody-positive women, and that up to 4% of all post-partum women would be affected when less-severe depressive states are included. The lack of association with more severe depressed states is in accordance with the finding that women admitted to hospital with mental disorder in the six months after giving birth do not have an excess of thyroid disorder (Stewart *et al*, 1988).

Impairment of concentration (and possibly memory), together with increased carelessness and making mistakes, has been claimed by Hayslip (1988), although there is no evidence for impairment of reaction time and digit-span memory (Mallett *et al*, 1992). Such impairment might well have an effect on the mother–baby relationship and interaction. There is also evidence indicating that the newborn children of antibody-positive women have significantly slower growth rates than those of antibody-negative women, so there may well be far-reaching consequences in terms of the newborn baby (Bech *et al*, 1991). Usually the thyroid dysfunction is transient, and treatment of the depression should consist of treatment of the thyroid condition along symptomatic lines (i.e. thyroid hormone may be prescribed in hypothyroid states and beta-blockers in hyperthyroid states), together with antidepressants where mood disorder persists. However, the question arises as to what happens to the condition in the longer term. Tachi *et al* (1988) showed that in 83% of episodes (59 in 44 women) there was recovery within one year post-partum, the women remaining euthyroid. The remaining 17% of episodes developed into permanent hypothyroidism, necessitating long-term treatment. Thus the condition, though mostly transient, has some similarities to Hashimoto's disease, in that sometimes a transient hyperthyroidism precedes the hypothyroidism, and those individuals who develop *permanent* hypothyroidism may be regarded as true cases of Hashimoto's disease, exacerbated by the autoimmune rebound of the post-partum period. Identification of such women is thus important and easy, and can be achieved by testing for plasma thyroid antibodies and thyroid function (i.e. T_3, T_4, and TSH), the course of the condition indicating the need for long-term follow-up.

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