Pituitary Disorders and Pregnancy

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The sella turcica of the sphenoid bone, lined by dura mater, is occupied by the pituitary gland. The dura covering the roof, called the diaphragm sella, is perforated centrally by the pituitary stalk. Directly above this diaphragm, and anterior to the stalk, lies the optic chiasm. The gland consists of two lobes, anterior (adenohypophysis) and posterior (neurohypophysis), the former accounting for five sixths of the volume of the gland. The pituitary stalk not only comprises the direct neural connections between the hypothalamic nuclei and the posterior lobe but also is the vascular link between the hypothalamus and the anterior lobe, thus enabling hypothalamic neurohormonal secretions to influence the activity of the anterior lobe cells. Paired superior hypophyseal arteries, arising from the internal carotids anastomose around the upper part of the stalk. These terminate within elongated coiled capillary loops into which the hypothalamic hormones are discharged. The capillary bed drains into portal veins that empty into sinusoids of the anterior lobe (Fig 1). Paired inferior hypophyseal arteries supply the posterior lobe. The venous drainage of both lobes is into the cavernous sinuses.

The adenohypophysis produces gonadotropins (luteinizing hormone [LH], follicle-stimulating hormone [FSH]), growth hormone, thyrotropin (TSH), prolactin, corticotropin (ACTH), and its related peptide melanocyte-stimulating hormone. Since 1947, when Green and Harris formulated the concept that the control of the anterior pituitary is exerted by neurohormonal mechanisms, several peptides have been isolated from the hypothalamus that indeed function in this capacity. Thus, thyrotropin-releasing hormone (TRH) causes release of TSH (and incidentally, also of prolactin), gonadotropin releasing-hormone (GnRH) allows release of LH and FSH, and corticotropin-releasing factor releases ACTH. In addition, substances with an inhibitory rather than stimulatory influence have been isolated: somatostatin inhibits the release of growth hormone (and many other hormones, too), and dopamine inhibits the release of prolactin. This inhibition of the lactotroph is clinically important; disturbances of the stalk or vascular dissociation of the hypothalamus from the anterior pituitary result in deficiency of all anterior pituitary hormones with the exception of prolactin. Thus, the lactotroph is normally under predominantly inhibitory control.

Physiologic Changes During Pregnancy

During pregnancy the anterior lobe may double or triple in size due to massive proliferation of the lactotrophs. Magnetic resonance imaging studies of normal primigravid patients have confirmed progressively increasing pituitary volumes during gestation: at the end of pregnancy there was an overall increase in pituitary gland size of 136% as compared with control nulliparous subjects. The major accompanying physiologic change is a progressive increase in serum prolactin concentrations, with approximately a 10-fold increase during gestation (Fig 2). Its role is in the preparation of the breasts for initiation and maintenance of lactation. Despite this dramatic increase, the lactotroph maintains its ability to respond to TRH, its releasing hormone (in contradistinction to prolactinomas when this response is usually blunted or absent).

Other physiologic changes during pregnancy include the following: (1) a decline in gonadotropin concentrations with a progressively diminishing response to GnRH; (2) blunting of growth hormone response to its normal stimuli, for example, insulin or arginine; (3) an increase in ACTH concentrations, occurring despite a rise in both bound and free plasma cortisol, suggesting that factors besides cortisol may regulate its release (or that an alternate source of ACTH exists). The diurnal variation of cortisol, although blunted, is preserved during pregnancy. Thyrotropin, free thyroxine, and tri-iodothyronine concentrations remain unchanged; that is, the hypothalamic-ip
Pituitary-thyroidal axis is essentially unaffected by pregnancy. Total serum thyroxine and tri-iodothyronine concentrations, of course, increase due to doubling of thyroxine-binding globulin levels.

Oxytocin and vasopressin, produced by neurons of the paraventricular and supraoptic hypothalamic nuclei, are released into the blood vessels of the neurohypophysis. Vasopressin plays a central role in osmolarity and volume regulation, osmoreceptors are located in the anterior hypothalamus, and vasopressin release increases when plasma osmolality rises. Early in pregnancy plasma osmolality decreases to values 5 to 10 mOsm/kg below the normal mean of 285 mOsm/kg in nonpregnant women. However, plasma levels of vasopressin and its response to water loading and dehydration are normal in pregnancy, indicating a resetting of the threshold; that is, vasopressin is secreted at a lower plasma osmolality. Similarly, the plasma osmolality at which thirst is experienced is lowered in the pregnant state.

Oxytocin is involved in the process of parturition and in suckling. Although the role of oxytocin in the initiation of labor is unclear, there is a significant preterm increase in plasma concentrations of oxytocin. During nursing, nipple stimulation initiates a neurogenic reflex which is transmitted to the hypothalamus, thus triggering oxytocin release from the posterior pituitary. Oxytocin then induces contraction of myoepithelial cells and mammary duct smooth muscle, resulting in milk ejection.

Disorders of the Anterior Lobe

Most commonly, tumors and, less commonly, vascular mishaps and inflammatory changes may afflict the anterior lobe. In their evaluation consideration has to be given to both anatomic derangements and the effects of excess or deficient hormones that may accompany these disorders. Given the additional physiologic changes in pregnancy outlined above, the combination of pregnancy and pituitary disorders poses a challenge to the obstetrician and endocrinologist in their endeavor for a safe outcome for both mother and child.

Pituitary Tumors

Pituitary tumors may be classified into hormonally functioning and functionless lesions. Examples of the former include growth-hormone-producing tumors resulting in acromegaly, ACTH-producing tumors giving rise to Cushing's disease, and prolactinomas. Prolactinoma is by far the most common pituitary tumor encountered in pregnancy. Less commonly, hormonally functionless pituitary tumors may occur. As these are relatively asymptomatic in their early stages, they tend
to be larger at diagnosis, and the patient should be appropriately treated surgically before becoming pregnant.

**Prolactinoma**

The advent of prolactin radioimmunoassay in the early 1970s enabled the correct diagnosis of prolactinoma to be made in many patients previously thought to have functionless pituitary tumors. Because of the negative impact of excess prolactin on the hypothalamic-pituitary-gonadal axis, the majority of these women, who were also in their childbearing years, presented with amenorrhea and many had a desire to achieve pregnancy. Parallel with the development of the prolactin assay and improved radiologic techniques for diagnosing these tumors came the development and refinement of transphenoidal microsurgical techniques and a powerful new drug, bromocriptine mesylate, which is capable of suppressing elevated prolactin concentrations to normal. Numerous pregnancies resulted from restoring normal gonadal function in these women, and over the last decade information pertaining to these pregnancies has been consolidated. Given the physiologic changes that occur in the pituitary in a normal pregnancy, namely enlargement of the gland and hyperplasia of the lactotrophs with a 10-fold increase in serum prolactin, concerns about women with prolactinomas becoming pregnant were very reasonable.

**Effect of the prolactinoma and its treatment on pregnancy and the fetus: Safety of bromocriptine in pregnancy.** Bromocriptine mesylate is an ergot derivative with potent dopamine receptor agonist activity. Administered orally, it is a potent inhibitor of prolactin secretion, the effects lasting usually only for the duration of treatment. Numerous accounts of the use and safety of bromocriptine in pregnancy are available, but they are best summed up by Krupp and Monker from the Drug Monitoring Center, Clinical Research, Sandoz, Basle, Switzerland. They collected data from 2,587 pregnancies in 2,437 women treated with bromocriptine during some stage of gestation. The results showed that its use was not associated with an increased risk of spontaneous abortion, multiple pregnancy, or the occurrence of congenital malformation in their progeny. In addition, they followed 546 children postnatally up to 9 years and found no adverse effect on postnatal development. In the majority of the women treated, bromocriptine was discontinued upon confirmation of pregnancy. These results are important insofar as investigations indicate that bromocriptine crosses the placental barrier and can be found in dose-related concentrations in fetal blood and in the amniotic fluid.

**Effects of pregnancy on the prolactinoma.** In a review of the subject with data collected and combined from many studies, Albrecht and Betz noted the following: of 352 pregnancies in patients with untreated microadenomas (<10 mm in size), 8 (2.3%) developed visual disturbances, 17 (4.8%) developed headaches, and 2 (0.6%) had diabetes insipidus; the corresponding figures for 144 pregnancies in women with macroadenomas (>10 mm in size) were visual disturbances in 22 (15.3%), headaches in 22 (15.3%), and diabetes insipidus in 2 (1.4%). In the same review, the outcome of 318 pregnancies in patients with treated (surgery, radiation therapy or both) adenomas (both microadenoma and macroadenoma) were analyzed: there were visual disturbances in 10 (3.1%), headaches in 12 (3.8%), and diabetes insipidus in 1 (0.3%). Symptoms related to a pregnancy-induced increase in the size of a pituitary tumor may begin as early as the first trimester with the mean time for the onset of visual symptoms at 14 weeks' gestation; headaches usually precede visual disturbances.

![Figure 3](image-url)  
**Figure 3.** Time from beginning of pregnancy to onset of symptoms (ie, either headache or visual disturbances) in 91 pregnancies in women with previously untreated pituitary tumors. Occurrence of symptoms is evenly distributed throughout pregnancy. (Reprinted with permission.)  

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changes. The time from beginning of pregnancy to onset of symptoms in 91 pregnancies in women with previously untreated pituitary tumors is shown in Fig 3.

Based on these data patients with prolactinomas planning pregnancy can be counseled, and definitive treatment of macroadenomas before pregnancy is currently recommended, especially if associated with destruction of the sella turcica or with suprasellar extension. Recommendations for management of patients with prolactinomas before and during pregnancy are outlined in Tables 1 and 2. Monthly measurement of serum prolactin is not necessary. Prolactin concentrations measured in a group of patients with surgically untreated microadenomas were found to be elevated early in gestation but did not increase further with advancing gestation, in contrast to normal pregnant controls (Fig 4).

Management of tumor complications during pregnancy. Before the bromocriptine era and in the early stages of its use, the management of tumor complications in pregnancy was difficult and included surgery, radiotherapy, and/or early delivery. Fortuitously, it was soon observed that bromocriptine may, in addition to its prolactin-lowering effects, shrink the volume of pituitary tumors, including large macroadenomas causing visual fields defects. Given the lack of known adverse effects of bromocriptine use in pregnancy, and the predicament of a pregnant patient with symptomatic tumor enlargement, bromocriptine has been successfully used in the treatment of such complications and is the treatment of choice. The medicine should be administered with food and the dose adjusted according to symptoms (eg, 2.5 to 5 mg two or three times daily). Glucocorticoids may also be given to expedite recovery of visual defects. Surgery is recommended only if there is no response to bromocriptine.

An indicated previously, the majority of patients with microadenomas have uncomplicated pregnancies, whereas a disturbing number of patients with untreated macroadenomas have symptomatic tumor enlargement. Given the tumor-shrinking properties of bromocriptine, it is not surprising that the continuous use of bromocriptine in pregnancy has been advocated and indeed used in patients with macroadenomas. However, until the safety of such therapy on the developing fetus is established, such therapy cannot presently be recommended except in special circumstances. Although the rates of abortion and perinatal mortality do not differ in women with pituitary tumors that are untreated or treated before or during pregnancy, there is a significant increase in prematurity in those treated (surgery and/or radiotherapy) during pregnancy (P < .005, v a untreated group; P < .05, v a group treated before pregnancy).

Breast-feeding and postpartum care. There is no reason to avoid breast-feeding when a patient...
wishes to nurse her child. In a small study of 14 women with microadenomas who breast-fed for 6 to 14 months, serum prolactin was not significantly higher than prepregnancy. In another study (Fig 5), the increase in prolactin associated with suckling was absent in women with pathologic hyperprolactinemia. For those wishing to inhibit lactation, bromocriptine is the treatment of choice, with a dose of approximately 2.5 mg three times daily usually being appropriate. Estrogen should not be used to inhibit lactation, as expansion of the tumor can occur. Ophthalmologic and radiologic evaluation and determination of serum prolactin concentrations are in order 6 to 8 weeks postdelivery. In most instances, the sella returns to its original size and prolactin decreases to previous levels. Further pregnancies are not contraindicated in patients with prolactinomas.

**Acromegaly**

Acromegaly is the result of excessive growth hormone secretion in adults, this usually being associated with acidophilic or chromophobic pituitary adenomas. When clinical evidence exists, a glucose tolerance test is performed; lack of suppression of growth hormone below 5 ng/mL during this test is in keeping with a diagnosis of acromegaly. Because the biologic effect of growth hormone is mediated through somatomedin C, elevation of serum concentrations of this growth factor is not only considered a useful confirmatory test but has been used to monitor the progression of the disease. However, in the context of pregnancy, somatomedin C concentrations should be interpreted with caution as they may be elevated.

Menstrual irregularity or amenorrhea is an extremely frequent finding in acromegalic women. Nonetheless, pregnancy may occur in women with acromegaly and may be accompanied by tumor expansion necessitating hypophysectomy. Definitive treatment before conception is the treatment of choice in acromegalics desiring children. The observation that l-dopa causes a paradoxical decrease in growth hormone in acromegaly led to the use of dopaminergic agonists in the treatment of acromegaly. In two reported cases pregnancy occurred in acromegalics during bromocriptine therapy, and with continuation of treatment during pregnancy tumor expansion was not observed.

**Cushing’s Syndrome**

Cushing’s syndrome is a state of hypercortisolism and may arise from excess ACTH produced by the pituitary or an ectopic source such as a tumor. In addition, an adrenal lesion (adenoma or carcinoma) may itself be the direct source of excess
Pregnancy is uncommon in patients with this syndrome because of its association with a high incidence of menstrual disturbances and anovulation. Cushing’s disease or pituitary-dependent Cushing’s, although the most common etiology in nonpregnant patients, is relatively less commonly associated with pregnancy, hyperfunctioning adrenal adenomas being more common in pregnant patients with Cushing’s syndrome. Of 31 pregnant patients with Cushing’s syndrome, 11 had pituitary-dependent Cushing’s, 12 had adrenal adenomas, 4 had adrenocortical carcinomas, and in the remaining 4 the etiology was not known. The diagnosis of Cushing’s syndrome in pregnancy may be rendered more difficult because weight gain, hypertension, striae, edema, and pigmentation may occur in normal pregnancy. More specific signs, such as thinning of the skin, spontaneous bruising, and muscle weakness should be sought. Furthermore, the laboratory diagnosis is complicated by the changes in adrenal function that occur in normal pregnancy, namely an elevation of plasma cortisol and diminished diurnal variation. Because urinary-free cortisol excretion is elevated during normal pregnancy, a prolonged low-dose dexamethasone suppression test (2 mg/d for 8 days) with measurement of plasma and urinary steroids is the appropriate test for diagnosis, and failure of suppression is in keeping with Cushing’s syndrome. To distinguish pituitary-dependent Cushing’s from hyperfunctioning adrenal tumors, a prolonged high-dose dexamethasone suppression test is recommended (8 mg/d for 8 days). Significant (≥50%) suppression of plasma cortisol is the rule in pituitary-dependent Cushing’s, and failure of suppression to high-dose dexamethasone, along with low or undetectable ACTH concentrations, would strongly suggest an adrenal source. The adrenal glands, as well as the pituitary, may be evaluated during pregnancy using magnetic resonance imaging.

In a review of 35 pregnancies in the 31 women with Cushing’s syndrome previously mentioned, there were 5 abortions (1 therapeutic), 1 neonatal death, 3 stillbirths, and only 26 successful births. In addition, preterm labor was common. The stage of gestation was recorded in 22 of the 26 with successful outcomes; 12 delivered between 28 and 37 weeks, and only 10 had deliveries at or beyond 38 weeks. Twenty-two of the 31 patients received no treatment for Cushing’s during the pregnancy; 7 had adrenalectomy, 1 had pituitary irradiation, and 1 received metyrapone for control of Cushing’s during gestation. Metyrapone is an inhibitor of 11-B-hydroxylation. A normal infant was delivered at 37 weeks of gestation, but urinary estriol excretion was markedly deficient and thought to be due to metyrapone-induced inhibition of placental C19 hydroxylation. In patients with pituitary-dependent Cushing’s, transphenoidal hypophysectomy during pregnancy is also a therapeutic option. Neonatal adrenal insufficiency in association with Cushing’s syndrome has also been reported and is presumably due to suppression of the fetal hypothalamic-pituitary-adrenal axis from transplacental transport of excess maternal cortisol. With this possibility present, the baby should be monitored carefully for adrenal insufficiency.

**Hyppopituitarism**

Diminished or decreased production of anterior pituitary hormones results in inadequate activity of target organs such as the thyroid, adrenal, and gonads. The deficiency may be partial, affecting trophic hormones in varying degrees or it may be complete, resulting in panhypopituitarism. The role of the obstetrician-gynecologist in this context is twofold: (1) to be alert to and aware of the possibility of two disease processes that may affect the pregnant patient, namely Sheehan’s syndrome and lymphocytic hypophysitis; and (2) to recognize and treat hypopituitarism in a pregnant patient, thus avoiding unpleasant consequences.

**Sheehan’s Syndrome**

In 1937, Sheehan drew attention to the relationship between postpartum hemorrhage and anterior pituitary necrosis. Because the syndrome is distinctly uncommon with other conditions associated with shock and vascular collapse, it is assumed that the hyperplastic gland in pregnancy is more vulnerable to an inadequate blood supply. In a retrospective survey by Hall, pregnant patients admitted for hemorrhagic collapse were subsequently traced and evaluated for hypopituitarism, the incidence being approximately 3.6%. There is said to be no direct correlation between the severity of the hemorrhage and the occurrence of Sheehan’s syndrome, but the major part of the pituitary must be destroyed before symptoms become evident.

In a series of 25 cases, half the patients had permanent amenorrhea, the remainder having
rare and scanty menses. Only 1 had normal menstruation. In most, but not all, cases lactation was poor or absent. Four had coma episodes and two thirds had fatigue, cold intolerance, or frank hypothyroidism. A similar proportion had genital atrophy. There was a surprisingly long interval between the obstetric event to diagnosis (more than 10 years in over half the cases).

Although pregnancy in hypopituitary patients is rare, failure to establish the diagnosis and institute proper therapy may have lethal consequences for both the mother and the fetus. In one patient, seven pregnancies terminated in spontaneous abortions. Hormonal replacement therapy during the eighth pregnancy was associated with the delivery of a normal premature infant at 32 weeks' gestation. In this same report, pregnancy among patients with Sheehan's syndrome was reviewed. There were 87% live births, 13% abortions, and no stillbirth or maternal death in 15 pregnancies in patients receiving hormone replacement therapy. In sharp contrast, in 24 pregnancies among 11 women, in whom hormone replacement was not provided, there were 58% live births, 42% abortions, a stillbirth, and 3 maternal deaths.

In nonpregnant patients suspected of having Sheehan's syndrome the diagnosis and the extent of pituitary damage can be determined by tests of target organ function (eg, thyroid function tests, cortisol concentration) as well as tests of pituitary reserve, namely a GnRH test of gonadotropin reserve, a TRH test of TSH and prolactin reserve, and an insulin tolerance test to assess growth hormone and ACTH reserves. Because an ongoing pregnancy does not constitute evidence against the diagnosis of Sheehan's syndrome, it should be considered in all patients with a past history of postpartum hemorrhage. Hypopituitarism may not be suspected because nausea, vomiting, and fatigue are common in normal pregnancy. In the evaluation of pituitary function during pregnancy, it is important to remember that gonadotropin concentrations remain low in a normal pregnancy. Induction of hypoglycemia is undesirable, and growth hormone concentrations can be determined after sleep or exercise. Likewise, TRH testing is usually unnecessary, the finding of a low serum thyroxine and low-normal TSH being in keeping with secondary hypothyroidism. Low cortisol concentrations (compared with those of normal pregnant women) and failure of cortisol and ACTH to increase during times of stress would be in keeping with diminished ACTH reserve.

Treatment of pituitary insufficiency during pregnancy does not present special problems. Oral L-thyroxine (0.1 to 0.2 mg/d) and cortisol (20 mg AM, 10 mg PM) or prednisone (5 mg AM, 2.5 mg PM) are administered. There is no need for mineralocorticoids. As in the nonpregnant state, glucocorticoid requirements may increase during episodes of intercurrent illness. During labor a good state of hydration should be maintained and parenteral glucocorticoids administered. This is most easily achieved by the intravenous infusion of hydrocortisone. The dose may be adjusted as appropriate for the patient's state, ranging from 25 mg to 75 mg every 6 hours. Following delivery, parenteral glucocorticoids should be continued, in the smaller doses, for a few days along with intravenous fluids.

**Lymphocytic Hypophysitis**

In 1962, Goudie and Pinkerton described the case of a 22-year-old woman who died of circulatory collapse 8 hours postappendectomy. She was 14 months postpartum following a normal pregnancy and delivery, but had developed secondary amenorrhea postpartum. Her autopsy revealed lymphocytic infiltration of the pituitary and also of the thyroid, and the authors postulated an autoimmune mechanism to explain both. In a review of the literature since then, a total of 25 pathologically confirmed cases have been found, 24 of which were in women. In 18 of these the disease occurred in relation to a pregnancy. The features of these 18 patients are outlined in Table 3. In 10 the symptoms were noted postpartum, as outlined by the first case described; in the other 8 initial symptoms occurred during the pregnancy and included headache, lethargy, weight loss, and in one case collapse and death during labor. Thirteen of these 18 patients had varying degrees of hypopituitarism and 7 had evidence of an autoimmune disorder. Given this association and the prior documentation of a pituitary autoimmunity, the presence of antipituitary antibodies was sought in 3 cases and were positive in 1. Six of these patients also had hyperprolactinemia and/or galactorrhea; pituitary stalk disturbance with relative lack of the prolactin inhibitory factor, dopamine, has been suggested as the mechanism likely to explain this phenomenon. In 6 the
Table 3. Characteristics of 18 Women With
Pregnancy-related and Pathologically Documented
Lymphocytic Hypophysitis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean 28 yr</td>
</tr>
<tr>
<td></td>
<td>Range 22-37 yr</td>
</tr>
<tr>
<td>History of onset</td>
<td>8 During gestation</td>
</tr>
<tr>
<td></td>
<td>10 Postpartum</td>
</tr>
<tr>
<td>Hypopituitary</td>
<td>13 Cases</td>
</tr>
<tr>
<td>Visual disturbance</td>
<td>8 Cases</td>
</tr>
<tr>
<td>Hyperprolactinemia/galactorrhoea</td>
<td>6 Cases</td>
</tr>
</tbody>
</table>

Associated disorders

- Thyroiditis: 4 Cases
- Thyroiditis and adrenalitis: 1 Case
- Pernicious anemia: 1 Case
- Positive smooth muscle antibody: 1 Case

Diagnosis

- Autopsy: 6 Cases
- Biopsy (tumor suspected): 12 Cases

Diagnosis was established at autopsy; the remaining 12 had pituitary surgery for suspected tumors, and the appropriate diagnosis was made by biopsy of the material obtained.

The close temporal association of this disease with pregnancy is most intriguing. Flare-up of autoimmune disease processes in the postpartum period has been well documented, but given the relative immunologic tolerance during pregnancy the occurrence of lymphocytic hypophysitis during a pregnancy is less well explained. Exacerbation of the disease postpartum, even when it initially presents in pregnancy, has also been described.

The importance of this condition is that it is a potentially life-threatening but treatable disease affecting young women during or after a pregnancy. Thus, the diagnosis should be considered in women of reproductive age presenting with signs and symptoms of anterior pituitary hormone deficiencies, isolated or in combination, antepartum or postpartum (especially in the absence of significant bleeding during labor). In the absence of a threat to vision, such patients should be treated medically with hormone replacement and their progress observed. Magnetic resonance imaging should be used to delineate and follow the anatomic defects.

Disorders of the Posterior Lobe

Diabetes Insipidus

Vasopressin and oxytocin, produced in the supraoptic and paraventricular nuclei of the hypothalamus, are released into the posterior lobe and hence into the circulation. No disease process has yet been described with oxytocin deficiency or excess. However, lack of vasopressin results in diabetes insipidus, and this may occur as a primary or idiopathic disorder (approximately 30% of cases) or be acquired secondary to a variety of pathologic lesions including cranial injuries (16%), infections, sellar and suprasellar tumors (25%), and vascular lesions. The main symptoms are polyuria, polydipsia, with low urinary specific gravity. The diagnosis is made by water deprivation; increasing serum osmolality, in the face of low urine osmolality and a return toward normal after vasopressin, is diagnostic.

Effect of diabetes insipidus on pregnancy. Hendricks, in a comprehensive review, concluded that the prior existence of diabetes insipidus in a woman did not appear to alter her fertility, the course of pregnancy, the effectiveness of labor, or lactation. Since oxytocin is also produced in the same hypothalamic nuclei, diabetes insipidus is of particular interest in the pregnant woman because of the possible relationship of decreased oxytocin with decreased uterine contractions during labor. However, despite a report of uterine atony, it would appear that labor is normal in most patients with diabetes insipidus.

Effect of pregnancy on diabetes insipidus. The effect of pregnancy on diabetes insipidus is variable. In a review of the subject, Hime and Richardson found that 58% deteriorated, 20% improved, 15% remained the same. Interestingly, in a few cases in whom pre eclampsia developed, the diabetes insipidus improved. Placental destruction of vasopressin and its failure have been put forward as explanations for the deterioration in pregnancy and improvement with preeclampsia.

Treatment. t-diamino-8-d-arginine vasopressin (DDAVP) or desmopressin acetate, a synthetic analog of vasopressin, administered intranasally, is currently the treatment of choice in patients with diabetes insipidus. Because of lack of information, DDAVP has not been recommended in pregnancy, but the drug has been used successfully in a few pregnant women. Dosages range from 10 to 25 μg given once or twice daily. In a study by Burrow et al the drug was administered and DDAVP concentrations measured as vasopressin by radioimmunoassay in maternal serum and breast milk. Whereas maternal serum concentrations rose about seven-fold, breast milk concentrations
showed little change. This suggested that, given the low levels of DDAVP in milk, these mothers might also breast-feed.

Summary

In conclusion, the physiologic changes that occur in the pituitary during pregnancy make women harboring pituitary tumors more vulnerable to tumor complications, namely tumor expansion resulting in either visual defects or hormone deficiencies. Fortunately, vast experience with the most common of these tumors (prolactinomas) allows us to make specific recommendations to women with such tumor embarking upon pregnancy. These recommendations have been outlined. In addition to tumors, the anterior lobe of the pituitary may be the site of two rare conditions (Sheehan’s syndrome and lymphocytic hypophysitis) that afflict pregnant women predominantly. Their importance lies in the fact that hypopituitarism, sometimes requiring urgent treatment, may result. Finally, pregnancy may have an unfavorable impact upon women with diabetes insipidus, necessitating careful observation. Given the availability of a specific and highly effective therapeutic agent, desmopressin acetate, the management of these women is rarely problematic.

Acknowledgment

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References

2. Green JD, Harris GW: The neurovascular link between the neurohypophysis and adenohypophysis. J Endocrinol 5:136-146, 1947
60. Moses AM, Notman DD: Diabetes insipidus and syndrome of inappropriate antidiuretic hormone secretion, in Stullerman GH (ed): Advances in Internal Medicine, vol 27, Chicago, IL, Year Book Medical, 1982, pp 73-100