Endocrine disorders in pregnancy

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Abstract

Endocrine disorders in pregnancy are common. Good outcomes can be achieved with multi-disciplinary care in pregnancy. The primary objective of this review is to provide the reader with an overview of national guidelines and where applicable, recent advances with regard to care of women with endocrine disorders in pregnancy. We have outlined care for a broad range of conditions ranging from diabetes and thyroid disorders, to the rarer conditions such as phaeochromocytoma. In addition to the reading list below, we would encourage the reader to keep up to date with reports from the United Kingdom Obstetric Surveillance Service (UKOSS) which studies a range of uncommon conditions in pregnancy as well as the confidential enquiry into maternal and child death [Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK)]. The latter is especially useful for lessons learnt from past maternal deaths, the most common cause of which were indirect maternal deaths from pre-existing medical conditions.

Keywords cushing's; diabetes; endocrine; pregnancy; thyroid

Introduction and background

Collectively, endocrine disorders in pregnancy constitute the most commonly encountered medical disorders. In the presence of an endocrine disorder, normal physiological changes of pregnancy can perturb the stability of these conditions. This may lead to complications and directly contribute to fetal and maternal comorbidity and mortality. As with most medical conditions in pregnancy, multidisciplinary medical and obstetric input can optimize both maternal and fetal outcomes.

Our aims are to provide the reader with an overview of the common endocrine disorders encountered in clinical practice, taking a systematic approach to the subject matter. When considering medical disorders in pregnancy, one should consider both the effects of pre-existing medical conditions (and medications) on pregnancy, and vice versa. These effects can broadly be categorized into six epochs: pre-pregnancy, 1st trimester, 2nd trimester, 3rd trimester, labour and delivery, and finally the postpartum period.

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Diabetes

In the UK approximately 5% of pregnancies are complicated by diabetes. Approximately over 87% of these are due to gestational diabetes, and 12 % have pre-existing type 1 or type 2 diabetes.

Pre-existing diabetes

Diabetes in pregnancy can be associated with a number of important maternal and fetal complications. Pregnancy in turn, can complicate pre-existing diabetes by causing a deterioration in diabetic retinopathy, renal function and occasionally peripheral neuropathy. Rarely, poor glycaemic control can also result in maternal death due to hypoglycaemia or diabetic ketoacidosis. Pre-pregnancy counselling and good antenatal care with multidisciplinary input is important.

Some women with pre-existing diabetes may also have co-existing hypertension, cardiovascular and renal disease. As a result, they may be on pharmaceutical agents that are not appropriate for pregnancy. Examples of such medications include statins, ACE-II inhibitors, loop diuretics, sulphonylureas and clopidogrel. Independently of the pharmaceutical agents, there is an increased risk of congenital malformations (47.6/1000 Type 1 Diabetes and 44.8/1000 for Type 2 Diabetes) [National Pregnancy in Diabetes Audit (NPiDA 2017)]. Stillbirth rate is twice that of the general population, and neonatal death rate is four times more. Importantly, 1st trimester HBA1c is directly correlated to congenital anomaly rates.

Current national guidelines recommend a HbA1c level below 48 mmol/mol prior to embarking on pregnancy. Women with HbA1c level of above 86 mmol/mol are advised not to become pregnant. The NPIDA demonstrated that only 8% of women with pre-existing diabetes achieved a HbA1c <48 mmol/mol, used 5 mg of folic acid and avoided potentially harmful medications prior to embarking on pregnancy. As a higher HbA1c and/or high BMI are also found to be associated with high risk of hypertensive disorder in pregnancy, low dose aspirin (LDA) is recommended as soon as viable intrauterine pregnancy is confirmed. The prevalence of pre-eclampsia in pregnancies with type I diabetes is estimated to be 5 to 6 times more than that in the general populations. Risk factors which found to increase the risk of pre-eclampsia include diabetic nephropathy, microalbuminuria, diabetic retinopathy, and pre-existing hypertension. In high risk populations, LDA reduces the risk of pre-eclampsia.

The aim of pre-pregnancy care is therefore to optimize glycaemic and blood pressure control, BMI, and review the medication history as well as commencing 5 mg folic acid for all women with pre-existing diabetes. Assessment for pre-existing complications of diabetes should occur in the first trimester. This involves retinal assessment, urinalysis for micro- and macroalbuminuria, and cardiac symptoms.

Antenatal care in women with pre-existing diabetes focuses on the prevention of pregnancy associated complications, identification of fetal structural heart anomalies by undertaking fetal echocardiography, and optimizing glycaemic control to prevent fetal macrosomia.

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In a recent systemic review, the use of continuous insulin in pregnancy was found to be associated with lower insulin requirements and found to achieve better glycaemic control in the first trimester. However this effect was not observed in subsequent trimesters. It was also found to be associated with higher gestational weight gain and infants were more likely to be large for gestational age.

For women with Type 2 diabetes, Metformin and insulin may be used in combination. If required, corticosteroids for suspected preterm delivery should be accompanied by the use of a variable rate insulin sliding scale to improve glycaemic control.

Induction of labour is indicated at 37–38 weeks owing to the increased perinatal mortality rate in women with pre-existing diabetes. Intrapartum care involves hourly blood sugar monitoring to avoid neonatal hypoglycaemia. Establishment of early feeding in the post-natal period reduces this further. Insulin regimes should return to pre-pregnancy rates.

Gestational diabetes

Gestational diabetes (GDM) in pregnancy is defined by World Health Organization (WHO) as "carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy".

The diagnostic criteria for GDM -are lower than those for overt diabetes, due to the association between maternal glucose levels below those diagnostic of diabetes with fetal and maternal complications. These risks were clarified in many large studies such as the HAPO study which took place between 2000 and 2006 and included over 25,000 thousand pregnant women. The study found strong associations between maternal hyperglycaemia and increased birth weight at levels below those diagnostic of diabetes. Hyperglycaemia was also found to be positively associated with complications such as maternal pre-eclampsia and premature delivery, shoulder dystocia, and neonatal admission to intensive care. Therefore, tight glycaemic control is paramount for successful pregnancy outcomes.

GDM is more likely in the second half of pregnancy, as sensitivity to insulin reduces due to increase in placental hormones such as placental lactogen, and placental growth hormone. Therefore, the standard screening period in the UK is between 24 and 28 weeks. However, there are currently studies which are investigating whether earlier screening (18–22 weeks) and intervention improve pregnancy outcomes.

There is observed increase in prevalence of gestational diabetes in recent years, this is thought to be associated with increase obesity as well as increase in maternal age. Interventions which range from dietary measures to insulin therapy have been shown to improve maternal perinatal outcomes.

In newly diagnosed gestational diabetes, counselling and education on life style and dietary intervention have been shown to be very effective in reducing the requirement of drug therapy. A Large Cochrane overview of 14 systemic reviews into management of GDM found that lifestyle interventions versus usual care reduces the fetal risk of large-for-gestational age.

The introduction of Metformin has revolutionized the care of women with GDM by avoiding or delaying commencement of insulin therapy. The efficacy and safety of using Metformin in addition to dietary changes (alone or with supplemental insulin) has been investigated in many RCTs for the treatment of type II diabetes and GDM. The safety of Metformin has been investigated in comparison to insulin as it crosses the placenta freely. Metformin was not associated with increased perinatal complications as compared with insulin and trials also found that women preferred metformin to insulin treatment. However, the metformin versus insulin for the treatment of GDM trial found that a significant proportion of women (40%) required Insulin for adequate control of hyperglycaemia.

As Metformin does not stimulate the production of insulin it has the advantage that it can be used in women who are overweight without causing additional weight gain associated with the use of insulin.

Nice guidelines recommend induction of labour (IOL) for diabetes before term as evidence showed that this reduce the risk of birth trauma such as shoulder dystocia, and brachial plexus injury associated with fetal macrosomia. A Cochrane review based on good quality RCTs analysed the risks of elective IOL for women with diabetes at 38–39 weeks of gestation and indicated that this may reduce the risk of stillbirth and shoulder dystocia associated with fetal macrosomia without increasing the risk of caesarean section.

Thyroid disease

Thyroid disease is the second commonest endocrine disorder in pregnancy. Hypothyroidism affects up to 2–3% of pregnancies whereas the incidence of hyperthyroidism is approximately 0.2–0.4% of pregnancies, and is usually due to Grave's disease.

Changes in maternal physiology and specifically those due to the human chorionic gonadotrophin (hCG) thyrotropic effect, results in increase in thyroid volume and thyroid hormone levels and hence suppression of thyroid stimulating hormone (TSH). These effects are compensated by a rise in hepatic synthesis of thyroid-binding globulin (TBG), which keeps free T3 and T4 hormone levels within the normal range. Although maternal TSH does not cross the placenta, circulating T4 and T3 do cross the placenta in small quantities and are important for early fetal growth. Poorly managed thyroid dysfunction in pregnancy is associated with many maternal and fetal complications.

Hypothyroidism

Hypothyroidism is usually auto-immune secondary to Hashimoto thyroiditis and caused by antithyroid-peroxidase (TPO) antibodies. Overt hypothyroidism is defined as serum TSH above the normal trimester-specific reference range and serum free T4 below the normal trimester-specific reference range. It is important to consider iatrogenic causes of hypothyroidism. Treatment with radio-active iodine for women with Graves' disease or surgical resection goitre or thyroid cancer may have taken place. Whilst this could have rendered the patient hypothyroid, the implications of the underlying diagnosis is still important (see below). Most women with hypothyroidism are diagnosed prior to pregnancy by virtue of presenting with non-specific symptoms that prompt investigation in primary care.

The total body thyroxine pool must increase by 40–50% to maintain a euthyroid state and in non-hypothyroid women this is driven by high levels of hCG stimulating pituitary TSH release. In women with hypothyroidism the hCG-driven stimulation of TSH

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is absent and generally women are advised to independently increase their dose of levothyroxine by 20–30% upon finding of a positive pregnancy test. This is most easily done by doubling the pre-pregnancy dose of levothyroxine on 2 days of the week.

Thyroid function control should ideally be optimised at the pre-conception stage, aiming to keep TSH below 2.5 mIU/l. This is vital for the fetal neurodevelopment during pregnancy. The fetal thyroid gland is not fully functional until the 16th to 20th week of pregnancy. Until then the foetus relies on adequate maternal thyroid hormones to be transferred across the placenta.

Overt hypothyroidism in the mother has been associated with higher risk of pregnancy complications such as premature delivery, low birth weight, miscarriage and pre-eclampsia as well as deleterious effects on neurodevelopment. Subclinical hypothyroidism (raised serum TSH and normal serum fT4) and isolated hypothyroxinaemia (i.e. a pregnancy-specific condition of low fT4 and normal TSH) have been associated with similar complications although the definition of subclinical hypothyroidism is not the same in all studies and there is ongoing debate regarding the upper limit of normal for TSH concentrations during pregnancy.

In addition, women with raised levels of TPO antibodies are at increased risk of developing thyroid dysfunction during pregnancy and TPO antibody positivity per se have been associated with increased risk of miscarriage and premature delivery.

No randomized controlled trials of levothyroxine treatment for overt hypothyroidism have been conducted during pregnancy, although the general consensus is that overt hypothyroidism during pregnancy should be treated as early as possible. There have been two large randomized controlled trials of levothyroxine replacement in women with mild thyroid hypofunction (subclinical hypothyroidism or isolated hypothyroxinaemia). Neither trial showed beneficial effect on child IQ evaluated at 3–5 years, which was the primary outcome nor were there significant effects on obstetric outcomes which were studied in secondary analyses. It has to be noted that levothyroxine was started relatively late in both trials, at a median gestational age of 13 and 17 weeks respectively. In addition, the levothyroxine replacement dosage of 150 μg daily in the CATS trial may have been too high and other studies have indicated worse cognitive outcomes and increased risks of autism in mothers with high fT4 concentrations during pregnancy.

Whilst there is no clear evidence of benefit of treatment of subclinical hypothyroidism during pregnancy most current guidelines recommend treatment especially in women with raised TPO antibodies. Thresholds to start treatment are generally >2.5 mIU/L in TPO-positive women and >4.0 mIU/L in TPo-negative women. Importantly a recent study has indicated that levothyroxine in subclinical hypothyroidism has beneficial effects on pregnancy loss rates but is associated with increased risks of preterm delivery, gestational diabetes and pre-eclampsia.

The recently completed TABLET trial (Thyroid Antibodies and Levothyroxine trial) which studied the effects of 50 μg levothyroxine versus placebo in euthyroid TPO-antibody positive women with a history of miscarriage or subfertility, has indicated no benefit of thyroid hormone replacement in achieving live births at or beyond 34 weeks nor any effects on other pregnancy outcomes. Increased rates of miscarriage were found confirming adverse obstetric outcomes in women with thyroid autoimmunity but this may not be driven by effects on thyroid function.

Hyperthyroidism

Overt hyperthyroidism is defined as a serum TSH below the trimester specific level, with an elevated freeT3 (fT3)or free (fT4). The main challenge is to distinguish endogenous causes of hyperthyroidism form transient gestational thyrotoxicosis which is caused by stimulation of the thyroid gland by high levels of hCG and is typically found in women with hyperemesis gravidarum. This is generally a self-limiting condition which required supportive treatment only. Hyperthyroidism due to endogenous causes has been associated with an increased risk of severe pre-eclampsia, placental abruption, stillbirth, and intrauterine growth restriction. Uncontrolled hyperthyroidism can also complicate the maternal physiology resulting in elevations in heart rate and cardiac output causing life threatening arrhythmias and heart failure.

95% of hyperthyroidism in pregnancy can be attributed to Graves' disease since that is the most prevalent aetiology in women of childbearing age. Clinical features can be difficult to ascertain due to shared symptomatology with pregnancy such as heat intolerance and palpitation. More rare causes of endogenous hyperthyroidism include toxic nodular hyperthyroidism, drug induced thyrotoxicosis and hyperthyroidism caused by trophoblastic disease. Measurement of TSH receptor antibodies (TRAb) and serum fT3 concentrations are useful in distinguishing Graves' disease from transient gestational thyrotoxicosis. Further factors which may help differentiate the conditions include the presence of a family history and clinical features of Graves' ophthalmopathy which are usually absent in pregnancy-induced thyrotoxicosis. In patients with a palpable goitre, ultrasound assessment will provide important information regarding the size of the thyroid and possible tracheal compression, which may have implications for intubation.

Treatment of endogenous causes of hyperthyroidism is with antithyroid drugs, propylthiouracil or carbimazole. Radioactive iodine is contra-indicated in pregnancy but women may decide to have definitive treatment of hyperthyroidism prior to embarking on pregnancy. Pregnancy should be avoided for 6 months following the administration of radioactive iodine. If women develop severe side-effects to antithyroid drugs and remain very thyrotoxic, thyroidectomy may be considered during pregnancy and ideally should be undertaken in the second trimester by an experienced surgeon.

There is ongoing debate regarding the choice of antithyroid drugs during pregnancy. Carbimazole and its active component methimazole, the drug of choice outside pregnancy has been associated with increased risks of fetal abnormalities including choanal atresia and aplasia cutis. Propylthiouracil has been linked to liver failure both inside and outside the setting of pregnancy and is also associated with birth defects albeit to a lesser extent than carbimazole. Current guidelines recommend that Propylthiouracil is the drug of choice before and during the first trimester of pregnancy and if antithyroid drugs are still needed in the second trimester a switch to Carbimazole at around 16 weeks' gestation is usually recommended. The lowest possible dose of antithyroid drugs should be used and often antithyroid drugs can be discontinues since Graves' disease often gets better during pregnancy but flares up following delivery.

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Titration regimes with antithyroid drugs are recommended since block and replace regimens carry an increased risk of fetal hypothyroidism as antithyroid drugs cross the placenta more readily than levothyroxine.

Uncontrolled hyperthyroidism is associated with spontaneous abortion, growth restriction, premature labour and perinatal mortality. Graves' disease is caused by stimulating TSH receptor antibodies (TRAb) which can also cross the placenta, causing fetal hyperthyroidism and fetal goitre. The incidence of neonatal thyrotoxicosis is 1–5% with mortality rates as high as 12–20%. Therefore, in women with Graves' disease TRAb levels should be tested in pregnancy at approximately 20 weeks' gestation in order to assess the risk of fetal Graves' disease. Serum TRAb more than three times the upper limit of normal significantly increase the risk of fetal Graves' disease, independently of the maternal thyroid status. In these cases, close monitoring of fetal growth and heart rate with monthly scans and weekly heart auscultations is required to diagnose persistent fetal tachycardia.

Provided a mother with Graves' disease is euthyroid in pregnancy, no changes to intrapartum care is required. In the post-natal period either PTU or Carbimazole can be used and both are safe in breastfeeding if doses of less than 20 mg daily of Carbimazole or less than 400 mg daily of PTU are used. Thyroid function testing of a baby born to a mother with Graves' disease is required prior to discharge due to possible transplacental transfer of TRAb. Input from endocrinologists and cardiologists may be required in the event of poorly controlled hyperthyroidism, as heart failure can occur, particularly at the time of delivery.

Prolactinomas

Prolactinomas are common pituitary tumours inside and outside pregnancy. They are classified radiologically according to their size into macroprolactinomas (>10 mm) and microprolactinomas (≤10 mm).

In pregnancy the anterior pituitary gland increases in size due to hyperplasia and hypertrophy of prolactin-secreting cells. This normal physiological change results in increase in prolactin levels by up to ten times the normal range with levels falling to the pre-pregnancy range within 2 weeks postnatally in non-lactating women.

Prolactinomas are commonly diagnosed prior to pregnancy due to symptoms such as secondary amenorrhoea, and infertility. Macroprolactinomas may also present with frontal headache and visual field defect due to compression of the optic disc usually causing bitemporal hemianopia. During pregnancy there is increased risk of tumour enlargement, particularly in the case of macroprolactinomas which can increase up to 30% and cause visual impairment. Nevertheless, this is not known to have any impact on pregnancy outcomes.

Dopamine agonist treatment if the first line management option for prolactinomas. These medications exploit the physiological inhibition of prolactin secretion, by increasing dopamine production and treatments such as bromocriptine and cabergoline can also supress prolactinoma growth. Bromocriptine can normalize prolactin levels in 80–90% of microprolactinomas and 70% of macroprolactinoma, although it is associated with side effects such as nausea and vomiting, headaches and postural hypotension.

Cabergoline is thought to have a better profile in terms of efficacy and tolerability, however, Bromocriptine has a safer profile in early pregnancy. Dopamine agonist therapy is usually discontinued during pregnancy in patients microprolactinomas but continued in macroprolactinomas due to the risk of further expansion of the tumour. Bromocriptine is usually used but due to its worse side-effect profile, carbergoline is often used.

Surgical management of prolactinomas is indicated in selected cases where is there no response to medical treatment or in the case of tumour re-expansion.

During the intrapartum stage, there is no indication for continuous electronic fetal monitoring. Duration of pushing is in accordance with NICE Intrapartum Care Guidelines unless there is symptomatic tumour enlargement. In which case a planned caesarean section should be considered to prevent pituitary apoplexy.

In the postnatal period there is no contraindication for breastfeeding in women with prolactinomas, as there are no known risks of tumour growth during lactation. Often dopamine agonists are discontinued at 36 weeks of pregnancy to allow successful breastfeeding. An MRI scan is required in the postpartum period to assess for tumour growth. If there is evidence of enlargement, dopamine agonists should be restarted, however this will cause suppression of lactation impact on breastfeeding.

Cushing's syndrome

Cushing's syndrome is rarely seen in pregnancy as high cortisol and androgen levels supress gonadotropin releasing hormone resulting in anovulation and infertility. Benign adrenal adenoma is said to be the most common cause of Cushing's syndrome in pregnancy as its most likely to be purely cortisol-producing, not affecting ovulatory function.

Cushing's syndrome is very difficult to diagnose in pregnancy due to overlap with normal physiological changes that are commonly seen in pregnancy such as weight gain, central obesity, abdominal striae and hypertension. Furthermore, due to the relative hypercortisolaemia in pregnancy, dexamethasone suppression tests can be difficult to interpret.

Nevertheless, due to high rate of serious complications in pregnancy, it is an important condition to diagnose and treat. Serious and common maternal complications include hypertension, pre-eclampsia, diabetes and heart failure. This is associated with increased maternal mortality. Fetal complications may result in pregnancy loss, fetal growth restriction, premature delivery, and neonatal adrenal insufficiency.

Studies have shown that the treatment and management of Cushing's syndrome during pregnancy improves pregnancy outcomes. The first line recommended treatment is surgery of either the adrenal or pituitary gland depending on the cause of Cushing's syndrome and is ideally timed during the second trimester.

Medical therapy is used in cases of surgical failure or contraindication to surgery. Metyrapone is the most commonly used anti-adrenogenic during pregnancy and although it crosses the placenta, there are no reported fetal abnormalities with its use. Other anti-androgenic medications are avoided in pregnancy due to teratogenicity and inadequate efficacy.

Adrenal tumours

Phaeochromocytoma is a rare catecholamine-secreting adrenal tumour. They are very difficult to diagnose in pregnancy as they can be masked by physiological hypotension in the first and

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second trimesters. Nonetheless they should not be missed in pregnancy since they can result in significant maternal and fetal complications. Phaeochromocytoma may potentially be fatal as it can result in hypertensive crisis and maternal death due arrhythmias and cardiovascular disease (up to 15%). It is also associated with high risk of fetal death. Although catecholamines do not cross the placenta, elevation of blood pressure can cause placental abruption, and the rebound episodes of hypotension may lead to severe hypoxia and fetal compromise.

Phaeochromocytoma can present with sudden labile blood pressure, which to be confused with pre-eclampsia, which usually occurs after 20 weeks. Therefore, phaeochromocytoma should be suspected in pregnant women with persistent hypertension, particularly in the absence of proteinuria and oedema.

Diagnostic tests include measurement of serum or urinary catecholamines. Imaging with an MRI scan of the adrenal glands is used to localize adrenal tumours.

Management of phaeochromocytoma in pregnancy aims to prevent hypertensive crisis in pregnancy. Management of hypertension usually starts with an alpha blocker such as phenoxybenzamine, which can cross the placenta and may cause transient hypotension in the neonates. Beta blockers, are also used to control signs of tachycardia, however, they are not used before alpha blockers in the case of phaeochromocytoma as they can result in dramatic blood pressure elevations due to unopposed α-adrenergic effects by catecholamines.

β-Blockers are associated with increased risk of fetal growth restriction, and therefore serial growth scans are required during the third trimester antenatal care. Magnesium sulphate can also be used in the management severe hypertension, in addition to its vasodilator effects, it is thought to inhibit catecholamine release from the adrenal tumour and block peripheral catecholamine receptors.

Elective caesarean section is recommended due an increased risk of intrapartum malignant hypertension and maternal death. Nevertheless, there are recent reports of successful outcomes with regional analgesia and close monitoring.

Surgery can be curative for phaeochromocytoma; however, if diagnosed during pregnancy surgery is usually delayed until fetal maturity and then timed with a caesarean section or during the postpartum period.

Primary and secondary adrenal suppression

In pregnancy corticotrophin-releasing hormone (CRH) and adrenocorticotropic hormone and subsequently cortisol levels increase due to additional CRH and ACTH production by the placenta as well as decreased in catabolism.

The fetal adrenal gland provides large quantities of steroids predominantly in the form of dehydroepiandrosterone (DHEA). DHEA is an important steroid used for placental oestrogen production, hence the development and function of the fetal adrenal gland is vital for placental steroid production.

Primary adrenal insufficiency in the mother usually requires regular hydrocortisone and fludrocortisone, with increased doses during episode of increase systemic stress. The hydrocortisone replacement requirements usually increase during the second trimester of pregnancy and dose adjustments are required. If adrenal insufficiency is adequately treated with appropriate steroid replacement during pregnancy, there is no associated maternal or fetal morbidity.

During the intrapartum stage, corticosteroids are replaced intravenously either with a continuous 200 mg hydrocortisone infusion (or 50 mg IV 6 hourly), due to the additional systemic stress to prevent an adrenal crisis. Fludrocortisone is not usually required as hydrocortisone is given in high doses and will therefore have sufficient mineralocorticoid effects.

There are no contraindications to breastfeeding and pre-pregnancy doses of steroid replacement therapy can be recommenced usually within 72 h post-delivery unless there is ongoing systemic stress. ◆

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Practice Points

- Pre-pregnancy care significantly improves pregnancy outcomes especially for women with pre-existing medical conditions such as diabetes and thyroid disorders.
- A multi-disciplinary approach can improve obstetric outcomes.
- Pregnancy provides an opportunity for ongoing health promotion in women with endocrine disorders such as diabetes.
- Rarer disorders such as phaeochromocytoma should be considered in refractory hypertension and requires specialist input.
- Women with primary or secondary adrenal suppression require steroid replacement in situations of systemic stress in the intrapartum period or if surgical procedures are required.

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