

# Autoimmune Diseases and Pregnancy – Is There a Greater Risk of Giving Birth to a Sick Child?

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## Abstract

This study aims to describe the impact of some of the most common autoimmune diseases, such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD), myasthenia gravis (MG), chronic inflammatory bowel disease (IBD), type 1 diabetes (T1D), autoimmune thyroid disease, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriasis, vasculitis, and antiphospholipid syndrome (APS), on pregnancy in women. This review investigates the risk to the offspring of the women; that is, whether the mother's disease may affect fertility or disturb fetal development.

## Keywords

Autoimmune disease • Pregnancy • Pregnant woman • Multiple sclerosis • IBD • T1D

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## List of abbreviations

anti-CCP: Anti-Cyclic Citrullinated Peptide antibodies; anti-La/SSB: Anti-La/SSB antibodies; anti-Ro/SSA : Anti-Ro/SSA antibodies; Anti-TNF: Anti-Tumor Necrosis Factor; CI: Confidence Interval; CU: Chronic Urticaria; DMARDs: Disease-Modifying Antirheumatic Drugs; HLA-B: Human Leukocyte Antigen B; HLA-C: Human Leukocyte Antigen C; HLA-DP: Human Leukocyte Antigen DP; HLA-DQ: Human Leukocyte Antigen DQ; HLA-DR: Human Leukocyte Antigen DR; ICAM: Intercellular Adhesion Molecule; IFN- $\gamma$ : Interferon gamma; IL-1: Interleukin 1; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; PE: Pulmonary Embolism (lub Physical Examination – zależnie od kontekstu); TNF: Tumor Necrosis Factor; TSH-R: Thyroid-Stimulating Hormone Receptor; UVB: Ultraviolet B; VCAM: Vascular Cell Adhesion Molecule.

## 1. Introduction

With the growth of awareness about autoimmune diseases, there are better ways of diagnosing them and new treatment possibilities. Most of the theories suggest that the development of an autoimmune disease requires a genetic predisposition and environmental factors that trigger the immune pathways that lead ultimately to the disease development. Regardless of extensive research, there are no genetic tools that can be used clinically to anticipate the risk of autoimmune disease (Wang et al. 2015). The possibility of autoimmune

disease in identical twins is 12%–67%. Because of this fact, there are most important environmental factors in the pathophysiology of the disease and also the potential effect of stochastic or epigenetic aspects (Gupta and Hawkins 2015). Additionally, autoimmune diseases pose significant challenges during pregnancy, as they can influence maternal health, fertility, and fetal development. Previous researches suggest that maternal autoimmune diseases are associated with a higher risk of adverse pregnancy outcomes, such as preeclampsia, preterm birth, and growth restriction in the fetus. These conditions may also influence long-term health outcomes in offspring, potentially through mechanisms such as epigenetic modifications or immune system dysregulation (Andrawus et al. 2022; Singh et al. 2024). This study aims to examine the effects of some of the most common autoimmune diseases on pregnancy outcomes in women, as well as the birth and health outcomes in their offspring. This review investigates the risk to the offspring of the women; that is, whether the mother's disease may affect fertility or disturb fetal development.

## 2. Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorders (NMOSD)

MS is a neurodegenerative disease, which is characterized by demyelination, inflammation, and axonal damage in the central nervous system (Varytė et al. 2021). It is an active intermittent disease (relapsing-remitting MS) in most cases; however, about 15% of the affected people experience primary progressive MS (Vidal-Jordana and Montalban 2017).

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It is more common in women, usually appearing at the age of 20–40 years old, which coincides with their reproductive time (Varytė et al. 2021).

The most common symptoms of MS are muscle stiffness and muscle spasms, fatigue, dizziness, clumsiness, loss of balance and coordination, and difficulty with cognitive function. The diagnosis of this disease is based on clinical examination and neuroimaging such as lesions visible on magnetic resonance imaging (Dobson and Giovannoni 2019).

NMOSD are characterized by long segments of spinal cord inflammation and severe optic neuritis. The patient often presents bouts of intractable vomiting and hiccoughs (area postrema syndrome) (Huda et al. 2019).

Having MS or NMOSD neither affects the fertility nor the course of pregnancy itself. During pregnancy, many women find that their symptoms stay the same or even improve (Shosha et al. 2017; Vukusic et al. 2019). The latest research even suggests that nulliparous women with MS develop a progressive form of MS at a younger age (Zeydan et al. 2020). In women who suffer from MS or NMOSD and get pregnant, relapse in the disease usually appears after the pregnancy (Confavreux et al. 1998). This is caused due to the necessity of changing treatment during pregnancy. Moreover, it can be said that the pregnancy period is a protective state for women with autoimmune diseases because the fetus is an allograft due to the paternal proteins and immunizes in the woman's body. This applies to various autoimmune diseases described in this study, not only to patients with MS or NMOSD (Voskuhl and Momtazee 2017).

A safe drug for the fetus is interferon (IFN)- $\beta$  because it does not cross the placenta (Neuhaus et al. 2007). Hellwig et al. (2020) have collected data from 26 countries of the European Economic Area about pregnant women with MS exposed to IFN- $\beta$  during pregnancy or within 1 month before conception. No significant differences were compared between IFN- $\beta$  a-exposed pregnancies with the general population with regard to spontaneous abortions or congenital anomalies in live births (Hellwig et al. 2020). Similar results were obtained from Finnish and Swedish studies, in which there were no differences detected in infants whose mothers were treated with IFN- $\beta$  in birth weight, length, and head circumferences compared with the control group (Hakkarainen et al. 2020). What is more, breastfeeding under IFN- $\beta$  is not related to any adverse outcomes in the first year of life in the child as only a small amount of IFN- $\beta$  passes to the milk (Ciplea et al. 2020). There are similar conclusions when it comes to the other MS drug – glatiramer acetate (GA). GA due to its large size does not cross the placental barrier. GA is a complex polypeptide with a similar molecular weight compared to IFN- $\beta$ . GA treatment before conceiving and during pregnancy does not relate to an increased risk for inborn abnormalities compared with the general population (Varytė et al. 2021).

Other specifics for MS dimethyl fumarate are not recommended during pregnancy due to insufficient investigation into the subject of its toxicity for the fetus (Varytė et al. 2021). Another contraindicated drug for patients with MS who are planning to conceive is teriflunomide. In animal studies, it was confirmed for its teratogenicity and embryotoxicity (Varytė et al. 2021). Recent studies by Vukusic et al. (2019) present that there is no higher risk of spontaneous abortions or inborn abnormalities in pregnancies occurring during teriflunomide than in the general population. Similar reports were presented by Henson et al. (2020) investigating the parent compound of teriflunomide – leflunomide. Interestingly, Vukusic et al. (2019) observed in their research that there were no signs of teratogenicity noticed in women with male partners receiving teriflunomide or leflunomide. Despite this information, these drugs and their influence on embryogenesis need to be further investigated and, currently, it is recommended to avoid teriflunomide treatment and eliminate the substance from the organism using activated charcoal or cholestyramine. Due to the small molecular weight, this drug should also be withdrawn during the breastfeeding period (Varytė et al. 2021).

Recombinant humanized monoclonal antibody, alemtuzumab, is also one of the drugs in the treatment of MS and NMOSD. Due to an increased risk of autoimmune thyroiditis and the fetal risks related to it, including premature birth, preeclampsia, reduced birth weight, and neurocognitive impairment, it is not recommended to be taken by pregnant women (Decallonne et al. 2018). It is also not recommended to breastfeed during treatment by alemtuzumab (European Medicines Agency 2019).

Humanized monoclonal antibody, natalizumab, is used in the treatment of MS or NMOSD. It is better to discontinue the treatment with natalizumab early in pregnancy instead of before conception, which results in a reduction of disease relapses. Landi and Marfia (2020) presented that natalizumab continuation later into pregnancy resulted in lower annualized relapse rates compared with discontinuance before or early in pregnancy.

Treatment by another recombinant humanized monoclonal immunoglobulin, ocrelizumab, is advised to be accompanied by the use of effective birth control while receiving ocrelizumab for up to 12 months; however, some research claims that it is safe to use this drug during pregnancy (Oreja-Guevara et al. 2019).

In summary, maternity planning is achievable for patients with MS or NMOSD, but pregnancies in these individuals should be closely managed by an experienced obstetrician in collaboration with a neurologist to ensure optimal care. Additionally, further research is essential to evaluate the long-term effects of medications used in the treatment of MS and NMOSD on children. To improve clarity, the author should specify which

drugs require further research and which have sufficient evidence to guide pregnancy use. For example, GA and IFN- $\beta$  are relatively well-studied and often considered safer during pregnancy whereas drugs like rituximab, fingolimod, and natalizumab have limited long-term data. Clear delineation would help clinicians make informed decisions, prioritize research, and support patients in understanding the risks and benefits of treatment during pregnancy.

### 3. Myasthenia Gravis (MG)

MG is an autoimmune disorder that affects 30 cases per 100,000 population (Bourque and Breiner 2018). The most common symptom is fatigable weakness of the ocular, bulbar, respiratory, axial, and limb muscles, which worsens during activity (Hehir and Silvestri 2018). The disease is caused by antibodies against the acetylcholine receptor (AChR), which produce a compromise in the end-plate potential, reducing the safety factor for effective synaptic transmission (Hughes et al. 2004). Women are more often affected by this disease than men. However, 20–40-year-old women and men (who have a higher incidence of thymoma that is associated with MG) are most commonly affected. Usually, the symptoms appear in their second and third decades of life (Bourque and Breiner 2018). This is why it affects their reproductive life. Although MG does not reduce fertility, as the age of the first pregnancy is currently receding, more women suffering from myasthenia get pregnant than in recent years. The serum quantity, obtained by radioimmunoprecipitation, allows the detection of all types of anti-AChR antibodies, including those against the fetal form of the receptor (Béhin et al. 2008). Almost all generalized MG patients have antibodies to both the adult and fetal forms of AChR (Shi et al. 2012). There is a term called neonatal myasthenia with persistent retractions and myopathic features. In this condition, antibodies selectively inhibit the function of the fetal gamma unit and cross the placenta at a critical period in fetal development (Norwood et al. 2014).

Myasthenia exacerbates in nearly half of the females during pregnancy; it is also connected with higher rates of preterm premature rupture of membranes and cesarean delivery. Ducci et al. (2017) observed that transient neonatal MG occurred in 12.9% of live-born infants; however, no predictors were found. Myasthenia exacerbation is more often in the first trimester or post-partum (Roche and Bouhour 2021). This is important to observe respiratory function in pregnant women, as the growing uterus restricts diaphragm expansion. This may increase problems with breathing in myasthenic patients (Roche and Bouhour 2021).

There may also be problems with delivery in women suffering from MG. Hoff et al. (2007) wrote about more frequent complications in delivery than in the general population. It was more frequent even in asymptomatic patients (Hoff et al. 2004).

Vaginal delivery is possible, however, there may be a necessity of using instrumental assistance (Roche and Bouhour 2021). Cesarean section should be performed under epidural anesthesia while doctors should abstain from general anesthesia (Tsurane et al. 2019).

Interestingly, in both mothers who do give birth to children with myasthenia disease and in those who give birth to asymptomatic children, there are the same anti-Rach antibodies with the same antigenic specificities. There was no pattern of transmission of the disease and there was no correlation found between the severity of maternal disease (Tzartos et al. 2008). It was observed that myasthenia in infants correlates with a high ( $>2$ ) anti-fetal/adult AChR antibody ratio (Gardnerova et al. 1997). Neonatal myasthenia often occurs in other pregnancies (Bourque and Breiner 2018), which may be avoided by performing a thymectomy before pregnancy (Hoff et al. 2007). Neonatal myasthenia presents symptoms like hypotonia, difficulty in sucking, and weak cries which resolve for up to 3 months (Lindroos et al. 2024). There were also several patients presenting transient neonatal anti-muscle-specific kinase (anti-MuSK) myasthenia. In such patients, there are MuSK autoantibodies instead of the AChR (Niks et al. 2008).

Physiologic transformations during the first trimester (vomiting, increase in blood volume, modification of intestinal absorption) should be taken into account to adjust medication along with teratogenic features of the medications (Ducci et al. 2017). Teratogenic features present methotrexate (MTX) and mofetil mycophenolate, which is why these two drugs should be discontinued, respectively, for 3 months and 6 weeks before pregnancy (Ibarra Barrueta et al. 2023). Also, patients who receive rituximab should be on contraception for a year after the last infusion. During the pregnancy, women may use anticholinesterase inhibitors, corticosteroids, and azathioprine (Massey and De Jesus-Acosta 2014).

In conclusion, there is no reason to discourage pregnancy in women with MG; however, each case should be managed by a multidisciplinary team to ensure optimal care for both the mother and the child. This approach allows for tailored treatment plans and maternity care that address individual needs. For researchers, future studies should focus on evaluating the safety and feasibility of natural childbirth in women with MG. Specifically, research should investigate factors that influence the choice of delivery method, potential risks during labor and delivery, and strategies to minimize complications. Additionally, more data are needed on the long-term effects of MG and its treatments on both maternal and neonatal health outcomes.

### 4. Chronic Inflammatory Bowel Disease (IBD)

Among chronic IBD, we may list Crohn's disease (CD) and ulcerative colitis (UC). Most people present symptoms in

their 20s and 30s (Abhyankar et al. 2013). CD characterizes abdominal pain and diarrhea caused by transmural inflammation that occurs anywhere along the gastrointestinal tract, and the lesions occur discontinuously (Ballester Ferré et al. 2018). In UC patients, continuous superficial inflammation localized to the colon and rectum results in bloody diarrhea (Ordás et al. 2012). Diagnosis of each of the diseases is based on clinical presentation and the results of endoscopic evaluation with biopsy (Bruner et al. 2023).

As the disease often affects people in their third and fourth decades of life, the cases of pregnant women with IBD are not rare. Overall, fertility rates for women with IBD are comparable to rates in the normal population (Calderwood and Kane 2004). Some people decide to remain childless due to the fear of disease transmission to their child; however, current research results show a low transmission rate, about 7% when one of the parents has CD and even less when one of the patients is UC affected. The risk for both parents suffering from IBD is 37% (Yang et al. 1993). In some patients, the inflammation of the bowel situated near the fallopian tubes or ovaries may decrease fertility (Calderwood and Kane 2004).

Costa et al. (2022) conducted a retrospective descriptive analysis of 47 pregnant patients with IBD. The study utilized medical records from routine gastroenterology and obstetrics visits, as well as urgent care visits, to collect data on medical history, demographics, disease characteristics (type, activity, severity), therapies, and outcomes related to pregnancy, labor, postpartum, and newborn health.

They reported obstetric and neonatal complications in 55.3% and 14.6% of the IBD population, respectively, with a higher prevalence among UC patients. Active IBD was associated with increased adverse outcomes, such as fetal growth restriction (FGR) and low birth weight (LBW). Conversely, women with IBD receiving medical treatment experienced fewer obstetric/neonatal complications and required fewer cesarean sections. However, the analysis lacked clarity on the specific variables adjusted for to account for potential bias, which limits the interpretation of these findings (Costa et al. 2022).

What is more, hormonal, immunological, and microbial changes occurring during normal pregnancy may influence the course of IBD. However, there were contradictory conclusions obtained in different studies. Castiglione et al. (1996) observed that the incidence of relapses in the first 3 years after pregnancy is lower than in the pre-pregnancy period. On the contrary, Pedersen et al. (2013) claimed that child-bearing women with CD have a similar disease course during and after pregnancy compared with non-pregnant women with this disease. Active IBD increases the risk of pregnancy complications and adverse pregnancy outcomes (Abhyankar et al. 2013).

What is more, a beneficial effect of pregnancy on epithelial barrier function was observed, with relatively small fluctuations of pregnancy hormones already affecting the gut barrier. Moreover, an overall image of the induction of tolerance and suppression of immune responses during gestation is ascending (van der Giessen et al. 2019).

Vaginal delivery is a safe option except for pregnant women with active anoperineal lesions. If it comes to delivery by cesarean section, it should be systematically discussed in women with ileal pouch-anal anastomosis (Foulon et al. 2020).

When it comes to the treatment options, except for MTX and leflunomide, typically used treatment options are safe. Nielsen et al. (2022) have conducted a systematic review and meta-analysis of biological drugs that are used routinely in pregnant women with IBD such as anti-tumor necrosis factor (TNF), anti-integrins, and anti-cytokines.

In women with a severe course of the disease, there is a risk of malnutrition that may lead to disturbed fetal development (Calderwood and Kane 2004). Pregnant patients with IBD should be closely monitored by obstetricians and supported by clinical dietitians to ensure comprehensive care. Researchers should prioritize studies that analyze obstetric and neonatal outcomes, with a particular emphasis on identifying potential complications and tracking disease progression in both mothers and their offspring in the years following delivery.

## 5. Type 1 Diabetes (T1D)

Of all cases of diabetes, T1D accounts for 10% of cases. This disease is caused by autoimmune destruction of insulin-producing  $\beta$  cells in the pancreas by CD4<sup>+</sup> and CD8<sup>+</sup> T cells and macrophages infiltrating the islets (Gillespie 2006). T1D is the major type of diabetes in children and young people, accounting for  $\geq 85\%$  of all diabetes cases in people <20 years of age worldwide. In general, the incidence rate increases from birth and peaks between the ages of 10 years and 14 years (Maahs et al. 2010). As it affects the patients for all their lives, many feminine T1D patients become pregnant. The most common symptoms of T1D are polyuria, polydipsia, and weight loss (Gillespie 2006). Diagnosis of T1D can be made based on the sugar blood test and clinical presentation. T1D is not a hereditary disease, but people with T1D have a genetic predisposition to autoimmune diseases and this tendency to autoimmunity can be inherited (Gillespie 2006).

The basic drug used in the treatment of patients with T1D is insulin. A patient with newly diagnosed diabetes requires hospital treatment. Initially, insulin is administered by continuous intravenous infusion using an external drug delivery pump. The only way to treat T1D is by insulin therapy, which must be accompanied by a systematically



followed appropriate diabetic diet. To maintain proper blood glucose levels, the patient must conduct self-monitoring, that is, measure the blood glucose level using a glucometer (Gillespie 2006).

Treatment of a patient with T1D usually involves four subcutaneous injections (sometimes more) of insulin a day or administering insulin using a personal insulin pump. Short-acting human insulin or a fast-acting analog should be used before meals. Using insulin is safe during pregnancy (Mathiesen et al. 2011).

Hypoglycemia is a state when the blood glucose level is  $<4.0$  mmol/L, and this is very dangerous during pregnancy (McCance and Casey 2019). Interestingly, Ringholm et al. (2012) have investigated that in T1D patients, severe hypoglycemia occurs three to five times more often in early pregnancy than before pregnancy. What is important is that there are no long-term consequences of maternal hypoglycemia on the child. The risks are to the woman herself, such as loss of consciousness, seizures, hospital admission, and death (Rizzo et al. 1991). Furthermore often in women with diabetes, hypertension occurs. It complicates 1 in 10 pregnancies (Schaefer-Graf et al. 2018).

Insulin resistance is a phenomenon that progresses from mid-pregnancy to the end of the third trimester, when it reaches the level observed in type 2 diabetes (T2D). Insulin resistance, which is essential to the development of most T2D cases, is a state of reduced insulin sensitivity. Insulin sensitivity is the ability of insulin to lower plasma glucose levels. It is achieved by stimulating glucose uptake and use in skeletal muscle and adipose tissue and reducing hepatic glucose production (Fujimoto 2000). Although insulin resistance is typically associated with T2D, recently researchers have highlighted the role of insulin resistance in the pathophysiology of T1D (Gutaj et al. 2015). In T1D, insulin resistance is clinically recognized by an increased requirement for insulin (Kilpatrick et al. 2007). Insulin sensitivity in late pregnancy is 45%–70% lower compared with the period before pregnancy. The decrease in insulin sensitivity in the mother's tissues causes an increase in insulinemia, which is possible due to an increase in the mass of  $\beta$  cells (10%–15%), an increase in insulin production, and glucose-dependent insulin secretion. Changes in the production and action of insulin enable the storage of nutrients after meals and their rapid use in the postabsorptive period. Maternal postprandial hyperinsulinemia inhibits lipolysis and ketogenesis and increases amino acid uptake, promoting fat storage and protein synthesis by tissues. Glucose utilization by the placenta and fetus causes a decrease in maternal glycemia and insulin in the postabsorptive period. Hypoglycemia triggers a response from the sympathetic nervous system in the form of hepatic gluconeogenesis and the utilization of fat stores, manifested by an increase in the concentration of free fatty acids and

ketogenesis. Maternal insulin resistance is compensated by increased insulin production. This is caused by an increase in the expression of prolactin receptors in the pancreatic islets, which also bind placental lactogen. Lactotropic hormones stimulate  $\beta$ -cell proliferation, insulin gene expression, and glucose-dependent insulin secretion (Ballester Ferré et al. 2018). Temple (2002) has proved that improper controlling of blood sugar in the early stages of pregnancy correlates with a fourfold increase in the risk of spontaneous miscarriage and a ninefold increase in the risk of congenital defects in women. Congenital defects in newborns of diabetic mothers concern the heart, nervous system, digestive tract, musculoskeletal system, and urinary system. The above defects occur much less frequently in planned pregnancies compared with unplanned ones. This may be because planned pregnancies allow for better glycemic control and the avoidance of medications contraindicated in early pregnancy, reducing the risk to the fetus (Depla et al. 2021). A characteristic defect of diabetes is caudal regression syndrome with shortening of the femur, but this defect is very rare (Taylor et al. 2019). The most common defects are the cardiovascular and nervous systems. The most common heart defect is hypertrophic cardiomyopathy (Desoye and Herrera 2021).

One of the severe states, which are very serious in T1D patients, is ketoacidosis (Sibai and Viteri 2014), which results in increased rates of perinatal morbidity and mortality (Calimag et al. 2023). It is treated with aggressive volume replacement, initiation of intravenous insulin therapy, alteration of acidosis, alteration of electrolyte abnormalities, and observation of maternal–fetal response to treatment (Sibai and Viteri 2014).

Pregnant T1D women should be under the care of an obstetrician, endocrinologist, midwife, nurse, and a specialist dietitian, who knows about diabetes management (McCance and Casey 2019). Worldwide guidelines for women with gestational diabetes recommend delivery at 38–40 weeks' gestation to prevent the risk of stillbirth or macrosomia. Following these guidelines, a large number of women undergo induction of labor (IOL). IOL is controversially discussed as a potential risk factor for sudden C-Section (Weschenfelder et al. 2022). Further research should focus on understanding the impact of hormonal changes during pregnancy and developing strategies to prevent hypoglycemia and manage insulin resistance in women.

## 6. Autoimmune Thyroid Disease

Autoimmune thyroid disease is the most frequent organ-specific autoimmune disease. Those are Graves' disease and Hashimoto's thyroiditis (Vargas-Uricoechea 2023).

Graves' disease is the most common reason for hyperthyroidism, which is a type of thyrotoxicosis caused by inadequate

synthesis of thyroid hormones and their secretion by the thyroid gland (Ross et al. 2016). The autoimmune aspect of Graves' disease consists of autoantibodies stimulating the thyrotropin receptor (TSH-R). These autoantibodies by binding to receptors in the thyroid are responsible for creating more and more thyroxine and triiodothyronine (McIver and Morris 1998).

Thyrotoxicosis caused by high levels of thyroid hormones is characterized by symptoms like palpitations, emotional lability, worsened concentration, weakness of muscles, heat intolerance, and sweating. Signs of thyrotoxicosis confirmed by physicians are tachycardia, hypertension, higher risk of atrial fibrillation, weight loss, and goiter (Gilbert 2017). There are two manifestations of disease typical for Graves' disease – orbitopathy and dermopathy. The former is manifested by retraction of the eyelids, protrusion of the eye anteriorly out of orbit – this state is called exophthalmos, and dysfunction of the extraocular muscles (Sharma and Stan 2019). The latter presents signs of acropachy – swelling and deformities of the fingers (Mota et al. 2007). The frequency of symptoms caused by Graves' disease is higher in the first trimester and lower in the second and third trimesters. High concentrations of thyroid hormones lead to pre-eclampsia, pregnancy loss, heart failure, and preterm delivery. Treatment of hyperthyroidism during pregnancy is similar to that in non-pregnant women and consists of using drugs or excision of the thyroid gland. The main difference is the contraindication of radioactive iodine ablation, which is teratogenic. The preferred drug during the first weeks of pregnancy is propylthiouracil, which demonstrates a lower risk of serious defects in the fetus than different drugs used as antithyroids. The second trimester is the most appropriate time for thyroidectomy when there is a lower risk of complications linked to anesthesia and preterm labor (Lee and Pearce 2022). All children whose mothers had levels of autoantibodies 3.7 times higher than the upper limit of the reference should be examined after delivery. Moreover, blood from the placenta should be drawn to measure thyroid hormones and autoantibodies of the child. It is necessary for eventual treatment with antithyroid drugs. Sometimes, higher levels of thyroid hormones impact on inhibition of the hypothalamus–pituitary–thyroid axis, which can be the reason for hypothyroidism in children (van Trotsenburg 2020).

Hashimoto thyroiditis is the most common autoimmune thyroid disease and is one of the most frequent autoimmune diseases. It is an inflammation of the thyroid gland leading to goiter and hypothyroidism caused by interstitial infiltration of lymphocytes. Autoantibodies against thyroperoxidase and thyroglobulin are considered markers of the disease with the former being more specific and sensitive (Caturegli et al. 2014). The symptoms of Hashimoto's thyroiditis are directly linked to hypothyroidism – a condition where the thyroid hormones are lowered. These hormonal changes lead to decreased cardiac output, atherosclerosis, increased risk of

coronary artery disease, and increase in cholesterol (Udovcic et al. 2017), bradycardia, edema, hypothermia, depression, fatigue, memory impairment, and weight gain (Wilson et al. 2021). Hypothyroidism is treated by using levothyroxine – a synthetic thyroid hormone similar to thyroxine (Antonelli et al. 2021). Pregnant women treated with levothyroxine require higher doses, because in pregnancy the human chorionic gonadotropin stimulates TSH-Rs which leads to lower synthesis of thyroid hormones. Untreated hypothyroidism gives rise to miscarriage, preeclampsia, preterm delivery, and placenta impairment. Moreover, high levels of thyroperoxidase also increase the risk of spontaneous abortion and preterm birth (Wilson et al. 2021). Researchers should focus on understanding how maternal hormones in autoimmune thyroid disease influence fetal development and contribute to pregnancy complications such as preeclampsia or miscarriage. Identifying effective strategies to mitigate these hormonal effects on the fetus and to improve maternal health outcomes during pregnancy is crucial.

## 7. Rheumatoid Arthritis (RA)

RA is an autoimmune systemic disease characterized by joint inflammation and extra-articular involvement. It begins in the small peripheral joints, is usually symmetrical, and progresses to the proximal joints if left untreated. Arthritis over time leads to joint destruction with cartilage loss and bone erosions. RA is caused in many cases through environmental factors and gene interaction, and the development of the disease is also influenced by tobacco. RA with symptoms lasting <6 months is referred to as early RA, and when symptoms last >6 months, it is referred to as persistent RA. Untreated RA is a progressive disease, causing morbidity and increased mortality (Chauhan et al. 2024). Patients with RA often complain of general symptoms such as fever, malaise, and fatigue. Dry eyes associated with keratoconjunctivitis sicca (in about 45% of patients), xerostomia due to sialadenitis (40%), subcutaneous rheumatoid nodules on the extensor surface of the forearm (35%), numbness in the hands and feet associated with compression neuropathy (25%), and dyspnea on exertion or dry cough due to interstitial pneumonia (15%) are frequently observed (Tanaka 2020). Tissues with synovitis are characterized by vasodilation, angiogenesis, synoviocyte proliferation, and lymphocyte accumulation. In tissues with diffuse inflammation, the accumulation of memory T and B lymphocytes can promote the formation of structures that are similar to nucleated centers and lymphoid follicles. In these structures, high expression of pro-inflammatory cytokines and co-stimulators and close cellular interactions are characteristic (Smolen et al. 2018). Among RA patients, about 80% of patients are positive for rheumatoid factors, but this also happens in healthy individuals. Both the sensitivity and specificity of anti-CCP antibodies are 90% or higher, and patients with RA test positive before the onset of symptoms. In patients with

high levels of anti-CCP antibodies or rheumatoid factors, the progression of joint destruction is rapid. Due to inflammation, there is normocytic hypochromic anemia and an elevated white blood cell count (Tanaka 2020).

Delivery by cesarean section has been demonstrated to be more common among women with RA across multiple cohorts with wide-ranging geographic locations (Nørgaard et al. 2010). Several studies have shown an increased risk of preeclampsia in women with RA, and an increased risk of preterm birth has also been demonstrated.

There is conflicting evidence about the impact of RA on infant birth weight. While some research has found a significant connection between RA and LBW, other studies have not observed this relationship. A recent investigation indicated that increased disease activity during the third trimester is associated with a lower birth weight, with a relative risk of 1.45 (95% CI: 1.12–1.78). In addition, higher disability scores, such as those from the Health Assessment Questionnaire, were associated with a reduced gestational age at birth (OR = 2.10, 95% CI: 1.20–3.80). The discrepancies between studies may be attributed to differences in disease activity levels across cohorts, which could affect these findings (Makol and Krause 2016). It is well-documented that partial improvement of disease activity in RA patients often occurs during pregnancy. However, the risk of increased disease activity postpartum rises significantly, with 62% of women experiencing elevated disease activity at 6 months postpartum, peaking at around 12 weeks postpartum. This heightened activity is mediated by changes in cytokine patterns, immune cells, and hormones after childbirth. Studies indicate that prolonged breastfeeding (>17 months) may further increase the risk of RA disease activity (Li et al. 2021).

A subgroup analysis of four studies involving 3761 RA patients reported maternal and neonatal complications: 33.2% of women had cesarean sections, 7.3% experienced preeclampsia, 14.8% had preterm labor, and 9.5% of newborns had LBW. These rates suggest that women with RA face a higher risk of these complications compared with the general pregnant population. For example, Betran et al. (2021) found that the cesarean section rate in the general population is 21.1%. Similarly, preeclampsia occurs in 2%–15% of all pregnancies (Chang et al. 2023), preterm labor affects about 12% pregnant women (da Fonseca et al. 2020) while LBW worldwide is supposedly about 14.7% (Okwaraji et al. 2024). Drugs that may be safely used during pregnancy include corticosteroids, NSAIDs, and several DMARDs, including hydroxychloroquine and sulfasalazine. Drugs recommended to be stopped before pregnancy include MTX and leflunomide, plus the biologics: anti-TNF agents, abatacept, and rituximab. What is important is a treatment regimen that stabilizes a woman's disease before conception, using drugs that can be safely continued throughout pregnancy. Controlling disease activity

during pregnancy is important for both maternal and fetal health. Additional studies should investigate strategies that physicians can employ to prevent preeclampsia and preterm birth in pregnant women with RA, focusing on early detection, management approaches, and effective interventions to improve pregnancy outcomes.

## 8. Systemic Lupus Erythematosus (SLE)

SLE is a systemic autoimmune disease with the involvement of multiple systems. The disease has different varieties differing in clinical manifestations: there is a mild variety with mucocutaneous manifestations as well as multi-organ and severe central nervous system involvement (Justiz Vaillant et al. 2024). Hormonal influence and female sex are significant risk factors for SLE. Estrogen stimulates CD4<sup>+</sup> and CD8<sup>+</sup>, T cells, B cells, thymocytes, macrophages, the release of some specific cytokines (e.g., IL-1), and the expression of HLA and endothelial cell adhesion molecules (VCAM, ICAM). Moreover, prolactin and estrogens promote autoimmunity, increase the B-cell activation factor production, and modulate lymphocyte and plasmacytoid dendritic cells activation (Justiz Vaillant et al. 2024). The most common genetic predisposition is located at the major histocompatibility (MHC) locus. The MHC contains genes for antigen-presenting molecules (class I human leukocyte antigens [HLA-A, -B, and -C] and class II HLA molecules [HLA-DQ, -DR, and -DP]) (Justiz Vaillant et al. 2024). Environmental factors such as UVB radiation, toxins, and infections trigger a loss of immune tolerance in genetically susceptible individuals and lead to aberrant activation of autoimmunity (Ameer et al. 2022). Most SLE risk loci are located within or near genes that encode products functioning in the clearance of lymphocyte signaling, immune complexes, and type I IFN signaling (Ameer et al. 2022). Exacerbations of the disease can occur during pregnancy in women with SLE, particularly in those who have a history of kidney disease or have active disease at the time of conception. The consequence of these exacerbations is an increased number of adverse pregnancy outcomes, including fetal loss, premature birth, preeclampsia, and young children of gestational age. Women with anti-Ro/SSA and anti-La/SSB antibodies require special monitoring because their offspring are at risk for congenital complete heart block and neonatal lupus (Dao and Bermas 2022). One of the most important predictive factors for a good pregnancy outcome is stable disease under pregnancy-compatible medication; the European Alliance of Associations for Rheumatology (EULAR) and the American College of Rheumatology (ACR) have published evidence-based recommendations on treatment in pregnancy and lactation (Zucchi et al. 2023). SLE can achieve better pregnancy outcomes by monitoring associated predictive indicators, raising major concerns for severe complications (Zhang et al. 2022). Fetal-neonatal

complications include preterm birth, miscarriage, intrauterine growth retardation (IUGR), congenital heart block, and neonatal lupus. Hydroxychloroquine is beneficial for improving pregnancy outcomes and is extensively used (Tan et al. 2022). During pregnancy, lupus is generally treated with low-dose prednisone, hydroxychloroquine, pulse intravenous methylprednisolone, and azathioprine. If a woman with SLE has antiphospholipid (aPL) antibodies, prophylactic treatment with aspirin and/or low-molecular-weight heparin is indicated to prevent fetal loss (Baer et al. 2011). Preconception counseling, planned pregnancy, pregnancy monitoring, and therapeutic management are necessary (Tan et al. 2022). It is crucial to investigate effective methods for suppressing disease exacerbations during pregnancy in women with SLE, ensuring that both maternal and fetal health are maintained throughout the pregnancy.

## 9. Psoriasis

Psoriasis is a chronic, autoimmune disease with a worldwide prevalence of about 2%. As the prevalence varies depending on the region, in Caucasian and Scandinavian populations it is up to 11%, but it is lower in the African and Asian populations (Rendon and Schäkel 2019). Although the prevalence of the disease in women of reproductive age is around 1%, studies on prevalence of psoriasis in pregnant women are still limited (Simionescu et al. 2021). The disease affects both sexes but its onset is earlier in females and those with a family history (Raharja et al. 2021). There are different types of this disease, but 90% of psoriasis cases are psoriasis vulgaris, also called plaque-type psoriasis. The other types are inverse, guttate, and pustular psoriasis.

The underlying mechanism of psoriasis development is impaired function of the immune cells. The outermost layer of the skin is made up of keratinocytes (Rendon and Schäkel 2019), which recruit inflammatory dendritic cells to release interleukins 12 and 23 (IL-12, IL-23). These interleukins activate T-cells that are starting to produce IL-17, IL-22, IFN- $\gamma$ , and TNF- $\alpha$ . T-cell activity causes hyperproliferation of the epidermal skin cells. Due to this, as normal epidermal regeneration occurs every 21–28 days, in psoriasis, the epidermis turns over at every 3–4 days (Menter 2016).

Psoriasis typically manifests with a well-demarcated salmon pink plaque with a silver scale. The most common locations are extensor areas like the elbows and knees, but also on the trunk and scalp. Plaques are usually located symmetrically. With psoriasis is associated the Auspitz sign and the Koebner phenomenon. The first one is bleeding spots that occur after removing the scales and the second one is the appearance of psoriasis in skin areas that were damaged (Raharja et al. 2021). Psoriasis is associated with arthritis and uveitis, but it has also been found that psoriasis increases the risk

of cardiovascular and cerebral diseases and shortens the lifespan of affected individuals to around 6 years (Yamazaki 2021).

Pregnancy seems to have a positive influence on the course and severity of psoriasis (Vena et al. 2015). There are a few studies that examined how psoriasis influences pregnancy. Lamb et al. (2020) did not find any evidence of impaired fertility in women affected by psoriasis, but there is an increased risk of pregnancy hypertension, premature rupture of membranes, cleft palate, and large for gestational age. A different conclusion came from a Bandoli et al. (2020) which revealed that women with psoriasis were more likely to have preterm birth (50% increased risk), cesarean delivery (22% increased risk), and small for gestational age. One-third of preterm births and 12% of cesarean delivery were associated with preeclampsia (Bandoli et al. 2020). The cohort study from Psoriasis Longitudinal Assessment and Registry (PSOLAR) examined 220 women with 298 pregnancies, of which 244 were live births. The annual fertility of women with psoriasis was lower than in the general US population: 59.1 per 1000 women vs. 18.9 per 1000 women, respectively. The rate of congenital abnormalities was lower than in the general population, but there was no difference in preterm births and spontaneous abortion rates (Kimball et al. 2021). An interesting conclusion came from a nationwide case–control study from Denmark. They investigated whether psoriasis increases the risk of spontaneous abortion, ectopic pregnancy, intrauterine fetal death, and stillbirth. After analysis of 491,274 women, a connection between psoriasis and the risk of ectopic pregnancy was found. It turns out that women with psoriasis have a 2.48% higher risk of ectopic pregnancy than women without psoriasis (Johansen et al. 2022). Due to divergent conclusions from research, this topic needs further investigation. The treatment of psoriasis varies depending on the severity of the disease. Mild to moderate psoriasis is usually treated with glucocorticoids, vitamin D analogs, and phototherapy while severe psoriasis requires systemic treatments. Traditional systemic treatment consists of MTX, cyclosporin A, and retinoids, but nowadays biological treatments are increasingly used. Biologic treatments are monoclonal antibodies and receptor fusion proteins which target IL-23/Th17 axis and TNF- $\alpha$  signaling. TNF- $\alpha$  signaling is inhibited by etanercept, infliximab, adalimumab, and certolizumab, while IL-23/Th17 axis is treated by ustekinumab, guselkumab, tildrakizumab, risankizumab, secukinumab, ixekizumab, and brodalumab (Rendon and Schäkel 2019). Due to the teratogenicity of many drugs used in the therapy of psoriasis, the treatment in pregnancy varies from regular treatment. The first-line treatment in pregnancy is a topical treatment consisting of emollient creams, moisturizers, tacrolimus, and dermatocorticosteroids. The second line is a combination of UVB phototherapy with topical treatment. In severe psoriasis systemic therapies are used, such as cyclosporine, systemic corticosteroids, and TNF- $\alpha$  inhibitors. Currently,



there are only three biologics that can be used in psoriasis treatment during pregnancy. Currently, the following biologics can be used to treat psoriasis: adalimumab, etanercept, and infliximab (Simionescu et al. 2021). The PSOLAR study showed no difference in pregnancy outcomes between women with biologic treatment and those with non-biologic treatment (Kimball et al. 2021). Given the varying conclusions regarding the connection between infertility and psoriasis, further research is needed to clarify this relationship and identify potential underlying factors that may contribute to infertility in women with psoriasis.

## 10. Vasculitis

The term vasculitides refers to a heterogeneous group of diseases which are characterized by inflammation of the blood vessels (Torp et al. 2021). They are classified mostly by the size of the vessels they affect. The Chapel Hill Consensus Conference from 2012 divided vasculitis into Large vessel vasculitis, Medium vessel vasculitis, Small vessel vasculitis, Variable vessel vasculitis, Single-organ vasculitis, Vasculitis associated with systemic disease, and Vasculitis associated with probable etiology (Jennette 2013). In this research, we focused mainly on the influence of the primary systemic vasculitides on pregnancy. Primary systemic vasculitides that affect women of childbearing age are mainly Takayasu arteritis (TAK), polyarteritis nodosa (PAN), anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV), immune-complex small-vessel vasculitis (IgA vasculitis), and Behçet's disease (BD) (Ross et al. 2020).

Pregnancy causes changes in the endocrine and immune systems. Due to increased levels of cortisol, estradiol, progesterone, and testosterone, the Th-2 cytokine undergoes polarization both at the feto-maternal interface and at the systemic level. These changes may lead to improvement of Th-1 mediated vasculitis like TAK and BD and worsening of Th-2-driven ones like Wegener granulomatosis or the Churg–Strauss syndrome (Gatto et al. 2012).

TAK affects large vessels like the aorta and its branches. Comarmond et al. (2020) analyzed 505 pregnancies of 373 patients with TAK from articles published between 1980 and 2019. According to their research, hypertension was the most common complication in pregnancy and it reached 35%, while in the general population it occurs in 3%–9%. The other obstetric complications that occur more frequently in TAK than in the general population are preeclampsia, spontaneous abortion, IUGR, preterm birth, and cesarean section (Comarmond et al. 2020). The standard treatment for TAK is oral corticosteroid therapy by prednisone. Experts suggest using immunosuppressants such as MTX on the first line of therapy to reduce the use of steroids. Also, biotherapy is used in TAK, like infliximab, adalimumab, etanercept, and tocilizumab (Saadoun et al. 2021). During pregnancy, prednisone is given 1 mg/kg/day until disease control is obtained

and then reduced to a minimally effective dose. If prednisone is not sufficient, azathioprine is recommended (Doria et al. 2008).

PAN is necrotizing arteritis of the medium or small arteries without glomerulonephritis or vasculitis in the arterioles, capillaries, or venules, which is not associated with ANCA. It can be idiopathic or associated with infectious etiology (Howard et al. 2014). There are only 19 reported cases of PAN during pregnancy, from which 14 healthy babies were born. The other five cases ended in abortion, of which three were spontaneous and two therapeutic. There are very serious prognoses when it comes to the onset of the disease during pregnancy. Seven out of eight of those cases ended up in maternal death during gestation or within 42 days of delivery (Damian et al. 2018). Due to the high risk of death if PAN is diagnosed during pregnancy, therapeutic abortion is recommended, and in late pregnancy high-dose corticosteroid and cyclophosphamide (CYC) (Doria et al. 2008). Outside pregnancy, the first-line treatment is using corticosteroids that indicate remission in 50% of patients. The addition of CYCs causes remission or cure in up to 90% of the patients. In refractory cases, plasma exchange/plasmapheresis is used (Howard et al. 2014).

AAVs are granulomatosis with polyangiitis (GPA), microscopic polyangiitis and eosinophilic granulomatosis with polyangiitis (EGPA). EGPA was previously known as the Churg–Strauss syndrome. They usually affect the capillaries, arterioles, and venules (Kitching et al. 2020). The most common pregnancy complication in AAV patients is preterm delivery, which ranges at 20%–50%. Interestingly, in *de novo* AAV and vasculitis with high activity, the percentage of premature pregnancies reaches 90%. Pregnancy losses and pregnancy-related high blood pressure disorders occur more frequently in AAV patients. There are two reported cases of pulmonary and renal disease of the newborn secondary to the transfer of maternal myeloperoxidase-antineutrophil cytoplasmic antibodies. If it is necessary, corticosteroid therapy, azathioprine, and intravenous immunoglobulins may be used in AAV treatment during pregnancy. Drugs like MTX, leflunomide, mycophenolate mofetil (MMF), as well as CYC, avacopan, and mepolizumab, used outside pregnancy, must be stopped before conception (Pecher et al. 2022).

Immunoglobulin A (IgA) vasculitis (IgAV) also called Henoch–Schönlein purpura (HSP) affects the small vessels and is the most common form of vasculitis in children. Usually, it manifests by palpable purpura, arthritis or arthralgia, abdominal pain, and hematuria or proteinuria (Song et al. 2021). Feldmann et al. (2002) described nine cases of HSP during pregnancy, from which four were diagnosed before pregnancy, three during, and two after. The only reported obstetrical complication of HSP is pregnancy-induced hypertension. They also suggest that as immunoglobulins cannot cross the

normal placenta, there is probably no risk of IgA vasculitis in the fetus (Feldmann et al. 2002). Côté et al. (2018) in their case report summed up 22 case reports from the years 1980 to 2015. There was one case of preeclampsia. Two cases were complicated by severe renal failure with anasarca, hypertension, and oliguria. Both were diagnoses of new-onset HSP and both required renal replacement therapy (Côté et al. 2018). The European recommendations for IgAV treatment suggest varying the treatment depending on severity. Therapies of IgAV are combinations of renin–angiotensin system blockers in the case of proteinuria, corticosteroids, azathioprine, cyclosporine, MMF, and CYC (Hastings et al. 2022). We did not find any recommendation for IgAV treatment during pregnancy.

BD is a persistent multisystemic inflammation of idiopathic genesis. The main symptoms are recurrent mouth and genital sores, lesions in the skin, and eye diseases (Skef 2015). Barros et al. (2021) studies compared 49 pregnant women in 27 with BD to 98 pregnant women without any diseases as the control group. Women suffering from BD had a higher risk of spontaneous abortion and FGR (Barros et al. 2021) – a state when the fetus is too small for its gestational age (Shrivastava and Master 2020). There were 12 miscarriages and 4 FGR cases in the group of women with BD, whereas in the control group no spontaneous abortion was confirmed and only one child was affected with FGR. No other complications were confirmed (Barros et al. 2021). Due to inconsistent findings regarding the relationship between vasculitis and infertility, additional research is necessary to better understand how vasculitis may impact fertility and to identify potential factors that could influence reproductive outcomes in affected women.

## 11. aPL Syndrome

Antiphospholipid syndrome (APS) is an autoimmune disease causing hypercoagulation which manifests with thrombotic and pregnancy morbidity (Petri 2020). Primary APS is characterized by occurring in isolation (Ambati et al. 2023) while “secondary” is associated with other diseases like SLE. One-third of patients with lupus erythematosus present aPL antibodies and about half of APS patients have another autoimmune disease (Petri 2020). The mechanisms of aPL antibodies-induced thrombosis are inhibition of anticoagulant cascades, procoagulant activation of endothelial cells, complement activation, reduced fibrinolytic activity, and increased platelet aggregation. As not all aPL-positive patients develop thrombosis, there has to be a triggering factor. This is called the concept of “two-hit” (D’Ippolito et al. 2023). The first hit creates a procoagulant state by aPL while triggering a stimulus (second hit) like injury, pregnancy, or surgery which causes inflammation or vascular injury that leads to thrombosis (Knight and Kanthi 2022). There are three aPL

antibodies listed in the APS criteria: lupus anticoagulant, anticardiolipin, and anti- $\beta$  2 glycoprotein 1. The aPL antibodies bind to  $\beta$  2 glycoprotein 1 on platelets which causes its activation and as a result aggregation (Petri 2020).

Although thrombosis in APS may affect all sizes of vascular beds, the most common locations of thrombi are the lower deep veins and the cerebral arteries (Knight and Kanthi 2022). There is a special type of APS caused by multiple microthrombosis called catastrophic antiphospholipid syndrome (CAPS). It usually presents with fever, thrombocytopenia, cognitive impairment, weakness of muscles, abdominal pain, and renal failure. According to the classification criteria, CAPS damages three or more organs within a week (Bitsadze et al. 2024).

APS causes obstetric complications such as pregnancy losses and premature births as a result of placental insufficiency or severe preeclampsia. Obstetric APS (OAPS) has been described as a different clinical entity apart from vascular APS (D’Ippolito et al. 2023). OAPS criteria include over three consecutive miscarriages before 10 weeks of gestation, at least one feta loss after week 10 of gestation, and at least one premature birth before week 34 of gestation due to PE/eclampsia or placental insufficiency with positive aPL antibody results in laboratory tests for at least 12 weeks (Alijotas-Reig et al. 2022). A cohort study of 1000 patients with APS from 13 European countries revealed that early pregnancy loss was observed in 17.1% of pregnancies while 35% of live births were premature birds (Cervera et al. 2015). The positivity of the laboratory antibodies positivity test seems to make a difference when it comes to the percentage of live births. Women with more than one positive antibody showed a lower rate of live births.

As not all of the OAPS placentas showed thrombosis, other mechanisms apart from thrombosis must be involved in pregnancy morbidity. Animal models revealed that there might be direct functional damage on placental tissue mediated by aPL. The other possibility is a complement cascade causing inflammation. All of these mechanisms may act together leading to miscarriages or preeclampsia (D’Ippolito et al. 2023).

A European cohort study analyzed 134 children born to mothers with APS. They were examined at 3 months, 9 months, 24 months, and at 5 years; 60% of the children were born before 37 weeks and 14% weighed under 2500 g at birth. Four of the children (3%) showed behavioral abnormalities, which is more than in general society where the prevalence of neurodevelopmental abnormalities is near 1%. Only one of the children with behavioral abnormalities was positive for anticardiolipin antibodies (Mekinian et al. 2013). Because of the small cohort, this needs further investigation.

Regular treatment and treatment during pregnancy are different. Asymptomatic aPL carriers should receive low-dose aspirin (LDA) and patients after first unprovoked venous

thrombosis should start treatment with vitamin K antagonists with target international normalized ratio (INR) between 2 and 3. Patients who suffer recurrent arterial or venous thrombosis despite adequate treatment should increase their INR target to 3–4, add LDA, or switch to heparin. During pregnancy, the treatment consists of LDA and a prophylactic dosage of heparin (Tektonidou et al. 2019). What more needs to

**Table 1.** Medications used and contraindicated during pregnancy for autoimmune diseases and related conditions

Disease	Drugs used during pregnancy	Drugs forbidden during pregnancy
MS and NMOSD	IFN- $\beta$ GA	Dimethyl fumarate Teriflunomide Leflunomide Alemtuzumab Natalizumab Ocrelizumab
MG	Anticholinesterase inhibitors corticosteroids azathioprine	MTX Mofetil mycophenolate Rituximab
Chronic IBD	Anti-TNF	MTX Leflunomide
T1D	Insulin	
Autoimmune thyroid disease	Propylthiouracil (preferred over other, category D) levothyroxine	Radioactive iodine ablation
RA	Corticosteroids Hydroxychloroquine Sulfasalazine	MTX Leflunomide Anti-TNF agents Abatacept Rituximab
SLE	Prednisone Hydroxychloroquine Methylprednisolone Azathioprine	
Psoriasis	Topical treatment: emollient creams moisturizers tacrolimus dermatocorticosteroids	
	Systemic: cyclosporine corticosteroids adalimumab, etanercept, infliximab	
Vasculitis	Prednisone Azathioprine Intravenous immunoglobulins	MTX Leflunomide MMF CYC Avacopan Mepolizumab
aPL syndrome	LDA heparin	Vitamin K antagonists

aPL, antiphospholipid; CYC, cyclophosphamide; GA, glatiramer acetate; IFN- $\beta$ , interferon- $\beta$ ; LDA, low-dose aspirin; MG, myasthenia gravis; MMF, mycophenolate mofetil; MS, multiple sclerosis; MTX, methotrexate; NMOSD, neuromyelitis optica spectrum disorders; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; T1D, type 1 diabetes; TNF, tumor necrosis factor.

be known? Further research is required to determine whether preterm delivery can be effectively prevented. Investigators should focus on understanding the molecular mechanisms behind the role of antibodies in pregnancy complications and explore strategies to prevent their impact on maternal and fetal health.

12. Conclusion

Autoimmune diseases affect many women in their childbearing age causing obstetric complications. Pregnancy causes significant changes in women’s immune systems, which can result in improvement or worsening of the course of disease. For some diseases, like vasculitides, information is very limited and research is based on little data. Nearly all diseases, besides diabetes type 1, which is treated by insulin both during and outside pregnancy, have limited treatment during pregnancy due to their teratogenic effects. Obstetric complications were observed in the course of every researched disease and infant complications in nearly all of them. Maternity plans in patients suffering from autoimmune disease are possible to be implemented but require prior preparation such as discontinuation of certain drugs with teratogenic effects. Such pregnancy should be supervised by an experienced obstetrician. All the most important information is presented in Table 1.

Statement of Originality

We hereby confirm that the submitted manuscript is original, has not been published previously (except in the form of an abstract or preliminary communication, which is indicated in the Acknowledgements section), and is not under consideration for publication elsewhere. All authors have approved the manuscript and agree with its submission to Archivum Immunologiae et Therapiae Experimentalis.

Conflict of Interest Statement

The authors declare no conflict of interest related to this manuscript.

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**References**

- Abhyankar A, Ham M, Moss AC (2013) Meta-analysis: the impact of disease activity at conception on disease activity during pregnancy in patients with inflammatory bowel disease. *Alimentary Pharmacol Ther* 38:460–466. <https://doi.org/10.1111/apt.12417>
- Alijotas-Reig J, Esteve-Valverde E, Anunciación-Llunell A et al. (2022) Pathogenesis, diagnosis and management of obstetric antiphospholipid syndrome: a comprehensive review. *J Clin Med* 11:675. <https://doi.org/10.3390/jcm11030675>
- Ambati A, Knight JS, Zuo Y (2023) Antiphospholipid syndrome management: a 2023 update and practical algorithm-based approach. *Curr Opin Rheumatol* 35:149–160. <https://doi.org/10.1097/BOR.0000000000000932>
- Ameer MA, Chaudhry H, Mushtaq J et al. (2022) An overview of systemic lupus erythematosus (SLE) pathogenesis, classification, and management. *Cureus* 14:e30330. <https://doi.org/10.7759/cureus.30330>
- Andrawus M, Sharvit L, Atzmon G (2022) Epigenetics and pregnancy: conditional snapshot or rolling event. *Int J Mol Sci* 23:12698. <https://doi.org/10.3390/ijms232012698>
- Antonelli A, Wartofsky L, Miccoli P (2021) Editorial: levothyroxine therapy in patients with hypothyroidism. *Front Endocrinol* 12:734895. <https://doi.org/10.3389/fendo.2021.734895>
- Baer AN, Witter FR, Petri M (2011) Lupus and pregnancy. *Obstet Gynecol Surv* 66:639–653. <https://doi.org/10.1097/OGX.0b013e318239e1ee>
- Ballester Ferré MP, Boscá-Watts MM, Mínguez Pérez M (2018) Enfermedad de Crohn. *Med Clí* 151:26–33. <https://doi.org/10.1016/j.medcli.2017.10.036>
- Bandoli G, Singh N, Strouse J et al. (2020) Mediation of adverse pregnancy outcomes in autoimmune conditions by pregnancy complications: a mediation analysis of autoimmune conditions and adverse pregnancy outcomes. *Arthritis Care Res* 72:256–264. <https://doi.org/10.1002/acr.24037>
- Barros T, Braga A, Marinho A et al. (2021) Behçet's disease and pregnancy: a retrospective case-control study. *Yale J Biol Med* 94:585–592. PMID: 34970095
- Béhin A, Mayer M, Kassis-Makhoul B et al. (2008) Severe neonatal myasthenia due to maternal anti-MuSK antibodies. *Neuromuscul Disord* 18:443–446. <https://doi.org/10.1016/j.nmd.2008.03.006>
- Betran AP, Ye J, Moller AB et al. (2021) Trends and projections of caesarean section rates: global and regional estimates. *BMJ Glob Health* 6:e005671. <https://doi.org/10.1136/bmjgh-2021-005671>
- Bitsadze V, Yakubova F, Khizroeva J et al. (2024) Catastrophic antiphospholipid syndrome. *Int J Mol Sci* 25:668. <https://doi.org/10.3390/ijms25010668>
- Bourque PR, Breiner A (2018) Myasthenia gravis. *Can Med Assoc J* 190:E1141–E1141. <https://doi.org/10.1503/cmaj.180656>
- Bruner LP, White AM, Prokcell S (2023) Inflammatory bowel disease. *Prim Care* 50:411–427. <https://doi.org/10.1016/j.pop.2023.03.009>
- Calderwood AH, Kane SV (2004) IBD and pregnancy. *MedGenMed* 6:14. PMID: 15775841
- Calimag APP, Chlebek S, Lerma EV et al. (2023) Diabetic ketoacidosis. *Dis Mon* 69:101418. <https://doi.org/10.1016/j.disamonth.2022.101418>
- Castiglione F, Pignata S, Morace F et al. (1996) Effect of pregnancy on the clinical course of a cohort of women with inflammatory bowel disease. *Ital J Gastroenterol* 28:199–204. PMID: 8842834
- Caturegli P, De Remigis A, Rose NR (2014) Hashimoto thyroiditis: clinical and diagnostic criteria. *Autoimmun Rev* 13:391–397. <https://doi.org/10.1016/j.autrev.2014.01.007>
- Cervera R, Serrano R, Pons-Estel GJ et al. (2015) Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients. *Ann Rheum Dis* 74:1011–1018. <https://doi.org/10.1136/annrheumdis-2013-204838>
- Chang KJ, Seow KM, Chen KH (2023) Preeclampsia: recent advances in predicting, preventing, and managing the maternal and fetal life-threatening condition. *Int J Environ Res Public Health* 20:2994. <https://doi.org/10.3390/ijerph20042994>
- Chauhan K, Jandu JS, Brent LH et al. (2024) Rheumatoid arthritis. *StatPearls* [Internet], Treasure Island (FL).
- Ciplea AI, Langer-Gould A, Stahl A et al. (2020) Safety of potential breast milk exposure to IFN- $\beta$  or glatiramer acetate. *Neurol*



- Neuroimmunol Neuroinflamm 7:e757. <https://doi.org/10.1212/NXI.0000000000000757>
- Comarmond C, Saadoun D, Nizard J et al. (2020) Pregnancy issues in Takayasu arteritis. *Semin Arthritis Rheum* 50:911–914. <https://doi.org/10.1016/j.semarthrit.2020.08.001>
- Confavreux C, Hutchinson M, Hours MM et al. (1998) Rate of pregnancy-related relapse in multiple sclerosis. *N Engl J Med* 339:285–291. <https://doi.org/10.1056/NEJM199807303390501>
- Costa RV, Simões C, Correia L et al. (2022) Inflammatory bowel disease and pregnancy: is it a marker for adverse outcomes? *Rev Bras Ginecol Obstet* 44:915–924. <https://doi.org/10.1055/s-0042-1756149>
- Côté JM, Meunier RS, Tremblay JA et al. (2018) Henoch-Schönlein purpura in pregnancy: a case report. *Obstet Med* 11:195–197. <https://doi.org/10.1177/1753495X17745391>
- da Fonseca EB, Damião R, Moreira DA (2020) Preterm birth prevention. *Best Pract Res Clin Obstet Gynaecol* 69:40–49. <https://doi.org/10.1016/j.bpobgyn.2020.09.003>
- Damian L, Pamfil C, Fodor M et al. (2018) Polyarteritis nodosa in pregnancy. *Ochsner J* 18:94–97. <https://doi.org/10.1043/TOJ-17-0025>
- Dao KH, Bermas BL (2022) Systemic lupus erythematosus management in pregnancy. *Int J Womens Health* 14:199–211. <https://doi.org/10.2147/IJWH.S282604>
- Decallonne B, Bartholomé E, Delvaux V et al. (2018) Thyroid disorders in alemtuzumab-treated multiple sclerosis patients: a Belgian consensus on diagnosis and management. *Acta Neurol Belg* 118:153–159. <https://doi.org/10.1007/s13760-018-0883-2>
- Depla AL, De Wit L, Steenhuis TJ et al. (2021) Effect of maternal diabetes on fetal heart function on echocardiography: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 57:539–550. <https://doi.org/10.1002/uog.22163>
- Desoye G, Herrera E (2021) Adipose tissue development and lipid metabolism in the human fetus: The 2020 perspective focusing on maternal diabetes and obesity. *Prog Lipid Res* 81:101082. <https://doi.org/10.1016/j.plipres.2020.101082>
- D'Ippolito S, Barbaro G, Paciullo C et al. (2023) Antiphospholipid syndrome in pregnancy: new and old pathogenetic mechanisms. *Int J Mol Sci* 24:3195. <https://doi.org/10.3390/ijms24043195>
- Dobson R, Giovannoni G (2019) Multiple sclerosis – a review. *Eur J Neurol* 26:27–40. <https://doi.org/10.1111/ene.13819>
- Doria A, Bajocchi G, Tonon M et al. (2008) Pre-pregnancy counselling of patients with vasculitis. *Rheumatology* 47(Suppl. 3):iii13–iii15. <https://doi.org/10.1093/rheumatology/ken152>
- Ducci RD, Lorenzoni PJ, Kay CS et al. (2017) Clinical follow-up of pregnancy in myasthenia gravis patients. *Neuromuscul Disord* 27:352–357. <https://doi.org/10.1016/j.nmd.2017.01.021>
- European Medicines Agency. (2019). Lemtrada SPC.
- Feldmann R, Rieger W, Sator PG et al. (2002) Schönlein-Henoch purpura during pregnancy with successful outcome for mother and newborn. *BMC Dermatol* 2:1. <https://doi.org/10.1186/1471-5945-2-1>
- Foulon A, Chevreau J, Yze C et al. (2020) Maladie chronique inflammatoire de l'intestin et grossesse: de la conception à la naissance. *Gynécol Obstét Fertil Sénol* 48:514–519. <https://doi.org/10.1016/j.gofs.2020.02.013>
- Fujimoto WY (2000) The importance of insulin resistance in the pathogenesis of type 2 diabetes mellitus. *Am J Med* 108:9–14. [https://doi.org/10.1016/S0002-9343\(00\)00337-5](https://doi.org/10.1016/S0002-9343(00)00337-5)
- Gardnerova M, Eymard B, Morel E et al. (1997) The fetal/adult acetylcholine receptor antibody ratio in mothers with myasthenia gravis as a marker for transfer of the disease to the newborn. *Neurology* 48:50–54. <https://doi.org/10.1212/WNL.48.1.50>
- Gatto M, Iaccarino L, Canova M et al. (2012) Pregnancy and vasculitis: a systematic review of the literature. *Autoimmun Rev* 11:A447–A459. <https://doi.org/10.1016/j.autrev.2011.11.019>
- Gilbert J (2017) Thyrotoxicosis – investigation and management. *Clin Med* 17:274–277. <https://doi.org/10.7861/clinmedicine.17-3-274>
- Gillespie KM (2006) Type 1 diabetes: pathogenesis and prevention. *Can Med Assoc J* 175:165–170. <https://doi.org/10.1503/cmaj.060244>
- Gupta B, Hawkins RD (2015) Epigenomics of autoimmune diseases. *Immunol Cell Biol* 93:271–276. <https://doi.org/10.1038/icb.2015.18>
- Gutaj P, Sawicka-Gutaj N, Brązert M et al. (2015) Insulin resistance in pregnancy complicated by type 1 diabetes mellitus. Do we know enough? *Ginekol Pol* 86:219–223. <https://doi.org/10.17772/gp/2065>
- Hakkarainen KM, Juuti R, Burkill S et al. (2020) Pregnancy outcomes after exposure to interferon beta: a register-based cohort study among women with MS in Finland and Sweden. *Ther Adv Neurol Disord* 13:5628642095107. <https://doi.org/10.1177/1756286420951072>
- Hastings MC, Rizk DV, Koryluk K et al. (2022) IgA vasculitis with nephritis: update of pathogenesis with clinical implications. *Pediatr Nephrol* 37:719–733. <https://doi.org/10.1007/s00467-021-04950-y>
- Hehir MK, Silvestri NJ (2018) Generalized myasthenia gravis. *Neurol Clin* 36:253–260. <https://doi.org/10.1016/j.ncl.2018.01.002>
- Hellwig K, Geissbuehler Y, Sabidó M et al. (2020) Pregnancy outcomes in interferon-beta-exposed patients with multiple sclerosis: results from the European Interferon-beta Pregnancy Registry. *J Neurol* 267:1715–1723. <https://doi.org/10.1007/s00415-020-09762-y>
- Henson LJ, Afsar S, Davenport L et al. (2020) Pregnancy outcomes in patients treated with leflunomide, the parent compound of the multiple sclerosis drug teriflunomide. *Reproduct Toxicol* 95:45–50. <https://doi.org/10.1016/j.reprotox.2020.04.073>
- Hoff JM, Daltveit AK, Gilhus NE (2004) Asymptomatic myasthenia gravis influences pregnancy and birth. *Eur J Neurol* 11:559–562. <https://doi.org/10.1111/j.1468-1331.2004.00900.x>
- Hoff JM, Daltveit AK, Gilhus NE (2007) Myasthenia gravis in pregnancy and birth: identifying risk factors, optimising care. *Eur J Neurol* 14:38–43. <https://doi.org/10.1111/j.1468-1331.2006.01538.x>
- Howard T, Ahmad K, Swanson JA et al. (2014) Polyarteritis nodosa. *Tech Vasc Intervent Radiol* 17:247–251. <https://doi.org/10.1053/j.tvir.2014.11.005>

- Huda S, Whittam D, Bhojak M et al. (2019) Neuromyelitis optica spectrum disorders. *Clin Med* 19:169–176. <https://doi.org/10.7861/clinmedicine.19-2-169>
- Hughes B, De Casillas M, Kaminski H (2004) Pathophysiology of myasthenia gravis. *Semin Neurol* 24:21–30. <https://doi.org/10.1055/s-2004-829585>
- Ibarra Barrueta O, García Martín E, López Sánchez P et al. (2023) Biological and immunosuppressive medications in pregnancy, breastfeeding and fertility in immune mediated diseases. *Farm Hosp* 47:39–49. <https://doi.org/10.1016/j.farma.2022.12.005>
- Jennette JC (2013) Overview of the 2012 revised International Chapel Hill Consensus Conference nomenclature of vasculitides. *Clin Exp Nephrol* 17:603–606. <https://doi.org/10.1007/s10157-013-0869-6>
- Johansen CB, Egeberg A, Jimenez-Solem E et al. (2022) Psoriasis and adverse pregnancy outcomes: a nationwide case-control study in 491,274 women in Denmark. *JAAD Int* 7:146–155. <https://doi.org/10.1016/j.jdin.2022.03.009>
- Justiz Vaillant AA, Goyal A, Varacallo M (2024) Systemic lupus erythematosus. *StatPearls* [Internet], Treasure Island (FL).
- Kilpatrick ES, Rigby AS, Atkin SL (2007) Insulin resistance, the metabolic syndrome, and complication risk in type 1 diabetes. *Diabetes Care* 30:707–712. <https://doi.org/10.2337/dc06-1982>
- Kimball AB, Guenther L, Kalia S et al. (2021) Pregnancy outcomes in women with moderate-to-severe psoriasis from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). *JAMA Dermatol* 157:301. <https://doi.org/10.1001/jamadermatol.2020.5595>
- Kitching AR, Anders HJ, Basu N et al. (2020) ANCA-associated vasculitis. *Nat Rev Dis Primers* 6:71. <https://doi.org/10.1038/s41572-020-0204-y>
- Knight JS, Kanthi Y (2022) Mechanisms of immunothrombosis and vasculopathy in antiphospholipid syndrome. *Semin Immunopathol* 44:347–362. <https://doi.org/10.1007/s00281-022-00916-w>
- Lambe M, Bergstrom AV, Johansson ALV et al. (2020) Reproductive patterns and maternal and pregnancy outcomes in women with psoriasis—A population-based study. *J Am Acad Dermatol* 82:1109–1116. <https://doi.org/10.1016/j.jaad.2019.05.099>
- Landi D, Marfia GA (2020) Exposure to natalizumab during pregnancy and lactation is safe – yes. *Mult Scler* 26:887–889. <https://doi.org/10.1177/1352458520915814>
- Lee SY, Pearce EN (2022) Assessment and treatment of thyroid disorders in pregnancy and the postpartum period. *Nat Rev Endocrinol* 18:158–171. <https://doi.org/10.1038/s41574-021-00604-z>
- Li R, Ma D, Su YZ et al. (2021) Adverse effects of maternal rheumatoid arthritis during pregnancy on children. *Chin Med J* 134:1113–1115. <https://doi.org/10.1097/CM9.0000000000001374>
- Lindroos JLV, Björk MH, Gilhus NE (2024) Transient neonatal myasthenia gravis as a common complication of a rare disease: a systematic review. *J Clin Med* 13:1136. <https://doi.org/10.3390/jcm13041136>
- Maahs DM, West NA, Lawrence JM et al. (2010) Epidemiology of type 1 diabetes. *Endocrinol Metab Clin North Am* 39:481–497. <https://doi.org/10.1016/j.ecl.2010.05.011>
- Makola A, Krause M (2016) Management of rheumatoid arthritis during pregnancy: challenges and solutions. *Open Access Rheumatol* 23:23–36. <https://doi.org/10.2147/OARRR.S85340>
- Massey JM, De Jesus-Acosta C (2014) Pregnancy and myasthenia gravis. *Continuum (Minneapolis)* 20:115–127. <https://doi.org/10.1212/01.CON.0000443840.33310.bd>
- Mathiesen ER, Ringholm L, Damm P (2011) Therapeutic management of type 1 diabetes before and during pregnancy. *Expert Opin Pharmacother* 12:779–786. <https://doi.org/10.1517/14656566.2011.540388>
- McCance DR, Casey C (2019) Type 1 diabetes in pregnancy. *Endocrinol Metab Clin North Am* 48:495–509. <https://doi.org/10.1016/j.ecl.2019.05.008>
- McIver B, Morris JC (1998) The pathogenesis of Graves' disease. *Endocrinol Metab Clin North Am* 27:73–89. [https://doi.org/10.1016/S0889-8529\(05\)70299-1](https://doi.org/10.1016/S0889-8529(05)70299-1)
- Mekinian A, Lachassinne E, Nicaise-Roland P et al. (2013) European registry of babies born to mothers with antiphospholipid syndrome. *Ann Rheum Dis* 72:217–222. <https://doi.org/10.1136/annrheumdis-2011-201167>
- Menter A (2016) Psoriasis and psoriatic arthritis overview. *Am J Manag Care* 22(8 Suppl.):s216–24. PMID: 27356193
- Mota A, Borrione P, Santiago M (2007) Thyroid acropachy. *J Clin Rheumatol* 13:360. <https://doi.org/10.1097/RHU.0b013e31815c6ccc>
- Neuhaus O, Kieseier BC, Hartung HP (2007) Pharmacokinetics and pharmacodynamics of the interferon-betas, glatiramer acetate, and mitoxantrone in multiple sclerosis. *J Neurol Sci* 259:27–37. <https://doi.org/10.1016/j.jns.2006.05.071>
- Nielsen OH, Gubatan JM, Juhl CB et al. (2022) Biologics for inflammatory bowel disease and their safety in pregnancy: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 20:74–87. e3. <https://doi.org/10.1016/j.cgh.2020.09.021>
- Niks EH, Verrips A, Semmekrot BA et al. (2008) A transient neonatal myasthenic syndrome with anti-MuSK antibodies. *Neurology* 70:1215–1216. <https://doi.org/10.1212/01.wnl.0000307751.20968.f1>
- Nørgaard M, Larsson H, Pedersen L et al. (2010) Rheumatoid arthritis and birth outcomes: a Danish and Swedish nationwide prevalence study. *J Intern Med* 268:329–337. <https://doi.org/10.1111/j.1365-2796.2010.02239.x>
- Norwood F, Dhanjal M, Hill M et al. (2014) Myasthenia in pregnancy: best practice guidelines from a UK multispecialty working group. *J Neurol Neurosurg Psychiatry* 85:538–543. <https://doi.org/10.1136/jnnp-2013-305572>
- Okwaraji YB, Krasevec J, Bradley E et al. (2024) National, regional, and global estimates of low birthweight in 2020, with trends from 2000: a systematic analysis. *Lancet* 403:1071–1080. [https://doi.org/10.1016/S0140-6736\(23\)01198-4](https://doi.org/10.1016/S0140-6736(23)01198-4)
- Ordás I, Eckmann L, Talamini M et al. (2012) Ulcerative colitis. *Lancet* 380:1606–1619. [https://doi.org/10.1016/S0140-6736\(12\)60150-0](https://doi.org/10.1016/S0140-6736(12)60150-0)
- Oreja-Guevara C, Wray S, Buffels R et al. (2019) Pregnancy outcomes in patients treated with ocrelizumab. In: Presented at the

- 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); 11–13 September 2019. Stockholm, Sweden.
- Pecher AC, Henes M, Henes JC (2022) Optimal management of ANCA-associated vasculitis before and during pregnancy: current perspectives. *Arch Gynecol Obstet* 308:379–385. <https://doi.org/10.1007/s00404-022-06744-5>
- Pedersen N, Bortoli A, Duricova D et al. (2013) The course of inflammatory bowel disease during pregnancy and postpartum: a prospective European ECCO-EpiCom study of 209 pregnant women. *Aliment Pharmacol Ther* 38:501–512. <https://doi.org/10.1111/apt.12412>
- Petri M (2020) Antiphospholipid syndrome. *Transl Res* 225:70–81. <https://doi.org/10.1016/j.trsl.2020.04.006>
- Raharja A, Mahil SK, Barker JN (2021) Psoriasis: a brief overview. *Clin Med (Lond)* 21:170–173. <https://doi.org/10.7861/clinmed.2021-0257>
- Rendon A, Schäkel K (2019) Psoriasis pathogenesis and treatment. *Int J Mol Sci* 20:1475. <https://doi.org/10.3390/ijms20061475>
- Ringholm L, Pedersen-Bjergaard U, Thorsteinsson B et al. (2012) Hypoglycaemia during pregnancy in women with type 1 diabetes. *Diabet Med* 29:558–566. <https://doi.org/10.1111/j.1464-5491.2012.03604.x>
- Rizzo T, Metzger BE, Burns WJ et al. (1991) Correlations between antepartum maternal metabolism and intelligence of offspring. *N Engl J Med* 325:911–916. <https://doi.org/10.1056/NEJM199109263251303>
- Roche P, Bouhour F (2021) Myasthenia gravis and pregnancy. *Rev Neurol* 177:215–219. <https://doi.org/10.1016/j.neurol.2020.09.015>
- Ross C, D'Souza R, Pagnoux C (2020) Pregnancy outcomes in systemic vasculitides. *Curr Rheumatol Rep* 22:63. <https://doi.org/10.1007/s11926-020-00940-5>
- Ross DS, Burch HB, Cooper DS et al. (2016) 2016 American thyroid association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid* 26:1343–1421. <https://doi.org/10.1089/thy.2016.0229>
- Saadoun D, Bura-Riviere A, Comarmond C et al. (2021) French recommendations for the management of Takayasu's arteritis. *Orphanet J Rare Dis* 16(S3):311. <https://doi.org/10.1186/s13023-021-01922-1>
- Schaefer-Graf U, Napoli A, Nolan CJ et al. (2018) Diabetes in pregnancy: a new decade of challenges ahead. *Diabetologia* 61:1012–1021. <https://doi.org/10.1007/s00125-018-4545-y>
- Sharma A, Stan MN (2019) Thyrotoxicosis: diagnosis and management. *Mayo Clin Proc* 94:1048–1064. <https://doi.org/10.1016/j.mayocp.2018.10.011>
- Shi QG, Wang ZH, Ma XW et al. (2012) Clinical significance of detection of antibodies to fetal and adult acetylcholine receptors in myasthenia gravis. *Neurosci Bull* 28:469–474. <https://doi.org/10.1007/s12264-012-1256-0>
- Shosha E, Pittock SJ, Flanagan E et al. (2017) Neuromyelitis optica spectrum disorders and pregnancy: interactions and management. *Mult Scler* 23:1808–1817. <https://doi.org/10.1177/1352458517740215>
- Shrivastava D, Master A (2020) Fetal growth restriction. *J Obstet Gynecol India* 70:103–110. <https://doi.org/10.1007/s13224-019-01278-4>
- Sibai BM, Viteri OA (2014) Diabetic ketoacidosis in pregnancy. *Obstet Gynecol* 123:167–178. <https://doi.org/10.1097/AOG.000000000000060>
- Simionescu AA, Danciu BM, Stanescu AMA (2021) State-of-the-art review of pregnancy-related psoriasis. *Medicina* 57:804. <https://doi.org/10.3390/medicina57080804>
- Singh M, Wambua S, Lee SI et al. (2024) Autoimmune diseases and adverse pregnancy outcomes: an umbrella review. *BMC Med* 22:94. <https://doi.org/10.1186/s12916-024-03309-y>
- Skef W (2015) Gastrointestinal Behçet's disease: a review. *World J Gastroenterol* 21:3801. <https://doi.org/10.3748/wjg.v21.i13.3801>
- Smolen JS, Aletaha D, Barton A et al. (2018) Rheumatoid arthritis. *Nat Rev Dis Primers* 4:18001. <https://doi.org/10.1038/nrdp.2018.1>
- Song Y, Huang X, Yu G et al. (2021) Pathogenesis of IgA vasculitis: an up-to-date review. *Front Immunol* 12:771619. <https://doi.org/10.3389/fimmu.2021.771619>
- Tanaka Y (2020) Rheumatoid arthritis. *Inflamm Regen* 40:20. <https://doi.org/10.1186/s41232-020-00133-8>
- Tan Y, Yang S, Liu Q et al. (2022) Pregnancy-related complications in systemic lupus erythematosus. *J Autoimmun* 132:102864. <https://doi.org/10.1016/j.jaut.2022.102864>
- Taylor RAM, Mackie A, Mogra R et al. (2019) Caudal regression syndrome in a fetus of a glucokinase-maturity-onset diabetes of the young pregnancy. *Diabet Med* 36:252–255. <https://doi.org/10.1111/dme.13844>
- Tektonidou MG, Andreoli L, Limper M et al. (2019) EULAR recommendations for the management of antiphospholipid syndrome in adults. *Ann Rheum Dis* 78:1296–1304. <https://doi.org/10.1136/annrheumdis-2019-215213>
- Temple R (2002) Association between outcome of pregnancy and glycaemic control in early pregnancy in type 1 diabetes: population based study. *BMJ* 325:1275–1276. <https://doi.org/10.1136/bmj.325.7375.1275>
- Torp CK, Br uner M, Keller KK et al. (2021) Vasculitis therapy refines vasculitis mechanistic classification. *Autoimmun Rev* 20:102829. <https://doi.org/10.1016/j.autrev.2021.102829>
- Tsurane K, Tanabe S, Miyasaka N et al. (2019) Management of labor and delivery in myasthenia gravis: a new protocol. *J Obstet Gynecol Res* 45:974–980. <https://doi.org/10.1111/jog.13922>
- Tzartos SJ, Efthimiadis A, Morel E et al. (2008) Neonatal myasthenia gravis: antigenic specificities of antibodies in sera from mothers and their infants. *Clin Exp Immunol* 80:376–380. <https://doi.org/10.1111/j.1365-2249.1990.tb03296.x>
- Udovcic M, Pena RH, Patham B et al. (2017) Hypothyroidism and the heart. *Methodist DeBakey Cardiovasc J* 13:55. <https://doi.org/10.14797/mdcj-13-2-55>

- van der Giessen J, Huang VW, van der Woude CJ (2019) Modulatory effects of pregnancy on inflammatory bowel disease. *Clin Transl Gastroenterol* 10:e00009. <https://doi.org/10.14309/ctg.0000000000000009>
- van Trotsenburg ASP (2020) Management of neonates born to mothers with thyroid dysfunction, and points for attention during pregnancy. *Best Pract Res Clin Endocrinol Metab* 34:101437. <https://doi.org/10.1016/j.beem.2020.101437>
- Vargas-Uricoechea H (2023) Molecular mechanisms in autoimmune thyroid disease. *Cells* 12:918. <https://doi.org/10.3390/cells12060918>
- Varytė G, Arlauskienė A, Ramašauskaitė D (2021) Pregnancy and multiple sclerosis: an update. *Curr Opin Obstet Gynecol* 33:378–383. <https://doi.org/10.1097/GCO.0000000000000731>
- Vena GA, Cassano N, Bellia G et al. (2015) Psoriasis in pregnancy: challenges and solutions. *Psoriasis (Auckl)* 18:83–95. <https://doi.org/10.2147/PTT.S82975>
- Vidal-Jordana A, Montalban X (2017) Multiple sclerosis. *Neuroimaging Clin N Am* 27:195–204. <https://doi.org/10.1016/j.nic.2016.12.001>
- Voskuhl R, Momtazee C (2017) Pregnancy: effect on multiple sclerosis, treatment considerations, and breastfeeding. *Neurotherapeutics* 14:974–984. <https://doi.org/10.1007/s13311-017-0562-7>
- Vukusic S, Hellwig K, Truffinet P (2019) Pregnancy outcomes in female partners of male patients treated with teriflunomide or leflunomide (an in vivo precursor of teriflunomide). In: Abstract (1146) at the ECTRIMS 2019 congress.
- Wang L, Wang F, Gershwin ME (2015) Human autoimmune diseases: a comprehensive update. *J Intern Med* 278:369–395. <https://doi.org/10.1111/joim.12395>
- Weschenfelder F, Herrmann E, Lehmann T et al. (2022) Predictors of a successful vaginal delivery in women with type 1 diabetes: a retrospective analysis of 20 years. *Arch Gynecol Obstet* 305:1445–1452. <https://doi.org/10.1007/s00404-021-06255-9>
- Wilson SA, Stem LA, Bruehlman RD (2021) Hypothyroidism: diagnosis and treatment. *Am Fam Physician* 103:605–613. PMID: 33983002
- Yamazaki F (2021) Psoriasis: comorbidities. *J Dermatol* 48:732–740. <https://doi.org/10.1111/1346-8138.15840>
- Yang H, McElree C, Roth MP et al. (1993) Familial empirical risks for inflammatory bowel disease: differences between Jews and non-Jews. *Gut* 34:517–524. <https://doi.org/10.1136/gut.34.4.517>
- Zeydan B, Atkinson EJ, Weis DM et al. (2020) Reproductive history and progressive multiple sclerosis risk in women. *Brain Commun* 2:fcaa185. <https://doi.org/10.1093/braincomms/fcaa185>
- Zhang S, Han X, Liu W et al. (2022) Pregnancy in patients with systemic lupus erythematosus: a systematic review. *Arch Gynecol Obstet* 308:63–71. <https://doi.org/10.1007/s00404-022-06718-7>
- Zucchi D, Fischer-Betz R, Tani C (2023) Pregnancy in systemic lupus erythematosus. *Best Pract Res Clin Rheumatol* 37:101860. <https://doi.org/10.1016/j.berh.2023.101860>



## Graphic Abstract

