

RHEUMATOID ARTHRITIS

- This chronic inflammatory disease stems from immunological dysfunction, and infiltrating T cells secrete
- cytokines to cause inflammation, polyarthrititis, and systemic symptoms. The cardinal feature is inflammatory
- synovitis that usually involves the peripheral joints. The disease has a propensity for cartilage destruction,
- bony erosions, and joint deformities. Pain, aggravated by movement, is accompanied by swelling and
- tenderness.
- Extraarticular manifestations include rheumatoid nodules, vasculitis, and pleuropulmonary
- symptoms. Other complaints are fatigue, anorexia, and depression

- . The worldwide prevalence of rheumatoid arthritis is 0.5 to 1 percent, women are three times more than men, and peak onset is from 25 to 55 years .There is a genetic predisposition, and
- heritability is estimated at 15 to 30 percent
• .Genome-wide associated studies have identified more than 30 loci involved in rheumatoid arthritis pathogenesis

- There is an association with the class II major histocompatibility complex molecule HLA-DR4 and HLA-DRB1 alleles,. Pregnancy provides a protection against rheumatoid arthritis development, and this may be related to HLA-disparate fetal microchimerism, •

- Management
- Treatment is directed at pain relief, inflammation reduction, protection of articular structures, and
- preservation of function. Physical and occupational therapy and self-management instructions are essential.
- Until recently, aspirin and other NSAIDs were the cornerstone of therapy, but they do not retard disease progression.

NSAIDs serve as adjunctive therapy but are •
important to pregnancy
because methotrexate is contraindicated. •
Conventional NSAIDs nonspecifically inhibit
both cyclooxygenase-
1 (COX-1), which is an enzyme critical to •
normal platelet function, and COX-2, which
mediates inflammatory response mechanisms

In one systematic review, a higher rate of cardiac malformations was found in newborns exposed to NSAIDs in the first trimester. In addition, NSAIDs are associated with early spontaneous abortions, ductus arteriosus constriction, and neonatal pulmonary hypertension. Thus, risks versus benefits of these medications must be considered.

Glucocorticoid therapy in low-to-moderate doses is given to achieve more rapid symptom control. Of these, prednisone, 7.5 mg orally daily for the first 2 years of active disease, substantively reduces progressive joint erosions.

The American College of Rheumatology recommends •
several DMARDs that may reduce or prevent joint
damage Leflunomide, like methotrexate, is teratogenic •
(, Angiotensin-
Converting Enzyme Inhibitors and Angiotensin- •
Receptor Blocking Drugs). Sulfasalazine and
hydroxychloroquine are safe for use in pregnancy •
.These, combined with COX-2 inhibitors and
with relatively low-dose prednisone—7.5 to 20 mg •
daily—usually successfully treat flares. In one review of
drug exposure, a fourth of women with rheumatoid •
arthritis took a DMARD within 6 months of conception

Biological DMARDs have revolutionized the treatment of rheumatoid arthritis. These include tumor necrosis

factor alpha (TNF- α) inhibitors—infliximab, adalimumab, golimumab, certolizumab, and etanercept. Their use in pregnancy is limited, and fetal safety is a concern

There is also little known regarding pregnancy effects of anakinra (an interleukin-1 receptor antagonist) or of rituximab (an antagonist to the B-cell CD20 antigen)

Pregnancy and Rheumatoid Arthritis

- In up to 90 percent of women with rheumatoid arthritis, their disease will improve during pregnancy.
- In one review, a postpartum flare was more common if women were breastfeeding
- Some studies report a protective effect of pregnancy against developing new-onset rheumatoid arthritis. In a
- case-control study of 88 affected women, there was a protective effect of pregnancy in the long term, but the
- likelihood of new-onset rheumatoid arthritis was increased sixfold during the first 3 postpartum months
- Pikwer and colleagues reported a significant reduction in the risk of subsequent arthritis in women who breastfed longer than 12 months

- These findings may reflect the interference of sex hormones with several putative processes involved in arthritis pathogenesis, including immunoregulation . First, Unger and associates reported that amelioration of rheumatoid arthritis correlated with serum levels of pregnancy-associated alpha2-glycoprotein. This compound has immunosuppressive properties. Second, Nelson and coworkers
- noted that amelioration of disease was associated with a disparity in HLA class II antigens between mother and fetus. They suggested that the maternal immune response to paternal HLA antigens may play a role in pregnancy-induced remission of arthritis. In addition to monocyte activations, there also may be Tlymphocyte activation. •

Juvenile Rheumatoid Arthritis

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- Juvenile Rheumatoid Arthritis
- This group of diseases is the most frequent cause of chronic arthritis in children and persists into adulthood.
- In 76 pregnancies of 51 affected Norwegian women, pregnancy had no effects on clinical presentation, but
- disease activity usually became quiescent or remained so during pregnancy. Postpartum flares were common as was discussed for rheumatoid arthritis. Joint deformities often developed in these women, and 15 of 20 cesarean deliveries were done for contracted pelvis or joint prostheses

- This arthritis portends few adverse pregnancy outcomes. The risk for preterm birth is increased, but later fetal development is normal .Disease severity in early
- pregnancy was predictive of preterm delivery and fetal-growth restriction in a cohort study .Another study of 190 pregnancies followed from first trimester to delivery found patients with low disease activity scores in the first trimester were likely to have low disease activity or remission in the third trimester
- . In a study of 1807 births, Remaeus and associates reported increased incidences of preterm birth, fetal-growth restriction, and preeclampsia

- If the cervical spine is involved, particular attention is warranted during pregnancy. Subluxation is common,
- and pregnancy, at least theoretically, predisposes to this because of joint laxity. Importantly, there are
- anesthesia concerns during endotracheal intubation.
- Following pregnancy in women with rheumatoid arthritis and its juvenile form, contraceptive counseling
- may include combination oral contraceptives. These are a logical choice because of their effectiveness and their potential to improve disease (Farr, 2010). That
- said, all methods of contraception are appropriate.

SYSTEMIC SCLEROSIS—SCLERODERMA •

- This is a chronic multisystem connective tissue disorder of unknown etiology. It is characterized by microvascular damage, immune system activation leading to inflammation, and excessive deposition of collagen in the skin and often in the lungs, heart, gastrointestinal tract, and kidneys. It is uncommon,
- displays a 5-to-1 female dominance, and typically affects those aged 30 to 50 years).
- This strong prevalence of scleroderma in women and its greater incidence in the years following childbirth give credence to the hypothesis that microchimerism is involved as discussed earlier •

- The hallmark is overproduction of normal collagen. In the more benign form—limited cutaneous systemic
- sclerosis—progression is slow. With diffuse cutaneous systemic sclerosis, skin thickening progresses rapidly,
- and skin fibrosis is followed by gastrointestinal tract fibrosis, especially the distal esophagus. Pulmonary interstitial fibrosis along with vascular changes may cause pulmonary hypertension, which develops in 15 percent of patients. Antinuclear antibodies are found in 95 percent of patients, and immunoincompetence often develop

- Raynaud phenomenon, which includes cold-induced episodic digital ischemia, is seen in 95 percent of patients, and there may also be swelling of the distal extremities and face. Half of patients have symptoms from esophageal involvement, especially fullness and epigastric burning pain. Pulmonary involvement is frequent and causes dyspnea. The 10-year cumulative survival rate is 70 percent in those with pulmonary fibrosis, and pulmonary arterial hypertension is the main cause of death . Women
- with limited cutaneous disease such as the CREST syndrome—calcinosis, Raynaud phenomenon, esophageal involvement, sclerodactyly, and telangiectasia—have milder • disease.

- Overlap syndrome refers to systemic sclerosis with features of other connective tissue disorders. Mixed connective tissue disease is a term used for the syndrome involving features of SLE, systemic sclerosis, polymyositis, rheumatoid arthritis, and high titers of anti-ribonucleoprotein (RNP) antibodies. The disorder is also termed undifferentiated connective tissue disease .
- Although systemic sclerosis is incurable, treatment directed at end-organ involvement can sometimes relieve symptoms and improve function. Renal involvement and hypertension are often comorbid. At times, ACE inhibitors may be required for blood pressure control despite their known teratogenicity. Scleroderma renal crisis develops in up to a fourth of these patients and is characterized by obliterative vasculopathy of the renal cortical arteries. This leads to renal failure and malignant hypertension. Interstitial restrictive lung disease is common and frequently becomes life threatening. Associated pulmonary hypertension is treated with bosentan or sildenafil

Pregnancy and Systemic Sclerosis

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- The prevalence of scleroderma in pregnancy approximates 1 in 22,000 pregnancies.
- These women usually have stable disease during gestation if their baseline function is good. As perhaps expected, dysphagia and reflux esophagitis are aggravated by pregnancy (Steen, 1999). Dysphagia results from loss of esophageal motility due to neuromuscular dysfunction. A decrease in amplitude or disappearance of peristaltic waves in the lower two thirds of the esophagus is seen using manometry. Symptomatic treatment for reflux is described in Chapter 54 (Gastroesophageal Reflux Disease).
- Women with renal insufficiency and malignant hypertension have a higher incidence of superimposed preeclampsia. With rapidly worsening renal or cardiac disease, pregnancy termination should be considered. As discussed, renal crisis is life threatening and is treated with ACE inhibitors, but it does not improve with delivery. Pulmonary hypertension usually contraindicates pregnancy •

- Vaginal delivery may be anticipated, unless the soft tissue thickening wrought by scleroderma produces dystocia requiring cesarean delivery. Tracheal intubation for general anesthesia has special concerns because of limited ability of these women to open their mouths widely. Because of
- esophageal dysfunction, aspiration is also more likely, and epidural analgesia is preferable. Warming the delivery room and intravenous fluids, extra blankets, and socks and gloves are recommended to improve impaired circulation from Raynaud phenomenon. If corticosteroids were used frequently, stress doses of hydrocortisone are recommended .

- Maternal and fetal outcomes correlate with underlying disease severity. In a review of 214 gravidas with systemic sclerosis, 45 percent had disseminated disease. Major complications included renal crisis in three and greater rates of preterm birth . Chung and coworkers also reported elevated rates of preterm delivery, fetal-growth restriction, and perinatal mortality. A multicenter study of 109 pregnancies from 25 centers reported higher rates of preterm delivery, fetal-growth restriction, and very-low-birthweight newborns . These are likely related to placental abnormalities that include decidual
- vasculopathy, acute atherosclerosis, and infarcts .
- Scleroderma may be associated with subfertility For women who do not
- choose pregnancy, several reversible contraceptive methods are acceptable. However, hormonal agents, especially combination oral contraceptives, probably should not be used, especially in women with pulmonary, cardiac, or renal involvement. Due to the often unrelenting progression of systemic sclerosis, permanent sterilization is also considered