

# Arthritis and Other Auto-immune Conditions

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**A**rthritis and rheumatic conditions are among the most frequently occurring chronic medical conditions and they have substantial impact of the health and quality of life of women with disabilities, as well as on the utilization of health care resources. Most rheumatic diseases cause chronic pain which inflicts not only enormous personal suffering but also economic loss to individuals and society. Disability, not death, is the principle consequence of chronic painful conditions. Pain is a subjective experience that cannot be measured objectively. Furthermore, there is not a direct relationship between tissue injury and the severity of pain.

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## ASSESSMENT OF DISABILITY

Arthritis and rheumatic disorders can lead to significant long-term disability. This disability can take many forms, including the anxiety and depression commonly seen in fibromyalgia, the chronic joint aches of osteoarthritis, and the functional losses incurred by progressive rheumatoid arthritis. Being able to meaningfully assess disability and recognize when interventions should be implemented are two essential skills for the astute clinician.

In an effort to quantify disability, many scales and mechanisms have been proposed. Beyond the activities of daily living (ADL) and instrumental activities of daily living (IADL) commonly used for a variety of disabling conditions<sup>1</sup>, quality of life questionnaires, such as the SF-36 or QOL-16 may provide further insight into the burdens faced by disease, and have been correlated with severity of disease in fibromyalgia<sup>2</sup>. Another study suggested that patients with osteoarthritis of the knee or hip often develop a cascade of cause-and-effect type changes leading to muscle weakness and negative effect<sup>3</sup>. It is rare for the disability resulting from even "minor" joint disease to be limited to the involved joint; usually many aspects of a patient's life are affected.

Attempts have been made to assess the spectrum of disability as it pertains to each condition. Large studies of these diseases suggest that rheumatoid arthritis is likely to cause clear-cut physical disability but less commonly leads to psychological or pain-related disability. In contrast, disorders such as low back pain, neck pain, and fibromyalgia have been found to result in far more psychological and pain-related issues. Fibromyalgia and rheumatoid arthritis both seem to affect the activities of daily living, while spinal pain is considerably less likely to compromise these essential skills<sup>4</sup>.

Autoimmune conditions are unique in the realm of disability because unlike the steady course of injury-related or developmental disabilities, these conditions can range from progressively debilitating to eventually remitting. By applying assessment tools tailored to the pattern of disability most commonly seen in each disorder, the astute clinician can more quickly determine where focus should be placed.

These psychological effects of musculoskeletal disorders are more difficult to ascertain but no less important in terms of disability. The Americans with Disabilities Act, passed in 1990, helped to legitimize psychiatric disability and gave legal implications to such a diagnosis. It is approximated that 13% of cases now filed under the ADA alleging employment discrimination cite psychiatric disability as the cause<sup>4</sup>. This means that conditions such as fibromyalgia in which there are no obvious physical deficits may legally qualify as disabling because of associated anxiety or depression.

The assessment of disability in autoimmune and joint disorders is vital to the well being of the patients who must cope with difficult diagnoses and sometimes uncertain outcomes. Being able to choose effective tools to measure disability and provide some insight into future patient livelihood are essential skills for the physician to develop. As more effective treatments become available for diseases such as rheumatoid arthritis and lupus, the importance of early intervention and longitudinal measurement of disability are amplified. In the 18-year long longitudinal rheumatoid arthritis study done by Hawle & Wolfe in 1991, once patients became work disabled, they averaged a loss of income by approximately 35% and were more likely to suffer worse symptoms, greater pain, anxiety, and depression<sup>5,6</sup>. Patients suffer debilitation in the form of forced lifestyle changes caused by the disease itself and by the financial constraints with which the disease burdens them.

***Summary Points:***

- Disability has both clinical and legal implications; psychiatric disability is legally recognized and may be the most compromising aspect of a patient's disease
- Many tools exist to quantify severity of disability and screen for patients at risk for future disability
- Rheumatoid arthritis usually causes physical disability with some resultant psychological disability, while fibromyalgia and chronic back pain seem to develop almost simultaneously with pain-related and psychiatric disability
- Longitudinal assessment is more valuable than single-visit assessment in predicting long-term disability in autoimmune disease

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## SEX HORMONES AND AUTOIMMUNE DISEASES

Since the first observation by Hench in 1938 of the remission of RA in pregnancy, it has been recognized that a woman's reproductive characteristics and hormonal milieu may have a profound effect on the course of rheumatic disease<sup>7, 12</sup>. Classical teaching states that physiological levels of estrogens were thought to stimulate the immune response and make hormones to suppress it<sup>9</sup>. Among the collagen vascular diseases, rheumatoid arthritis, systemic lupus erythematosus and systemic sclerosis have prevalence rates that are three to nine times higher in women than men. Estrogens lead to an increase in autoantibody production by stimulating B-cell response and a decrease in suppressor T-cell reactivity. These findings are found in vitro and do not explain the effects of estrogens on other normal immune responses such as inhibiting immune responses during pregnancy. It appears that estrogen has a biphasic dose effect with lower levels enhancing and higher levels inhibiting specific immune activities<sup>9, 12</sup>.

Pregnancy interacts with rheumatic diseases in various ways. Rheumatoid arthritis, while remitting during pregnancy, may be exacerbated in the post partum period. Pregnancy does not seem to adversely affect fetal outcome in rheumatoid arthritis. The course of systemic lupus erythematosus in pregnancy is unpredictable. Patients are about equally likely to see their disease improve, worsen, or remain unchanged. There is, however, an increase in adverse fetal outcome (prematurity, intrauterine growth retardation and pregnancy loss)<sup>10, 11</sup>.

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## INFLAMMATORY ARTHROPATHIES

The inflammatory autoimmune diseases are an array of disease conditions that manifest with varying degrees of inflammatory arthritis with joint swelling and pain, constitutional symptoms including fatigue, malaise, and low grade fever, and non-articular expressions such as alopecia, skin rashes, hematologic disorders, and neurologic sequelae. As a group, the inflammatory autoimmune diseases tend to selectively afflict women over men. They dramatically impact a woman's life – from her basic ability to get around and perform activities of daily living to her ability to perform a job and work outside the home to her more personal feelings about her own body, her femininity, and even her ability to conceive children. This section will focus on two such conditions – rheumatoid arthritis and systemic lupus erythematosus – and will look at the disease processes and how their various features and in some cases even treatment options can affect a woman's quality of life.

### *Rheumatoid Arthritis*

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease with extensive joint and systemic involvement. The current American College of Rheumatology criteria for diagnosis includes at least four of the following components:

**Table 1**

1.	Morning stiffness for at least one hour
2.	Swelling of three or more joints
3.	Swelling of hand joints (PIP, MCP or wrist joints)
4.	Symmetrical swelling
5.	Subcutaneous nodules
6.	Presence of serum rheumatoid factor
7.	Erosions and/or periarticular osteopenia in hand or wrist joints seen on radiograph

Of these seven criteria the first four must be present for at least six weeks, and criteria two through five must be observed by a physician<sup>13</sup>.

The Norfolk arthritis register is a prospective population-based database established to document new cases of inflammatory arthritis and follow these cases to unravel the natural history of the disease. They report an annual incidence of rheumatoid arthritis of 35.9 per 100,000 for women and 14.3 for men. The prevalence of the disease is generally reported between 0.5% and 1% of the adult population, and the prevalence among women has been demonstrated to be approximately double that in men<sup>14</sup>. The prevalence increases with age and the peak onset is most frequent between the fourth and sixth decades. Economic studies have estimated lifetime per patient cost (direct or medical expense cost) of RA to range between \$61,000 and \$122,000. Indirect costs, which are estimates of output loss because of cessation or reduction of productivity, are over twice those of direct expenses, leading to total RA-related costs of approximately \$26 to \$32 billion annually in the United States alone<sup>18</sup>.

The joint involvement in RA is typically symmetrical and polyarticular and usually involves the proximal interphalangeal joint, the metacarpophalangeal joint, the wrist, elbow, shoulder, knee and metatarsophalangeal joints. Morning joint stiffness is a prominent feature of the disease and can be severely limiting and impair a woman's ability to perform daily activities including household work. Besides limitations on physical activity there are other practical implications of joint disease for women with RA. In pregnant women with RA, severe hip disease may prevent normal vaginal delivery. Also, patients who have cervical spine disease and who require cesarean section under general anesthesia are at risk from complications of atlantoaxial subluxation leading to neurological deficits<sup>19</sup>.

The course of the disease is varied. Early in the disease the inflammation activity may fluctuate. In most patients, however, joint deformities and variable degrees of disability do occur with time. Therefore, assessment of functional capacity is very important<sup>15</sup>.

In fact, the term rheumatoid arthritis might be deemed a misnomer as it is a systemic illness and it might be more appropriately referred to as rheumatoid disease. Some of the extra-articular manifestations that can impair a woman's lifestyle include the constitutional symptoms such as low-grade fever, malaise, fatigue and weakness. Neurologically, RA can cause peripheral neuropathies secondary to the proliferating synovium causing nerve compression. Carpal tunnel and a similar variant involving the

anterior tibial nerve (tarsal tunnel syndrome) are common<sup>15</sup>. Women comprise a major portion of the office-staff workforce whose work demands a good amount of computer-based activity. Having a stronger propensity to develop carpal tunnel syndrome could potentially limit a woman's ability to earn a living. A secondary Sjogren's syndrome or autoimmune exocrinopathy, which can occur in both rheumatoid arthritis, systemic lupus erythematosus, as well as systemic sclerosis and polymyositis, can also appreciably impact a woman's lifestyle. In addition to the more commonly recognized dry eye, dry mouth and parotid gland enlargement components of the syndrome, women with Sjogren's syndrome may also have dry skin, dry throat, involvement of pancreatic exocrine glands leading to intestinal malabsorption, and a profound vaginal dryness which could impair sexual activity.

The goals of treating the inflammatory autoimmune diseases including rheumatoid arthritis are: 1) relief of pain and stiffness 2) reducing inflammation to protect and preserve joints 3) maintaining as normal a lifestyle as possible. To achieve these goals patients most commonly require a multi-disciplinary approach which should include medical management with appropriate NSAIDs as well as the newer disease modifying and immunomodulating drugs (i.e., infliximab and etanercept), physical therapy and appropriate exercise, education about the disease process to better cope with the changes that may occur in one's body and lifestyle, and emotional support via counseling and the more formal psychological therapies.

Several research studies have focused on the nature of disability in rheumatoid arthritis. Parker demonstrated a significant relationship between level of pain and the perceived level of disability<sup>16</sup> (by contrast the degree of joint swelling and serum inflammatory markers often correlate to the radiologic picture of the disease). Similarly there are a number of psychological markers that can significantly impact on a rheumatoid patient's life and ability to cope with the disease. Rheumatoid arthritis patients who had a higher level of cognitive distortions (i.e. catastrophizations, or inaccurate/all-encompassing beliefs that their disease irrevocably reduced their viability as people) had higher levels of depression, disability and lower levels of physical and psychological functioning. Patients who perceived a lower level of social support had increased physical disability. Similarly, patients who reported high levels of spousal criticism related higher levels of psychological distress and disability<sup>17</sup>.

A landmark 18-year study of work disability in 823 rheumatoid arthritis patients attempted to ascertain how frequently and quickly the condition leads to disability and what factors are most predictive of such a progression. The analysis revealed that 25% of rheumatoid patients were work disabled at 6.4 years after disease onset, and 50% were disabled by 20.9 years. Disability at the initial visit correlated well with measures of the disease flare severity, job demands, and functional status; however, this "spot" assessment was not nearly as accurate in predicting the course of disease or future disability. Factors measured in follow-up assessment that were independently predictive of subsequent disability include persistent ESR elevation, pain, presence of rheumatoid factor, and disability criteria by the Health Assessment Questionnaire<sup>18</sup>.

## *Systemic Lupus Erythematosus*

Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder that produces varying combinations of signs and symptoms. The criteria for SLE are as follows:

<b>Table 2</b>
1. Malar rash : butterfly rash which spares the nasolabial folds
2. Discoid rash: erythematous raised patches with adherent keratosis scaling and follicular plugging
3. Photosensitivity
4. Oral ulcers
5. Arthritis
6. Serositis
7. Renal involvement
8. CNS involvement
9. Hematologic disorder
10. Immunologic disorder – positive test for antiphospholipid antibodies OR Anti-DNA antibody OR Anti-Sm antibody OR false-positive test for syphilis
11. ANA antibody – abnormal titer of antinuclear antibody in absence of any drugs associated with “drug-induced lupus” syndrome

A diagnosis of SLE is made when a person has 4 of the 11 clinical and/or laboratory criteria – note: these findings can be present serially or simultaneously over length of time of observation<sup>20</sup>.

SLE has an age onset between 16 and 55, with eighty five percent of patients between ages 20 and 40 years of age. Since SLE affects such a young group, the disabilities associated with this disease represent a potentially large economic burden. Clarke et al calculated a conservative estimate of the indirect costs of SLE to be \$15,598 per year (Canadian dollars)<sup>21</sup>. In adults the female to male ratio ranges from 8:1 to 13:1. Most cases of SLE occur in the non-white population. In the US the highest incidence of SLE is found among Asians in Hawaii, blacks and some Native Americans. Black American females have a 1 in 250 risk of developing the disease.

Since lupus has such pervasive manifestations there are clearly many ways in which the disease can particularly impact on a woman's life. Although the arthritis of lupus is not as destructive as RA (i.e., no radiologic evidence of joint destruction) these symptoms can be just as troubling and place severe limitations on a woman's capacity to perform work both inside and outside the home as well as her ability to enjoy recreational activities. SLE has many skin manifestations which can be very troubling as they are often difficult to treat and they can dramatically impair a young woman's sense of well-being and her personal view of her own attractiveness and femininity. The

photosensitive malar rash occurs in more than 50% of lupus patients. The more permanent and disfiguring discoid lupus lesions occur in 25% of lupus patients. Discoid lesions on the scalp typically result in permanent hair loss. Additional skin problems include diffuse thinning of hair on the scalp which tends to follow flares of the disease, stressful life events, pregnancy and the use of steroids.

SLE has sexual and reproductive implications as well. In one study examining SLE patients and sexual function, compared with controls, patients with SLE had a significantly higher rate of abstinence, a lower frequency of sexual activity among the sexually active, diminished vaginal lubrication, and poorer general sexual adjustment<sup>22</sup>.

Just as in RA, there are also some additional concerns for women with SLE interested in getting pregnant. 25 to 40% of SLE pregnancies end in miscarriage<sup>23</sup>. SLE women are at an increased risk of having a premature delivery and a low-birth-weight baby<sup>19</sup>. Finally, there is some data suggesting a relationship between SLE and having children with learning disabilities. Lahita found dyslexia and other learning disorders were present in 45% (24/55) of male offspring of female SLE patients<sup>24</sup>.

Unfortunately even treatment modalities can sometimes cause side-effects that result in loss of quality of life. In particular, SLE patients who develop extensive renal involvement such as diffuse proliferative glomerulonephritis may require high doses (i.e., 1 mg/kg/day) of prednisone. Additionally, if azotemia is present (i.e., creatinine level greater than 1.2 mg/dL) an immunosuppressive agent such as cyclophosphamide may be needed. The side effects of prednisone are far ranging and can be as awful as the disease they are being used to treat. Patients may develop acne, gain weight, develop cushingoid features thus worsening their physical appearance. The metabolic effects of steroids are well known including osteoporosis and osteonecrosis which can result in further physical deterioration. Female patients who receive cyclophosphamide may become permanently infertile<sup>25</sup>.

There are a number of factors that may impact the extent of disability in SLE patients. Lower socioeconomic status has been correlated with higher morbidity and mortality from the disease<sup>26</sup>. Alison Partridge et al focused on risk factors for early work disability in SLE. They concluded that early work disability in SLE was predicted by lower levels of education (high school or less), physical demands of a job and greater disease activity at time of diagnosis. They also suggested that vocational education targeted at SLE patients with less education might lower disability rates and improve health outcomes<sup>27</sup>.

Our current model of disease has evolved from the purely biomedical model to a biopsychosocial paradigm that recognizes the contribution that our emotional state and social environment can have on our health. The inflammatory arthropathies, and indeed all diseases, should be viewed from the perspective of the multitude of ways in which they can change a person's life. In doing so, physicians will be in a better position to provide comprehensive and effective health care for all of their patients.

***Learning Points:***

1. RA is a systemic disease.
2. The prevalence of RA among women has been demonstrated to be approximately double that in men.
3. Economic studies have estimated lifetime per patient cost (direct or medical expense cost) of RA to range between \$61,000 and \$122,000. Indirect costs which measure lost productivity are much higher.
4. RA not only affects women more than men but it can have very specific implications for women. For example, severe high disease in RA may prevent women from having a normal vaginal delivery.
5. SLE is primarily a young women's disease. Indirect costs for this disease can be very high.
6. SLE has many cutaneous manifestations including Raynaud's phenomenon, photosensitive malar rash, discoid lupus lesions, alopecia.
7. Treatments for these diseases can also result in disability. For example, the use of cyclophosphamide is associated with infertility.
8. Social support and emotional adjustment to these diseases can have a major impact on the patient's level of disability.

***Noninflammatory Arthritic and Rheumatic Diseases:*****Osteoarthritis**

Osteoarthritis (OA) is manifested by morphologic, biochemical, molecular and biomechanical changes of both cells and matrix which lead to a softening, fibrillation, ulceration and loss of articular cartilage, sclerosis and eburnation of subchondral bone, osteophytes and subchondral cysts. When clinically evident, OA is characterized by joint pain, tenderness, limitation of movement, crepitus, occasional effusion and variable degrees of local inflammation<sup>28</sup>.

Osteoarthritis is the most common form of arthritis and the second most common cause of long-term disability among adults in the United States<sup>28, 29</sup>. Epidemiological factors including age, ethnic populations, occupation, gender and trauma predispose patients to getting osteoarthritis. The frequency of OA is about equal in the genders between age 45 and 55, but after 55 OA is much more common in women. Women are more likely to have the inflammatory form of OA of the hands, involving the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints producing Heberden's nodes and Bouchard's nodes respectively. In obese women there is a high probability of finding osteoarthritis of the knees with the associated anserine bursitis<sup>30</sup>.

Hip involvement is potentially the most painful and disabling joint involvement in OA. In patients between the ages of 20 and 50 years who have hip pain often may have a history of having hip dysplasia, Legg-Calve-Perthes disease or slipped capital femoral epiphysis that may have gone undetected, but have predisposed the patients to develop OA<sup>39</sup>.

Pain and disability are not solely related to physical mechanical impairment. Several factors have been linked to the inclination to be disabled in patients with osteoarthritis. They include older age, lower educational level, lower income, unmarried status and non-Caucasian race<sup>31</sup>. Reassurance, counseling and education by the physician are important in trying to minimize the negative effects of psychosocial factors. Weight loss groups and a stable social support system may be helpful in a concerted effort at weight reduction for obese patients. Patients can often have sexual problems secondary to the symptomatology from their osteoarthritis but may be reluctant to discuss this unless specifically queried. In a study done by Currey on osteoarthritis of the hip joint and sexual activity, it appeared that this problem was actually due to joint pain caused by coitus, difficulty due to stiffness of the hip joint(s), and loss of libido. Local mechanical factors were clearly more important than any loss of sexual drive<sup>32</sup>. Counseling and psychosocial counseling may be effective in this setting. Also depression may be present and once recognized it must be treated<sup>33</sup>.

It has been estimated that if a Caucasian woman lives to be 90 years of age, she has a 32% chance of sustaining a hip fracture. Also, the death rate within 3 months of a hip fracture is 12 to 20%, usually complications of surgery or prolonged hospitalization. Repeated fractures are all too likely in survivors as is loss of independent ambulatory ability<sup>40</sup>.

### **Fibromyalgia Syndrome**

Fibromyalgia Syndrome (FMS) is the most common rheumatic cause of chronic diffuse pain. It reportedly affects 2-5% of the general population and is much more prevalent in women than men.<sup>34</sup> Symptoms include diffuse soft tissue pain, stiffness and fatigue, accompanied by identification of multiple tender points in specific areas. The criteria proposed by the American College of Rheumatology include identification of at least 11 or 18 of these tender points.<sup>34</sup> (citation) [include picture of 18 points] Patients often have morning stiffness, which may fluctuate in severity through the course of the day and be exacerbated by factors such as physical or emotional stress, humidity, or poor sleep. Several other associated problems include tension headaches, irritable bowel syndrome, and upper extremity paresthesias and sensations of swelling. Non-restorative sleep is also present as a significant symptom in many patients. There is often symptom overlap with several other musculoskeletal diseases like myofascial pain syndrome, and with systemic diseases, such as hypothyroidism. In addition, the diagnosis of FMS may be obscured by the identification of another underlying problem, such as Rheumatoid Arthritis.<sup>34</sup>

The etiology of FMS is unknown but several hypotheses have been proposed. Suggestions of psychiatric, endocrinologic, and neurologic causes have been made. Often, the lack of objective findings often lead to impressions that there is a nonorganic basis for the patient's illness. However, recent arguments suggest that there may be less of an inflammatory process as an etiology than previously thought..

Treatment is multifaceted and directed toward improving function and symptoms. Modalities, which have been found to be effective in treatment of FMS, include exercise, pharmacologic intervention to improve sleep and help treatment such as biofeedback, injection of tender points, and acupuncture. In the past, Tricyclic antidepressants, such as Amitriptyline were effectively used to treat the associated sleep disturbances of FMS and concomitant symptoms of depression. The goal was to initiate treatment at the lowest dose of the medication prior to bedtime, and to adjust until the patient regained restorative sleep or until adverse side effects were experienced. The often unfavorable side effect profile of these medications include the range of anticholinergic effects such as dry mouth and eyes, daytime drowsiness, urinary retention and constipation, and the more severe risk of cardiac effects at higher doses. More recently, treatment of FMS has included the Selective Serotonin Reuptake Inhibitors, i.e. Fluoxetine and Sertraline. These have been associated with a more favorable side effect profile and greater effectiveness in treating associated depression in FMS. However, they may not be considered superior in treatment of the pain and sleep disorder of FMS.<sup>36</sup> NSAIDs have not been found to be effective as a single agent for treatment.<sup>34</sup> There may be some utility in their use for treatment of an underlying pain or arthritic disorder. The use of antiepileptic medications like Gabapentin have helped with treating the chronic pain associated with FMS.<sup>36</sup> Finally, short acting benzodiazepines like Alprazolam may be used to treat anxiety as well. The key to effective treatment of FMS is to utilize a multidisciplinary approach. The combination of low impact exercise for three to four days a week, mental health counseling to identify the patient's stresses, education about the patient's illness and the use of pharmacologic agents may prove to be of great benefit to the woman with FMS.<sup>34</sup>

Fibromyalgia has often been referred to as a "silent" disability as it is not associated with abnormalities in laboratory tests, imaging studies and histopathology. The range of disability associated with FMS may range from simple "nuisance" to total inability to live a functional life.

In terms of emotional effects of the disease, it has been found that not only are depression and anxiety associated with the syndrome, but also they are independently associated with the severity of the pain symptoms<sup>35</sup>. The presence of depression and anxiety may be attributed to several factors, including the fear of having a life threatening illness with no cure, the frustrations of others not believing the validity of the individual's pain, the inability to carry out daily activities, and the economic repercussions of not being able to work or function in society.

There are also components of economic disability associated with FMS. FMS is an increasingly frequent source of disability claims and payments. In fact, in one study of affected patients in Rheumatology clinics, 35% had received disability payments<sup>36</sup>. Financially, the burden of frequent office visits and tests is significant. In a study performed to evaluate service utilization and costs of patients with FMS, it was found that on average, the individual would have 10 office visits a year with the yearly expense greater than \$2,200<sup>37</sup>.

These patients have high lifetime utilization rates for all medical service types, and more symptoms and comorbid conditions are reported than in all other rheumatic diseases.

Disability in arthritic and rheumatic diseases is affected by disease process, comorbidity, psychological profile of the patient, chronic pain and disuse, and various medical and surgical interventions. An appreciation of medical and psychosocial factors is essential to understand the issue of disability from musculoskeletal diseases. The physician's ultimate responsibility is to the patient. While medical and legal definitions of disability differ, it is the physician's obligation to be the patient's advocate.

## APPENDIX

Disease	Medication Commonly used for Management	Common Dose Range	Common Side Effects	Issues Specific to Women
Inflammatory Rheumatic Diseases: Including: Rheumatoid Arthritis Systemic Lupus Vasculitis	Corticosteroids:  Methylprednisolone  Prednisone  Hydrocortisone	Dosage is highly variable and determined by the rheumatic disease to be treated. In general the lowest dose should be used and the dose should be taken with food. It is very important that Corticosteroids when used long term should not be stopped abruptly and should be tapered	Cushing's syndrome, osteoporosis, cataracts, hypertension, increased appetite, elevated blood sugar, indigestion, insomnia, mood changes, nervousness or restlessness, cramps, immune suppression.	Menstrual irregularities, hirsutism, found in breast milk so mothers should be advised not to breast-feed infants.
	Azathioprine	50 to 159 mg per day in 1 to 3 doses, based on body weight.	Loss of appetite, nausea or vomiting, skin rash, bone marrow suppression, infection, malignancy, pancreatitis.	Contraindicated in pregnancy, teratogenic, found in breast milk.
	Cyclophosphamide	50 to 150mg per day.	Infertility in men and women, loss of appetite, bone marrow suppression, infection, hemorrhagic cystitis, malignancy.	Infertility, teratogenic, contraindicated in pregnancy.

Disease	Medication Commonly used for Management	Common Dose Range	Common Side Effects	Issues Specific to Women
	Hydroxychloroquine	200 to 600mg per day.	Diarrhea, loss of appetite, nausea, stomach cramps or pain, skin rash, retinopathy, neuromyopathy.	Contraindicated in pregnancy.
	Gold	3 to 9mg per day	Abdominal cramps or pain, bloated feeling, decrease or loss of appetite, loose stools, nausea or vomiting, photosensitivity, skin rash.	Pregnancy category C, found to be teratogenic in animal models, found in breast milk.
	Etanercept	25mg IM injection biweekly	Immunosuppression, increased risk of malignancies, headache, nausea, rhinitis, injection site reaction.	Pregnancy category B, Drug should only be used during pregnancy only if needed, may be excreted in breast milk and either the drug should be stopped or breast-feeding discontinued.
	Methotrexate	7.5 to 25mg per week	Cough, diarrhea, hair loss, loss of appetite, unusual bleeding or bruising, fever, pneumonitis, infection, stomatitis.	Contraindicated in pregnancy.
	Infliximab	IV (in combination with methotrexate therapy): 3mg/kg followed by an additional 3mg/kg at 2 and 6 weeks after the first dose then repeat every 8 weeks thereafter.	Hypersensitivity, hypotension, lupus-like syndrome, sepsis	Pregnancy category B; use during pregnancy if only needed; breast feeding is not recommended.

Disease	Medication Commonly used for Management	Common Dose Range	Common Side Effects	Issues Specific to Women
Fibromyalgia	Serotonin-Norepinephrine Reuptake Inhibitors:  Amitriptyline	10 to 100mg per day	Difficulty concentrating, dizziness, drowsiness, dry mouth, headache, increased appetite, nausea, sleep disturbances, unpleasant taste, urinary retention, weight gain.	Pregnancy category D, Unsafe in pregnancy;
	Selective Serotonin Reuptake Inhibitors :  Fluoxetine	20 to 40mg per day	Serotonin syndrome, Insomnia, nausea, diarrhea, tremor, headache, anorexia, decreased libido, weight gain, anorgasmia, rash, sedation, pruritis, abnormal dreams.	Pregnancy category C, Uncertain safety; no human or animal studies show an adverse effect. Fluoxetine crosses the placenta.
	Sertraline	50 to 100mg per day	Similar side effect profile to Fluoxetine	Pregnancy category C, Uncertain safety; no human or animal studies show an adverse effect

Disease	Medication Commonly used for Management	Common Dose Range	Common Side Effects	Issues Specific to Women
	Anticonvulsants:  Gabapentin	Day 1: 300mg per day Day 2: 300mg twice a day Day 3: 300mg three times a day (max: 1200mg/day)	Leukopenia, somnolence, dizziness, ataxia, fatigue, nystagmus, tremor, nausea, weight gain, amnesia, dyspepsia, depression, periorbital edema, myalgias, dry mouth.	Pregnancy category C, Uncertain safety; no human or animal studies show an adverse effect. Excreted in human breast milk.
	Alprazolam	.025-.05mg three times a day as needed	Drowsiness, lightheadedness, syncope, tachycardia, respiratory depression, dry mouth, depression, headache, constipation, diarrhea, confusion, blurred vision, dermatitis	Pregnancy category D, Unsafe in pregnancy;
Non-Inflammatory Pain	Acetaminophen	1,000 to 4,000mg per day.	Usually free of side effects.	Pregnancy category B
	NSAIDS	Take as directed.	Abdominal pain, dizziness, drowsiness, fluid retention, gastric ulcers and bleeding, greater susceptibility to bleeding, heartburn, indigestion, lightheadedness, nausea, rash, ringing in ears. Used in caution in people with pre-existing heart or kidney disease.	Pregnancy category B and D especially during third trimester.

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