

Rheumatoid Arthritis

Rheumatoid arthritis is a chronic autoimmune disease characterized by a persistent inflammatory synovitis and multisystem involvement - most importantly cricoarytenoid & c-spine involvement resulting in potential difficult airway along with insidious cardiorespiratory involvement. These patients require a thorough workup including airway, c-spine, respiratory & medications & they often need awake fiberoptic intubation

ANESTHETIC CONSIDERATIONS:

- Potential for difficult airway
- Potential for unstable C-spine
- **Multisystem disease:**
 - Resp: interstitial fibrosis, pulmonary HTN, pleural effusions
 - CVS: pancarditis, AI, pericardial effusions, conduction system defects
 - Renal: CRF
 - Chronic anemia
- Medications with significant side effects:
 - Corticosteroids
 - NSAIDs
 - Immunosuppressives: cyclosporine, cyclophosphamide, MTX
 - Chronic pain meds
- Technical difficulties with lines and patient positioning, fragile skin
- Co-existing diseases – increased risk IHD, cancer, infection, PUD, DM, osteoporosis

ANESTHETIC GOALS:

- Assume unstable c-spine unless radiographic evidence to the contrary
- Preoperative optimization of extraarticular manifestations – respiratory/cardiac involvement.
- Difficult airway should be anticipated
- Careful positioning and documentation of pre-existing neurologic symptoms

HISTORY

- **Airway**
 - **Careful airway history and exam**
 - Limited mouth opening due to TMJ synovitis / arthritis
 - Cricoarytenoid arthritis
 - Limitation of vocal cord movement and generalized erythema and edema of the laryngeal mucosa that may progress to airway obstruction
 - Acutely, presents as hoarseness, pain on swallowing, dyspnea and stridor +/- tender to palpation of neck
 - Erythema and swelling of arytenoids seen on direct laryngoscopy
 - Chronically, can be asymptomatic or hoarseness, dyspnea, stridor
 - Cricoarytenoid arthritis may make endotracheal intubation difficult
 - Mandibular hypoplasia with JRA
- **Cervical spine issues**
 - Laxity of the ligaments, not joint disease, can cause atlantoaxial subluxation (AAS) and consequent separation of the atlanto-odontoid articulation
 - Flexion of the head in the presence of atlantoaxial instability could result in the displacement of the odontoid process into the cervical spine and medulla (causing compression) and/or occlusion of the vertebral arteries; This may precipitate quadriplegia, spinal shock, and death
 - Neck pain radiating to the occiput may be the first sign of cervical spine involvement
 - AAS symptoms = occipital headaches, dysphagia, dysphonia, diplopia (cranial nerve root compression), persistent or progressive neck / arm pain (subaxial radicular entrapment), dizziness, upper extremity numbness (long tract compression, vertebral artery insufficiency), myelopathy
 - Subluxation can be asymptomatic
 - Anterior (80%) – avoid flexion
 - Posterior (3-7%) – avoid extension
 - Vertical (10-20%), most dangerous as it may cause compression of cervical medulla – avoid extension
 - Direct laryngoscopy should be avoided in patients with vertical or posterior subluxation
 - Lateral / rotational (2-5%) may cause compression of vertebral arteries, cervical nerves or non-reducible head tilt – avoid rotation
 - Subluxation of other cervical vertebrae can also occur
 - Sub-axial subluxation (usually C5-6) – limited movement with neutral stabilization during laryngoscopy
 - Ankylosing spondylitis of cervical spine
 - Prior cervical spine surgery / fusion
 - A careful history may elicit neurologic deficits, neck and upper extremity pain, and a crunching sound with neck movement
- **Joints**
 - The onset of rheumatoid arthritis in adults may be acute, involving single or multiple joints, or insidious with symptoms such as fatigue, anorexia, and weakness preceding overt arthritis
 - Several joints, often the hands, wrists, knees, and feet, are affected in a symmetrical distribution
 - Pain and stiffness in multiple joints common - usually the wrists and metacarpophalangeal joints are involved; this distinguishes RA from osteoarthritis, which often affects distal interphalangeal joints
 - RA is characterized by morning stiffness often lasting more than 1 hour after initiating activity
 - When the disease is progressive and unremitting, nearly every joint is affected except for the thoracic and lumbosacral spine
- **Extra-articular features**
 - Pulmonary Disease
 - Pleural effusions – most common but usually small
 - Pulmonary nodules may mimic TB, carcinoma

- Pulmonary fibrosis/ interstitial lung disease → reduced diffusion capacity and pulmonary HTN
 - Obstructive lung disease
 - Costochondral involvement may produce restrictive lung changes with decreased lung volumes and vital capacity → ventilation-perfusion mismatch and decreased arterial oxygenation
 - Organizing pneumonia
 - Obliterative bronchiolitis (associated with gold, penicillamine, sulfasalazine)
 - CVS
 - Pericarditis → acute pericarditis, chronic constrictive pericarditis or pericardial effusion (30%), cardiac tamponade (rare)
 - Myocarditis (rare) & coronary arteritis
 - Rheumatoid nodules in conduction system → dysrhythmias
 - Aortitis (aortic root dilation, aortic valve regurgitation)
 - Cardiac valve fibrosis
 - Accelerated coronary atherosclerosis and coronary artery disease
 - The often severely limited functional status in these patients masks ischemic symptoms
 - Heart failure: consider differential
 - Ischemic cardiomyopathy
 - Infiltrative cardiomyopathy (amyloid deposition in longstanding RA)
 - HF is exacerbated by anti-TNF agents, nonselective NSAIDs, COX-2 selective inhibitors, antimalarials, and glucocorticoids
 - LV systolic and diastolic dysfunction due to RA (LVEF < 40% in 5% of RA patients)
 - GI
 - Mildly abnormal liver function common, hepatitis
 - PUD from NSAIDs – care with anticoagulation
 - Renal
 - Renal dysfunction (glomerulonephritis) and failure
 - Secondary to drugs (gold, NSAIDs, cyclosporine, penicillamine), vasculitis, amyloidosis
 - Hematologic
 - Anemia of chronic disease - secondary to drugs or decrease in erythropoiesis
 - Thrombocytopenia or platelet dysfunction → ASA / NSAIDs
 - Felty's syndrome = RA, leukopenia, splenomegaly
 - Neurologic
 - Polyneuropathies, peripheral nerve compression (eg. carpal tunnel syndrome), myopathies (loss of strength in skeletal muscles adjacent to joints with active synovitis)
 - Mononeuritis multiplex is presumed to be caused by deposition of immune complexes in blood vessels supplying the affected nerves
 - Cervical nerve root compression
 - Rheumatoid vasculitis may affect cerebral blood vessels, producing a cerebral necrotizing vasculitis
 - Dural nodules can cause cord compression
 - Psych
 - Chronic pain, depression
 - Other
 - Scleritis
 - Corneal ulceration
 - Raynaud's
 - Digital necrosis

PHYSICAL

- **A/W** – Careful examination of the airway looking for edematous mucosa, arthritis of larynx (hoarseness, stridor), C-spine involvement (gentle assessment of ROM of neck and any associated discomfort or symptoms to assess if there is interference with vertebral artery blood flow during flexion/extension/rotation of head and C-spine; flexion deformity/ability to straighten neck), and TMJ involvement (extent of mouth opening)
- **CVS** - Careful cardiac exam for pericarditis (S3, loud P2, rales, diastolic murmur [A1], distant HS, pericardial rub, other murmurs of valvulopathy); restrictive pericarditis (dyspnea, right heart failure, fever, chest pain, pericardial friction rub, and pulsus paradoxus); pericardial effusion (muffled heart sounds, pericardial rubs), and enlarged heart
- **RESP** - Careful respiratory exam for fibrosis with pneumonitis (progressive dyspnea, chronic cough, fine crackles), pleural effusions (crackles, dullness, decreased breath sounds)
- **CNS** - Spinal cord compression, neurologic dysfunction (sensory deficits, motor deficits, ROM of neck)
- **MSK** - Arthritis (swelling, pain with motion, restricted motion)
 - The rheumatoid joints are usually boggy, tender to the touch, and warm
 - Patients may have prominent epitrochlear, axillary, and cervical lymph node enlargement
 - Subcutaneous nodules (rheumatoid nodules) may surround joints, extensor surfaces, and bony prominences
- **Neuro** - Preoperative documentation of deformities and neurologic deficits is important to establish a baseline level of function

INVESTIGATIONS

- **Labs**
 - CBC, lytes, BUN, Cr → anemia, renal insufficiency
 - Rheumatoid factor (an immunoglobulin G antibody) is elevated in up to 90% of patients with rheumatoid arthritis (but not specific to rheumatoid arthritis)
 - Elevated CRP and ESR – can be used to monitor the course of RA
- **Imaging**
 - C-spine X-rays

- Patients who have neurologic deficits or symptoms or long-standing, severely deforming disease or who are scheduled to undergo procedures requiring manipulation of the cervical spine or special positioning, such as turning prone, require anteroposterior and lateral cervical spine radiographs with special flexion, extension, and open-mouth odontoid views
 - Radiographic demonstration that the distance from the anterior arch of the atlas to the odontoid process exceeds 3 mm confirms the presence of atlantoaxial subluxation
 - Risk factors for AA subluxation: seropositive, males, severe arthropathy and longstanding disease
 - The duration, severity, or symptoms of the disease do not correlate with cervical spine subluxation
 - Significant abnormalities (anterior atlas-dens interval >9 mm or posterior interval <14 mm) may benefit from consultation with a neurologist or neurosurgeon
 - MRI – for better imaging and to confirm cervical spine involvement
 - EKG → conduction system abnormal, ischemia, pericardial effusion
 - CXR → pleural effusion, fibrosis
 - +/- ECHO if suspect pericardial effusion
- **Other**
 - PFT and ABG → if significant lung disease

OPTIMIZATION

- Consider consult regarding stability of c-spine if elective case
 - Patients with symptoms or evidence of cervical cord compression can be fitted with a cervical collar preoperatively to minimize the risk of overmanipulation of the neck during surgery
- Consider ENT consult for patients with significant hoarseness to assess mobility of the vocal cords and the degree of cricoarytenoid arthritis
 - Severe cricoarytenoid arthritis may require awake tracheostomy
- Consider cardiology and pulmonary consults depending on cardiopulmonary status
 - The need for postoperative ventilatory support should be anticipated if severe pulmonary disease is present.
- Consider optimization of anemia with preoperative iron or EPO, or other blood conservation strategies appropriate to the procedure (cell saver, ANH)
- Because rheumatoid arthritis is a multisystem disease and the clinical manifestations are so diverse, individualized preoperative evaluation is important in the identification of systemic effects
- Considerations of Drugs used to treat RA
 - Drug therapy is used to provide analgesia, control inflammation, and produce immunosuppression
 - Monotherapy is unlikely to be completely successful, thus patients are often on multiple drugs
 - NSAIDs -symptomatic relief of rheumatoid arthritis but have little role in changing the underlying disease process (decrease swelling in affected joints and relieve stiffness) and are thus used in conjunction with DMARDs
 - RA patients taking NSAIDs should be assessed for gastrointestinal side effects and renal complications
 - Corticosteroids -potent anti-inflammatory drugs that decrease joint swelling, pain, and morning stiffness in patients with rheumatoid arthritis; high doses are required and are often associated with significant long-term side effects including osteoporosis, osteonecrosis, increased susceptibility to infection, myopathy, hyperglycemia, adrenal suppression and poor wound healing
 - Prednisone doses greater than 10 mg/day are rarely indicated for joint disease, but higher doses may be needed to treat other manifestations of rheumatoid arthritis, especially vasculitis
 - Patients taking significant quantities of glucocorticoids need stress-dose steroids for their operations
 - DMARDs -a group of drugs that have the potential to slow or halt the progression of the disease (generally take 2 to 6 months to achieve their effects)
 - Methotrexate is the preferred DMARD, given in a once-a-week dosing regimen (primarily anti-inflammatory)
 - Monitoring hematologic parameters and liver function tests are necessary in individuals being treated with methotrexate because of the risks of bone marrow suppression and cirrhosis
 - Also lung toxicity
 - Daily folic acid therapy can decrease methotrexate toxicities
 - Tumor necrosis factor inhibitors such as infliximab (Remicade) and etanercept (Enbrel) are quite effective and act more rapidly than other DMARDs
 - Long-term toxicities such as increased susceptibility to infection (tuberculosis) and demyelinating syndromes are a concern
 - Gold, the oldest DMARD, is extremely effective therapy for some patients with rheumatoid arthritis, but it is not commonly used because of its frequent toxicities
 - Lung and kidney toxicity
 - Continuation of steroids and chronic pain medications is optimal, but drugs with antiplatelet effects are generally discontinued and immunosuppressants may have to be temporarily stopped to allow normalization of blood counts

Table 25-13 Adverse Effects of Drugs Used to Treat Collagen Vascular Diseases

CLASS OF DRUGS	EFFECTS
Immunosuppressants	
Methotrexate	Hepatotoxicity, anemia, leucopenia
Azathioprine	Biliary stasis, leucopenia
Cyclosporine	Renal dysfunction, hypertension hypomagnesemia
Cyclophosphamide	Leukopenia, hemorrhagic cystitis, inhibition of pseudochoolinesterase
Lefunomide	Hepatotoxicity, weight loss, hypertension
Mycophenolate mofetil	Nausea, vomiting, diarrhea
TNF Antagonists	
Etanercept	Infections, tuberculosis
Infliximab	Lymphoma, heart failure

Adalimumab	
Interleukin-1 Antagonists	
Anakinra	Infection, skin irritation
T-Cell Inhibitors	
Abatacept	Infection
Interleukin-6 Antagonists	
Tocilizumab	Infection, headache, stomatitis, fever
CD20 Monoclonal Antibody	
Rituximab	Infection, infusion reaction
Corticosteroids	
	Hypertension, fluid retention, osteoporosis, infection, glucose intolerance
Aspirin	
	Platelet dysfunction, peptic ulcer, hypersensitivity
NSAIDs	
	Peptic ulcer, leukopenia, coronary artery disease
COX-2 Inhibitors	
	Renal dysfunction
Adverse cardiovascular events	
Gold	
	Aplastic anemia, dermatitis, nephritis
Antimalarials	
	Myopathy, retinopathy
Penicillamine	
	Glomerulonephritis, myasthenia, aplastic anemia
TNF, tumor necrosis factor; NSAIDs, nonsteroidal anti-inflammatory drugs; COX-2, cyclooxygenase-2.	

ANESTHETIC OPTIONS

- General, neuraxial, regional anesthesia OK (thoracolumbar spine usually unaffected)
 - **Advanced** planning for the management of identified or potential difficult airways is important
 - **Regional** techniques may be preferable to avoid instrumentation of the A/W
 - **Awake fiberoptic** intubation is recommended for GA
 - **LMA** positioning may be difficult due to malposition of larynx

ANESTHETIC SETUP

- **Drugs**
 - Standard emergency drugs
- **Equipment**
 - Standard CAS plus 5-lead EKG
 - Invasive monitors as dictated by cardiopulmonary status / procedure
 - Careful positioning and padding
 - Sicca – lubricating eye gel

MANAGEMENT OF ANESTHESIA

- **Induction**
 - Consider awake FOI if any indication of AAS or difficult airway
 - Smaller than usual ETT
 - Involvement of the cricoarytenoid joints by arthritic changes can result in narrowing of the glottic opening and interference with transalaryngeal passage of the tracheal tube or an increased risk of cricoarytenoid joint dislocation
 - Cricoid arthritis produces erythema and edema of the vocal cords and may reduce the size of the glottic inlet
 - Adjuvant techniques:
 - Bougie, light-wand, Glidescope
 - NB - emergency tracheostomy almost impossible in severe cases
 - Difficult IV access d/t deformity, delicate skin and vessels
 - No specific contraindications to common induction agents
 - The degree of cardiopulmonary involvement by the rheumatoid process influences the selection of the type of anesthesia
 - Greater decreases in BP secondary to myocardial dysfunction
 - Increased risk of aspiration pneumonitis
 - Careful positioning –restricted joint mobility; minimize risk of neurovascular compression and further joint injury
 - Preoperative examination of joint motion will help determine how the extremities should be positioned
- **Maintenance**
 - Based on type of surgery
 - Historical: drug-induced hepatic dysfunction; potential for halothane hepatitis
 - Exaggerated CV effects of volatile anesthetics
- **Emergence**
 - Extubation when fully awake as regaining airway may be difficult

DISPOSITION & MONITORING

- Postextubation laryngeal obstruction may occur in patients with cricoarytenoid arthritis
- Patients with atlantoaxial subluxation require postoperative monitoring with pulse oximetry and judicious administration of narcotic analgesics because emergent airway management, including tracheotomy, is extremely difficult
- Postoperative ventilation may be required if severe restrictive lung disease present perioperatively

COMPLICATIONS

- Difficult tracheal intubation

- Increased neurologic deficits secondary to cervical spine degeneration
- Post-extubation laryngeal edema or cricoarytenoid joint dislocation → stridor

PATHOPHYSIOLOGY

- Prevalence ~1% of adults
- Female:Male 2-3:1
- The most common chronic inflammatory arthritis
- RA is characterized by persistent joint synovial tissue inflammation leading to bone erosion, destruction of cartilage, and loss of joint integrity
- Characterized by symmetric polyarthropathy
 - Morning stiffness
 - MCPs and PIPs commonly involved in the upper body
 - Knees commonly involved in the lower body
- RA also is a systemic disease, affecting multiple organ systems
- RA often progresses through multiple exacerbations and remissions, but 20% to 30% of affected individuals become permanently disabled within 3 years of diagnosis
- The etiology of rheumatoid arthritis is unknown, but it is suspected to be a complex interaction between genetic and environmental factors and the immune system
 - Activation of cellular immune responses in genetically susceptible hosts?
 - The autoimmune response may be initiated by viral induced activation of B lymphocytes
 - This leads to synovitis
- Pathogenesis:
 - Activated endothelial cells attract adhesion molecules that bind to proteins and initiate a sequence of events that stimulate T cells and B lymphocytes
 - Cytokines (tumor necrosis factor, interleukin-1, interleukin-6) are released that accelerate the inflammatory cascade. B lymphocytes produce autoantibodies (rheumatoid factor) that enhance cytokine production and can be found in 75% of patients with rheumatoid arthritis
 - The pathologic changes of rheumatoid arthritis begin with cellular hyperplasia of the synovium followed by invasion of the synovium by lymphocytes, plasma cells, and fibroblasts
 - Cartilage and articular surfaces are ultimately destroyed
- Many of the systemic manifestations of rheumatoid arthritis are a result of small and medium-sized artery vasculitis due to deposition of immune complexes
- Systemic involvement is usually most obvious in patients with severe articular disease

CONSIDERATIONS IN PREGNANCY

- Pregnancy has a beneficial, ameliorating effect on the activity of rheumatoid arthritis
- Effects on fetus:
 - Women with RA are more likely to experience intrauterine growth restriction and/or premature rupture of membranes and also are more likely to have a cesarean delivery than women without rheumatoid arthritis
 - In the absence of vasculitis, fetal outcome is good
- Medications for RA:
 - Aspirin - no evidence suggests that it is teratogenic, and it is most likely the safest antirheumatic agent during pregnancy
 - Potential complications (particularly when high doses are continued until delivery) include anemia, post-term delivery, prolonged labor, antepartum and postpartum hemorrhage, neonatal cephalohematoma, neonatal renal failure and oligohydramnios, neonatal pulmonary HTN and intracranial hemorrhage in preterm infants
 - Most of these complications occur at delivery; therefore aspirin should be discontinued near term
 - Most nonsteroidal anti-inflammatory drugs (NSAIDs) do not seem to be a major problem during pregnancy, although dystocia has been attributed to their use
 - An international consensus conference on the use of NSAIDs in pregnancy concluded that all NSAIDs except low-dose aspirin should be discontinued at 32 weeks' gestation (premature closure of ductus)
 - Corticosteroids and antimalarial agents appear safe and should be continued during pregnancy
 - Gold and d-penicillamine typically are discontinued, although few problems have been attributed to their use during pregnancy
 - Azathioprine may be used safely during pregnancy at doses less than 2 mg/kg/day, but other immunosuppressive agents (e.g., methotrexate, cyclophosphamide, chlorambucil) are highly teratogenic and should be discontinued before conception
 - Cyclosporin, tacrolimus, and intravenous immunoglobulin may all be used in pregnancy
 - An attempt is often made to reduce the dose of all antirheumatic agents during pregnancy and, if possible, to discontinue them in the final weeks of gestation
- Vaginal delivery is preferred for parturients with rheumatoid arthritis, and cesarean delivery should be reserved for obstetric indications
 - A major concern is maternal positioning during labor
 - Patients with juvenile rheumatoid arthritis may have a small mandible, temporomandibular joint (TMJ) dysfunction, cricoarytenoid arthritis, and laryngeal deviation, and these findings may complicate direct laryngoscopy
 - Cervical spine involvement is not common in young patients but may occur in patients with disease of long duration and in those with severe, deforming disease—typically, patients with juvenile rheumatoid arthritis
 - Cervical spine radiographs should be evaluated in pregnant women who have severe erosive disease, neck symptoms, or a history of disease of 10 or more years' duration
 - The cardiac and pulmonary features of rheumatoid arthritis are not common in young patients, but signs and symptoms of pleural and pericardial effusions and pulmonary parenchymal involvement should be sought
 - No evidence contraindicates the administration of spinal or epidural anesthesia in patients with rheumatoid arthritis
 - Care should be taken to avoid excessive manipulation of the neck during administration of general anesthesia

REFERENCES

- Coexisting Chpt 18
- Barash Pg. 636-638
- Miller Chpt 34, 70
- Chestnut Chpt 48