

1. Rheumatoid Arthritis

# Rheumatoid Arthritis

Elena M. Massarotti, MD

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2. Objectives

## Objectives

- Define types of **chronic** inflammatory arthritis
- Define the concept of **pattern recognition**
- Present the **clinical features** of RA
- Discuss the **pathogenesis** of RA

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3. Patient Presentation

## Patient Presentation

- 34 year old **woman** with no significant PMH presents with **pain and swelling of hands** for the last **6 months**
- Malaise and fatigue prominent
- **Morning stiffness** lasts hours
- No rashes, fevers, anorexia, Raynaud's phenomenon

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4. Patient Presentation, Cont'd

## Patient Presentation, Cont'd

- Physical examination showed swelling in the **MCP and PIP** joints of both hands, and bilateral **knee swelling**
- Laboratory tests: **ESR 95** mm/hr (normal  $\leq$  30 mm/hr); negative ANA; **RF 120 IU** (normal  $\leq$  20)
- Synovial Fluid analysis: **WBC 15,790** cells/mm<sup>3</sup> (normal  $\leq$  2000 )

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5. Salient Features

## Salient Features

- Female patient with symmetric small joint arthritis of 6 months duration
- Elevated acute phase reactants
- Positive rheumatoid factor
- Inflammatory joint effusion

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6. The Normal Synovium

## The Normal Synovium

- Lines diarthrodial joints
- Lacks a basement membrane
- Is primarily composed of two cellular types with macrophage and fibroblast-like features
- Is highly vascular

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7. Chronic Inflammatory Arthritis

## **Chronic Inflammatory Arthritis**

- The synovium is the target lesion
- Villous hypertrophy is characteristically seen, along with the formation of lymphoid follicles composed of a round cell infiltrate
- Hypertrophied synovium releases proteinases that lead to erosion of joints, and ultimately to joint instability

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8. Types of Chronic Inflammatory Arthritis

## **Types of Chronic Inflammatory Arthritis**

- Rheumatoid Arthritis
- The Seronegative Spondyloarthropathies: ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease-related, reactive arthritis
- Lyme arthritis

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## Patterns

# Patterns

- Monoarticular/Oligoarticular/Polyarticular
- Symmetric/Asymmetric
- Small joint/Large joint

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## Patterns of Arthritis

# Patterns of Arthritis

- *Symmetric Polyarthritis*: SLE, RA
- *Oligoarticular Arthritis*:  
Spondyloarthropathies, Crystal Induced  
Disease, Lyme Arthritis
- *Large Joint Monoarticular Arthritis*:  
Septic arthritis

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11. Rheumatoid Arthritis: Epidemiology

## Rheumatoid Arthritis: Epidemiology

- The most common chronic inflammatory arthritis, affecting 1% of the North American population
- Women are predominantly affected, at a ratio of 3:1
- Age of onset between ages thirty and fifty
- Associated with smoking

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12. Rheumatoid Arthritis: Risk Factors

## Rheumatoid Arthritis: Risk Factors

- Lack of a formal education
- Positive family history
- Poor prognostic indicators include high amounts of rheumatoid factor, polyarticular presentation, systemic features, presence of **HLADRβ1\*0401, 0404, 0408 alleles**

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13. Rheumatoid Arthritis: Clinical Features

## **Rheumatoid Arthritis: Clinical Features**

- Symmetric polyarthritis affecting large and small joints
- **Typical joints** involved in classic RA include the MCP and PIP joints; wrists often involved; DIP joints **spared**
- **Other joints:** high cervical spine, elbows, knees, hips, MTP joints and ankles; thoracic and lumbar spine usually **spared**

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14. Rheumatoid Arthritis: Extrarticular Features

## **Rheumatoid Arthritis: Extrarticular Features**

- Constitutional symptoms: fever, weight loss, night sweats, fatigue
- Sicca complex (secondary Sjogren's Syndrome)
- Nodules
- Pericarditis
- Pleural Effusions
- Vasculitis

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15. Rheumatoid Arthritis: Laboratory Features

## Rheumatoid Arthritis: Laboratory Features

- Increased levels of acute phase reactants: ferritin, ESR, CRP
- Normochromic, normocytic anemia
- 80% of patients have an elevated rheumatoid factor

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16. Rheumatoid Factor

## Rheumatoid Factor

- Antibody directed against the Fc portion of IgG
- Is *not* diagnostic of RA
- Can be seen with other diseases in which polyclonal stimulation of B cells is seen (chronic infections)
- Does *not* follow clinical disease activity

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17. Rheumatoid Arthritis: Pathogenesis

## Rheumatoid Arthritis: Pathogenesis

- Pathogenetic principle: *certain triggers (eg., infectious agents) in genetically susceptible individuals may induce an untoward immune response with autoreactive features that leads to chronic arthritis*
- Rheumatoid Arthritis: no trigger identified; multiple genetic alleles known

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18. T cells provide immune response to antigens

### T cells provide immune response to antigens

- Macrophages digest foreign bodies into small peptides
- Peptides are presented on major histocompatibility complex (MCH) proteins
- T-cell receptors bind to MCH-peptide complex
- Helper T cells respond to antigens by secreting cytokines

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19. Rheumatoid Arthritis: Treatment Considerations

## **Rheumatoid Arthritis: Treatment Considerations**

- Relieve pain
- Preserve joint function
- Minimize toxicity

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20. Rheumatoid Arthritis: Treatment Considerations

## **Rheumatoid Arthritis: Treatment Considerations**

- Pharmacological therapies
- Nonpharmacological therapies

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21. Nonsteroidal Antinflammatory Agents

## Nonsteroidal Antinflammatory Agents

- Provide symptomatic relief
- Do not reverse joint damage, or prevent joint damage
- COX-1 and COX -2 inhibitors equally effective but differing side effect profiles

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22. DMARDS (Disease Modifying AntiRheumatic Drugs)

## DMARDS (Disease Modifying AntiRheumatic Drugs)

- Should be used in all patients with diagnosed rheumatoid arthritis within three months of disease onset
- Have different mechanisms of action, directed at minimizing synovial proliferation

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DMARDs, Cont'd

## **DMARDs, Cont'd**

- Intramuscular gold salts
- Weekly pulse methotrexate
- Oral azathioprine
- Oral leflunomide
- Hydroxychloroquine

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Biological Therapies

## **Biological Therapies**

- AKA Targeted therapies
- Directed against specific immune modulators in RA
- Examples: inhibitors of TNF- $\alpha$ , Il-1

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Role of B Cells in RA

## **Role of B Cells in RA**

- May function as antigen presenting cells
- Provide costimulatory signals required for CD4 positive effector functions
- The synovial membrane of RA patients contains antibody producing plasma cells
- T cell activation requires B cell involvement
- RF is a disease marker and prognosticator

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Other B Cell Targets

## **Other B Cell Targets**

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Treatment

## Treatment

- Naproxen Sodium twice daily
- Weekly pulse methotrexate instituted with less than optimal therapy after 6 months
- Etanercept 50 mg once weekly added with resultant improvement

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