

# PROGRESS IN THE THERAPY OF RHEUMATOID ARTHRITIS

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# RHEUMATOID ARTHRITIS (RA)



- Sex : F:M 3:1
- Prevalence : 0.5-1% of population
- Incidence : 4-5 per 100,000/year
- Outcome 2-20 years : progressive joint damage & disability, reduced quality of life
- Pathogenesis : immune mediated inflammation of synovium
- Structural damage early & progressive

# THE PROBLEM

## **SYMPTOMS:**

**Fatigue, stiffness, pain**

## **SIGNS:**

**Swollen, deformed joints**

## **PATHOLOGY:**

**Inflammation**

**Most have progressive joint destruction**

## **QUALITY OF LIFE:**

**Inability to look after household, children**

**Inability to work**

**Earnings reduced**

## **DURATION OF LIFE:**

**Reduced**

**Early atherosclerosis and stroke**

**Infection**

**Lymphomas**

# CURRENT STATUS

*A partial solution: 'Newer' oral drugs*

**Disease modifying drugs 'DMARDs'**

**Methotrexate: popularized by M. Weinblatt etc.**

**Leflunomide**

**Sulfasalazine, Hydroxychloroquine**

**All of these have significant toxicity issues**

**Many non responders**

**Transient responders (< 3 years)**

*Patients don't feel good*

# CURRENT STATUS

*A partial solution: New Biologic Therapies:*

## 1. TNF Blockade

**Monoclonal Antibodies** - infliximab (Remicade®)  
- adalimumab (Humira®)

**Receptor Fc** - etanercept (Enbrel®)

**Advantage:** useful in 2/3 oral drug non responders

**Over  $10^6$  treated patients**

**Marked joint protection, onset repair**

**Relatively non-toxic: *patients feel good***

## *A partial solution: 'Newer' oral drugs*

2. **IL-1 Blockade - IL-1 receptor antagonist**  
**- Anakinra (Kineret®)**  
**Disdvantage: Less effective than TNF blockade daily injection. Rarely used**
  
3. **T cell/APC blockade (CTLA4-Ig):**  
**- Abatacept (Orencia®)**
  
4. **B cells lysis (anti CD20):**  
**- Rituximab (Rituxan®)**

Video

# UNMET NEEDS IN 2006

## Gold Standard - TNF blocker plus MTX

### For TNF Responders:

1. Safer but just as effective
2. Orally available
3. Cheaper: current cost leads to rationing
4. Greater efficacy: nearer remission
5. A cure: long term remission without long term treatment

### For TNF non-responders:

1. Other options:
2. Other treatment that can be used with anti TNF

# APPROACHES TO GETTING THERE

**Good therapeutic targets:**

**TNF**

**other cytokines e.g. IL-6**

**B cells**

**Combination treatment:**

**safety issues**

**Small molecules:**

**advantage of**

**rapid reversibility**

**oral delivery**

**Better monitoring:**

**biomarkers**

**imaging**

**Quicker trials with imaging**

**Realization that even late stage disease is treatable  
and joint repair possible**