

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 10⁶ 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**