Kristian Stengaard-Pedersen
Department of Rheumatology, Aarhus University Hospital
Reumatoid arthritis
Main conclusions of the Health Technology Assessment Report 2002 of early referral, diagnosis, and pharmacotherapy

Kristian Stengaard-Pedersen
Department of Rheumatology
Aarhus University Hospital
HTA - REUMATOID ARTHRITIS
A major health problem in Denmark

- Prevalence 35000
- Incidence per year 1700
- Specialist treatment 18000
- Operations yearly 4000
- Disablement pension 50%
- Reduced life expectancy 8-10 years
EPIDEMIOLOGY OF RA

- Prevalence 0.5 – 1.0%
- Incidence
  - M 0.2 – 0.4/1000/year
  - K 0.1 – 0.2/1000/year
- Peak incidence 50-60 yrs
- Affects 2 - 3 times as many women as men
RHEUMATOID ARTHRITIS
AETIOLOGY
RHEUMATOID ARTHRITIS
JOINT DAMAGE LEADS TO INFLAMMATION
THE REVERSAL OF THE CLINICAL PARADIGM

Inflammation
(disease activity)
Cells, cytokines, prostaglandins,
metalloproteases, acute phase
reactants, autoimmunity,
immune complexes, ...

Joint damage
Cartilage and bone breakdown
products, neoepitopes

Disability

Ann Rheum Dis 2009;68:159-62
DEVELOPMENT OF RHEUMATOID ARTHRITIS RISK FACTORS

Genes
• **Shared epitope, HLA-DRB1 genotype**
• TNF-alpha receptor genotype polymorphism
• RANKL genotypes polymorphism
• Female sex
• Others

Environment
• **Cigarette smoking**
• Hormones
• Diet
• Infection
• Occupation

*Complex interaction between shared epitope, cigarette smoking, and other factors influence the development of RA*
GENETICS
First generation of relatives to RA patients have 16 times higher risk for developing RA than the general population.

A concordance of 15-30% in monozygotic twins and 5% in dizygotic twins.

HLA-DRB1 allele genes are markers for susceptibility and for more severe erosive RA.
RA: CONTRIBUTING GENETIC FACTORS

Certain human leukocyte antigen (HLA) proteins, coded on chromosome 6, have been linked to RA.
STRUCTURE OF HLA MOLECULES: FUNCTIONAL IMPLICATIONS
<table>
<thead>
<tr>
<th>Serumology</th>
<th>Cellular typing</th>
<th>Oligonucleotide typing</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Recognition by multiparous serum or monoclonal antibodies)</td>
<td>(Recognition by T-cells in a mixed lymphocyte culture)</td>
<td>(Hybridization of labeled probe with specific DNA sequence)</td>
</tr>
</tbody>
</table>

- DR4
- Dw4
- Dw10
- Dw13
- Dw14
- Dw15
- Dw'KT2'

- DRB1*0401
- DRB1*0402
- DRB1*0403
- DRB1*0407
- DRB1*0404
- DRB1*0408
- DRB1*0405
- DRB1*0406
- DRB1*0409
- DRB1*0410
- DRB1*0411

... etc.
The HLA-DRB1 allele genes (0401, 0404, 0101) on chromosome 6 encodes the class II histocompatibility antigens that form the human leucocyte antigen HLA (types) which are markers for susceptibility and for more severe erosive RA.
AETIOLOGY OF RHEUMATOID ARTHRITIS

ENVIRONMENTAL FACTORS

- Infections / autoantigens
- Smoking
- Diet
- Others
SMOOKING
HISTOLOGY RA

- Synovial cell proliferation
- Leukocyte infiltration
- Angiogenesis

\[
\text{Inflammation} \downarrow \\
\text{Citrullination} \downarrow \\
\text{Anti-CCP ab}
\]
DEIMINATION (CITRULLINATION) OF ARGinine BY PEPTIDYLARGININE DEIMINASE (PAD)

Arginine + PAD → Citrulline
DEIMINATION (CITRULLINATION) OF ARGinine
BY PEPTIDYLARGININE DEIMINASE (PAD)
Macrophage phagocytosis of apoptotic neutrophils is compromised by matrix proteins modified by cigarette smoke and lipid peroxidation products

Kirkham PA, Spooner G, Rahman I, Rossi AG

Biochem Biophys Res Commun 2004 21;318:32-7
RELATIVE RISK OF DEVELOPING RA
A NEW MODEL FOR AN ETIOLOGY OF RA

CONCLUSIONS

Smoking in the context of HLA-DR SE genes may trigger RA-specific immune reactions to citrullinated proteins.

The data suggests an etiology for RA involving a specific genotype, an environmental provocation, and the induction of specific autoimmunity, all restricted to a distinct subset of RA.

*Arthritis Rheum* 2006;54:38-46
RHEUMATOID ARTHRITIS RISK FACTORS

ALCOHOL CONSUMPTION IS ASSOCIATED WITH DECREASED RHEUMATOID ARTHRITIS: RESULTS FROM TWO SCANDINAVIAN CASE-CONTROL STUDIES

ANN RHEUM DIS 2009;68:222-7
ALCOHOL CONSUMPTION, HLA-DRB1 SE ALLELES AND RISK OF ACPA POSITIVE RA

Ann Rheum Dis 2009;68:222-7
DEVELOPMENT OF RHEUMATOID ARTHRITIS RISK FACTORS

Genes
- Shared epitope, HLA-DRB1 genotype
- TNF-alpha receptor genotype polymorphism
- RANKL genotypes polymorphism
- Female sex
- Others

Environment
- Cigarette smoking
- Hormones
- Diet
- Infection
- Occupation

Complex interaction between shared epitope, cigarette smoking, and other factors influence the development of RA
PATHOGENESIS
RHEUMATOID ARTHRITIS
INFLAMMATION LEADS TO JOINT DESTRUCTION
THE TRADITIONAL PARADIGM

- Innate immune system triggered
  - MBL, NK cells, macrophages

- Adaptive immune system triggered
  - Cells: APC, T- and B-lymphocytes
  - Humoral: AB, immune complexes, complement

- Synovial cells
  synoviocytes, fibroblasts, endothelial cells

- Osteoclasts, chondrocytes

Ann Rheum Dis 2009;68:159-62
RHEUMATOID ARTHRITIS
HISTOLOGY

Synovial cell proliferation
Leukocyte infiltration
Angiogenesis
ACTIVATED T CELLS ORCHESTRATE THE INFLAMMATORY RESPONSE IN RA

DC = dendritic cell; T = T cell; B = B cell; FLS = fibroblast-like synoviocyte; Mφ = macrophage; MMPs = matrix metalloproteinases.
CYTOKINE NETWORK

Swollen and tender joints

Joint destruction

Acute phase proteins
TNF-alpha inhibitors
Infliximab
Adalimumab
Etanercept
Key Actions Attributed to TNF-α

- **Macrophages**
  - ↑ pro-inflammatory cytokines
  - ↑ chemokines
  - Increased inflammation

- **Endothelium**
  - ↑ adhesion molecules
  - ↑ vascular endothelial growth factor (VEGF)
  - Increased angiogenesis

- **Hepatocytes**
  - ↑ acute phase response
  - Increased CRP in serum

- **Synoviocytes**
  - ↑ metalloproteinase synthesis
  - Articular cartilage degradation

References:
T-LYMFOCYTE MODULATOR

ABATACEPT

- Selective Co-stimulator Modulator
ACTIVATION OF T CELLS IN RA

Antigen Generates Signal 1

- MHC class II
- Antigen
- TCR

CD28 Costimulation Provides Signal 2

- CD80/CD86
- CD28

Activated T cell

DC = dendritic cell; MHC class II = major histocompatibility complex class II molecule; TCR = T cell receptor; T = T cell.
ABATACEPT
CHIMERIC FUSION PROTEIN OF HUMAN CTLA4 MOLECULE AND HUMAN IgG

ACTIVATION OF T CELLS IN RA

DC = dendritic cell; MHC class II = major histocompatibility complex class II molecule; TCR = T cell receptor; T = T cell; CTLA4 = cytotoxic T-lymphocyte–associated antigen 4.
THE ROLE OF B-CELLS IN RA

CARTILAGE LOSS

Bone erosion

Inflamed synovia

IL-8

TNF-α

IL-10

Mature B cell

B cell

Plasma cell

Bone erosion

Inflamed synovia

Cytokine secretion

Intracellular signaling

Autoantibody production and self-perpetuation

Antigen presentation
<table>
<thead>
<tr>
<th>Autoantigens</th>
<th>Foreign antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type II collagen</td>
<td>Bacteria</td>
</tr>
<tr>
<td>Proteoglycans</td>
<td>Superantigens</td>
</tr>
<tr>
<td>Human cartilage glycoprotein 39</td>
<td>Viruses</td>
</tr>
<tr>
<td>Heat-shock proteins – hsp60, hsp70, BiP</td>
<td></td>
</tr>
<tr>
<td>Citrullinated proteins</td>
<td></td>
</tr>
<tr>
<td>Normal cell components, e.g. enzymes</td>
<td></td>
</tr>
<tr>
<td>Nuclear antigens</td>
<td></td>
</tr>
<tr>
<td>Glucose-6-phosphate isomerase</td>
<td></td>
</tr>
</tbody>
</table>
RHEUMATOID ARTHRITIS AUTO-ANTIBODIES

- Rheumatoid factors
- Anti-CCP antibodies
- Anti-BIP/p68 antibodies
- Anti-calpastatin
- Anti-collagen type II antibodies
- Anti-GPI antibodies
- Anti-RA33 antibodies
- Anti-SA antibodies
- ANA
- ANCA

RHEUMATOID FACTORS

IgM RF

IgG RF

Fc

Fab

IgG

IgG
B-LYMFOCYTE MODULATOR

RITUXIMAB

- Selective anti-CD20 antibodies
TARGETING THE LYMPHOCYTES IN THE TREATMENT OF AUTOIMMUNE DISEASES

1 = Anti-CD20, DAS of B-cells
2 = Anti-CD40L, inhibition of B-cell activation
3 = Anti-cytokine BlyS inhibition of B-cell survival
4 = LJP394, B-cell functional inactivation

Cytokine Signaling Pathways Involved in RA

Choy EHS, Panayi GS. *N Engl J Med* 2001;344:907-916. ©2001, Massachusetts Medical Society. All rights reserved.
BONE REMODELING

Quiescent Phase

Resorptive Phase

Reversal Phase

Formative Phase

Completed Osteon
BONE REMODELING

BONE RESORPTION
Osteoclastic activity, stimulated by PTH, cytokines (IL-1, TNF-alpha), inhibited by calcitonin, sex steroids and other cytokines

BONE FORMATION
Osteoblast secretes osteoid that is mineralized by hydroxyapatite. Stimulated by PTH, sex steroids, IGF-1 and cytokines
RHEUMATOID ARTHRITIS

CLINICAL MANIFESTATIONS
RHEUMATOID ARTHRITIS

6 months

1 year
RHEUMATOID ARTHRITIS

4 years
RHEUMATOID ARTHRITIS

12 years
RHEUMATOID ARTHRITIS

20 years
RHEUMATOID ARTHRITIS
RHEUMATOID ARTHRITIS
RHEUMATOID ARTHRITIS
RHEUMATOID ARTHRITIS
RHEUMATOID ARTHRITIS
RHEUMATOID ARTHRITIS

temporo-mandibular 30%
cervical spine 40%
cricoarytenoid 10%
acromio-clavicular 50%
shoulder 60%
sterno-clavicular 30%
elbow 50%
hip 50%
wrist 80%
MCPs, PIPs 90%
knee 80%
ankle, subtalar 80%
MTPs 90%
REUMATOID NODULI
REUMATOID ARTHRITIS
KARPALTUNNELSYNDROM
REUMATOID ARTHRITIS
EPISCLERITIS
Reumatoid Arthritis
Nodules in the lungs
RHEUMATOID ARTHRITIS
Reumatoid Arthritis

Ekstraartikulære manifestationer

eye
- scleritis
- keratoconjunctivitis

pleura
- effusions

lung
- fibrosis, nodules

lymph node
- reactive
- lymphadenopathies

pericardium
- effusions

spleen
- splenomegaly

kidney & gut
- amyloidosis

bone marrow
- anemia
- thrombocytosis

muscle
- wasting

skin
- thinning, ulceration

nervous system
- peripheral
- neuropathy
## KLINISKE MANIFESTATIONER VED REUMATOID ARTHRITIS

<table>
<thead>
<tr>
<th>Polyarthritis</th>
<th>Ekstraartikulære manifestationer</th>
</tr>
</thead>
<tbody>
<tr>
<td>hænder, håndled</td>
<td>tenosynovitis, bursitis</td>
</tr>
<tr>
<td>fødder, fodled</td>
<td>myopati</td>
</tr>
<tr>
<td>knæled</td>
<td>noduli rheumatici</td>
</tr>
<tr>
<td>hofteled</td>
<td>vasculitis</td>
</tr>
<tr>
<td>columna cervicalis</td>
<td>lunger, pleurae</td>
</tr>
<tr>
<td>andre led</td>
<td>hjerte, pericardium</td>
</tr>
<tr>
<td></td>
<td>nervesystem</td>
</tr>
<tr>
<td></td>
<td>øjne</td>
</tr>
<tr>
<td></td>
<td>nyrer</td>
</tr>
<tr>
<td></td>
<td>lymfeknudenesvulst</td>
</tr>
<tr>
<td></td>
<td>almene symptomer</td>
</tr>
<tr>
<td></td>
<td>osteoporose</td>
</tr>
<tr>
<td></td>
<td>m.fl.</td>
</tr>
</tbody>
</table>
RHEUMATOID ARTHRITIS
DISEASE COURSE
RA Progression

Graph: Adapted from Kirwan JR. *J Rheumatol* 2001;28:881-886.
Photo: Copyright © American College of Rheumatology.
RHEUMATOID ARTHRITIS
DIAGNOSIS
Diagnosis of Rheumatoid Arthritis
American College of Rheumatology (ACR) Criteria

• At least four of the following criteria

  • Morning stiffness >1 hour
  • Arthritis of ≥3 joint areas
  • Arthritis of hand joints
  • Symmetric arthritis

Must be present for at least 6 weeks

• Rheumatoid nodules
• Serum rheumatoid factor
• Radiographic changes

RHEUMATOID ARTHRITIS
AUTO-ANTIBODIES
DIAGNOSTIC AND PROGNOSTIC VALUES

• Rheumatoid factor (RF)
  IgG-, IgA, and IgG-M-RF

• Anti-cyclic citrullinated peptide antibodies
  Anti-CCP ab

IgM-RF and anti-CCP ab have the same diagnostic sensitivity but for specific early diagnosis and prognosticating radiographically destructive joint disease anti-CCP seems better than IgM-RF
RHEUMATOID ARTHRITIS

PROGNOSIS
## The Natural History of Rheumatoid Arthritis

### Work disability in RA

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Disabled %</th>
<th>Years After Disease Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Makisara</td>
<td>405</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Yelin (1987)</td>
<td>822</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Reisine (1989)</td>
<td>206</td>
<td>43</td>
<td>&gt;5</td>
</tr>
<tr>
<td>Wolfe (1994)</td>
<td>826</td>
<td>25</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Approximately 50% is disabled after 10 years

*J. Rheumatol 1996: (suppl 44) 23:13-22, Frederick Wolfe*
10 YEARS SURVIVAL ACCORDING TO QUANTITATIVE MARKERS IN RHEUMATOID ARTHRITIS

Pincus T, Callahan LF, Vaughn WK. J Rheumatol 1987 Apr;14(2):240-51
Rheumatoid arthritis

Prognosis year 2000

• Irreversible joint damage after 2 year
• Disablement pension, 50% after 10 yrs
• Reduced life time, approx. 8 years
Rheumatoid arthritis
Prognostic factors

- Many joints affected at start of disease
- Rapidly erosive progression
- Bone marrow oedema on MRI
- High RF and anti-CCP
- Low social status
RHEUMATOID ARTHRITIS

Progression of joint damage in early rheumatoid arthritis: association with HLA-DRB1, rheumatoid factor, and anti-citrullinated protein antibodies in relation to different treatment strategies


Arthritis Rheum. 2008 May;58:1293-8
RHEUMATOID ARTHRITIS
Progression of joint damage
Influence of HLB-DRB1

Sequential monotherapy
Step-up combination therapy
Initial combi + prednisone
Initial combi + infliximab

Arthritis Rheum 2008;58:1293-8
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Step-up combination therapy

Initial combi + prednisone

Initial combi + infliximab

Arthritis Rheum 2008;58:1293-8
RHEUMATOID ARTHRITIS
Progression of joint damage
Conclusions

- HLA-DRB1 status is associated with radiographic progression
- Rheumatoid factor and anti-citrullinated peptide antibodies are predictive of progressive disease in sequential mono-therapy but not other therapies
- Effective treatment can prevent radiographic progression even in patients with risk factors for severe damage

Arthritis Rheum 2008;58:1293-8
RHEUMATOID ARTHRITIS

EARLY TREATMENT IS IMPORTANT
RHEUMATOID ARTHRITIS TREATMENT
RHEUMATOID ARTHRITIS
TREATMENT

INFLAMMATION (ARTICULAR, EXTRAARTICULAR)
- DMARDs: traditional, biologiclas
- Glucocorticoids: Local, systemic
- NSAIDs: selective, non-selective
- Analgesics: paracetamol, opioids

JOIN DESTRUCTION (CERVICAL SPINE, HANDS, FEET, OTHER JOINTS)
- Non-pharmacological treatment
- Analgesics, NSAIDs
- Orthopaedic Surgery: prosthetics, bone fusion, tendon repair etc.
American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis


Arthritis Rheum 2008;59:762-84
ACR Recommendations

RA Duration < 6 months

RA duration 6 – 24 months

RA duration > 24 months

Arthritis Rheum 2008;59:762-84
Management of Rheumatoid Arthritis

- Facilitate early diagnosis
  - Early suspicion
  - Rapid referral
- Consider early, aggressive treatment
- Select appropriate RA therapy
Early Treatment With DMARDs

- Delayed treatment (median treatment lag time, 123 days; n = 109)
- Early treatment (median treatment lag time, 15 days; n = 97)

*P<0.05 vs. delayed-treatment group
Key Therapeutics for RA

Use of key therapeutics for RA treatment


Gold  Steroids  NSAID  SSZ  MTX  Combo  Biologics
Penicillamine  Hydroxychloroquine
# Reumatoid Artritis

## Pharmacological Treatment

<table>
<thead>
<tr>
<th>DMARD</th>
<th>Biologicals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>Infliximab (Remicade)</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>Etanercept (Enbrel)</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Adalimumab (Humira)</td>
</tr>
<tr>
<td>Aurothiomalate</td>
<td>Anakinra (Kineret)</td>
</tr>
<tr>
<td>Penicillamine</td>
<td>Mabthera (Rituximab)</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td></td>
</tr>
<tr>
<td>Azathioprin</td>
<td></td>
</tr>
<tr>
<td>Ciclosporin</td>
<td></td>
</tr>
<tr>
<td>DMARD</td>
<td>Time to D/C (mo)†</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Antimalarial</td>
<td>20</td>
</tr>
<tr>
<td>IM gold</td>
<td>15</td>
</tr>
<tr>
<td>SSZ</td>
<td>10</td>
</tr>
<tr>
<td>MTX</td>
<td>33</td>
</tr>
<tr>
<td>Oral gold</td>
<td>9</td>
</tr>
<tr>
<td>D-pen</td>
<td>14</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
</tr>
</tbody>
</table>

*Retrospective audit of records of 1,132 patients with RA onset between January 1985 and June 1994 who received a total of 2,296 DMARDs; †Median.

D/C = Discontinuation; IM = Intramuscular.
Konventionelle DMARD-lægemidler er effektive
Men langvarig behandlingseffekt fastholdes ikke

TNF-alfa kraftigt betændelsesfremmende samt brusk og knogleødelæggende

Etanercept

- Binds soluble and membrane TNF-α and TNF-β (lymphotoxin)
- Moderate- to high-binding affinity to TNF-α
- Half-life of 4-5 days
- Inject sc every 3-4 days
- Standard dose only
- With MTX or monotherapy (monotherapy only in EU)
TEMPO Study Design: A Three-Arm Trial

- European and Australian, 92-site, double-blind trial of 686 patients

Randomized (N=686)  
ITT Population (N=682)

Failure on ≥1 DMARD  
No recent MTX

Baseline

Endpoints

ACR-N 24 Weeks

Total Sharp Score 52 Weeks

Enbrel® (etanercept) + MTX (n=231)

ENBREL (n=223)

MTX (n=228)

- Withdrawals: MTX, 30%; ENBREL, 24%; ENBREL + MTX, 16%

ACR Response at 52 Weeks

MTX (n=228)
Enbrel® (etanercept) (n=223)
Enbrel® + MTX (n=231)

*p<0.01 vs. MTX
†p<0.05 vs. Enbrel
‡p<0.01 vs. Enbrel

Analysis using last observation carried forward (LOCF).

Primary Radiographic Endpoint: Change in Total Sharp Score From Baseline at 52 Weeks\(^1\)

- **MTX (n = 212)**
  - 2.8
  - 95% CI (1.08 – 4.51)

- **Enbrel® (etanercept) (n = 212)**
  - 0.52\(^*\)
  - 95% CI (-0.1 – 1.15)

- **Enbrel® + MTX (n = 218)**
  - -0.54\(^{††}\)
  - 95% CI (-1.00 – -0.07)

One year value imputed by linear extrapolation if needed.

Conclusions: Efficacy

• Benefits of anti-TNF therapy in RA
  – Rapid, clinically significant, and sustained improvement in signs and symptoms of disease beyond what is generally seen with traditional DMARDs
  – Inhibition of radiographic progression
  – Improvement in HR QOL and disability

• Overall risk-benefit of TNF inhibitors in RA is strongly positive
SIDE EFFECTS OF BIOLOGICALS

Specific side effects
- Injection site reactions
- Allergic reactions (infliximab)
- Human anti-chimeric antibodies (HACAs: inflixomab)
- Leukocyclastic vasculitis (CD4-Ak IDEC-CE9.1)
- Pancytopenia (etanercept)
- Neurologic symptoms (MS-like; etanercept)

General side effects
- Autoimmunity (ANA- and dsDNA-antibodies, SLE)
- Infections (tuberculosis, coccidiomycosis)
- Malignant disorders
BIOLOGISKE LÆGEMIDLER

Skræddersyet behandling ved kronisk leddeget

Anti-cytokinbehandling
• Anti-TNF-alpha
• Mab to IL-1, IL-6, IL-12, IL-15, IL-18, MIF

Receptorblokadebehandling
• IL-1Ra
• CCR-2 blokade

Celleaktivering
• T-lymfocytter (CTLA-4Ig)
• B-lymfocytter (anti-CD20)
• Monocytter (CCR-2)
RHEUMATOID ARTHRITIS
DMARD treatment

- Early diagnosis, early aggressive DMARD treatment
- Tight control, measurement of disease activity and quick escalation of DMARD
- DMARD in combination is better than monotherapy
- MTX + TNF-alpha inhibitor is the best combination therapy
- Steroid intraarticular or systemic as bridging therapy
TREATMENT STRATEGY IN RA

DMARDs

- MTX or (SSZ)
- MTX + SSZ + chloroquine
  MTX + cyclosporine or MTX + leflunomide
- MTX + TNF inhibitor
  - Adalimumab
  - Etanercept
  - Infliximab
- MTX + Other biologicals
TREATMENT STRATEGY IN RA DMARDs CT.

- MTX + TNF inhibitor failure (1-2 used sequentially)
- MTX + abatacept or MTX + rituximab
TECHNIQUE OF GLUCOCORTICOID INJECTION

- Aseptic procedures obligatory
- Skin desinfection with iodinated solution or chlorhexidine alcohol twice before puncture
- Use of sterile gloves, sterile disposable syringes and needles. Handling by "non-touch-technique"
- Knowledge of anatomy, inflammatory pathology and the injection procedure
- Interval of at least 4-6 weeks between joint injections
- Maximum 3-4 intra-articular injections per year in the same joint
- Injections in bursae and tendon sheets can be repeated up to 3 times with 1-3 weeks interval
MUSCULOSKELETAL ULTRASONOGRAPHY
INDIKATIONER FOR INTRAARTIKULÆRE GLUKOKORTIKOIDINJEKTIONER

- Arthritis in a knee joint
- Arthritis in a MCP-joint
- Carpal tunnel syndrome
- Lateral epicondylitis
RHEUMATOID ARTHRITIS TREATMENT

INFLAMMATION (ARTICULAR, EXTRAARTICULAR)
- DMARDs: traditional, biologiclas
- Glucocorticoids: Local, systemic
- NSAIDs: selective, non-selective
- Analgesics: paracetamol, opioids

JOIN DESTRUCTION (CERVICAL SPINE, HANDS, FEET, OTHER JOINTS)
- Non-pharmacological treatment
- Analgesics, NSAIDs
- Orthopaedic Surgery: prosthetics, bone fusion, tendon repair etc.
RHEUMATOID ARTHRITIS

THANK YOU FOR YOUR ATTENTION!

Kristian Stengaard Pedersen
Department of Rheumatology, Aarhus University Hospital