

Kvartsexponering och reumatoid artrit

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Rheumatoid Arthritis (RA) A disease defined by clinical criteria

At least 4 of the following criteria should be fulfilled

- Morning stiffness > 1 hour
- Swollenness in ≥ 3 joints
- Swollenness in hand joints
- Symmetric joint involvement
- Typical joint destruction by X-ray
- Rheumatid nodules
- Presence of rheumatoid factors in serum

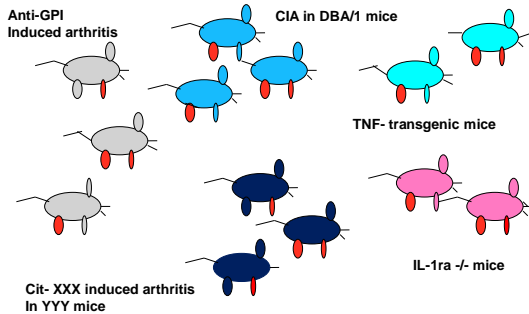


Early RA
Inflammation



Advanced RA
Destruction

The mouse lesson: Many ways of getting and many ways of curing arthritis – genes and environment are the determinants



EIRA

Epidemiologic Investigation of
Rheumatoid Arthritis

Aim: To study the interaction between genes, environmental factors and immunity in RA

EIRA

A population based
case-control study

Data collection started 1996

EIRA

Information:

- **Questionnaire:** information on environmental/lifestyle factors among cases and controls
- **Plasma, Serum/DNA:** genetic and immunologic information

Study start – 1996

→ Data collection still on-going.



2015

So far we have included about 3900 cases and 6100 controls

Less than one year between disease onset and inclusion in EIRA for 85% of the cases

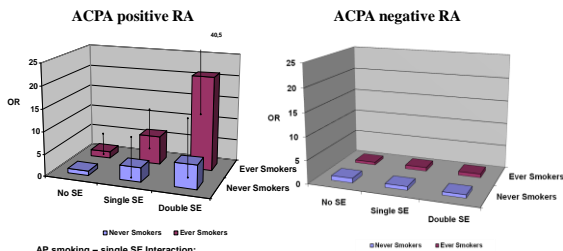
EIRA

Interaction between the two major established riskfactors:

- HLA-DRB1 shared epitope
- Smoking

Interaction between smoking and HLA-DRB1 SE in ACPA + RA and ACPA - RA .

Odds ratios for different combinations of smoking and HLA-DRB1 SE alleles regarding risk of developing **ACPA positive RA** and **ACPA negative RA**.



AP smoking - single SE Interaction:
0.4 (0.2 - 0.7)
AP smoking - double SE Interaction:
0.7 (0.5 - 0.9)

Klareskog et al Arthritis Rheum 2006;54:38-46

A hypothesis on an etiology

- Smoking causes citrullination of proteins
- An immune reaction against citrullinated proteins is triggered preferentially in individuals carrying the HLA-DRB1 SE genotype

(The same immune reaction can cause arthritis in mice)

Andra luftvägsexponeringar också relaterade till risk för RA?

Kvarts?

Kvartsexponering

- frågor angående specifika yrkesexponeringar och under vilka tidsperioder:

"Ange om du har kommit i kontakt med något av följande i ditt arbete - i så fall under vilket/vilka år"

- indexår

Kvartsexponering

Personer som rapporterat följande exponeringar före eller under indexåret:

- stenkrossning
- bergbörning
- stendamm/betongdamm

Odds ratio (OR) with 95% CI of developing **ACPA-positive** RA, among men exposed to stone dust, rock drilling, stone crushing and silica overall, respectively, compared with men unexposed to silica

Exposure	Number of cases/controls	OR	95% CI
Stone dust	44/58	1.60	1.04-2.44
Rock-drilling	18/17	2.34	1.17-4.68
Stone crushing	11/13	2.03	0.88-4.67
Silica overall	54/69	1.67	1.13-2.48

Stolt P, et al. Ann Rheum Dis. 2010 Jun;69(6):1072-6.

Enbart män analyserades

577 fall och 659 kontroller ingick i analysen.

Andelen silica-exposed var 14% bland fallen och 10.5% bland kontrollerna.

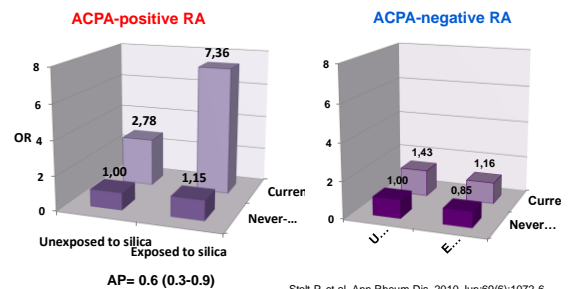
Odds ratio (OR) with 95% CI of developing **ACPA-negative** RA, among men exposed to stone dust, rock drilling, stone crushing and silica overall, respectively, compared with men unexposed to silica

Exposure	Number of cases/controls	OR	95% CI
Stone dust	17/58	1.02	0.57-1.82
Rock-drilling	5/17	0.96	0.34-2.67
Stone crushing	5/13	1.34	0.45-3.97
Silica overall	20/69	0.98	0.57-1.66

Men rökning då ?

Interagerar kvartsexponering med rökning?

Odds ratio (OR) of developing RA among men with different combinations of silica exposure status and cigarette smoking



Stolt P, et al. Ann Rheum Dis. 2010 Jun;69(6):1072-6.

Diskussion

Vår studie är den största hittills och den med bäst kontroll för confounding.

Tillförlitligheten av exponeringsklassificeringen hög

Enbart samband för ACPA positiv RA

Slutsatser

Kiselexponering i kombination med rökning bland män är associerat med en förhöjd risk att utveckla ACPA-positiv RA.

Resultaten indikerar att olika luftburna exponeringar kan samverka i etiologin till ACPA-positiv RA

Collaborators



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Thank you



SWEDISH FOUNDATION for
STRATEGIC RESEARCH



Diskussion

Odds ratios were adjusted for potential confounding from age and residential area.

Adjustment for social class, joint injury and physical work load was also conducted, but only marginally changed the estimates and was not retained in the final analyses.

Sambandet mellan silika och RA observerat i 6 tidigare mindre studier.