NEDERLANDSE FEDERATIE VAN UNIVERSITAIR MEDISCHE CENTRA

VWS-erkenning ECZA

vasculitis STICHTING

ERN ReCONNET

rita
Primary Immunodeficiencies / Autoinflammatory Disorders
Autoimmune Diseases / Paediatric Rheumatic Diseases

the rotterdam eye hospital

R.O.I.
rotterdams oogheelkundig instituut
rotterdam ophthalmic institute

ISBD
INTERNATIONAL SOCIETY FOR BEHCET'S DISEASE

Webinar: Imuunziekten, vermoeidheid en werk

J.A.M. van Laar, UHD, internist-immunoloog
Zeldzame Immunologische Aandoeningen
Sectie Klinische Immunologie
Afdelingen Interne Geneeskunde & Immunologie

Papendal, 12-05-2023

Erasmus MC
Universitair Medisch Centrum Rotterdam

Disclosure belangen spreker

Dienstverband(en)	Stafarts Interne Geneeskunde, sectie Klinische Immunologie EMC
Eigen onderneming(en) en aandelen	-
Adviseurschappen en honoraria incl. sprekersvergoedingen > €500	Amgen, Eusa pharm, NOG/NIV
Sponsoring en onderzoeksgelden	Selectra

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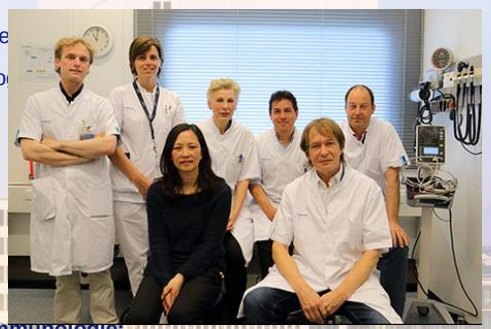
Team BD

Data en Onderzoek

Bart Humer, master student

Sophie den Otter, master student-rese

Saskia Rombach, internist-immunoloo



Vrijwilligers

C Post

A Kaddour

Polikliniek-assistenten Klinische Immunologie:

Kader Oymaci

Berit Aaldijk

Souad El Morabit

Karima Molhout

Vasculitis.nl

Peter Verhoeven, voorzitter Vascultis Stichting

Interne geneeskunde & immunologie

Martin van Hagen

Tim van der Houwen

Paul van Daele

Wim Dik

Oogheelkunde

Alberta Thiadens

Lise Sels

Tom Missotten

Mirjam van Veldhoven

Robert Kuijpers

Dermatologie

Bing Thio

Collette van Hees

Reumatologie

Roos Padmos

Neurologie

Beatrice Wokke

Joost Smulders

KNO/ Mond en tandheelkunde

M Koudstaal

Epidemiologie and genetica

Andre Uitterlinden

Fernando Rivadeneira

Internationale samenwerking

G. Wallace

G Emmi

A Gül

M. Soylu

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Wat is er bereikt?

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Werk en immuunziekten in de wereldliteratuur?

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SUBSTANTIAL WORK DISABILITY AND EARNINGS LOSSES IN INDIVIDUALS LESS THAN AGE 65 WITH OSTEOARTHRITIS: COMPARISONS WITH RHEUMATOID ARTHRITIS*

THEODORE PINCUS,[1,†] JEAN M. MITCHELL[2] and RICHARD V. BURKHAUSER[3]

[1]Division of Rheumatology and Immunology, Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232, [2]Department of Economics, Florida State University, Tallahassee, FL 32306 and [3]Department of Economics, Vanderbilt University, Nashville, TN 37232, U.S.A.

(*Received in revised form* 4 *August* 1988)

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AI & Maatschappij $

2011

The Cost Burden of Autoimmune Disease: The Latest Front in the War on Healthcare Spending

American Autoimmune Related Diseases Association (AARDA)

National Coalition of Autoimmune Patient Groups (NCAPG)

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Wat "kost" het dan?

The Cost Burden of Autoimmune Disease:

The Latest Front in the War on Healthcare Spending

"The burden of a human disease should be counted not only in terms of dollars spent on health care for people directly affected, but as the total cost to society."

National Institutes of Health (NIH), "Progress in Autoimmune Disease Research" Report

AI-ziekte is een maatschappelijk probleem

Prevalence Data for Selected Autoimmune Diseases Listed Alphabetically

Autoimmune Disease	Hospital and Non-Hospital-Based Data	
	Studies from Europe, North America, Australia, New Zealand	
	Rate per 100,000	Study Area
Addison's disease	11-14	UK, Italy, Norway
Alopecia	1700	US
Chronic active hepatitis	11-17	Spain, Sweden, Norway
Crohn's disease	96-201	US, Spain, Denmark, New
Diabetes type 1 – age < 20 yrs.	227-355	US, New Zealand
Multiple sclerosis	177-358	US, Canada
Myasthenia gravis	8-15	Greece, Estonia, Croatia, Netherlands, Sweden, UK
Polymyalgia rheumatica – age ≥ 50 yrs.	739	US
Primary biliary cirrhosis	4-20	US, Australia
Psoriasis	696-1527	US, UK
Psoriatic arthritis	140-190	US, Iceland, Norway, Den-
Rheumatoid arthritis	310-380	France, Hungary, Spain, Turkey, Greece, UK
Sjögren's syndrome – ages 30-60	110	Denmark
Systemic lupus erythematosus	34-150	US, Spain, Greece
Systemic sclerosis	5-34	US, France, Greece, Spain,
Systemic vasculitis	9-14	France, UK
Thyroid-hyper	500	US
Thyroid-hypo	300	US
Ulcerative colitis	143-294	US, Hungary, Denmark,
Uveitis	69-115	US, Finland
Wegener's granulomatosis	2-10	France, Norway, Australia,

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Centjes

The Estimated Cost of Selected Autoimmune Diseases

Autoimmune Disease	Base Yr	Country	Indirect Costs	Direct Costs	Total Est'd Costs
Crohn's disease	2008	US			$10.9-$15.5 billion
Ulcerative colitis	2008	US	Est'd at 40 percent of direct costs	$3.4–8.6 billion	$8.1–$14.9 billion
SLE	2008	US	$8,659/pt/yr	$12,643/pt/yr.	$2.2-$9.6 billion
MS	1994	US			$6.8 billion
RA	2005	US	$8.4 billion	$10.9 billion	$19.3 billion
Psoriasis	2010	US	$4.5 billion	$6.7 billion	$11.2 billion
Scleroderma	1997	US			$1.5 billion

Centjes II

Annual Indirect and Direct Costs of SS, RA and Controls

	INDIRECT COSTS		DIRECT COSTS	TOTAL COSTS
	Low Range	High Range	*Not including cost of biologics*	
Control Group	£892 or US $1,418	£3,382 or US $5,353	£949 or US $1,509	£1,841 - £4,331 or US $2,927 – $6,862
SS Patients	£7,677 or US $12,150	£13,502 or US $21,369	£2,188 or US $3,479	£9,865 - £15,690 or US $12,185 – $24,848
RA Patients	£10,444 or US $16,530	£17,070 US $ 27,061	£2,693 or US $4,282	£13,137 - £19,763 or US $20,812 - $31,343

Notes:
US $ is based on £1.00 = $1.59; All figures rounded up or down to the nearest whole number.
Direct Costs = The costs paid to health services by patient and insurance companies (includes lab work, medications, any inpatient care by doctor or hospital)
Indirect Costs = All non-medical costs due to autoimmune disease, including time lost from current work (lower range) and time lost from inability to work at all or to work full-time (higher range). Indirect costs also include the cost of hiring help for tasks that the patients cannot do due to their illness (such as housework and yard work).

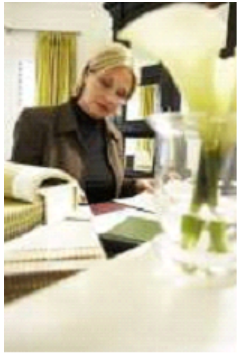
AUTOIMMUNE NEWS

THE LATEST AUTOIMMUNE TREATMENTS, THERAPIES, AND CURES. CALL YOUR US REPRESENTATIVE AND US SENATORS TO DEMAND MORE FUNDING FOR CURES. CALL THE FDA AND DEMAND THESE RESEARCH DISCOVERIES BE USED IN HUMAN TRIALS TODAY! TOMMORROW IS TOO LATE.

THURSDAY, FEBRUARY 19, 2009

Autoimmune Induced Fatigue Cause Found

My son, Paul, has psoriasis, psoriatic arthritis, and ankylosing spondylitis. He is tired all the time. He used to be a ball of non stop energy--running to his college classes at UCSD instead of taking the slow tram. Now especially as he gets closer to needing his next Remicade infusion, he gets more and more tired.



informedhealthonline

Updated health information you can trust

independent, objective and evidence-based

Tailored physical exercise programmes and energy conservation techniques can reduce fatigue in people who have multiple sclerosis, rheumatoid arthritis or lupus.

Autoimmune diseases are long-term (chronic) conditions. The person's body acts as though its own tissues are foreign, and constantly mounts an immune response against itself. This means that the symptoms and damage to the body that the disease causes will generally get worse over time.

Multiple sclerosis (MS), rheumatoid arthritis (RA) and lupus or SLE (systemic lupus erythematosus) are autoimmune diseases. Each of these diseases has flares and remissions, and they develop in individual people in quite different and unpredictable ways. In each of the conditions, inflammation or swelling of tissues plays a part.

Overzicht

Algemene toets kennis immunologische ziekten (herhaald op einde)

Cases (interactief)

Kliniek en achtergronden (theorie)

- Ziektebeelden
  - SLE
  - Sarcoïdose
  - Syndroom van Sjögren
  - (RA)

Mogelijke implicaties ziekte op werk? (interactieve sessie)

SLE

1. SLE:
    a. Is een ziekte die vaker bij mannen voorkomt dan bij vrouwen
    b. De moeheid is op het einde van de dag het meest ernstig
    c. Nierlokalisatie is gerelateerd met een slechtere prognose
    d. Behandeling met immuunsuppressiva wordt getritreerd op het bestaan van orgaanbedreiging
    e. In Curacao zijn SLE patiënten vaker moe dan in Nederland
    f. Hoe vermoeider de SLE patiënt, des te minder deze werkt

Sarcoïdose

1. Sarcoïdose:
    a. Wordt gekenmerkt door granulomen
    b. Presenteert zich vooral in de longen
    c. Gaat meestal vanzelf over
    d. Wordt met anti-TNF-alpha behandeld
    e. Gaat dikwijls gepaard met moeheid

Syndroom van Sjögren

1. Syndroom van Sjögren
    a. Is een systeemziekte
    b. Kan fataal verlopen
    c. Is het minst onderzocht op vermoeidheid
    d. Heeft meestal geen immuunsuppressie nodig
    e. QoL is significant lager indien verergering ziekte

RA

1. RA:
    1. Wordt gediagnosticeerd bij positieve IgM-RF
    2. Reageert goed op NSAIDs
    3. Is een aandoening van de grote gewrichten
    4. Kenmerkt zich door cystes in de gewrichten

2. Ziekteverzuim bij RA op de werkvloer:
    a. Is hoger bij mannen dan bij vrouwen
    b. Is 10% per aangedaan gewricht extra
    c. Is pas relevant bij meer dan 5 gewrichten aangedaan
    d. Ligt hoger als de heupen aangedaan zijn dan handen of knieën

Casus 1; vrouw 27 jaar

24 jr	witte handen in de kou
	‘eczeem’
27 jr	moeheid
	toename huidafwijkingen
	rode vlekken wangen door de zon
	pijn en stijve gewrichten
	zweertjes in de mond
	haaruitval
	dikke enkels
familie	nichtje SLE
Beroep:	opleiding politie agente

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Lichamelijk onderzoek

Fit, atletisch, half Indonesisch

RR 125/85

Huid:

Gewrichten;

artitis MCP I, II

Enkel oedeem

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Wat zou u nu doen?

"Het slachtoffer zit met veel vragen.
Diegene aan de juiste hulp helpen,
lost al veel problemen op."

- letselschade specialist van Slot Letselschade

Erasmus MC

Verwijzen?!

Google

de beste internist van nederland

Web | Afbeeldingen | Maps | Video's | Nieuws | Meer | Zoekhulpmiddelen

Ongeveer 177.000 resultaten (0,29 seconden)

in

Zoek naar personen, vacatures, bedrijven en meer

jan van laar

Internist-immunologist

Rotterdam en omgeving, Nederland | Hoger onderwijs

Huidig	Erasmus University Rotterdam, Erasmus MC
Vorig	St Elisabeth Hospital, Roswell Park Cancer Institute
Opleiding	Erasmus Universiteit Rotterdam

Profiel weergeven als

290
connecties

het grootste zakelijke netwerk ter wereld en stelt professionals als jan **van** ...

Masteronderzoek onderwerpen
asklepios.eur.nl/mi/keuze/kijk.php?nummer=106
Dr. **J.A.M. van Laar**, internist, immunoloog, j.vanlaar@erasmusmc.nl, kamer D 419, tel. 010-4635954 email. Beschrijving, Achtergrond: Hemofagocytose, of ...

Rooster voor docent J.A.M. van Laar - Roosters

specialists!”

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Wat gaat u (of wij) doen?

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Lab

Hb 6.5, MCV 99, L 1.2, Thr 34

Kreat 80 -> 240, bili 46, LDH 666, haptoglob 0.01, reticulocytes; 130

Coombs pos

ANA 1: 1260, Sm +, anti ds DNA 1: 56

Urine; L++, ery ++, cilinders ++, eiwit 5 g/l

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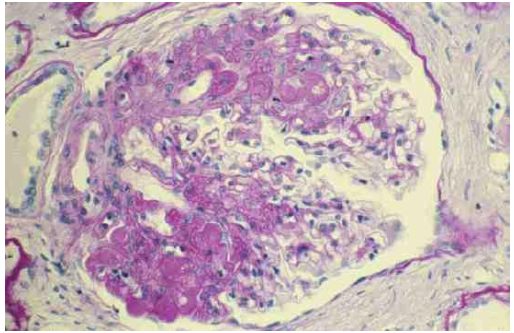
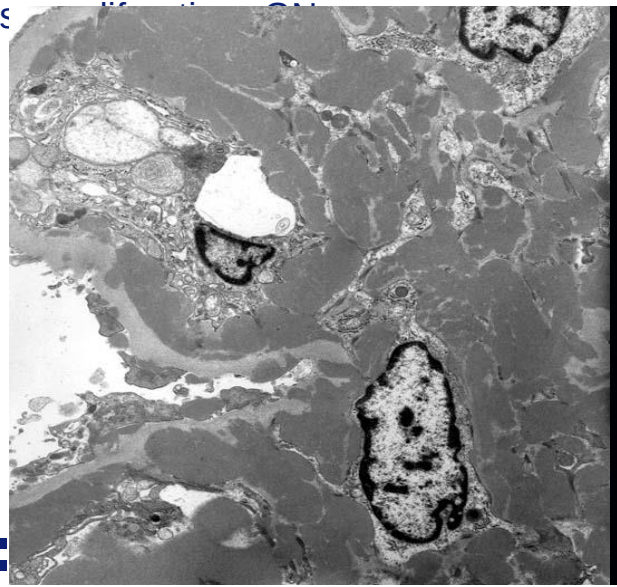
Histologie

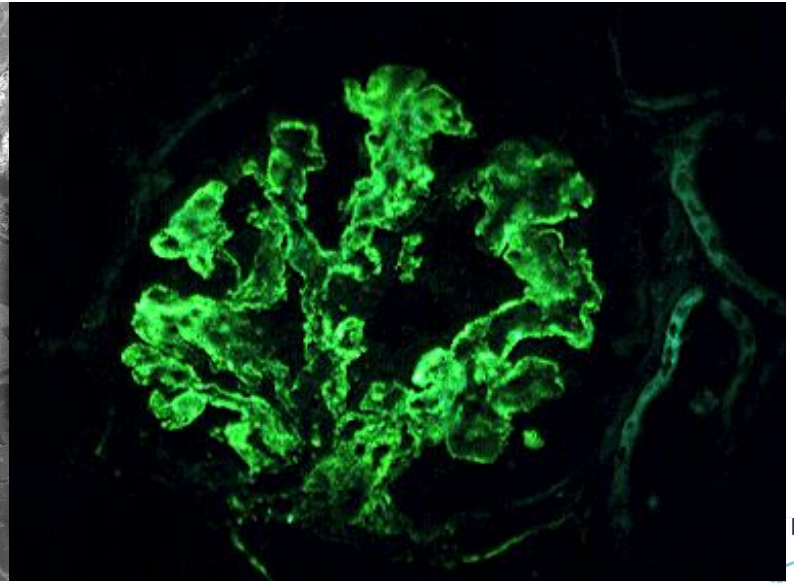


PA: destructie basaal membraan en architectuur glomerulus

IF: C3 deposities BM en capillairen

EM: diffus





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Diagnose?

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SLE

diagnose bij ≥ 4 items

1. vlinderfiguur
2. discoïde uitslag
3. fotosensitiviteit
4. orale ulcera
5. artritis
6. serositis
7. nierafwijkingen
8. neurologische afwijkingen
9. hematologische afwijkingen
10. anti-DNA, anti-Sm of APLA
11. ANA

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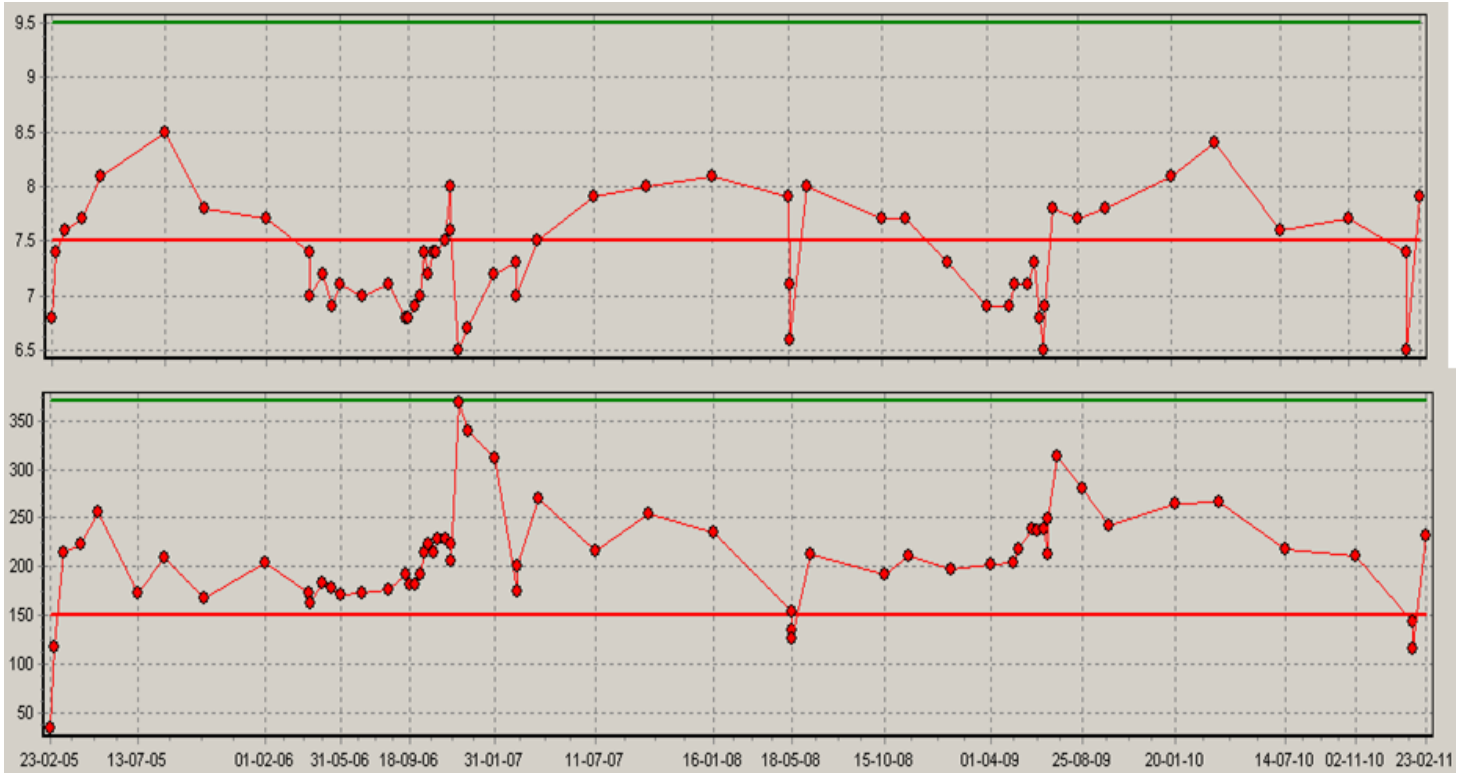
Casus 1: behandeling

- hydroxychloroquine 200 mg/dag
- prednison 60 mg/dag afbouwschema
- mycofenolaat 2 dd 1500mg

=> azathioprine 150 mg/dag na 6 maanden

Beloop



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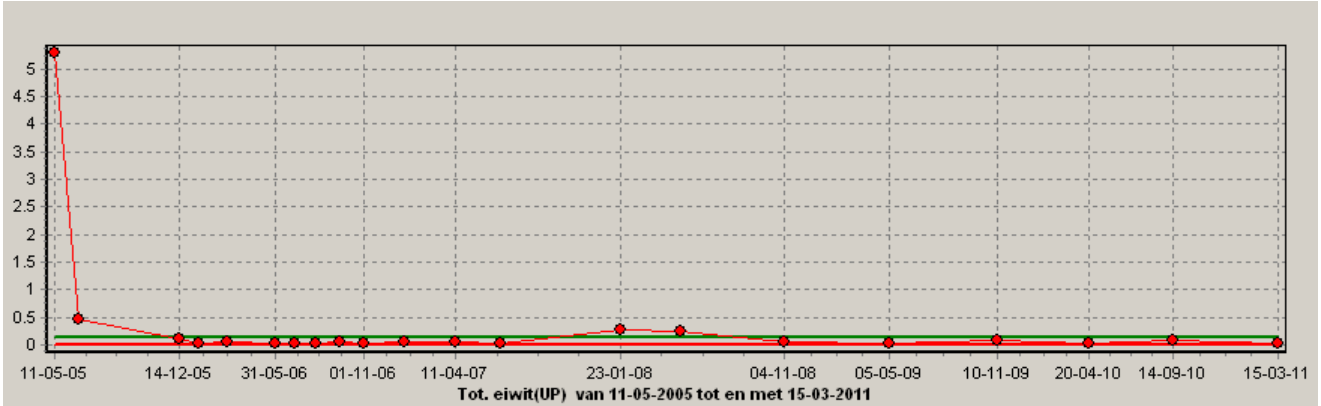
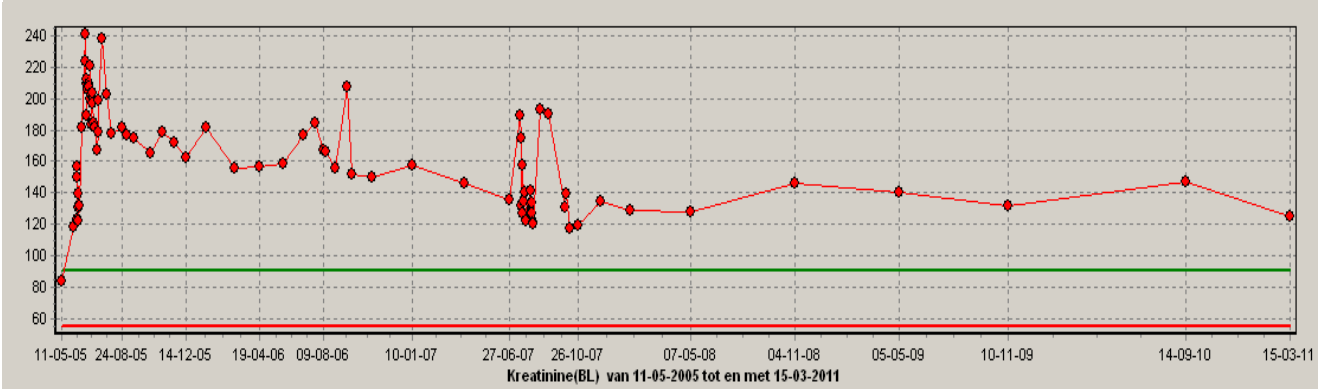
Beloop





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Beloop

Wisselende arthralgiën

2 gezonde kinderen, “ongecompliceerd” beloop SLE

Minder moe, doch ook minder belastbaar

Opleiding net afgemaakt

Omgeschoold naar kantoorfunctie (3 dagen) binnen politie

Komt zichzelf steeds meer tegen bij intensivering werkfrequentie

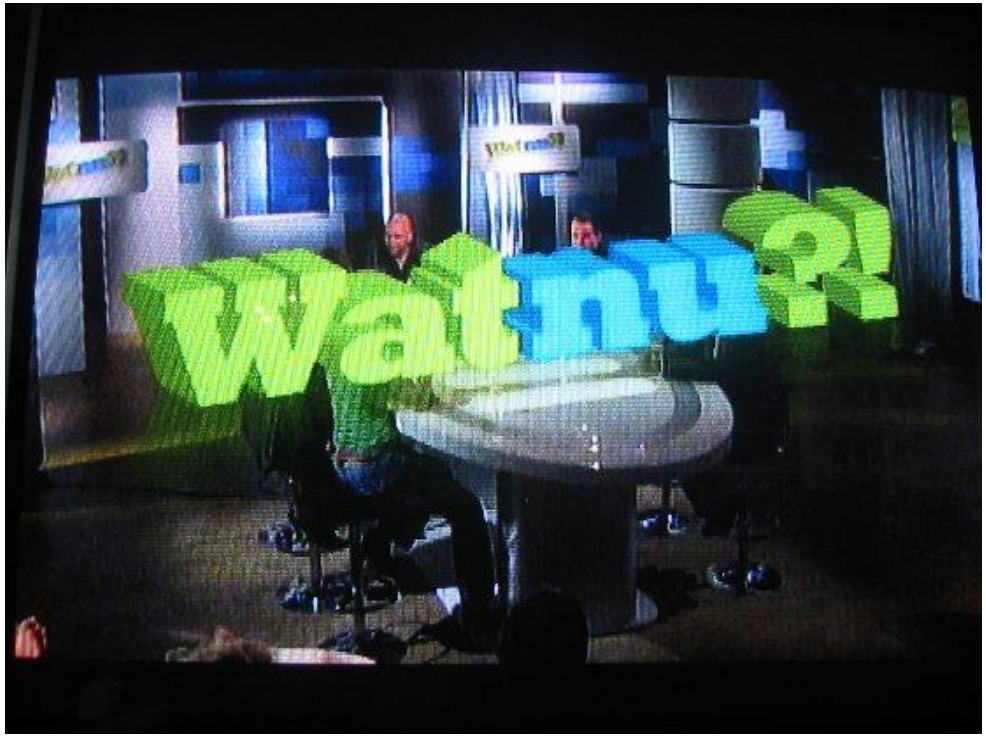
Casus 2, vrouw 37 jaar

andere patiënt

13 jr	fenomeen van Raynaud
>10 jr	droge huid en vagina
8 jr	speekselklierzwellingen
5 jr	moeheid, pijnlijke gewrichten
4 jr	gebitsproblemen (wsch. tandhalscariës)
3 jr	droge mond (cracker sign) en oogirritatie

Werk: administratief

Casus 2



laboratorium

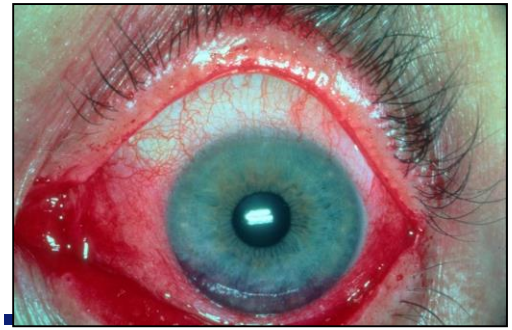
• *BSE*	*36 mm*
• *CRP*	*7 mg/l*
• *amylase*	*60 U/l*
• *IgG*	***27,0** g/l*
• *eiwitspectrum*	*polyklonaal*
• *anti-SSA/Ro*	***positief***
• *anti-SSB/La*	***positief***
• *reumafactor*	***400 IE***
• *anti-CCP*	*negatief*

Oogtesten

Schirmertest *3-4 mm*
normaal >5

andere patiënten

bengaalsrood-kleuring *6*
normaal <4



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Diagnose

Primair Syndroom van Sjögren

conform de Amerikaans-Europese criteria, op basis van*

- *kenmerkende oogklachten*
- *kenmerkende mondklachten*
- *afwijkende oogtesten*
- *antistoffen tegen SSA/Ro en/of SSB/La*

**Vitali et al. Ann Rheum Dis 2002;61:554-8*

Casus 2: behandeling

- *kunsttranen*
- *pilocarpine 4 dd 4 mg*
- *hydroxychloroquine (Plaquenil)*
- *toegespitste aanpassing werkomgeving*

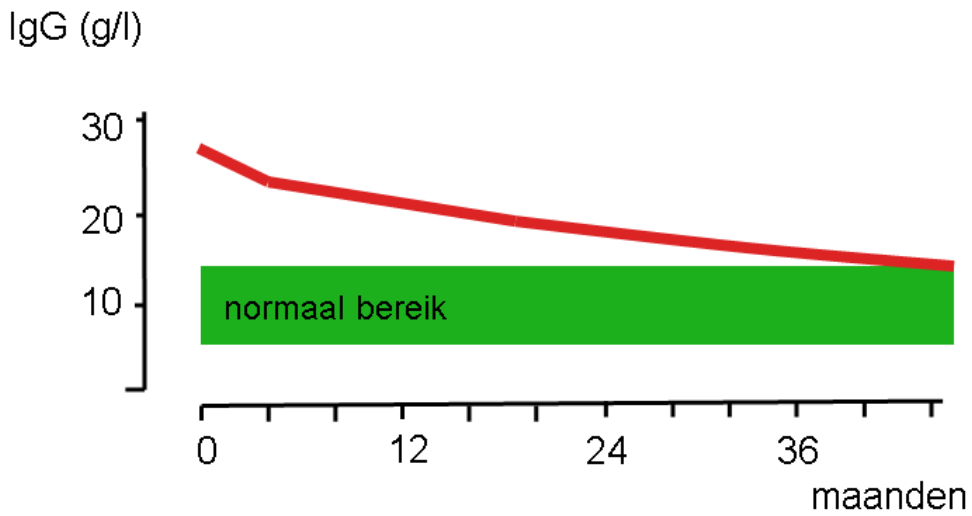
Beloop

Oogvochtproductie neemt toe

Raynaud loopt in de pas

Arthralgiën blijven, maar zijn acceptabel

Moedheid geleidelijk aan minder



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Casus 3, man, 28 jaar

RvK; verwijzing oogarts ivm “bobbels”

Forse pan-uveitis, type granulomateus: visus ODS 0.4/0.3

Huidafwijkingen

Moe

Dyspnoe

Gewrichtsklachten

Opleiding ICT, werkeloos ivm klachten

Lichamelijk onderzoek

Huid:

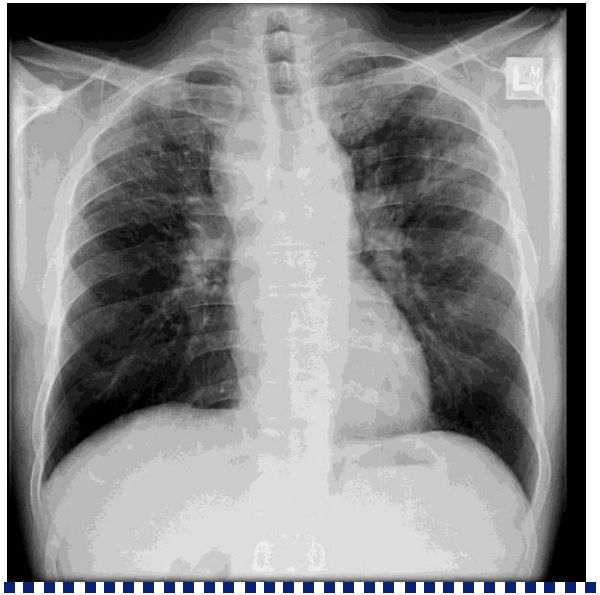
EN

Diverse lymfoompjes < 1cm, geen hepatospenomegalie

Aanvullend onderzoek

Bloedbeeld, LE, NF, CRP, BSE: normaal

ACE 145, Ca 2.89



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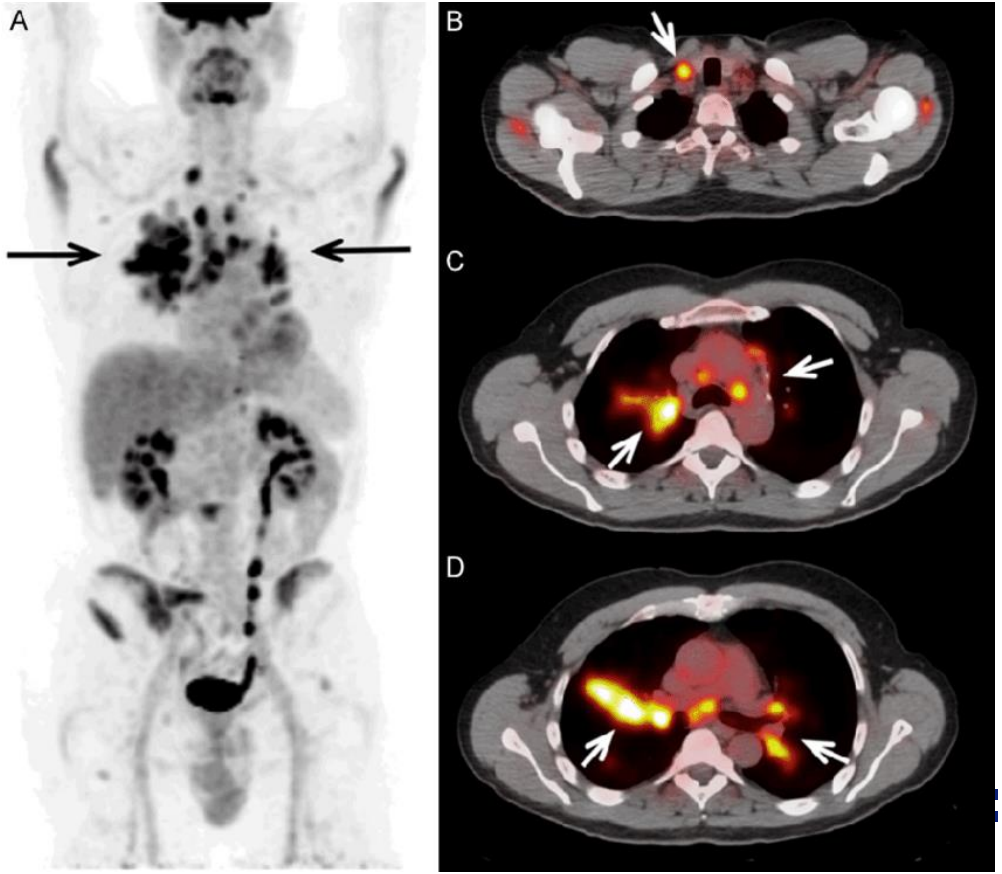
PET-CT scan



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Diagnose?

Jonge man met:

Uveitis, granulomateus

Verdikte tattoos

Lymfadenopathie, ook bihilair

SMS uptake

Verhoogd ACE en Calcium

(D) Diagnose?

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Diagnose?

PA

Via longarts en dermatoloog:

Granulomen in bronchusbiopt en tattoo

Diagnose?

Beloop

Behandeling:

Immuunsuppressiva (plaquenil, prednison, neoral, azathioprine en later Humira)

Ondersteunend: FT, NSAIDs, pijnstilling

Parameters:

- Uveitis
- X-thorax
- Longfunctie

Beloop

oog
het oogziekenhuis rotterdam
the rotterdam eye hospital

De weledelzeergeleerde heer
Dr. J.A.M. van Laar, internist
EMC
Postbus 2040
3000 CA Rotterdam

Betreft: dhr. 5-06-1978, wonend Rotterdam.

Geachte collega,

Bovengenoemde patient(e) zag ik op het spreekuur op 04-02-11.
Hij is bekend met sarcoïdose, waarvoor in het verleden omgeschakeld is naar Humira.

Onderzoek:
De visus OD is 0.7.
De visus OS is 0.6.
Er zijn toenemende lensopaciteiten maar geen actieve inflammatie.
Er is nu een chalazion, waarvoor Terracortril en ooglidhygiëne werd voorgeschreven alsmede warme compressen.

Alles is rustig en dus wij gaan verder met Humira 1x per 2 weken.
Predforte 1dd, Tropicamide 1dd en Plaquenil oraal 200 mg per dag.

Controle: 3-4 maanden of eerder indien het chalazion in het linker bovenooglid nog zou storen.

Met collegiale groet,

Erasmus MC

Longfunctie

	1	%	2	%	3	%	4	%
Meting	260508		031008		141009		110111	
Tijd	08:51		08:30		14:33		09:45	
Subst.								
Lab No	C		F		A		E	
TLC-He	6.86	97	6.95	98	6.91	98	6.90	98
FRC-He	3.23	97	3.27	98	2.82	85	2.44	73
FRC %	47.05	93	47.04	93	40.84	81	35.40	70
RV-He	1.41	79	1.26	70	1.33	74	1.52	85
RV%TLC	20.51	78	18.08	68	19.29	73	22.08	83
VC MAX	5.74	109	5.44	104	5.32	101	5.38	103
FEV 1	4.57	109	4.57	109	4.09	98	3.96	94
FEV1%M	79.56	98	83.94	103	76.90	94	73.53	90
PEF	9.52	99	9.60	100	8.67	90	10.04	104
PI Ave								
PE Ave								
TLCOc	125.82	62	130.22	64	124.10	61	153.79	75
KCOc	21.11	81	21.88	84	21.24	81	23.69	91
KCO RCL		76		80				93
Hb	9.47		9.97		9.60		9.20	
PC20 h								
PC20 m								
Gew.	83		81		94		98	

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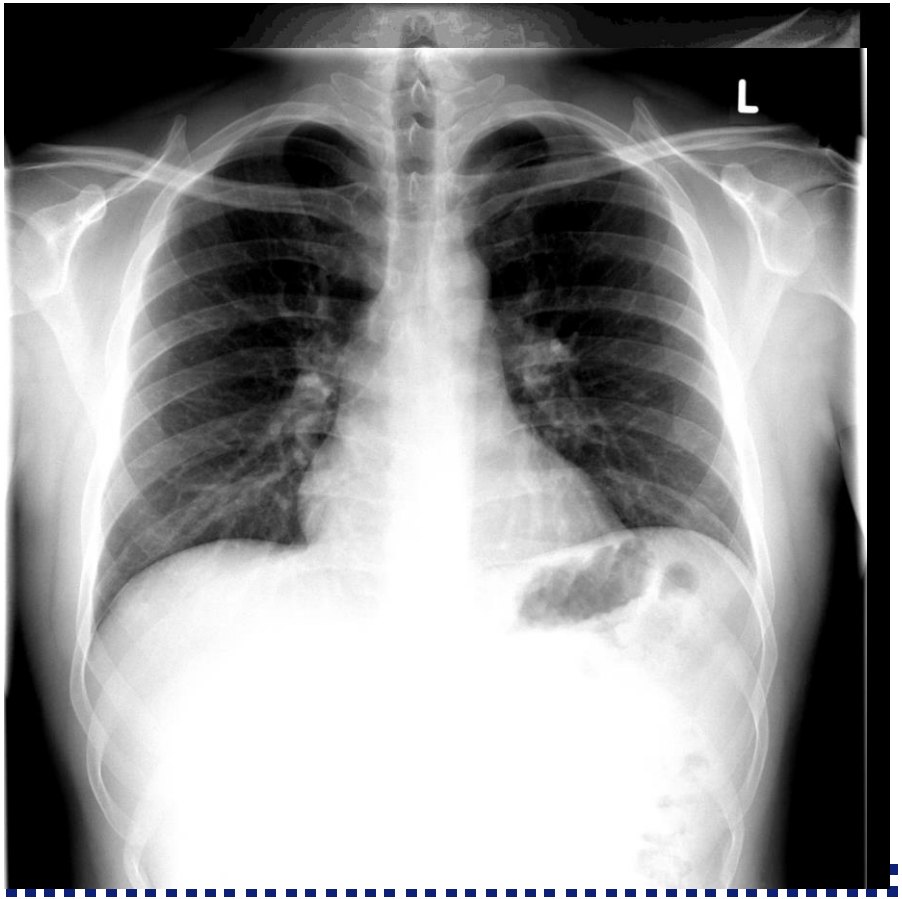
X-thorax



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Beloop patient?

Artralgieën minder

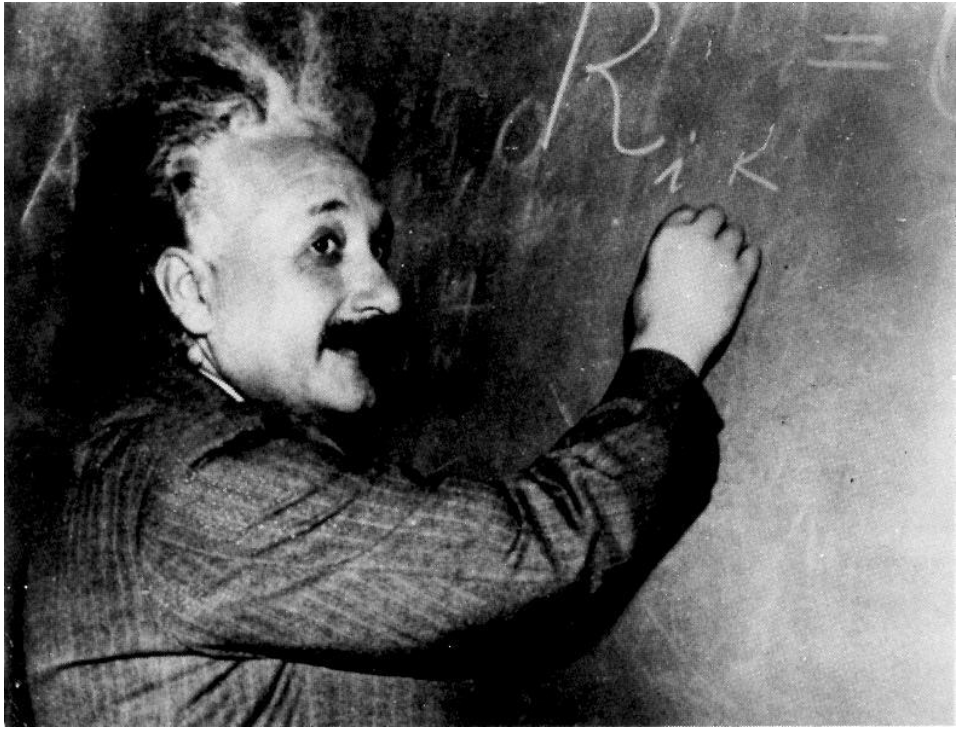
Moe

Nog werkeloos

Aangekomen

PC20 h				
PC20 m				
Gew.	83	81	94	98

Theorie en achtergronden

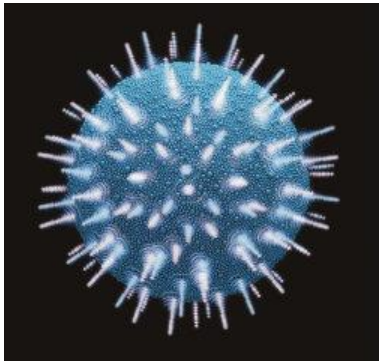


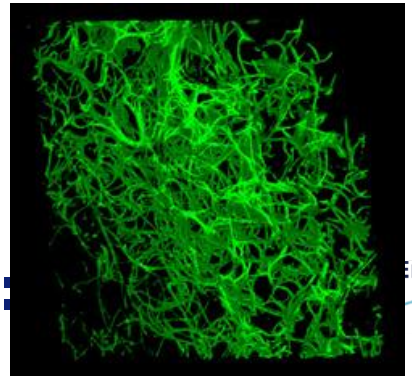
Erasmus MC

Immuun systeem

Doel afweerapparaat is het beschermen van het eigen lichaam tegen:

- Micro-organismen
- Kwaadaardige cellen





Erasmus MC

Afweer:

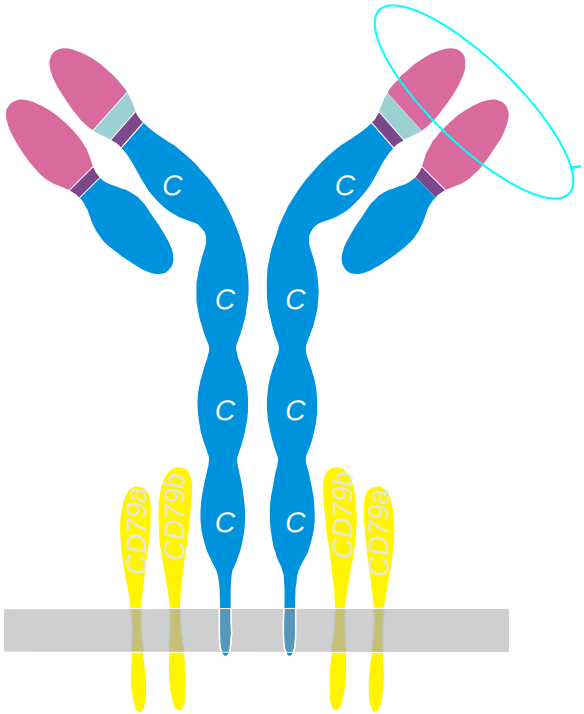
Aangeboren:

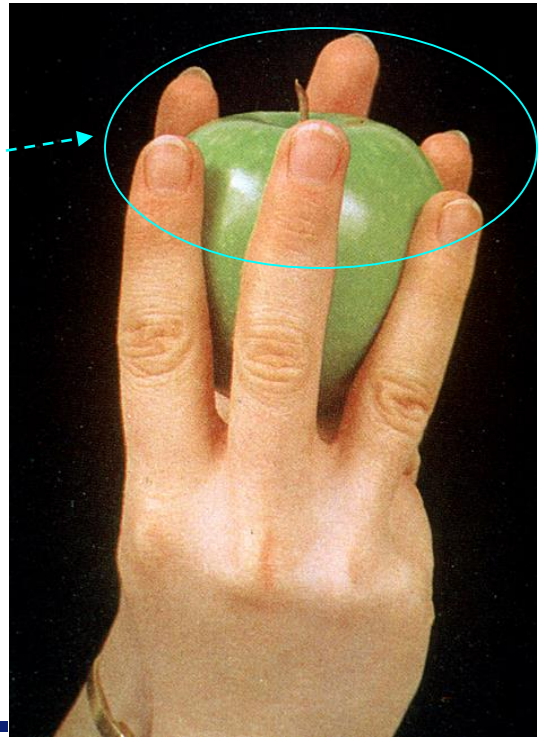
- Immunisatie niet nodig
- Geen geheugen
- Fysieke barriere

Verworven:

- B/T-cel activatie
- Immunologisch geheugen
- Antilichamen en cytotoxische T-cellen

Immuunglobuline: structuur

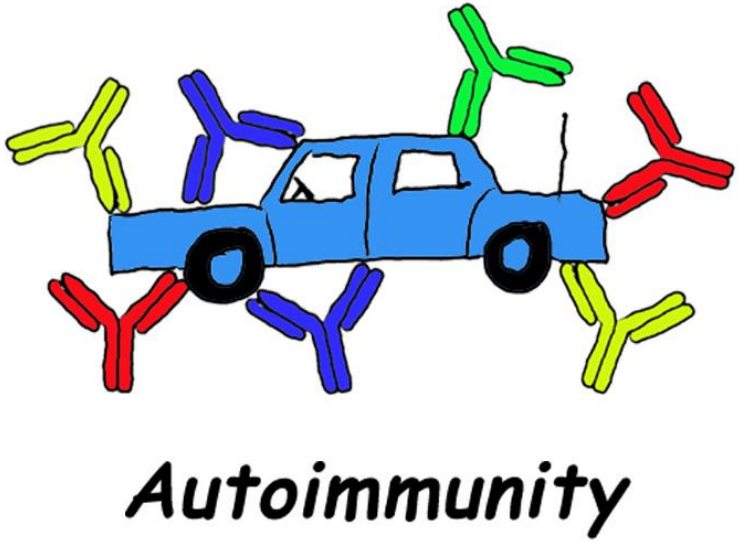




Erasmus MC

Auto-immuunziekte

“Ziekte waarbij de afweer gericht is tegen het eigen organisme”



Autoimmune Disorders: Factors to Evaluate in Clinical Management

TESTS FOR AI FACTORS

CCP antibodies
c-RP
Ferritin
Thyroid status
Endocrine profiles
Nutritional status profile
Large intestine dysbiosis
Small intestine overgrowth
Intestinal permeability
Secretory IgA
Urogenital swab/culture
Nasopharyngeal swab/culture

Autoimmune disorders MUST be overseen if not managed by a medical physician. Onset and flare-ups may be extremely serious.

This map is offered as an overview of management considerations and suggests factors to evaluate based upon published literature.

Three important keys to managing the autoimmune disorders are:

Balance of organisms in the intestinal tract and elsewhere
State of inflammation based upon nutritional status and history
Hormonal balance across systems

NF-kB (INFLAMMATION) MODULATING NUTRIENTS

Lipoic acid
N-A-cysteine
Willow bark
Vitamin D
Rosemary
Co-Q-10
Resveratrol
I3C
Curcumin
Vitamin C
Green tea
Grape seed extract
GLA
EPA
Propolis
Zinc
Selenium
Boswellia
More

Manage dysbiosis

- Genitourinary
- Oropharyngeal
- Gastrointestinal
- May be multiple locations
- May be multiple organisms
- Changing diet may be sufficient
- Botanical antibiotics may often help

Hormonal tendencies

- Low DHEA
- Low cortisol
- High prolactin
- High estradiol
- Low testosterone
- Thyroid may be high or low
- Dietary correction may suffice
- Some replacement may be required

Initial treatment

- Treat factors involved
- "Paleo" diet
- Multivitamin
- Vitamin D
- Probiotic
- Essential fatty acids

Follow-up treatment

- Eliminate wheat
- Periodic fasting
- Hormone balance
- Dysbiosis treatment
- Management of inflammation
- Remove mold from environment

Foods to avoid/reduce

- Wheat
- Corn oil
- Linoleic acid
- Saturated fats
- Allergenic foods
- Arachidonic acid
- Low nutrient foods
- High glycemic acid foods

Links

- Paleo Diet
- Dr. Alex Vasquez
- Alternative Medicine
- Integrative Rheumatology
- Functional Medicine Institute

AVOID WHEAT

Wheat oligosaccharides can be inflammatory, even in the absence of celiac disease or gluten allergy.

MOLD CONTAMINATION

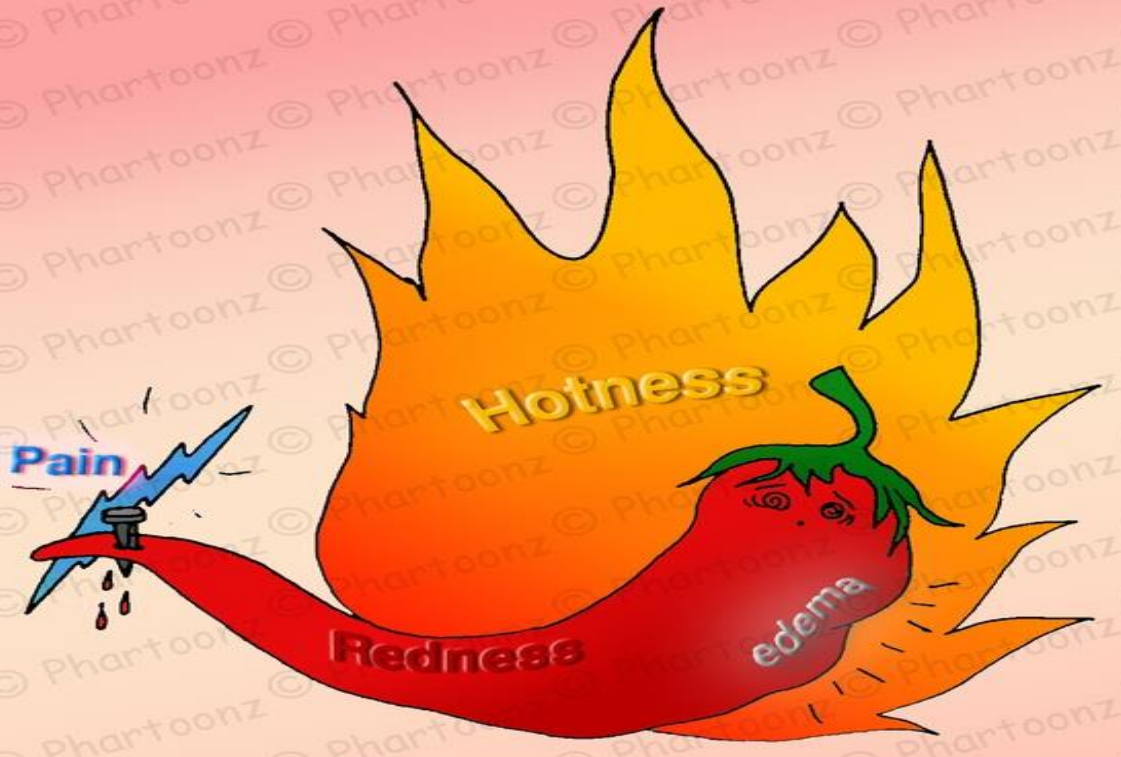
Toxic mycotoxicosis can cause autoimmune disorders affecting joints.

BOTANICAL ANTIBIOTICS

Berberine
Artemesia
Oregano oil
St. John's wort
Bismuth
Probiotics
Saccaromyces boulardii

LOCATE A FUNCTIONAL MEDICINE PRACTITIONER.

Erasmus MC



© Phartoonz

Auto-immuun ziekten

- Orgaan specifiek
- Systemisch

The spectrum of autoimmune disease

Organ Specific Autoimmune Diseases

Graves Disease	(Thyroid: TSHR Abs, TPO Abs)
Hashimoto Thytreoiditis	(Thyroid: TPO Abs, Tg Abs)
Diabetes Type I	(Pankreas: GAD II Abs, IA2 Abs, ICA)
Goodpasture Syndrome	(Kidney: GBM Abs)
Pernicious Anemia	(Stomach: Parietal Cell Abs)
Primary Biliary Cirrhosis	(Liver, Bile: AMAbs)
Myasthenia Gravis	(Muscles: AChR Abs)
Dermato-/Polymyositis	(Skin / Muscles: Jo 1 Abs)
Vasculitis	(Vessels: ANCA)
Rheumatoid Arthritis	(Joints: CRP, RF, RA33 Abs, Sa Abs)
MCTD	(RNP Abs)
Scleroderma	(Scl 70 Abs, CENP Abs, PM/Scl Abs)
SLE	(ANA, Cardiolipin Abs, Beta 2 GP I Abs)

Multi-systemic Autoimmune Diseases

Alle organen kunnen aangedaan zijn.

Erasmus MC

Behandeling

Erasmus MC

Ziektebeelden

SLE

Syndroom van Sjögren

Sarcoidose

Reumatoïde Artritis

M Wegener

Church-Strauss

M Behçet

Relapsing Polychondritis

CVID

Ziektebeelden

SLE

Syndroom van Sjögren

Sarcoidose

Reumatoïde Artritis

M Wegener

Church-Strauss

M Behçet

Relapsing Polychondritis

CVID

Systemic lupus erythematosus (SLE)

Een gegeneraliseerde auto-immuunziekte gekenmerkt door:

typische huidafwijkingen

- gevoeligheid voor zonlicht
- immuuncomplexen (IgG en complement) op basale membraan (ook van normale huid)

antinucleaire antistoffen

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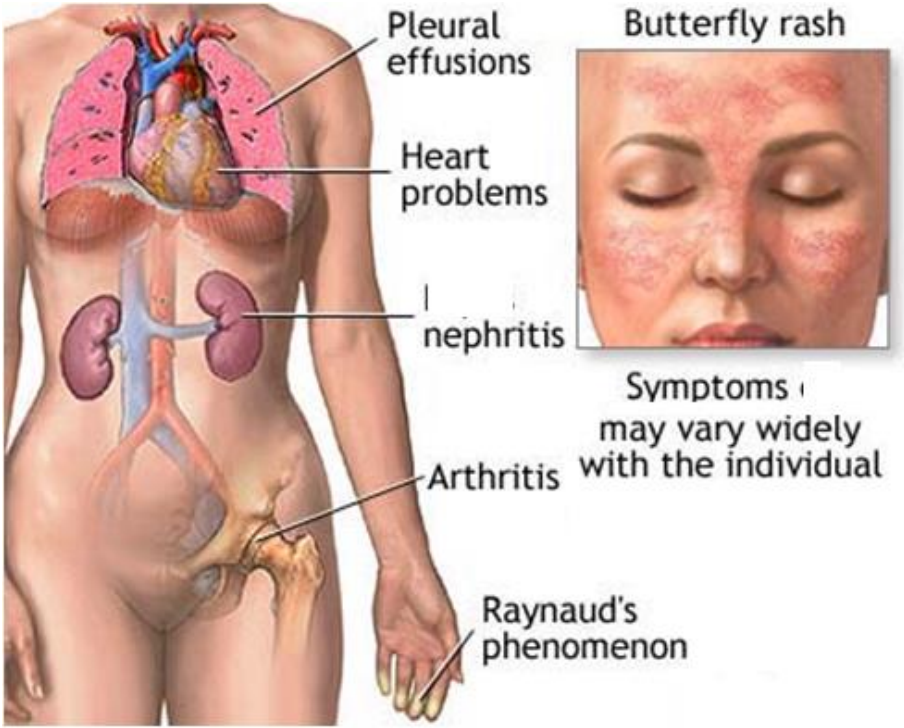
Systemic lupus erythematosus (SLE)



New EULAR/ACR criteria for the classification of SLE

Clinical domains	Points
Constitutional domain	
Fever	2
Cutaneous domain	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous or discoid lupus	4
Acute cutaneous lupus	6
Arthritis domain	
Synovitis or tenderness in at least 2 joints	6
Neurologic domain	
Delirium	2
Psychosis	3
Seizure	5
Serositis domain	
Pleural or pericardial effusion	5
Acute pericarditis	6
Hematologic domain	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Renal domain	
Proteinuria > 0.5 g/24 hr	4
Class II or V lupus nephritis	8
Class III or IV lupus nephritis	10

Immunologic domains	Points
Antiphospholipid antibody domain	
Anticardiolipin IgG > 40 GPL *or* anti-β2GP1 IgG > 40 units *or* lupus anticoagulant	2
Complement proteins domain	
Low C3 *or* low C4	3
Low C3 *and* low C4	4
Highly specific antibodies domain	
Anti-dsDNA antibody	6
Anti-Sm antibody	6

REFERENCE: Aringer et al. Abstract #2928. 2018 ACR/ARHP Annual Meeting

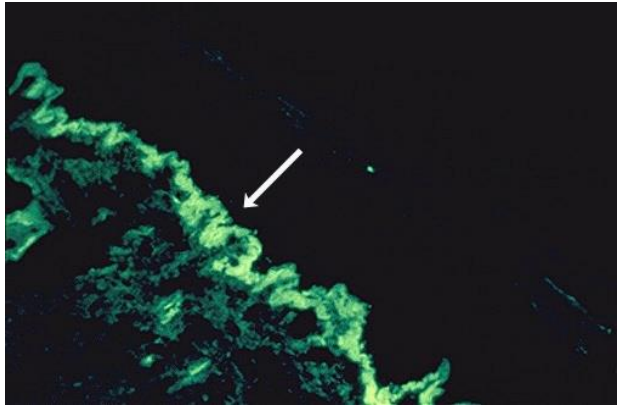
- ✓ **Classification criteria are not diagnosis criteria**
- ✓ All patients classified as having SLE must have ANA ≥ 1:80 (entry criterion)
- ✓ Patients must have ≥ 10 points to be classified as SLE
- ✓ Items can only be counted for classification if there is no more likely cause
- ✓ Only the highest criterion in a given domain counts
- ✓ SLE classification requires points from at least one clinical domain

@Lupusreference

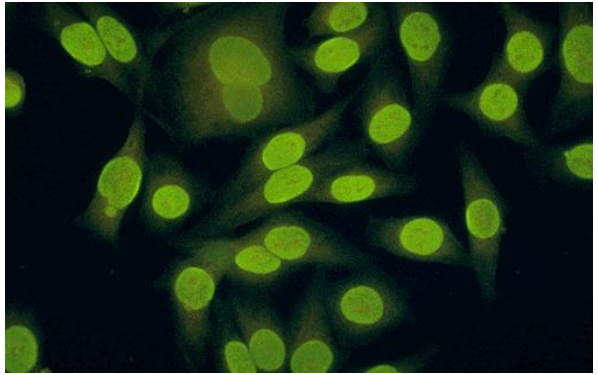
SLE: verschijnselen

- moeheid
- fenomeen van Raynaud
- pijn en ontsteking gewrichten (niet-destructief)
- erytheem, diffuse alopecia
- pericarditis, endocarditis
- pleuritis, pneumonitis
- glomerulonefritis
  - membraneus: nefrotisch syndroom
  - diffuus proliferatief: hypertensie, uremie
- neuropsychiatrische afwijkingen
- cytopenie: granulocyten, erytrocyten, trombo's

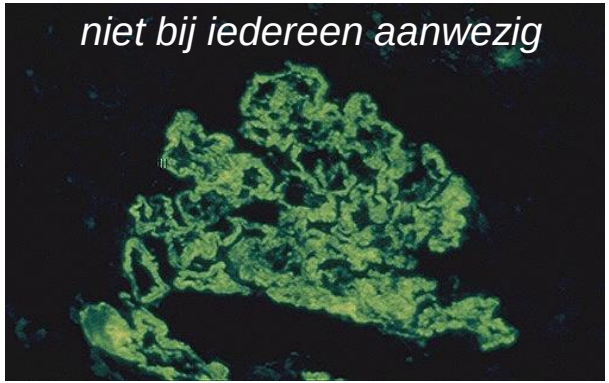
vlinderfiguur



BM immunofluorescentie

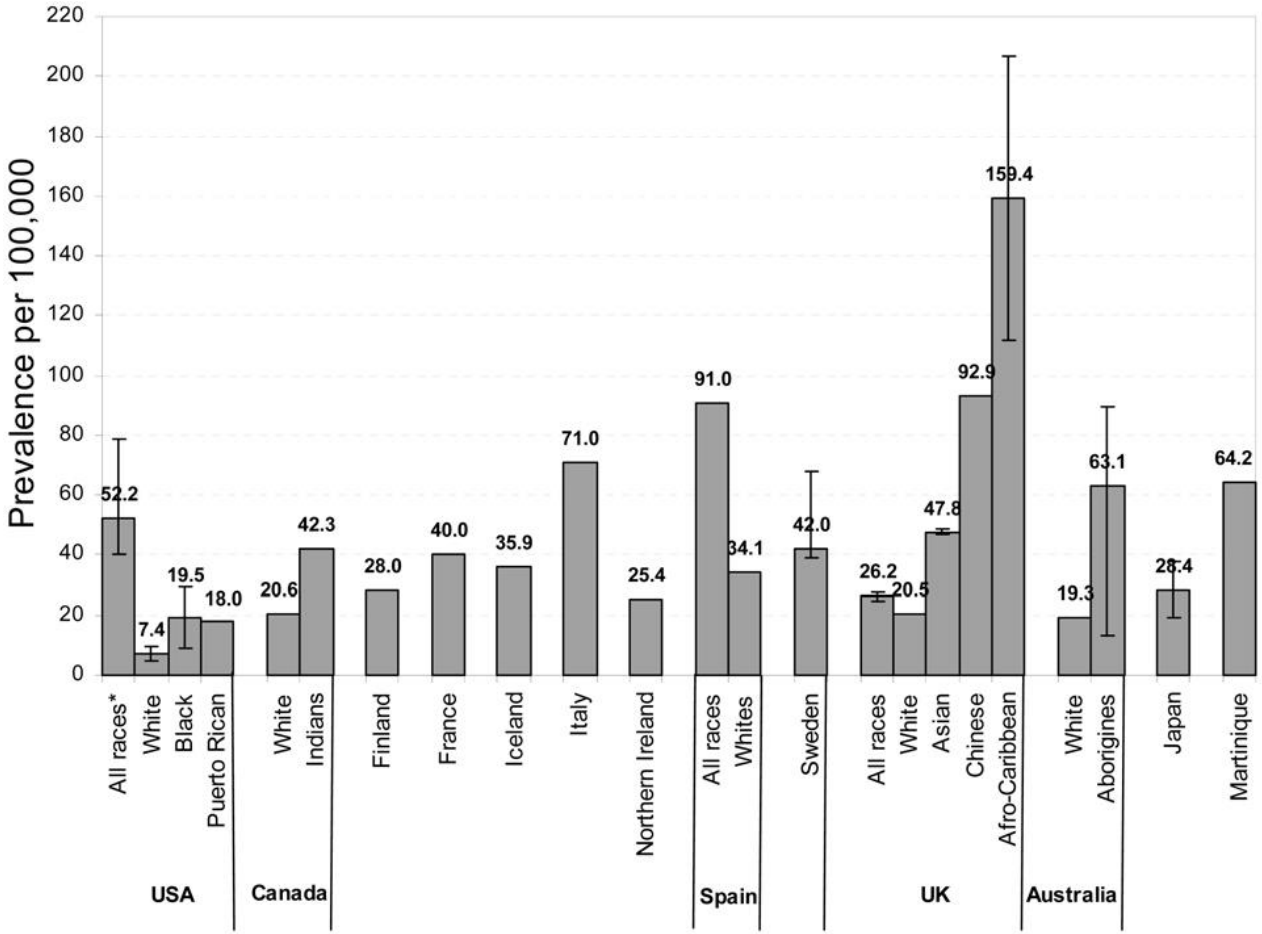


ANA



glomerulonefritis

Erasmus MC



Danchenko N et al. Lupus 2006;15:308-18

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SLE prevalentie Europa

sterk afhankelijk van geslacht én ras:

veel vaker vrouwen en niet-blanken

	vrouwen	mannen
blank	1 : 2.500	1 : 25.000
niet-blank	1 : 1.250	1 : 12.500

Danchenko N et al. Lupus 2006;15:308-18

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SLE Behandeling

disease modifying – laat effect

- hydroxychloroquine
- azathioprine, ciclosporine
- mycofenolaat mofetil
- cyclofosfamide

symptomatisch – snel effect

- corticosteroïden
- NSAID's waaronder selectieve cox-2 remmers* (celecoxib, etoricoxib)

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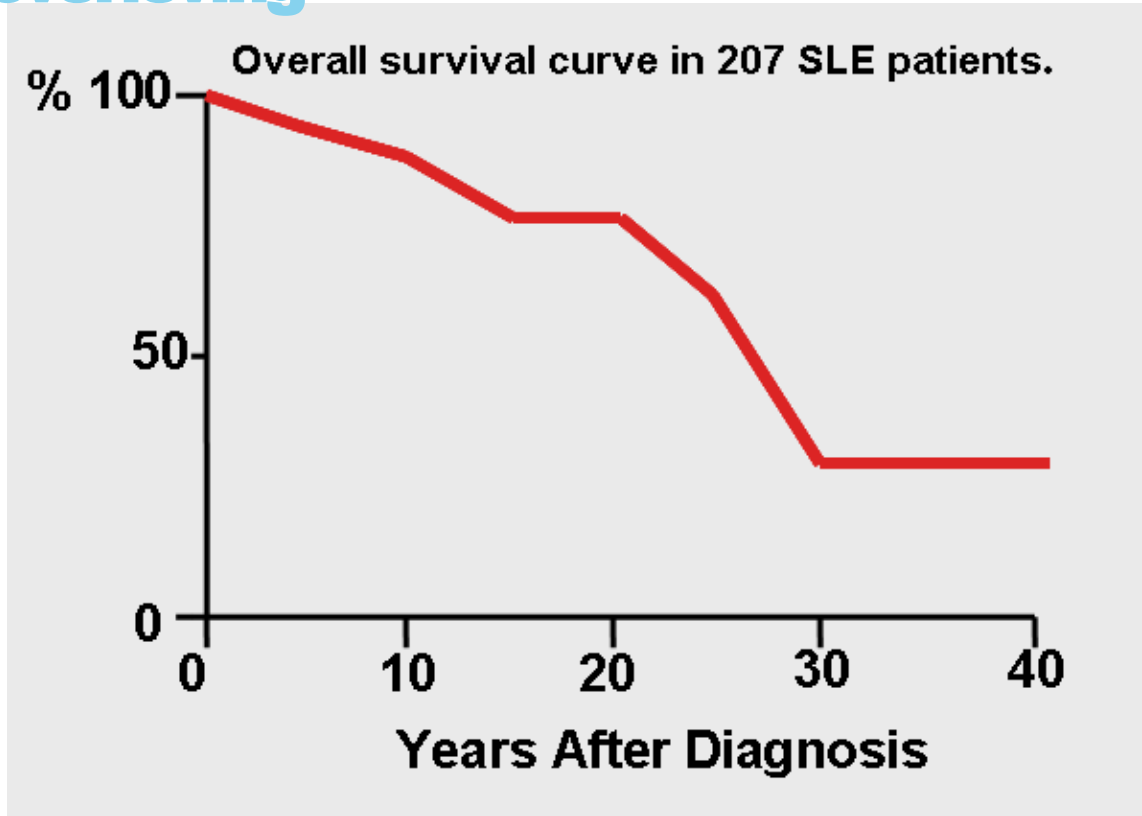
SLE overleving



Doria A et al Am J Med

Erasmus MC

SLE overleving

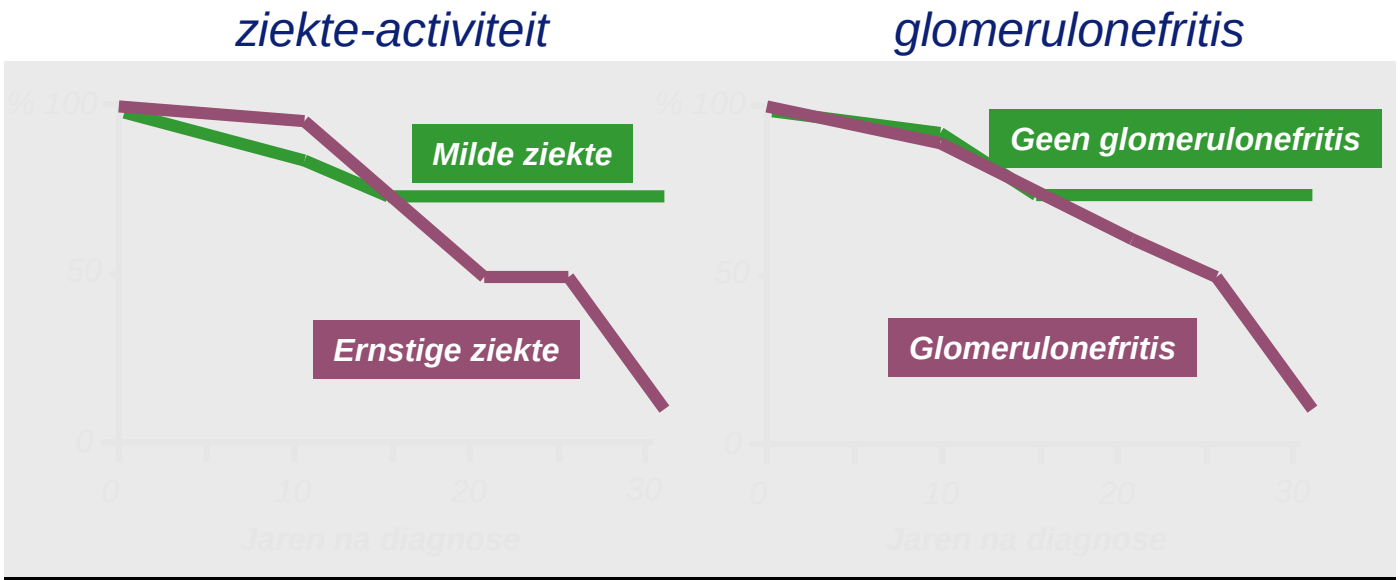
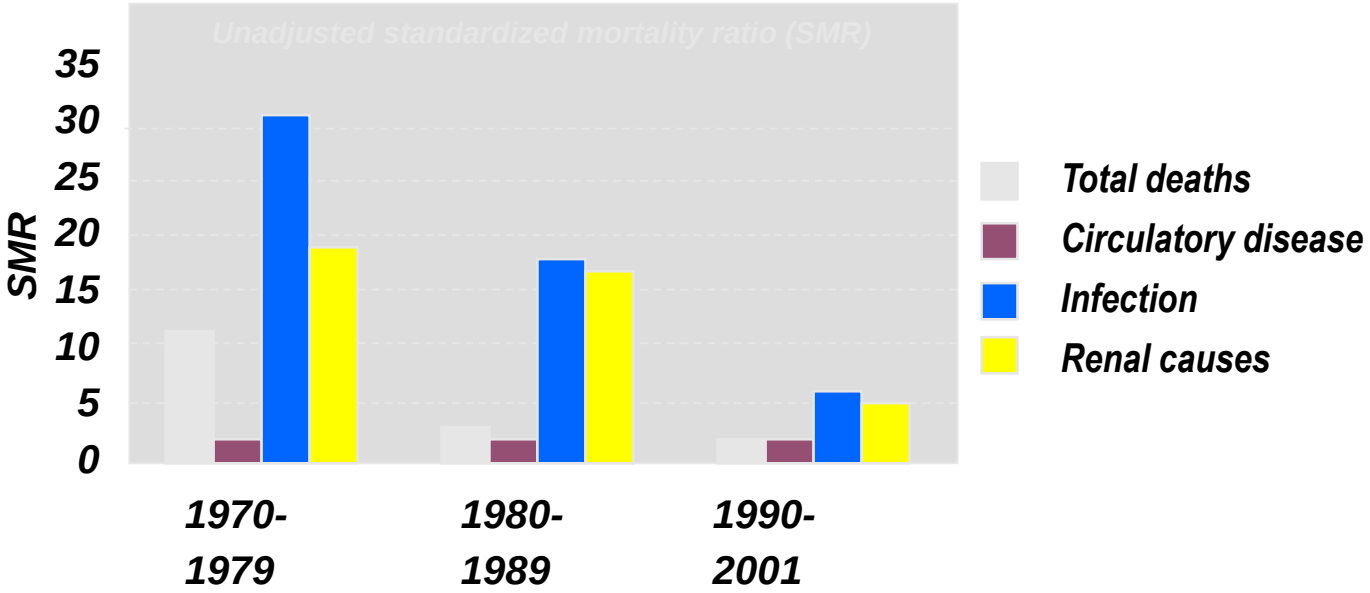


Figure 2. *Survival curve in 207 SLE patients. Comparison between patients with severe disease and those with mild disease (**A**). Comparison between patients with and without glomerulonephritis (**B**).*

Doria A et al Am J Med

Erasmus MC

SLE: SMR=ratio of deaths observed to deaths expected



Bernatsky S et al.. J Rheum 2008

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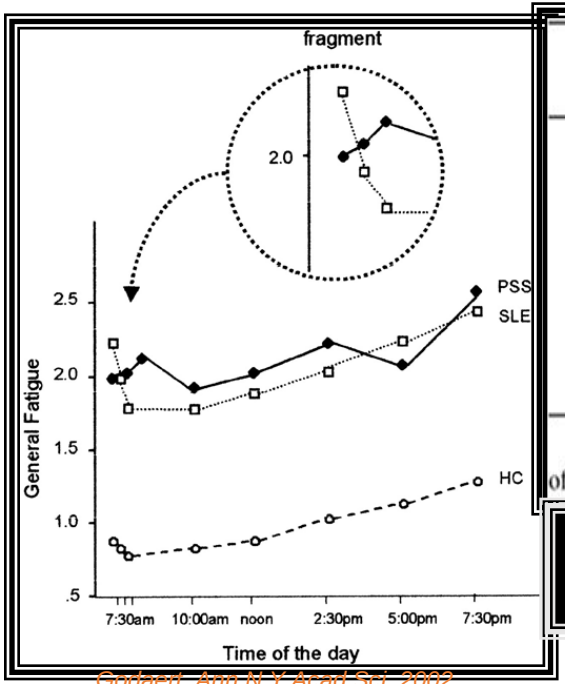
SLE en moeheid



Godbert, Ann N Y Acad Sci, 2002

	General Fatigue	Physical Fatigue	Reduced Activity	Reduced Motivation	Mental Fatigue
Difference between groups	$F = 7.76$ $p = 0.001$	$F = 4.26$ $p = 0.02$	$F = 2.69$ $p = 0.07$	ns	ns
SLE vs. HC	$p = 0.004$	$p = 0.03$	$p = 0.09$	$p = 0.05$	ns
PSS vs. HC	$p = 0.001$	$p = 0.01$	$p = 0.03$	ns	ns
Time-of-Day Quadratic Contrast	$F = 7.21$ $p = 0.009$	$F = 11.37$ $p = 0.001$	$F = 8.10$ $p = 0.001$	ns	ns

NOTE: The values in this table reflect repeated measures analysis of variance of day (2) × time of day (8) × subgroup (3) with the covariate of age.

PSS; primair Sjögrens Syndroom

HC: gezonde controle

Erasmus MC

Syndroom van Sjögren

Syndroom van Sjögren

Gegeneraliseerde auto-immuunziekte met betrokkenheid van:

- traanklieren en speekselklieren

vaak algemene verschijnselen:

- vermoeidheid
- gewrichts- en spierpijn
- grieperig gevoel

→ verminderde kwaliteit van leven, nog minder dan bij reumatoïde artritis

Syndroom van Sjögren

prevalentie vlg Amerikaans-Europese criteria

40-44 jaar: 0,22%

71-74 jaar: 1,40%

- *vrouwen : mannen = 10 : 1*
- *sensitiviteit criteria: 50%*

  40-44 jaar: 0,44%

  71-74 jaar: 2,80%

<u>bij vrouwen</u>

40-44 jr: 1 op 300

71-74 jr: 1 op 40

- *tussen eerste verschijnselen en diagnose: gemiddeld 9 jr*
- *niet erfelijk, maar erfelijke factoren spelen een rol*

het Syndroom van Sjögren is na reumatoïde artritis de meest voorkomende gegeneraliseerde auto-immuunziekte

Erasmus MC

Syndroom van Sjögren

kenmerkende klachten
Dagelijks hinderlijke last van ogen en mond:

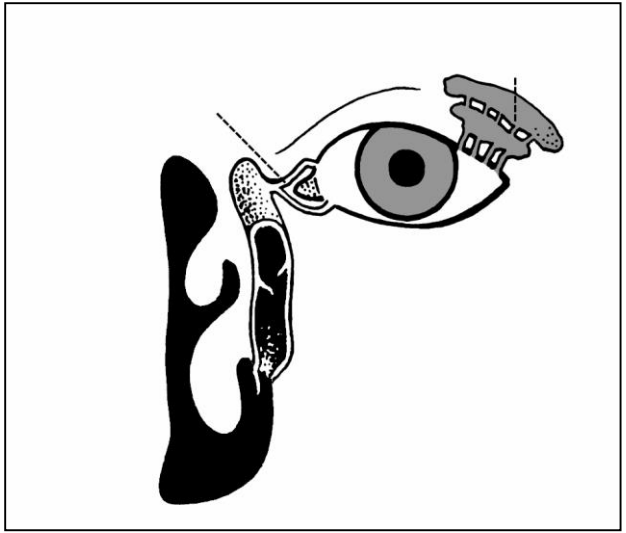
ogen:

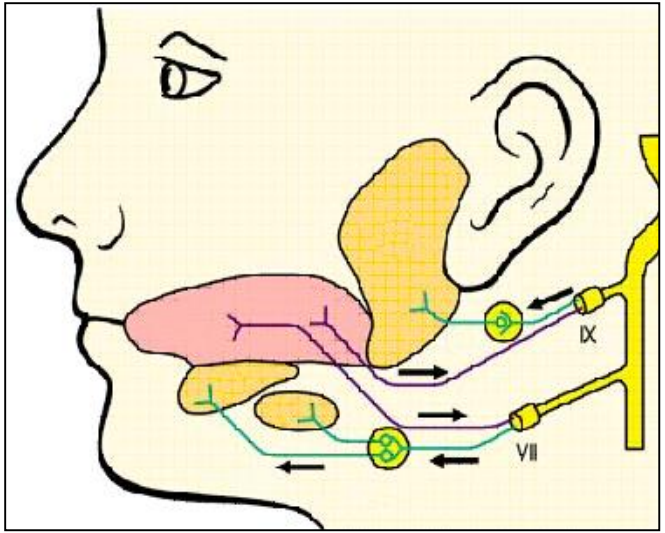
- branderige ogen
- zandkorrelgevoel
- rode, vermoeide ogen
- meer last bij tocht, rook, lezen, tv-kijken
- **spontane klacht van droge ogen zeer zeldzaam**

mond: droge mond
het moeten drinken bij eten (*cracker sign*)

vooral verminderde *functie* van traan- en speekselklieren
dus gewoonlijk niet door destructie

oorzaak van de droogteklachten





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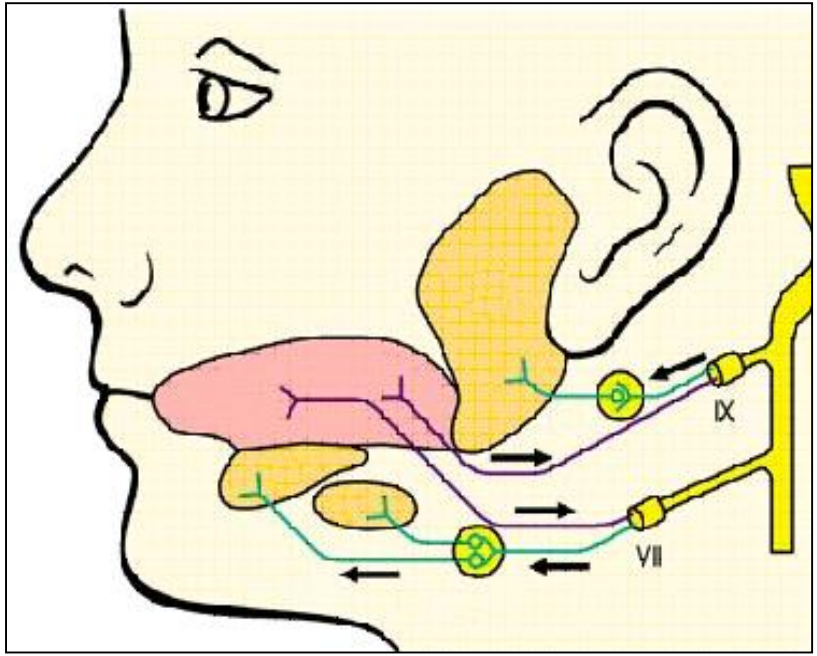
Syndroom van Sjögren

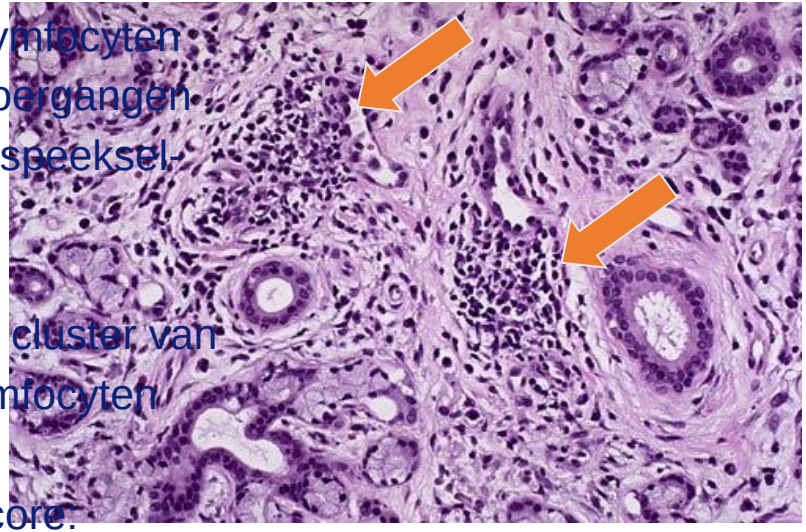


speekselklieren zijn maar bij 1/3 van de patiënten vergroot en bij de helft daarvan éénzijdig

Syndroom van Sjögren

histologie speekselklieren

focale ophoping
van T-lymfocyten
om afvoergangen
van de speeksel-
klieren



<u>focus</u> = cluster van
≥ 50 lymfocyten

<u>focusscore</u>:
aantal foci / 4 mm^2
(normaal <1)

Syndroom van Sjögren kliniek

altijd (per definitie)

kenmerkende droogteklachten van de ogen en mond

bij >50%

- *gewrichtspijn of -ontsteking (vluchtig, symmetrisch, niet erosief)*
- *spierpijn, moeheid, grieperig gevoel*
- *droge huid, neus, vagina*

Syndroom van Sjögren

bij 25-50%

polyneuropathie

leukopenie

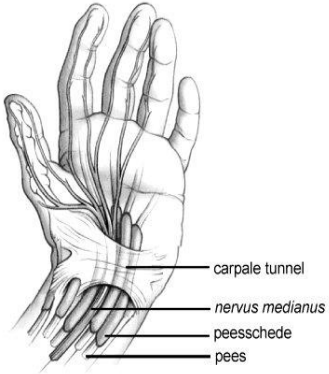
fenomeen van Raynaud

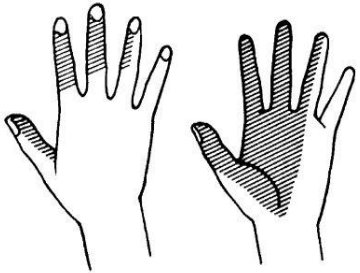
vasculitis

bij 5-25%

- *non-Hodgkin lymfoom*
- *antifosfolipiden syndroom*
- *schildklierziekte*
- *carpaal tunnel syndroom*

fenomeen van Raynaud





carpaal tunnel syndroom

Erasmus MC

Table 2 Revised international classification criteria for Sjögren's syndrome

I. Ocular symptoms: a positive response to at least one of the following questions:

1. Have you had daily, persistent, troublesome dry eyes for more than 3 months?
2. Do you have a recurrent sensation of sand or gravel in the eyes?
3. Do you use tear substitutes more than 3 times a day?

- **Criteria**
  1. Ocular symptoms
  2. Oral symptoms
  3. Ocular signs (Schirmer's or Rose Bengal test)
  4. Diagnostic histopathologic features in salivary gland biopsy
  5. Presence of abnormality in at least one salivary gland study: parotid sialography, salivary scintigraphy, or unstimulated salivary flow
  6. Presence of at least one: Ro/SS-A, La/ SS-B antibodies, antinuclear antibodies, rheumatoid factor
- **Exclusion:** preexisting lymphoma, AIDS, sarcoidosis, chronic GVHD
- **Primary Sjogren's:** 4 of 6 criteria

VI. Autoantibodies: presence in the serum of the following autoantibodies:

1. Antibodies to Ro(SSA) or La(SSB) antigens, or both

asmus MC

Syndroom van Sjögren: diagnose

1. kenmerkende oogklachten
2. kenmerkende mondklachten en/of speekselklierzwelling
3. oogtesten (Schirmertest <= 5 mm en/of bengaalsroodkleuring (van Bijsterveldscore >= 4)
4. lipbiopt: focusscore >= 1
5. speekselklierfunctie (scan, flow); sialogram
6. auto-antistoffen (anti-SSA/Ro en/of –SSB/La)

diagnose: $\geq$4 items, of 3 van items 3-6
voor beide moet item 4 of 6 aanwezig zijn

Vitali C et al. Ann Rheum Dis 2002; 61:554-8.

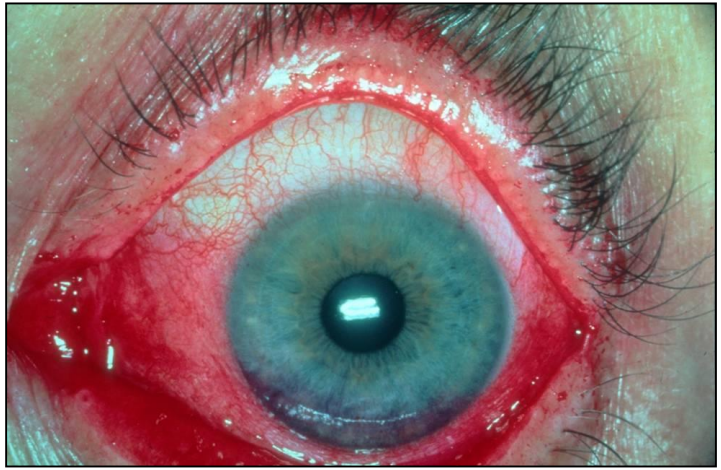
Schirmertest

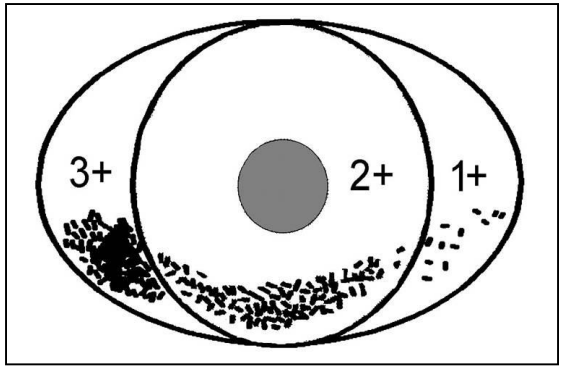
foto: Dr. O.P. van Bijsterveld

normaal > 5 mm in 5 minuten

Erasmus MC

Bengaalsroodkleuring





van Bijsterveldscore:
som van 3 gebieden
per oog (max. 9)
normaal < 4

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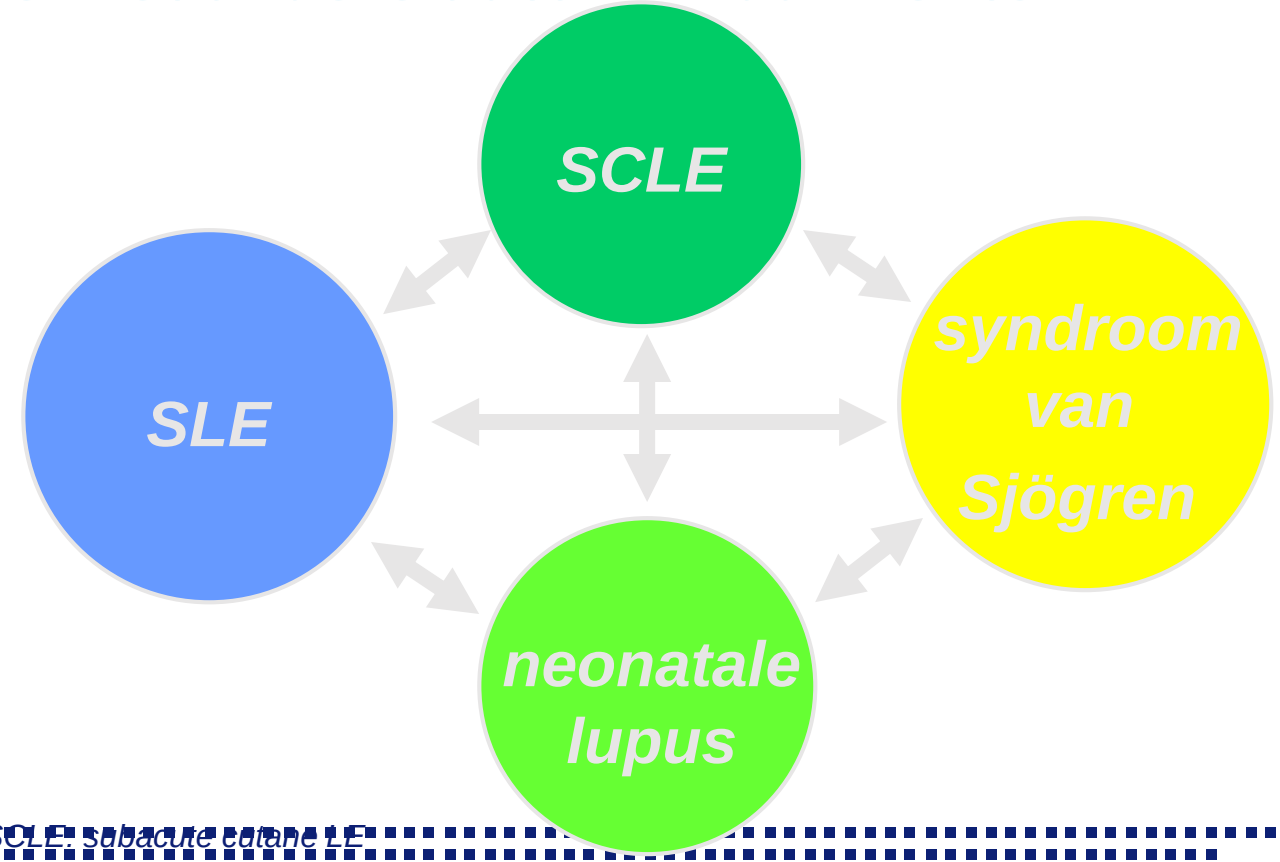
Relatie met andere auto-immuunziekten



SCLE: subacute cutane LE

hypersensitivity vasculitis

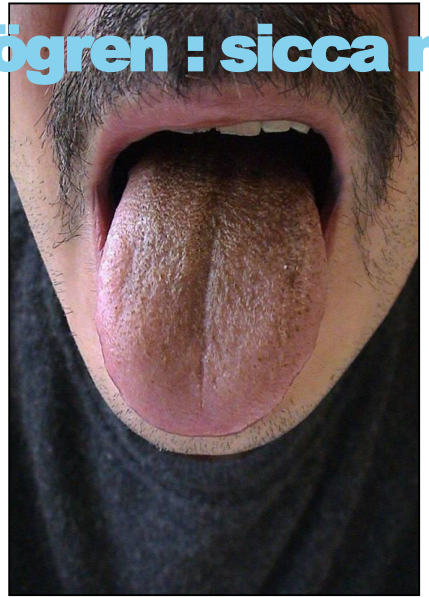
PA: leukocytoclastische vasculitis

immuuncomplexen

antistof

complement

Syndroom van Sjögren : sicca mond



bruine haartong

erythemateuze candidiasis

infectie met Candida en evt. bacteriën

brandende tong en gehemelte kapotte mondhoeken

Erasmus MC

Syndroom van Sjögren: pathofysiologie

droogte wordt veroorzaakt door onvoldoende stimulatie van de muscarine M3-receptoren (M3R) door blokkerende antistoffen tegen de M3R

droogte kan optreden bij relatief normale speeksel- en traanklieren

verklaart gunstig effect op vochtproductie van de M3R-agonist pilocarpine ongeacht de ziekteduur

Syndroom van Sjögren: behandeling

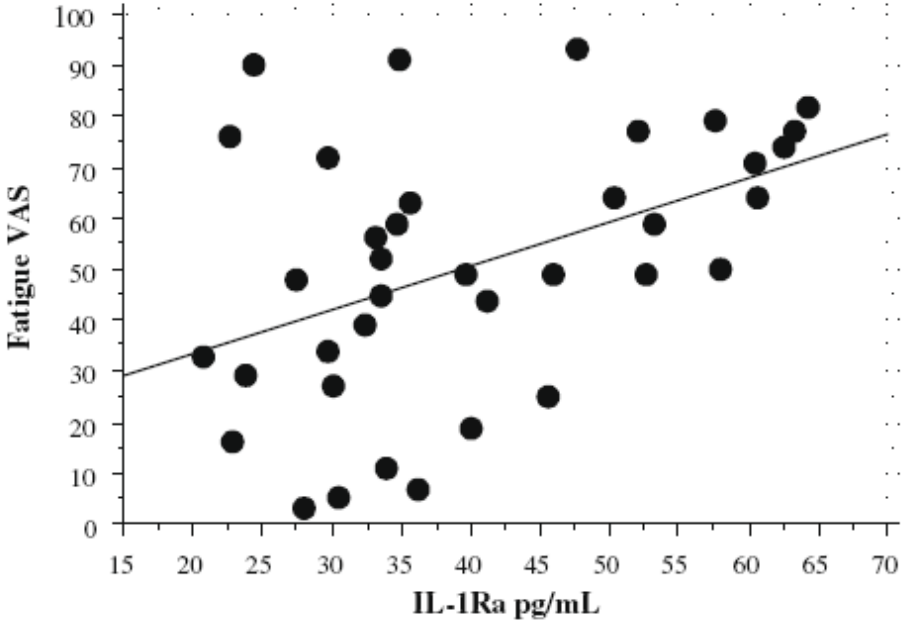
substitutie vocht (kunsttranen, kunstspeeksel)

ontstekingsremming en ziekte-modulatie (hydroxychloroquine)

stimulatie exocriene klieren met M3R agonisten (pilocarpine)

behandeling complicaties (o.a. orale candidiasis)

Syndroom van Sjögren: verklaring moeheid?



Harboe et al, Brain, Behavior, and Immunity, 2009

Erasmus MC

Sarcoïdose

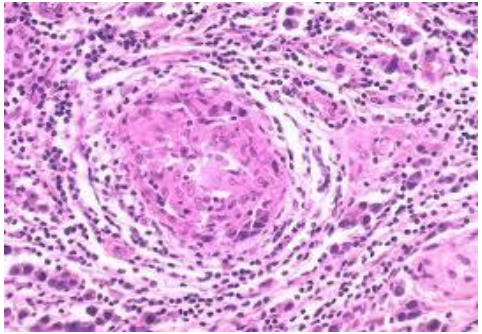
Multisysteem ziekte van onbekende etiologie

Niet-necrotiserende granulomen

< 50 jaar

Prevalentie wereldwijd 1-50:100.000

Prevalentie Nederland 45:100.000



Beloop:

- Subklinisch (50%?)
- Löfgren 90% spontane remissie < 6 maanden
- Algemeen: 30 – 80% spontane remissie, afhankelijk stadium
- Chronisch indien > 2 – 3 jaar actieve ziekte

Oorzaken?

A Case Control Etiologic Study of Sarcoidosis

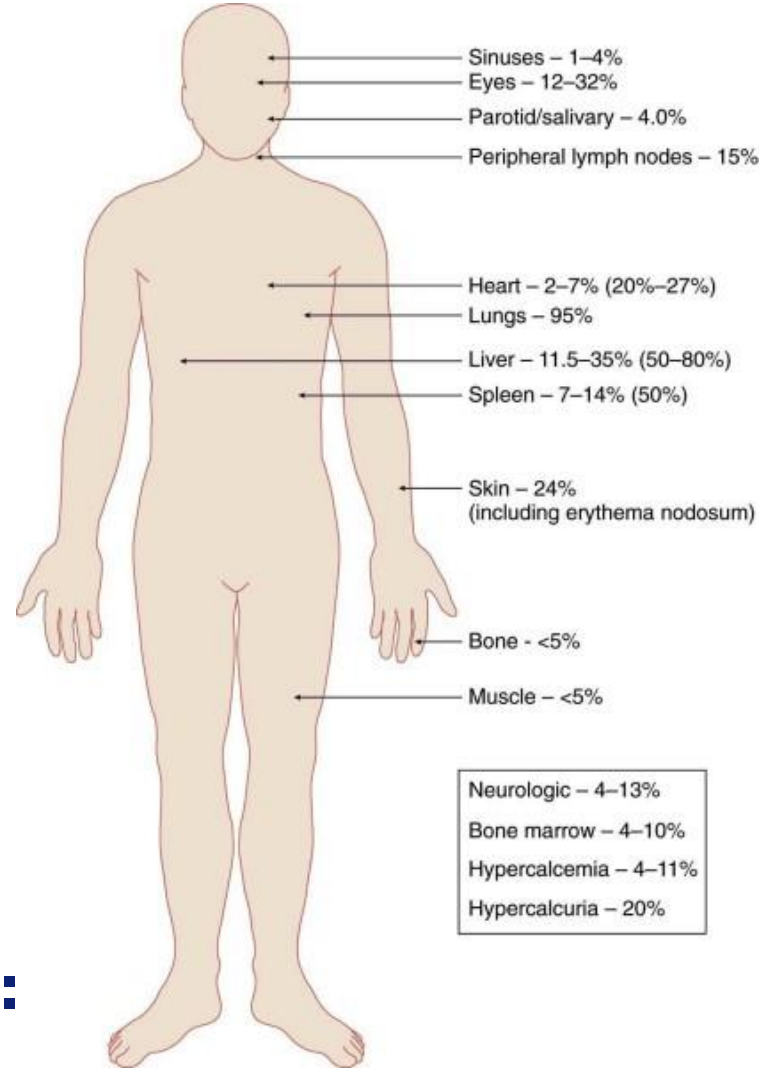
Environmental and Occupational Risk Factors

Lee S. Newman, Cecile S. Rose, Eddy A. Bresnitz, Milton D. Rossman, Juliana Barnard, Margaret Frederick, Michael L. Terrin, Steven E. Weinberger, David R. Moller, Geoffrey McLennan, Gary Hunninghake, Louis DePalo, Robert P. Baughman, Michael C. Iannuzzi, Marc A. Judson, Genell L. Knatterud, Bruce W. Thompson, Alvin S. Teirstein, Henry Yeager, Jr., Carol J. Johns†, David L. Rabin, Benjamin A. Rybicki, Reuben Cherniack, and the ACCESS Research Group*

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 170 2004

agricultural employment	OR 1.46, CI 1.13–1.89
insecticides at work	OR 1.52, CI 1.14–2.04
exposures to microbial bioaerosols	OR 1.61, CI 1.13–2.31
work in areas with musty odors	OR 1.62, CI 1.24–2.11
occupational exposure to insecticides	OR 1.61, CI 1.13–2.28

Lokatie



Erasmus MC

Sarcoïdose en moeheid

Study	Incidence of fatigue *n* (%)	Assessment of fatigue	Conclusions about fatigue
[21]	44 (73%)	FAS	Clinical or serological parameters, except D_LCO, did not predict fatigue.
[3]	83 (57%)	FAS, symptom inventory	Tired patients reported a worse QOL, and clinical parameters were unrelated to fatigue.
[23]	83 (55%)	FAS	The Croatian translation of the FAS is reliable and valid.
[9]	837 (80%)[b]	FAS, WHOQOL-100 facet Energy & Fatigue	The FAS is a promising measure to assess fatigue.
	68 (85%)[b]		
[25]	98 (69%)	FAS	Fatigue was related with 6MWD and with dyspnea.
[15]	27 (73%)[c]	Interview	Fatigue was a major complaint, and QOL was related to the perception of complaints.
[14]	28 (76%)[c]	WHOQOL-100, interview	WHOQOL-100 is a sensitive instrument to measure fatigue. The facet Energy & Fatigue was related to depression, but unrelated to the domain Psychological Health and lung function.
[28••]	10 (100%)[d]	FAS, FACIT-F	Treatment with d-MPH was associated with a significant improvement in fatigue
[27••]		Fatigue Scale	Patients with extrapulmonary involvement are more fatigued than patients with pulmonary involvement.
[19]	599 (73%)	WHOQOL-100, symptom inventory	Fatigue was related to pain.
[17]	28 (76%)	Interview	Sarcoidosis patients reported as much fatigue as patients with RA, and more than controls.
[26]	88 (60%)	WHOQOL-100, symptom inventory	Fatigue predicted QOL after controlling for demographics and clinical parameters.
[5]	25 (66%)	WHOQOL-100 facet Energy & Fatigue, symptom inventory	Fatigue was related to an acute phase response, but not to markers of disease activity. Tired patients suffered more frequently from dyspnea, exercise intolerance, muscle pain, eye problems and needed more sleep.
[22]		FAS	Fatigue was related to perceived stress, when the role of depression was partialed out.
[18]		SHQ	SHQ is appropriate to measure fatigue in sarcoidosis, including fatigue.
[24]	22 (100%)[d]	Domain fatigue of CRDQ, Borg score fatigue, 6MWD	Quadriceps peak torque was negatively associated with fatigue. Patients reported more fatigue than healthy controls.
[20]		Vitality subscale SF-36	Vitality was related to inspiratory muscle endurance.
[12]	6 (33%)[c]	Interview	Fatigued patients had lower maximum expiratory muscle pressures than those without fatigue.
[16]	720 (74%)	Symptom inventory	Women reported more fatigue, and women who used oral steroids reported more fatigue.
[13]	728 (71%)	Symptom inventory	The most frequently reported symptom was fatigue. Symptoms and corticosteroids were not related. Women suffered more frequently from fatigue.

6MWD, 6-minute walking distance; CRDQ, Chronic Respiratory Disease Questionnaire; D_LCO, diffusing capacity of the lung for carbon monoxide; FACIT-F, Functional Assessment of the Chronic Illness Therapy-Fatigue; FAS, Fatigue Assessment Scale; QOL, quality of life; RA, rheumatoid arthritis; SF-36, Short Form 36; SHQ, Sarcoidosis Health Questionnaire; WHOQOL-100, World Health Organization questionnaire of Quality of Life.
[a] Information about sarcoidosis patients is presented; no information about controls or other patient groups is included.
[b] 837 members of Dutch Sarcoidosis Society and 68 outpatients.
[c] Percentage among patients with current symptoms.
[d] Fatigue was an inclusion criterion.

Fatigue in sarcoidosis: a systematic review.
de Kleijn, Willemien; De Vries, Jolanda; Lower, Elyse; Elfferich, Marjon; Baughman, Robert; Drent, Marjolein

Current Opinion in Pulmonary Medicine. 15(5):499-506, September 2009.
DOI: 10.1097/MCP.0b013e32832d0403

Erasmus MC

Sarcoidose, indicatie behandeling

- Bedreiging organen:
- Ogen
- Longen
  - Achteruitgang foto’s
  - TLC/ VC/ DCO < 70%
- Gewrichten
- Cerebraal
- Neuropathie

Behandeling sarcoïdose

Table 3

Medications Used in Sarcoidosis

Medication	Usual Dose	Toxicity/Adverse Events	Comments
Prednisone equivalent	Initial: 20-60 mg/d or every other day Maintenance: 5-10 mg daily or every other day	Diabetes, osteoporosis, hypertension, insomnia, decreased immune system	First-line therapy for sarcoidosis
Methotrexate	10-20 mg/wk	Myelosuppression, nausea, hepatotoxicity, pulmonary fibrosis; useful for chronic patients	May not see full effect for up to 6 mo
Azathioprine	50-150 mg/d	Myelosuppression, nausea	Not as widely studied as methotrexate
Chloroquine Hydroxychloroquine	500 mg/d 200-400 mg/d	Ocular toxicity, nausea	Useful for skin disease and hypercalcemia
Cyclophosphamide	50-150 mg/d	Myelosuppression, cystitis, nausea, carcinogenic	Third-line due to toxicity; use limited to refractory cases
Pentoxifylline	400-1200 mg/d	Nausea	Reports limited to use in acute disease
Infliximab	5 mg/kg IV wk 0, wk 2, and wk 6, then every 8 wk	Increased rate of infection, especially TB infusion reaction	Limited data; contraindicated in CHF patients
Etanercept	25 mg SQ twice a week	Increased rate of infection, especially TB	Limited data; conflicting results
Adalimumab	40 mg SQ every other week	Increased rate of infection, especially TB	Limited data

CHF: congestive heart failure; SQ: subcutaneous; TB: tuberculosis.
Source: Reference 18.

Erasmus MC

Behandeling erger dan de kwaal?

The effect of corticosteroids on quality of life in a sarcoidosis clinic: The results of a propensity analysis

Marc A. Judson [a,*], Haroon Chaudhry [a], Amanda Louis [b], Kevin Lee [b], Recai Yucel [c]

Respiratory Medicine (2015) 109, 526–531

ELSEVIER

Erasmus MC

Studie: effect steroïden op KvL

Rationale:

Prednison vermindert KvL (zelfde groep, Chest 2004)

Matching was done on age, sex, race, number of organs involved (one organ versus more than one organ), the presence or absence of a stage IV chest radiograph, the presence or absence of lupus pernio, forced vital capacity (FVC) % predicted, and the need for additional anti-sarcoidosis drugs.

KvL: SHQ of SAI

Kliniek

“Propensity score” gematchte cases na multivariate analyse

Resultaten

Table 3 Mean scores after propensity score matching by the two corticosteroid dose groups*.

PRO module	>500 mg prednisone/year	<=500 mg prednisone/year	Minimum important difference**	p-Value
SHQ total [+]	4.18 (0.37)	4.17 (0.33)	N/A	0.88
SHQ physical [+]	4.73 (0.70)	4.46 (0.69)	N/A	0.05
SHQ daily [+]	4.01 (0.41)	4.17 (0.48)	N/A	0.08
SHQ emotional [+]	3.79 (0.51)	3.81 (0.45)	N/A	0.35
SAT pain [−]	54.5 (10.0)	51.8 (10.1)	3.2	0.18
SAT fatigue [−]	54.8 (11.4)	48.9 (10.6)	3.1	<0.0001
SAT satisfaction [+]	46.5 (10.7)	51.5 (11.8)	3.0	0.03
SAT daily activities [+]	42.1 (7.5)	45.8 (9.5)	3.0	0.03
SAT lung [−]	45.7 (9.1)	42.7 (9.5)	2.7	0.12

SHQ: Sarcoidosis Health Questionnaire; SAT: sarcoidosis assessment tool; *: standard deviations given in the parentheses; **previously established (REF# 16); [+]: higher score indicates better quality of life; [−]: lower score indicates better quality of life; N/A: not applicable as minimum important difference has not been determined for the Sarcoidosis Health Questionnaire.

Diagnose

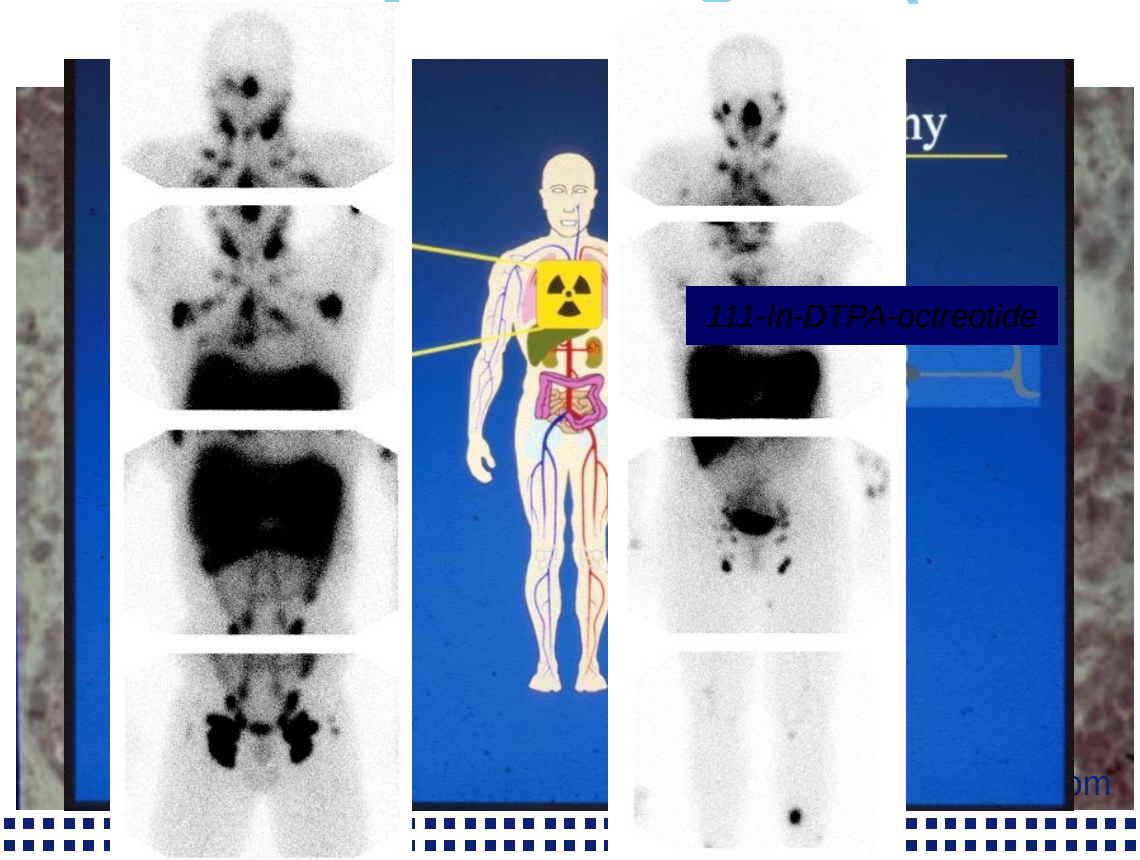
Kliniek

Histologie

Beeldvorming

- Thoraxfoto
- SMS-scan

Somatostatine receptor scintigrafie (SMS-scan)



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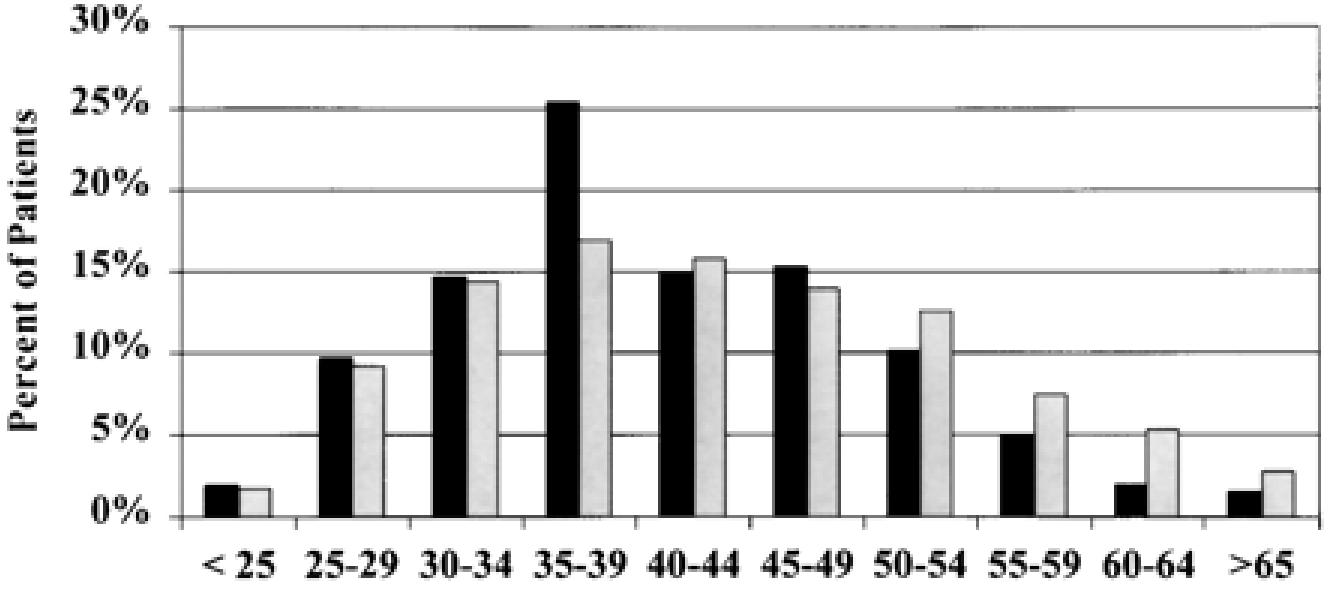
Sarcoidose demografie



Baughman et al. Am. J. Respir. Crit. Care Med, 2001

Erasmus MC

Methoden

Radiologisch stadium sarcoïdose (X-thorax/CT-scan)

I

II

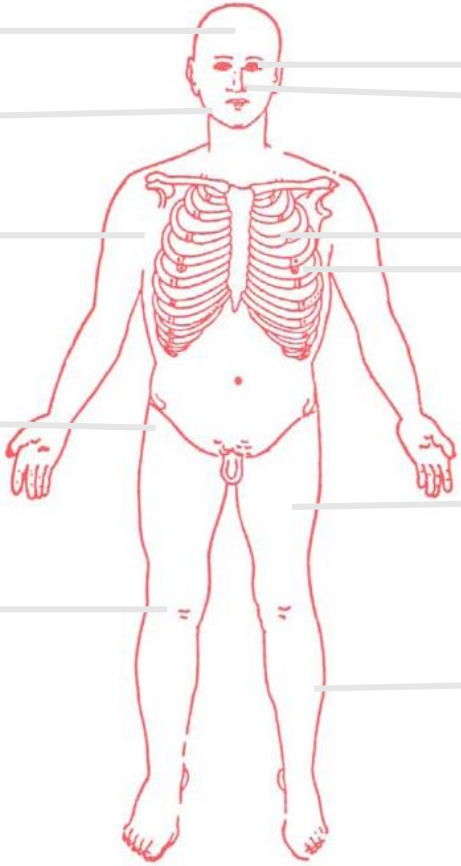
III

IV

Ziekte-activiteit parameters

- ACE
- Soluble interleukin 2 receptor (sIL-2R)

Lokalisatie



n = 218 sarcoïdose patiënten

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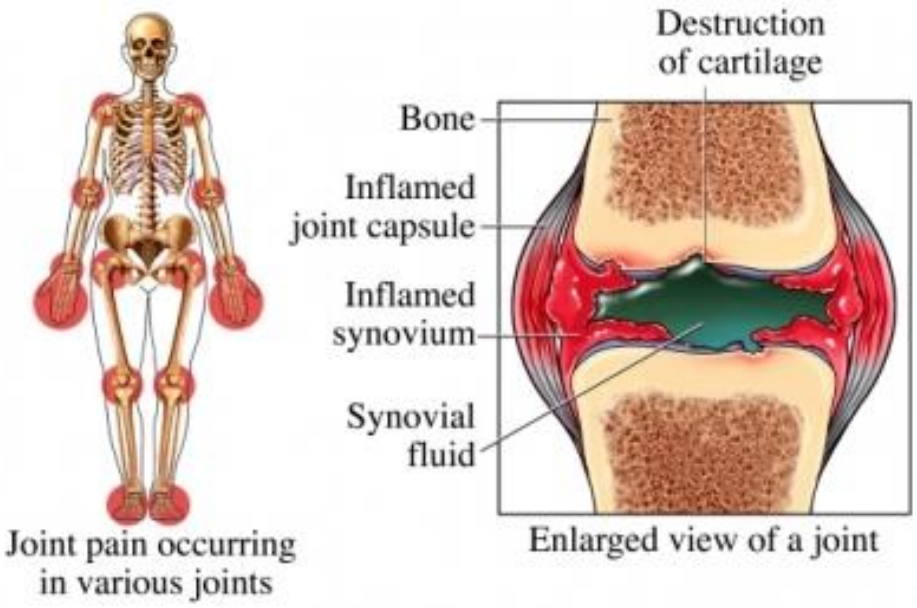
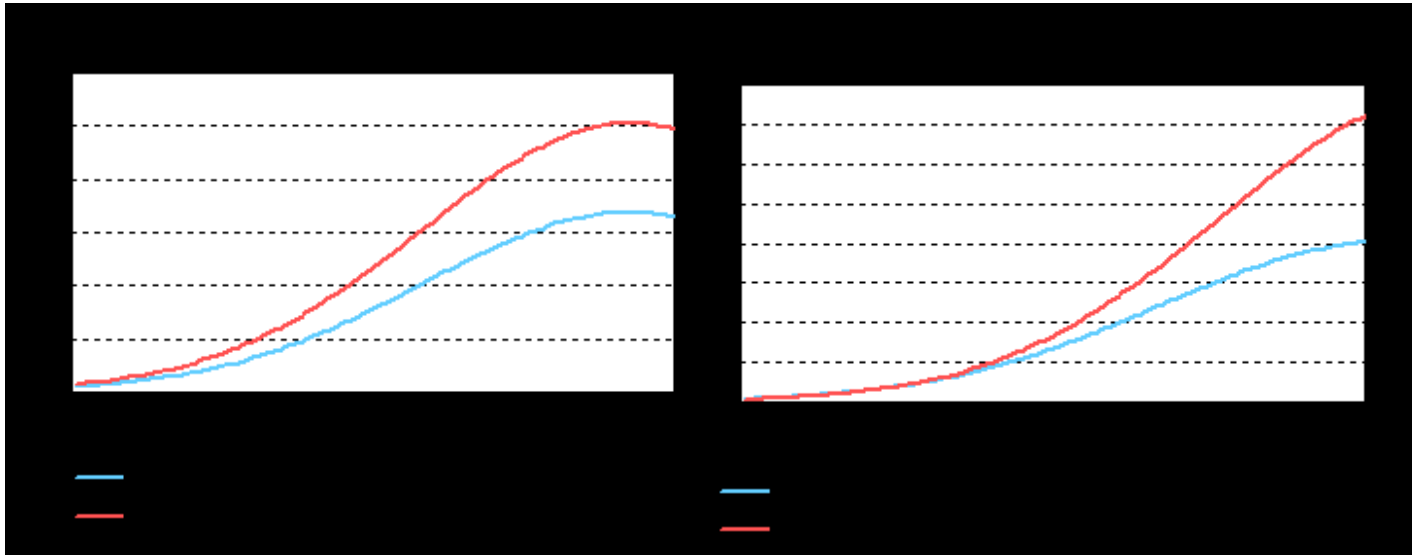
Reumatoïde artritis



Voorkomen RA



148.300 personen met RA in NL in 2007

15.600 nieuwen in 2007

RA: kliniek en immunologisch actieve cellen

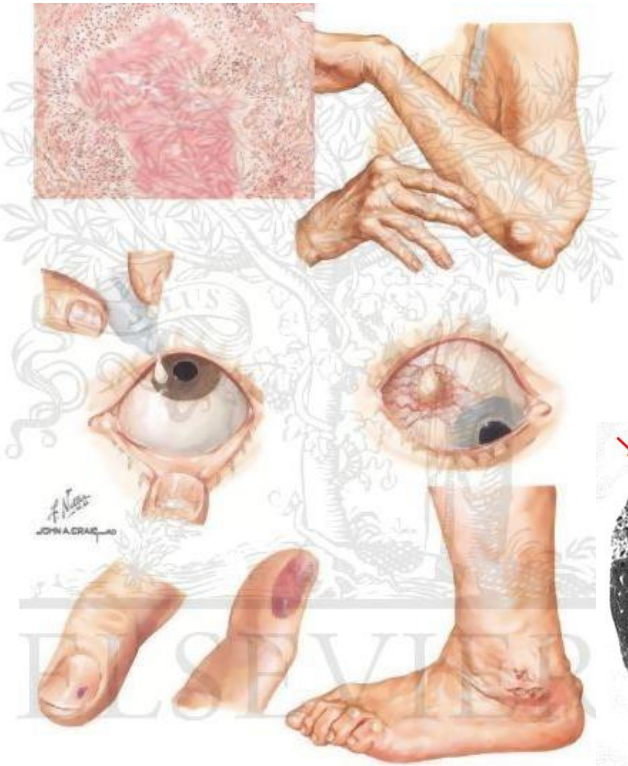
Erasmus MC

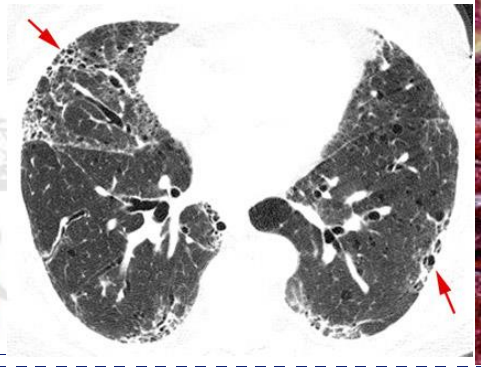
RA: diagnose volgens ACR criteria

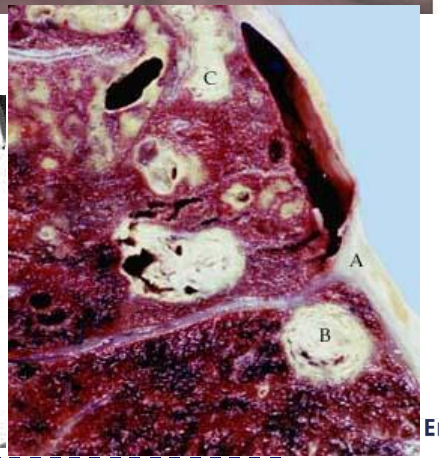
Tabel 3. Classificatiecriteria voor RA volgens de American College of Rheumatology (ACR). De diagnose RA wordt gesteld indien aan ten minste 4 van de 7 criteria wordt voldaan, waarbij criteria 1 t/m 4 ten minste 6 weken moeten bestaan om geldig te zijn.

Criterium	Definitie
1 ochtendstijfheid	gewrichtsstijfheid die niet binnen een uur geheel is verdwenen
2 artritis in drie of meer gewrichten	door een arts waargenomen zwelling of hydrops
3 artritis in de handgewrichten	zwelling of hydrops van pols, metacarpofalangeale of proximale interfalangeale gewrichten
4 symmetrische artritis	gelijktijdige ontsteking van dezelfde gewrichten aan beide zijden van het lichaam
5 noduli	door een arts waargenomen subcutane of periostale knobbels
6 reumafactoren	aanwezigheid in serum van antilichamen tegen IgG, aangetoond met een agglutinatietest
7 radiologische afwijkingen	aanwezigheid van erosies op röntgenfoto's van handen en polsen

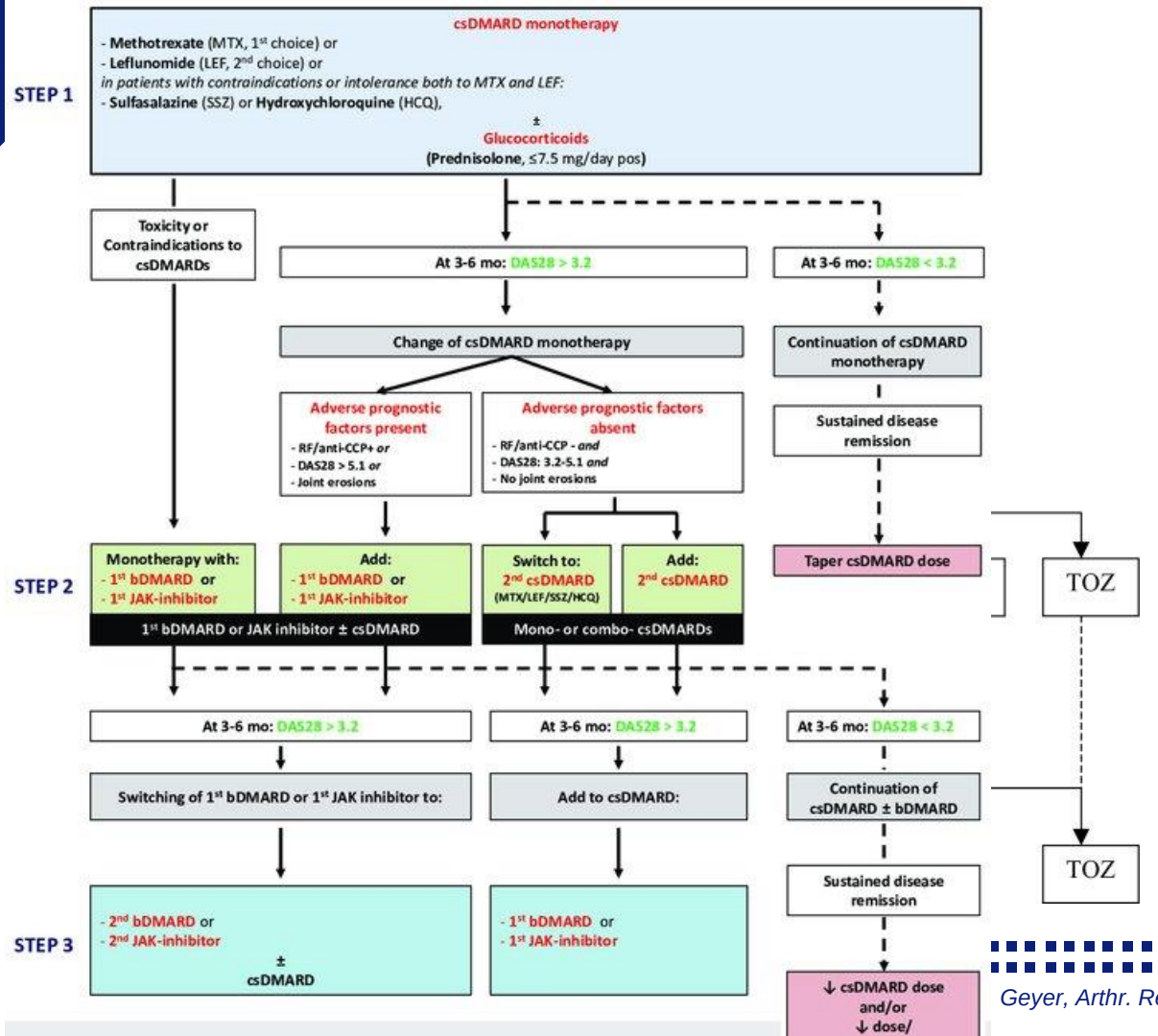
Reumatoïde artritis extra-articulair







Erasmus MC

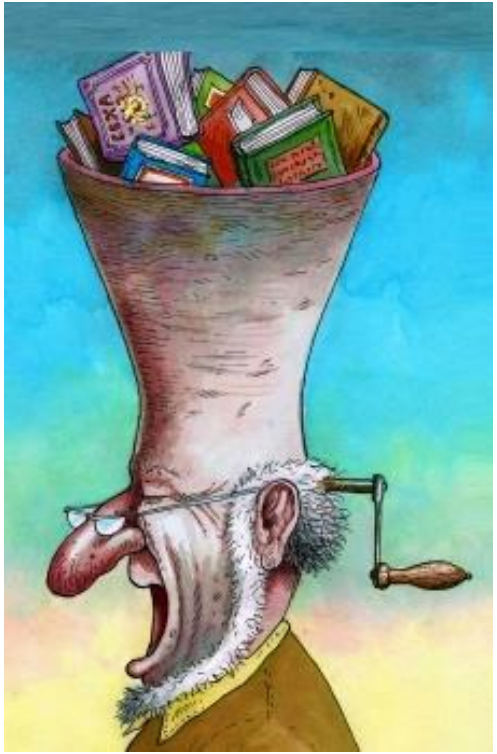


Erasmus MC

Geyer, Arthr. Res. Ther., 2010/ Vasilopoulus, Med. J Rheum, 2020

Werk en AI-ziekte?

Tijd om samen met de groep aan het werk te gaan!



Erasmus MC

RA

1. RA:
    1. Wordt gediagnosticeerd bij positieve IgM-RF
    2. Reageert goed op NSAIDs
    3. Is een aandoening van de grote gewrichten
    4. Kenmerkt zich door cystes in de gewrichten

2. Ziekteverzuim bij RA op de werkvloer:
    a. Is hoger bij mannen dan bij vrouwen
    b. Is 10% per aangedaan gewricht extra
    c. Is pas relevant bij meer dan 5 gewrichten aangedaan
    d. Ligt hoger als de heupen aangedaan zijn dan handen of knieën

RA

Table 1. Disability and work status of individuals with arthritis age 18 64 in 1978 U.S. population*

Category of individuals	Total number (thousands)	Percent of population	Disability status: Percent not disabled	Disability status: Percent moderately disabled	Disability status: Percent severely diabled	Work status: Percent working
Women						
a. Total female population	64,012	100.0%	82.2%	8.1%	9.6%	58.0%
b. No arthritis†	51,520	80.5%	90.1%	5.4%	4.5%	61.6%
c. Symmetric polyarthritis§	1511	2.4%	22.2%	26.8%	51.0%	31.0%
d. Asymmetric oligoarthritis	2687	4.2%	33.1%	19.3%	47.5%	35.5%
Men						
a. Total male population	62,670	100.0%	81.4%	8.5%	7.2%	87.1%
b. No arthritis†	54,033	86.2%	90.6%	5.8%	3.7%	89.4%
c. Symmetric polyarthritis§	855	1.4%	29.7%	23.3%	47.0%	56.1%
d. Asymmetric oligoarthritis¶	1574	2.5%	28.6%	26.9%	44.5%	66.7%

Table 2. Disability and work status of individuals age 18–64 in 1978 U.S. population according to involvement of specific joints

Category of Individuals	Women: Percent not disabled	Women: Percent severely disabled	Women: Percent working	Men: Percent not disabled	Men: Percent severely disabled	Men: Percent working
No arthritis	90.1%	4.5%	61.6%	90.6%	3.7%	89.3%
Symmetric polyarthritis*						
Two knees	18.9%	62.4%	31.3%	29.7%	44.0%	60.0%
Two hips	8.9%	76.4%	19.3%	3.9%	62.6%	40.0%
Two hands	24.0%	45.5%	30.8%	25.0%	52.8%	51.5%
Asymmetric oligoarthritis*						
One knee	29.8%	43.3%	41.1%	25.7%	54.7%	58.6%
One hip	48.8%	44.5%	23.6%	24.9%	48.3%	71.6%
One hand	25.6%	47.9%	50.1%	23.0%	53.0%	52.2%

Pincus, JCE, 1989

Erasmus MC

RA

Table 3. Disability status and work status in individuals age 18–64 according to number of joints with pain and swelling

Number of joint problems	Estimated number of persons	Percent of working age population	Disability status: Percent not diabled	Disability status: Percent moderately disabled	Disability status: Percent severely disabled	Work status: Percent working*
None	108,709	85.6%	89.3%	6.1%	4.6%	77.4%
One joint	5200	4.1%	62.4%	16.8%	20.8%	69.2%
Two joints	5522	4.3%	53.1%	22.2%	24.7%	69.2%
Three joints	1823	1.4%	47.1%	18.1%	34.8%	58.1%
Four joints	2041	1.6%	43.8%	23.2%	33.0%	62.7%
Five or six joints	1476	1.2%	28.6%	29.7%	41.7%	49.6%
Seven to nine joints	1017	0.8%	16.9%	27.9%	55.2%	38.9%
Ten or more joints	1259	1.0%	11.3%	27.6%	55.0%	39.0%

Pincus, JCE, 1989

RA

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RA

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SLE

1. SLE:
    a. Is een ziekte die vaker bij mannen voorkomt dan bij vrouwen
    b. De moeheid is op het einde van de dag het meest ernstig
    c. Nierlokalisatie is gerelateerd met een slechtere prognose
    d. Behandeling met immuunsuppressiva wordt getritreerd op het bestaan van orgaanbedreiging
    e. In Curacao zijn SLE patiënten vaker moe dan in Nederland
    f. Hoe vermoeider de SLE patiënt, des te minder deze werkt

SLE

Rheumatology 2005;44:751–755
Advance Access publication 9 March 2005

Concise Report

The systemic lupus erythematosus tri-nation study: longitudinal changes in physical and mental well-being

P. Panopalis[1], M. Petri[4], S. Manzi[5], D. A. Isenberg[6], C. Gord

Objective. We have shown that SLE patients in Canada and the UK incurred 20% and 13% lower health costs than those in the US, respectively, but did not experience worse outcomes as expressed by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. We now compare change in quality of life in these patients.

Patients and methods. Seven hundred and fifteen SLE patients (Canada 231, US 269, UK 215) completed the SF-36 annually over four years. The annual change in the SF-36 Physical and Mental Component Summary (PCS and MCS) scores over the course of the study were summarized by estimating a linear trend for each individual patient using hierarchical modelling. Cross-country comparison of the slopes in the PCS and MCS scores was then performed using simultaneous regressions.

Results. The estimated mean annual changes (95% credible interval [CrI]) in the PCS scores in Canada, the US, and the UK were 0.18 (−0.07, 0.43), −0.05 (−0.27, 0.17), and 0.03 (−0.20, 0.27), respectively; the mean annual changes in the MCS scores were 0.15 (−0.04, 0.34), 0.23 (0.09, 0.37), and 0.08 (−0.10, 0.27), respectively. Regression results showed that the mean annual changes in PCS and MCS scores did not substantially differ across countries.

Conclusion. Quality of life remained stable across countries. Despite Canadian and British patients incurring lower health costs, on average, patients experienced similar changes in physical and mental well-being.

Erasmus MC

SLE en werk?

Burden of Systemic Lupus Erythematosus on Employment and Work Productivity: Data From a Large Cohort in the Southeastern United States

CRISTINA DRENKARD,[1] GAOBIN BAO,[1] GREG DENNIS,[2] HONG J. KAN,[3] PRITI M. JHINGRAN,[3] CHARLES T. MOLTA,[4] AND S. SAM LIM[1]

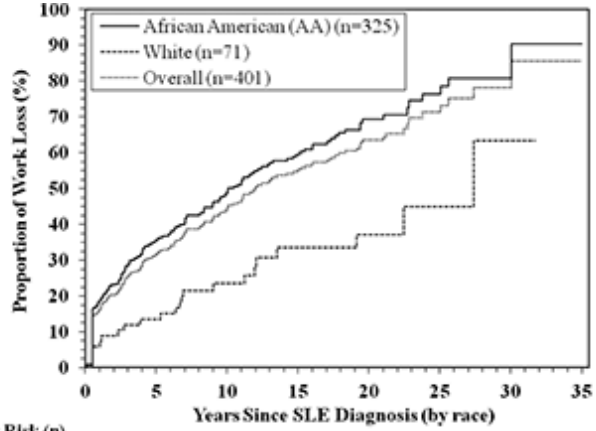
Arthritis Care & Research
Vol. 66, No. 6, June 2014, pp 878–887

Significance & Innovations

- We examined the impact of systemic lupus erythematosus (SLE) on work outcomes in a large population-based SLE cohort in the southeastern US. By analyzing a representative sample of SLE patients that included a substantial number from disadvantaged sociodemographic subgroups, our findings advance the understanding of the complete burden of SLE on work outcomes.
- To our knowledge, this is the first population-based study in the US that reports the excess risk of unemployment in SLE compared with standards from the general population in the same geographic area, and further examines the burden of unemployment across demographic and disease severity subgroups.

Erasmus MC

SLE en werk Wh vs Bl



At Risk (n)								
Overall	401	244	164	85	44	15	3	1
AA	325	186	123	60	28	11	2	1
White	71	54	38	23	15	4	1	0
Work Loss (%)								
Overall	0	32	44	55	63	71	78	85
AA	0	36	49	60	69	76	81	90
White	0	14	23	33	37	45	63	-

Gecorrigeerd

Table 2. Standardized unemployment ratios (SURs) for SLE*

Category	SLE cases†	Unemployment Observed (SLE)	Unemployment Expected (GP)	SUR (95% CI)‡
Overall	570	318	88	3.61 (3.24–4.03)
Demographics				
Men	34	23	5	4.60 (3.06–6.92)
Women	536	295	84	3.51 (3.13–3.94)
African American	463	283	80	3.54 (3.15–3.97)
White	99	30	8	3.75 (2.62–5.36)
African American women	434	260	76	3.42 (3.03–3.86)
White women	94	30	7	4.29 (3.00–6.13)
Disease-related factors				
Disease duration, years				
0–5	101	59	17	3.47 (2.69–4.48)
6–15	235	123	36	3.42 (2.86–4.08)
>15	182	98	26	3.77 (3.09–4.59)
Disease activity score				
Mild (0–10)	143	55	21	2.62 (2.01–3.41)
Moderate (11–16)	129	53	19	2.79 (2.13–3.65)
Severe (≥17)	298	210	48	4.38 (3.82–5.01)
Organ damage score				
None (0)	158	53	24	2.21 (1.69–2.89)
Mild (1–3)	288	165	46	3.59 (3.08–4.18)
Severe (≥4)	124	100	18	5.56 (4.57–6.76)

* Values are the number unless indicated otherwise. SLE = systemic lupus erythematosus; GP = general population; 95% CI = 95% confidence interval.
† All SLE patients working for pay or being employed/disabled at the time of wave 1 survey.
‡ SUR adjusted by age, sex, and race using employment status data from the 2011 American Community Survey.

Erasmus MC

Moeheid en werk bij SLE?

Table 3. Work productivity impairment in SLE as a function of disease activity and organ damage*

Variable	Cases, no.	Adjusted WPI, mean (95% CI)†	P
Disease activity score			
Mild (0–10; reference)	80	14.9 (3.8–26.0)	–
Moderate (11–16)	66	37.7 (27.6–47.9)	< 0.0001
Severe (≥17)	79	49.5 (38.6–60.4)	< 0.0001
Organ damage score			
None (reference)	98	33.6 (23.0–44.2)	–
Mild (1–2)	83	28.7 (18.5–38.9)	0.24
Severe (≥3)	44	39.8 (28.1–51.6)	0.22
Disease activity by organ system score			
Fatigue			
Absent (0; reference)	26	17.6 (3.2–32.0)	–
Mild (1)	58	20.0 (7.7–32.3)	0.73
Moderate (2)	89	33.0 (22.6–43.4)	0.015
Severe (3)	52	50.6 (38.7–62.5)	< 0.0001
Skin			
Absent (0; reference)	73	16.6 (4.9–28.3)	–
Present (1)	152	38.9 (28.7–49.1)	< 0.0001
Lung			
Absent (0; reference)	78	20.2 (8.5–31.9)	–
Mild (1)	79	30.4 (19.4–41.5)	0.029
Moderate (2)	45	45.0 (32.2–57.8)	< 0.0001
Severe (3)	23	49.5 (35.5–63.5)	< 0.0001
Stroke syndrome			
Absent (0; reference)	101	25.9 (14.8–36.9)	–
Mild (1)	57	38.5 (26.5–50.5)	0.011
Moderate (2)	48	40.3 (27.4–53.2)	0.005
Severe (3)	19	52.1 (35.5–68.8)	0.0005
Cognitive			
Absent (0; reference)	54	20.7 (8.5–33.0)	–
Mild (1)	71	29.9 (18.6–41.1)	0.078
Moderate (2)	69	36.2 (25.0–47.5)	0.0034
Severe (3)	31	56.8 (43.0–70.5)	< 0.0001
Muscle			
Absent (0; reference)	57	19.8 (7.8–31.8)	–
Mild (1)	71	29.5 (19.0–40.1)	0.054
Moderate (2)	61	42.4 (30.0–54.7)	< 0.0001
Severe (3)	36	56.2 (43.3–69.0)	< 0.0001
Joint			
Absent (0; reference)	37	16.6 (3.7–29.5)	–
Mild (1)	78	28.4 (17.5–39.3)	0.037
Moderate (2)	74	40.7 (29.2–52.1)	< 0.0001
Severe (3)	36	53.8 (40.6–66.9)	< 0.0001

* SLE = systemic lupus erythematosus; WPI = work productivity impairment; 95% CI = 95% confidence interval.
† WPI adjusted by age, race, educational attainment, and disease duration.

SLE

1. SLE:
    a. Is een ziekte die vaker bij mannen voorkomt dan bij vrouwen
    b. De moeheid is op het einde van de dag het meest ernstig
    c. Nierlokalisatie is gerelateerd met een slechtere prognose
    d. Behandeling met immuunsuppressiva wordt getritreerd op het bestaan van orgaanbedreiging
    e. In Curacao zijn SLE patiënten vaker moe dan in Nederland
    f. Hoe vermoeider de SLE patiënt, des te minder deze werkt

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Sarcoïdose

1. Sarcoïdose:
    a. Wordt gekenmerkt door granulomen
    b. Presenteert zich vooral in de longen
    c. Gaat meestal vanzelf over
    d. Wordt met anti-TNF-alpha behandeld
    e. Gaat dikwijls gepaard met moeheid

Sarcoidose

Table 1 Quality of Life (QOL) and Health Status (HS) Questionnaires Utilized in Sarcoidosis

Questionnaires	QOL/HS Measure	Items Number	Required Time (min)	Quality in Sarcoidosis
CRQ	HS	20	20–30	Not good*
SF-36	HS	36	10	Good*
SGRQ	HS	76	15–20	Good*
SHQ	HS	29	10	Good*
SIP	HS	136	20–30	Unknown
WHOQOL-100	QOL	100	15–20	Good
Q-LES-Q	QOL	93	??	Unknown

*Validated in interstitial lung disease sample including 10 sarcoidosis patients.
CRQ, Chronic Respiratory Questionnaire; SF-36, Medical Outcome Study Short Form-36; SGRQ, St. George Respiratory Questionnaire; SHQ, Sarcoidosis Health Questionnaire; SIP, Sickness Impact Profile; WHOQOL-100, World Health Organization Quality of Life assessment instrument-100; Q-LES-Q, Quality of Life Enjoyment and Satisfaction Questionnaire.

SHQ

TABLE 2. IMPACT SCORES (FREQUENCY × IMPORTANCE SCORE) FOR SARCOIDOSIS HEALTH QUESTIONNAIRE ITEMS BY DOMAIN FOR DEVELOPMENT STUDY PATIENTS

SHQ Item	Frequency with which Patients Reported Problem	Importance	Impact	Cronbach's α
Daily Functioning				0.92
Felt you were full of energy	0.84	4.43	3.72	
Felt bodily pain	0.79	4.27	3.37	
Felt you need medications to function day to day	0.77	4.44	3.50	
Felt confidence in yourself and your abilities	0.74	4.57	3.38	
Felt that you accomplished all that you wanted	0.72	4.09	2.94	
Felt that everything you did took a lot of effort	0.69	4.12	2.84	
Been discouraged by recent weight gain	0.67	4.13	2.77	
Felt sarcoidosis controls your life	0.67	3.92	2.63	
Had a good night's sleep	0.65	4.18	2.72	
Bothered by sarcoidosis skin or hair problems	0.63	3.83	2.41	
Felt you were as healthy as others your age	0.63	4.04	2.54	
Felt your physical problems interfered in your social activities with family and friends	0.62	4.21	2.61	
Bothered by eye or eyesight problems	0.61	4.01	2.45	
Physical Functioning				0.84
Felt your breathing was completely comfortable during your normal daily activities	0.81	4.48	3.63	
Felt shortness of breath walking up stairs, the length of a city block, or up a small hill	0.79	4.44	3.50	
Had joint pains	0.75	4.16	3.12	
Had a cough	0.73	4.01	2.93	
Been bothered by headaches	0.69	4.07	2.81	
Experienced wheezing	0.69	4.07	2.80	
Emotional Functioning				0.87
Worried sarcoidosis might flare up or worsen	0.83	4.50	3.74	
Expect your health to be good in the future	0.80	4.58	3.67	
Satisfied with the support of family and friends	0.80	4.43	3.54	
Worried about the amount of pain and discomfort	0.75	4.26	3.19	
Felt mood swings	0.73	4.19	3.06	
Felt depressed	0.67	4.14	2.82	
Felt satisfied with the appearance of your body	0.65	4.31	2.80	
Felt that you could concentrate easily	0.62	4.29	2.65	
Been discouraged by physical limitations in performing your normal daily activities or your job	0.60	4.12	2.51	
Felt that your emotional problems affected your relationships with family, friends, or coworkers	0.60	4.16	2.50	

Definition of abbreviation: SHQ = Sarcoidosis Health Questionnaire.

Erasmus MC

SF 36 (10 vragen)

4. Heeft u in de afgelopen 4 weken, een van de volgende problemen bij uw werk of andere dagelijkse bezigheden gehad, ten gevolge van uw lichamelijke gezondheid?

(omcirkel één cijfer op elke regel)

	JA	NEE
a. U besteedde **minder tijd** aan werk of andere bezigheden	1	2
b. U heeft **minder bereikt** dan u zou willen	1	2
c. U was beperkt in het **soort** werk of andere bezigheden	1	2
d. U had **moeite** om uw werk of andere bezigheden uit te voeren (het kostte u bv. extra inspanning)	1	2

5. Heeft u in de afgelopen 4 weken, een van de volgende problemen ondervonden bij uw werk of andere dagelijkse bezigheden ten gevolge van emotionele problemen (zoals depressieve of angstige gevoelens)?

(omcirkel één cijfer op elke regel)

	JA	NEE
a. U besteedde **minder tijd** aan werk of andere bezigheden	1	2
b. U heeft **minder bereikt** dan u zou willen	1	2
c. U deed uw werk of andere bezigheden niet zo **zorgvuldig** als gewoonlijk	1	2

8. In welke mate bent u de afgelopen 4 weken door pijn gehinderd in uw normale werk (zowel werk buitenshuis als huishoudelijk werk)?

(omcirkel één cijfer)

Helemaal niet	1
Een klein beetje	2
Nogal	3
Veel	4
Heel erg veel	5

Erasmus MC

Table 2 Impact of Drug Intervention Therapy for Sarcoidosis on Health-Related Quality of Life, Health Status, and Fatigue

Year	Reference	Intervention	*N*	Design	Disease Manifestation	Follow-up Interval	Instrument(s) Used	HRQOL Findings
2002	[43]	Fluticasone in patients starting on prednisone	22	DBRT	Pulmonary	48 weeks	SF-36	All patients felt "health" better on prednisone, no difference between treatment groups
2006	[66]	Infliximab	138	DBRT	Pulmonary	12 months	SGRQ	Both arms improved from baseline, no significant difference between groups
2006	[67]	Infliximab	19	DBRT	Pulmonary	6 weeks	SF-36	No difference between groups
2006	[68]	Thalidomide	10	Open label	Pulmonary	24 weeks	SF-36	No change with therapy
2008	[58]	d-Methylphenidate	10	DBRT with crossover	Fatigue	16 weeks each arm	SGRQ, SHQ, FAS, FACIT-F	Significant improvement in FAS and FACIT-F while on active drug, SGRQ-S+ improved while on active drug, no difference for other components of SGRQ or SHQ
2009	[69]	Iloprost	21	Open label	Pulmonary hypertension	16 weeks each arm	SGRQ, SF-36	Significant improvement in SGRQ-A++ for 13 patients who completed all 16 weeks of therapy, no difference from baseline for SF-36, SHQ, FAS, or other components of SGRQ
2010	[7]	Anti-TNF-α: infliximab or adalimumab	42	Open label	Fatigue, cognitive failure, and systemic sarcoidosis	6 months	FAS, CFQ	Significant improvement in FAS and CFQ score

DBRT, double-blind, randomized trial; SF-36, Medical Outcome Study Short Form-36; SGRQ-S, Saint George Respiratory Questionnaire—symptoms; SGRQ-A, Saint George Respiratory Questionnaire—activity; SHQ, Sarcoidosis Health Questionnaire; FAS, Fatigue Assessment Scale; FACIT-F, Functional Assessment of the Chronic Illness Therapy—Fatigue; CFQ, cognitive failure questionnaire; TNF, tumor necrosis factor.

De Vries, et al. 2010SEMINARS IN RESPIRATORY AND CRITICAL CARE MEDICINE, 31: 485

Erasmus MC

Sarcoïdose

1. Sarcoïdose:
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    b. Presenteert zich vooral in de longen
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    d. Wordt met anti-TNF-alpha behandeld
    e. Gaat dikwijls gepaard met moeheid

Syndroom van Sjögren

1. Syndroom van Sjögren
    a. Is een systeemziekte
    b. Kan fataal verlopen
    c. Is het minst vaak onderzocht op vermoeidheid
    d. Heeft meestal geen immuunsuppressie nodig
    e. QoL is significant lager indien verergering ziekte

Syndroom van Sjögren

RHEUMATOLOGY

Rheumatology 2010;49:844–853
doi:10.1093/rheumatology/keq009
Advance Access publication 10 February 2010

Re

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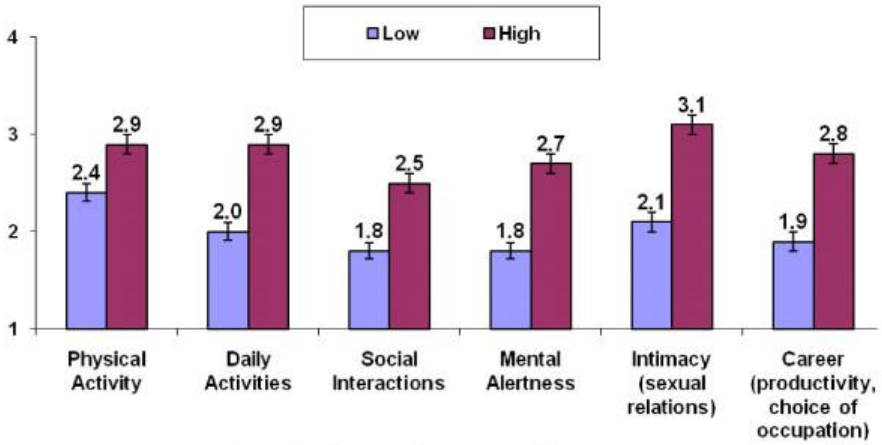
70% quality
of life. In this article, we review the instruments used for evaluating pSS-related fatigue, our current understanding of the underlying psychosocial and physiological mechanisms of fatigue in pSS and the therapeutic strategies that have been studied in the management of fatigue in pSS.

Rheumatology key messages

- Fatigue is a common and debilitating symptom in pSS.
- Further research to define the underlying psycho-physiological mechanisms and to develop effective management strategies is needed.

Syndroom van Sjögren



Note: Mean score and Standard Errors for ratings of impact on various aspects of life

Segal et al, Health Qual Life Outcomes. 2009 May 27;7:46.

Erasmus MC

Syndroom van Sjögren

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    a. Is een systeemziekte
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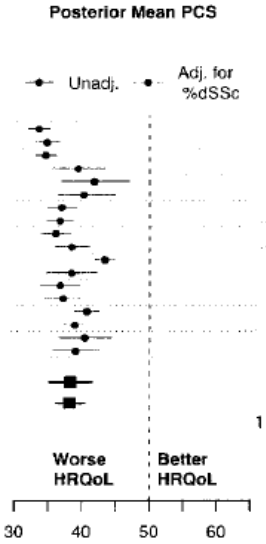
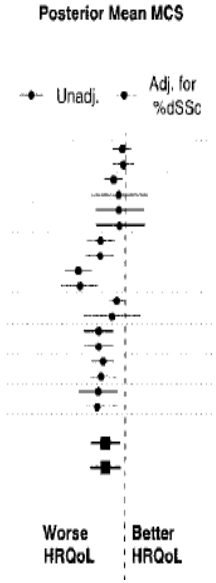
    d. Heeft meestal geen immuunsuppressie nodig
    e. QoL is significant lager indien verergering ziekte

Systemische sclerose

Study	Raw Study Estimates PCS	SE	N	Posterior Mean PCS (95% CI) Unadj.	%dSSc Adj
Khanna SLS '07	33.4	0.9	158	33.6 (32.0,35.2)	34.9 (33.0,36.7)
Khanna Rlx '07	34.5	0.8	196	34.7 (33.1,36.2)	39.5 (35.7,43.5)
Rannou '07	43.8	3.0	50	41.8 (37.0,47.0)	40.3 (36.5,45.0)
Khanna HV '07	36.9	1.1	107	37.0 (34.9,39.1)	36.8 (34.7,38.8)
Georges '06	36.0	1.2	89	36.2 (34.0,38.4)	38.5 (35.9,41.2)
Glidden '06	43.6	0.8	187	43.4 (41.8,45.0)	38.5 (34.7,42.3)
Johnson '06	36.6	1.6	68	36.8 (33.9,39.7)	37.2 (34.5,39.8)
Danieli '05	40.9	1.0	76	40.7 (38.9,42.6)	38.9 (36.9,41.1)
DelRosso '04	41.1	2.2	24	40.4 (36.6,44.4)	39.1 (35.8,42.6)
Pooled	**37.8**	**0.4**	**955**	**38.3 (35.2,41.5)**	**38.2 (36.2,40.4)**



Raw Study Estimates MCS	SE	N	Posterior Mean MCS (95% CI) Unadj.	%dSSc Adj
49.7	0.8	158	49.5 (47.8,51.0)	49.6 (47.9,51.5)
48.1	0.8	196	48.0 (46.4,49.6)	48.9 (44.1,54.0)
50.7	2.7	50	48.9 (44.9,53.3)	49.0 (44.9,53.5)
45.5	1.4	107	45.7 (43.3,48.1)	45.6 (43.1,48.1)
41.0	1.2	89	41.8 (39.5,44.1)	42.2 (38.9,45.2)
48.7	0.8	187	48.5 (47.1,50.0)	47.7 (42.8,52.6)
45.1	1.4	68	45.4 (42.8,47.9)	45.4 (42.8,48.0)
46.1	1.0	76	46.2 (44.2,48.1)	45.9 (43.3,48.4)
44.8	2.0	24	45.4 (42.0,48.7)	45.2 (41.5,48.6)
47.2	**0.4**	**955**	**46.6 (44.2,49.1)**	**46.6 (44,49.2)**



Hudson et al, Arthritis & Rheumatism, 2009

Wat heb je hier als bedrijfs/ verzekeringsarts aan?

Site reumafonds

Op zoek naar een ziekenhuis?
Kies uw Reumazorg
› Klik hier

Aanpassingen
Uw bedrijfsarts kan u in contact brengen met een ergonomisch medewerker van de arbodienst. Deze geeft u advies over hoe u uw taken op een lichtere manier kunt doen, of welke aanpassingen of hulpmiddelen u bij uw taken kunnen helpen.

Bij het UWV kan uw werkgever een vergoeding aanvragen voor aanpassingen die u nodig heeft.

Blijf betrokken
Ook als u een poosje niet kunt werken is het verstandig om contact te houden met uw collega's. U toont daarmee uw interesse in het werk. Kijk of het bijvoorbeeld lukt om nog wel naar teambesprekingen of belangrijke bijeenkomsten te gaan. Zo weet u wat er op uw werk speelt. En uw collega's weten hoe het met u gaat.

Laat u coachen
Voor uzelf opkomen kan lastig zijn. Misschien voelt u zich een buitenbeentje op het werk of loopt u tegen onbegrip aan. Geef uzelf de tijd om uit te zoeken hoe u hier het beste mee om kunt gaan. Bij het Centrum Chronisch Ziek en Werk vindt u professionele coaches die zelf ervaring hebben met reuma. Wilt u graag dat iemand met u meedenkt en kijkt hoe u omgaat met reuma op de werkvloer? Of wilt u bijvoorbeeld een steuntje in de rug bij re-integratie? Neem dan contact op met het Centrum Chronisch Ziek en Werk.

Houd regie
Alleen u weet precies hoe het met u op het werk gaat. U doet er daarom goed aan om uw eigen grenzen in de gaten te houden. Trek op tijd aan de bel bij uw werkgever of bedrijfsarts als u ergens tegenaan loopt. Heeft u zelf ideeën over mogelijke oplossingen? Informeer dan of daar iets mee gedaan kan worden. Zo houdt u de regie zo veel mogelijk in eigen hand.

Meer informatie
Wilt u handige tips en oplossingen voor het omgaan met beperkingen op het werk? Er bestaat een checklist met ideeën en aandachtspunten voor u, uw werkgever en uw bedrijfsarts. Deze vindt u op de website van het platform Fit For Work.
In de folder 'Reuma en behoud van werk' leest u wat u kunt doen en wie u kan helpen om aan het werk te blijven. De folder is geschreven voor mensen met reumatoïde artritis (RA), maar is ook geschikt voor mensen met andere vormen van reuma.

Erasmus MC

Wat heb je hier als bedrijfs/ verzekeringsarts aan?

Te verwachten problemen:

A-specifiek:

Moeheid

Algemeen onwelbevinden

Verhoogd infectie risico bij immuunsuppressiva

Atrhralgiëen en artritis

Wat heb je hier als bedrijfs/ verzekeringsarts aan?

Specifiek:

SLE; fotosensitiviteit, thrombopenie, psychiatrisch

Sarcoïdose; dyspnoe, neurologisch

S Sjögren; sicca

RA; artritis

Raynaud

En wat moet je er dan mee?

Moeheid en onwelbevinden:

Mobiliseren/ belasten op geleide patiënt

Optimaliseren immunologische behandeling

Infectierisico:

Overleg specialist

Arthralgiëen:

Belasten op geleide pijn

En wat moet je er dan mee?

Fotosensitiviteit:

Buitenwerken liever vermijden

Minimaal factor 30

Thrombopenie:

Overleg specialist

Voorkom trauma’s/ of werk met hoog risico hierop

Psychiatrisch:

Herkenning!

Dient soms immuunsupressief behandeld te worden

En wat moet je er dan mee?

Dyspnoe:

Voorko

Tunnel Excavation Triggering Pulmonary Sarcoidosis

AMERICAN JOURNAL OF INDUSTRIAL MEDICINE 55:390–394 (2012)

L.B. Kawano-Dourado, MD,[1]* C.R.R. Carvalho, MD,[1] U.P. Santos, MD,[1]
M. Canzian, MD,[2] E.N.A. Coletta, MD,[3] C.A.C. Pereira, MD,[4] and R.A. Kairalla, MD[1]

Genetic susceptibility to beryllium: a case–referent study of men and women of working age with sarcoidosis or other chronic lung disease

Nicola Cherry,[1] Jeremy Beach,[2] Igor Burstyn,[3] Jillian Parboosingh,[4,5]
Janine Schouchen,[2] Ambikaipakan Senthilselvan,[6] Larry Svenson,[7]
Niko Yiannakoulias[8]

Cherry N, *et al*. *Occup Environ Med* 2015;**72**:21–27. doi:10.1136/oemed-2014-102359

Conclusions The gene–environment interaction supports the hypothesis that some cases diagnosed as sarcoidosis result from occupational beryllium exposure.

Erasmus MC

En wat moet je er dan mee?

Neurologisch:

Herkening

Sicca:

Problemen bij

- droge/ winderige werkomgeving
- Luchtverontreiniging, incl rokers en andere irriterende factoren
- Ziekenhuis OK/ recovery
- Computers

Luchtbevochtiging, kunsttranen, vochtconserverende oogbeschermers

TH/OM

Systeemziekten:

- Geven een breed scala aan klachten
- Zijn zeldzaam
- Zijn geassocieerd met moeheid
- Worden vaak met immuunsuppressiva behandeld
- Patiënten zijn dikwijls jong
- En zien er vaak opvallend goed uit
- Hebben een grote impact op de kwaliteit van leven en socio-economisch functioneren

In het kort

Artritis:

Blijven be

Verminde

Rekening

Raynaud

Voorkom

Kleding

Voorkom

Stop roke

Voorkom

Voorkom

Erasmus MC

Vragen

rasmus MC