류마티스질환에 흔히 시행하는 혈액검사

2019. 09.22

삼성창원병원 류마티스내과 황지원

Common & important questions

- 류마티스 인자가 양성이면 류마티스 관절염이다 ?
- 항 CCP 항체는 류마티스관절염에 특이적이다 ?
- 류마티스 인자와 항 CPP 항체가 음성이면 류마티스 관절염이 아니다 ?
- ESR, CRP는 감염 질환에서만 유용하다 ?
- 항핵항체가 양성이면 전신홍반루푸스다 ?
- HLA-B27 양성이면 강직성척추염으로 진단한다 ?
- 혈청 요산수치가 높으면 통풍이다 ? / 요산수치가 정상이면 통풍이 아니다 ?

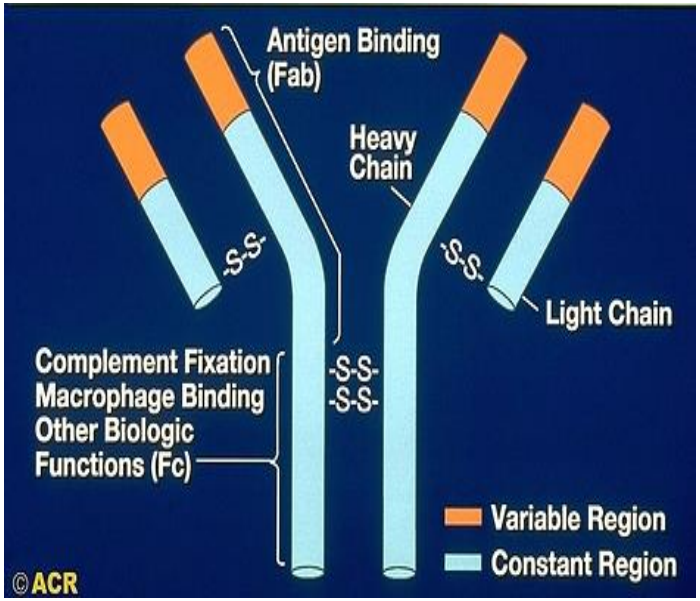
Adopted from prof.Sangil Lee's slide of 2016 KCR 24th training lecture

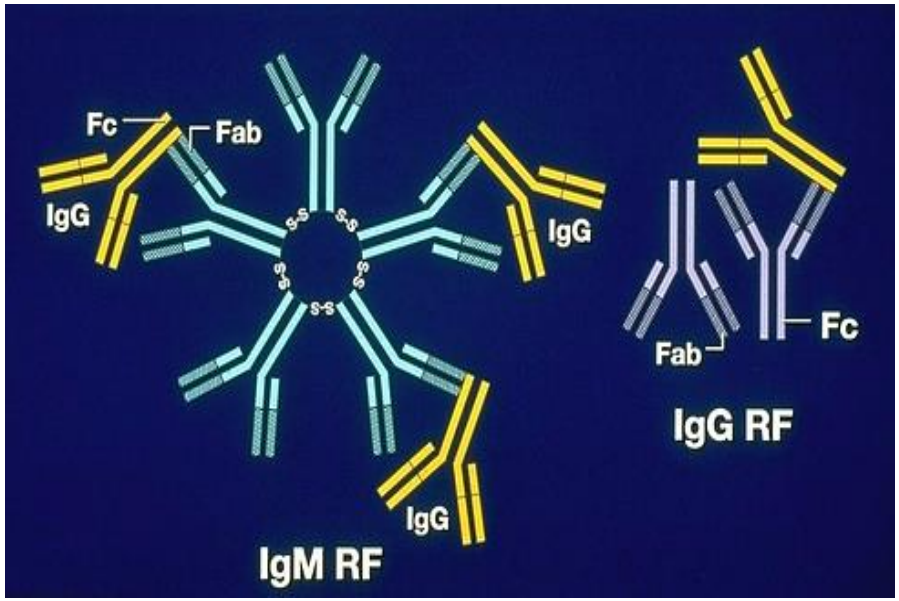
Purpose of laboratory tests

- ✓ Screening
- ✓ Confirming diagnosis
- ✓ Establishing disease stage
- ✓ Determining prognosis
- ✓ Gauging disease activity
- ✓ Following response to treatment
- ✓ Monitoring side effects of drug

Contents

류마티스인자 (Rheumatoid factor; RF) (I)





- Autoantibody that binds to directed to the Fc region of IgG
- The most common RF isotype : IgG, IgM, IgA, in some cases IgD and IgE
- Usually measure IgM

류마티스인자 (II)

- In rheumatoid arthritis (RA)
  - Sensitivity70-80 %, approximately 50% in early RA
  - Far from specific for RA
    - ✓ 류마티스 관절염 환자의 70-80%에서 양성; 20-30%에서 음성
    - ✓ 류마티스인자 음성이라 해서 류마티스 관절염을 배제해서는 안된다
  - Low titer < 3 times UNL; high titer > 3 times UNL
  - Higher titers of RF : More severe disease
    - ✓ 류마티스인자 역가가 높을수록 심한 활막염, 관절 파괴, 관절외증상 (피부결절, 혈관염, 신경병증, 족부궤양 등) 빈도가 높다
    - ✓ 류마티스관절염 환자의 예후 평가 지표로 사용될 수 있다

류마티스인자 (III)

- Incidence of RF in Rheumatic disease other than RA
  - Sjogren's syndrome: 90%
  - Cryoglobulinemia: > 90%
  - SLE: 40%
  - AS: < 15%
  - JIA: 20%
  - Reiter's syndrome: negative
  - Psoriatic arthritis: negative

류마티스인자 (IV)

Condition in non-rheumatic diseases	Frequency of RF (%)
Aging (>age 60)	5 – 25
Infection	Viral infections: HIV, CMV, viral hepatitis, influenza, after vaccination (man yield falsely elevated titers of antiviral antibodies) Parasitic infections: trypanosomiasis, kala-azar, malaria, schistosomiasis, filariasis Chronic bacterial infections: tuberculosis, leprosy, yaws, syphilis, brucellosis, subacute bacterial endocarditis, salmonellosis Neoplasms: lymphoproliferative diseases Other hyperglobulinemic states: hypergammoglobulinemic purpura, cryoglobulinemia, chronic liver diseases, sarcoidosis, other chronic pulmonary diseases
Pulmonary disease	
Miscellaneous diseases	
After multiple immunizations	

* Disorders that may cause symptoms suggestive of rheumatoid arthritis.

Adopted from AJM 1991;91(5):528-534.

류마티스인자 (V)

✓ 류마티스인자가 양성이라고 무조건 류마티스관절염으로 진단하면 안된다

Table 2 Prevalence of RF positivity in health screening subjects and subjects with HBs antigen by age and sex

Age (years)	Men			Women			Health screening subjects	Subjects with HBs antigen	Subjects with anti-HCV (+)
	Total (n = 23,269)	HBV (+) (n = 1,030)	HCV (+) (n = 72)	Total (n = 14,391)	HBV (+) (n = 464)	HCV (+) (n = 60)			
10–30	0	0	–	3.4	0	–	1.7	0	–
31–40	3.1	10.4	8.7	4.1	12.7	28.6	3.5	11.2	8.3
41–50	3.5	9.2	8.8	4.9	20.1	18.2	4.0	12.2	12.5
51–60	4.3	22.6	11.1	4.0	9.5	0	4.2	17.3	6.7
61–70	4.8	14.3	16.7	5.8	20.5	14.3	5.3	17.6	15.4
71–	8.5			7.5			7.9		
Total	3.3	10.2	9.7	4.4	15.5	11.7	3.7	11.8	10.6

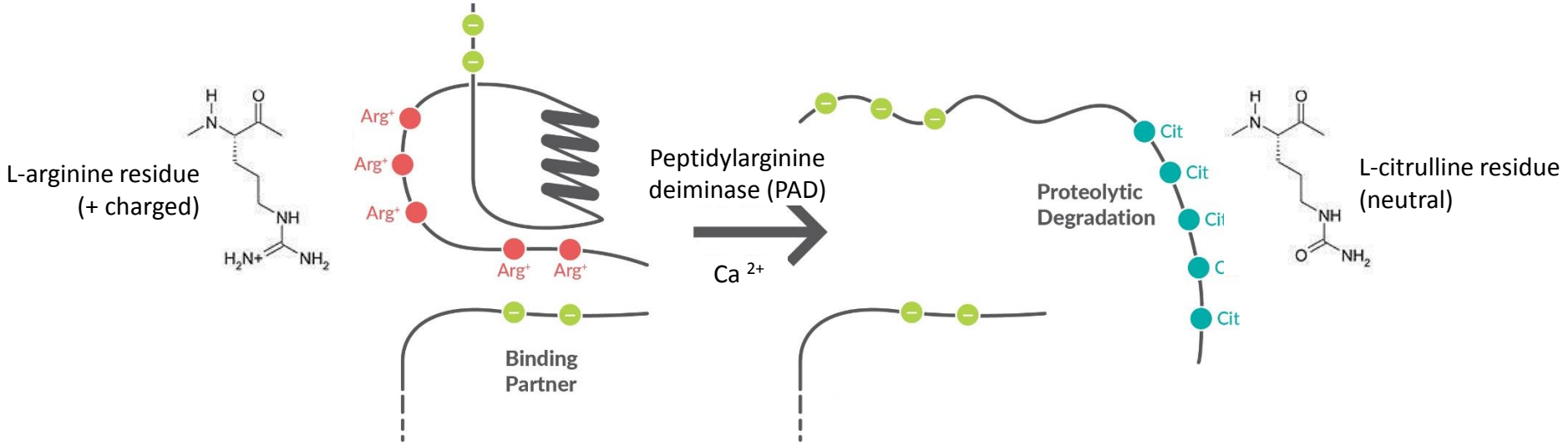
Unless otherwise indicated, values are percentages

HBsAg hepatitis B surface antigen, *HCV* hepatitis C virus

Mod Rheumatol. 2012;22(6):885-91.

항 CCP 항체 (I)

- Antibodies to citrullinated proteins (ACPA)
  - RA 환자가 citrulline 포함하는 peptide/protein에 대한 항체를 가짐 (1998)
- Citrullination
  - Result of deimination of arginine residues by activation of Ca^{2+}-dependent peptidyl-arginine-deiminase enzyme during inflammation-induced cell apoptosis



항 CCP 항체 (II)

- Effort to find out specific autoantibody in RA
  - In 1964, anti-perinuclear factor (APF)
    - Keratohyalin granules in buccal mucosa cells
  - In 1979, anti-keratin antibodies (AKAs)
    - Keratinized tissues of esophagus and cells of human hair follicles
  - In 1993, anti-filaggrin antibodies
    - Keratohyalin granules in terminally differentiated epidermal cells
  - In late 1990s, anti-citrullinated vimentin antibodies (Canada); anti-citrullinated peptide antibodies (Holland and France)
    - Target citrullinated parts of filaggrin (buccal mucosa), keratin (esophagus), vimentin (macrophage), fibrin (joints)
    - Detection of peptidyl-arginine deiminase (PAD)
    - Subsequently (auto)immunogenic

Adapted from Nat Rev Rheumatol. 2017;13(7):443-448.

항 CCP 항체 (III)

- In RA: sensitivity 80%, specificity 98%

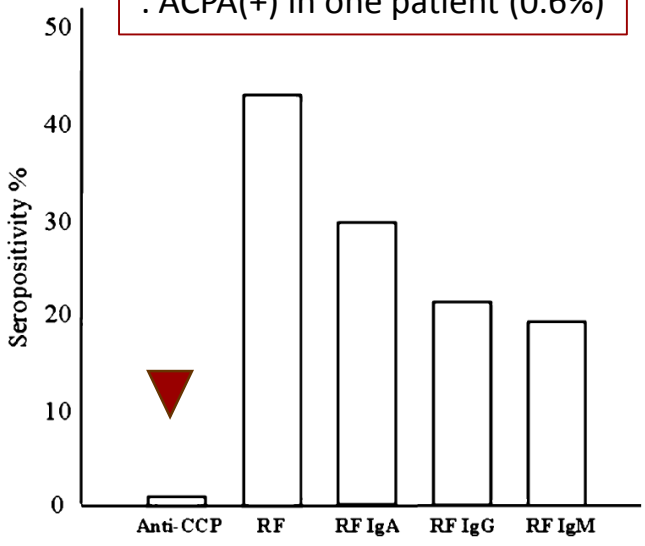
Author (year)	Subjects	Antigens (Methods)*	Sensitivity	Specificity
Simon (1993)	RA 48/control 56	human skin FA (IB)	75%	89%
Schellekens (1998)	RA 134/control 154	CCP (ELISA)	76%	96%
Schellekens (2000)	RA 134/control 154	CCP (ELISA)	68%	98%
	early arthritis 486	CCP (ELISA)	48%	96%
Goldbach-Mansky	arthritis <1 year 238	human skin FA (ELISA)	33%	93%
(2000)	(RA 106/others 122)	CCP (ELISA)	41%	91%
Bizzaro (2001)	RA 98/control 232	CCP (ELISA)	41%	97.8%
Vincent (2002)	RA 240/control 471	rat r-cFA (ELISA)	67%	98.5%
		human r-cFA (IB)	48%	
		CCP (ELISA)	58%	
Suzuki (2003)	RA 549/control 208	CCP (ELISA)	87.6%	88.9%
		human r-cFA (ELISA)	68.7%	94.7%
Rantapää-	RA 83 from blood	CCP (ELISA)	33.7%	98.2%
Dahlqvist (2003)	donors before onset			

Intern Med. 2005;44(11):1122-6.

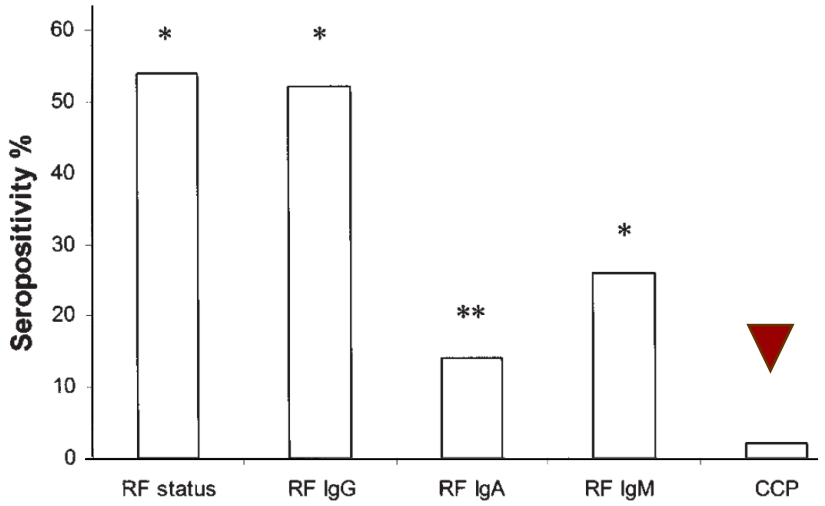
항 CCP 항체 (IV)

✓ 항 CCP 항체는 류마티스관절염에 특이적이다

176 non-arthritic patients with chronic hepatitis B infection
: ACPA(+) in one patient (0.6%)



50 non-arthritic patients with chronic hepatitis C infection
: ACPA weakly positive in one patient



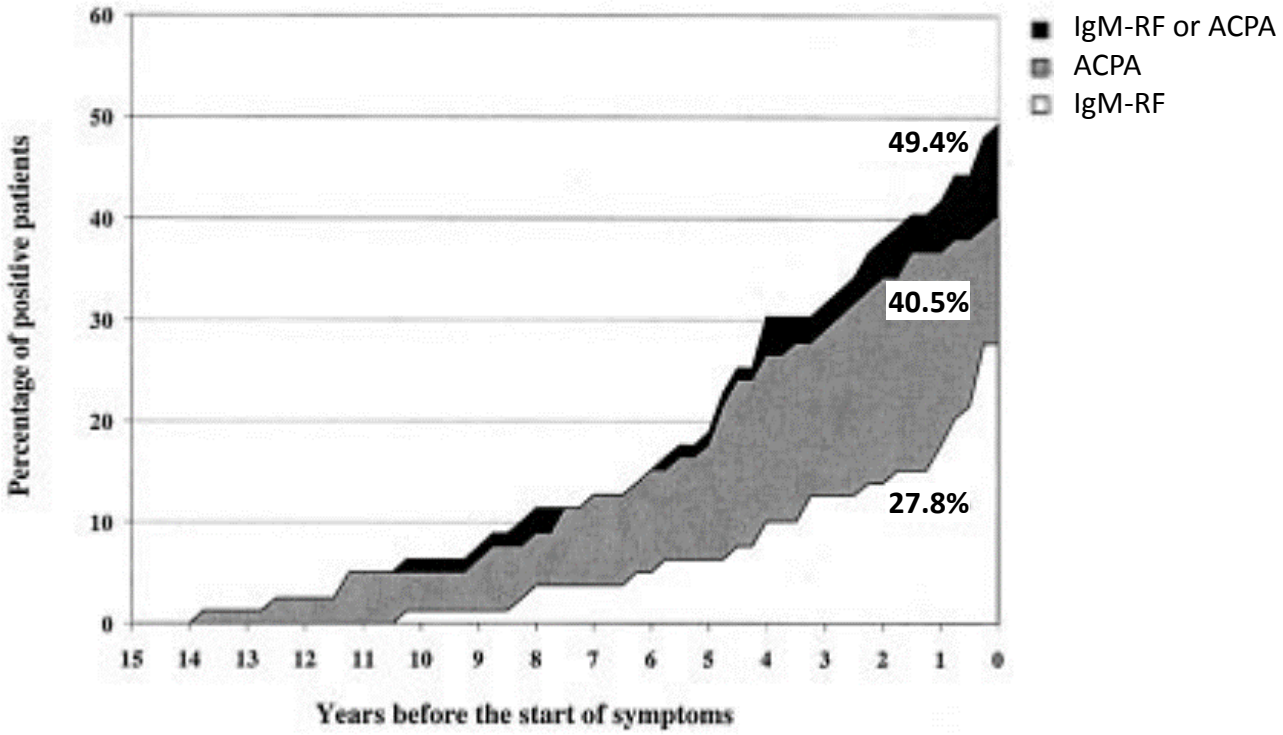
Clin Rheumatol. 2007;26(7):1079-82.
J Rheumatol. 2005;32(3):489-93.

항 CCP 항체 (V)

- Clinical usefulness
  - In the setting of seronegative patients suspected of having RA
    - Among RF-negative RA patients: ACPA-positivity 30-40%
  - In differential diagnosis
    - In patients with other forms of CTD who are RF positive
    - In patients with hepatitis B or C, or other infections

항 CCP 항체 (VI)

Cumulative percentages of patients with 1 or more positive test results for IgM-RF, ACPA, and IgM-RF and/or ACPA before the onset of RA symptoms



Arthritis Rheum. 2004;50(2):380-6.

항 CCP 항체 (VII)

- Implications in RA
  - In early RA, even antedate the onset of inflammatory synovitis
  - Better predictor of erosive disease than RF
    - A positive ACPA + a positive RF IgM

      → strongly with radiographic progression

  ✓ 질병 활성도 모니터를 위해서는 사용하지 않는다

급성기반응물질 (Acute phase reactants;APR)

- Heterogeneous group of proteins produced by hepatocytes
  - Reflection of both acute and ongoing chronic inflammation
  - Rapidly induced in a wide variety of inflammatory conditions including infections, trauma, malignancies, inflammatory rheumatic disorders and certain immune reactions to drug

➢ Positive APR
  - ESR, CRP, fibrinogen, ferritin, serum amyloid protein A, complement

➢ Negative APR
  - albumin, transferrin

✓ 임상적으로 염증 유무와 정도, 치료 반응을 평가하는데 유용하다

적혈구침강속도
Erythrocyte Sedimentation Rate (ESR)

- Rate at which RBC fall in a vertical tube (Westergren or Wintrobe) (mm/h)
  - Indirect measure of the acute phase response, particularly fibrinogen
  - Reference range: (age in years)/2 for men; (age in years + 10)/2 for women

➢ Increased by
  - Inflammatory process (infectious, immunologic, neoplastic, trauma, tissue injury/ischemia)
  - Any other condition that raise serum fibrinogen (diabetes, end stage renal disease, pregnancy), anemia, obesity (due to IL-6)
  - Tilting tube or high room temperature

➢ Lowered by
  - RBC shape change, extreme leukocytosis, hypofibrinogenemia, HF, cachexia
  - Sample clotting, delayed testing (>2hr), low room temperature, short tube

C-반응단백
C-reactive protein (CRP)

- Acute-phase protein of hepatic origin
  - C-polysaccharide of Streptococcus pneumoniae
  - Synthesized in response to tissue injury, depending on a sufficient concentration of inflammatory mediators
  - Rough correction for age, reference range (mg/dL)
    - (age in years)/50 for men; (age in years/50) + 0.6 for women

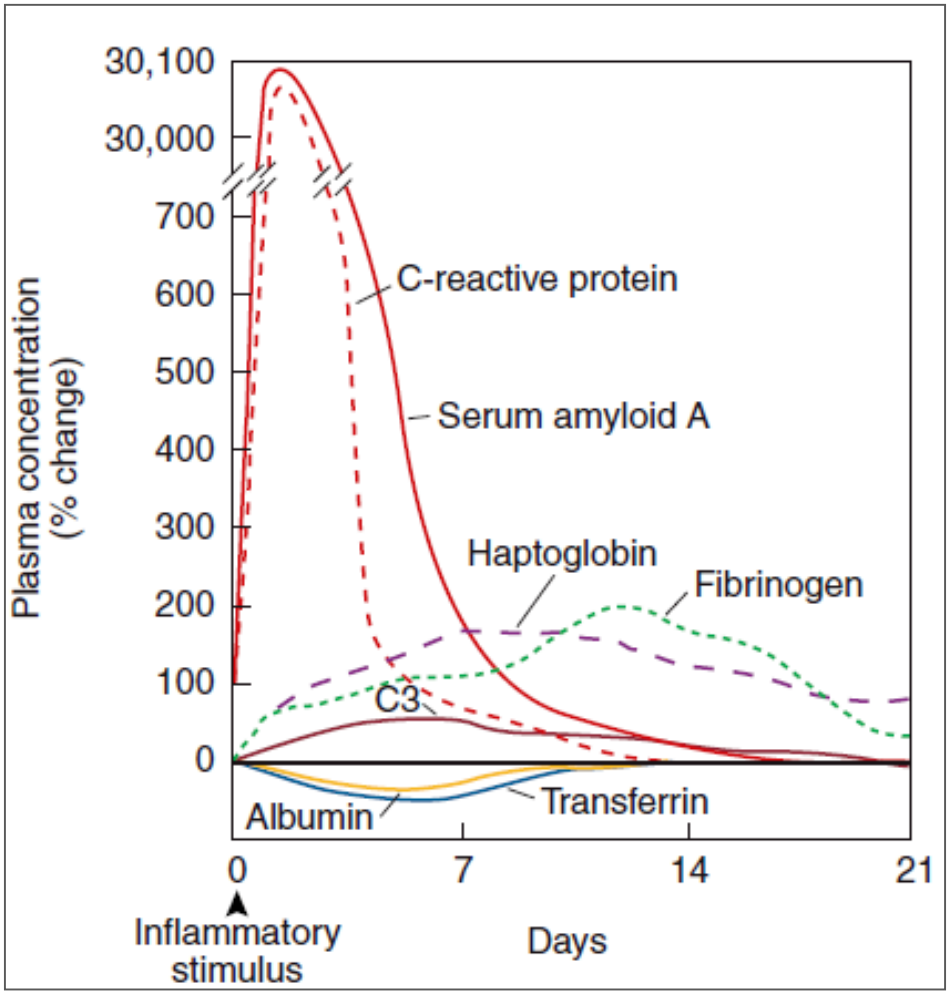
Normal or Minor Elevation (<1 mg/dL)	Moderate Elevation (1-10 mg/dL)	Marked Elevation (>10 mg/dL)
Vigorous exercise	Myocardial infarction	Acute bacterial infection (80%-85%)
Common cold	Malignancies	Major trauma
Pregnancy	Pancreatitis	Systemic vasculitis
Gingivitis	Mucosal infection (bronchitis, cystitis)	
Seizures	Most connective tissue diseases	
Depression	Rheumatoid arthritis	
Insulin resistance and diabetes		
Several genetic polymorphisms		
Obesity		

ESR vs. CRP

- Advantages
  - Familiarity, simplicity

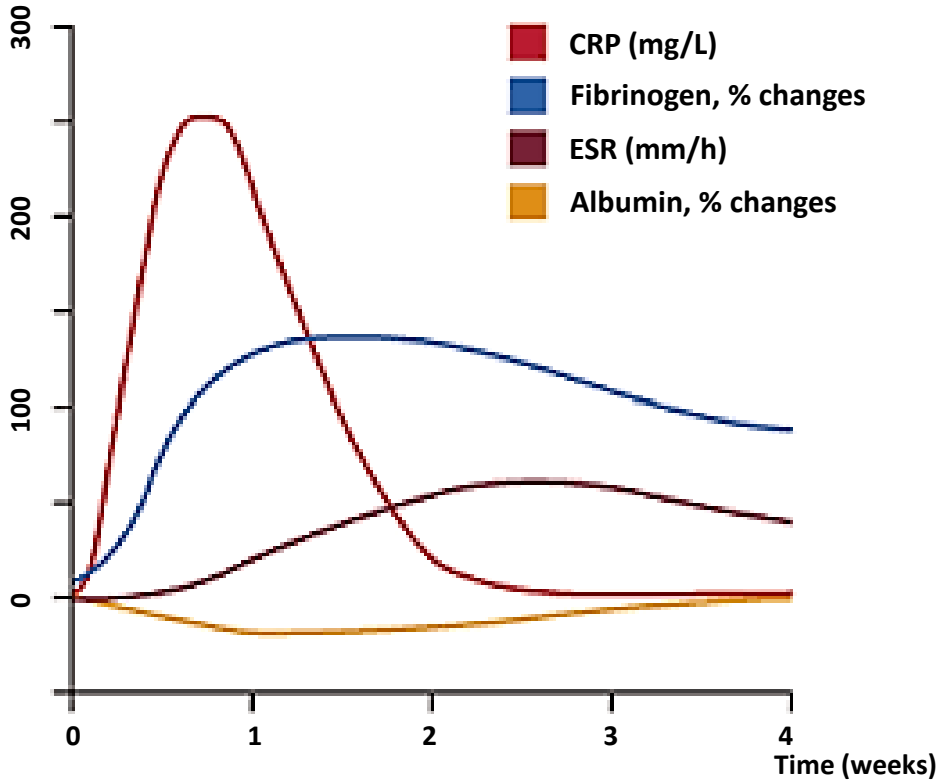
- Disadvantages
  - Indirect measurement
  - Change slowly upon control of inflammation
  - Influenced by RBC morphology and immunoglobulins
  - Increase with age in normal papulation
  - Sex difference (woman >> man)

Comparison of major component (I)



Firestein: Kelley's Textbook of Rheumatology, 8th ed. Figure 52-1.

Comparison of major component (II)



Serum conc. Of CRP goes rapidly up to 1,000 % serum baseline values after an inflammatory stimulus. ESR shows slower, smaller rise and a slower return to normal.

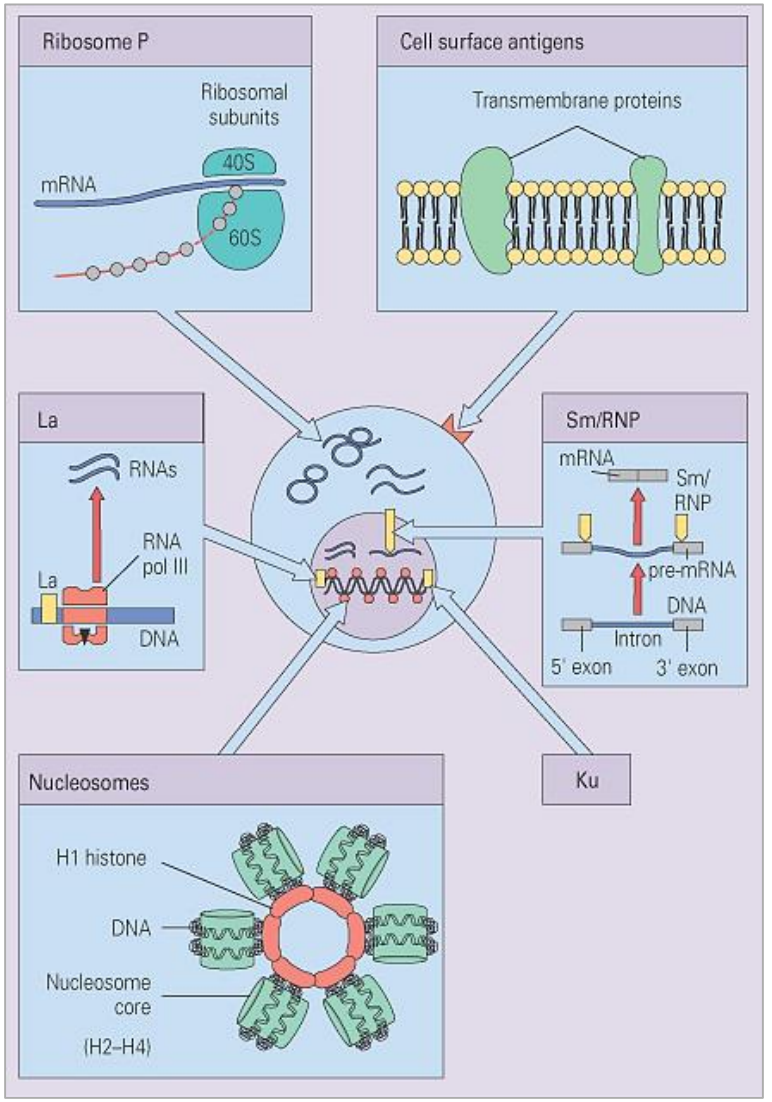
Clinical use of acute-phase reactants

- Measurement of ESR & CRP can be clinically helpful in
  1) Evaluating the extent or severity of inflammation
  2) Monitoring changes in disease activity over time
  3) Assessing prognosis

- In RA
  - Monitoring disease activity and response to therapy, prognostic indicators
  - CRP correlate better with disease activity
- In SLE
  - Many do not show even mild elevation of CRP
  - Substantial CRP elevation : infection >> activation of lupus
  - ESR correlates with disease activity and tissue damage rather than CRP

항핵항체 (Antinuclear antibodies; ANA)

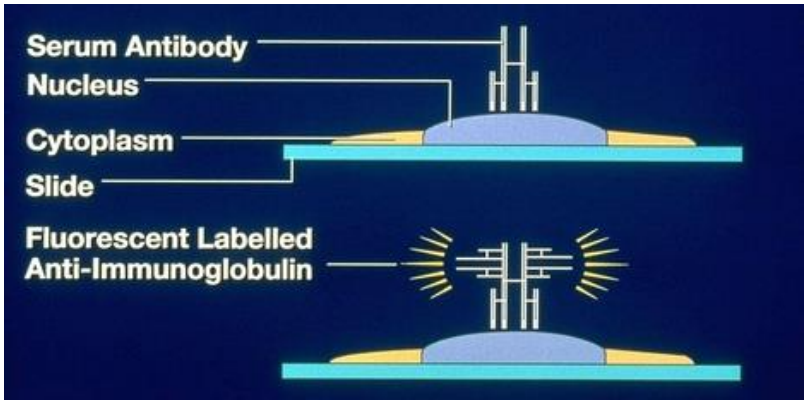
- Cellular autoantigens
- ANA
  - Autoantibodies that react with nuclear components including nucleic acids, histones & components of the centromere



Firestein: Kelley's Textbook of Rheumatology, 8th ed.

간접면역형광법
Indirect immunofluorescence test for ANA

- Reference method of choice for detection of ANA: FANA



- Monolayer of HEp-2 (Human epithelial type 2) cells fixed to glass slides
  - > Overlaid with diluted patient serum
    - > Wash to remove nonadherent immunoglobulins after initial incubation
      - > Incubated with a fluorescein-conjugated anti-human IgG
        - > Wash out to remove unbound fluoresceinated antibodies
          - > Immunofluorescence (ultraviolet)microscopy

FANA (I)

- Sensitive screening methods
  - high sensitivity (95-100%) but lov
  - Normal individuals : Positive at a
    - Usually older and female, or
    - ✓ 항핵항체가 양성인 사람에서

【판독결과】

< Anti-nuclear Antibody Report >

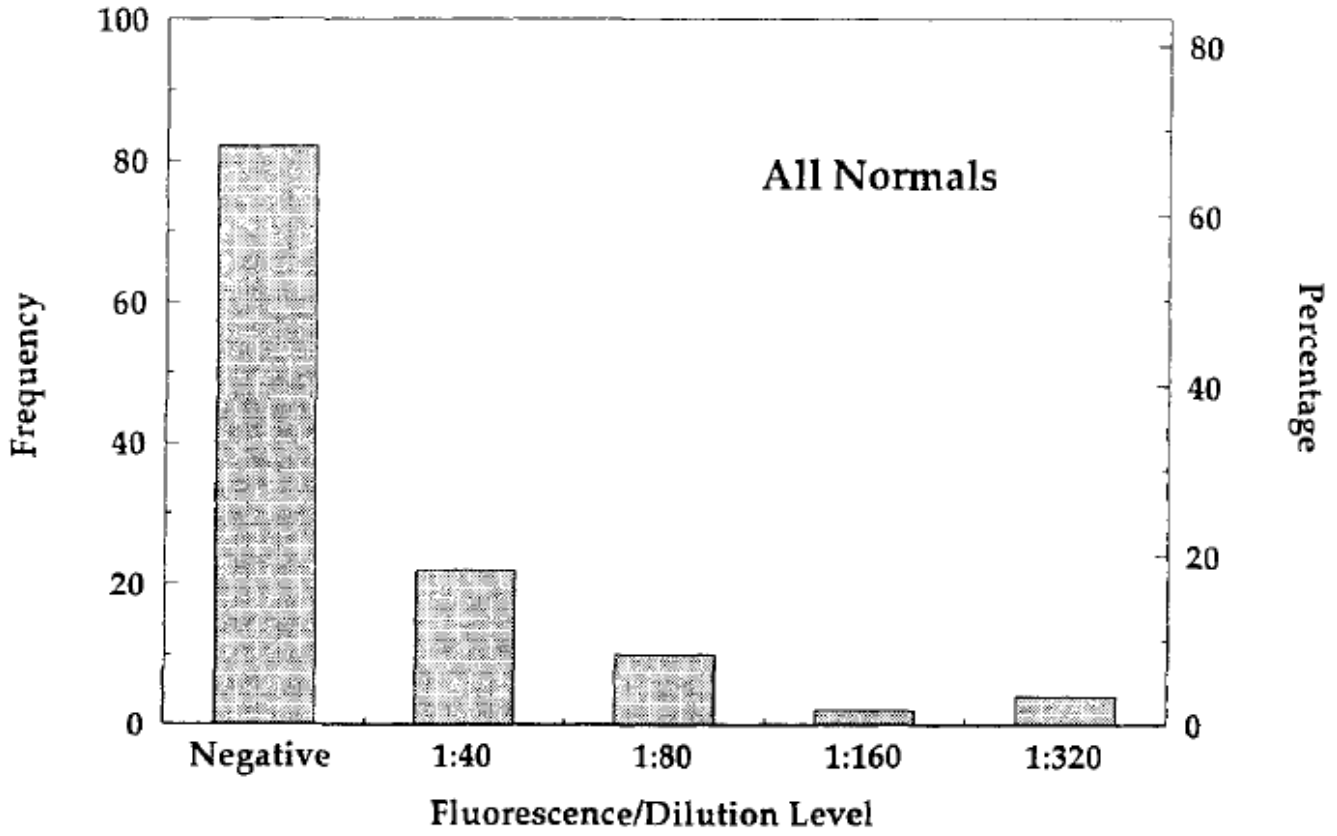
- Result

ANA (qualitative in 1 : 40)	: Positive
Nuclear pattern	: Homogeneous
Intensity (- to 4+)	: 4+
Quantitation (titer)	: 1:640
Cytoplasmic fluorescence	: Negative

- 참고치 : Negative

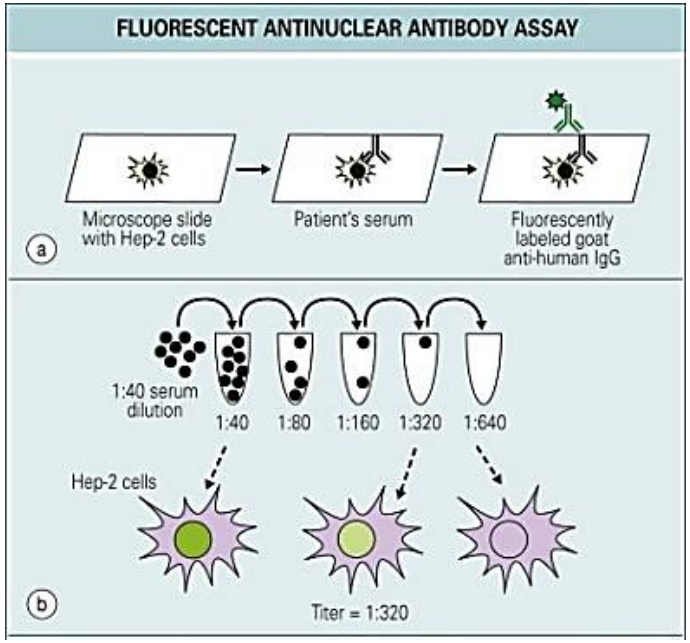
- Reported as pattern and titers
  - Pattern : morphologic descriptors
    - (Diffuse) homogeneous, speckled, centromere, nucleolar, peripheral, etc
  - Titer : 1:40 or greater being considered positive
  - High titer increases the likelihood that the presence of antibodies is related to a disease

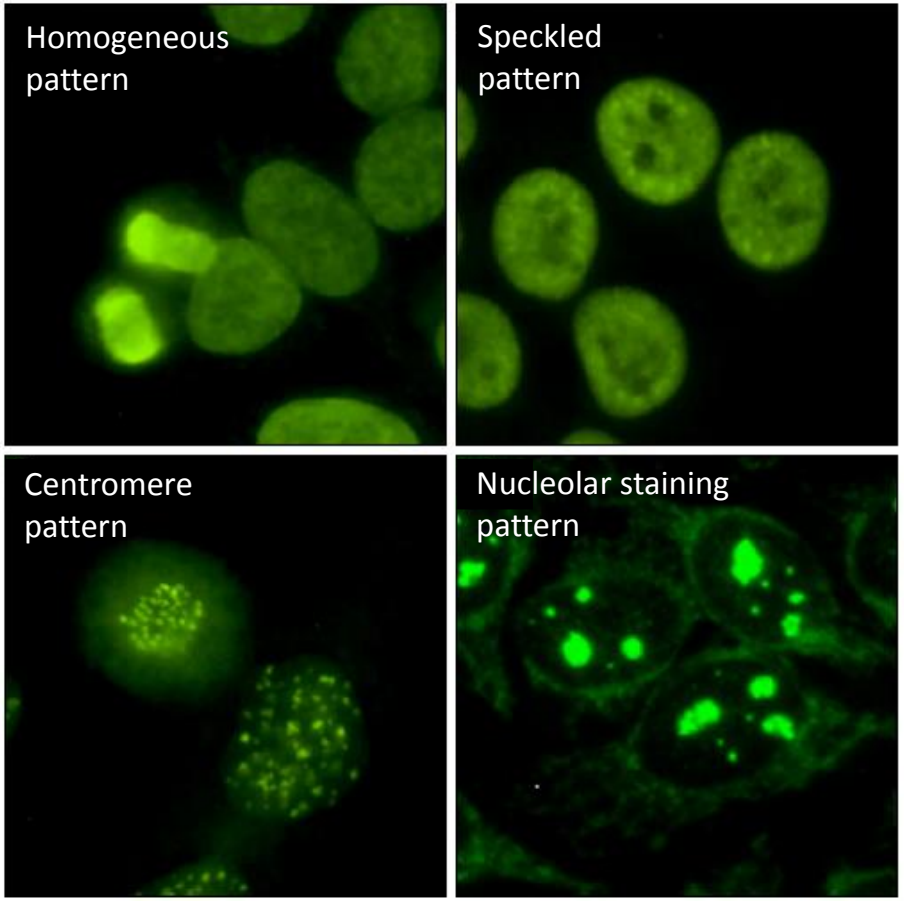
FANA in healthy persons



Arthritis Rheum. 2004;50(2):380-6.

FANA (II)





Firestein: Kelley's Textbook of Rheumatology, 8th ed.
UpToDate.

FANA (III)

Pattern	Nuclear antigen	Clinical association
Homogeneous	Double-stranded DNA	Systemic lupus erythematosus
Diffuse	Histon	Drug reaction Systemic lupus erythematosus
	Topoisomerase I	Systemic sclerosis
Speckled	Extractable nuclear antigen (Sm, RNP)	Mixed connective tissue disease Systemic lupus erythematosus
	Ro-SSA/La-SSB	Sjogren's syndrome
	Other	Poly/Dermatomyositis Various autoimmune disease Infection Neoplasia
Nucleolar	RNA-associated antigen	Systemic sclerosis
Peripheral	Double-stranded DNA	Systemic lupus erythematosus
Centromere	Centromere	Limited systemic sclerosis

Primer on the Rheumatic diseases, 13th edition.

Frequency of FANA

Disease	Sensitivity (%)
Autoimmune disease	
Systemic lupus erythematosus	95-100
Systemic sclerosis	60-80
Mixed connective tissue disease	100
Polymyositis/dermatomyositis	60
Rheumatoid arthritis	50
Rheumatoid vasculitis	30-50
Sjogren's syndrome	40-70
Drug-induced lupus	90
Discoid lupus	15
Juvenile idiopathic arthritis	70
Non-rheumatic diseases	
Hashimoto's thyroiditis	45
Graves' disease	50
Autoimmune hepatitis	50
Primary pulmonary hypertension	40

Rheumatology , 4th edition.

ANA-negative SLE

- Recognized since the 1970s: estimated 5%
  - Occurred by sera tested using rodent and not human tissues as the substrate
  - Subsequent substitution of HEp2 cells (human cell line): even fewer

- Nevertheless, exists on rare occasions
  - In the presence of anti-Ro antibodies
  - Presenting at an early stage of SLE disease
  - SLE patients who have longstanding disease and/or have undergone treatment → may lose ANA reactivity

  ✓ Repeated test using indirect immunofluorescence method with HEp-2 cells in a strong clinical suspicion for SLE and a negative ANA by a solid phase immunoassay

2012 SLICC/ACR classification criteria for SLE

✓ 항핵항체 양성만으로 전신홍반루푸스를 진단할 수 없다

Requirements: ≥ 4 criteria (at least 1 clinical and 1 laboratory criteria)
OR biopsy-proven lupus nephritis with positive ANA or Anti-DNA

Clinical Criteria

1. Acute Cutaneous Lupus*
2. Chronic Cutaneous Lupus*
3. Oral or nasal ulcers *
4. Non-scarring alopecia
5. Arthritis *
6. Serositis *
7. Renal *
8. Neurologic *
9. Hemolytic anemia
10. Leukopenia *
11. Thrombocytopenia (<100,000/mm^3)

Immunologic Criteria

1. ANA
2. Anti-DNA
3. Anti-Sm
4. Antiphospholipid Ab *
5. Low complement (C3, C4, CH50)
6. Direct Coombs' test (do not count in the presence of hemolytic anemia)

†SLICC: Systemic Lupus International Collaborating Clinics

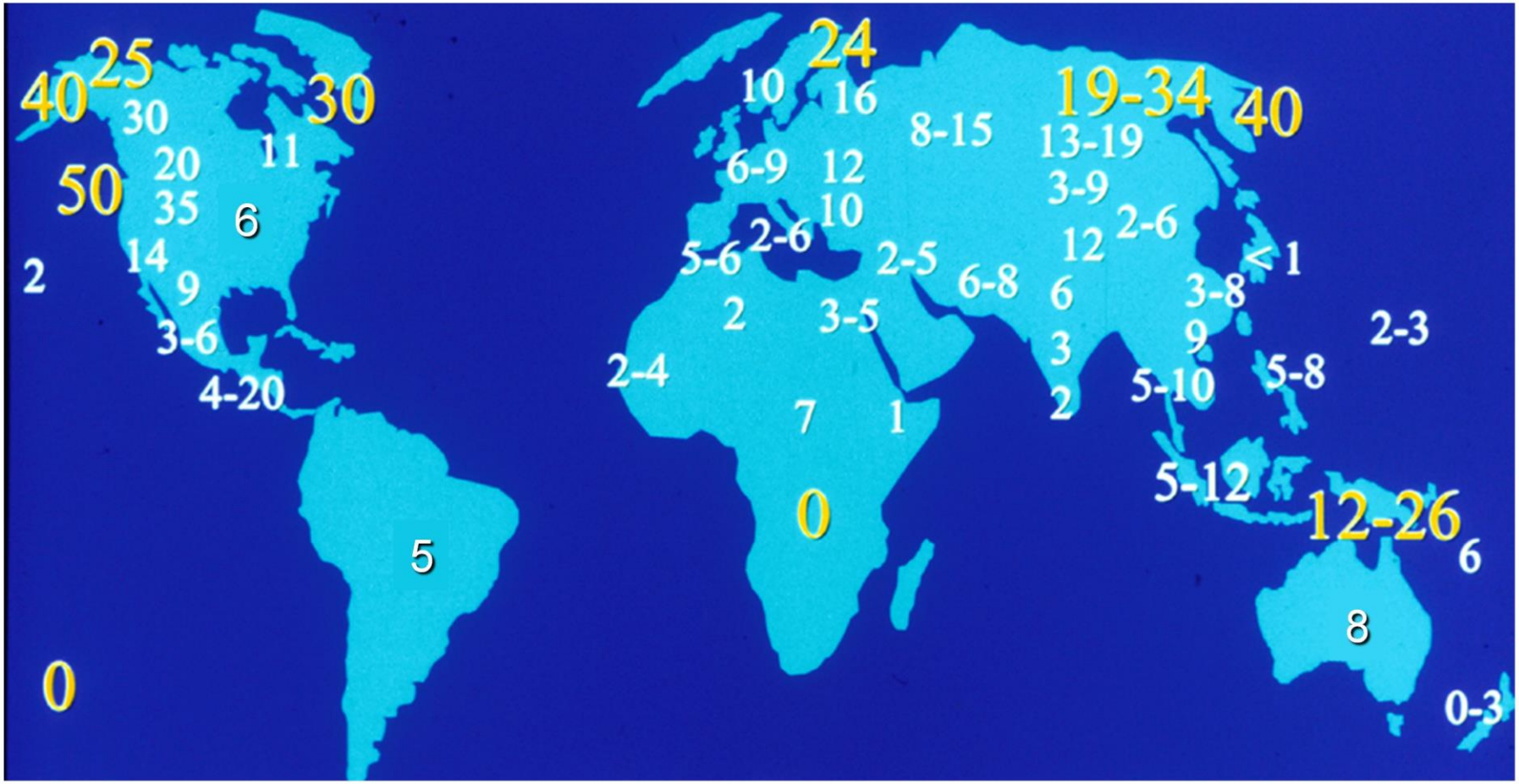
HLA-B27 (I)

HLA: gene complex encoding MHC
- MHC class I: HLA-A, B, C
  - Presenting peptides from inside the cell
- MHC class II: HLA-DP, DM, DO, DQ, DR
  - Presenting antigens from outside of the cell to T-lymphocytes
- MHC class III: encode components of complement system

- Human leukocyte antigen-B27
  - Class I surface antigen encoded by the B locus in the major histocompatibility complex (MHC) on chromosome 6
  - Subtypes B*2701-2759
    - Strongly associated with AS: HLA-B*2702, B*2703, B*2704, B*2705, B*2710
    - Not associated with AS: HLA-B*2706, B*2709

  - ➢ 85-90% of patients with ankylosing spondylitis: HLA-B27(+)
  - ➢ Probability of ankylosing spondylitis
    - In a subject with HLA-B27(+): 1-6%
    - In a subject with HLA-B27(+), who has family member with AS: 10-30%
    - Prevalence closely parallels HLA-B27 frequency in general population

Percentage Prevalence of HLA-B27 in Various Populations of the World



Khan MA Curr Opin Rheumatol 1995;7:263-9
Khan MA J Clin Rheumatol 2008;14:50-2
Khan MA. In Mehra N (Ed). The HLA Complex in Biology and Medicine. New Dehli, India 2010; 422-46.
Reveille J et al. Arthritis Rheum 2012;64:1407-11

ASAS

Ankylosing Spondylitis - Prevalence

Country	AS Prevalence	HLA-B27 Prevalence
US[1, 2]	0.52%	6%
The Netherlands[3]	0.1%	8%
Germany[4]	0.55%	9%
Norway[5]	1.1 – 1.4%	14%
Haida Indians[6]	6.1%	50%

[1]Helmick CG et al. Arthritis Rheum 2008;58:15-25; [2] Reveille JD et al. Arthritis Rheum 2012;64:1407-11; [3]van der Linden S et al. Arthritis Rheum.1984;27:241-9; [4]Braun J et al. Arthritis Rheum 2005;52:4049-50; [5]Gran T et al. Ann Rheum Dis 1985;44:359-67; [6]Gofton JP et al. Ann Rheum Dis 1966;25:525-7

HLA-B27 (II)

- 국내 HLA-B27 유전자 빈도 4.6-6.3%
  - HLA-B*2705: most frequent subtype in AS

JRD 2012;19(2):112-113.

- Genetic risk of AS in general population
  - Identified loci contribute 24% of the risk for developing disease
    - 이 중, 20% 가 HLA-B27 에 의한 것
    - Non-HLA genes: ERAP1 and ERAP2, TNF receptor family (TNFRSF1A, LTBR)
- Genetic influence to AS manifestation
  - Age of onset: 10 years later in B27-negative cases
    - No other genes definitely affect clinical manifestations of AS

✓ HLA-B27 양성만으로 강직척추염을 진단할 수 없다

Brief Funct Genomics 2011;10:249-257.
Nat Genet 2013;45:730-738.
ARD 2009;60:717-727.
ARD 2006;65:775-780.

Inflammatory back pain

	Inflammatory LBP
Age of onset	< 40 years
Type of onset	Insidious
Sx duration	> 3months
Morning stiffness	> 60min
Nocturnal pain	Frequent
Effect of exercise	Improvement
SI joint tenderness	Frequent
Back mobility	Loss in all planes
Chest expansion	Often decreased
Neurologic deficits	Unusual

ASAS Classification Criteria for Axial Spondyloarthritis (SpA)

In patients with ≥3 months back pain and age at onset <45 years

Sacroiliitis on imaging* **plus** **≥1 SpA feature**	**OR**	**HLA-B27** **plus** **≥2 other SpA features**

***Sacroiliitis on imaging**

- **active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA**
- **definite radiographic sacroiliitis according to the modified New York criteria**

SpA features:

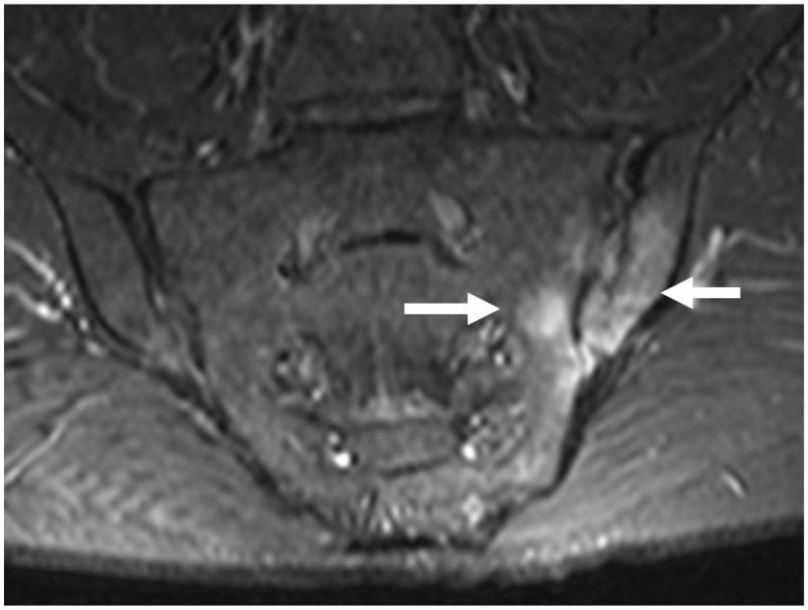
- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

n=649 patients with back pain;

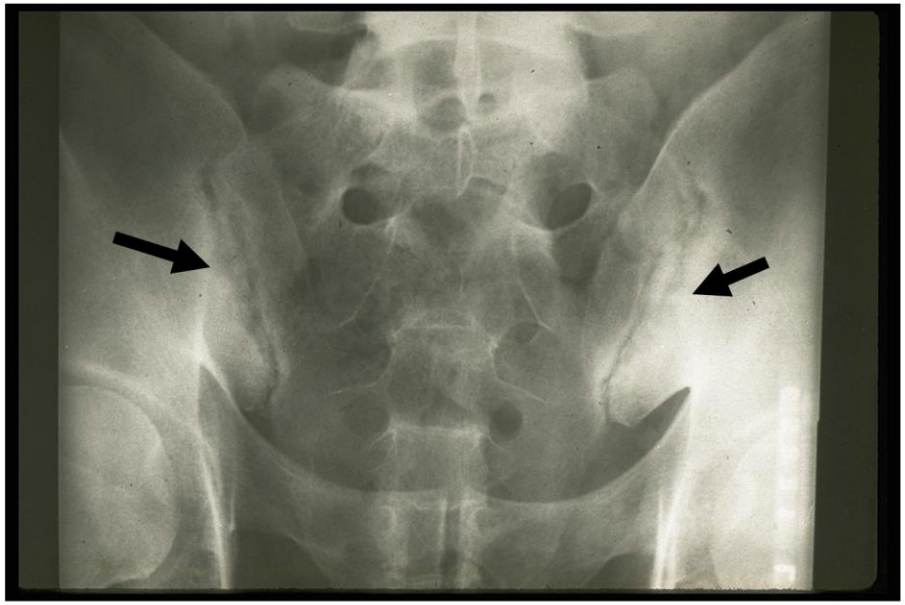
Overall
Sensitivity: 82.9%, Specificity: 84.4%
Imaging arm alone
Sensitivity: 66.2%, Specificity: 97.3%
Clinical arm alone
Sensitivity: 56.6%, Specificity: 83.3%

Rudwaleit M et al. Ann Rheum Dis 2009;68:777-783 (with permission)

Sacroiliitis by MRI and X-ray in Patients with Axial Spondyloarthritis



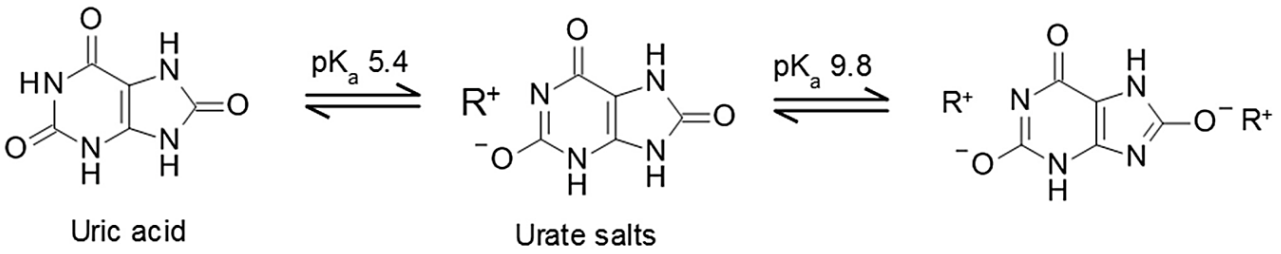
Active inflammatory sacroiliitis without bony changes



Sacroiliitis with bony changes (grade II)

Uric acid

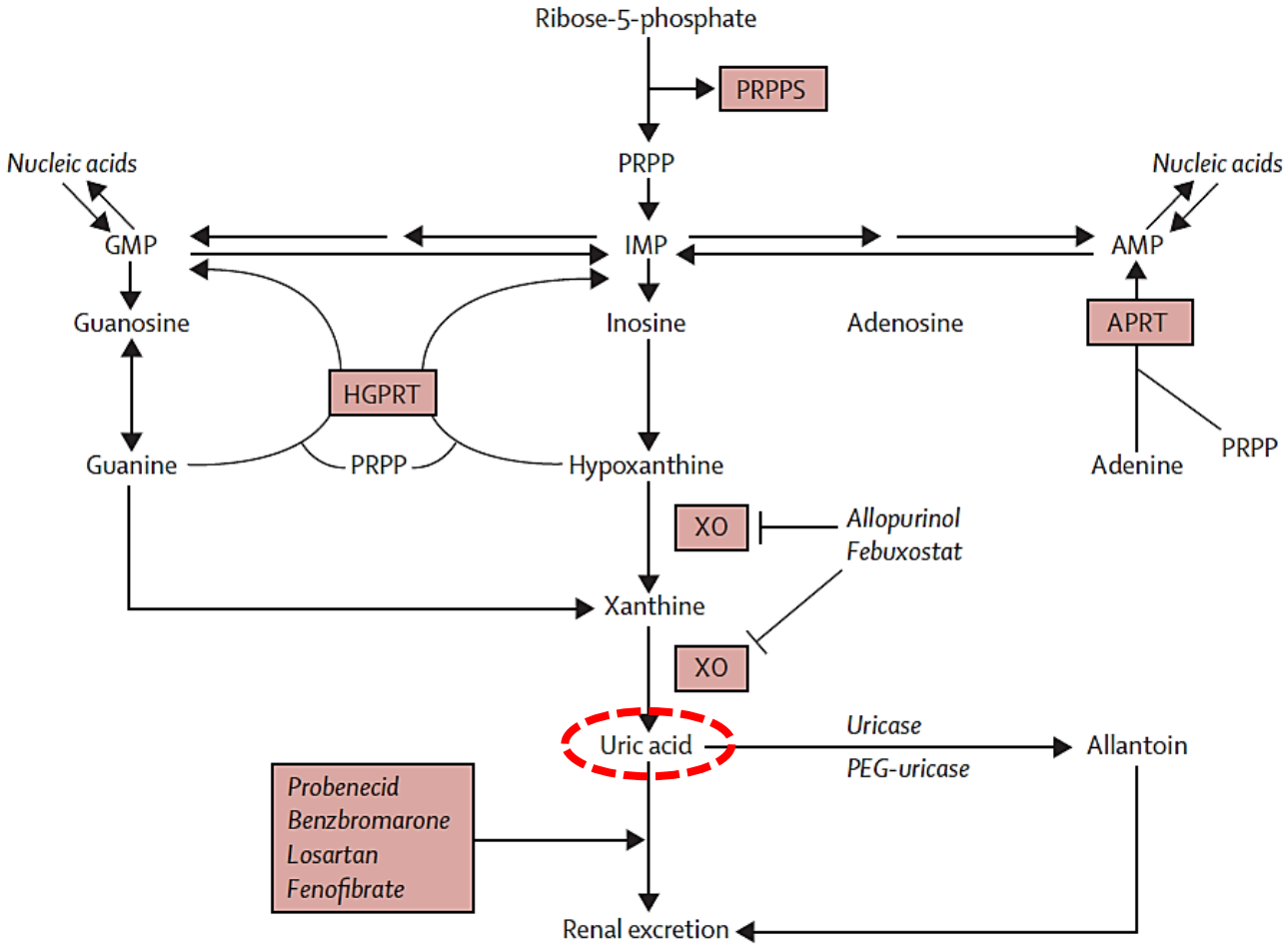
- Diprotic acid with aqueous pKa_1=5.4 and pKa_2=10.3



- In strong alkali (high pH), forms the dually charged full urate ion
- At physiological pH,
  - Predominantly (98-99%) deprotonated urate anion: Uric acid ↔ Urate– + H+
  - Solubility of uric acid: generally 6.8mg/dL at 37℃
    - Reference ranges for serum uric acid
      - 3.5 to 7.2 mg/dL in males → hyperuricemia > 7mg/dL
      - 2.6–6.0 mg/dL in premenopausal females → hyperuricemia > 6mg/dL

Front Med (Lausanne). 2018;5:160.

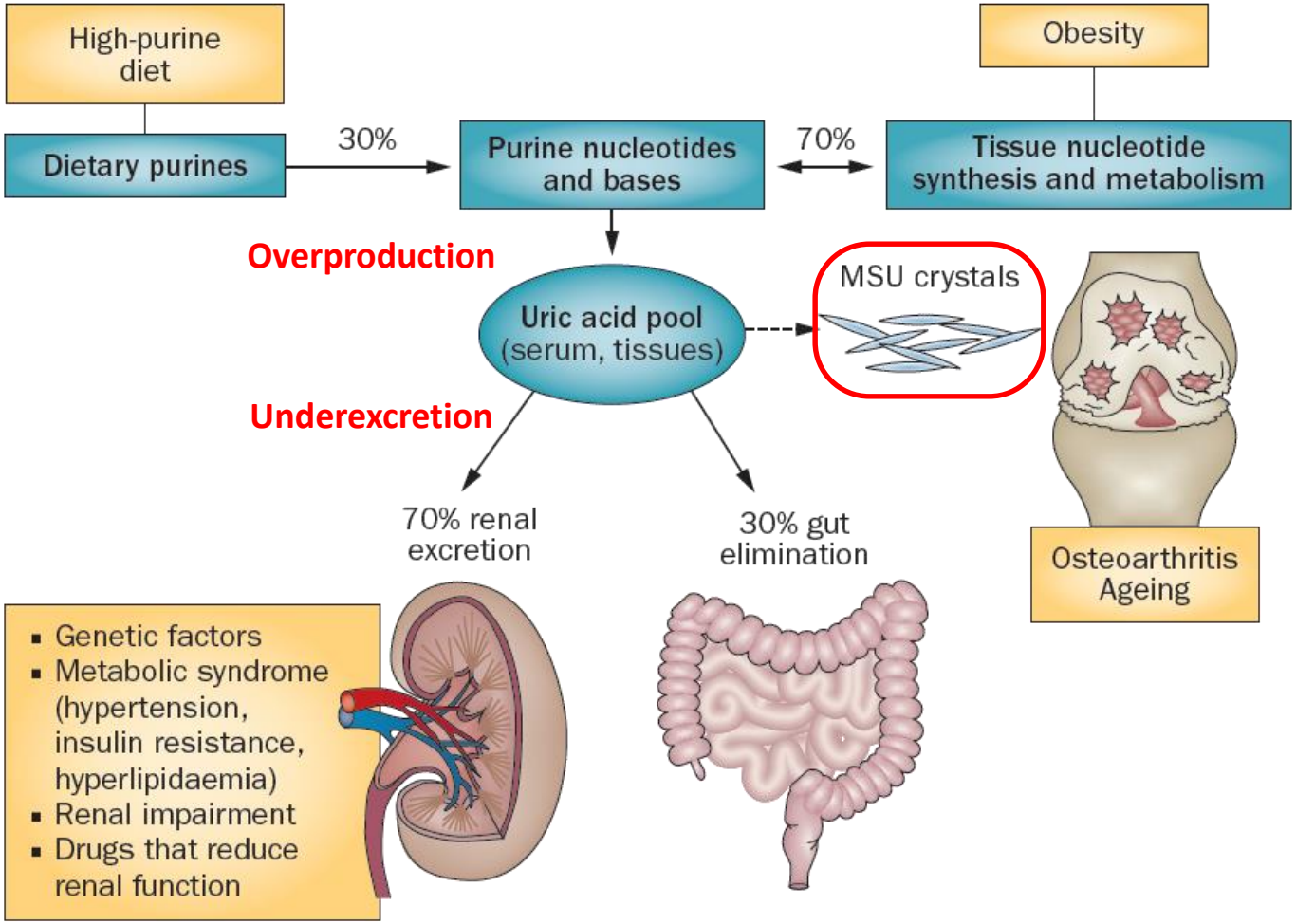
Purine synthesis, salvage, degradation



✓ End product of the metabolism of purine compounds in humans

Lancet 2010; 375: 318–28.

Uric acid pool



✓ Urate overproduction & decreased uric acid excretion, combined mechanism

Nat. Rev. Rheumatol. 2014; 10: 271–283.

Hyperuricemia ≠ Gout ?

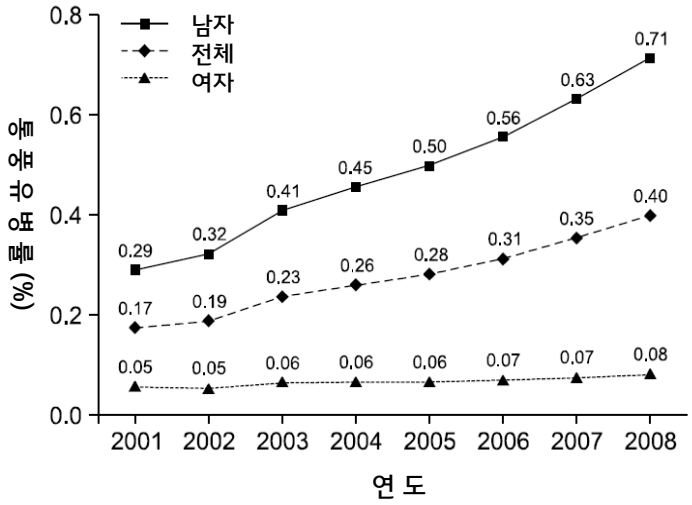
- Gout
  - A clinical disease associated with hyperuricemia
  - Inflammatory reaction caused by the deposition of monosodium urate crystals in and around the tissues of joints
  - Also non-articular (soft tissue) : tophi, urolithiasis

➢ ≈10% of people with hyperuricemia develop gout at some point in lifetime

- The risk of gout depends on the degree of hyperuricemia
  - 7 - 8.9 mg/dL: risk 0.5% per year
  - > 9 mg/dL: risk 4.5% per year
- Up to 20% of patients with gout develop kidney stones

- Can have a normal uric acid during severe attack of gout
- Do not treat asymptomatic hyperuricemia

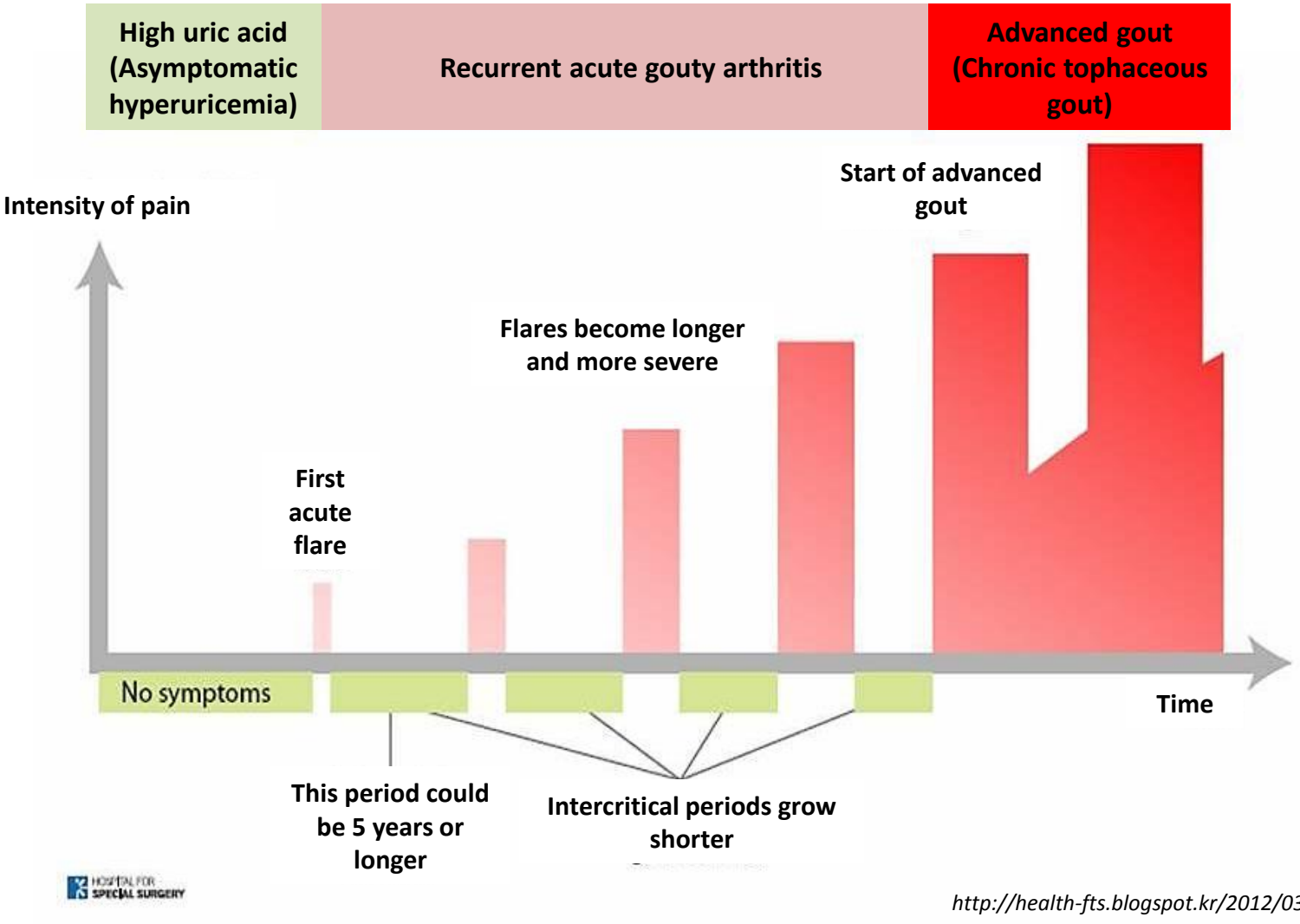
Gout (I)



- Prevalence
  - 인구집단에 따라 2.6% ~ 47.2%
  - 국내 : 2007년 16만 3000명 → 2011년 24만명
    - 5년간 7만 7000명 증가 (47.5%)
    - 연평균 증가율 10.2%

- Hereditary inclination
  - 가족력 빈도 11 ~ 80%
  - 지금까지 밝혀진 유전자는 요산의 신장배설과 관련
    - 유전자 변이로 설명이 가능한 요산 변화 6%
  - 통상적인 통풍 환자에서 유전자 검사시행은 제한적이며 유전성향을 예측할 수 없음

Gout (II)



http://health-fts.blogspot.kr/2012/03/gout.html

Gout (III)

- Who needs treatment (uric acid lowering therapy)?
  - ➢ Patients with gout
  - ~~➢ Patients without gout (asymptomatic hyperuricemic patients)~~

The ACR/EULAR gout classification criteria			
		Categories	Score
Step 1:	Entry criterion (only apply criteria below to those meeting this entry criterion)	At least 1 episode of swelling, pain, or tenderness in a peripheral joint or bursa	
Step 2:	Sufficient criterion (if met, can classify as gout without applying criteria below	Presence of MSU crystals in a symptomatic joint or bursa (ie, in synovial fluid) or tophus	
Step 3:	Criteria (to be used if sufficient criterion not met) ➢ Clinical ➢ Laboratory ➢ Imaging	Maximum possible score in the final criteria Threshold score that classifies an individual as having gout	23 ≥8

Ann Rheum Dis. 2015;74(10):1789-98 & Arthritis Rheumatol. 2015;67(10):2557-68.

The ACR/EULAR gout classification criteria			
Step 3:		Categories	Score
Clinical	Pattern of joint/bursa involvement during symptomatic episode(s) ever	Ankle or mid-foot (as part of monoarticular or oligoarticular episode without involvement of the first metatarsophalangeal joint	1
		Involvement of the first metatarsophalangeal joint (as part of monoarticular or oligoarticular episode)	2
	Characteristics of symptomatic episode(s) ever ▸ Erythema overlying affected joint (patient-reported or physician-observed) ▸ Can't bear touch or pressure to affected joint ▸ Great difficulty with walking or inability to use affected joint	One characteristic	1
		Two characteristics	2
		Three characteristics	3
	Time course of episode(s) ever Presence (ever) of ≥2, irrespective of anti-inflammatory treatment: ▸ Time to maximal pain <24 h ▸ Resolution of symptoms in ≤14 days ▸ Complete resolution (to baseline level) between symptomatic episodes	One typical episode	1
		Recurrent typical episodes	2
	Clinical evidence of tophus Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, located in typical locations: joints, ears, olecranon bursae, finger pads, tendons (eg, Achilles)	Present	4
Symptomatic episodes: periods of symptoms of any swelling, pain, and/or tenderness in a peripheral joint or bursa			

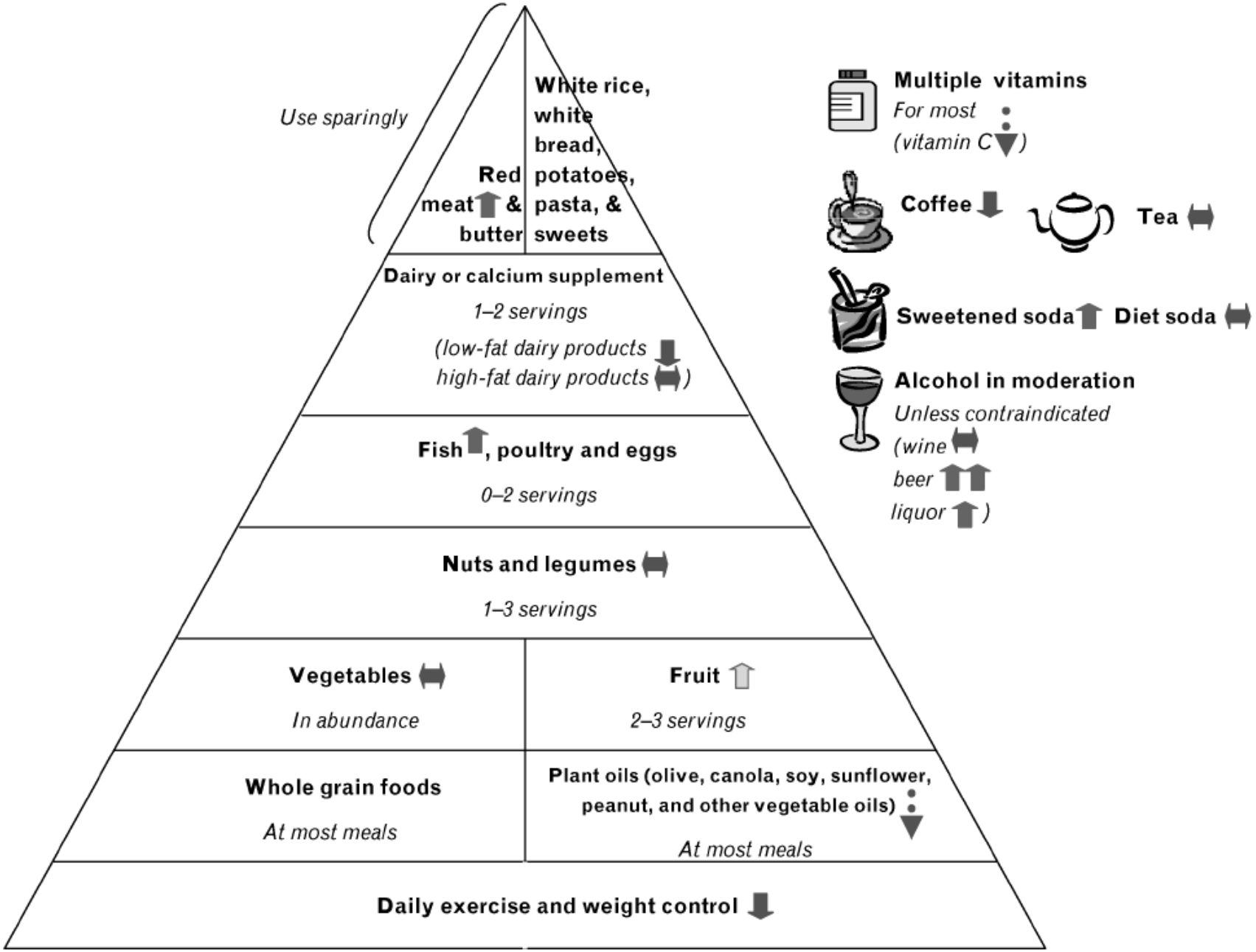
The ACR/EULAR gout classification criteria			
Step 3:		Categories	Score
Laboratory	Serum urate: Measured by the uricase method. Ideally should be scored at a time		

✓ 혈청 요산수치가 높은 것만으로 통풍이라고 진단할 수 없다

✓ 요산수치가 정상이라고 해서 통풍을 배제할 수 없다

	joint or bursa (should be assessed by a trained observer)‡		
Imaging	Imaging evidence of urate deposition in symptomatic (ever) joint or bursa: ultrasound evidence of double-contour sign¶ or DECT demonstrating urate deposition**	Present (either modality)	4
	Imaging evidence of gout-related joint damage: conventional radiography of the hands and/or feet demonstrates at least 1 erosion††	Present	4

Web-based calculator can be accessed at: http://goutclassificationcalculator.auckland.ac.nz
If serum urate level is ≥4 mg/dL – >6 mg/dL (≥0.24 – <0.36 mmoles/liter), score this item as 0.
If polarizing microscopy of synovial fluid from a symptomatic (ever) joint or bursa by a trained examiner fails to show monosodium urate monohydrate (MSU) crystals, subtract 2 points.
If synovial fluid was not assessed, score this item as 0.
If imaging is not available, score these items as 0.



Nat. Rev. Rheumatol. 2014; 10: 271–283.

경청해 주셔서 감사합니다