PARACLINIC In SLE

Importance of Paraclinic in SLE

Essential to make the diagnosis

Crucial in the follow up of patients

Serologic Abnormalities

Autoantibodies

CIC

Hypocomplemntemia

Hyperglobuline

Hypoalbuminemia

Elevation of ESR and CRP

Hargreaves ' description

- **Hargreaves ' description of the lupus erythematosus (LE) cell phenumenon (phagocytosis of relatively intact nuclear material by polymorphonuclear leukocytes) in 1948 was the first evidence that systemic lupus erythematosus (SLE) is an autoimmune disease .**

- **This was followed by the discovery that certain antinuclear antibodies (ANAs) were specific for DNA and/or histones .**

- **The discovery by Tan and Kunkel in 1966 that anti-Smith (anti-Sm) antibodies are specific for SLE**

LE Cell

Hargreaves LE Phenomenon 1948

First serologic marker in diagnosis of SLE

replaced by ANA Test

ANA

- **Useful screening test**
- **If negative patient has < 3% chance to have SLE**
- **Not diagnostic for SLE**

ANA Test

The standard technique is immunofluorescence (FANA)

Substrate is of very importance in FANA

Using Hep-2 sensitivity is 95%

Specifcity is low for SLE

In diluted serums sensitivity decreases and specificity increases

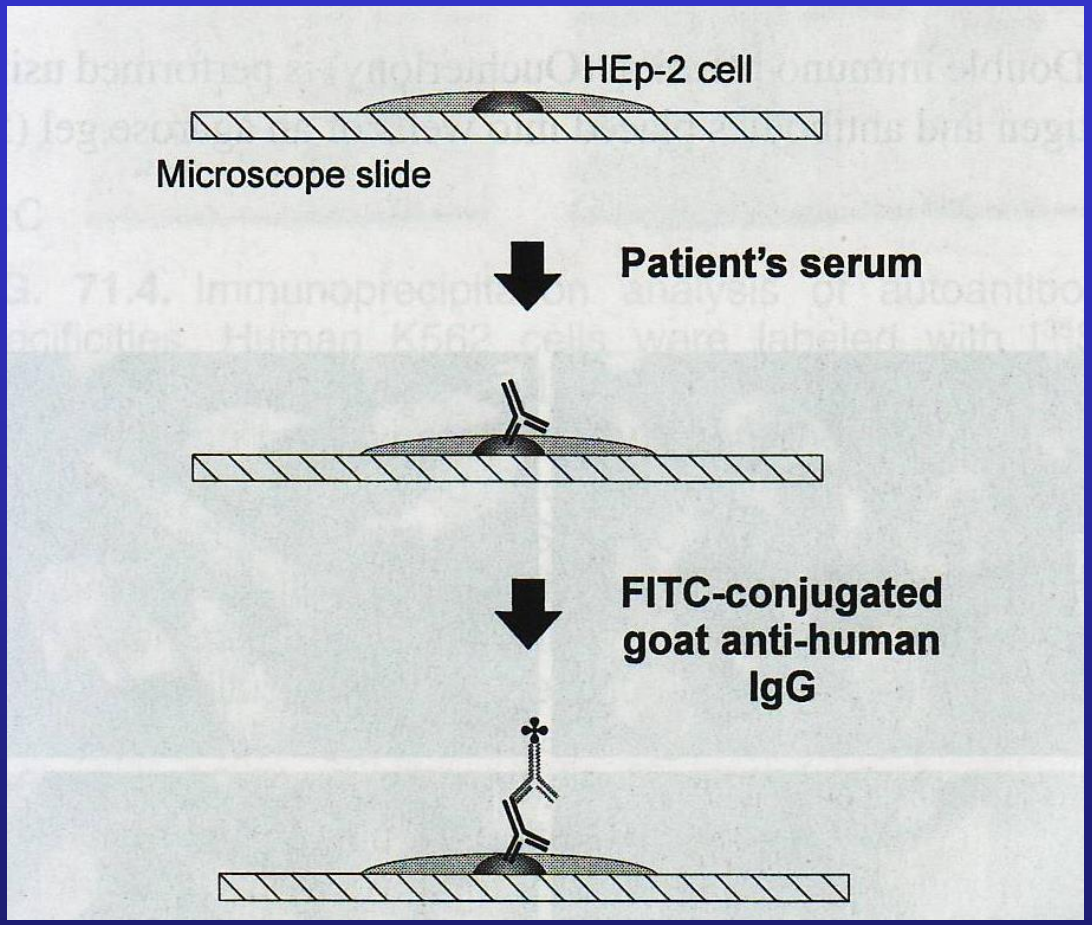
Optimal dilution is 1/160

The optimal balance between sensitivity and specificity is at a serum dilution of about 1:160.

With 1/40 30% of population are ANA positive

With 1/160 3% of population are ANA positive

FANA



Fluorescent antinuclear antibody technique. Adherent human cells (HEp-2 or HeLa) are grown on a microscope slide or coverslip until about two-thirds confluent.

They are fixed with methanol and incubated with medium containing bovine calf serum to block nonspecific sticky sites.

The cells then are incubated sequentially with diluted serum from a patient, followed by fluorescent isothiocyanate (FITC) conjugated goat antihuman IgG antibodies.

The slides are washed and viewed using an epifluorescence microscope equipped with an FITC filter.

Disadvantage of FANA

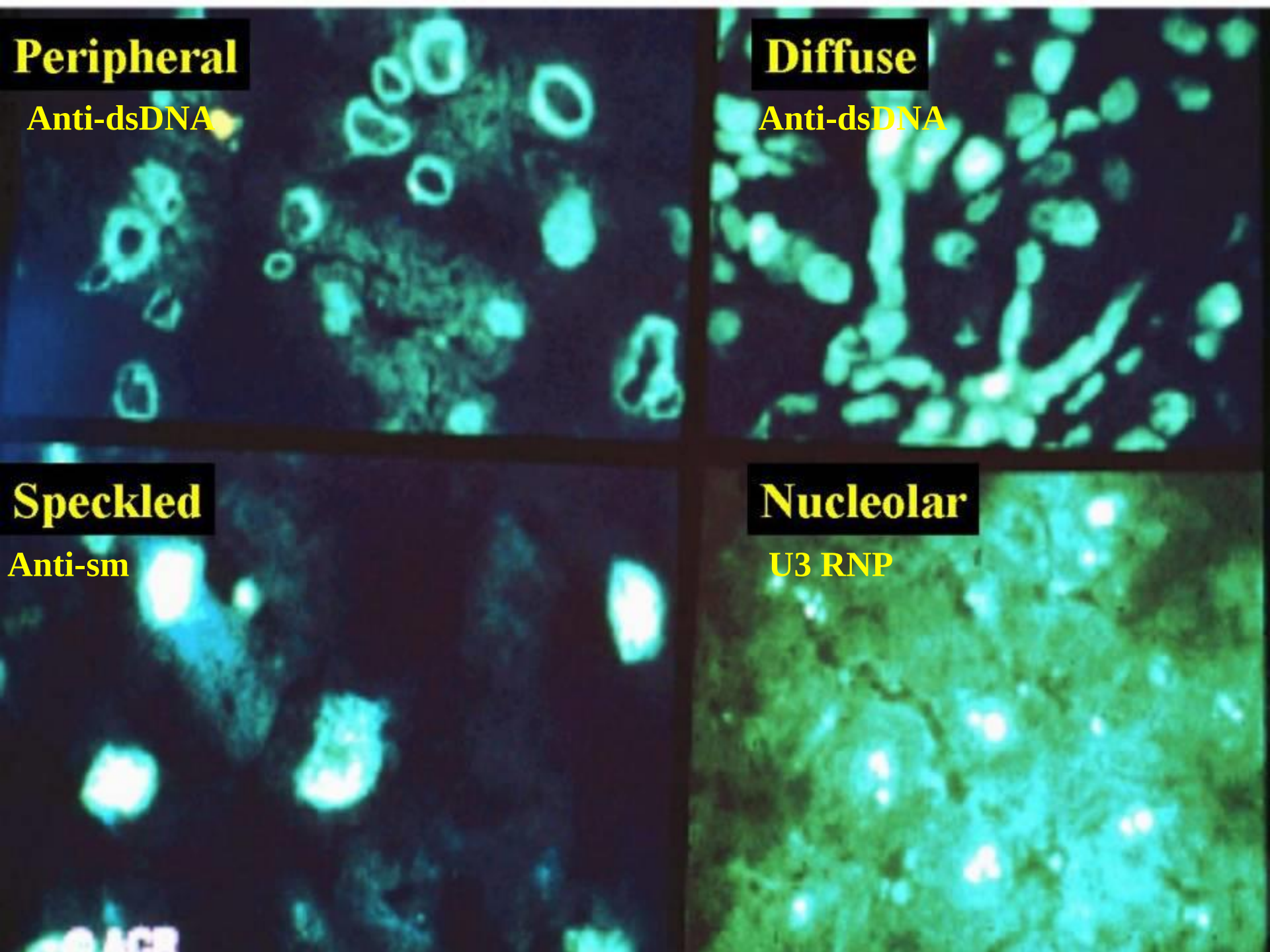
Interpretation of FANA depennds on the experience observer-dependent.

There is diference in the results between laboratories interlaboratory variability.

interlaboratory coefficients of variation ranged from 36% at a 1:320 dilution to 51% at a 1:40 dilution

Distinguishing between negative and postive is subjective

Nevertheless, the test can discriminate normal individuals from those with SLE, scleroderma, or Sjogren's syndrome most of the time.


Peripheral
Anti-dsDNA
Diffuse
Anti-dsDNA
Speckled
Anti-sm
Nucleolar
U3 RNP

ELISA

ELISA is the alternative technique

Sensitive but with high false positive rate

Enzyme-linked Immunosorbent Assays

- **ELISA is a simple, rapid, and sensitive approach used widely for screening .**

Plastic wells of a microtiter plate are coated with a purified antigen

and diluted test serum added,

followed by enzyme-labeled antiimmunoglobulin antibodies.

Binding of the labeled antibody is detected by adding a substrate for the enzyme, forming a colored product .

The product is quantified by determining absorbance in a spectrophotometer.

- **In view of their high sensitivity, ELISA must be standardized carefully to avoid measuring non specific binding.**

COMPARISON
ELISAS WITH THE FANA TEST

In one of six ELISAs with the FANA test,
the results difered substantially , although others have reported good agreement .

Further studies are needed to determine the utility of these tests, but it is difficult at present to recommend discarding the standard, but more labor-intensive, fluorescent ANA test.

ANA negative SLE

With human substrate 90% of ANA negative become ANA positive

AntiRO and AntiLa may be positive

Have DLE or SCLE

Have antiphospholipid syndrome

Early disease

Due to drugs

Lupus-like disease associated with complement deficiency

Truly ANA negative

SLE = 2%

Anti ds DNA

Highly characteristic for SLE

Prevalence in SLE is 60 to 70%

%Prevalence in SLE with active nephritis is 50 to 75

95% specific for SLE

At any given time about half of SLE patients are positive

High titers accompanied with low complement predict flare of disease

But some patients with no symptoms persistently have high titers

RECIPROCAL PATTERN

High titers accompanied with low complement predict flare of disease

But some patients with no symptoms persistently have high titers

Anti-dsDNA

60-70 %.

It may predict relapses as early as 10 weeks before a flare . Serial (prospective) measurement of anti-dsDNA may preferable to measuring C3 or C4 levels.

Moreover, treatment with prednisone as soon as a significant rise in the anti-dsDNA antibody level is documented by Farr assay may prevent relapse¸ .(is controvers)

Anti sm Antibody

discovered by Tan and Kunkel in 1966

like anti-dsDNA, also are virtually pathognomonic

Depending on ethnicity

Is present in 30%

Is considered specific for SLE

Has considerable diagnostic value

Is associated with mild CNS and renal disease

There is little evidence that either anti-nRNP or anti-Sm antibodies cause disease.

anti-Sm antibodies in other diseases,

Although there are reports of anti-Sm antibodies in other diseases, including schizophrenia and uveitis ,

There also are unverified reports that anti-Sm antibodies are associated with an increased frequency of Raynaud's phenomenon and mild renal or central nervous system disease .

disease activity constant levels

Although not as dramatic as the changes in levels of anti-DNA antibodies, it has been suggested that anti-Sm or nRNP antibody levels may reflect disease activity.

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However, it is widely accepted that once anti-nRNP or anti-Sm antibodies develop, they remain at relatively constant levels and do not disappear during periods of disease quiescence, unlike anti-DNA antibodies .

Anti Ro/SSA and Anti La/SSB

Strongly correlated with

ANA-negative SLE

Lupus-like syndrome

Neonatal Lupus syndrome

Is useful in diagnosis of ANA-negative SLE

1982 CLASSIFICATION CRITERIA SLE

Serositis
Oral ulcers
Arthritis
Photosensitive rash

Blood dyscrasias
Renal disorder
ANA
Immunologic disorder
Neurologic disorder

Malar rash
Discoid rash

Anti-DNA *or*
Anti-Sm *or*
LE cell

** SLE if 4 of 11 present serially or simultaneously

Sensitivity & specifity=96% in iran90%

Adapted from Hochberg MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 40:1725, 1997. Sensitivity & specifity=96% in iran90%

Malar rash	
Discoid rash	
Photosensitivity	
Oral ulcers	
Arthritis	
Serositis	
Renal disorder	
Neurologic disorder	
Hematologic disorder	
Immunologic disorder	
	Anti-DNA—antibody to native DNA in abnormal titer, *or*
	Anti-Sm—presence of antibody to Sm nuclear antigen, *or*
	Positive finding of antiphospholipid antibodies
ANA	