Rheumatoid Arthritis and Erythrocyte Sedimentation Rate (ESR)

PRACTICAL

IMMUNOLOGY

Lect- 2

Rheumatoid Arthritis

Rheumatoid Arthritis is a chronic systemic inflammatory disease of undetermined etiology involving primarily the synovial membranes and articular structures of multiple joints. The disease is often progressive and results in pain, stiffness, and swelling of joints. In late stages, deformity and ankylosis develop. Women are affected more than men, with a female: male ratio of 3:1; the disease onset reaches its apex between 35 and 50 years.

Causes

- **Genetic**: Certain **HLA-DR4** molecules associated with RA (e.g. **HLA-DR beta *0401, 0404, or 0405**); in addition, **HLA-DR1** (**HLA-DR beta *0101**) carries this shared epitope and confer risk, particularly in certain southern European areas.

- **Environmental:** for many decades, numerous infection agents have been suggested to induce RA. Among these are Mycoplasma organisms, Epstein Barr virus, rubella virus, cytomegalovirus and herpes virus.

- **Hormonal:** Sex hormones may play a role, as evidenced by the disproportionate number of females with RA, its amelioration during pregnancy, its recurrence in the early postpartum period, and its reduced incidence in women using oral contraceptives. Hyperprolactinemia may be a risk factor for RA.

pathophysiology
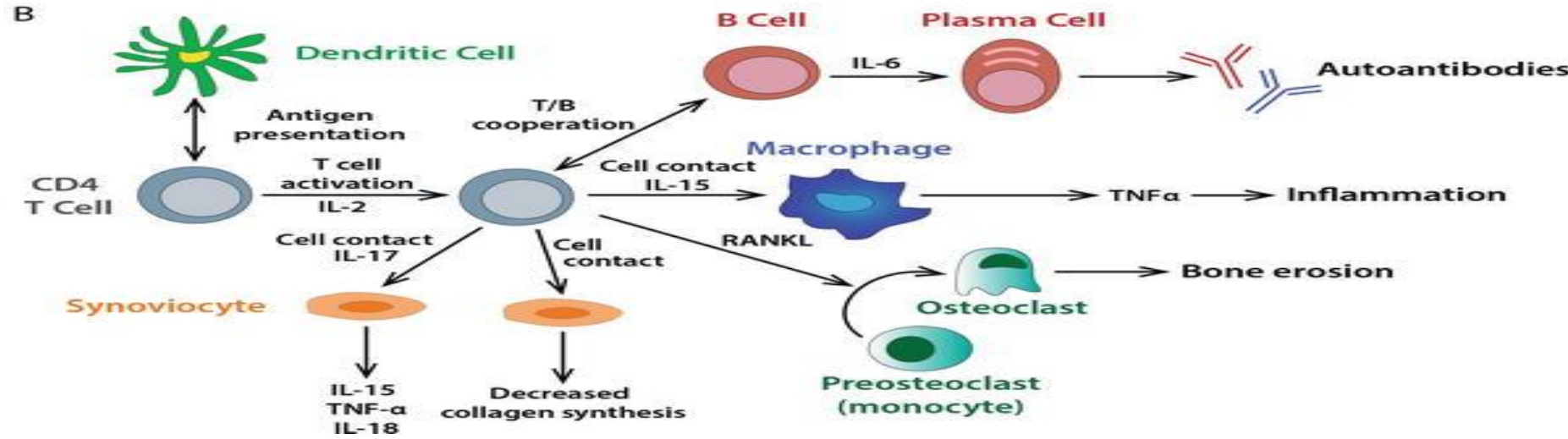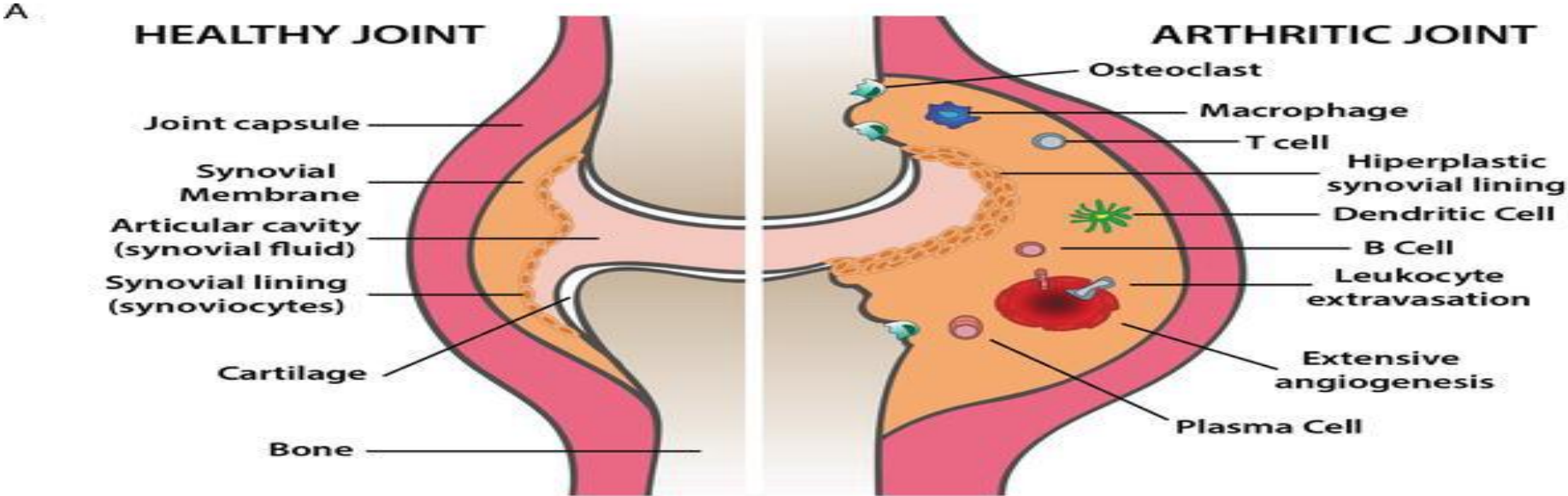
Laboratory diagnosis

- A. **Synovial fluid analysis**

1. Inflammatory synovial fluid (WBC count > 2000/μL) is present with WBC counts generally from 5,000-50,000/μL.

2. Usually, neutrophil predominance (60-70%) is observed in the synovial fluid(in contrast with mononuclear cell predominance in the synovium). Because of a transport defect, the glucose levels of pleural, pericardial, and synovial fluids in patients with RA are often low compared to serum glucose levels.

Laboratory diagnosis

B. **Immunological diagnosis** include autoantibodies (e.g., **RF, anti-RF33 (nuclear antigen), anti-CCP, ANA)**.

1. **Rheumatoid factor(RF)** refers only to the IgM antibody which binds aggregated IgG as antigen. During the first year of illness, rheumatoid factor is more likely to be negative with some individuals converting to seropositive status over time. RF is also seen in other illnesses, for example Sjögren's syndrome, Hepatitis C, chronic infections and in approximately 10% of the healthy population, therefore the test is not very specific.

2. **Anti-cyclic Citrullinated peptide** (**anti-CCP**) is the highly sensitivity (90-96%) for RA, can identify RA years before symptoms develop and is the most specific test for RA.

3. **Antinuclear antibodies** (**ANA**) are present in approximately 30% of patient with RA. This test is not routinely performed in the early disease.

4. **C-reactive protein (CRP)** for acute active arthritis.

Laboratory diagnosis

C. Hematological tests

1. Complete blood count (CBC) indicate the presence of anemia in normocytic and

normochromic.

2. Thrombocytosis may be present.

3. Erythrocyte sedimentation rate (ESR) is elevated inapproximately 90% of

patient with RA. This test is not routinely performed in the acute setting .

Introduction

Erythrocyte Sedimentation Rate (ESR) is a common hematological test for non specific detection of inflammation that may be caused by infection, some cancers and certain autoimmune diseases.

- **ESR** can be defined as a measurement of the rate at which the RBCs (erythrocytes) settle from the plasma in anticoagulated blood.

- It measures the amount of inflammation in your body.

- It is non specific test, meaning that it does not tell your doctor exactly where the inflammation is occurring in the body, or what is causing it, and also because it can be affected by other conditions besides inflammation. Thus, ESR is typically used in conjunction with some other tests.

• It is used an initial screening tool and also as a follow up test to monitor therapy and progression or remission of disease.

• **ESR** is helpful in diagnosis of two specific inflammatory diseases: temporalarteritis and polymyalgiarheumatica.

• The ESR test is easy to perform and inexpensive.

ESR
Erythrocyte Sedimentation Rate

plasma

Erythrocyes separated from blood sample

RBCs

Before

After 1 hour

Introduction

However , new studies have reported the following as normal ESR test results:

- Women under age 50 should have an ESR under 20 mm/hr.

- Men under age 50 should have an ESR under 15 mm/hr.

- Women over age 50 should have an ESR under 30 mm/hr

- Men over age 50 should have an ESR under 20 mm/hr.

- Newborns should have an ESR under 2 mm/hr.

Introduction

- ESR is determined by the interaction between factors that promote (fibrinogen) and factors that resist (negative charge of RBC)sedimentation.

- Normally, RBCs settle down slowly as they do not form rouleaux. Instead, they gently repel each other due to the negative charge on their surface.

- Rouleaux are stacks of many RBCs that become heavier and settle down faster.

- Plasma proteins ,especially fibrinogen, adhere to the red cell membranes and neutralize the surface negative charges, promoting cell adherence and rouleaux formation

Mechanism

ESR is directly proportional to the weight of the cell aggregate sand inversely proportional to the surface area.

•RBCs sediment by rouleaux formation, the RBCs aggregate one on the top of each other which will increase the speed of sedimentation. When an inflammatory process is taking place in the body ,the high proportion of fibrinogen in the blood causes RBCs to stick on each other. The RBCs form stacks called "rouleaux" which settle faster. Rouleaux formation canal so occur in association with some lymphoproliferative disorders in which one or more immunoglobulins are secreted in high munts.
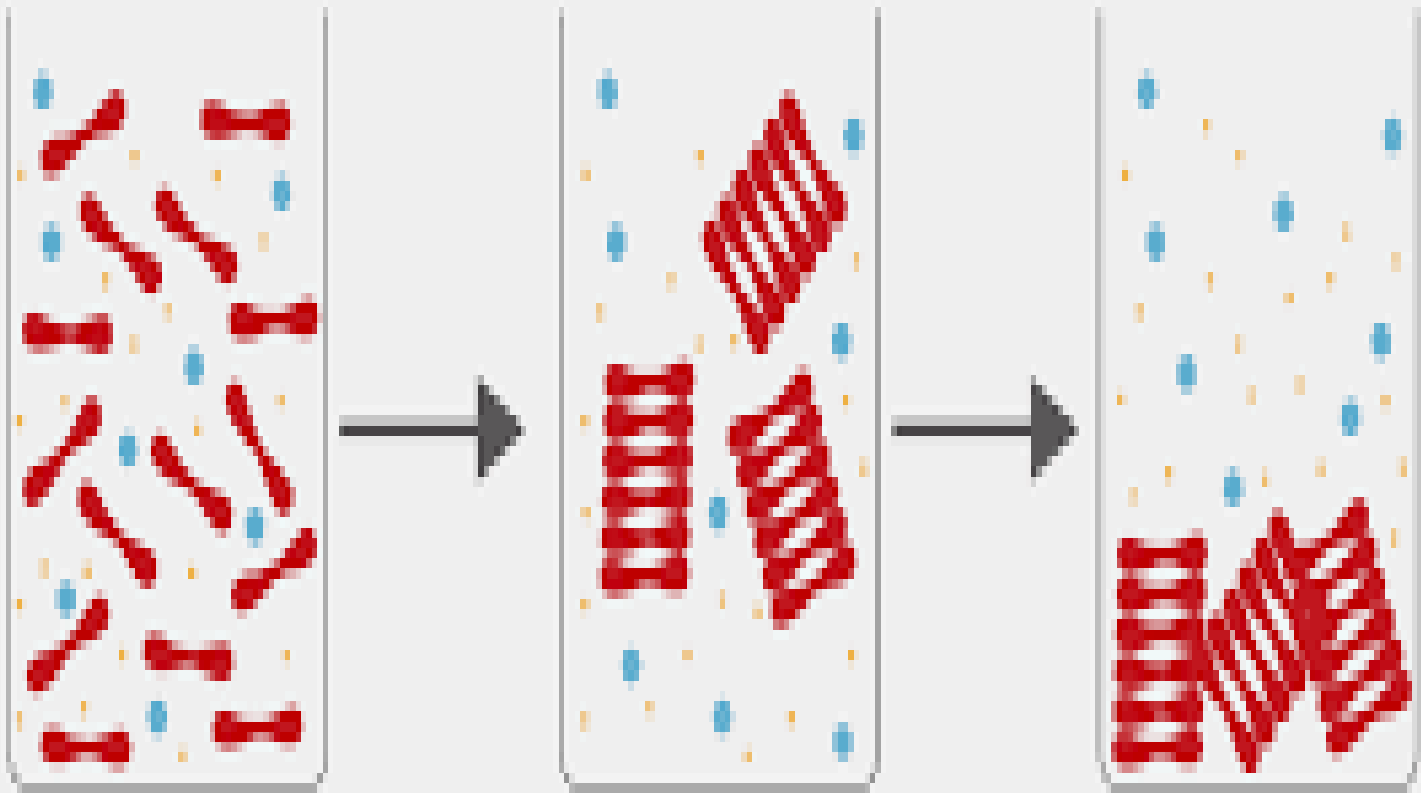
Rouleaux formation   Settling   Packing

3 stages of sedimentation

Principle of ESR

- When anticoagulated blood is allowed to stand in a narrow vertical glass tube, undisturbed for a period of time, the RBCs–under the influence of gravity settle out from the plasma. The rate at which they settle is measured as the number of millimeters of clear plasma present at the top of the column after one hour(mm/hr). This mechanism involves *three stages:*

- **Stage of aggregation**
- It is the stage of rouleaux formation/ aggregation. It occurs in the first 10-15min.
- **Stage of sedimentation**
- It is the stage of actual RBCs sedimentation, it occurs at constant rate. This occurs in 30-40 minutes out of 1 hr.
- **Stage of packing**
- This is the final stage and is also known as stationary phase. In this stage, there is as lower rate off alling during which packing of sedimenting RBCs in column occurs due to over crowding. It occurs in final10 minutes in 1 hour

Westergren Method

Widely used method for ESR estimation. **It is the method that we are going to use into day lab.**

WintrobeMethod

•Also used for ESR determination. Wintrobe tube is smaller than Westergren tube.

Procedure of Westergren Method

- Put 0.4 cc of Sodium Citrate in a plain test tube.
- Withdraw 2 cc of blood from the patient vein using a syringe.
- Immediately, add 1.6 cc of blood from the syringe in the plain tube and shake the tube for 2 min to ensure a good mixing of blood with Sodium Citrate.
- Fill the Westergren pipette exactly to 0 mark, make sure that there are no air bubbles at all in the blood.
- Place the pipette vertically on the rack and leave it undisturbed for 60 min. Avoid any vibration to the tube and do not expose it to a direct sunlight.
- At the end of the 60 min, read the number of millimeter the RBCs have fallen (i.e the height of clear plasma above the upper limit of the column of the sedimentating cells).
- Read the results in mm/hr.

An elevated ESR may be found in

1. Pregnancy (after the third month).

2. Acute and chronic infections.

3. Rheumatic fever.

4. Rheumatoid arthritis.

5. Myocardial infection.

6. Nephrosis.

7. Acute hepatitis.

8. Menstruation.

9. Tuberculosis.

10. Hypothyroidism.

11. Hyperthyroidism.

A decreased ESR will be present in:

1. Polycythemia.

2. Congestive heart failure.

3. Hypofibrinogenemia.

4. The presence of red blood cell abnormalities (poikilocytosis, spherocytes, and sickle cells).