SAWA UNIVERSITY

# اسم المادة و الكورس

## HEREDITARY SPHEROCYTOSIS


جامعـــــــة ســـــــــاوة الاهلية

Sawa University

كليـــــة التقنيـــات الصحيـة والطبيـة

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المرحلـــــــــــــة .....الثالثة..

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محاضرة رقم 10

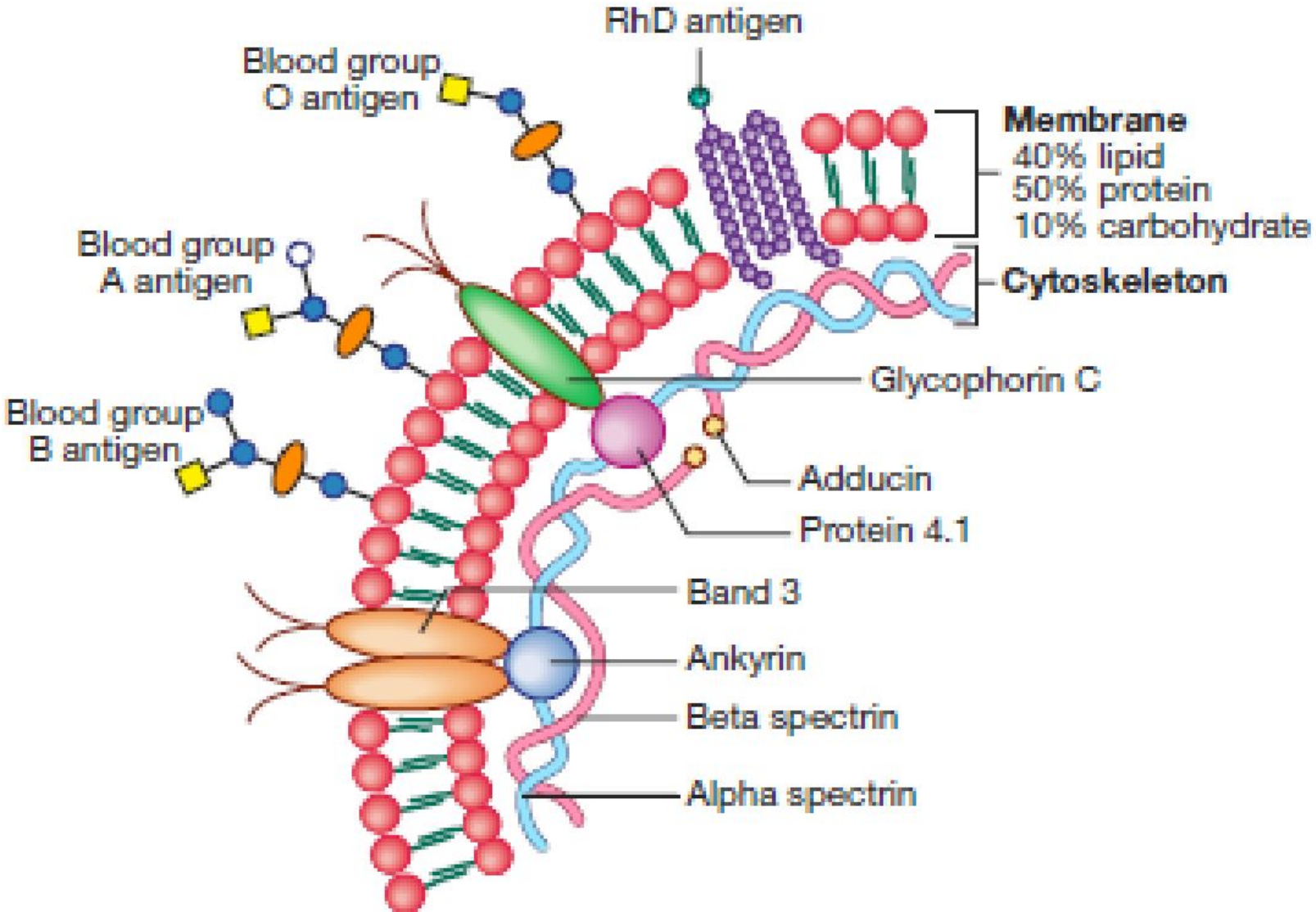
Lecture No. …10…..

الجانب النظري

Theoretical


... تدريسي المادة : ...د. وضاح علي

# Red cell membrane defects



# Introduction

Autosomal inherited disorder, caused by intrinsic defects in red cell membrane that render red cells spheroid, less deformable & vulnerable to splenic sequestration & destruction

Autosomal dominant inheritance :

75 % of cases

Autosomal recessive form :

Less common, more severe

# Introduction

**Morphologically, spherocytosis are rounded cells that have lost the ability to change shape.**

- Chronic hemolysis is the hallmark of HS
- . In most individuals, the condition is mild requires no specific therapy.
- In severe cases, it results in severe anemia, splenomegaly jaundice.
- Splenectomy sometimes is recommended as therapy for severe cases can result in amelioration of the disease.

# Pathophysiology

The abnormal red cells lysis is caused by a defect in cytoskeleton protein ： deficiency of ***spectrin*** (RBC membrane protein).

The spherical shape has *two* effects on RBC.

1.they become trapped in the splenic cord.

2.they have shortened life span.

The abnormal membrane also demonstrate an increased permeability of sodium

# pathogenesis

Regardless of the molecular basis for a case of HS, the common denominator of spectrin deficiency results in an unstable red cell membrane.

Disruptions of ankyrin, band 3, or the other structural proteins lead to common 2ry defects in spectrin assembly, resulting in unstable red cell membrane.

Four abnormalities in red cell membrane proteins have been identified and include

(1) spectrin deficiency alone,

(2) combined spectrin and ankyrin deficiency,

(3) band 3 deficiency, and

(4) protein 4.2 defects.

# Pathogenesis

- Spectrin deficiency is the most common defect.
- Each is associated with a variety of mutations that result in different protein abnormalities and varied clinical expression.
- Most cases of HS are heterozygous because homozygous states are lethal.
- Lipids are lost from the bi-layer as micro-vesicles.
- As the red cell progressively loses surface area, it changes from a biconcave disc to sphere.

# Pathogenesis

- As a result of this shape change, the red cells lose their ability to circulate freely through narrow capillaries in the body.

- The resulting spherocytes become trapped in the spleen as they course through the sinuses the red cells are engulfed by macrophages.

- Hemolysis causes elevations of unconjugated bilirubin the development of gallstones.

## Laboratory Evaluation

- Lab tests is helpful in both establishing the diagnosis of HS classifying the severity of illness.
- In the initial evaluation, it often is useful to study relatives as well as individual patients.

- Most patients have a (+ ve) F/H of HS.

- The peripheral blood smear in HS shows numerous spherocytosis that appear as red cells that do not have any central pallor, decreased mean corpuscular diameter, increased density are smaller than usual.
- Larger bluish cells (polychromasia) also may be seen.

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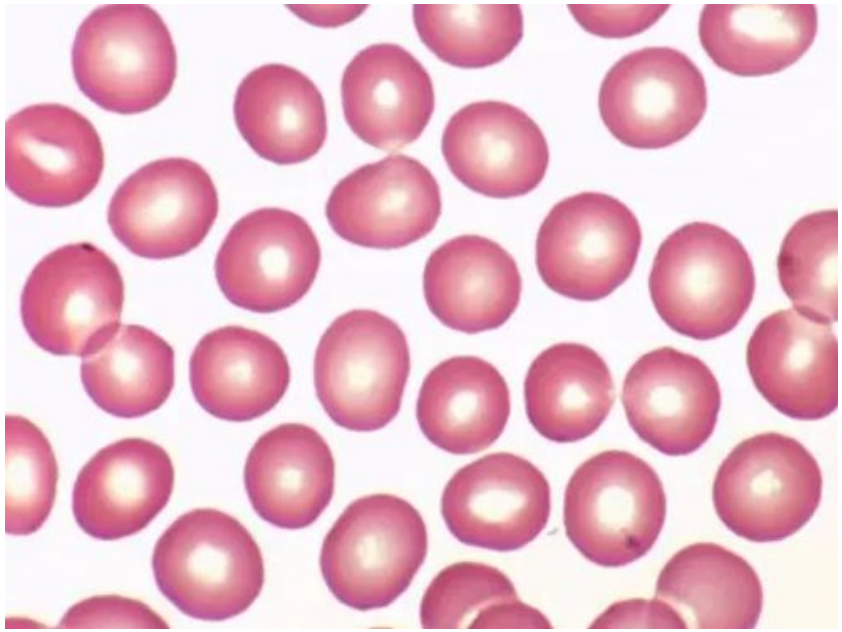
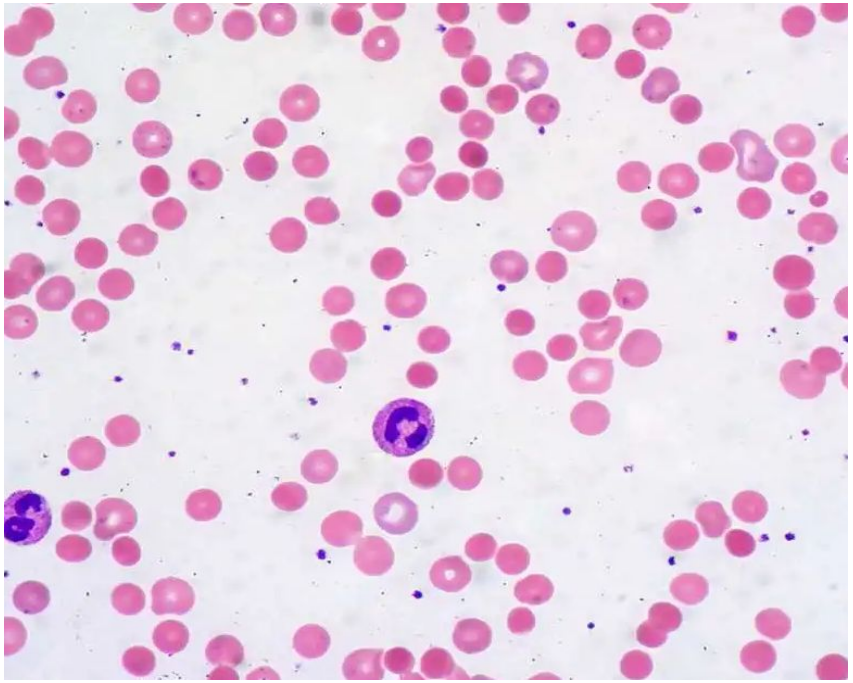




# Laboratory Evaluation

- The CBC count reveal a low Hb concentration and high Reticulocyte count.

- The mean corpuscular Hb concentration (MCHC) usually high 2ry to mild cellular dehydration.

- The mean corpuscular volume (MCV) may be low (this relatively low MCV reflect membrane loss and cell dehydration)
- or high if there is reticulocytosis

# Laboratory Evaluation

- most sensitive test to help detect HS is the incubated osmotic fragility test
  incubating RBCs for 18-24 hours under sterile conditions at 37C based on the principle that red cells swell and rupture when incubated in hypotonic solutions.

- Other tests results that support the diagnosis of HS include
- - Elevated unconjugated hyperbilirubinemia.
- - Elevated LDH level.
- - Low haptoglobin level.

# Osmotic fragility test

- Expose RBC to decreasing saline concentrations
- As saline decreases RBC absorb more

- Normal RBC can swell due to flexibility of membrane, therefore are more resistant to low saline

- Spherocytes are inflexible , therefore cannot absorb more - ? hemolysis

# Diagnosis

*Suggested by a family history of HS and characteristic finding on PBS i.e.* spherocytes.
Two studies are used to confirm the diagnosis.
*1. osmotic fragility test.*
A positive test shows lysis of the patients red cells at hypotonic saline solution compared to simple swelling in normal cells.
*2. Autohemolysis test* :
Normal autohemolysis is about 1% while HS cells will display Hb release rate of 3% or more

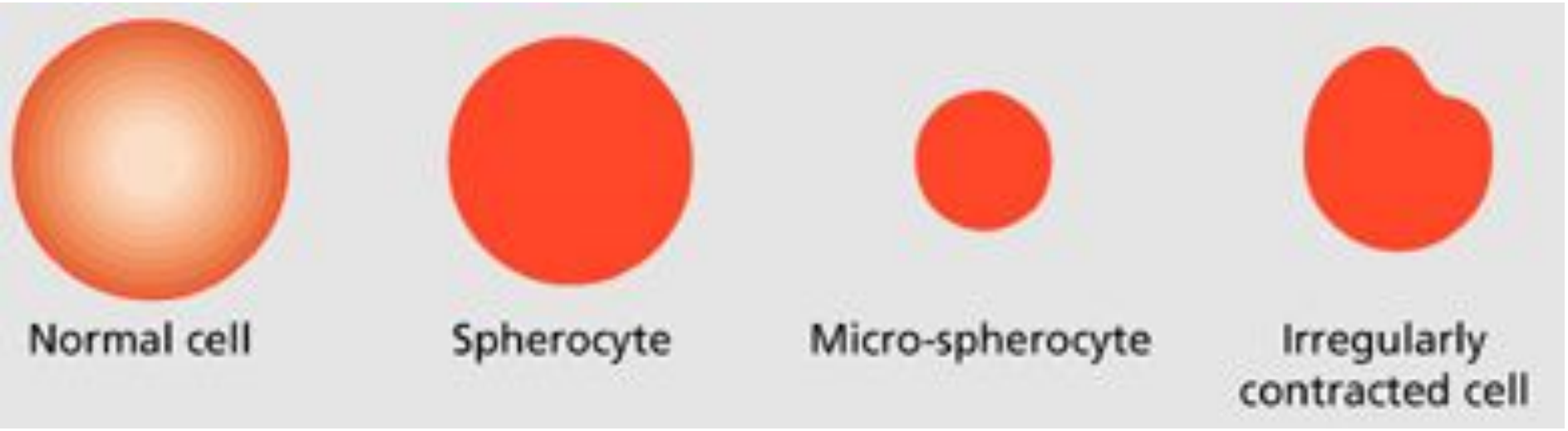
3-***flow cytometric***

tests, detecting binding of eosin-5-maleimide to red

cells, are recommended in borderline cases

# Clinical manifestation

The typical HS pts is relatively asymptomatic with well compensated hemolysis and palpable spleen.
The rare pts with severe HS may present early in childhood with life threatening hemolysis.
HS has the usual features of chronic hemolysis :
*symptoms of anaemia.
*splenomegaly.
*gall stones.
crisis *Aplastic crisis ,hemolytic and megaloblastic
#Family members have mild form of the disorder or are carrier.


Normal cell
Spherocyte
Micro-spherocyte
Irregularly contracted cell

# Treatment

1.Asymptomatic pts with compensated hemolysis should receive supportive treatment with folate supplements 5mg for life.

2.Aplastic crisis may require short period of blood transfusion.

3.Splenectomy is curative in most pts with HS.

# Guide line for performing splenectomy

1. performed only when necessaryi.e moderate to severe hemolysis with complication (pts who required blood transfusion,gall stones)
2. should be avoided in pts younger than 6 years of age ,associated risk (fatal pneumonia, sepsis)
3. may be performed with cholecystectomy to decrease the amount of hemolysis and the risk of gall stones development.

**Q1 Lab diagnosis of hereditary spherocytosis HS**

**Q2 Definition of osmotic fragility test**

**Q3 Type of red cell membrane proteins loss in HS**