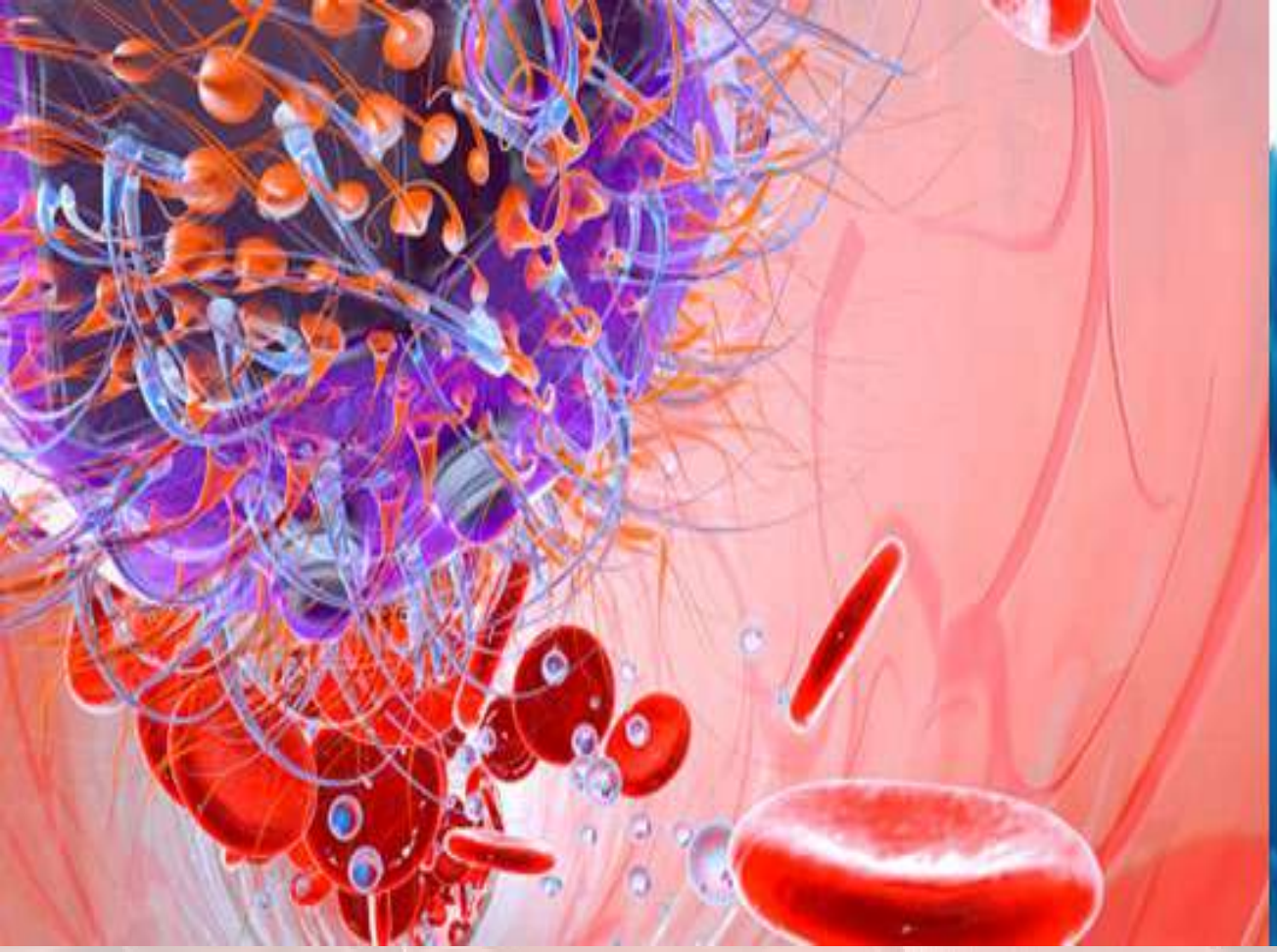


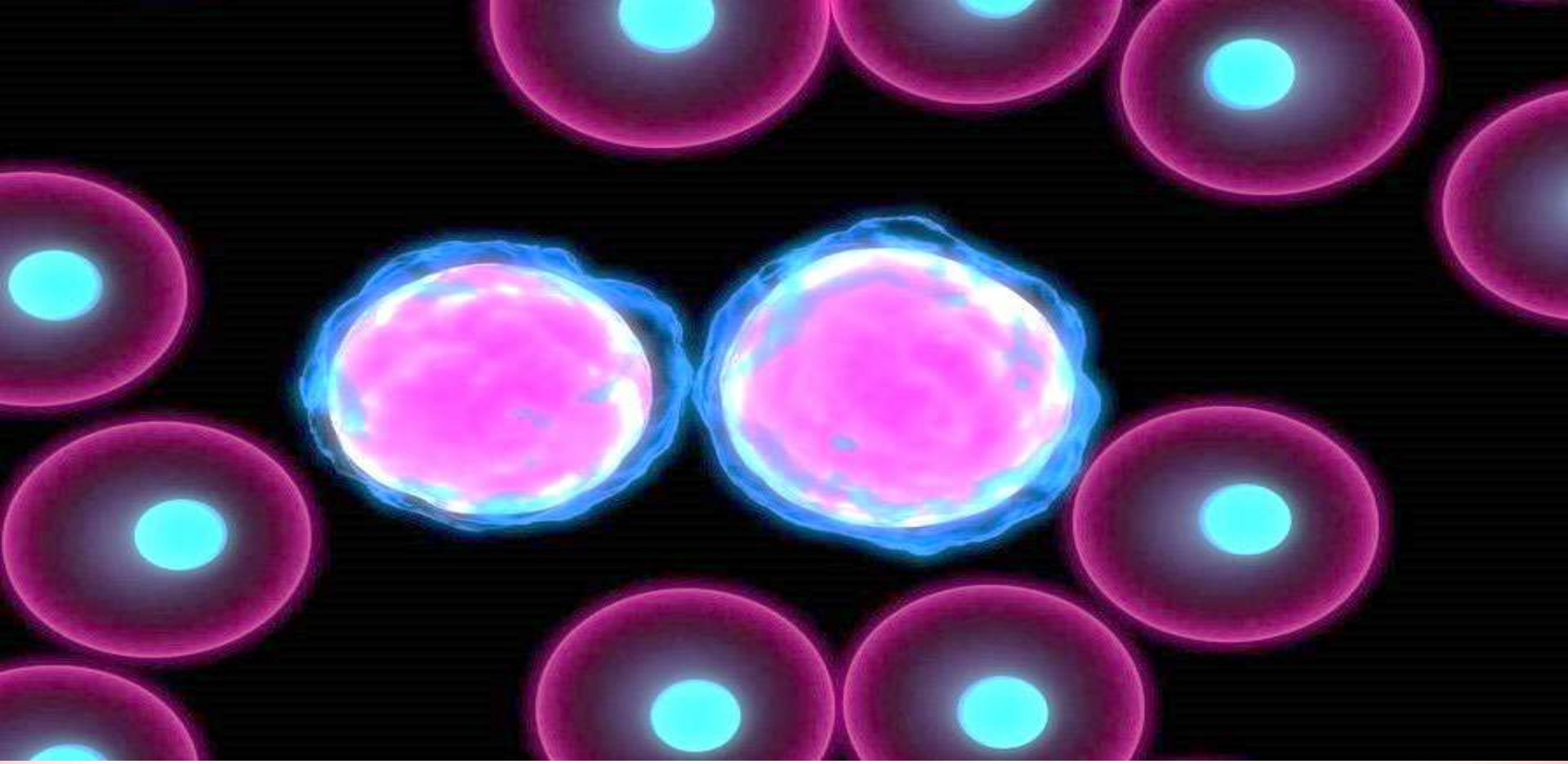
Haematology

Hematology

Dr. Abdulsalam Al-Ani
4th Year – Under Graduate
College of Medicine
University of Anbar

Objectives

1. Hemopoiesis.
2. **Anemia, Types and Related Disorders.**
3. Granulopoiesis and White Blood Cell Disorders.
4. Hematological Malignancies.
5. Hemostasis.
6. Transfusion Medicine.



ACQUIRED HEMOLYTIC ANEMIA

ACQUIRED HEMOLYTIC ANEMIA:

- Immune HA (IHA): due to antibodies (Abs) reaction against RBCs antigens, usually show *positive* Coombs' test.
- Non-immune HA: due to mechanisms, whether physical or chemical, not related to the immune system, with *negative* Coombs' test.
- The immune can be in the following forms;

  1- Autoantibodies

  2- Alloantibodies.

  3- Drug induced antibodies.

Caused of Acquired Immune HA;

Autoimmune	*Warm*	**Primary;** (Idiopathic)
		Secondary; Autoimmune diseases (ITP,SLE, RA) Lymphoproliferative disorders Infections (EBV) Ovarian cysts CA; Ovarian, and some other cancers Drugs
	Cold	Cold hemagglutinin disease (CHAD) Cold antibody syndromes; Infections (*M. pneumoniae*) & lymphoproliferative disorders
	Donath–Landsteiner Abs.	Paroxysmal cold hemoglobinuria (PCH); occurs Post viral, syphilis
Alloimmune	*Induced by red cell Ags;*	Hemolytic transfusion reactions Hemolytic disease of the newborn (HDN) Post-stem-cell allografts
	Drug dependent	Antibody/macrophage mediated Antibody/complement mediated Membrane modification Autoimmune

ITP; immune thrombocytopenia, SLE; systemic lupus erythematosus,
RA; Rheumatoid arthritis, EBV; Epstein–Barr virus

❖ Acquired Immune Hemolytic Anemia

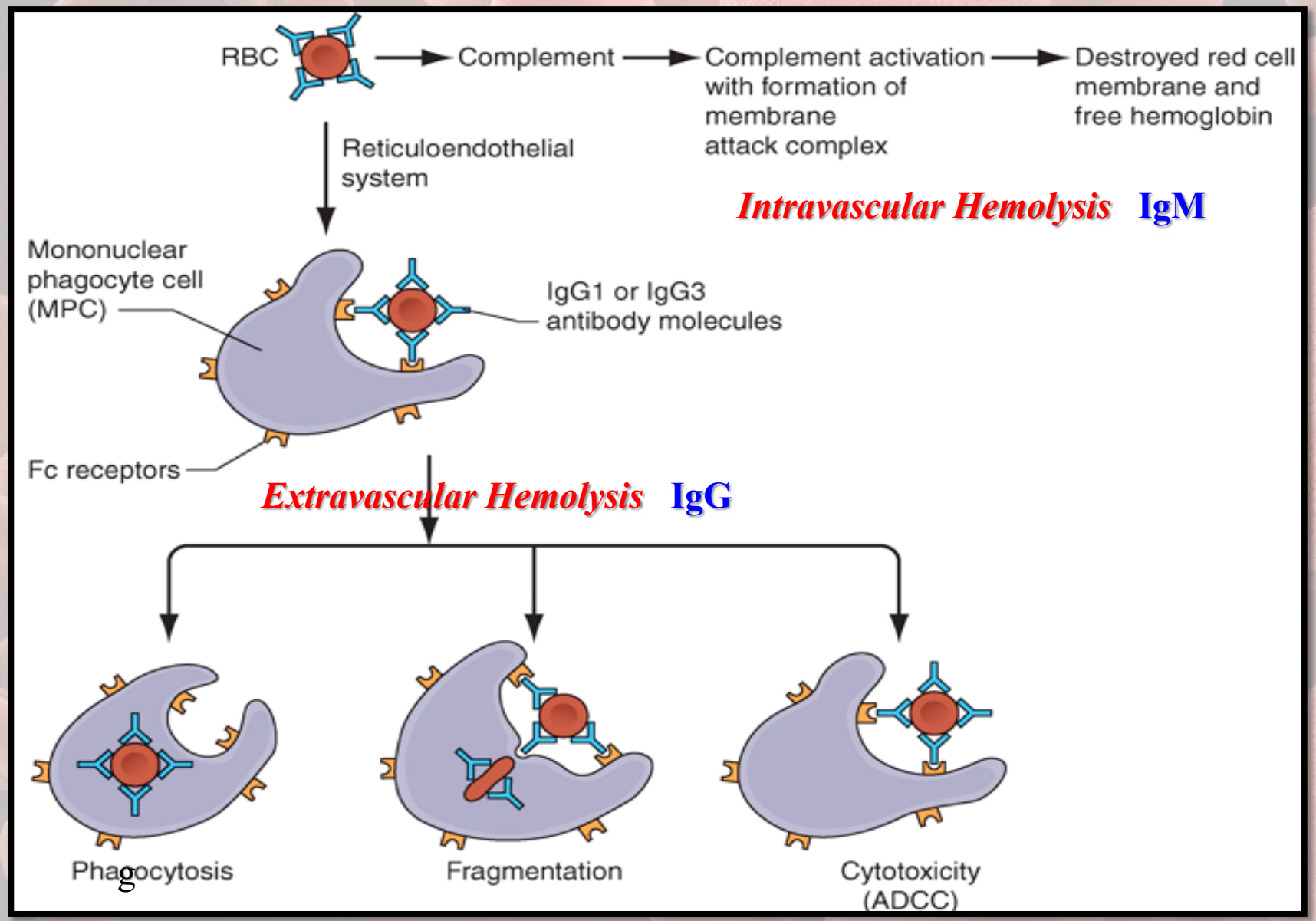
- Can be of autoimmune; in which the antibodies react against its own RBCs, or alloimmune in which the antibodies reacts against the RBCs of another person or drug induced.
- Immune HA; either warm or cold type, depending whether the Abs activity more strongly at 37°C or 4°C respectively.
- The warm AIHA; usually due to IgG Abs with or without complement, while the cold type of IgM and usually with complements.
- The warm AIHA usually of extravascular features of hemolysis, while the cold AIHA associated with intra- and extravascular features.

1- Autoantibodies;

- AIHA is caused by an autoantibody directed against a red cell antigen .
- Warm antibody of type IgG antibody. Leads to extravascular hemolysis, Spherocytes on blood smear and nucleated red blood cells. Positive direct Coombs test. High dose steroids often achieve remission, splenectomy may be of value in those who do not respond satisfactorily.
- Cold antibody of type IgM antibodies. Leads to intravascular hemolysis. Agglutinated RBCs on blood smear. May benefit from therapy with alkylating agents

- The autoantibody binds to the red cells. Once a red cell is coated by antibody, it will be destroyed by one or more mechanisms.
- In most cases the Fc portion of the IgG antibody will be recognized by the Fc receptor of macrophages, and this will trigger erythrophagocytosis in the spleen, liver, and bone marrow, with extravascular hemolysis.
- In some cases, the nature of the antibody (usually an IgM antibody) is able to activate complement (C). As a result, a large amount of membrane attack complex will form, and the red cells may be destroyed directly with intravascular hemolysis.

Antibody-mediated Immune Destruction of RBCs



❖ Clinical features

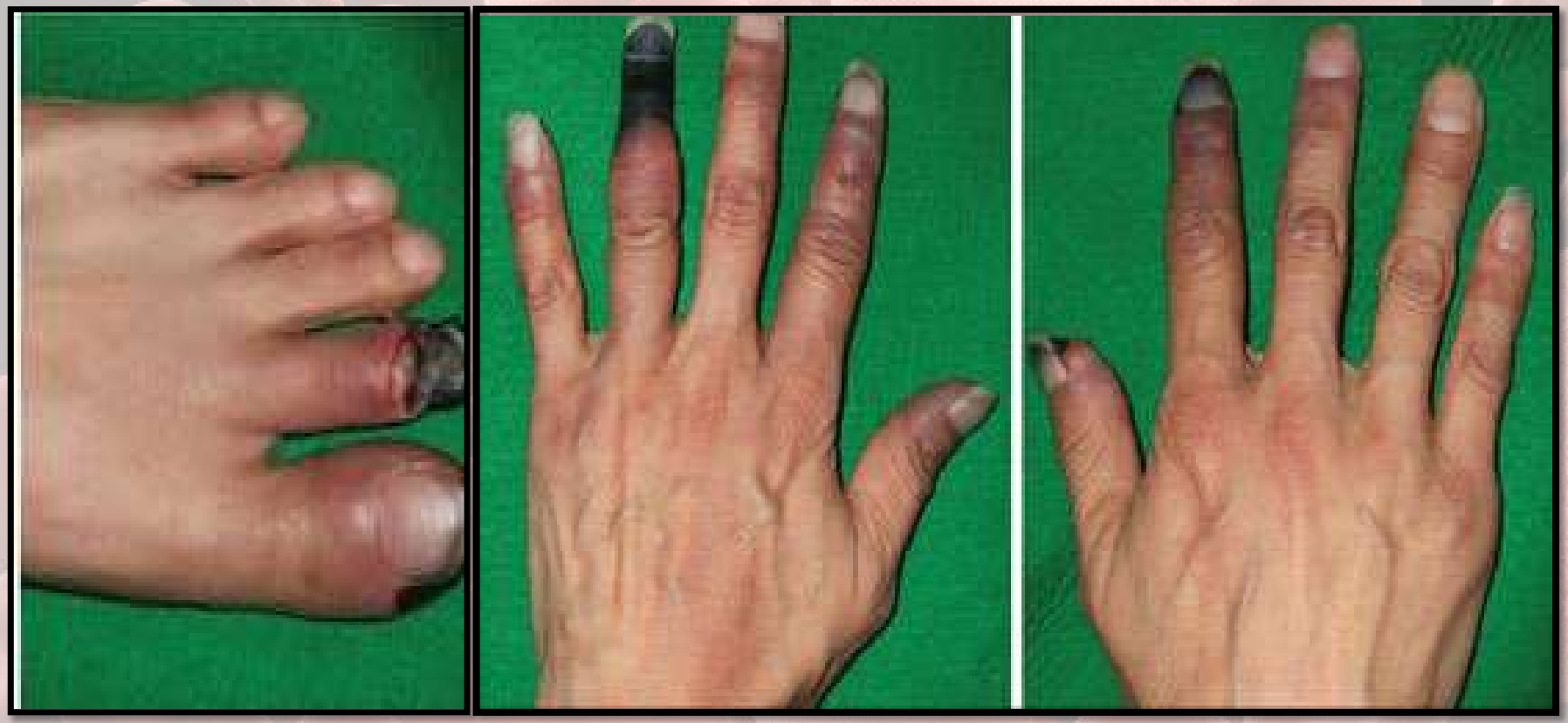
1- Worm HA;

- The disease may occur at any age, in either sex.
- Presents as a hemolytic anemia of varying severity of extravascular type.
- Th e spleen is often enlarged.
- The disease tends to remit and relapse.
- It may occur alone or in association with other diseases.

❖ Clinical features

2- Cold HA;

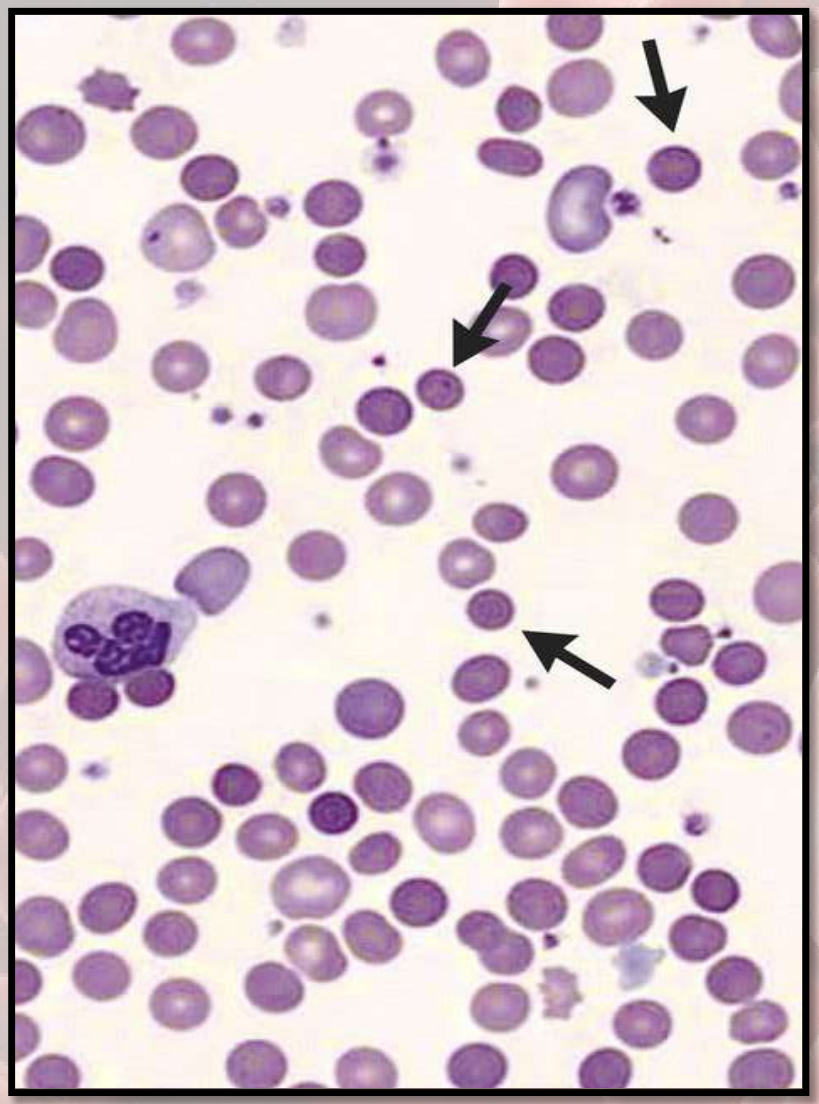
- The patient may have a chronic hemolytic anemia
- Hemolysis aggravated by the cold.
- Often associated with intravascular hemolysis.
- Mild jaundice and Splenomegaly may be present.
- The patient may develop acrocyanosis of the hands and feet as a purplish skin discoloration when exposed to cold whether.

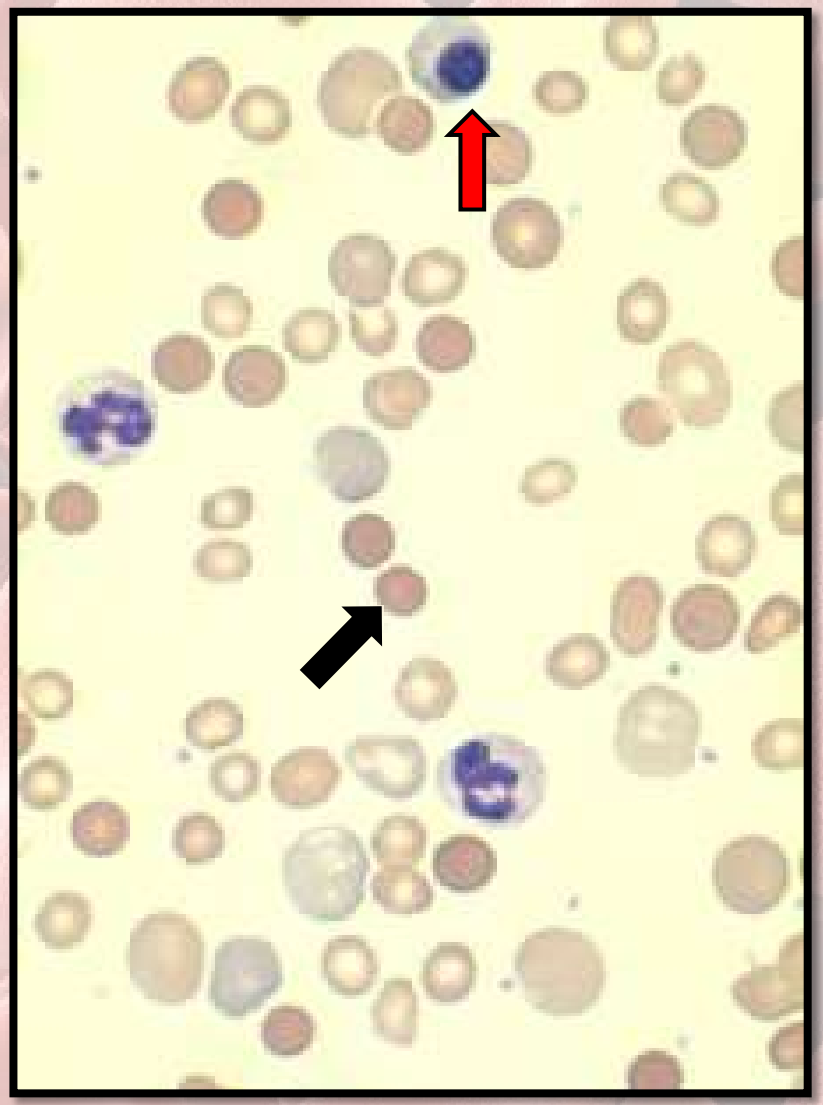


Acrocyanosis and digital gangrene, after cold exposure, rapidly appeared in the patient's hands and feet, with dark purple-to-gray discoloration of the skin in acral areas such as; fingertips, toes, nose, and ears.

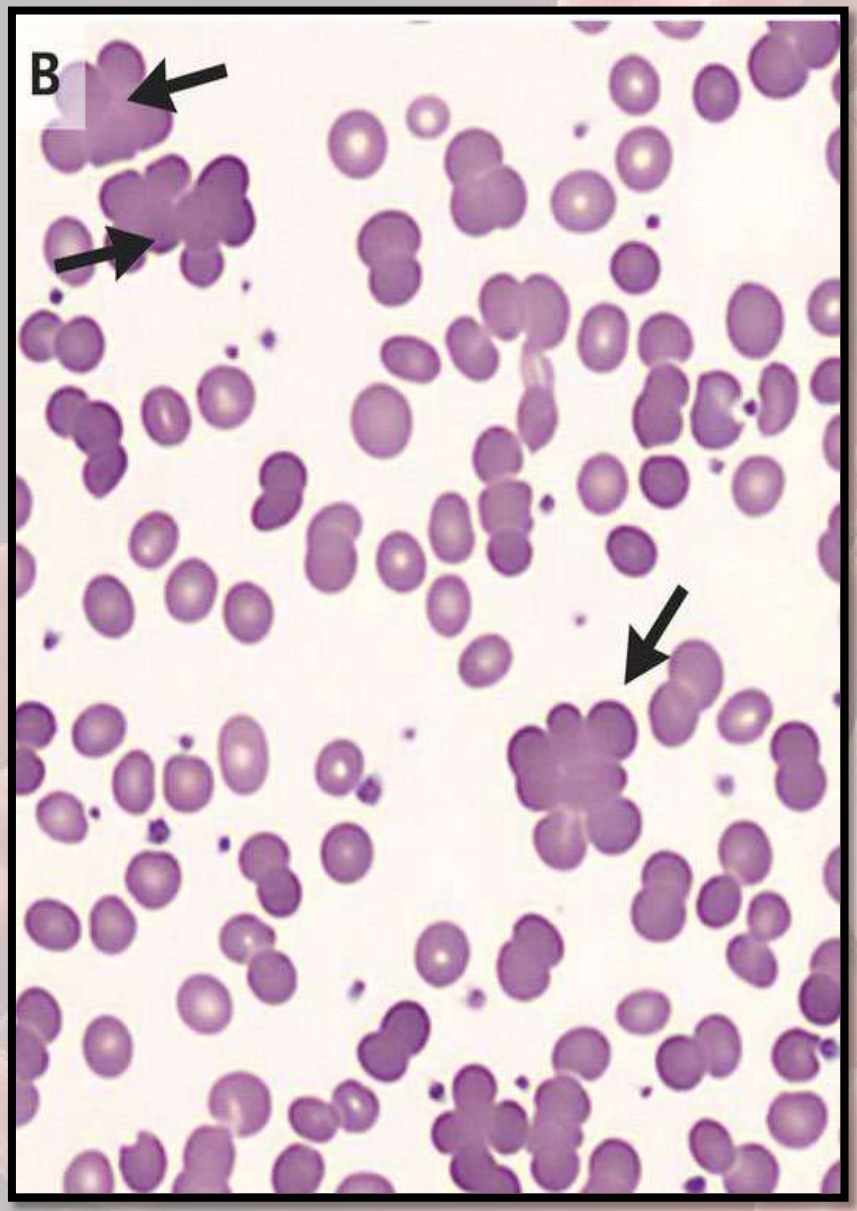
❖ Laboratory Findings

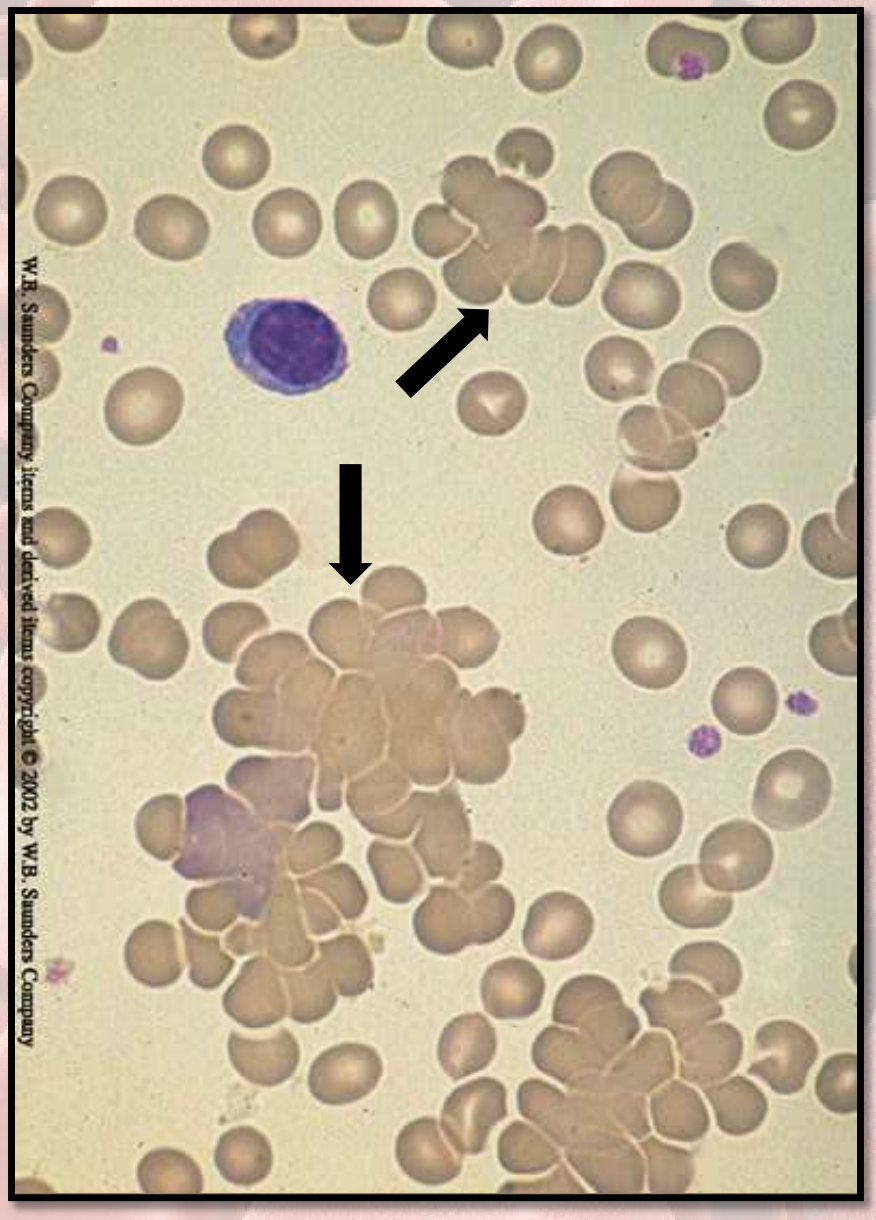
- **Warm** HA; the hematological and biochemical findings are typical of an extravascular hemolytic anemia, while in **Cold** HA; of intravascular with or without of extravascular (see lab. features of HA).
- Spherocytosis prominent in the peripheral blood, in **warm** HA.
- Red cell agglutination is present in films made at room temperature, in **cold** HA.





Warm AIHA; marked red cell *spherocytosis*, small round RBCs lacking central pallor (black arrows), *polychromasia* (green arrow) and *nucleated red blood cells* (red arrow).

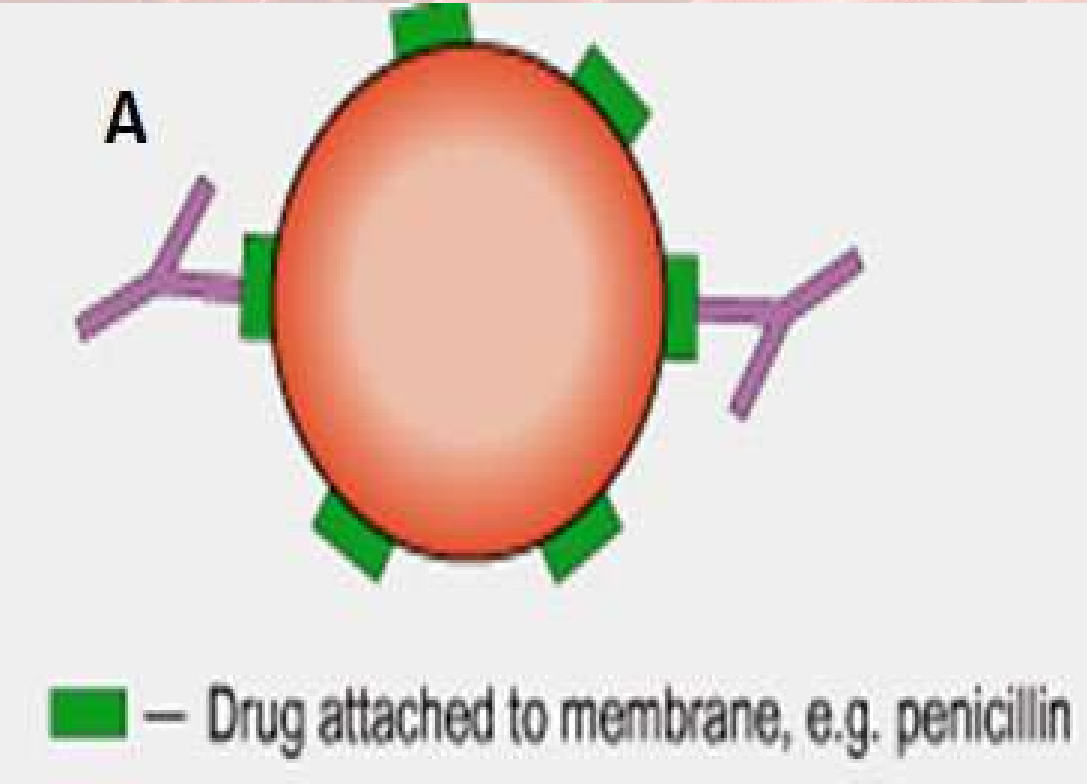




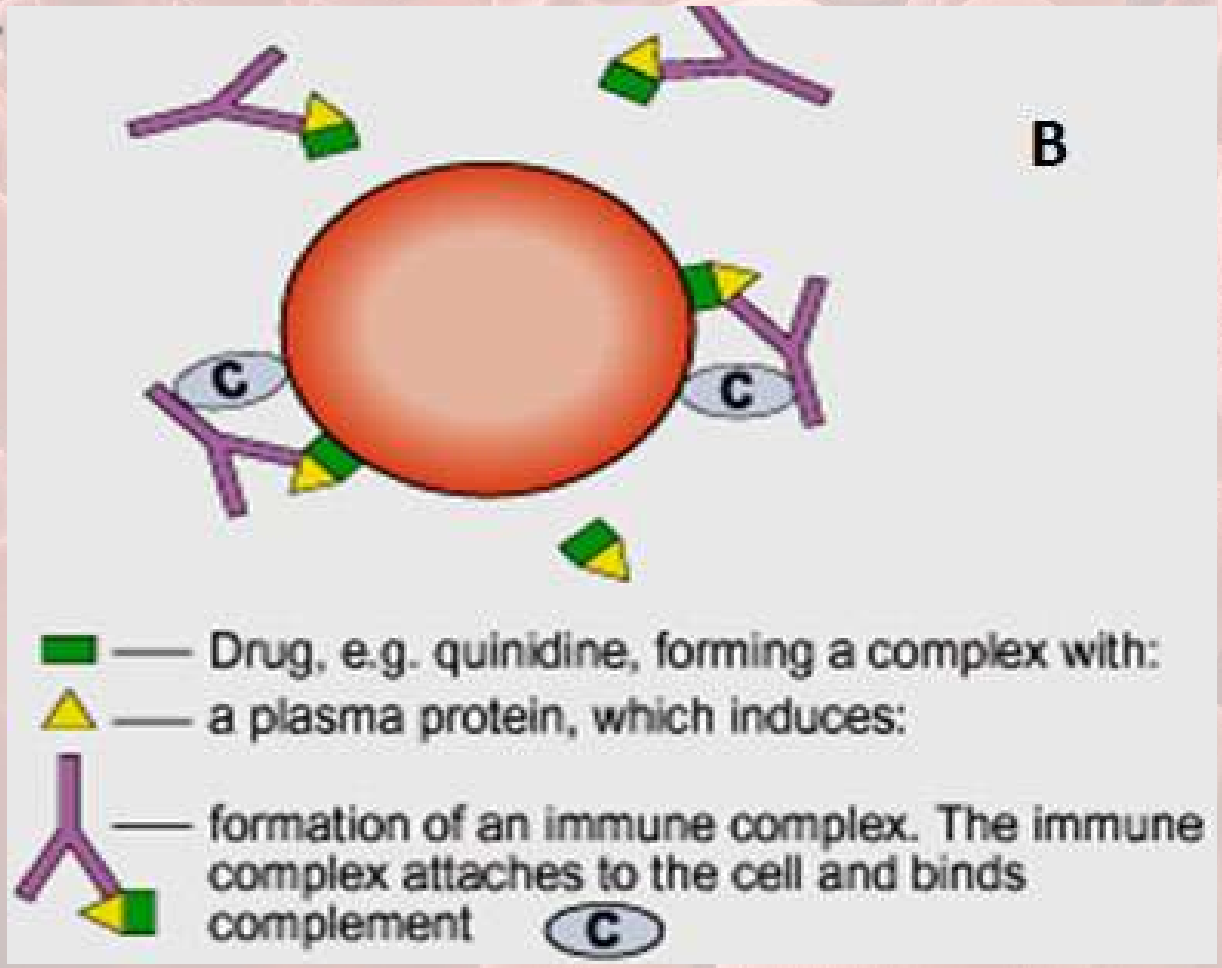
Cold type; irregular *clumps* of the red cells (arrow).

2. Drug induced antibodies

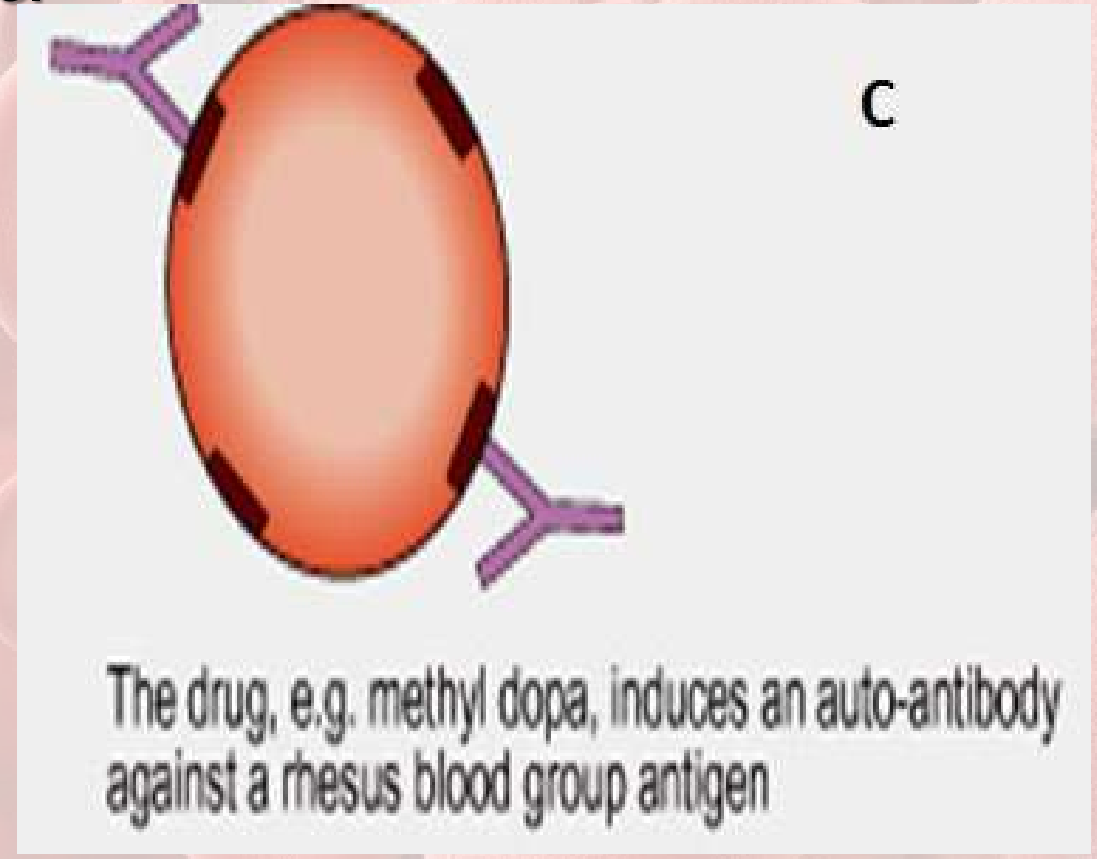
A. Hapten model (penicillin): Abs. against drug bound to the cell membrane, antibodies may be directed against a red cell membrane/drug complex.



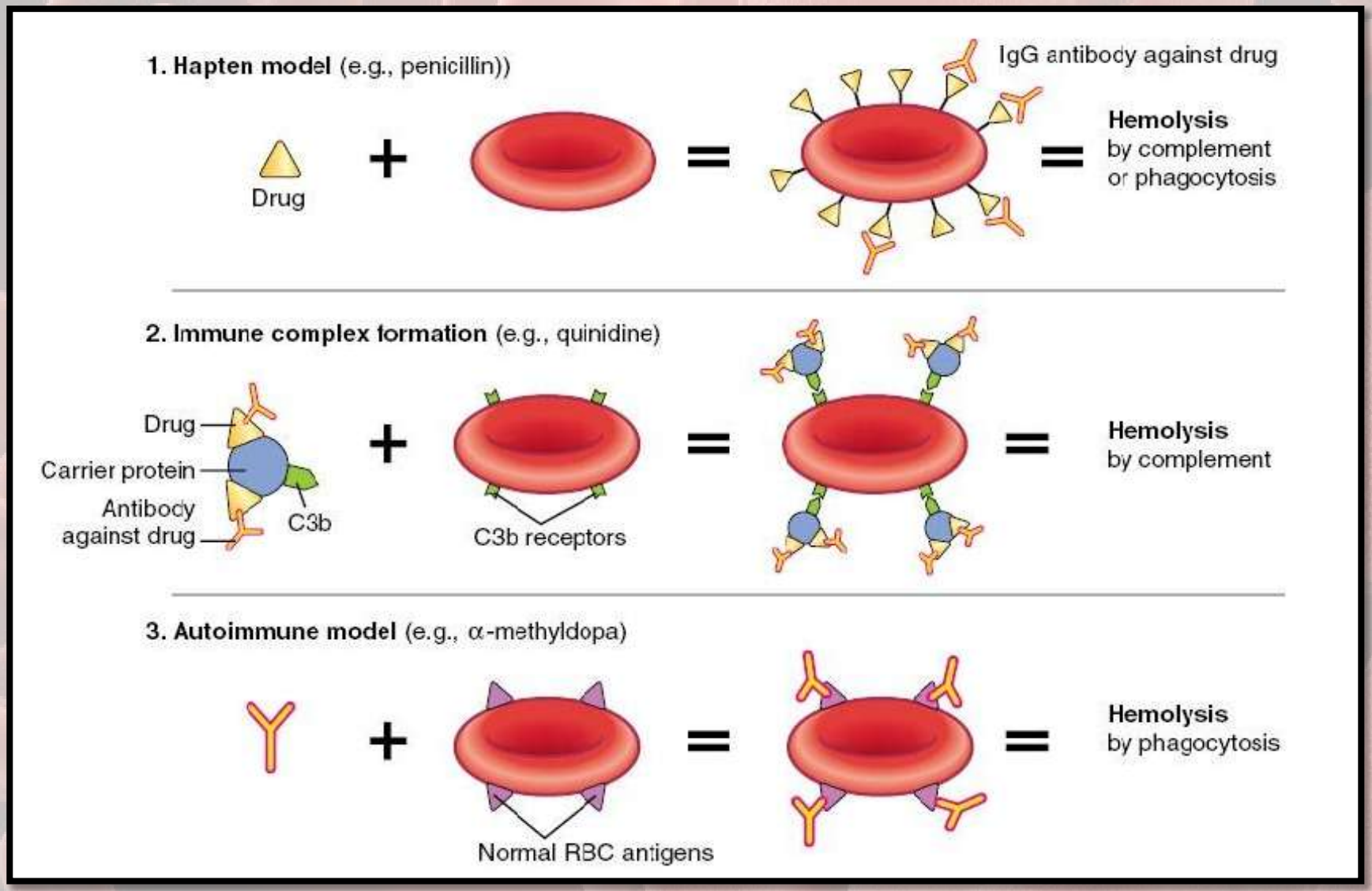
B. Antibody against a new Antigen (Quinine): determinant produced by drug bound to the cell membrane, may be deposition of a protein/antibody/drug complex on the red cell surface.



C. Autoantibody (Methyldopa); is the paradigm drug in autoimmune drug-induced hemolytic anemia. Typically, the DAT becomes positive about 6 weeks after its started and is strongly positive due to lgG on the red cell surface.



Mechanism of drug-induced IHA



3. Alloimmune;

- Induced by red cell antigens.

    A. Hemolytic transfusion reactions .

    B. Hemolytic disease of the newborn.

    C. Post-stem cell allografts.

➢ Non-Immune HA;

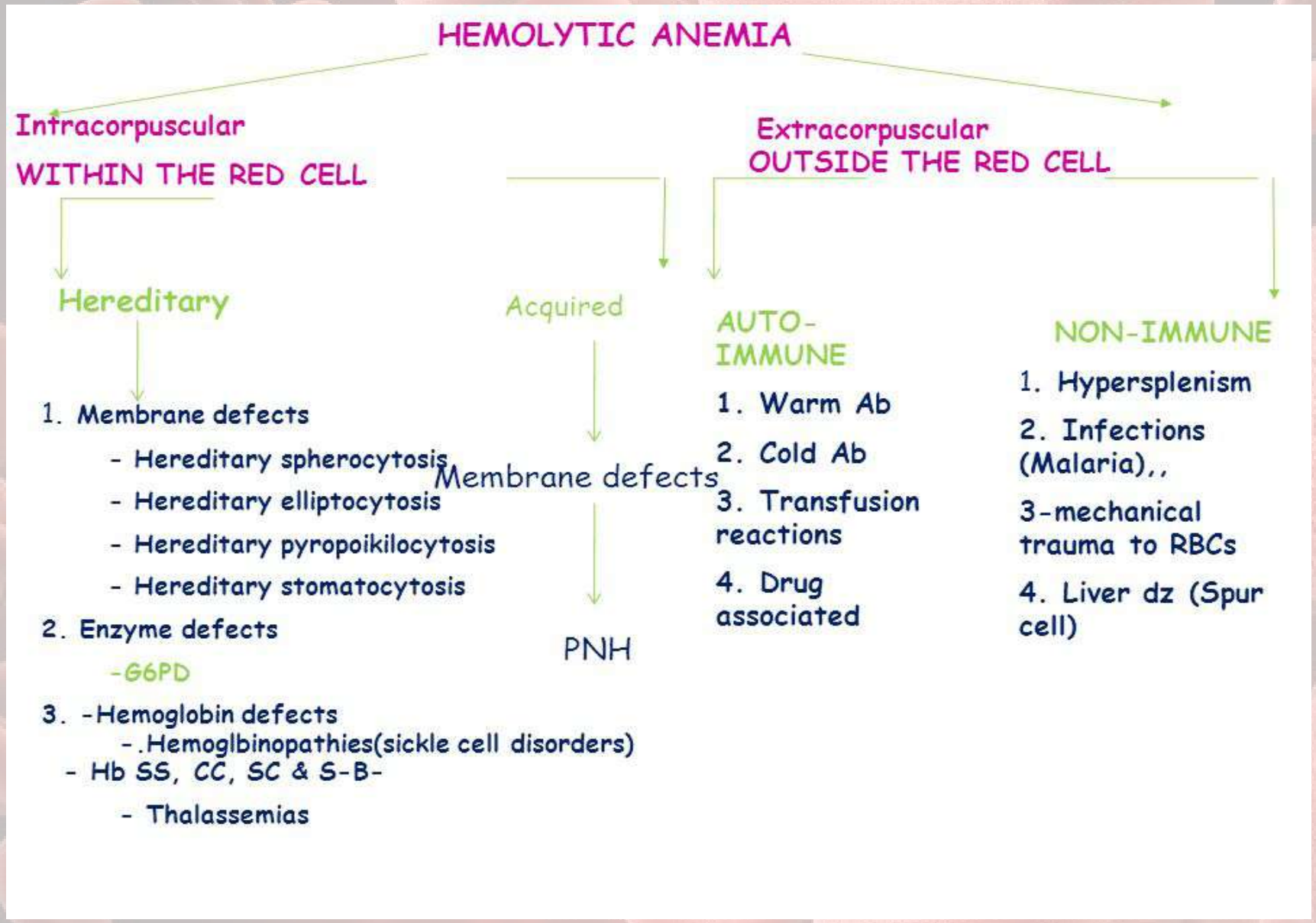
- Infections.
- Drug-induced
- Red cell fragmentation syndromes (artificial heart valves, arteriovenous malformations, disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP).
- March hemoglobinuria.
- Paroxysmal nocturnal hemoglobinuria (PNH); acquired clonal disorder affecting stem cell with mutation in X-chromosome. Associated with Hburia due to the IV hemolysis.

Caused of Non-Immune HA (Acquired);

Infections	• Falciparum malaria. • Bacterial sepsis (DIC)*. • viral infections.
Enzyme toxins	• Snake • Spider bites.
Chemical and physical agents	• Drugs • Burns. • Osmotic lysis (fresh water), dehydration of red cells (salt water)
Fragmentation (mechanical)	• Lysis on prosthetic surfaces (cardiac or valvular). • Microangiopathic hemolytic anemia(TTP** • March hemoglobinuria
Acquired membrane disorders	• Liver disease. • Paroxysmal nocturnal hemoglobinuria (Somatic mutation) (PNH)

DIC, disseminated intravascular coagulation,TTP;* **thrombotic thrombocytopenic purpura**

Classification of HA



Myelophthisic Anemia:

This form of normochromic normocytic anemia is caused by the extensive replacement (infiltration) of the marrow by neoplasms or other lesions;

- Can be produced by the following effects;

1- Destruction and replacement of normal hematopoietic stem cells.

2- Proinflammatory Cytokines; tumor necrosis factor (TNF), IL, and other substances are released.

3- Premature release of immature cells.

4- Stem and progenitor cells migrate to the spleen and Liver (extramedullary).

- Can be caused by;

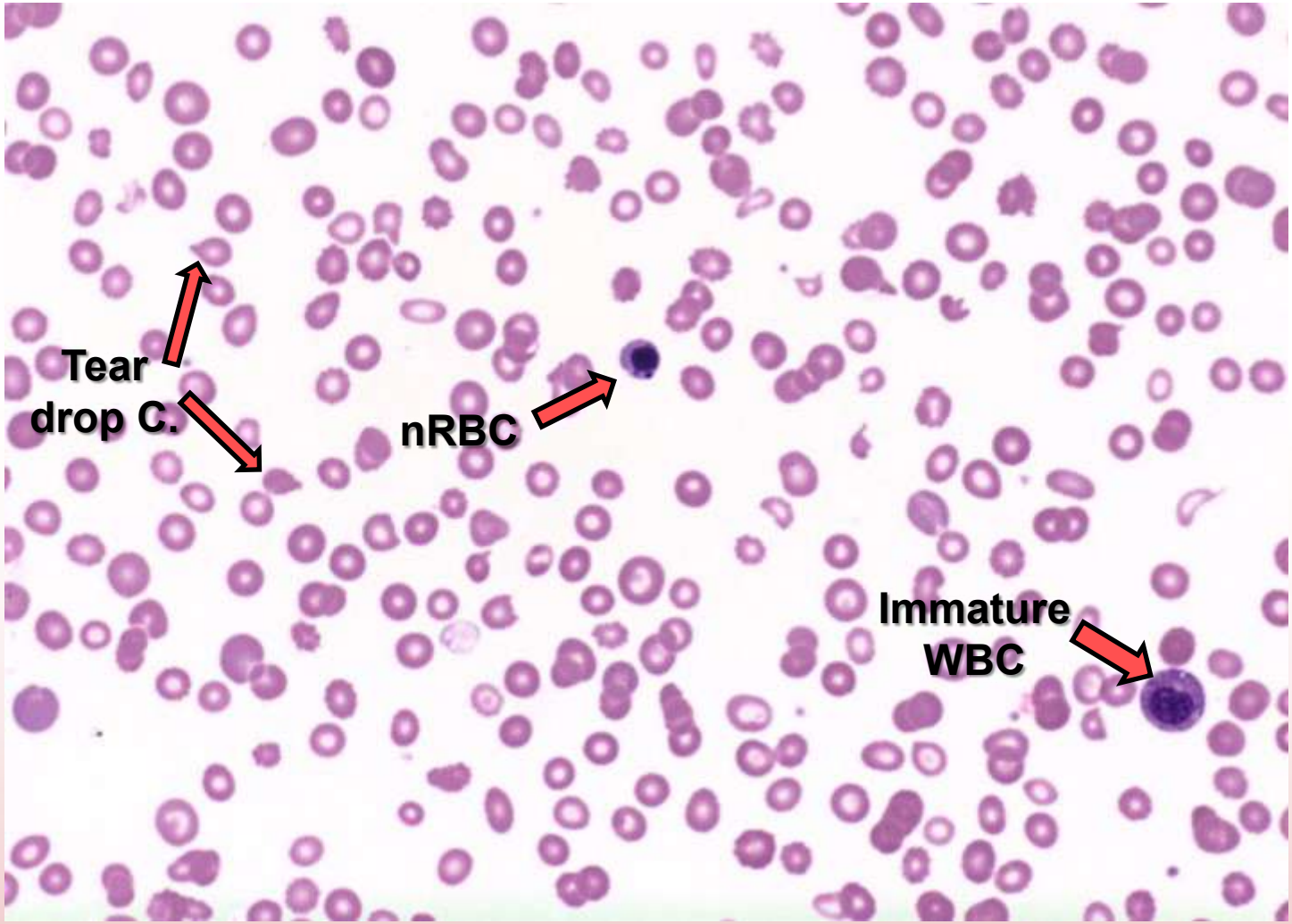
1- Metastatic carcinoma to the BM most commonly from breast, lung, or prostate primaries.

2- Advanced tuberculosis (T.B).

3- Lipid storage disorders.

4- Osteosclerosis.

- Characteristically anemia of normochromic normocytic.
- May be presented with thrombocytopenia.
- Red cells may show teardrops.
- Immature granulocytic and erythroid precursors may also be seen (**leukoerythroblastic** blood picture).



Variation in erythrocyte size, shape, and staining, a nucleated erythrocyte, with immature granulocytes (leukoerythroblastic)

شكراً جزيلاً
ngiyabonga
рахмат
danke
謝謝
spas
teşekkür ederim
Баярлалаа
mersi
kia ora
barka
welalin
tack
mahalo
tapadh leat
спасибо
faafetai lava
vinaka
blagodaram
dank je
misaotra
paldies
grazzi
matondo
спасибі
thank you
gracias
kiitos
dankie
nanni
nandri
dhanyavad
mauruuru
köszönöm
aciu
хвала
asante
manana
bedankt
bayarlalaa
gracie
hvala
dankon
akun
obrigada
murakoze
tenki
enkosi
djiere dieuf
tau
mochchakkeram
дякую
mamnun
dziękuję
chnorakaloutioun
gratias ago
gràcies
sulpáy
go raibh maith agat
chokrane
sobodi
dekuji
sagolun
sukriya
kop khun krap
taiku
obrigado
arigatô
takk
dakujem
trugarez
mèsi
didi madloba
ありがとう
najis tuke
grazie
tanemirt
rahmet
terima kasih
kam sah hamnida
rahmat
ευχαριστώ
diolch
dhanyavadagalu
shukriya
mercè
мерси
তোমাকে ধন্যবাদ
감사합니다
xiexie
merci