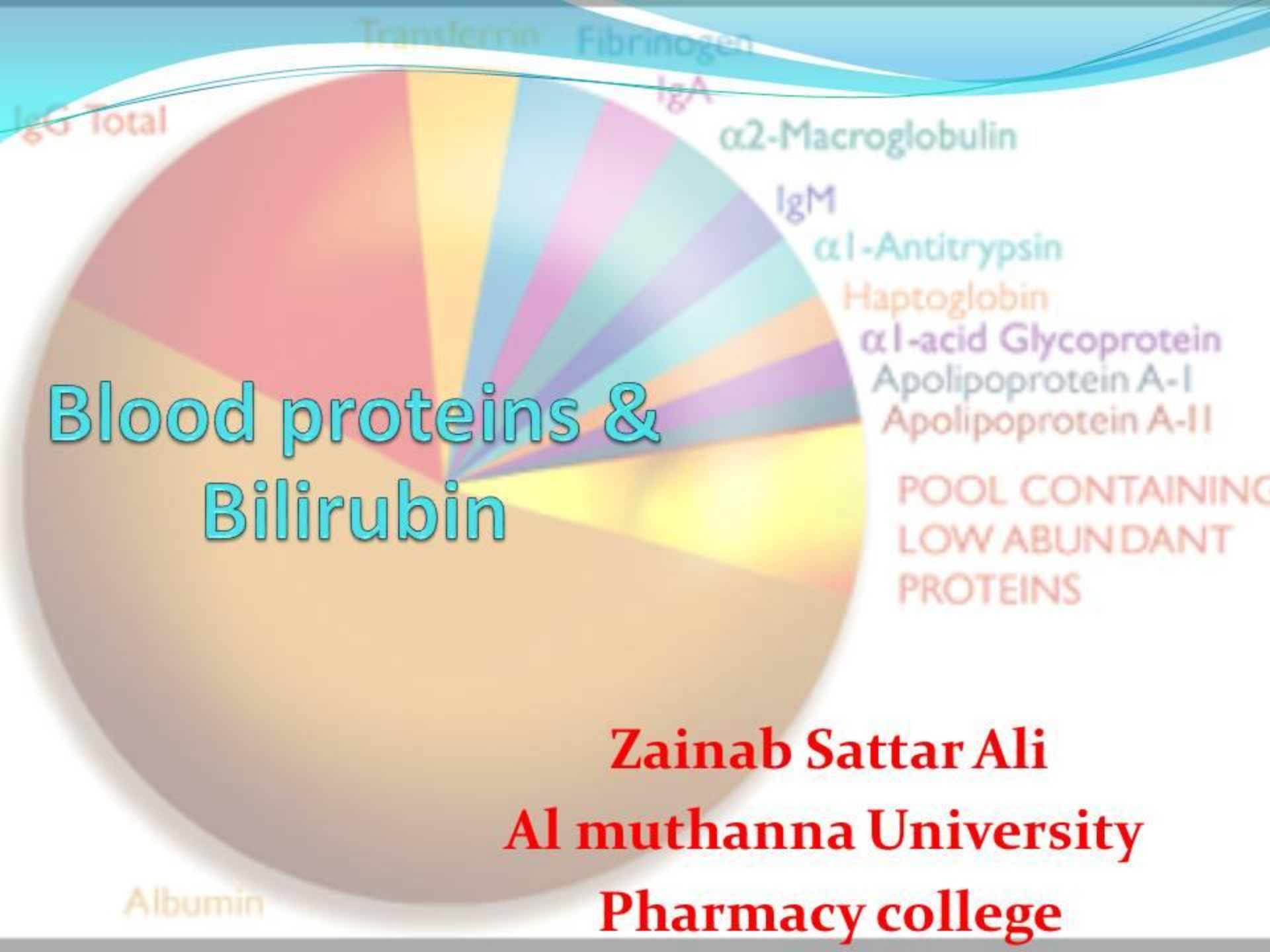


Blood proteins & Bilirubin

Zainab Sattar Ali

Al muthanna University

Pharmacy college

Bilirubin: is an orange-yellow pigment, a waste product primarily produced by the normal breakdown of heme "a component of hemoglobin in red blood cells (RBCs)". Bilirubin is ultimately processed by the liver to allow its elimination from the body. Bilirubin concentrations tend to be slightly higher in males than females. Two forms of bilirubin can be measured or estimated by laboratory tests:

- **Unconjugated bilirubin:** after RBCs normally degrade, the heme is released from hemoglobin, it is converted to bilirubin. Most (85%) of bilirubin is derived from damaged or degraded RBCs, with the remaining amount derived from the bone marrow or liver. This form of bilirubin is also called unconjugated bilirubin. Small amounts may be present in the blood.
- **Conjugated bilirubin:** Unconjugated bilirubin is carried by proteins to the liver; there, sugars are attached (conjugated) to bilirubin to form conjugated bilirubin.
- Conjugated bilirubin enters the bile and passes from the liver to

the small intestines; there, it is further broken down by bacteria and eventually eliminated in the stool. Thus, the breakdown products of bilirubin give stool its characteristic brown color.

Bilirubin direct serum 0 - 0.3 mg/dl

Bilirubin, total, serum 0.2 - 1.9 mg/dl.

Normally, no conjugated bilirubin is present in the blood.

Usually, a chemical test is used to first measure the total bilirubin level (unconjugated plus conjugated bilirubin). If the total bilirubin level is increased, the laboratory can use a second chemical test to detect water-soluble forms of bilirubin, called "direct" bilirubin. The direct bilirubin test provides an estimate of the amount of conjugated bilirubin present. Subtracting direct bilirubin level from the total bilirubin level helps estimate the "indirect" level of unconjugated bilirubin.

Bilirubin is measured to:

- Diagnose diseases of the liver and bile duct (e.g., cirrhosis, hepatitis, or gallstones), the level of conjugated bilirubin can

increase when the liver is able to process bilirubin but is not able to pass the conjugated bilirubin to the bile for removal.

- A practitioner usually orders a bilirubin test in conjunction with other laboratory tests (alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase) when someone shows signs of abnormal liver function.
- Evaluate people with sickle cell disease or other causes of hemolytic anemia; these people may have episodes called crises when excessive RBC destruction increases levels of unconjugated bilirubin may be increased when there is an unusual amount of RBC destruction (hemolysis) or when the liver is unable to process bilirubin (i.e., with liver diseases such as cirrhosis or inherited problems).

In newborns jaundice: may consequences of it damage include mental retardation, learning and developmental disabilities, hearing loss, eye movement problems, and death. This condition must be quickly detected and treated, usually with surgery, to prevent serious liver damage that may require liver transplantation

1- Increased total and unconjugated bilirubin levels are relatively common in the first few days after birth. This finding is called "physiologic jaundice of the newborn" and occurs because the newborn's liver is not mature enough to process bilirubin yet. Usually, physiologic jaundice of the newborn resolves itself within a few days.

2- in hemolytic disease of the newborn, RBCs may be destroyed because of blood incompatibilities between the baby and the mother; in these cases, treatment may be required because high levels of unconjugated bilirubin can damage the newborn's brain.

3- A rare (about 1 in 10,000 births) but life-threatening congenital condition called biliary atresia can cause increased total and conjugated bilirubin levels in newborns.

Jaundice:

If the bilirubin level increases in the blood, a person may appear jaundiced, with a yellowing of the skin and/or whites of the eyes.
Nausea/vomiting
Abdominal pain and/or swelling
Fatigue and general malaise that often accompany chronic liver disease
Dark, amber-colored urine(Bilirubin is not normally present in the urine. However, conjugated bilirubin is water-soluble and may be eliminated from the body through the urine if it cannot pass into the bile. Measurable bilirubin in the urine usually indicates blockage of liver or bile ducts, hepatitis, or some other form of liver damage and may be detectable early in disease).

- **Shows evidence of jaundice**

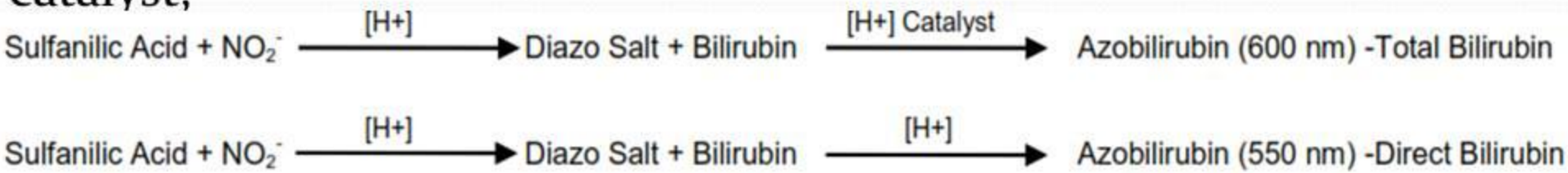
Has a history of drinking excessive amounts of alcohol
Has suspected drug toxicity
Has been exposed to hepatitis-causing viruses

Drugs :

can decrease total bilirubin include barbiturates, caffeine, penicillin, and high doses of salicylates.

The drug atazanavir increases unconjugated (indirect) bilirubin. Several inherited chronic conditions increase bilirubin levels in the blood and include Gilbert syndrome, Dubin-Johnson syndrome, Rotor syndrome, and Crigler-Najjar syndrome.

Total bilirubin assay protocol summary: (unconjugated + conjugated) concentration is determined in the presence of a catalyst,



Kit Contents:

Components	K553-100
Bilirubin Reagent 1	2.5 ml
Bilirubin Reagent 2	1 ml
Catalyst	15 ml
Total Bilirubin Probe	10 ml
Direct Bilirubin Probe	20 ml
Bilirubin Standard (0.2 µg/µl)	2 x 200 µl
DMSO (Anhydrous)	3.5 ml

where bilirubin reacts with a diazo- salt to form azobilirubin, which absorbs at 600 nm. Direct bilirubin (conjugated) is determined in the absence of catalyst (550 nm).

Protein C and protein S:

are two proteins in the blood that help regulate blood clot formation. This has the net effect of slowing down clot formation, if there is not enough protein C or S or they are not functioning normally, possibly leading to excessive clotting. Two separate tests for these proteins are often performed together as part of the investigation of a possible excessive clotting disorder.

- **Deficient or dysfunctional protein C or protein S due to:**
- **Acquired deficiencies:** Low protein C and low protein S may be seen with severe infections, inflammatory conditions, kidney disease, cancers, treatment with certain chemotherapeutic agents, HIV, mild and temporary during pregnancy and with warfarin (Coumadin®) anticoagulant therapy.
- **Inheriteddeficiencies:** passed from parent to child. About 1 out

of every 300 people has one normal gene and one abnormal gene (heterozygous)for protein C deficiency and about 1 in 20,000 people have protein S or C deficiencies that lead to symptoms.

There are two types of inherited protein C and Protein S deficiencies: **Type 1** :is related to quantity.

Type 2: is related to abnormal function and is less common than Type 1

Two types of tests may be used to evaluate protein C and protein S:

1- Functional tests: measure their activity and evaluate their ability to regulate and slow blood clotting.

2- Protein C and protein S antigen tests: measure the amount of the protein present. Tests for protein C and protein S are two separate tests that are often performed together to help investigate a possible excessive clotting (hypercoagulable) disorder and/or to help diagnose the cause of an inappropriate blood clot such as deep venous thrombosis (DVT) or a venous thromboembolism (VTE).

- A health practitioner will also likely order other tests to look for underlying diseases or conditions, such as liver disease, vitamin K deficiency, or cancer, that may cause inappropriate blood clotting (bleeding or thrombosis).
- Fresh frozen plasma contains protein C and protein S, and it can be used as a short-term preventative when a patient is having a surgical procedure
- **Total Protein and Albumin/Globulin (A/G) Ratio:**

Two major classes of proteins are found in the blood, albumin and globulin. Produced by the liver. albumin serves a variety of functions including as a carrier protein for many small molecules and ions, as a source of amino acids for tissue metabolism, and as the principle component involved in maintaining osmotic pressure (preventing fluid from leaking out of blood vessels). **In serum :Albumin 3.5 - 5.2 g/dl , total protein 6.0-8.0 gm/dl , globulin 3.0-2.0 g/dl.**

The globulin proteins are a varied group. They include enzymes, antibodies, hormones, carrier proteins, and numerous other types of proteins.

Total protein may decrease in conditions:

- malnutrition or severe liver disease, breakdown or loss of protein, such as kidney disease (nephrotic syndrome)
- That increase/expand plasma volume (diluting the blood), such as congestive heart failure

Total protein may increase with conditions that cause:

- Abnormally high production of protein (e.g., inflammatory disorders, multiple myeloma).
- Dehydration.

The A/G ratio: is calculated from measured total protein, albumin, and globulin (total protein-albumin). Normally, there is a little more albumin than globulins, giving a normal A/G ratio of slightly over 1.

A low A/G ratio may reflect overproduction of globulins, such as seen in multiple myeloma or autoimmune diseases, or underproduction of albumin, such as may occur with cirrhosis, or loss of albumin from the circulation, as may occur with kidney disease (nephrotic syndrome).

A high A/G ratio suggests underproduction of immunoglobulins as may be seen in some genetic deficiencies and in some leukemias.

Total protein and albumin tests are routinely included in :

- The panels of tests performed as part of a health examination, such as a comprehensive metabolic panel (CMP), so they are f used to evaluate a person's overall health status.
- Can reflect nutritional status and conditions that cause malabsorption, such as celiac disease or inflammatory bowel disease (IBD).
- To help diagnose kidney disease or liver disease, bone marrow disorder, or to investigate the cause of abnormal pooling of fluid in tissue (edema).
- Drugs that may decrease protein levels include estrogens and oral contraceptives.
- False elevated total protein when prolonged application of a tourniquet during blood collection.

Some examples of follow-up tests include protein: electrophoresis and quantitative immunoglobulins.