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ORIGINAL ARTICLES

Overview of bilirubin as criterion for higher military education admission

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Abstract: *This article was written because of the necessity of clarifying the recent biomedical selection criterion for the medical exam of the students who are applying for higher military education. In order to screen for or monitor liver disorders or hemolytic anemia the bilirubin is measured. The increased values of the bilirubin can be caused by multiple factors and they are presented in the following chapters.*

Keywords: *Bilirubin, liver, gall, alimentation, genetic diseases*

WHAT IS BILIRUBIN?

Bilirubin is a linear liposoluble tetrapyrrole derived from the enzymatic catabolism of the hem fraction from various hemoproteins in the body. Understanding changes in plasma levels of bilirubin under pathological conditions and differentiation of icteric syndromes involves a prior knowledge of the mechanism of formation, agglutination and elimination of this compound.

The normal values observed in the laboratory analysis are:
- Total bilirubin = 0.3 - 1.2 mg / dl, (or 0.1 - 1.2 mg / dl)
- Direct bilirubin = 0.1 - 0.35 mg / dl
- Indirect bilirubin = difference

Linear tetrapyrrole is the result of the enzymatic mechanism that catalysis the oxidative breakdown of the tetrapirolic (porphyrinic) ring of the hemoglobin heme molecule, primarily of the aged erythrocytes.

The process leads to hemoglobin formation in at least two stages. Bilirubin is mainly formed in the liver (about 80-85% up to 90% according to some authors), the rest having extrahepatic origin, in part reticuloendothelial (spleen, bone marrow).

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Involvement of the liver in bilirubin production

The main degradation product of porphyrins is bilirubin, the red-orange bile pigment, which still possesses the four pyrrole rings. In the plasma, the pigment circulates as total bilirubin, consisting of two components: bilirubin bound to unconjugated albumin, indirectly referred to as free glucuronide bilirubin (mono- and diglucuronate), related to the diazotation reaction, Hijmans Van Den Bergh. Total bilirubin level serum concentration is 0.1-1.2 mg/dL or 17 µmol/l. Under normal circumstances, bilirubin accounts for 85% of the erythrocyte hemoglobin degradation and the remaining 15% originates in the degradation of other hemproteins such as myoglobin, cytochromes and other hemic enzymes (catalases, peroxidases, cytochrom-oxidases).

Direct bilirubin (agglutinated with glucuronic acid) circulates freely in the blood. Indirect bilirubin (primary, unconjugated) is transported by binding to albumin, partially in the form of the albumin-phosphatide complex and in small amounts bound to both metals, amino acids, peptides or other small molecules. In the gall there are bilirubin esters with sulfuric

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acid and other acids. By binding the bilirubin to the elastic fibers of the skin and the conjunctiva the symptoms of jaundice appear (yellowing of the skin and conjunctiva).

Bilirubin production is 35 mg per gram of hemoglobin, yielding 250-300 mg daily bilirubin. Hemoglobin degradation in bilirubin is performed in Kupffer stellate cells in the hepatic reticulo-histocithic system (RHS), which is the primary location of the process, the spleen and bone marrow being organs involved in this activity.

The secretion of the gall

One of the most important functions of the liver is the production of its external secretion, the gall, which reaches the duodenum through the biliary tract. The gall fulfills two major functions:

• elimination of endogenous substances – end products of metabolism and foreign substances such as bromsulfonaphthalein (BSP) drugs and dyes;

•intervention in lipid digestion and reabsorption – the liver secreted by hepatocytes, the hepatic ball, differs in appearance and concentration of vesicular bile. The first one is clear, yellow-gold and almost isotonic with blood, and the second is of brownish green (oxidized bilirubin), cloudy and filthy. Vesicular vesicle is more concentrated than the liver due to water reabsorption through the bladder wall.

INCREASE IN BILIRUBIN VALUES

Without entering into anatomical and physiological details and the claim of accurately discovering the causes that cause the increase of bilirubin values, applying filters such as the elimination of neo-natal casuistry, serious diseases (cancerous disease, cirrhosis etc), which have a very low incidence at the age of the students, we can focus on two main directions that could underpin the rise of increased bilirubin at our students:

1. Physiological-behavioural and social.
2. Inherited, triggering some hereditary disease syndromes.

Prior to the two directions, two further specifications are required:

• The triggering of the studied phenomenon belongs mainly to the age of adolescent-premature.

• In specialty work, the possibility of recording normal values occurs once in 3-5 laboratory tests, at intervals of at least three weeks, repeated bilirubin tests can be associated with other investigations, to determine normal hepatic functionality.

1. On the liver tract, intrahepatic and extrahepatic, gall bladder, biliary bladder, we narrowed down the multitude of possibilities with pathological manifestation (even anicteric, cholestasis mild hepatitis, confirmed by Dr. Anton).

However, it is worth mentioning that hyperbilirubinemia has been reported in a different institution, namely the "Football Academy" (according to A. Constantinescu – Fundeni University Clinic)

We noticed an increase of bilirubin in the cases of:

• Automedication (we advise that medication is administered and supervised by the medic):
- Paracetamol, even a slightly increased dose,
- Oral contraceptives,
- Consumption of food supliments, protein for muscle mass.
- Energy drinks, sweet juices, fast food
• Alimentation (canteen, home or other sources):
- Lack of food diversity
- Lack of lipids in the diet

The most important aspects of nutrition belong to food adjuvants mainly preservatives:

- Sodium metabisulphite (E223) in biscuits, cakes, fast food, juices, pickles, medications.
- Monosodium glutamate (called "good taste") is less directly incriminating, but it induces fatigue, headaches, sometimes aggravating breathing, causing stress. It is omnipresent in soups, sausages, vegetable preserves, flavors etc. This heat-treated (E621) adjuvant gives the browning reaction resulting in very toxic compounds.
- Sodium benzoate, preservative (E211).
- Carbon tetrachloride, hepatotoxic.

An important factor is "pernicious anemia" - ineffective erythropoiesis, lack of vitamin B12 due to lack of food, or more severe, due to the lack of intrinsic Castle's factor in gastric juice, necessary for absorption. B12 or perhaps stress-related somatostatin secretion that inhibits the secretion of the Castle's factor.

Sure, the theme is vast. Surveillance over time and complementing with specific analyzes, not just laboratory (CT, eco) will explain the causes.

2. On the track from the liver, intra-, extracapsal, bile duct to gall bladder several hereditary transmission syndromes can be manifested with precise localization and with a slightly variable pathological manifestation. They are triggered at adolescent age, according to the algorithm for the interpretation of the functional - liver test results (according to Henry J.B.). The most common genetic diseases are:

- *The Gilbert syndrome*

It is characterized by chronic, benign, intermittent, familial

hyperbilirubinemia found in a routine control. It is caused by a defect in the transport and conjugation of unconjugated bilirubin. The jaundice is accentuated in feverish states, physical exertion or consumption of oral contraceptives.

- *The Crigler-Najjar syndrome*

Type I may be a homozygous of Gilbert's disease. Type II is characterized by partial glucuronide-transferase deficiency that bilirubin conjugates to the liver cell. Usually at adolescents, complications are rare and occur in the case of poor eating habits or by excluding lipids from the diet.

- *The Dubin- Johnson syndrome*

It is characterized by the inability to transport bilirubinuriuronide from hepatic cells to the tubule while the conjugation is normal. The stress periods are a factor. The jaundice is harmless and reversible and occurs after eating estrogen and contraceptives. It can be confused with mild viral hepatitis.

- *The Rotor Syndrome*

It is asymptomatic, benign; withdrawal and storage of conjugated bilirubin defect, and possibly related to transfer from liver to bile. Usually it is reported in adolescents (medication, exercise-physical stress). Other liver functions are normal.

- *Epstein-Barr virus infections (human herpesvirus 4)*

It induces bilirubin increases in about 30% of the patients, but if liver function abnormalities are not found, another diagnosis should be sought.

CONCLUSIONS

After analyzing the studied material together with the medical laboratory specialists (Chem. Stanciulescu C., Synevo, Biochem. Apircioaei O., former SMC), the two physicians mentioned above, Dr. Stanciulescu P., internal specialist and I tried to highlight some aspects of hyperbilirubinemia:

- Self-medication - forbidden.
- Nutrition - the main recommendations:
- Regular fresh fruits and vegetables consumption
- Reduced fast food and unhealthy drinks consumption.
- Reducing fast at the first deviations from the normal functioning of the body, especially during the body-growing period.
- Elimination, at least limitation of stress, in all forms of manifestation: physical, food, intellectual, psychosocial.
- Avoid fatigue of any kind (not enough sleep at night)

These landmarks must be all considered, taking care of only one recommendation cannot bring immediate positive results.

As for hereditary transmission diseases, unfortunately, the possibilities of reaction are very limited in Gilbert and Crigler - Najjar syndromes, phenobarbital brings a certain decrease (Jacques Wallach, p. 341, confirmed by Dr. Anton) only under the supervision of the doctor. The most important factor is however a varied diet, avoiding starvation and tiredness.

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