LIVER FUNCTION EVALUATION IN LEPTOSPIROSIS WITH COLLOIDAL GOLD ^{198}Au*.

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Eight patients with leptospirosis were studied with colloidal gold ^{198}Au. The radiocolloidal hepatic distribution was altered, presenting a non-homogeneous liver concentration in seven cases, and a minute to moderate splenic visualization in five. Two patients presented doubtful splenic image, and one seemed to be normal. Liver scanning with colloidal gold ^{198}Au is demonstrated to be a good liver function test.

INTRODUCTION

The Nuclear Medicine Tests have become more and more valuable to observe the metabolic and functional processes in man. Various radioactive compounds have been used for the detection of abnormalities in the liver (Table I). Among them, the most commonly employed are the Rose Bengal ^{131}I, the colloidal gold ^{198}Au and the sulfur colloid ^{99m}Tc. The first one has been mainly applied to evaluate the hepatocyte function and the biliary tract, as an excretion test. In pediatrics, it has a great value in the investigation of neotal jaundice[14]. It enters and leaves the polygonal cells by the active transport mecanism. Because of the physical caracteristics of the ^{123}I, Rose Bengal ^{123}I has been demonstrated to be an ideal radiocompound[10]. The last two agents give the physician science about the normality of the reticuloendothelial system. They principally deposit in the liver by phagocytosis through the Kupffer cells. Griffiths[5] stated that the sulfur colloid ^{99m}Tc does not, as it was thought, come through the Kupffer cells by phagocytosis, but stays in their membrane[5]. Other organs also concentrate these radioactive particals the same way as in the liver, but in very minute amount. Those organs are the spleen, the bone marrow, the lymph nodes and other magrophages.

It seems that the colloidal gold ^{198}Au is a better agent to study diffuse liver diseases than the sulfur colloid ^{99m}Tc, and that this one helps the physician note space occupying lesions more accurately than the colloidal gold ^{198}Au. There are two important advantages of the sulfur colloid ^{99m}Tc over the radioactive colloidal gold:

a) – its short half-life (T 1/2 = 6 hr.) and weak energy. (140 kev) make the patient recieve a lower radiation dose;

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Submitted to publication on June, 7, 1977.

b) – because of the two physical caracteristics said above in *"a"*, a larger activity dose may be administered into the patient, increasing the number of photons to obtain good quality images.

The primary application of the liver scanning with radiocolloid is to detect space occupying lesions, such as hepatoma, hepatic metastasis and liver abscesses[1,4,6,13] and to differentiate them from those diffuse: hepatitis, steatosis and cirrhosis, prior to any other traumatic diagnostic procedure.

The purpose of this work is to evaluate the liver function in leptospirosis, by means of the scintigraphic method, with colloidal gold ^{198}Au.

MATERIAL AND METHODS

Eight patients with clinical and biochemical blood tests suggestive of leptospirosis were investigated. The disease was proved by means of muscle and, or, liver biopsies. Colloidal gold ^{198} Au from São Paulo Atomic Energy Institute was used. Its specific activity was from 0.50 mCi/mg to 0.80 mCi/mg. Two views were taken (AP and PA) 30 minutes after intravenous injection of 350 uCi in all of them. The electronics was the SCINTMAT II – SIEMENS with a 3-inch-sodium iodide crystal activated with thallium NaI(Tl). The patients were scanned 12 to 29 days after the beginnig of the disease, and the time interval between the biochemical blood tests and the performanse of the examination was from 7 to 20 days. Careful attention to the liver and spleen sizes, and their radiocolloid concentration was given, specially to the borders and the hepatic left lobe, as well as to the bone marrow.

RESULTS

All of the patients had clinical suspition of leptospirosis. Therefore, biochemical blood tests and liver and, or, muscle biopsies were requested. The hepatic scintigraphy was performed before the histologic examination, which presented compatible appearances of leptospirosis.

The scintigraphic aspacts were as follow (Table II):

A) – **The liver.** Five patients had a uniform enlargement of the liver (cases I, II, III, IV and V). One had only a slight increase in size of the left lobe (case VI); another was questionable (case VII), and the last seemed to be normal (case VIII). The first five patients showed a regular and non-homogeneous concentration of the radiocolloid, with a diffuse "mottling" from discrete to moderate in the first four, and from moderate to accentuated in case V (Fig. 1). The borders and the left lobe of these five cases showed decreased uptake compared with the central area of the organ. Two patients presented good concentration, except in the borders and the left lobe (cases VI and VII), of which one bad a minimal "mottled" aspect (case VI). The last showed a normal pattern (case VIII).

b) – **The spleen.** In three cases splenic enlargement could be noted (cases II, IV and V); in two there was doubt (cases I and III), and the rest seemed to be normal (cases VI, VII and VIII). The spleen was visualized in five patients (cases II, III, IV, V and VII) with an "uptake" from moderate to minimal except in case V, which presented a moderate to high concentration; two had questionable "uptake" (cases I and VI). No splenic image could be noted in the last patient (case VIII).

C) – **The bone marrow.** No bone marrow image could be cought in any patients.

The last patient (case VIII) was the one who had his biochemical blood tests returned to the normal levels when he was subjected to scanning. The others presented abnormally high values in creatine, urea, bilirubin and transaminasis.

DISCUSSION

Liver scanning with radiocolloid has demonstrated to be an excellent liver function test, primarily for the detection of focal lesions[1,4,6,13]. It has an emphatic application to identify lesions different from those occupying ones, such as, cirrhosis[2,3,8]. In this kind of disease, the colloidal liver concentration is almost always non-homogeneous, presenting a "mottled" aspect, and spleen and bone marrow image, although this is not patognomonic[2,3,8].

Luthra and coworkers studied twenty one patients with hepatitis. Twenty of them had decreased intensity of liver uptake, and the borders were not well delineated. Eight of

TABLE I – Radiopharmaceuticals used to evaluate the liver function

Radiopharmaceuticals	Physical Caracteristics			Organ Uptake	Mecanism	Dose (mCi)
	Half-Life (T1/2)	Energy (Kev)				
Colloidal gold ^{198}Au	2.7 d	411	960	Liver, spleen, bone marrow, lymph nodes	Phagocytosis by the Kupffer cells	0.20 – 0.35
Sulfur Colloid ^{99m}Tc	6.0 hr	140	–	Liver, spleen, bone marrow, lymph nodes	Phagocytosis by the Kupffer cells (?)	2.0 – 4.0
Rose Bengal ^{131}I	8.1 d	364	610	Liver, kidney (in liver demage or biliary system block)	Active transport by the polygonal cells	0.20 – 0.35
Rose Bengal ^{123}I	13.0 hr	160	EC*	Liver, Kidney (in liver demage or biliary system block)	Active transport by the polygonal cells	2.0 – 4.0
Human serum albumin microaggregates ^{99m}Tc	6.0 hr	140	–	Liver	Phagocytosis. Active transporte (?)	2.0 – 4.0
Human serum albumin ^{99m}Tc	6.0 hr	140	–	Blood pool	Difusion	2.0 – 4.0
Transferrin ^{113m}In	8.1 d	364	610	Blood pool	Difusion	0.20 – 0.35
Human serum albumin ^{131}	1.7 hr	392	–	Blood poll	Difusion	2.0 – 8.0
Selemethionine ^{75}Se	120 d	265	121	Liver, pancreas, thyroid, parathyroids and neoplastic cells	Active transport	0.20 – 0.30

* Decay by Electron Capture

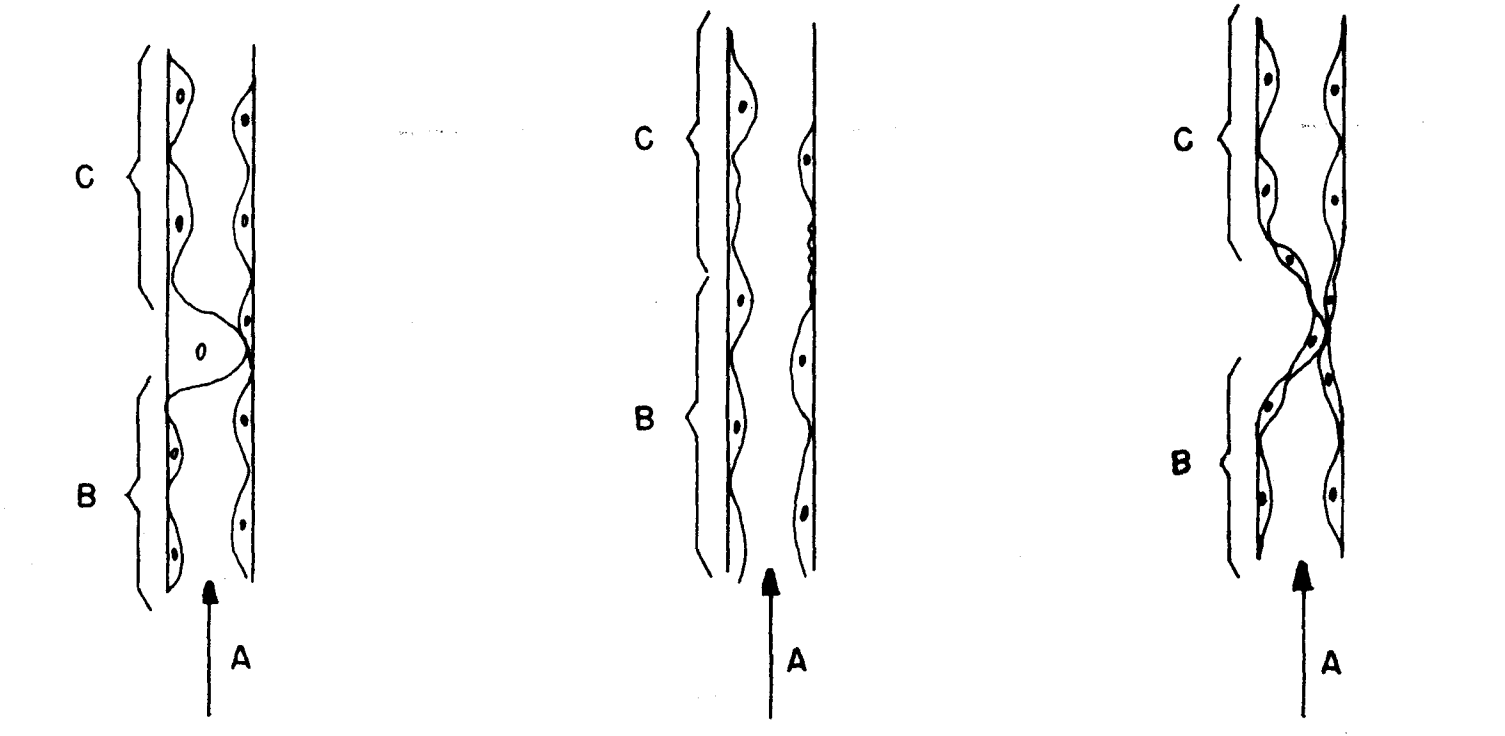
TABLE II — The scintigraphic aspects.

Cases	Liver		Spleen		Bone Marrow Image
	Increase In Size	Colloidal Concentration	Increase in Size	Image	
I	Uniform	Regular, non-homogeneous and diffuse "mottling", from Di — Mo, more evident in the borders and the left lobe.	?	?	No
II	Uniform	Regular, non-homogeneous and diffuse "mottling", from Di — Mo, more evident in the borders and the left lobe.	Yes	From Mi — Mo in AP and Di — Mo in PA	No
III	Uniform	Regular, non-homogeneous and diffuse "mottling", from Di — Mo, more evident in the borders and the left lobe.	?	Mi in Pa	No
IV	Uniform	Regular, non-homogeneous and diffuse "mottling", from Di — Mo, more evident in the borders and the left lobe.	Yes	Mi in AP and Mo in PA	No
V	Uniform	Regular, non-homogeneous and diffuse "mottling", from Mo — Ac, more evident in the borders and the left lobe.	Yes	Mo — Ac	No
VI	Slight increase in left lobe	Good concentration except in the left lobe and the borders, and Mi "mottling"	No	?	No
VII	?	Good concentration except in the borders.	No	Mi — Ab in PA	No
VIII	No	Normal	No	No	No

Legend of TABLE II

Di - discrete
Mi = minimal
Mo = moderate
Ab = absent
Ac = accentuated

Di — Mo = from discrete to moderate
Mo — Ac = from moderate to accentuated
Mi — Ab = from minimal to absent
? = questionable



1 Hypertrophy of the kupffer cells

2 Kupffer cell necrosis

3 Edema around the sinusoids

A – Blood flow in the sinusoids

B – Segment of normal activity

C – Segment of reduced activity

Fig. 1 – Explanation of the hepatic "mottling" pattern.

these had splenic activity, and three showed marrow image[7].

Using Rose Bengal ^{131}I, Schwartz and Herrera[8] investigated eight patients with hepatitis at varying stages. They disclosed impairment of liver function with diffuse "mottling" on the scan. In a work of ours on hepatitis, as well, we noted similar patterns. We had even observed bone marrow activity in one case[10].

Leptospirosis, as well, may present appearances almost like those found in hepatitis, although not so intensively "mottled", and the liver usually has a uniform size increase. We also noted that colloidal splenic uptake is less evident in this disease than in hepatitis, and that there was no bone marrow image[11]. We suppose that this is related to the degree of the liver impairment.

Normally, right after intravenous injection, the major part of the colloidal gold ^{198}Au is deposited in the liver through phagocytosis by the Kupffer cells. Very little quantity of this compound is taken up by the extrahepatic reticuloendothelial system. It is for this reason that the hepatic image is the one seen in normal subjects. Diminished hepatic concentration of the radiocolloid, splenic and sometimes bone marrow activity indicate liver failure that is proportional to the extrahepatic accumulation.

The mecanism to explain these patterns, that is, the "mottled" liver aspect, the splenic and sometimes the bone marrow images, has not been known yet, but it is supposed to be (Fig. 1):

1. For colloid excess. This might explain the reason why the spleen is visualized.

1.1. Absolute – excessive colloid injection.

1.2. Relative

1.2.1. For hypertrophy of the Kupffer cells which might block the pathway of the colloid to the next sinusoid segment (Fig. 1.)

1.2.2. For necrosis of Kupffer cell populations (Fig. 1.)

1.2.3. For edema around the sinusoids and the hepatic veins (Fig. 1.)

2. For reduced blood flow to the liver perifery, the farthest regions from the central vessels[2]. This would explain why the borders concentrate less activity than the perihilar areas.

3. For arteriovenous fistulas.

The spleen can be visualized, presumably, for the returning of the excessive colloid into the circulation. The excess of particals might happen in leptospirosis for the mecanisms stated in 1.2.1, 1.2.2 and 1.2.3. These mecanisms and probably the *"2"* might explain the "mottling" patterns found in the liver in this investigation. Thus, it is demonstrated that liver scanning with colloidal gold ^{198}Au is a good liver function test.

Ackowledgement: The authors wish to thank the drawer, Mr. Antonio Albuquerque.

RESUMO

Oito pacientes com Leptospirose foram investigados com ouro coloidal radioativo (^{198}Au). A distribuição intrahepática do radiocoloide era alterada, apresentando uma concentração hepática não-homogênea em 7 casos, e visualização esplênica de mínima a moderada em 5. Dois tinham dúvida quanto à imagem do baço, e um parecia normal. A cintigrafia hepática com ouro coloidal radioativo (^{198}Au) é demonstrada ser um bom teste de função hepática.

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