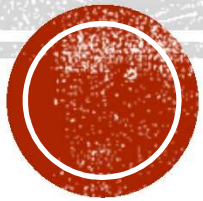
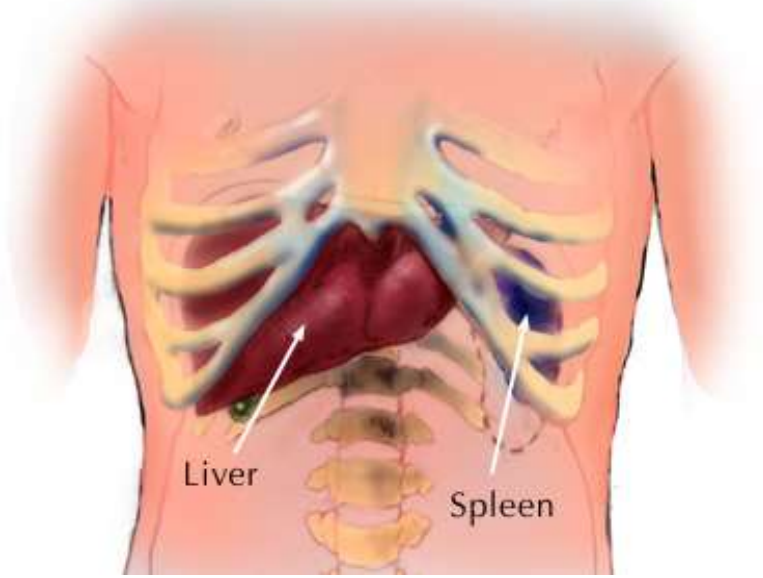
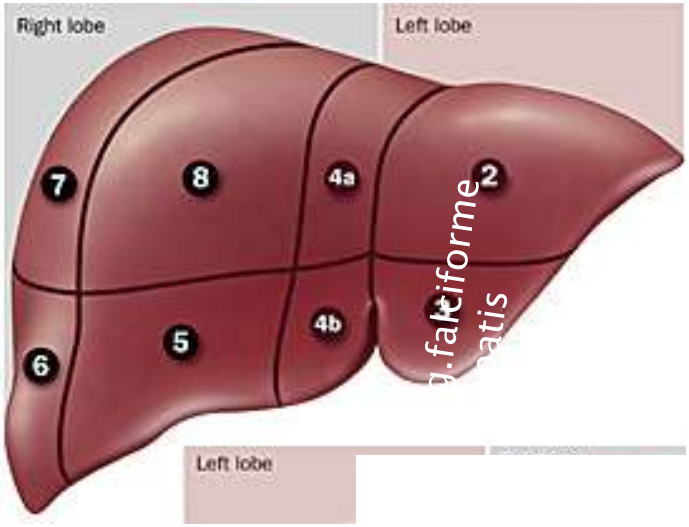
NUCLEAR MEDICINE IN EVALUATION OF LIVER AND BILIARY TRACT DISEASES

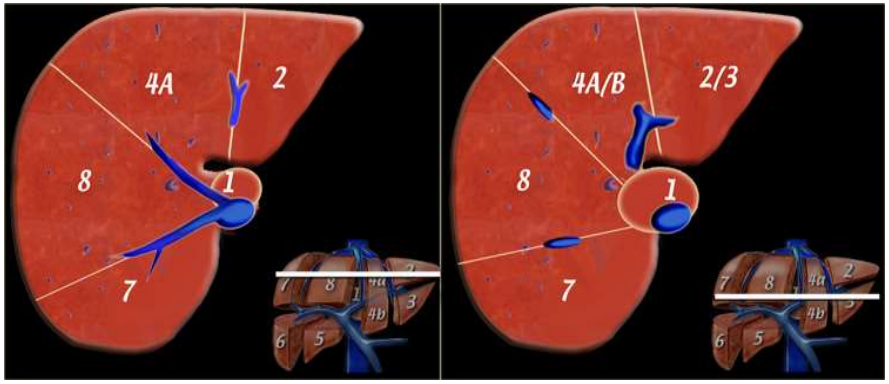


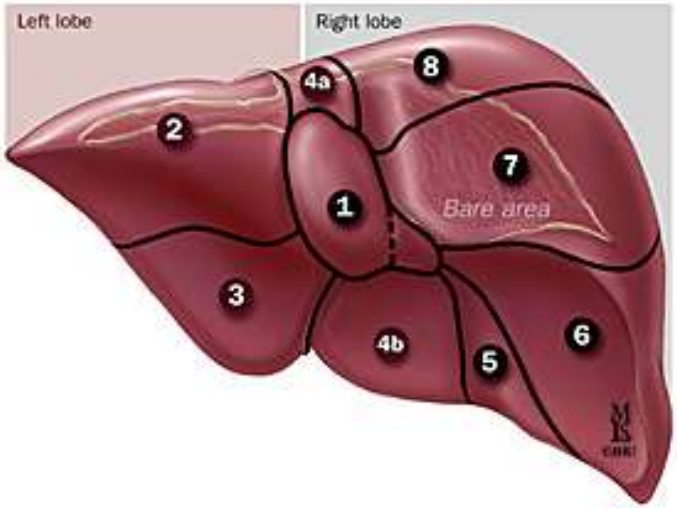
THE LIVER

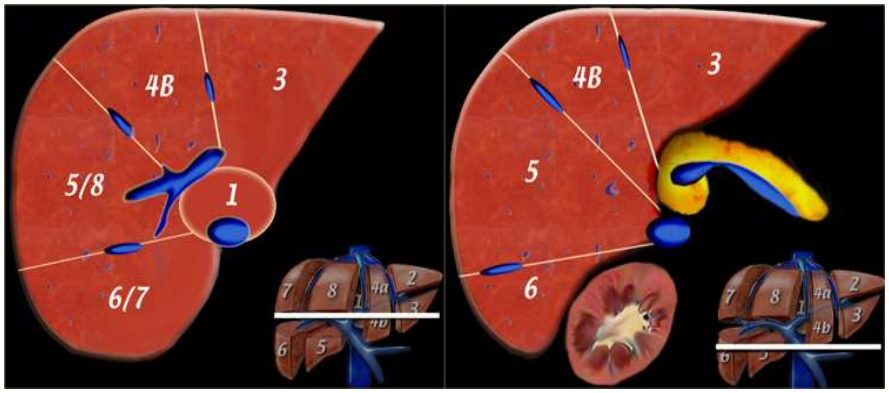
- is the largest organ in the body, weighing 1200–1500 g.
- in the right upper quadrant of the abdomen, protected by the ribcage.
- The liver receives about one-fifth of the resting cardiac output; 25% is via the hepatic artery and 75% via the portal vein

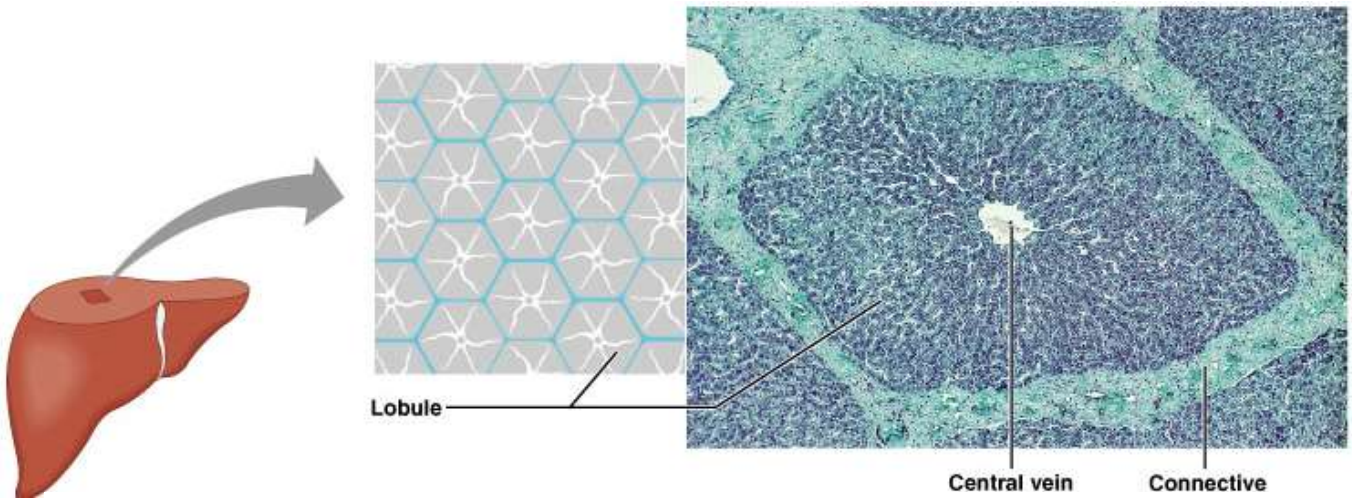


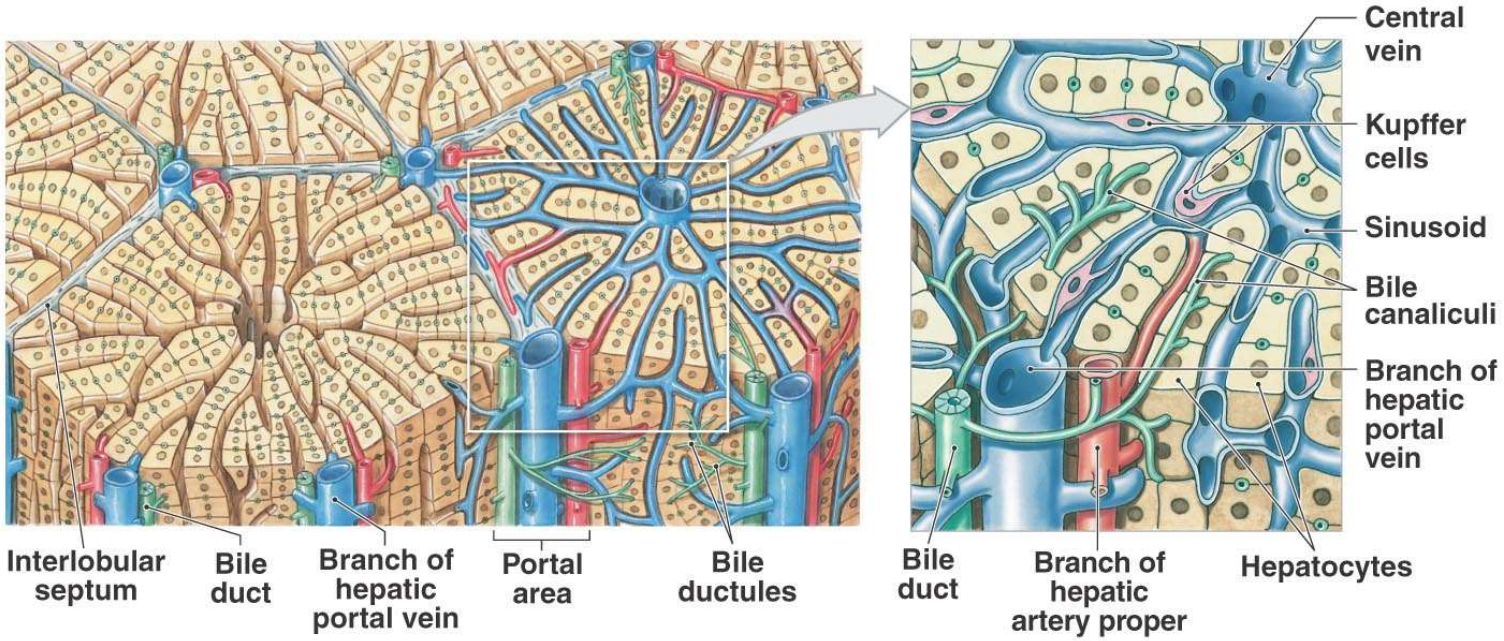

Right lobe
Left lobe
7
8
4a
2
6
5
4b
3
Left lobe


4A
2
8
1
7
4A/B
2/3
8
1
7


Left lobe
Right lobe
8
4a
2
7
1
Bare area
3
4b
5
6


4B
3
5/8
1
6/7
4B
3
5
6


Lobule
Central vein
Connective


Central vein
Kupffer cells
Sinusoid
Bile canaliculi
Branch of hepatic portal vein
Interlobular septum
Bile duct
Branch of hepatic portal vein
Portal area
Bile ductules
Bile duct
Branch of hepatic artery proper
Hepatocytes

BILIARY DRAINAGE

- Small canaliculi between the hepatocytes receive secreted bile and drain into bile ducts which run alongside the branches of the arterial and portal vein at the edge of the lobule. The bile ducts drain into the right and left hepatic ducts, which meet in the porta hepatis to form the common hepatic duct. The cystic duct connects the gallbladder to the common hepatic duct, forming the common bile duct which drains into the second part of the duodenum.
- Bile enters the gallbladder where it is concentrated and then discharged by gallbladder contraction during a meal.

BILE

- Bile contains salts which are emulsifying agents important for fat digestion. More than 95% of bile salts are reabsorbed in the terminal ileum and re-excreted via the biliary system (enterohepatic circulation).
- Malabsorption at the terminal ileum results in bile salt loss, reduced bile salt excretion, and thus fat malabsorption. The main waste product excreted is bilirubin, which is derived from the breakdown of hemoglobin.
- Excess bilirubin circulating in the blood (hyperbilirubinemia) gives rise to jaundice. This may be: "prehepatic", due to excess bilirubin production (hemolytic anemia); "hepatic", due to failure of hepatocytes to secrete bilirubin (e.g. inhepatitis); or "post-hepatic", due to bile duct obstruction (e.g. by gallstone or tumor).

COLLOID LIVER SCAN

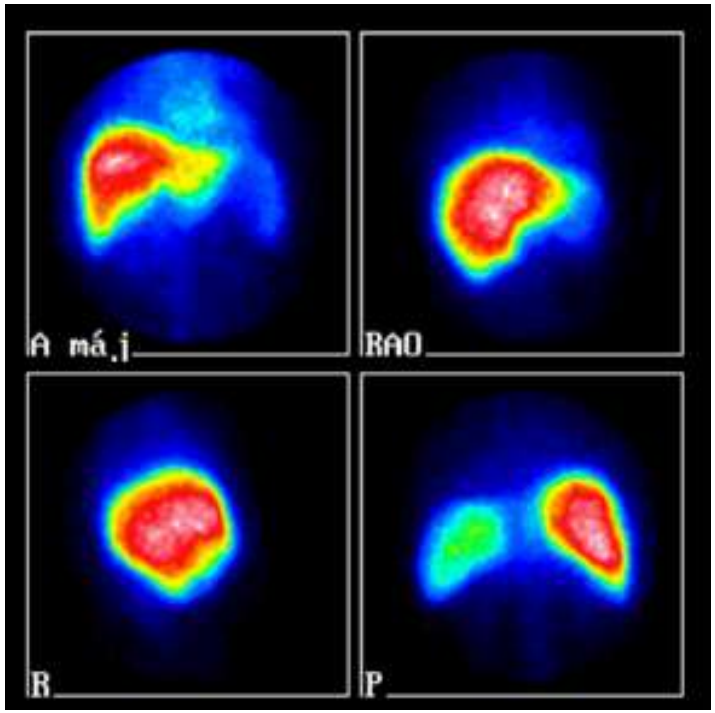
- colloid scan is used to examine the liver, spleen, and bone marrow.Colloid studies of the liver are currently performed to assess diffuse hepatic disease and less frequency to evaluate focal processes within the liver.
- Colloids are trapped and then taken up by the reticuloendothelial cells (Kupffer cells in liver); 70–80% of tin colloid is taken up by liver, 10–20% by spleen, and 5–10% by bone marrow.
- The distribution of colloid depends on its size, and the smaller colloid preparations (nanocolloid) have higher bone marrow and spleen uptake than larger tin colloids.

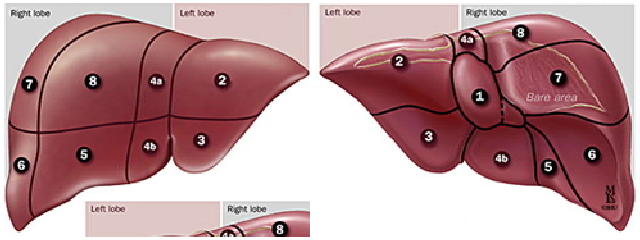
IMAGING

- Colloid should be administered into a vein (74-259MBq).
- Care must be taken to avoid formation of blood clot in the syringe due to repeated attempts at venipuncture as this may clump the colloid and result in lung extraction.
- Images are acquired 15 minutes after injection.
- The standard images are anterior and posterior images with right and left laterals.

COLLOID LIVER SCAN

- ^{99m}Tc-S(Sn)-colloid, ^{99m}Tc-phytate, ^{188}Re-S-colloid



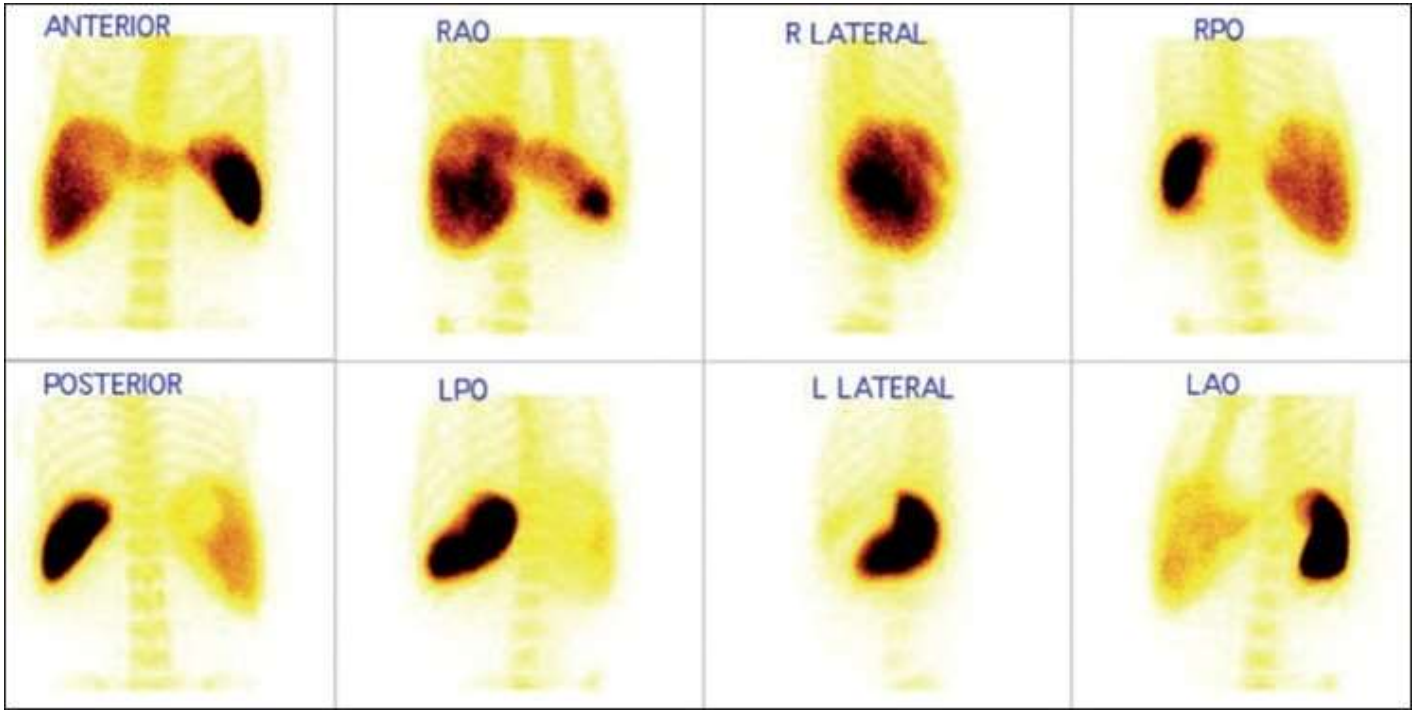


ANALYSIS AND INTERPRETATION

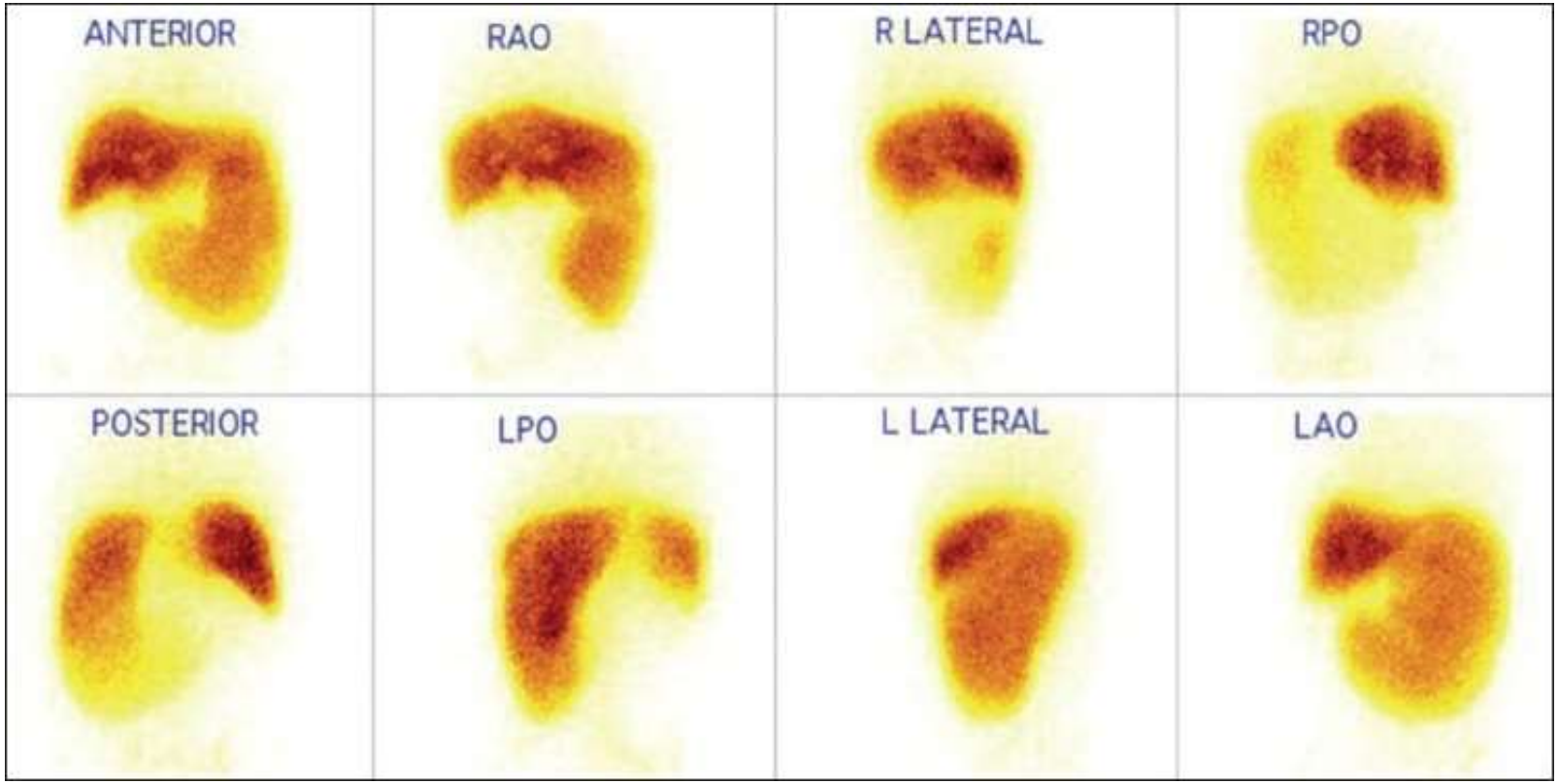
- The shape and amount of uptake in the liver is noted. The liver is examined for any photon-deficient areas.
- With cirrhosis there is reduced liver uptake, increased bone marrow uptake and with portal hypertension excessive splenic uptake.
- The liver disease detectable may be focal (metastases, hepatoma, cyst, and abscess) or the abnormality may be reduced diffuse uptake, which is encountered in generalized liver disease such as cirrhosis.

GENERALIZED LIVER DISEASE

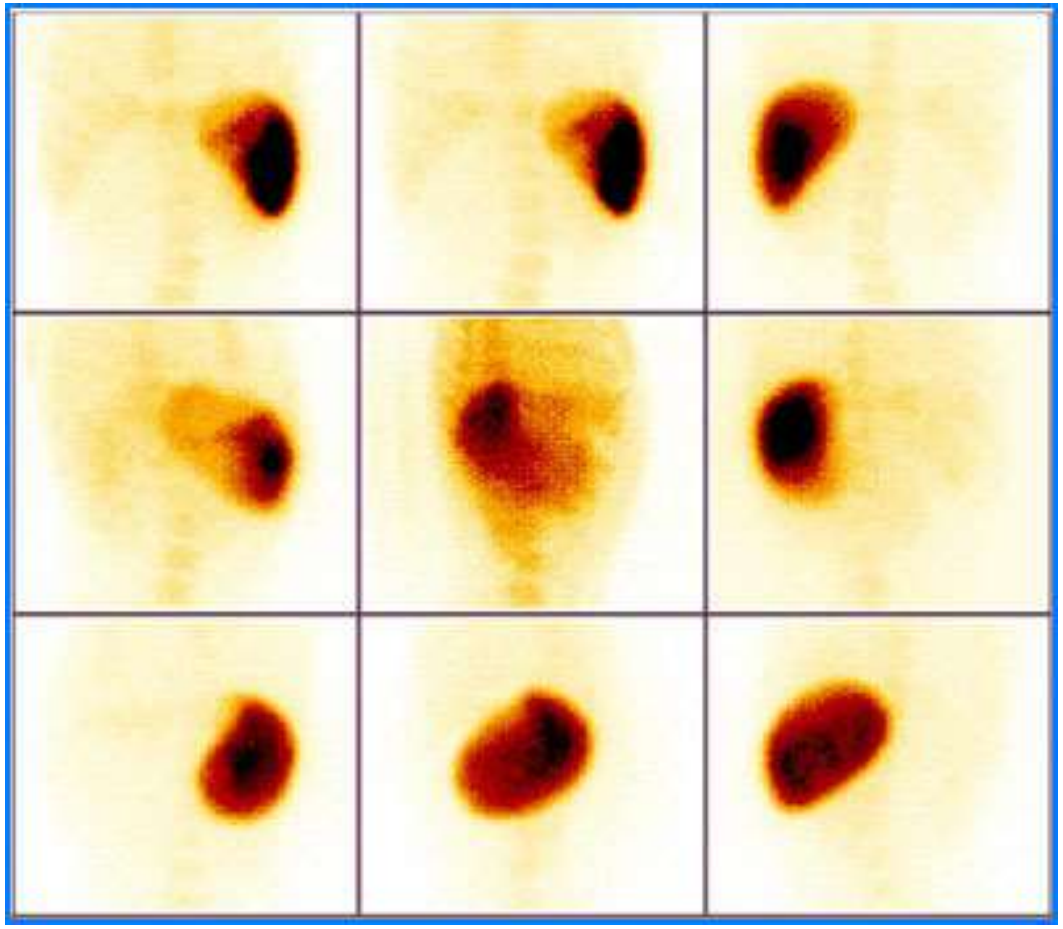
- Liver cirrhosis



GENERALIZED LIVER DISEASE



GENERALIZED LIVER DISEASE



- Colloid "shift" is not specific for hepatic dysfunction;
- factors including portal hypertension, hypersplenism, marrow-active anemia as a response to chemotherapy,and malignant melanoma may also result in this finding
- Splenomegaly is not a specific finding in hepatic disease, because other pathology, such as lymphoma, can alter splenic size

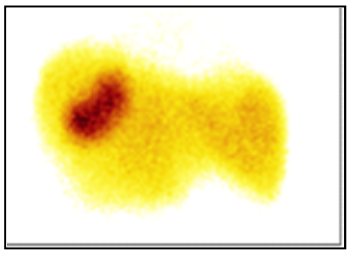
- Most true space-occupying processes within the liver, such as metastases and abscesses, are devoid of Kupffer cells, with resultant defects noted on SC imaging.
- In contrast, processes that simulate space-occupying lesions on radiographic studies, but do not disturb Kupffer cell function, such as regenerating nodules or fatty change within the liver, retain SC uptake
- Primary masses originating within the liver include HCC, focal nodular hyperplasia (FNH) and hepatic adenoma. HCC is devoid of uptake on SC studies. In FNH, lesions have variable degrees of Kupffer cell function, and consequently variable colloid uptake has been described in these lesions

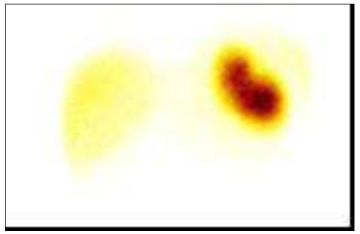
SPLENIC IMAGING

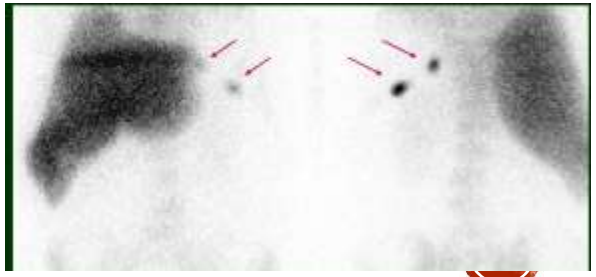
- The spleen will usually be imaged as part of a liver scan and this often provides sufficient information for clinical purposes. Splenic imaging may be performed in children to rule out congenital asplenia or polysplenia. Other indications include confirming presence of functional splenic tissue in cases of splenic auto-transplantation following splenic trauma or absence of such tissue in patients who have been treated previously with splenectomy for conditions such as idiopathic thrombocytopenic purpura (ITP). Splenic imaging can also be performed in order to characterize incidentally noted abdominal masses, which are thought to represent accessory spleens or splenic tissue
- A more specific way of showing the spleen is to use heat-denatured erythrocytes, which give excellent splenic visualization and are particularly useful if the splenic uptake is suspected to be poor.
- Red cells are first labeled with technetium as described, then they are heated to 39.5◦C (for 30 minutes). This distorts the red cell structure and the damaged cells are taken up by the functioning splenic tissue.

SPLENIC IMAGING

- After cooling to at least body temperature, the heat-damaged RBCs are administered intravenously, with imaging performed 20 to 30 minutes post injection
- If ectopic splenic tissue is a concern, the entire abdomen should be imaged. If the patient has had prior trauma that may have resulted in a diaphragmatic rupture, the chest also should be imaged.

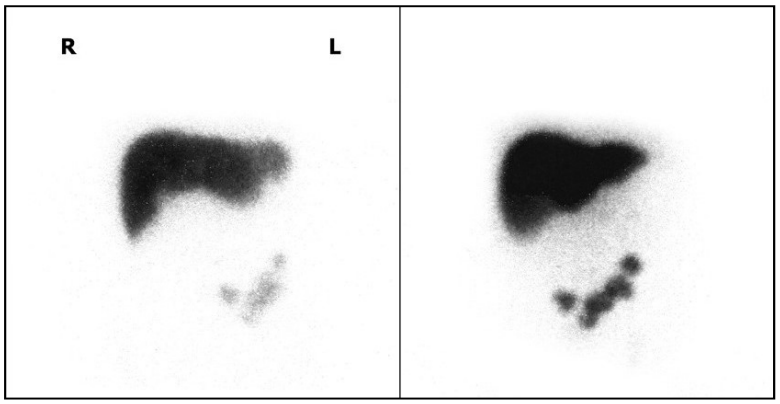




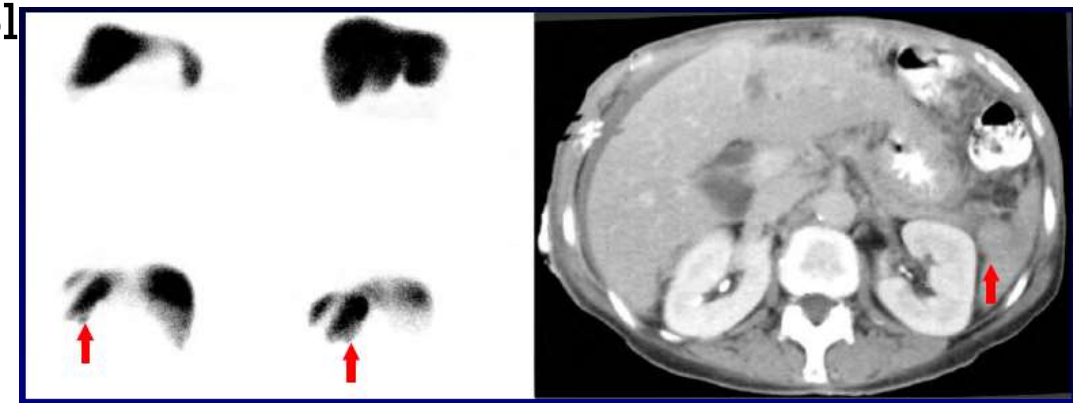


SPLENIC IMAGING

- splenosis



- accessory spl

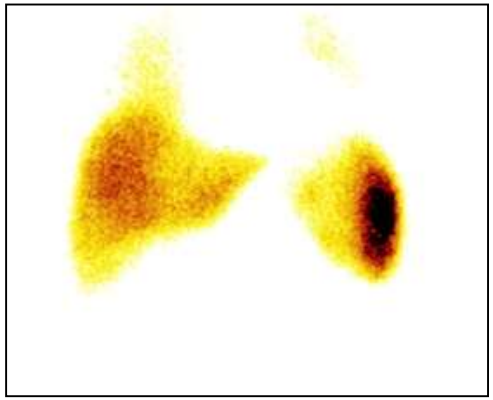


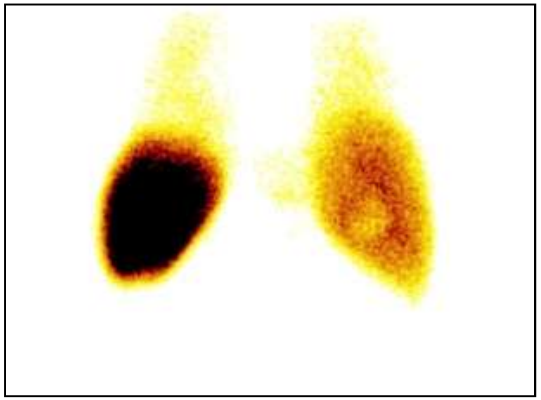
HEMANGIOMA IMAGING

- The most common benign lesion of the liver is hemangioma, occurring in up to 7% of the population and representing a frequent incidental finding in the course of imaging of the abdomen. Hemangiomas do not require any medical intervention or treatment, and a non-invasive and specific means of characterizing these lesions would serve to obviate further concern. Imaging of the liver with 99mTc-labeled RBCs fulfills this role.
- Delayed blood pool images, are acquired approximately 2–3 h following injection. SPECT will often be necessary to visualize small lesions, especially when deep within the liver parenchyma or not detected on planar views, and is useful for comparison to other cross-sectional imaging modalities.

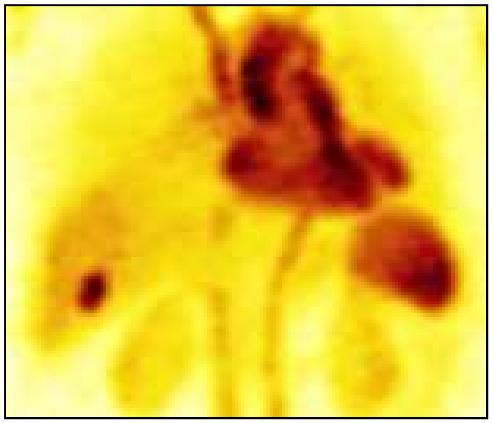
HEMANGIOMA IMAGING

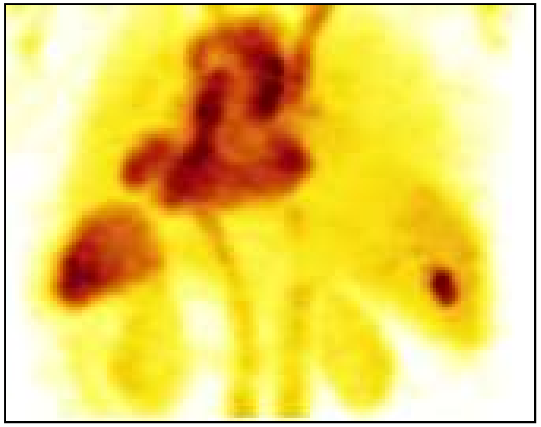
^{99m}Tc-Sn-colloid





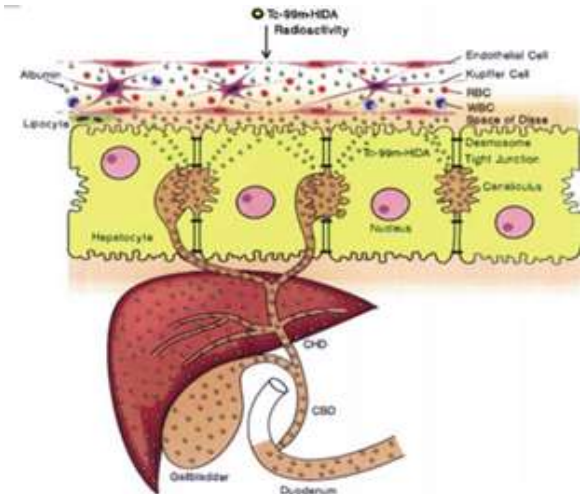
^{99m}Tc-Sn-RBC SPECT





HEPATOBILIARY SCINTIGRAPHY

- 99mTc-labeled iminodiacetic acid (IDA) derivatives have been used to investigate biliary excretion and the pathway from liver to small intestine.
- Tribromomethyl-HIDA (mebrofenin), DISIDA, is generally available. It is cleared from the circulation by the hepatic cells and secreted into the bile by mechanisms identical to bilirubin, they are not conjugated as is bilirubin.
- When liver function is poor there is proportionally increased kidney excretion. HIDA compounds accumulate into the gallbladder and are excreted into the small bowel. Once in the bowel it is possible to investigate and measure bile reflux from duodenum into the stomach.
- Hepatobiliary scintigraphy is also used to assess the hepatic uptake, bile duct patency, cystic duct patency, gallbladder function (chronic and acute infections), gallstones, common bile duct patency, and sphincter of Oddi dysfunction. Bile reflux studies are usually undertaken in patients after ulcer surgery. Symptoms of bile vomiting, epigastric pain, and heartburn may occur, especially in those who have had gastric resections, and it is important to establish the presence of reflux before corrective surgery is undertaken.



Agent	Liver uptake (% dose)	Urine excretion (% dose)	Liver excretion (T½, min)
Tc-99m-Mebrofenin (Choletec)	98	2.	17
Tc-99m-Disofenin (Hepatolite)	89	11	19

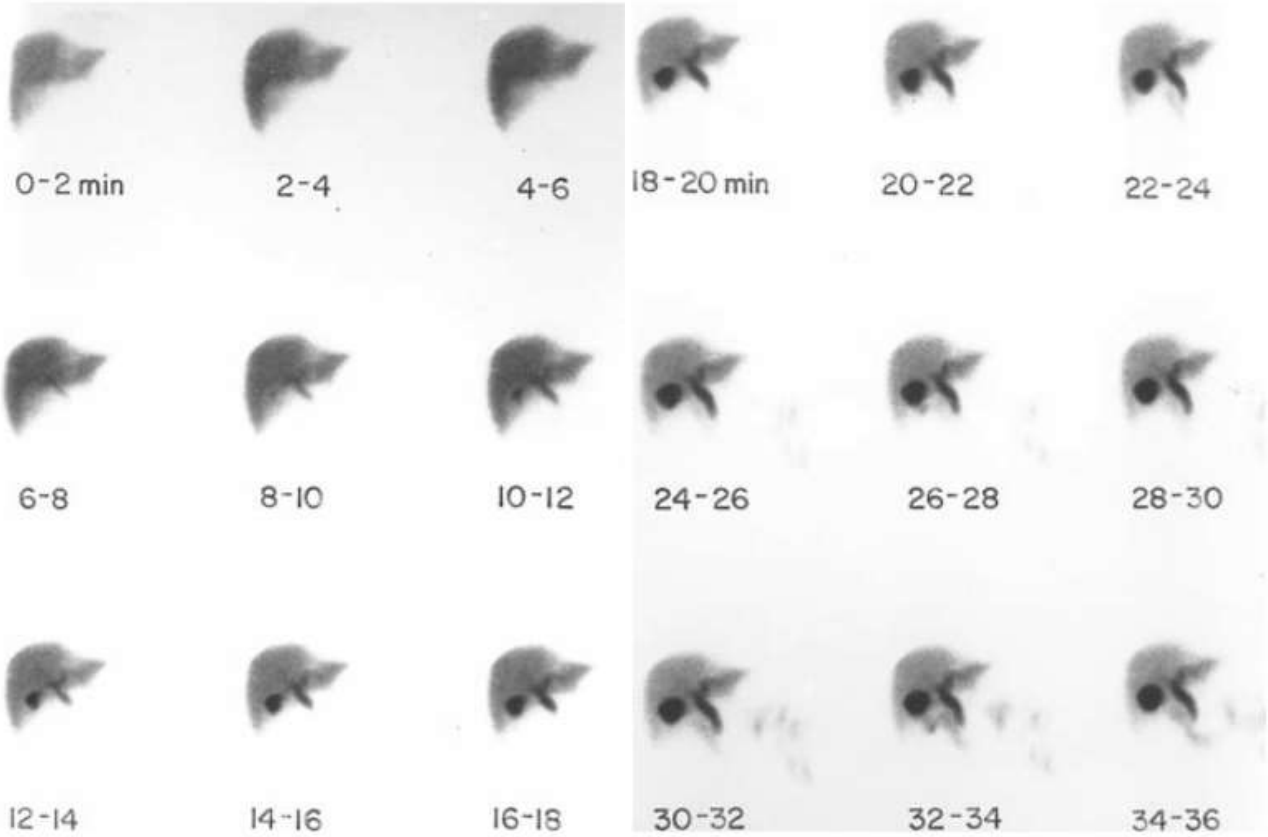
- The patient is positioned prone on a bed with the camera anteriorly so that heart, liver, and spleen are included in the field of view. The patient is then injected with 99mTc-labeled HIDA and acquisition started immediately.
- However, if only gallbladder function and reflux is being assessed then the injection can be given first and the patient brought in for imaging 20 minutes later.
- When gallbladder stimulation is required, either a liquid fatty meal or cholecystokinin (CCK) or its analogue may be given at 40 minutes after HIDA injection to provoke emptying of the bile ducts and gallbladder.

- The gallbladder is identified in the images and the region of interest is drawn around it. The ejection fraction, ejection period, and rate of ejection are calculated for the gallbladder using the time–activity curves.
- The images are checked for the time of appearance of activity in the small bowel and for evidence of reflux into the stomach/esophagus. It is important to note the time of appearance of the gallbladder. In chronic cholecystitis the gallbladder may be visualized later, but more commonly the rate and period of gallbladder ejection is prolonged while the ejection fraction is reduced

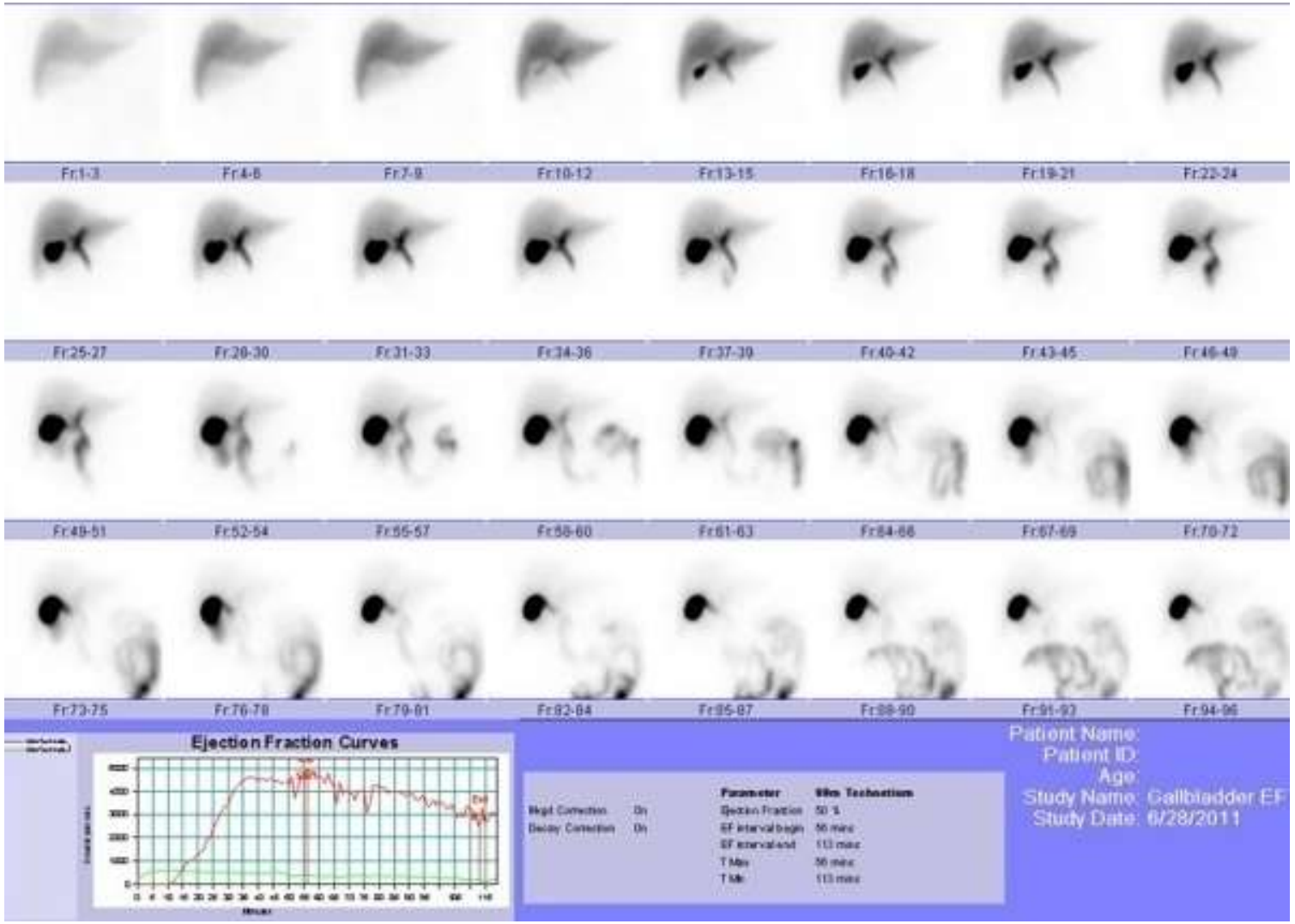
- In the presence of right upper quadrant pain, failure to visualize the gallbladder by 4 hours with normal passage of activity to the bowel is sign of acute cholecystitis, and indicates cystic duct obstruction.
- While delayed visualization of the gallbladder usually indicates chronic cholecystitis.
- Non-visualization of gallbladder, bile ducts, or small bowel may be due to acute biliary obstruction. In children with cystic fibrosis there is no activity in the small bowel; however, the bile ducts may be visualized in the late images.
- Other causes of non-visualization of gallbladder are previous cholecystectomy, and non-fasting patients.
- Biliary scintigraphy is helpful to differentiate the different causes of neonatal jaundice (neonatal hepatitis and biliary atresia). Imaging begins immediately post-injection and extends intermittently through several hours. If no bowel activity is observed, patients return for delayed imaging through 24 h. Any activity noted within the bowel or GB indicates patency of the CBD and excludes the diagnosis of biliary atresia

HEPATOBILIARY SCINTIGRAPHY

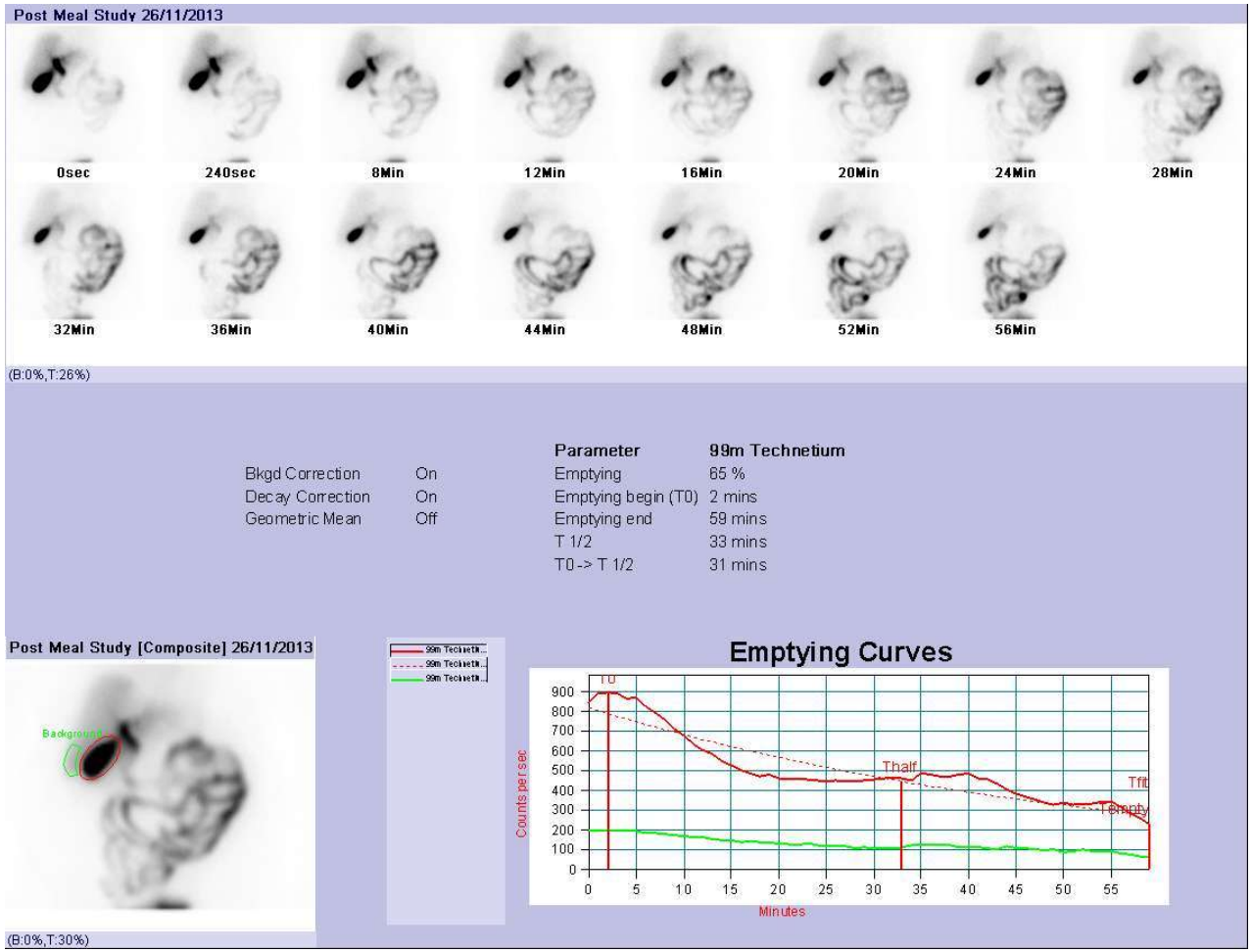
In the normal patient, hepatic uptake of a 99mTc-labeled IDA derivative is prompt, with blood-pool activity clearing by 5 min post-injection. There is rapid excretion of radiopharmaceutical by the liver, through the biliary tree, and into the duodenum and GB, both of which visualize within the first hour, the GB normally fills between 10 min and 1 h post-injection of radiopharmaceutical.



HEPATOBILIARY SCINTIGRAPHY

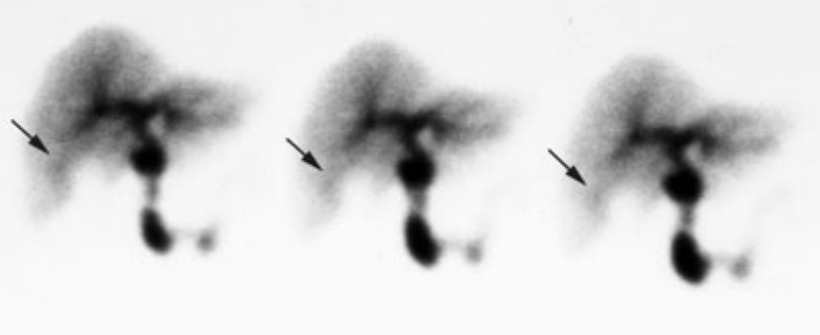


HEPATOBILIARY SCINTIGRAPHY



ACUTE CHOLECYSTITIS

- Clinical information of relevance prior to a hepatobiliary study includes history of previous surgeries, recent bilirubin and liver enzyme levels, and current medications, time of most recent food ingestion
- Complete non-visualization through 4 h in an acutely ill patient is both highly sensitive and specific for acute cholecystitis, reflecting cystic duct. This is usually caused by impaction of a stone in the cystic duct; however, acute acalculous cholecystitis will also cause non-visualization of the GB



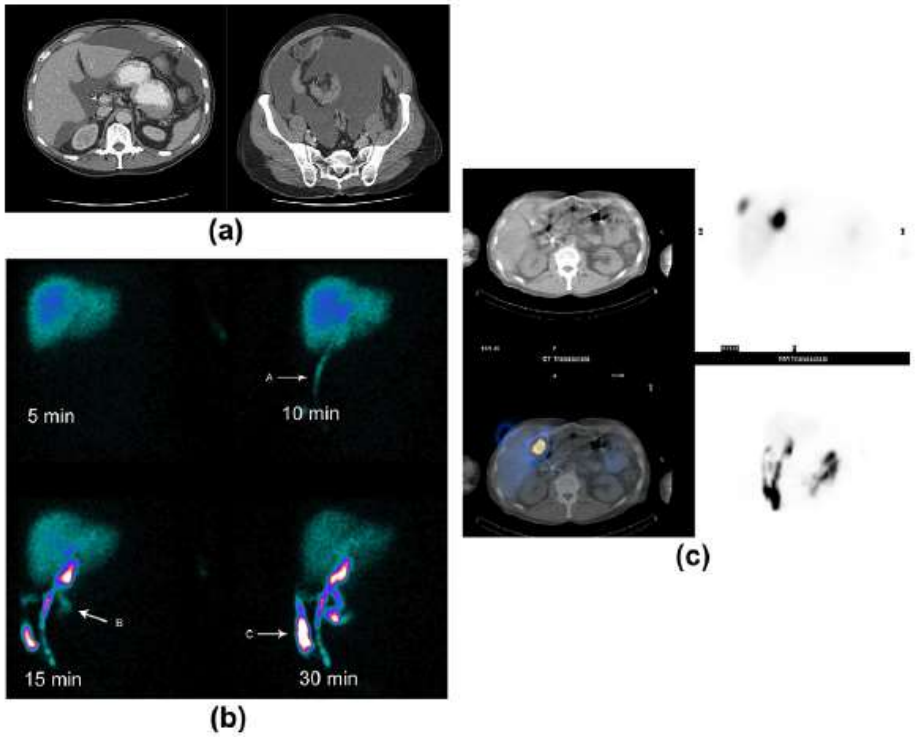
„Rim sign“

“rim” or “stripe” sign which consists of a band of increased activity at the lower margin of the liver in the region of the GB fossa is the suggestive of complicated acute cholecystitis,

- Occasionally, right upper quadrant pain persists following cholecystectomy. In these circumstances, quantitative scintigraphy may be used to assess the physiologic transit of radiotracer from the liver to the bowel, thereby evaluating function of the sphincter of Oddi.

BILE LEAK

- Bile leaks and bile duct injury has been the major postoperative complications described after laparoscopic cholecystectomy.
- HBS can determine whether a fluid collection seen on ultrasound or CT is of biliary origin.
- HBS can determine the rate of leakage and can be used as a follow-up tool. A common finding of a bile leak is the radiopharmaceutical's progressive accumulation outside the biliary system, either localized (bilomas) or diffuse
- Negative HBS study for significant bile leak can assure the surgeon to manage the patient conservatively.

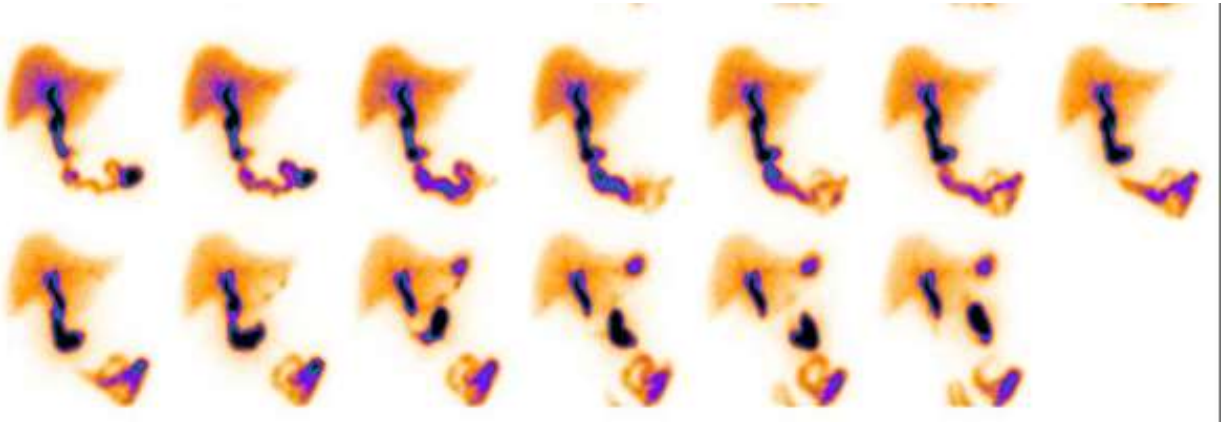


SPHINCTER OF ODDI DYSFUNCTION

- refers to a functional obstruction of the sphincter of Oddi leading to hepatobiliary-type pain. Historically, the gold standard for diagnosis of SOD has been the detection of elevated sphincter pressure via manometry; however, this is an invasive procedure that carries with it a substantial risk of inducing pancreatitis. Hepatobiliary scintigraphy with cholecystokinin (HIDA-CCK) stimulation is a less-invasive, alternative to manometry; however, its clinical utility in the context of SOD is unclear

ENTEROGASTRIC REFLUX

- is a frequent incidental finding (10%) on HIDA scans and may have important implications for patients with suspected cholecystitis. Detecting EGR may reveal the true etiology of pain in patients with normal HIDA scans.
- cholecystectomy is a risk factor for development of clinically significant EGR and therefore may worsen pre-existing EGR.

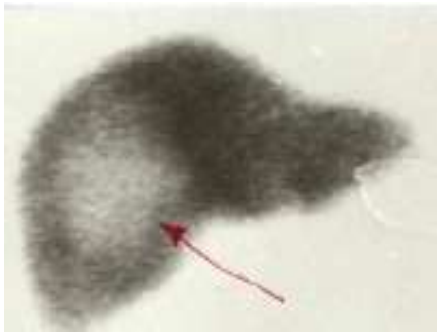


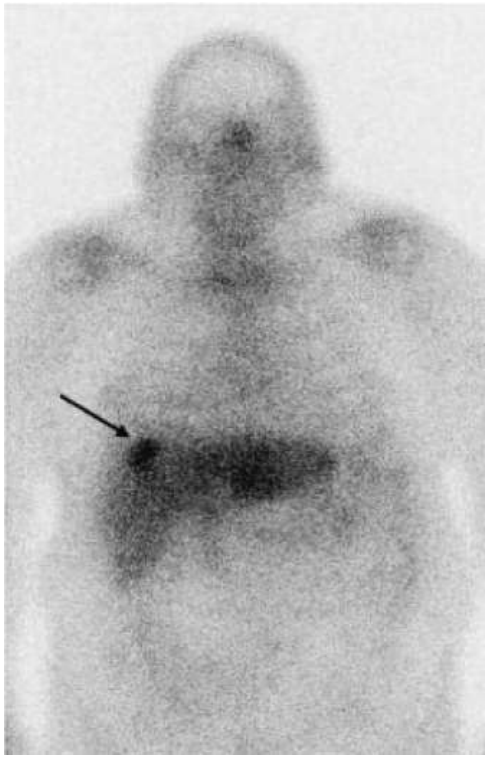
CHARACTERIZATION OF LIVER MASSES

- Uptake of hepatobiliary radiopharmaceutical indicates presence of functioning hepatocytes and thereby excludes masses of non-hepatic origin.
- 18F-Fluorodeoxyglucose (FDG) PET has become a mainstay of oncologic imaging. It is therefore not surprising that this modality has been successfully used in evaluating tumors of the liver and GI tract
- useful in the evaluation of liver metastases from a variety of primary malignancies
- Somatostatin receptor scintigraphy has been shown to be superior to FDG PET for diagnosing and staging carcinoid tumors;
- 67Ga-citrate has been known to accumulate in both malignant and infectious processes that affect the liver. More recently, the mechanism of localization of 67Ga-citrate in tumors has been understood to be receptor based, reflecting increased presence of transferrin receptors to which circulating 67Ga-transferrin complexes bind

CHARACTERIZATION OF LIVER MASSES

^{99m}Tc-Sn-kolid





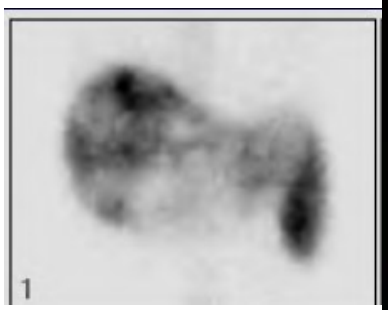
^{67}Ga-citrat

Hepatocellular carcinoma (HCC) usually displays marked arterial vascularity on dynamic perfusion imaging, its appearance on static colloid imaging (focally decreased activity) is nonspecific. Sulfur colloid imaging can be used to differentiate regenerating nodules from HCC in a cirrhotic liver

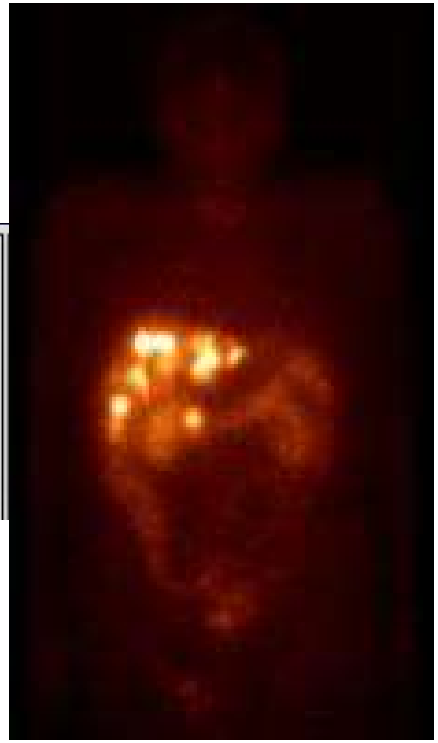
90–95% of HCCs are reported to have ^{67}Ga-citrate uptake

gallium-avid HCC replacing hepatic tissue in region of defects noted on the colloid study.

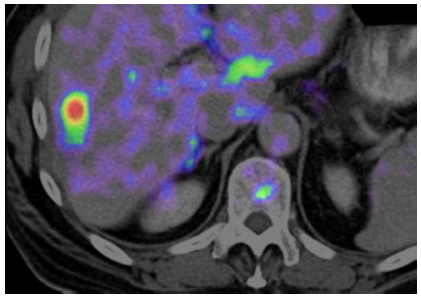
FDG SCANNING IN DETECTING HEPATIC METASTASES

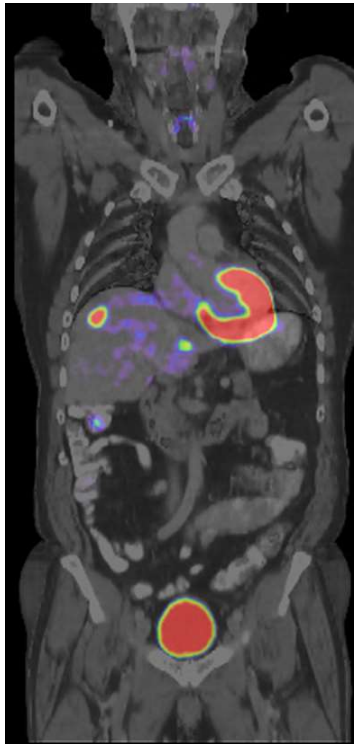


99m-Tc-colloid



^{18}F-FDG

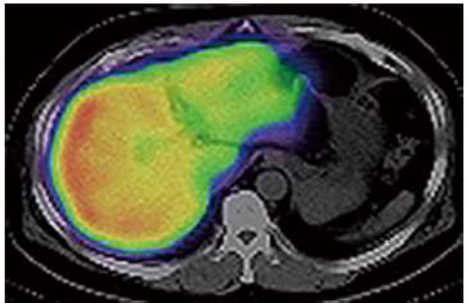




^{18}F-FDG

FUNCTIONAL HEPATIC MASS/RESERVE

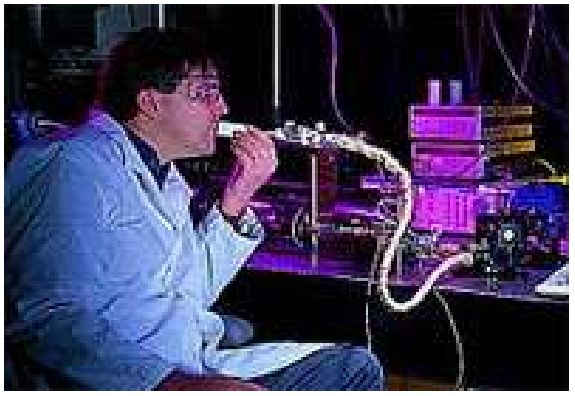
- It is important to assess the functional hepatic reserve prior to major hepatic resection because postoperative liver failure can significantly affect the clinical coursee
- Tc-99m-GSA appears to be the most widely used radiopharmaceutical for assessing functional hepatic reserve in a variety of clinical settings
- This tracer is taken up only by functional hepatocytes, independent of hepatic blood flow
- Tc-99m- GSA does not compete with bilirubin, which is an additional advantage in the evaluation of hepatic reserve in patients with hyperbilirubinemia.
- Overall, Tc- 99m-GSA imaging performed prior to surgery and/or other procedures such as a percutaneous transhepatic portal embolization appears to be a reliable method of predicting functional hepatic reserve



^{14}C-AMINOPYRINE EXPIRATION TEST

^{14}C-aminopyrine 2 µCi (74 KBq) per os or i.v.

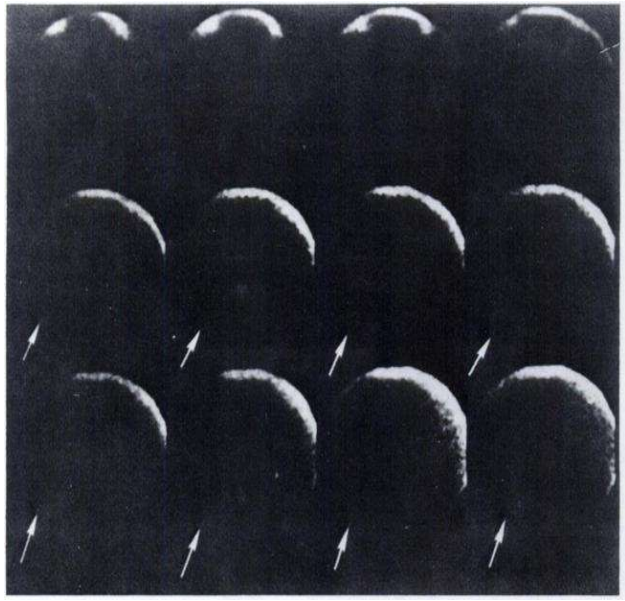
Microsomal enzymes play an important role in drug metabolism their activity may be reduced in liver disease. Aminopyrine breath test is a sensitive, non-invasive test and specific in liver function and therefore useful in the follow up of patients with known liver disease.The ^{14}CO2 exhaled after intravenous administration of 14C-aminopyrine gives quantitative information on the hepatic demethylation of the drug. Subsequently a breath test, after oral administration of (14C) aminopyrine, has been developed which provides a simple procedure for the quantitative assessment of microsomal function in man



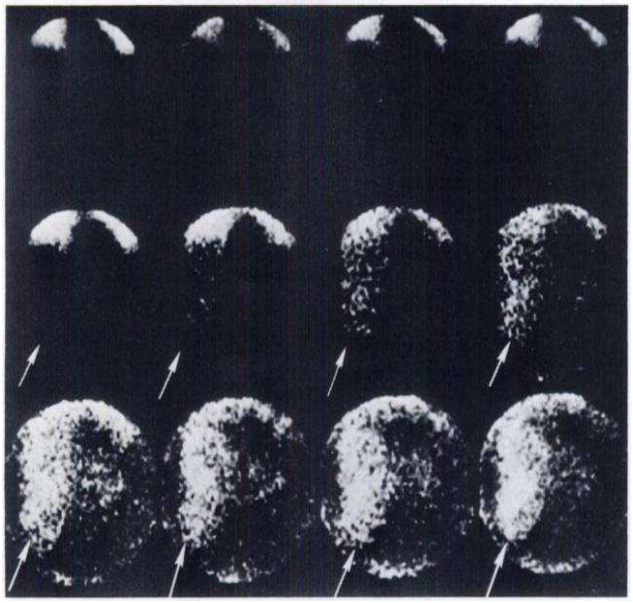
STEATOSIS HEPATIS ^{133}XENON

- Though not commonly performed today, radioactive xenon has historically been used to identify focal fatty changes in the liver, based on retention of the radioactive gas within the liver on delayed washout studies
- When the liver exhibits only a moderate degree of hepatic steatosis, a normal SC examination appears to be a more reliable and available means of excluding pathology.
- Xenon -133 is a readily diffusible gas which is neither utilized nor produced by the body. It passes through cell membranes, freely exchanges between blood and tissue, and tends to concentrate more in body fat than in blood, plasma, water or protein solutions. In the concentrations recommended for diagnostic studies, it is physiologically inactive

- Xenon Xe 133 decays by beta emission with a physical half life of 5.245 days'. The 81.0 keV gamma ray is useful for detection in imaging studies.
- Inhaled Xenon Xe 133 will enter the alveolar wall and enter the pulmonary venous circulation via the capillaries. Most of the Xenon Xe 133 that enters the circulation from a single breath is returned to the lungs and exhaled after a single pass through the peripheral circulation.
- INDICATIONS AND USAGE: MPI Xenon Xe 133 Gas may be used in inhalation studies for the evaluation of pulmonary function, for lung imaging and the assessment of cerebral blood flow.



Healthy liver



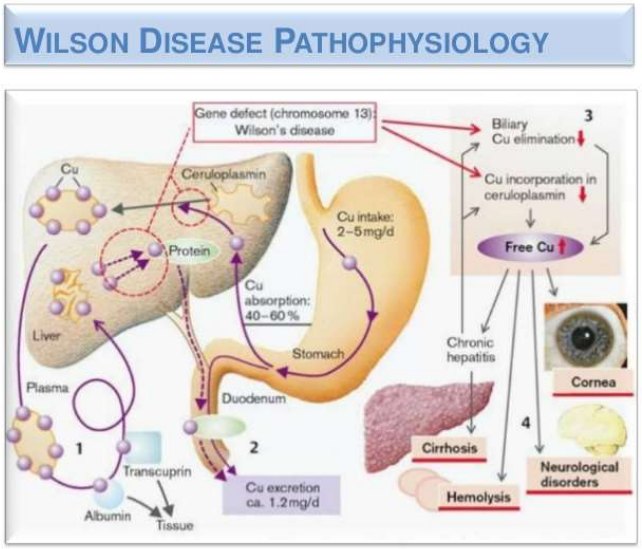
Steatosis

WILSON DISEASE

- Disappearance of copper from plasma roughly corresponds to the sequestration of the metal by liver. Untreated, symptomatic Wilson's disease patients show much delayed uptake of copper by the liver and slow clearance from plasma. Treatment with chelating agents restores the pattern towards that seen in presymptomatic patients.

- 64CuCl2 PET may change the management of WD patients because it could reflect the symptoms variation of WD and thus affect the treatment strategy. With more detailed information and a SUV cut-off value obtained from further validation of the methodology, 64CuCl2 PET could serve as a simple, straightforward, and noninvasive method for WD diagnosis

  - symptoms usually appear between the ages of 6 and 20 years, but cases in much older people have been described. Wilson's disease occurs in 1 to 4 per 100,000 people
  - The genetic defect, localized to arm 13q, has been shown to affect the copper-transporting adenosine triphosphatase (ATPase) gene (ATP7B-Wilson disease protein) in the liver.



- Radiolabeled copper testing directly assays hepatic copper metabolism. Blood is collected at 1, 2, 4, 24, and 48 hours after oral ingestion of radiolabeled copper (^{64}Cu or ^{67}Cu) for radioactivity in serum.
- In all individuals, radioactivity promptly appears after absorption, followed by hepatic clearance. In healthy people, reappearance of the radioactivity in serum occurs as the labeled copper is incorporated into newly synthesized ceruloplasmin and released into the circulation.
- Heterozygotes exhibit a slow, lower-level reappearance of radioactivity rather than the continued fall in radioactivity seen in persons with Wilson disease, but there may be considerable overlap between the 2 types of patients. Patients with Wilson disease, even those with normal ceruloplasmin levels, do not exhibit the secondary rise in radioactivity.