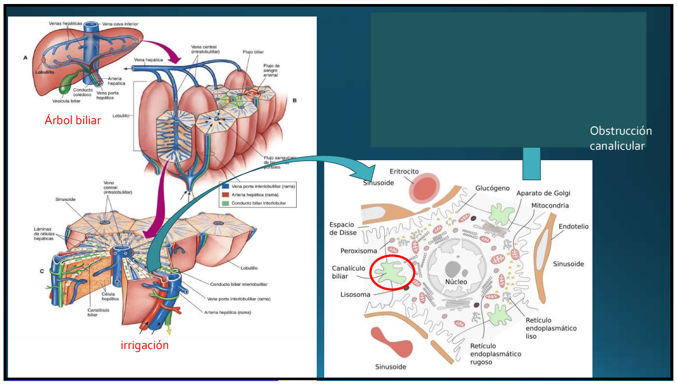
DIPLOMADO EN MVZ

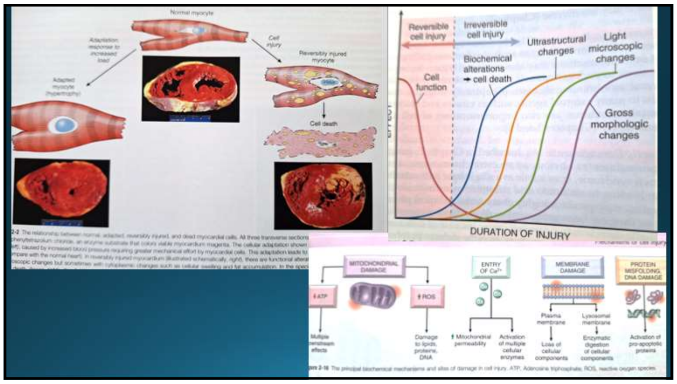
# HEPÁTICO


Venas hepáticas
Vena cava inferior
A
Lobulillo
Arteria hepática
Conducto colédoco
Vena porta hepática
Vesícula biliar
Vena hepática
Vena central (intralobulillar)
Flujo biliar
Flujo de sangre arterial
B
Lobulillo
Vena porta interlobulillar (rama)
Arteria hepática (rama)
Conducto biliar interlobular
Vena central (intralobulillar)
Sinusoide
Láminas de células hepáticas
C
Lobulillo
Conducto biliar interlobulillar
Vena porta interlobulillar (rama)
Arteria hepática (rama)
Célula hepática
Canalículo biliar
Eritrocito
Sinusoide
Glucógeno
Aparato de Golgi
Mitocondria
Espacio de Disse
Endotelio
Peroxisoma
Canalículo biliar
Núcleo
Sinusoide
Lisosoma
Retículo endoplasmático liso
Retículo endoplasmático rugoso
Sinusoide

Árbol biliar

irrigación

Obstrucción canalicular


Normal myocyte
Adaptation: response to increased load
Cell injury
Adapted myocyte (hypertrophy)
Reversibly injured myocyte
Cell death
Reversible cell injury
Irreversible cell injury
Ultrastructural changes
Light microscopic changes
Biochemical alterations → cell death
Cell function
Gross morphologic changes
EFFECT
DURATION OF INJURY
MITOCHONDRIAL DAMAGE
ENTRY OF Ca2+
MEMBRANE DAMAGE
PROTEIN MISFOLDING DNA DAMAGE
↓ATP
↑ROS
Multiple downstream effects
Damage to lipids, proteins, DNA
↑ Mitochondrial permeability
Activation of multiple cellular enzymes
Plasma membrane
Lysosomal membrane
Loss of cellular components
Enzymatic digestion of cellular components
Activation of pro-apoptotic proteins

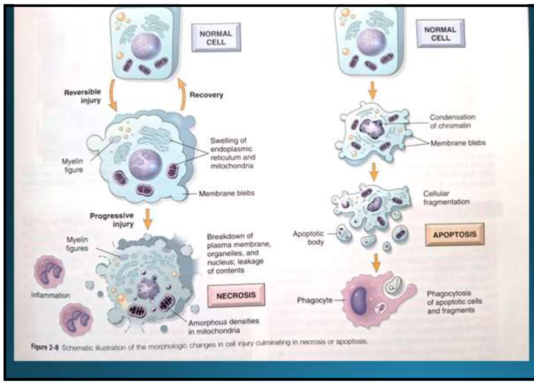
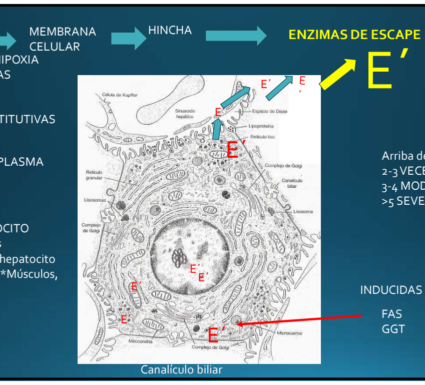

NORMAL CELL
Reversible injury
Recovery
Myelin figure
Swelling of endoplasmic reticulum and mitochondria
Membrane blebs
Progressive injury
Myelin figures
Breakdown of plasma membrane, organelles, and nucleus; leakage of contents
Inflammation
NECROSIS
Amorphous densities in mitochondria
NORMAL CELL
Condensation of chromatin
Membrane blebs
Cellular fragmentation
Apoptotic body
APOPTOSIS
Phagocyte
Phagocytosis of apoptotic cells and fragments

Figure 2-8 Schematic illustration of the morphologic changes in cell injury culminating in necrosis or apoptosis.


Célula de Kupffer
Sinusoide hepático
Espacio de Disse
Lipoproteína
Retículo liso
Complejo de Golgi
Canalículo biliar
Retículo granular
Lisosomas
Lisosoma
Complejo de Golgi
Microcuerpo
Mitocondria
Complejo de Golgi
E´
E´
E´
E´
E´
E´
E´
E´
E´
E´

**LESIÓN** → MEMBRANA CELULAR → HINCHA → **ENZIMAS DE ESCAPE**

E´

INFLAMACIÓN, HIPOXIA
TOXINAS, DRUGAS
NEOPLASIAS

CONSTITUTIVAS

| | CITOPLASMA |
|---|---|
| GATOS | ALT |
| CANINOS | AST |

DAÑO AL HEPATOCITO
Elevación en horas
ALT casi exclusiva hepatocito
AST otros tejidos: *Músculos, renales

Arriba del límite superior
2-3 VECES LEVE
3-4 MODERADO
>5 SEVERO

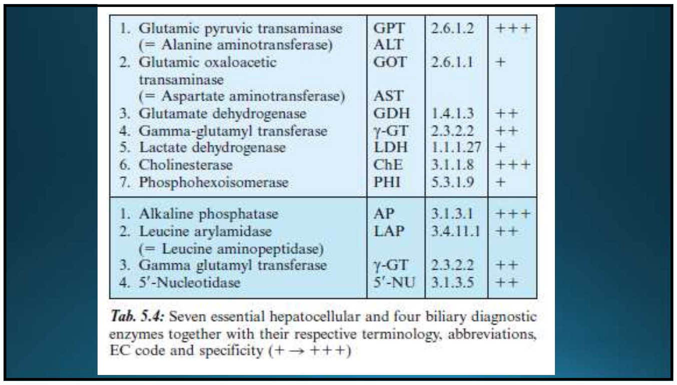
INDUCIDAS

| | |
|---|---|
| FAS<br>GGT | Colestasis intrahepática<br>FAS<br>GGT |

Canalículo biliar

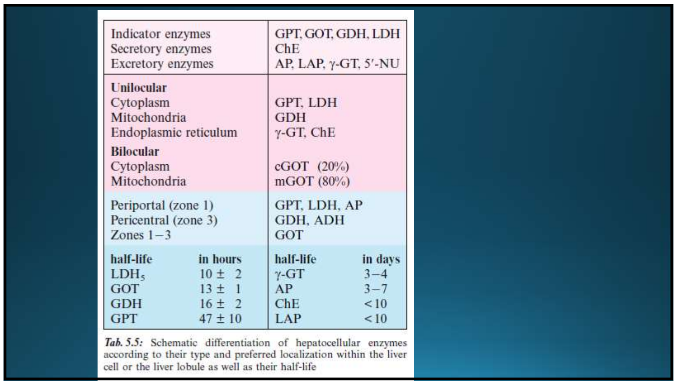
## ENZIMAS DE ESCAPE

| ENZIMA | NOMBRE |
|---|---|
| ALT<br>TGP | Aspartato Amino Transferasa<br>Transaminasa Glutámico Pirúvica |
| FAS (4) | Fosfatasa Alcalina Sérica (Isoenzimas) |
| LDH(5) | Lactato Deshidrogenasa (Isoenzimas) |
| GGT | Gama Glutamil Tansferasa |
| SD | Sorbitol Deshidrogenasa |



| | | | |
|---|---|---|---|
| 1. Glutamic pyruvic transaminase (= Alanine aminotransferase) | GPT<br>ALT | 2.6.1.2 | +++ |
| 2. Glutamic oxaloacetic transaminase (= Aspartate aminotransferase) | GOT<br>AST | 2.6.1.1 | + |
| 3. Glutamate dehydrogenase | GDH | 1.4.1.3 | ++ |
| 4. Gamma-glutamyl transferase | γ-GT | 2.3.2.2 | ++ |
| 5. Lactate dehydrogenase | LDH | 1.1.1.27 | + |
| 6. Cholinesterase | ChE | 3.1.1.8 | +++ |
| 7. Phosphohexoisomerase | PHI | 5.3.1.9 | + |
| 1. Alkaline phosphatase | AP | 3.1.3.1 | +++ |
| 2. Leucine arylamidase (= Leucine aminopeptidase) | LAP | 3.4.11.1 | ++ |
| 3. Gamma glutamyl transferase | γ-GT | 2.3.2.2 | ++ |
| 4. 5′-Nucleotidase | 5′-NU | 3.1.3.5 | ++ |

*Tab. 5.4:* Seven essential hepatocellular and four biliary diagnostic enzymes together with their respective terminology, abbreviations, EC code and specificity (+ → +++)



| | |
|---|---|
| Indicator enzymes<br>Secretory enzymes<br>Excretory enzymes | GPT, GOT, GDH, LDH<br>ChE<br>AP, LAP, γ-GT, 5′-NU |
| **Unilocular** | |
| Cytoplasm | GPT, LDH |
| Mitochondria | GDH |
| Endoplasmic reticulum | γ-GT, ChE |
| **Bilocular** | |
| Cytoplasm | cGOT (20%) |
| Mitochondria | mGOT (80%) |
| Periportal (zone 1) | GPT, LDH, AP |
| Pericentral (zone 3) | GDH, ADH |
| Zones 1−3 | GOT |

| **half-life** | **in hours** | **half-life** | **in days** |
|---|---|---|---|
| $LDH_5$ | 10 ± 2 | γ-GT | 3−4 |
| GOT | 13 ± 1 | AP | 3−7 |
| GDH | 16 ± 2 | ChE | < 10 |
| GPT | 47 ± 10 | LAP | < 10 |

*Tab. 5.5:* Schematic differentiation of hepatocellular enzymes according to their type and preferred localization within the liver cell or the liver lobule as well as their half-life

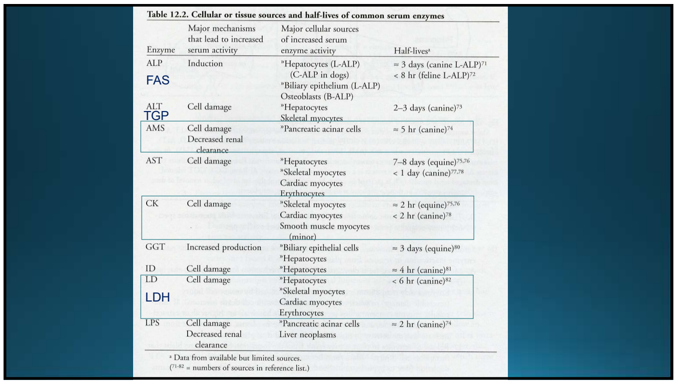
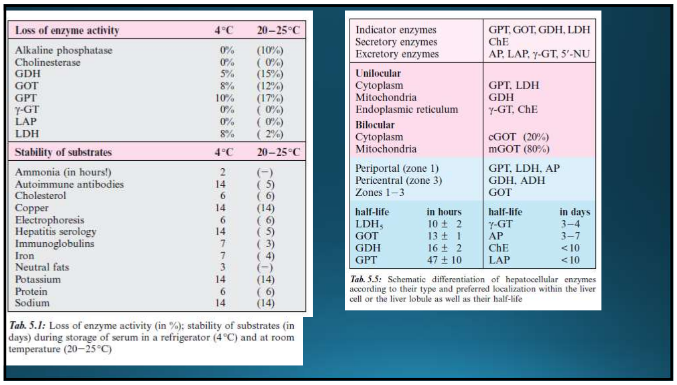


**Table 12.2. Cellular or tissue sources and half-lives of common serum enzymes**

| Enzyme | Major mechanisms that lead to increased serum activity | Major cellular sources of increased serum enzyme activity | Half-lives$^{a}$ |
|---|---|---|---|
| ALP<br>FAS | Induction | *Hepatocytes (L-ALP)<br>(C-ALP in dogs)<br>*Biliary epithelium (L-ALP)<br>Osteoblasts (B-ALP) | ≈ 3 days (canine L-ALP)$^{71}$<br>< 8 hr (feline L-ALP)$^{72}$ |
| ALT<br>TGP | Cell damage | *Hepatocytes<br>Skeletal myocytes | 2–3 days (canine)$^{73}$ |
| AMS | Cell damage<br>Decreased renal clearance | *Pancreatic acinar cells | ≈ 5 hr (canine)$^{74}$ |
| AST | Cell damage | *Hepatocytes<br>*Skeletal myocytes<br>Cardiac myocytes<br>Erythrocytes | 7–8 days (equine)$^{75,76}$<br>< 1 day (canine)$^{77,78}$ |
| CK | Cell damage | *Skeletal myocytes<br>Cardiac myocytes<br>Smooth muscle myocytes (minor) | ≈ 2 hr (equine)$^{75,76}$<br>< 2 hr (canine)$^{78}$ |
| GGT | Increased production | *Biliary epithelial cells<br>*Hepatocytes | ≈ 3 days (equine)$^{80}$ |
| ID | Cell damage | *Hepatocytes | ≈ 4 hr (canine)$^{81}$ |
| LD<br>LDH | Cell damage | *Hepatocytes<br>*Skeletal myocytes<br>Cardiac myocytes<br>Erythrocytes | < 6 hr (canine)$^{82}$ |
| LPS | Cell damage<br>Decreased renal clearance | *Pancreatic acinar cells<br>Liver neoplasms | ≈ 2 hr (canine)$^{74}$ |

$^{a}$ Data from available but limited sources.
($^{71-82}$ = numbers of sources in reference list.)



| Loss of enzyme activity | 4°C | 20−25°C |
|---|---|---|
| Alkaline phosphatase | 0% | (10%) |
| Cholinesterase | 0% | ( 0%) |
| GDH | 5% | (15%) |
| GOT | 8% | (12%) |
| GPT | 10% | (17%) |
| γ-GT | 0% | ( 0%) |
| LAP | 0% | ( 0%) |
| LDH | 8% | ( 2%) |
| **Stability of substrates** | **4°C** | **20−25°C** |
| Ammonia (in hours!) | 2 | (−) |
| Autoimmune antibodies | 14 | ( 5) |
| Cholesterol | 6 | ( 6) |
| Copper | 14 | (14) |
| Electrophoresis | 6 | ( 6) |
| Hepatitis serology | 14 | ( 5) |
| Immunoglobulins | 7 | ( 3) |
| Iron | 7 | ( 4) |
| Neutral fats | 3 | (−) |
| Potassium | 14 | (14) |
| Protein | 6 | ( 6) |
| Sodium | 14 | (14) |

*Tab. 5.1:* Loss of enzyme activity (in %); stability of substrates (in days) during storage of serum in a refrigerator (4°C) and at room temperature (20−25°C)

| | |
|---|---|
| Indicator enzymes<br>Secretory enzymes<br>Excretory enzymes | GPT, GOT, GDH, LDH<br>ChE<br>AP, LAP, γ-GT, 5′-NU |
| **Unilocular** | |
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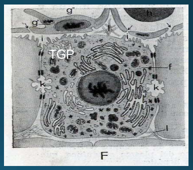
## TRANSAMINASA GLUTAMICO PIRÚVICA (TGP)
## ALANINA AMINO TRANSFERASA (ALT)

ALT1

- 1000 veces serica
- Vida media 24 h,
- magnitud directamente proporcional al daño
- Niveles permanecen por 12 horas
- Significado 2-3 veces de aumento
- Hasta 20-40 veces

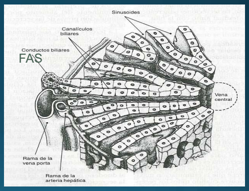
- Musculo esquelético ALT2
- Igual LDH

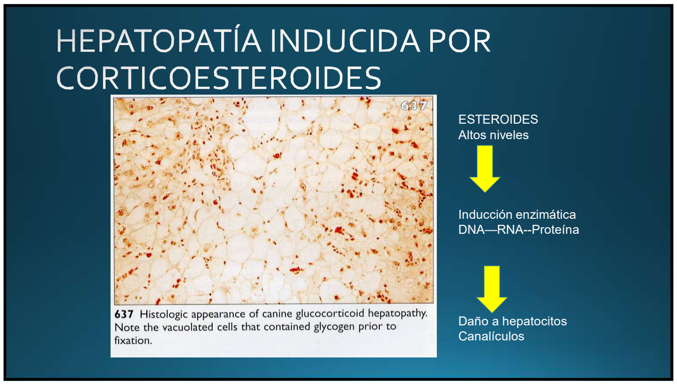


## FOSFATASA ALCALINA SÉRICA (FAS)

- ISOENZIMAS:
- CANINOS 4: v= 2-3 días
- Hueso (B-ALP), hepática (L-ALP),
- inducida por corticoesteroides (C-ALP)
- Origen desconocido

- FELINO 2: v=8 h
- hueso, hígado





## HEPATOPATÍA INDUCIDA POR CORTICOESTEROIDES

**637** Histologic appearance of canine glucocorticoid hepatopathy. Note the vacuolated cells that contained glycogen prior to fixation.

ESTEROIDES
Altos niveles

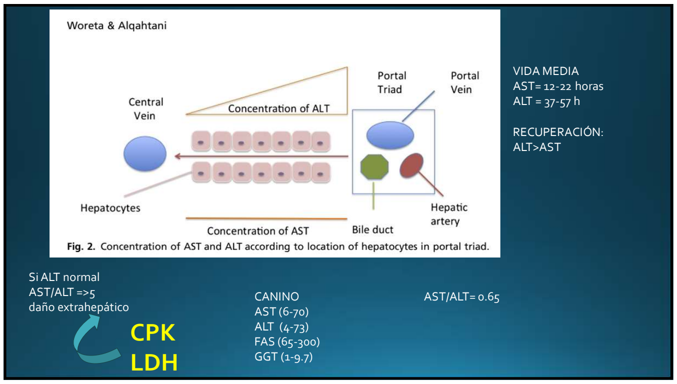
Inducción enzimática
DNA—RNA--Proteína

Daño a hepatocitos
Canalículos

## GAMA GLUTAMIL TRANSFERASA (GGT)

- Derivada del hígado (también riñón y páncreas)
- Felinos, mejor que FAS
- Lipoidosis hepática felina FAS +++, GGT+
- En general aumentan de 2-3 veces significativo
- Principalmente con fibrosis porque aumenta la colestasis por el desorden de la fibrosis

- ALTAMENTE ESPECÍFICA PARA COLESTASIS (JUNTO CON FAS)
- >90% Aumento de FAS y GGT
- 50% FAS
- 80% GGT



Woreta & Alqahtani

Central Vein
Concentration of ALT
Portal Triad
Portal Vein
Hepatocytes
Hepatic artery
Concentration of AST
Bile duct

**Fig. 2.** Concentration of AST and ALT according to location of hepatocytes in portal triad.

VIDA MEDIA
AST= 12-22 horas
ALT = 37-57 h

RECUPERACIÓN:
ALT>AST

Si ALT normal
AST/ALT =>5
daño extrahepático

**CPK**
**LDH**

CANINO
AST (6-70)
ALT (4-73)
FAS (65-300)
GGT (1-9.7)

AST/ALT= 0.65

R= ALT/FAS = 1.89

R<2 .- COLESTASIS
R=2-5 Mixto colestasis y hepatocelular
R>5 HEPATOCELULAR

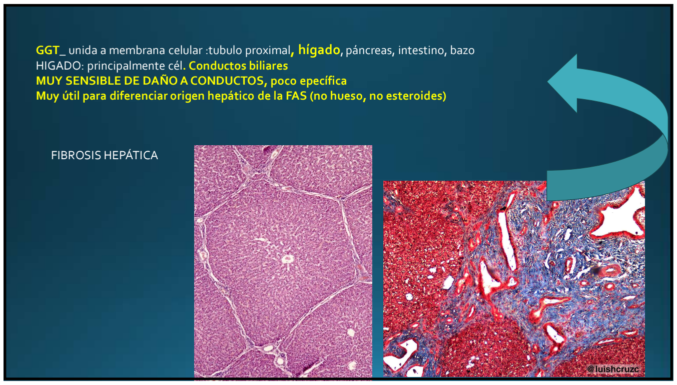
CANINO
AST (6-70)
**ALT** (4-73)
**FAS** (65-300)
GGT (1-9.7)

Arriba del límite superior
2-3 VECES LEVE
3-4 MODERADO
>5 SEVERO

ELEVACIÓN
ALT /70 = 1.65
FAS / 189 = 0.87

ALT/73= 2.73
FAS/300= 1.33

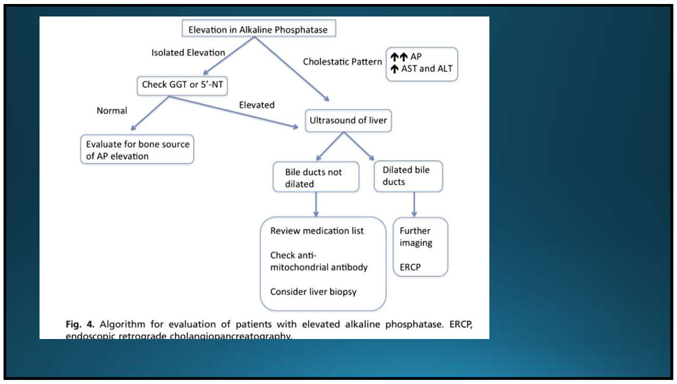
FAS.- Las isoenzimas más comunes que se encuentran en el suero de los perros son: la isoenzima hepática, la inducida por corticoesteroides y la ósea.



**GGT_** unida a membrana celular :tubulo proximal, **hígado**, páncreas, intestino, bazo
HIGADO: principalmente cél. **Conductos biliares**
**MUY SENSIBLE DE DAÑO A CONDUCTOS, poco epecífica**
**Muy útil para diferenciar origen hepático de la FAS (no hueso, no esteroides)**

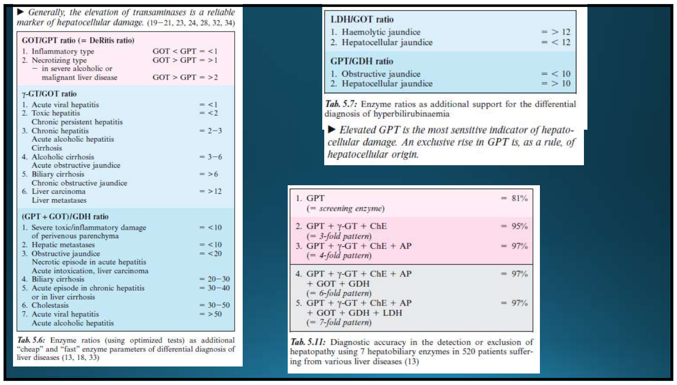
FIBROSIS HEPÁTICA

@luishcruzc



Elevation in Alkaline Phosphatase
Isolated Elevation
Cholestatic Pattern
↑↑ AP
↑ AST and ALT
Check GGT or 5'-NT
Normal
Elevated
Ultrasound of liver
Evaluate for bone source of AP elevation
Bile ducts not dilated
Dilated bile ducts
Review medication list
Check anti-mitochondrial antibody
Consider liver biopsy
Further imaging
ERCP

**Fig. 4.** Algorithm for evaluation of patients with elevated alkaline phosphatase. ERCP, endoscopic retrograde cholangiopancreatography.



▶ *Generally, the elevation of transaminases is a reliable marker of hepatocellular damage.* (19−21, 23, 24, 28, 32, 34)

| **GOT/GPT ratio (= DeRitis ratio)** | |
|---|---|
| 1. Inflammatory type | GOT < GPT = <1 |
| 2. Necrotizing type | GOT > GPT = >1 |
| − in severe alcoholic or malignant liver disease | GOT > GPT = >2 |
| **γ-GT/GOT ratio** | |
| 1. Acute viral hepatitis | = <1 |
| 2. Toxic hepatitis<br>Chronic persistent hepatitis | = <2 |
| 3. Chronic hepatitis<br>Acute alcoholic hepatitis<br>Cirrhosis | = 2−3 |
| 4. Alcoholic cirrhosis<br>Acute obstructive jaundice | = 3−6 |
| 5. Biliary cirrhosis<br>Chronic obstructive jaundice | = >6 |
| 6. Liver carcinoma<br>Liver metastases | = >12 |
| **(GPT + GOT)/GDH ratio** | |
| 1. Severe toxic/inflammatory damage of perivenous parenchyma | = <10 |
| 2. Hepatic metastases | = <10 |
| 3. Obstructive jaundice<br>Necrotic episode in acute hepatitis<br>Acute intoxication, liver carcinoma | = <20 |
| 4. Biliary cirrhosis | = 20−30 |
| 5. Acute episode in chronic hepatitis or in liver cirrhosis | = 30−40 |
| 6. Cholestasis | = 30−50 |
| 7. Acute viral hepatitis<br>Acute alcoholic hepatitis | = >50 |

*Tab. 5.6:* Enzyme ratios (using optimized tests) as additional "cheap" and "fast" enzyme parameters of differential diagnosis of liver diseases (13, 18, 33)

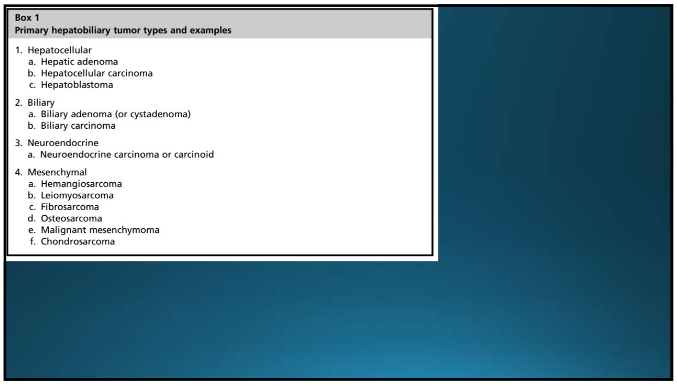
| **LDH/GOT ratio** | |
|---|---|
| 1. Haemolytic jaundice | = > 12 |
| 2. Hepatocellular jaundice | = < 12 |
| **GPT/GDH ratio** | |
| 1. Obstructive jaundice | = < 10 |
| 2. Hepatocellular jaundice | = > 10 |

*Tab. 5.7:* Enzyme ratios as additional support for the differential diagnosis of hyperbilirubinaemia

▶ *Elevated GPT is the most sensitive indicator of hepatocellular damage. An exclusive rise in GPT is, as a rule, of hepatocellular origin.*

| | |
|---|---|
| 1. GPT<br>(= *screening enzyme*) | = 81% |
| 2. GPT + γ-GT + ChE<br>(= *3-fold pattern*) | = 95% |
| 3. GPT + γ-GT + ChE + AP<br>(= *4-fold pattern*) | = 97% |
| 4. GPT + γ-GT + ChE + AP + GOT + GDH<br>(= *6-fold pattern*) | = 97% |
| 5. GPT + γ-GT + ChE + AP + GOT + GDH + LDH<br>(= *7-fold pattern*) | = 97% |

*Tab. 5.11:* Diagnostic accuracy in the detection or exclusion of hepatopathy using 7 hepatobiliary enzymes in 520 patients suffering from various liver diseases (13)



**Box 1**
**Primary hepatobiliary tumor types and examples**

1. Hepatocellular
    - a. Hepatic adenoma
    - b. Hepatocellular carcinoma
    - c. Hepatoblastoma
2. Biliary
    - a. Biliary adenoma (or cystadenoma)
    - b. Biliary carcinoma
3. Neuroendocrine
    - a. Neuroendocrine carcinoma or carcinoid
4. Mesenchymal
    - a. Hemangiosarcoma
    - b. Leiomyosarcoma
    - c. Fibrosarcoma
    - d. Osteosarcoma
    - e. Malignant mesenchymoma
    - f. Chondrosarcoma

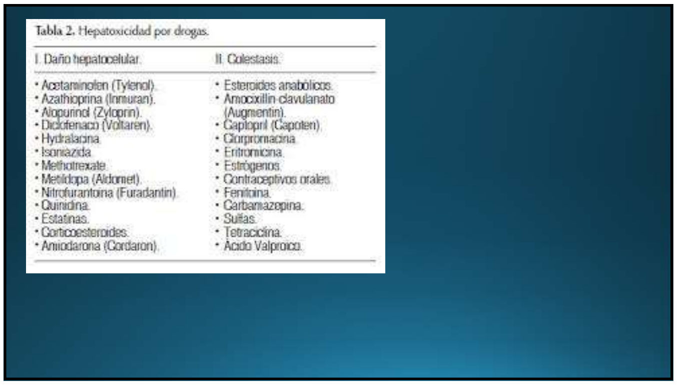
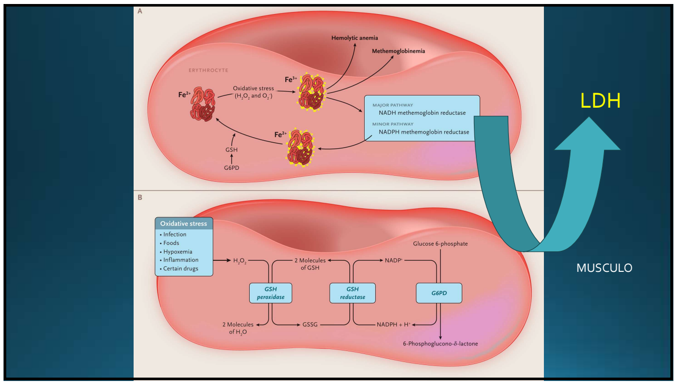


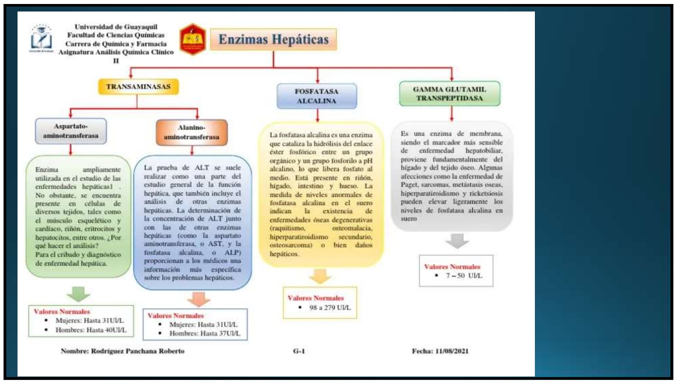
Tabla 2. Hepatoxicidad por drogas.

| I. Daño hepatocelular. | II. Colestasis. |
|---|---|
| • Acetaminofen (Tylenol). | • Esteroides anabólicos. |
| • Azathioprina (Inmuran). | • Amocixilin-clavulanato (Augmentin). |
| • Alopurinol (Zyloprin). | • Captopril (Capoten). |
| • Diclofenaco (Voltaren). | • Clorpromacina. |
| • Hydralacina. | • Eritromicina. |
| • Isoniazida. | • Estrógenos. |
| • Methotrexate. | • Contraceptivos orales. |
| • Metildopa (Aldomet). | • Fenitoina. |
| • Nitrofurantoina (Furadantin). | • Carbamazepina. |
| • Quinidina. | • Sulfas. |
| • Estatinas. | • Tetraciclina. |
| • Corticoesteroides. | • Acido Valproico. |
| • Amiodarona (Cordaron). | |



LDH

MUSCULO



**Universidad de Guayaquil**
**Facultad de Ciencias Químicas**
**Carrera de Química y Farmacia**
**Asignatura Análisis Químico Clínico II**

**Enzimas Hepáticas**

**TRANSAMINASAS**

**Aspartato-aminotransferasa**

Enzima ampliamente utilizada en el estudio de las enfermedades hepáticas1 . No obstante, se encuentra presente en células de diversos tejidos, tales como el músculo esquelético y cardíaco, riñón, eritrocitos y hepatocitos, entre otros. ¿Por qué hacer el análisis?
Para el cribado y diagnóstico de enfermedad hepática.

Valores Normales
- Mujeres: Hasta 31UI/L.
- Hombres: Hasta 40UI/L.

**Alanino-aminotransferasa**

La prueba de ALT se suele realizar como una parte del estudio general de la función hepática, que también incluye el análisis de otras enzimas hepáticas. La determinación de la concentración de ALT junto con las de otras enzimas hepáticas (como la aspartato aminotransferasa, o AST, y la fosfatasa alcalina, o ALP) proporcionan a los médicos una información más específica sobre los problemas hepáticos.

Valores Normales
- Mujeres: Hasta 31UI/L.
- Hombres: Hasta 37UI/L.

**FOSFATASA ALCALINA**

La fosfatasa alcalina es una enzima que cataliza la hidrólisis del enlace éster fosfórico entre un grupo orgánico y un grupo fosforilo a pH alcalino, lo que libera fosfato al medio. Está presente en riñón, hígado, intestino y hueso. La medida de niveles anormales de fosfatasa alcalina en el suero indican la existencia de enfermedades óseas degenerativas (raquitismo, osteomalacia, hiperparatiroidismo secundario, osteosarcoma) o bien daños hepáticos.

Valores Normales
- 98 a 279 UI/L

**GAMMA GLUTAMIL TRANSPEPTIDASA**

Es una enzima de membrana, siendo el marcador más sensible de enfermedad hepatobiliar, proviene fundamentalmente del hígado y del tejido óseo. Algunas afecciones como la enfermedad de Paget, sarcomas, metástasis oseas, hiperparatiroidismo y ricketsiosis pueden elevar ligeramente los niveles de fosfatasa alcalina en suero

Valores Normales
- 7 – 50 UI/L

**Nombre: Rodríguez Panchana Roberto** **G-1** **Fecha: 11/08/2021**

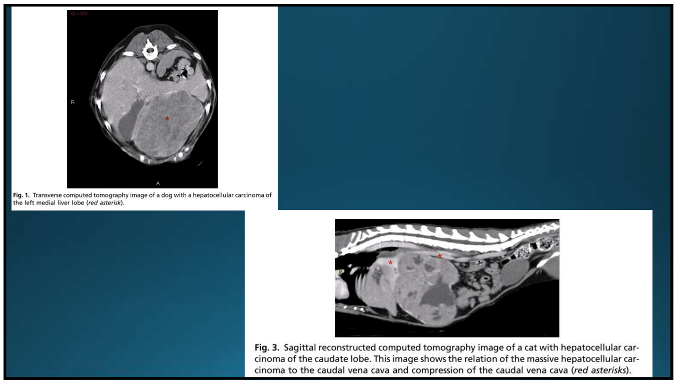
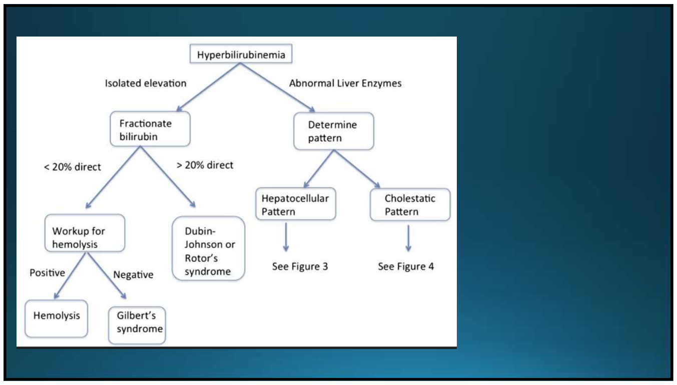


**Fig. 1.** Transverse computed tomography image of a dog with a hepatocellular carcinoma of the left medial liver lobe (*red asterisk*).

**Fig. 3.** Sagittal reconstructed computed tomography image of a cat with hepatocellular carcinoma of the caudate lobe. This image shows the relation of the massive hepatocellular carcinoma to the caudal vena cava and compression of the caudal vena cava (*red asterisks*).



Hyperbilirubinemia

Isolated elevation

Abnormal Liver Enzymes

Fractionate bilirubin

Determine pattern

< 20% direct

> 20% direct

Hepatocellular Pattern

Cholestatic Pattern

Workup for hemolysis

Dubin-Johnson or Rotor's syndrome

See Figure 3

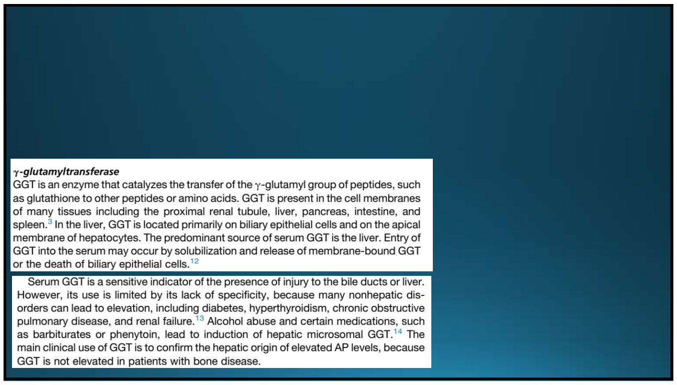
See Figure 4

Positive

Negative

Hemolysis

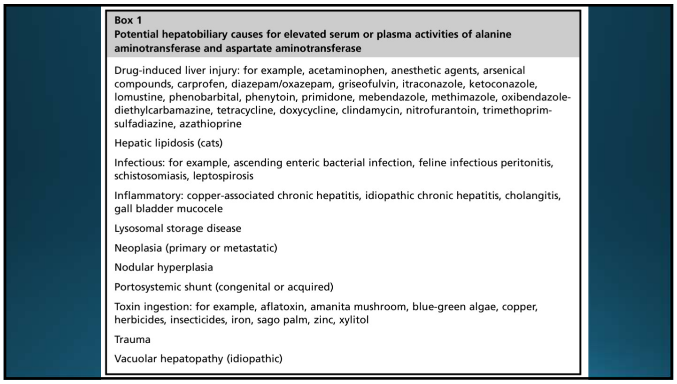
Gilbert's syndrome



***γ-glutamyltransferase***

GGT is an enzyme that catalyzes the transfer of the γ-glutamyl group of peptides, such as glutathione to other peptides or amino acids. GGT is present in the cell membranes of many tissues including the proximal renal tubule, liver, pancreas, intestine, and spleen.[3] In the liver, GGT is located primarily on biliary epithelial cells and on the apical membrane of hepatocytes. The predominant source of serum GGT is the liver. Entry of GGT into the serum may occur by solubilization and release of membrane-bound GGT or the death of biliary epithelial cells.[12]

Serum GGT is a sensitive indicator of the presence of injury to the bile ducts or liver. However, its use is limited by its lack of specificity, because many nonhepatic disorders can lead to elevation, including diabetes, hyperthyroidism, chronic obstructive pulmonary disease, and renal failure.[13] Alcohol abuse and certain medications, such as barbiturates or phenytoin, lead to induction of hepatic microsomal GGT.[14] The main clinical use of GGT is to confirm the hepatic origin of elevated AP levels, because GGT is not elevated in patients with bone disease.



**Box 1**
**Potential hepatobiliary causes for elevated serum or plasma activities of alanine aminotransferase and aspartate aminotransferase**

Drug-induced liver injury: for example, acetaminophen, anesthetic agents, arsenical compounds, carprofen, diazepam/oxazepam, griseofulvin, itraconazole, ketoconazole, lomustine, phenobarbital, phenytoin, primidone, mebendazole, methimazole, oxibendazole-diethylcarbamazine, tetracycline, doxycycline, clindamycin, nitrofurantoin, trimethoprim-sulfadiazine, azathioprine

Hepatic lipidosis (cats)

Infectious: for example, ascending enteric bacterial infection, feline infectious peritonitis, schistosomiasis, leptospirosis

Inflammatory: copper-associated chronic hepatitis, idiopathic chronic hepatitis, cholangitis, gall bladder mucocele

Lysosomal storage disease

Neoplasia (primary or metastatic)

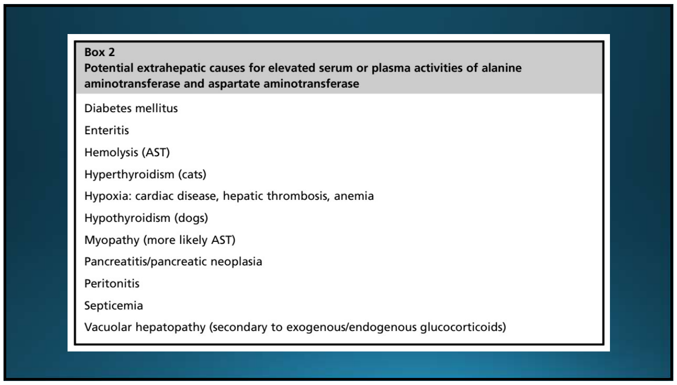
Nodular hyperplasia

Portosystemic shunt (congenital or acquired)

Toxin ingestion: for example, aflatoxin, amanita mushroom, blue-green algae, copper, herbicides, insecticides, iron, sago palm, zinc, xylitol

Trauma

Vacuolar hepatopathy (idiopathic)



**Box 2**
**Potential extrahepatic causes for elevated serum or plasma activities of alanine aminotransferase and aspartate aminotransferase**

Diabetes mellitus

Enteritis

Hemolysis (AST)

Hyperthyroidism (cats)

Hypoxia: cardiac disease, hepatic thrombosis, anemia

Hypothyroidism (dogs)

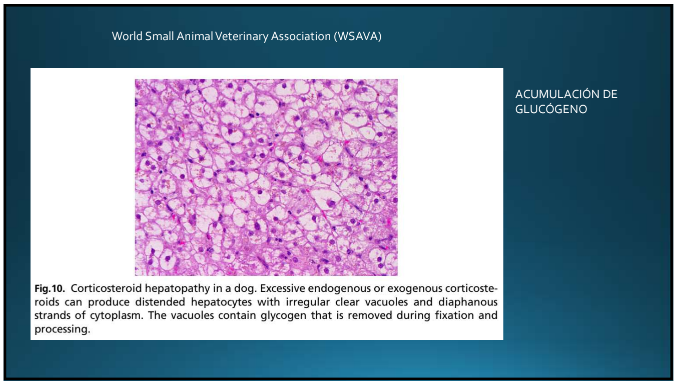
Myopathy (more likely AST)

Pancreatitis/pancreatic neoplasia

Peritonitis

Septicemia

Vacuolar hepatopathy (secondary to exogenous/endogenous glucocorticoids)



World Small Animal Veterinary Association (WSAVA)

ACUMULACIÓN DE GLUCÓGENO

**Fig. 10.** Corticosteroid hepatopathy in a dog. Excessive endogenous or exogenous corticosteroids can produce distended hepatocytes with irregular clear vacuoles and diaphanous strands of cytoplasm. The vacuoles contain glycogen that is removed during fixation and processing.

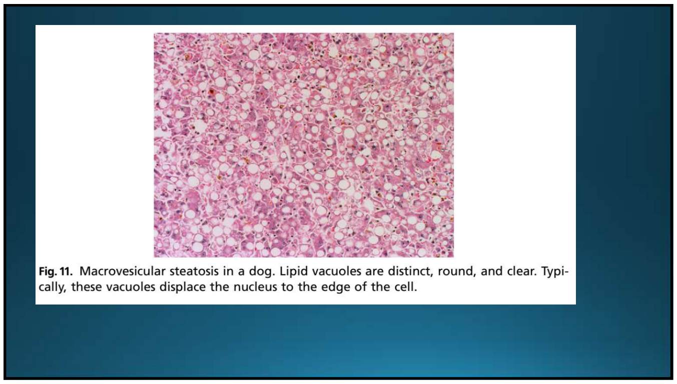


**Fig. 11.** Macrovesicular steatosis in a dog. Lipid vacuoles are distinct, round, and clear. Typically, these vacuoles displace the nucleus to the edge of the cell.

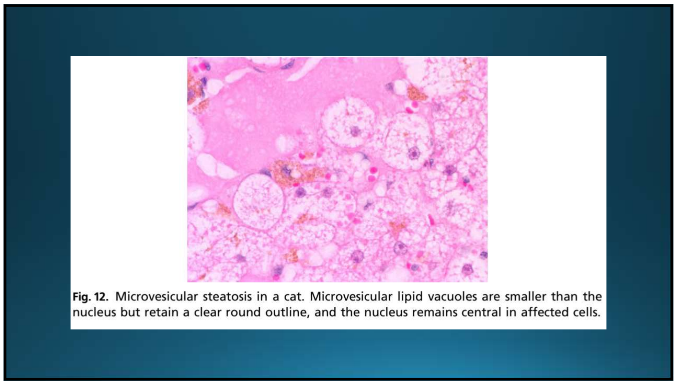


**Fig. 12.** Microvesicular steatosis in a cat. Microvesicular lipid vacuoles are smaller than the nucleus but retain a clear round outline, and the nucleus remains central in affected cells.

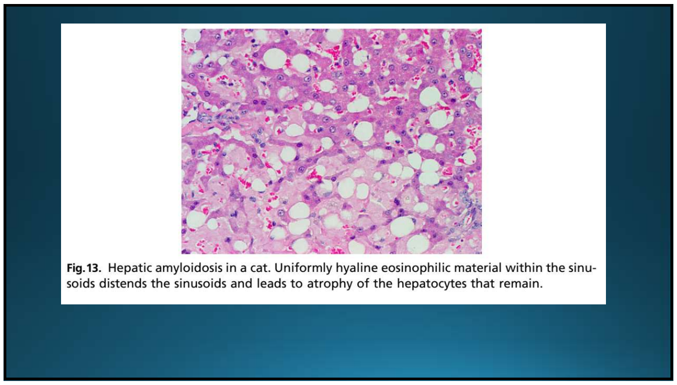
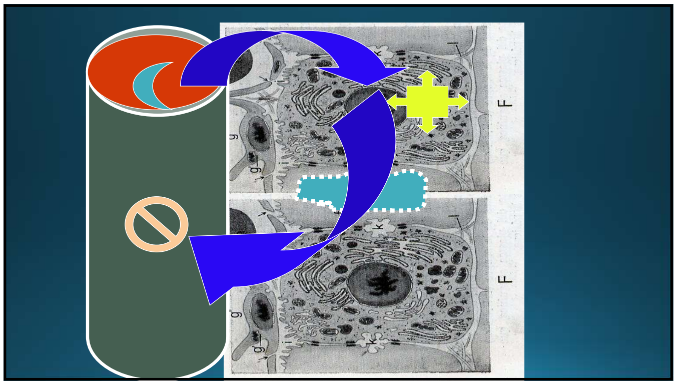
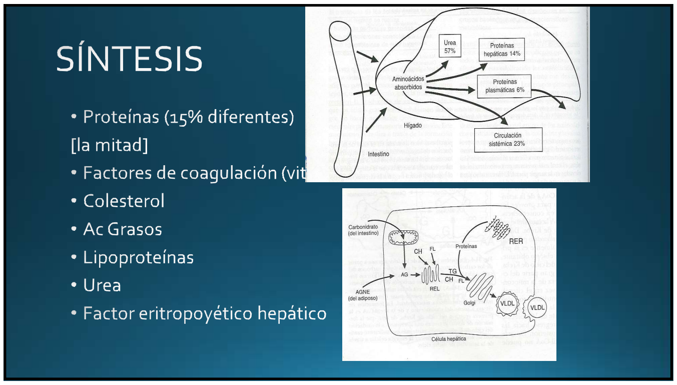


**Fig. 13.** Hepatic amyloidosis in a cat. Uniformly hyaline eosinophilic material within the sinusoids distends the sinusoids and leads to atrophy of the hepatocytes that remain.

## FUNCIONES DEL HÍGADO

- Producción de sustancias a la sangre.

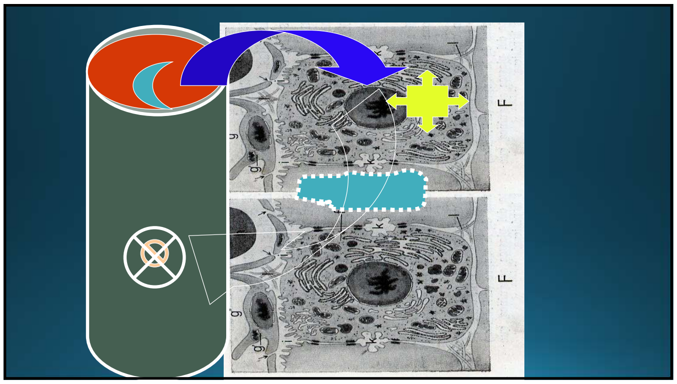


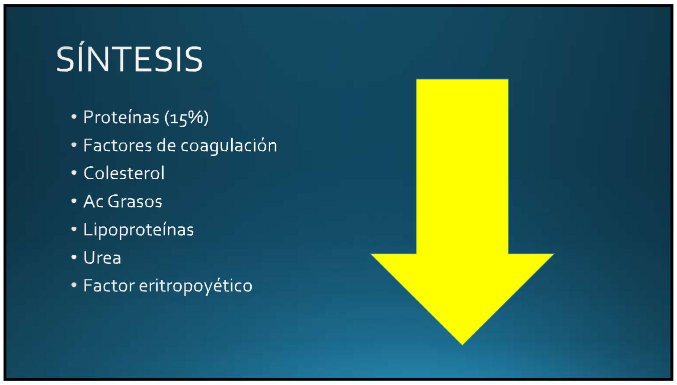


## SÍNTESIS

- Proteínas (15% diferentes) [la mitad]
- Factores de coagulación (vit
- Colesterol
- Ac Grasos
- Lipoproteínas
- Urea
- Factor eritropoyético hepático

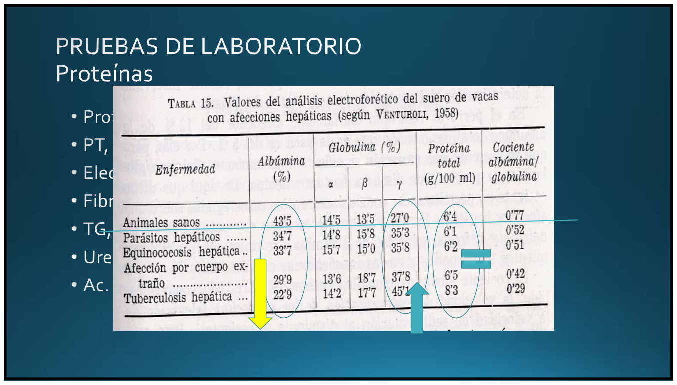
Urea 57%
Proteínas hepáticas 14%
Aminoácidos absorbidos
Proteínas plasmáticas 6%
Hígado
Circulación sistémica 23%
Intestino
Carbonidrato (del intestino)
CH
FL
Proteínas
RER
AG
TG
CH
FL
REL
AGNE (del adiposo)
Golgi
VLDL
VLDL
Célula hepática





## SÍNTESIS

- Proteínas (15%)
- Factores de coagulación
- Colesterol
- Ac Grasos
- Lipoproteínas
- Urea
- Factor eritropoyético



## PRUEBAS DE LABORATORIO
Proteínas

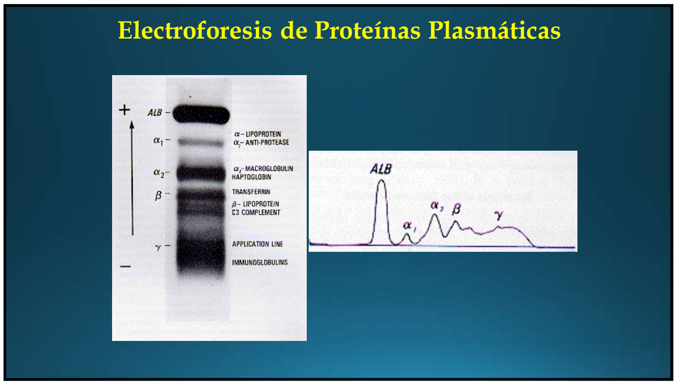
- Pro
- PT,
- Elec
- Fibr
- TG,
- Ure
- Ac.

TABLA 15. Valores del análisis electroforético del suero de vacas con afecciones hepáticas (según VENTUROLI, 1958)

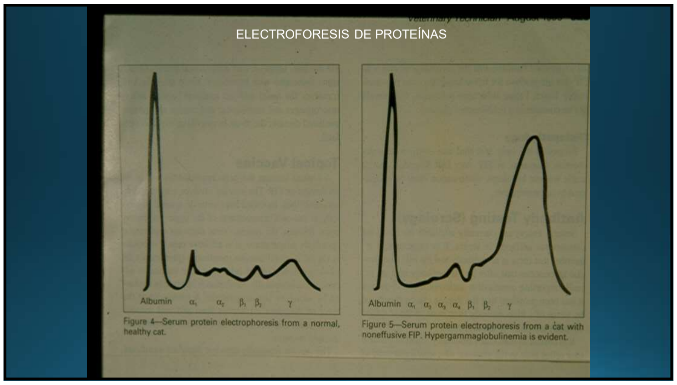
| *Enfermedad* | *Albúmina* (%) | *Globulina (%)* | | | *Proteína total* (g/100 ml) | *Cociente albúmina/globulina* |
|---|---|---|---|---|---|---|
| | | α | β | γ | | |
| Animales sanos | 43'5 | 14'5 | 13'5 | 27'0 | 6'4 | 0'77 |
| Parásitos hepáticos | 34'7 | 14'8 | 15'8 | 35'3 | 6'1 | 0'52 |
| Equinococosis hepática | 33'7 | 15'7 | 15'0 | 35'8 | 6'2 | 0'51 |
| Afección por cuerpo extraño | 29'9 | 13'6 | 18'7 | 37'8 | 6'5 | 0'42 |
| Tuberculosis hepática | 22'9 | 14'2 | 17'7 | 45'1 | 8'3 | 0'29 |

## Determinación de Proteínas

- Proteína total (BHc)
- Proteína total, albúmina, globulinas relación A/G
- Electroforesis de proteínas séricas.
- Proteínas en orina (tira reactiva)
- Proteínas en orina (químico, electroforesis)



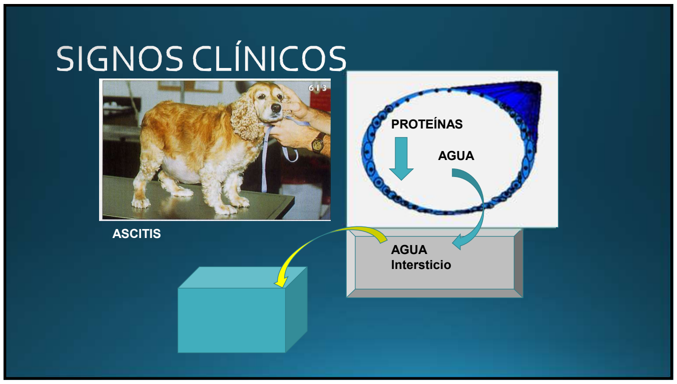
## Electroforesis de Proteínas Plasmáticas



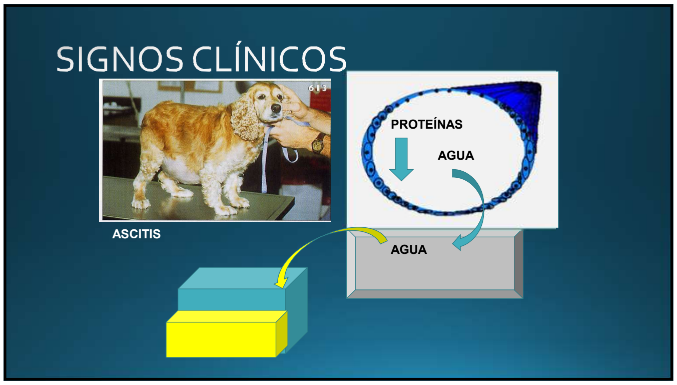
ELECTROFORESIS DE PROTEÍNAS

Figure 4—Serum protein electrophoresis from a normal, healthy cat.

Figure 5—Serum protein electrophoresis from a cat with noneffusive FIP. Hypergammaglobulinemia is evident.

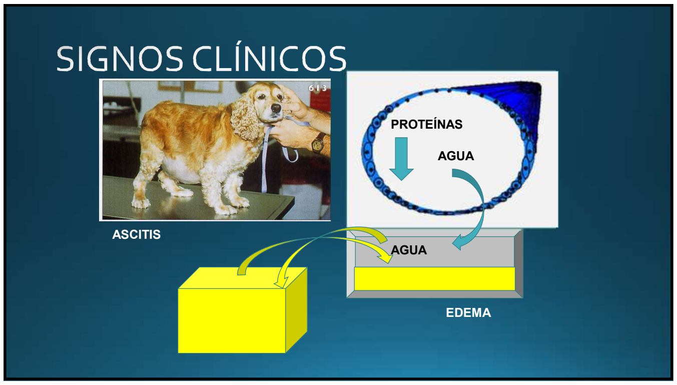


## SIGNOS CLÍNICOS



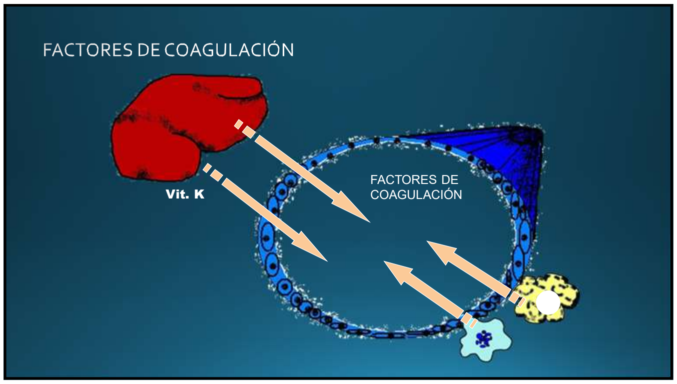
## SIGNOS CLÍNICOS

ASCITIS
PROTEÍNAS
AGUA
AGUA



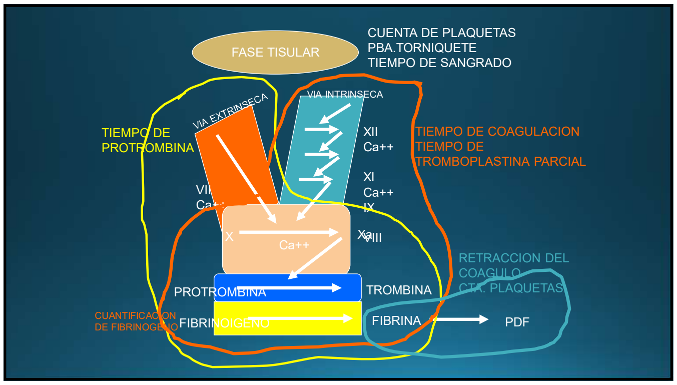
## SIGNOS CLÍNICOS

ASCITIS
PROTEÍNAS
AGUA
AGUA
EDEMA



## FACTORES DE COAGULACIÓN

Vit. K
FACTORES DE COAGULACIÓN



FASE TISULAR
CUENTA DE PLAQUETAS
PBA.TORNIQUETE
TIEMPO DE SANGRADO
VIA EXTRINSECA
VIA INTRINSECA
TIEMPO DE PROTROMBINA
XII
Ca++
TIEMPO DE COAGULACION
TIEMPO DE TROMBOPLASTINA PARCIAL
VII
Ca++
XI
Ca++
IX
X
Ca++
Xa
VIII
RETRACCION DEL COAGULO
CTA. PLAQUETAS
PROTROMBINA
TROMBINA
CUANTIFICACION DE FIBRINOGENO
FIBRINOIGENO
FIBRINA
PDF

## Pruebas de Coagulación

- Fibrinógeno ↓
- Tiempo de coagulación ↑
- TTP, TP

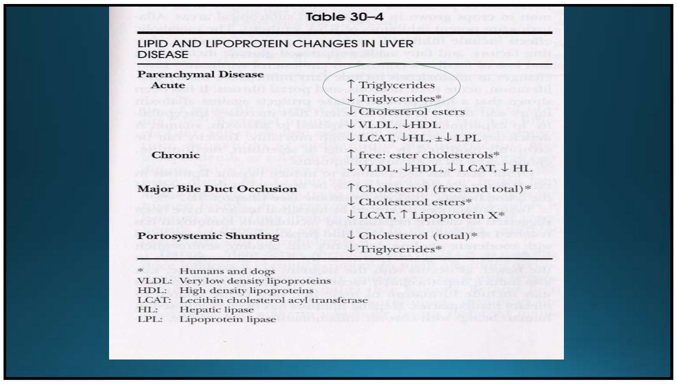
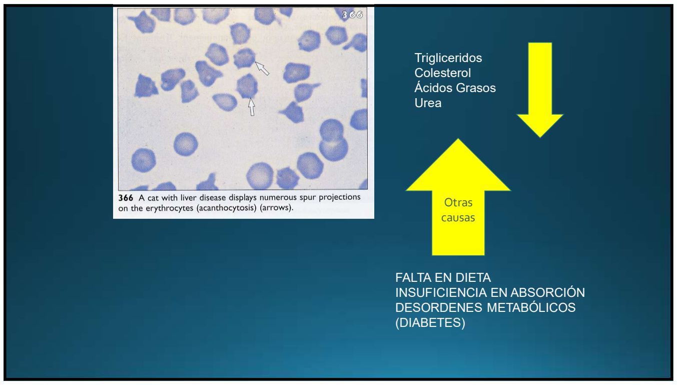


**Table 30–4**

LIPID AND LIPOPROTEIN CHANGES IN LIVER DISEASE

| | |
|---|---|
| **Parenchymal Disease** | |
| **Acute** | ↑ Triglycerides<br>↓ Triglycerides*<br>↓ Cholesterol esters<br>↓ VLDL, ↓HDL<br>↓ LCAT, ↓HL, ±↓ LPL |
| **Chronic** | ↑ free: ester cholesterols*<br>↓ VLDL, ↓HDL, ↓ LCAT, ↓ HL |
| **Major Bile Duct Occlusion** | ↑ Cholesterol (free and total)*<br>↓ Cholesterol esters*<br>↓ LCAT, ↑ Lipoprotein X* |
| **Portosystemic Shunting** | ↓ Cholesterol (total)*<br>↓ Triglycerides* |

| | |
|---|---|
| * | Humans and dogs |
| VLDL: | Very low density lipoproteins |
| HDL: | High density lipoproteins |
| LCAT: | Lecithin cholesterol acyl transferase |
| HL: | Hepatic lipase |
| LPL: | Lipoprotein lipase |



366 A cat with liver disease displays numerous spur projections on the erythrocytes (acanthocytosis) (arrows).

Triglicеridos
Colesterol
Ácidos Grasos
Urea

Otras causas

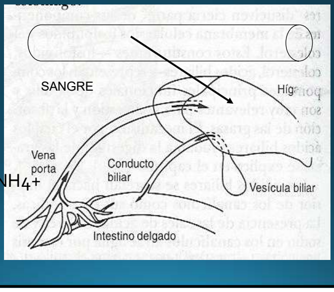
FALTA EN DIETA
INSUFICIENCIA EN ABSORCIÓN
DESORDENES METABÓLICOS (DIABETES)

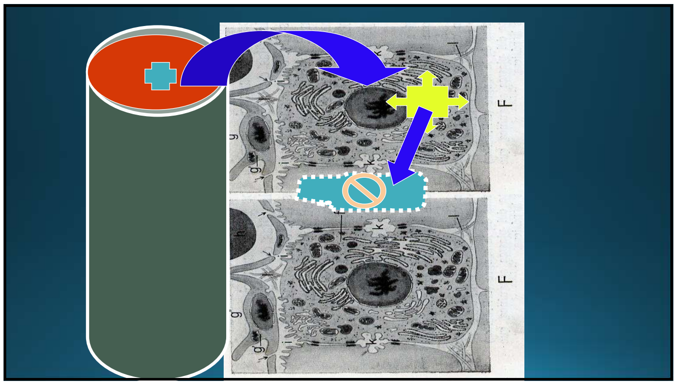
## FUNCIONES DEL HÍGADO

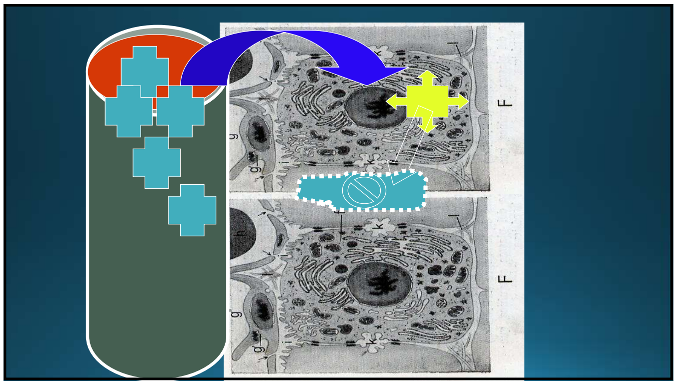
- Eliminación de sustancias de la sangre (destoxificación).

## EXCRESIÓN

- Bilirrubinas
- Hormonas, Esteroides
- Fármacos
- Anestésicos
- Antibióticos
- Toxinas
- Complejos amoniacales $NH_4^+$


SANGRE
Híga
Vena porta
Conducto biliar
Vesícula biliar
Intestino delgado





## PRUEBAS DE LABORATORIO

- Bilirrubinas : tot, dir, ind. (icteria >2-3 mg/dl)
- BSF.- 1g, 5 y 12 min. Vida media, (2.5-4.1)
- <5% 30 min.
- Amoniaco.
- Sales biliares

## Bilirrubinas

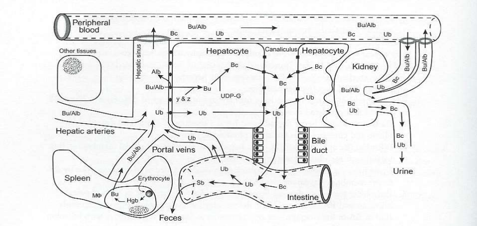

Peripheral blood
Other tissues
Hepatic sinus
Hepatocyte
Canaliculus
Hepatocyte
Kidney
Bu/Alb
Bc
Ub
Alb
Bu
y & z
UDP-G
Hepatic arteries
Portal veins
Bile duct
Spleen
Erythrocyte
MΦ
Hgb
Sb
Intestine
Feces
Urine

**Fig. 13.1.** Physiologic processes involving bilirubin. (Bu/Alb = Bu associated with albumin, Bδ-Alb = Bδ bonded to albumin, MΦ = macrophage, UDP-G = uridine diphosphoglucuronide, Sb = stercobilinogen, Ub = urobilinogen)

## Bilirrubinas

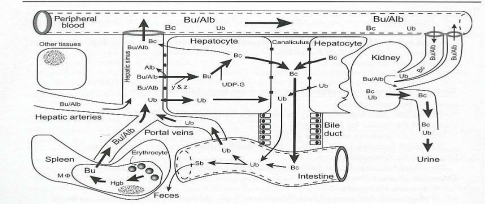
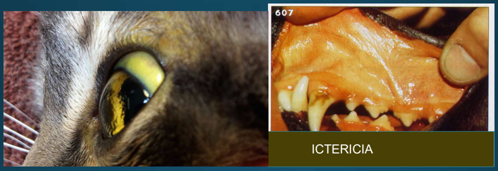

Peripheral blood
Other tissues
Hepatic sinus
Hepatocyte
Canaliculus
Hepatocyte
Kidney
Bu/Alb
Bc
Ub
Alb
Bu
y & z
UDP-G
Hepatic arteries
Portal veins
Bile duct
Spleen
Erythrocyte
MΦ
Hgb
Sb
Intestine
Feces
Urine

**Fig. 13.2.** Hemolytic icterus. (Bu/Alb = Bu associated with albumin, Bδ-Alb = Bδ bonded to albumin, MΦ = macrophage, UDP-G = uridine diphosphoglucuronide, Sb = stercobilinogen, Ub = urobilinogen)

Accelerated destruction of erythrocytes in macrophages of spleen (also liver and marrow) causes increased production and delivery of Bu to hepatocytes. If the rate of Bu formation exceeds the liver's ability to clear Bu from plasma, hyperbilirubinemia dominated by Bu will develop. Increased delivery of Bu to hepatocytes also causes increased Bc formation and biliary excretion. If Bc formation exceeds Bc transport to canaliculi, then Bc can be "regurgitated" to plasma. The increased [Bc] in plasma will result in increased Bc excretion in urine (bilirubinuria).

## SIGNOS CLÍNICOS


607
ICTERICIA

>2.5mg/dl

>1.6-1.8 mg/dl

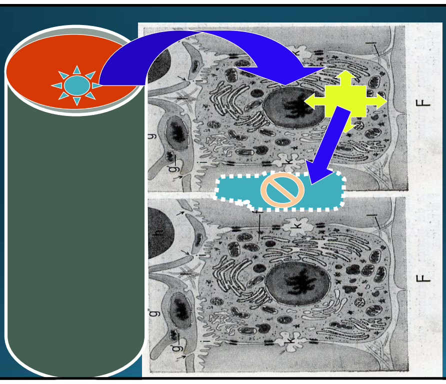
NORMAL Bil t <1.1 mg/dl (<18.8 umol/L
Bil i (0.3- 1.0 mg/dl (5-17 umol/L)

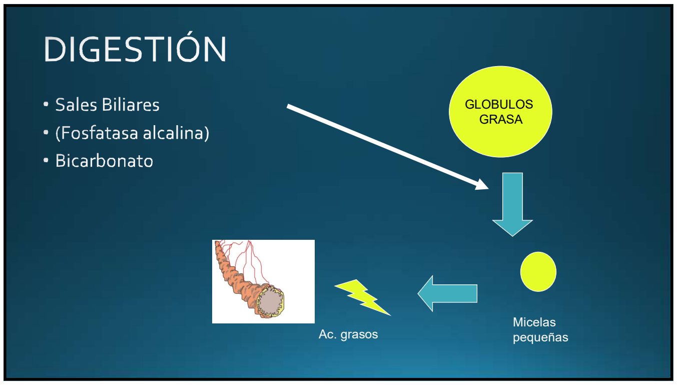
## FUNCIONES DEL HÍGADO

- Digestión (Ac.o sales biliares, bicarbonato ¿FAS?)

## FUNCIONES DE ACIDOS BILIARES

- Digestión de grasas
- Absorción de vitaminas liposolubles
- Homeostasis del colesterol
- Se originan del colesterol y glicerol
- Taurocólico, queno-deoxicólico
- Se reabsorben en intestino 95% (hasta 15 veces al día)

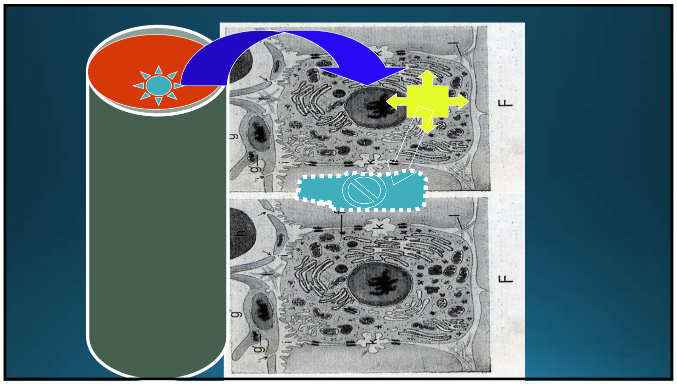


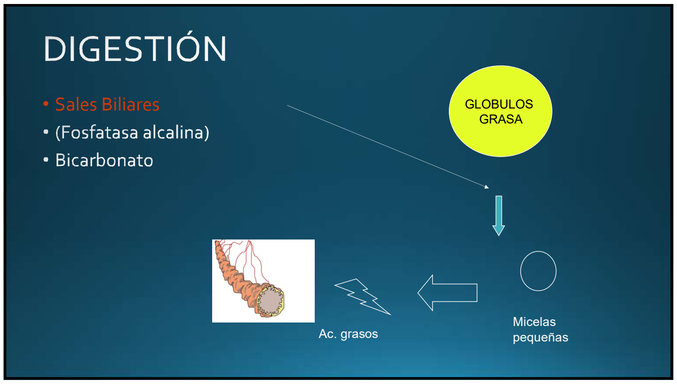


## DIGESTIÓN

- Sales Biliares
- (Fosfatasa alcalina)
- Bicarbonato

GLOBULOS GRASA
Micelas pequeñas
Ac. grasos





## DIGESTIÓN

- Sales Biliares
- (Fosfatasa alcalina)
- Bicarbonato

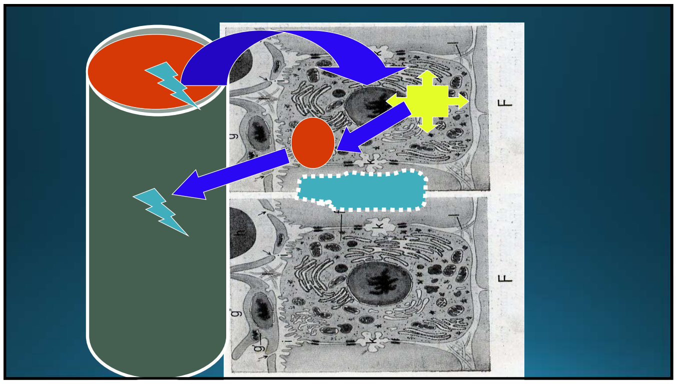
GLOBULOS GRASA
Micelas pequeñas
Ac. grasos

## PRUEBAS DE LABORATORIO

- Examen Coprológico
- Turbidez del plasma
- Ac. biliares suero
- Perros > 30mM/L (<10)
- Gatos > 20 mM/l (<5)

## FUNCIONES DEL HÍGADO

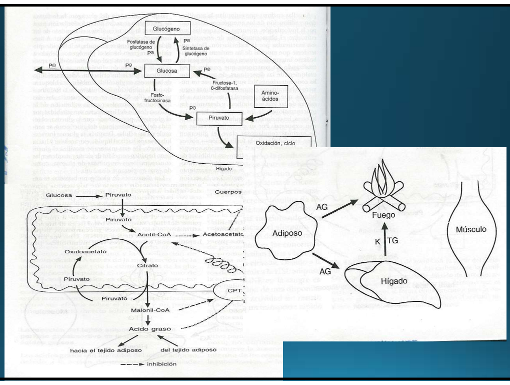
- Almacén de sustancias.

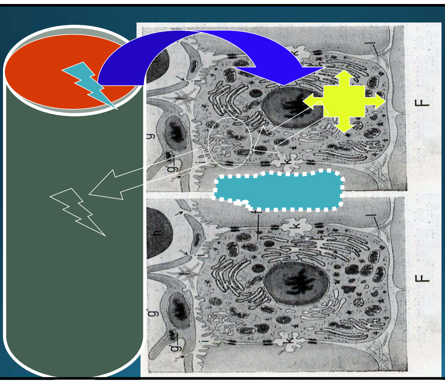


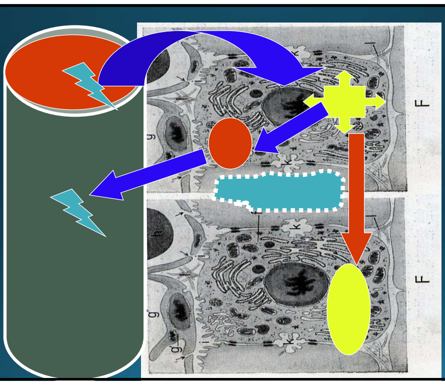
# ALMACÉN

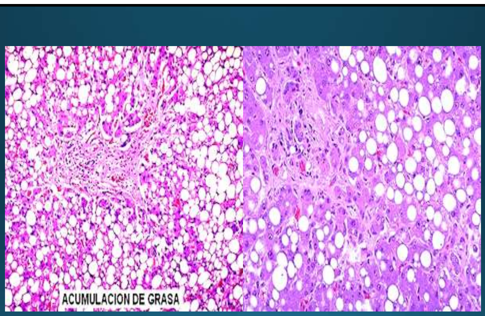
- **FISIOLÓGICO**
- Glucógeno
- Vitaminas
- Hierro
- Selenio
- Cobre

- **PATOLÓGICO**
- Grasa
- Glicoproteínas
- Agua
- Hierro
- Pigmentos
- Toxinas


Glucógeno
Fosfatasa de glucógeno
Sintetasa de glucógeno
Glucosa
Fructosa-1, 6-difosfatasa
Fosfo-fructocinasa
Amino-ácidos
Piruvato
Oxidación, ciclo
Hígado
Cuerpos
Glucosa
Piruvato
Piruvato
Acetil-CoA
Acetoacetato
Oxaloacetato
Citrato
Piruvato
Piruvato
CPT
Malonil-CoA
Acido graso
hacia el tejido adiposo
del tejido adiposo
inhibición
Adiposo
AG
AG
Fuego
K
TG
Hígado
Músculo

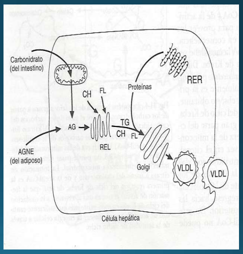





ACUMULACION DE GRASA

# LIPOIDOSIS

- Biosíntesis en hígado
- Rumiantes NO a partir de glucosa
- Formación alta de TG
- No exportación de TG


Carbonidrato (del intestino)
AGNE (del adiposo)
AG
CH
FL
REL
TG
CH
FL
Proteínas
RER
Golgi
VLDL
VLDL
Célula hepática

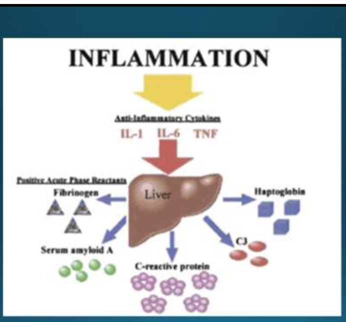
Fosfolípidos, triglicéridos, colesterol
Lípidos de Muy baja densidad.

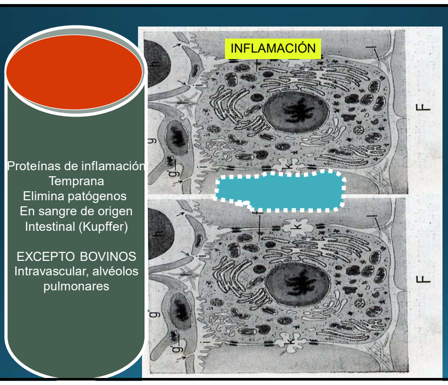
# CAUSAS DE LIPOIDOSIS

- Alto consumo de AG
- Alta producción de tej. Adiposo por demanda (Pico de lactación, finales de gestación, anorexia, Cetosis, endócrinopatias)
- Insuficiencia hepática en oxidación de AG
- Baja síntesis de apoproteínas y no exporta VLDL
- Falta de secreción de VLDL por hepatotoxinas o drogas
- Aumento de glucosa e insulina que produce altos TG, almacenados
- Alto ingreso de glucosa con alta producción de TG
- Hígado graso bovino: obesos, pocos días antes del parto, con anorexia

# FUNCIONES DEL HÍGADO

- *"Inflamatoria"*


INFLAMMATION
Anti-Inflammatory Cytokines
IL-1
IL-6
TNF
Positive Acute Phase Reactants
Fibrinogen
Liver
Haptoglobin
Serum amyloid A
C-reactive protein
C3


INFLAMACIÓN
F
F
g
h
k

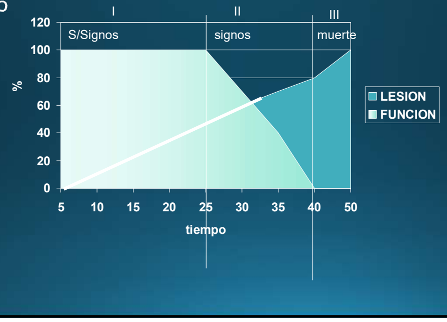
Proteínas de inflamación
Temprana
Elimina patógenos
En sangre de origen
Intestinal (Kupffer)

EXCEPTO BOVINOS
Intravascular, alvéolos
pulmonares

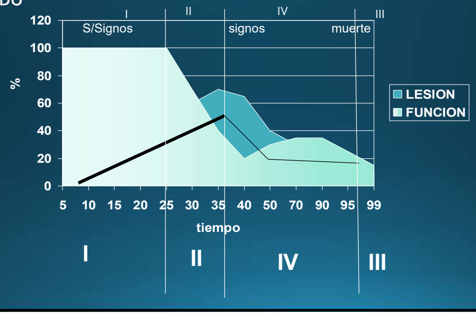
# PROTEÍNAS DE FASE AGUDA

- Más sensibles que leucocitosis o neutrofília.
- Muchas inflamaciones las aumentan
- Canino: PCR, Haptoglobina, ceruroplasmina

## RESERVA FUNCIONAL HÍGADO



## RESERVA FUNCIONAL HÍGADO



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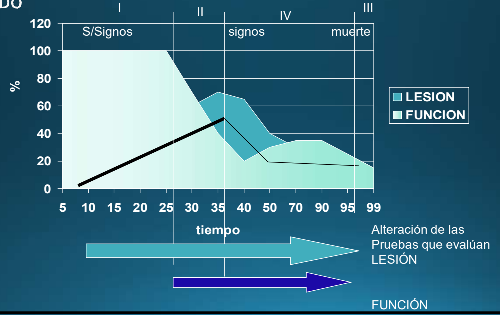
## RESERVA FUNCIONAL HÍGADO



Alteración de las Pruebas que evalúan LESIÓN

FUNCIÓN

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## CLASIFICACION DE LAS PRUEBAS DE LABORATORIO POR SU USO CLINICO

| LESION | FUNCION | AGENTE ETIOLOGICO |
|---|---|---|
| Histología | Histoquímica | Inmunohistoquimica |
| Citología | Hormonas | Anticuerpos |
| Enzimas de Escape | Pruebas de Funcionamiento | Cultivos |
| Radiografía simple | Radiografía con medio de contraste | PCR |
| Examen microscópico | Examen microscópico | Hibridación |
| Ultrasonido | Química sanguínea | Western Blotting |
| | | ELISA , IP , IF |

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## ALTERACIÓN EN LAS PRUEBAS DE LABORATORIO

| FASE | LESIÓN | FUNCIÓN | AGENTE |
|---|---|---|---|
| I | ++ | | + |
| II | +++++ | ++++ | ++ |
| IV | ++ | ++ | - |
| III | + | (+++++) | - /+++ |

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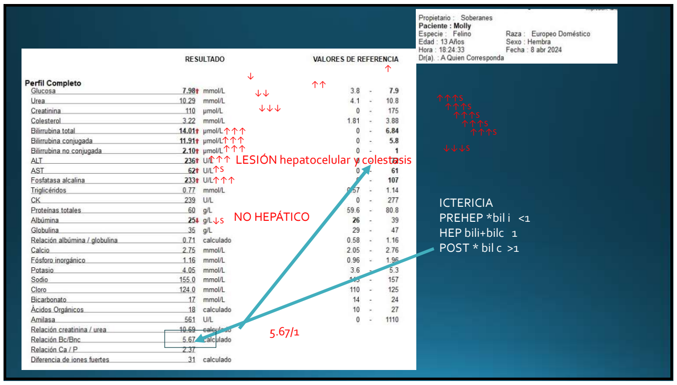

Propietario : Soberanes
**Paciente : Molly**
Especie : Felino
Raza : Europeo Doméstico
Edad : 13 Años
Sexo : Hembra
Hora : 18:24:33
Fecha : 8 abr 2024
Dr(a). : A Quien Corresponda

↓
↑↑
↑

**Perfil Completo**

| | RESULTADO | | VALORES DE REFERENCIA | | |
|---|---|---|---|---|---|
| Glucosa | **7.98↑** | mmol/L ↓↓ | 3.8 | - | **7.9** |
| Urea | 10.29 | mmol/L | 4.1 | - | 10.8 |
| Creatinina | 110 | µmol/L ↓↓↓ | 0 | - | 175 |
| Colesterol | 3.22 | mmol/L | 1.81 | - | 3.88 |
| Bilirrubina total | **14.01↑** | µmol/L ↑↑↑ | 0 | - | **6.84** |
| Bilirrubina conjugada | **11.91↑** | µmol/L ↑↑↑ | 0 | - | **5.8** |
| Bilirrubina no conjugada | **2.10↑** | µmol/L ↑↑↑ | 0 | - | **1** |
| ALT | **236↑** | U/L ↑↑↑ | 0 | - | [illegible] |
| AST | **62↑** | U/L ↑s | 0 | - | **61** |
| Fosfatasa alcalina | **233↑** | U/L ↑↑↑ | [illegible] | - | **107** |
| Triglicéridos | 0.77 | mmol/L | 0.57 | - | 1.14 |
| CK | 239 | U/L | 0 | - | 277 |
| Proteínas totales | 60 | g/L | 59.6 | - | 80.8 |
| Albúmina | **25↓** | g/L ↓s | **26** | - | 39 |
| Globulina | 35 | g/L | 29 | - | 47 |
| Relación albúmina / globulina | 0.71 | calculado | 0.58 | - | 1.16 |
| Calcio | 2.75 | mmol/L | 2.05 | - | 2.76 |
| Fósforo inorgánico | 1.16 | mmol/L | 0.96 | - | 1.96 |
| Potasio | 4.05 | mmol/L | 3.6 | - | 5.3 |
| Sodio | 155.0 | mmol/L | [illegible] | - | 157 |
| Cloro | 124.0 | mmol/L | 110 | - | 125 |
| Bicarbonato | 17 | mmol/L | 14 | - | 24 |
| Ácidos Orgánicos | 18 | calculado | 10 | - | 27 |
| Amilasa | 561 | U/L | 0 | - | 1110 |
| Relación creatinina / urea | 10.69 | calculado | | | |
| Relación Bc/Bnc | 5.67 | calculado | | | |
| Relación Ca / P | 2.37 | | | | |
| Diferencia de iones fuertes | 31 | calculado | | | |

LESIÓN hepatocelular y colestasis

NO HEPÁTICO

5.67/1

↑↑↑s
↑↑↑s
↑↑↑s
↑↑↑s
↑↑↑s

↓↓↓s

ICTERICIA
PREHEP *bil i <1
HEP bili+bilc 1
POST * bil c >1

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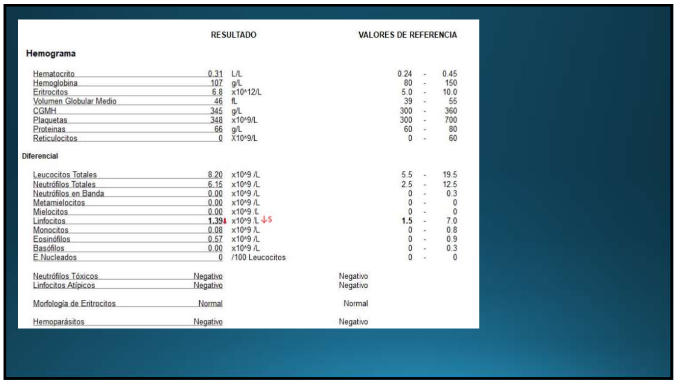

**Hemograma**

| | RESULTADO | | VALORES DE REFERENCIA | | |
|---|---|---|---|---|---|
| Hematocrito | 0.31 | L/L | 0.24 | - | 0.45 |
| Hemoglobina | 107 | g/L | 80 | - | 150 |
| Eritrocitos | 6.8 | x10^12/L | 5.0 | - | 10.0 |
| Volumen Globular Medio | 46 | fL | 39 | - | 55 |
| CGMH | 345 | g/L | 300 | - | 360 |
| Plaquetas | 348 | x10^9/L | 300 | - | 700 |
| Proteinas | 66 | g/L | 60 | - | 80 |
| Reticulocitos | 0 | X10^9/L | 0 | - | 60 |

**Diferencial**

| | RESULTADO | | VALORES DE REFERENCIA | | |
|---|---|---|---|---|---|
| Leucocitos Totales | 8.20 | x10^9 /L | 5.5 | - | 19.5 |
| Neutrófilos Totales | 6.15 | x10^9 /L | 2.5 | - | 12.5 |
| Neutrófilos en Banda | 0.00 | x10^9 /L | 0 | - | 0.3 |
| Metamielocitos | 0.00 | x10^9 /L | 0 | - | 0 |
| Mielocitos | 0.00 | x10^9 /L | 0 | - | 0 |
| Linfocitos | **1.39↓** | x10^9 /L ↓s | **1.5** | - | 7.0 |
| Monocitos | 0.08 | x10^9 /L | 0 | - | 0.8 |
| Eosinófilos | 0.57 | x10^9 /L | 0 | - | 0.9 |
| Basófilos | 0.00 | x10^9 /L | 0 | - | 0.3 |
| E.Nucleados | 0 | /100 Leucocitos | 0 | - | 0 |
| Neutrófilos Tóxicos | Negativo | | Negativo | | |
| Linfocitos Atípicos | Negativo | | Negativo | | |
| Morfología de Eritrocitos | Normal | | Normal | | |
| Hemoparásitos | Negativo | | Negativo | | |

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