

# Clinical Management of Common Liver Disease I

지 흥 민 | 재미한인수의사회 전회장

## I. 생리 기능적 세부

### A. 간세포

- ▶ 실질 세포가 간의 60% 차지
- ▶ 비실질 세포

1. Kupffer's Cell
2. Lipocytes
3. Endothelial Cells
4. Granular Lymphocytes (Pit Cells)

B. 간세포의 한쪽 면은 도양혈관 / space of Disse와 접하고 있습니다.

인접한 간세포들은 세관을 이룹니다.

C. 담즙계는 담즙 세관과 함께 시작하고 표면에 위치합니다.

D. 세관 연결망은 확대된 상피선 담즙관계로 배출되며 결국 총담즙관을 통해 십이지장에서 배출됩니다.

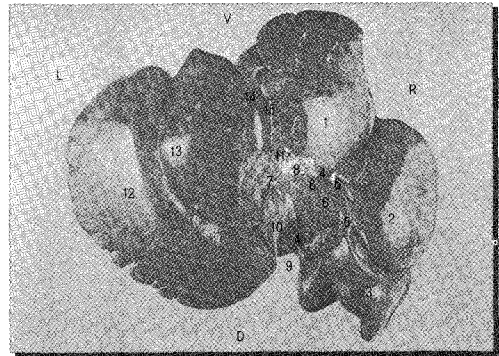
### E. 간 기능단위:

1. Classic Hepatic Lobule
2. Acinar

F. 간은 두 혈관으로부터 혈액을 공급받음

1. 간 동맥은 영양과 산소를 공급

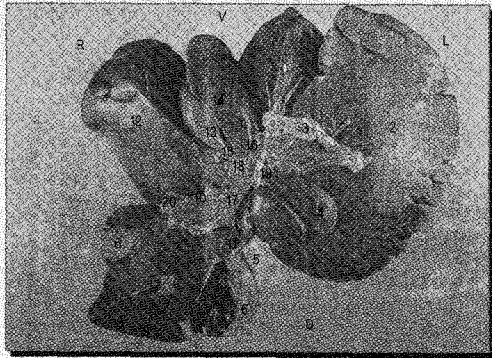
2. 간문맥 정맥은 위장관으로부터 흡수된 물질들과 췌장 호르몬을 운반합니다.



**Diaphragmatic surface of the liver of dog**

(Orientation ventrally(V), dorsally(D), left(L) and right(R) is indicated)

1. Right medial lobe
2. Right lateral lobe
3. Caudate lobe
4. Caudal vena cava
5. Right triangular ligament
6. Coronary ligament
7. Left triangular ligament
8. Oesophageal notch
9. Papillary ligament
10. Papillary process of Caudate lobe
11. Falciform ligament
12. Left lateral lobe
13. Left medial lobe
14. Quadrate lobe
15. Gall bladder

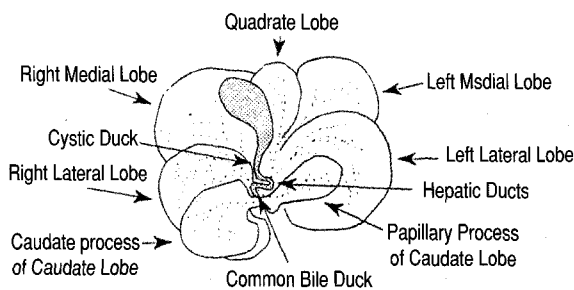


**Visceral surface of the liver of dog**

(Orientation ventrally(V), dorsally(D), left(L) and right(R) is indicated)

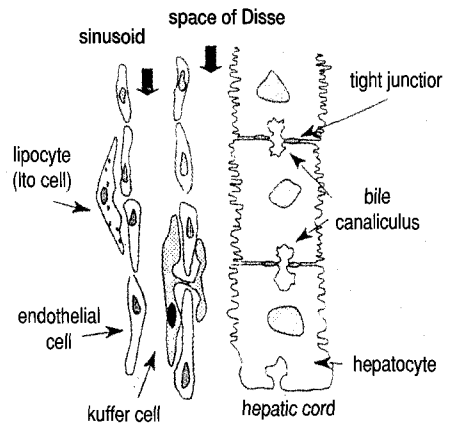
1. Left medial lobe
2. Left lateral lobe
3. Lesser omentum(hepatogastric ligament)
4. Papillary process of caudate lobe
5. Oesophageal notch

6. Right lateral lobe
7. Caudate process of caudate lobe
8. Renal fossa
9. hepatorenal ligament
10. Lesser omentum(hepatoduodenal ligament)
11. Caudal vena cava
12. Right medial lobe
13. Gall bladder
14. Quadrate lobe
15. Cystic duct
16. Hepatic duct
17. Bile duct
18. Portal vein
19. Hepatic artery
20. Gastroduodenal artery



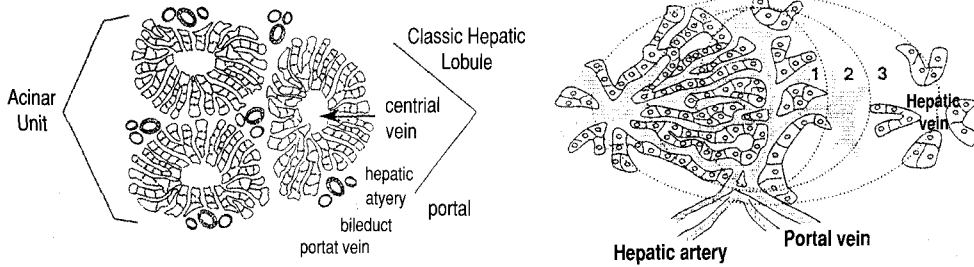
**Overview of gross liver lobe anatomy.**

Dotted line indicates anatomic of intrahepatic biliary tree.



Anatomic orientation of the cellular components of hepatic sinusoid and hepatic cords. Note the extraluminal position of lipocyte(Ito cell) and the intraluminal position of the Kupffer cell, with extending a pseudopod through sinusoidal fenestrations.

VI. Approach to the patient with Liver Disease



Zonal distribution of blood flow in an acinar unit that corresponds to zonal distribution of blood flow, hepatocellular functions, and certain histologic lesions.

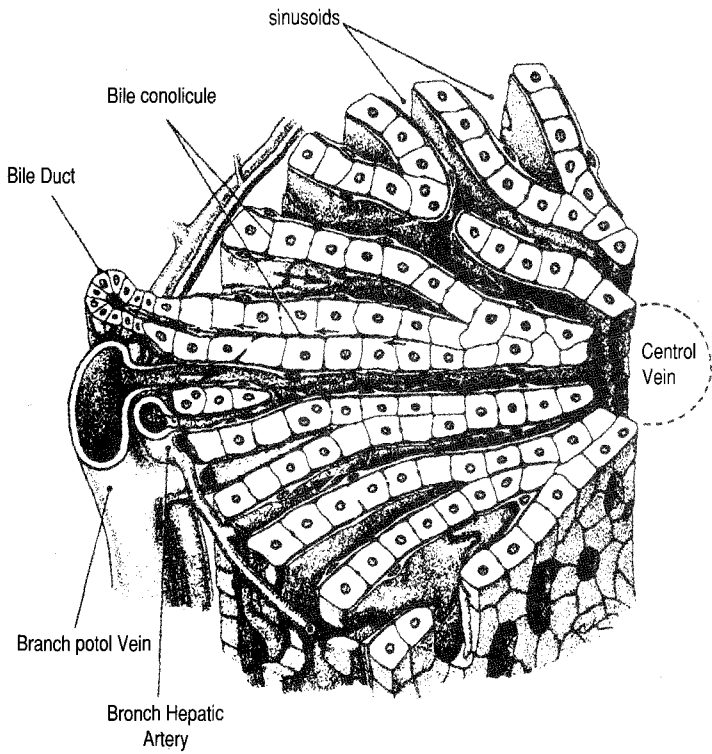


Figure 28-5. Hepatic microanatomy is complex and can be visualized in several ways. Note the relationship of the bile canaliculi to the bile ducts; the biliary system may be imagined as an acinar lens with the bile canaliculi forming a long narrow acinus. (Modified from Hamwal textbook of Histology, 5th ed. Philadelphia, JB Lippincott, 1965.)



### II. 간 질환의 개요

- A. 가장 큰 분비 기관. 단일 선 조직
- B. 현재까지 1,500개의 생리화학적 기능과 대사 기능이 밝혀짐
- C. 대단히 큰 여유 능력과 독성과 전염체에 대한 특별한 저항능력이 있음
- D. 간세포의 80% 이상 손상되기 전까지는 심각한 임상 증상을 유발하지 않음
- E. 손상 후 회복되는 능력이 매우 큼
- F. 다른 많은 기능들을 하는 일반 기관들은 다양한 독성물질과 감염체로부터 쉽게 손상 받지만 간은 쉽게 손상 받지 않음

### III. 병인론

- A. 일반적으로 다음의 요인들에 의해 간 질환이 유발됨
  - 1. 바이러스, 세균, 기생충 등 전염 가능성이 있는 병원체에 감염
  - 2. 독성물질의 흡수, 섭취를 통한 손상
  - 3. 심각한 영양 불균형에 의한 간 기능의 손상
  - 4. 원발성 또는 전이성 종양에 의한 손상
  - 5. 기타 : 외상(교통사고)  
대사 이상(고양이의 지방간)  
온도, 열사병
- B. 개와 고양이 급성 간 질환의 일반적인 원인
  - 1. 감염성 또는 기생충
    - a. 바이러스
    - b. 세균
    - c. 곰팡이
    - d. 원충성
    - e. 기생충
  - 2. 간독성물질
    - a. 약물과 마취제
    - b. 화학물질과 생물학적 물질

- c. 전신성, 대사성 이상
- d. 외상, 온도, 저산소성 손상

### IV. 간담도계의 주기능

- A. 탄수화물 대사
- B. 지방 대사
- C. 단백질 대사
- D. 비타민 대사
- E. 내분비물질, 호르몬 대사
- F. 면역 기능
- G. 저장 기능
- H. 혈액학적 기능
- I. 소화 기능
- J. 해독작용과 분비 기능

### V. 간담도계 질환의 임상 증상

- A. 일반적으로 질병 초기에는 모호한 증상들을 보임
- B. 담도계 폐쇄 시에는 72시간 후 황달이 나타나며 21일 후에는 출혈성 경향을 나타냄
- C. 선천적인 간문맥혈관계 이상 시에는 생후 2달 안에 간성뇌증을 보임
- D. 간담도계 질환의 주된 증상들
  - ▶ 식욕 저하, 구역질, 구토, 설사, 변비, 체중 감소 등을 포함한 위장관계 이상 증상
- E. 식욕저하는 고양이 간 질환에서 일반적으로 나타나는 증상임
- F. 위장관 궤양과 출혈
- G. 발열
- H. 출혈성 경향
- I. 황달
- J. 다음/다뇨

## MAJOR HEPATOBILIARY FUNCTIONS

### Carbohydrate Metabolism

Glucos homeostasis : gluconeogenesis ; glycogenolysis., insulin metabolism : glucagon metabolism  
Glycogen : metabolism and storage  
Insulin : degradation  
Glucagon : degradation  
Growth hormone : regulation

### Lipid Metabolism

Cholesterol : synthesis, esterification, excretion  
Bile acid : synthesis and regulation  
Ketogenesis  
Fatty acid : oxidation and mobilization  
Triglyceride: synthesis and release  
Phospholipid : metabolism

### Protein Metabolism

Albumin : synthesis : turnover  
Globulins ; acute-phase proteins ; transport proteins ; enertain immunoglobulins (bile)  
Apoproteins : synthesis(some)  
Coagulation proteins:  
Activators for : procoagulants and inhibitors  
inhibitors for : procoagulants and inhibitors  
Aminoacid : regulation  
Ammonia : synthesis and detoxification  
Urea : synthesis

### Vitamin Metabolism

Water-soluble : activation, synthesis, storage(B<sub>1</sub>, B<sub>6</sub> (pyridoxine), B<sub>12</sub> (cyanocobalamin), folic acid, nicotinic acid, and riboflavin)  
Fat-soluble : activation, synthesis, storage(vitamins E, D, A, and K)

### Immunologic Functions

Kupffer cell: population, Function : phagocytic protection, gut bacteria, toxins, particulate debris  
Complement metabolism  
Interleukin production

Immunomodulation(metabolic products)

### Endocrine Hormone Metabolism

Polypeptide homones : target organ influence, degradation  
steroid homones : conjugation : degradation and excretion

### storage Function

Water-soluble vitamins	fat-soluble vitamins
Triglycerides	Glycogen
Copper, iron, zinc	Blood

### Hematologic Functions

In utero : hematopoiesis  
Extramedullary hematopoiesis : severe anemia : marrow failure  
Coagulation system : factor synthesis, activation : overall homeostasis  
Reticuloendothelial function : senescent, RBC breakdown  
Transferrin synthesis  
Bilirubin : uptake, conjugation, excretion, enterohepatic circulation  
Hematopoietic factor storage and activation : B<sub>12</sub>, folate, iron  
Iron homeostasis

### Digestive Function

Bile acids : synthesis, regulation, enterohepatic circulation  
Bile : component synthesis-excretion, digestive release  
Bladder : bile storage, bile digestive interval release

### Detoxification and Excrete Funcions

bilirubin : conjugation, uptake, biliary excretion  
Ammonia : urea cycle  
Steroid homones : cortisol, androgens, estrongen, aldosterone  
Micosomal enzyme induction : dog especially

xenobiotic : e.g.	barbiturates	propoxyphene
	chloramphenical	pentazocine
	clindamycin	diazepam
	metronidazole	meperidine
	propranolol	lidocaine
	theophylline	aminophylline

Copper : biliary excretion, lysosomal storage

Cholesterol : biliary excretion

## HISTORICAL AND PHYSICAL SIGNS OF LIVER DISEASE

### ACQUIRED

#### Early Signs

vomiting  
Diarrhea/constipation  
Weight loss  
Pyrexia  
Normal bilirubinemia  
Polyuria/ polydipsia  
clear to yellow urine

#### Mojoir Bile Occlusion

Anorexia  
Vomintion  
Diarrhea/consripation  
Weight loss  
Pyrexia  
Jaundice Within 72 hours  
Polydipsia  
Orange urine  
Negative urobilinogen  
Bleeding tendencies  
Achollic(pale) feces  
Melenic feces if bleeding  
Jepatomegaly  
(firm, rounded borders)  
Palpable gallbladder(cat)  
gastroduodenal ulceration  
If chronic: > 6 wk - ascites

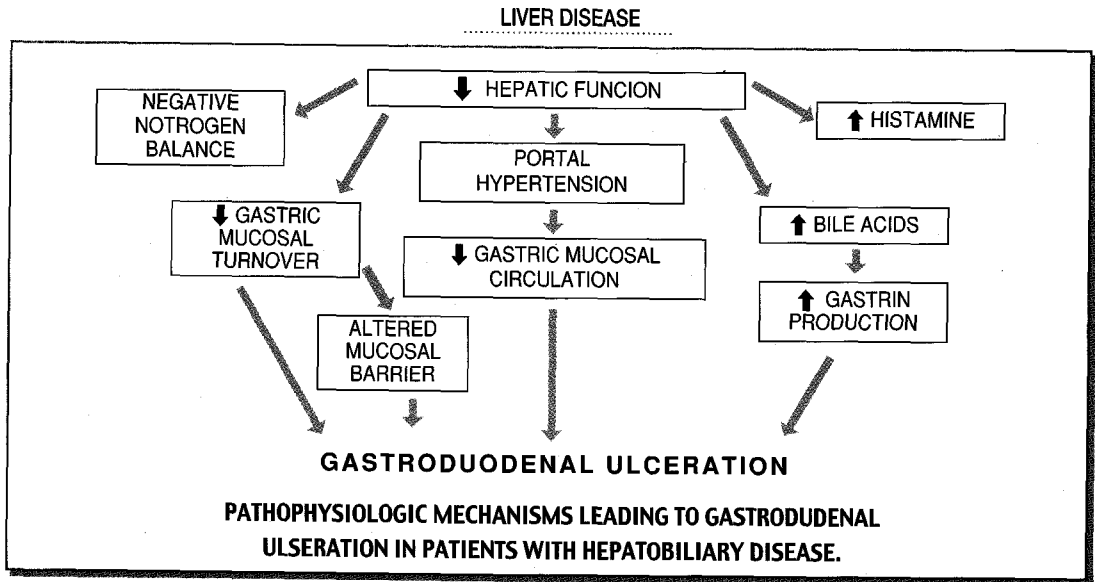
#### Severe hepatic Insufficiency

Anorexia  
Vomintion  
Diarrhea/consripation  
Weight loss  
Pyrexia  
Jaundice as disease advances  
Polydipsia/polydipsia  
Clear to orange urine  
urobilinigen "+"  
Bruising/bleeding tendencies  
Brown to melenic feces  
Green feces :  $\downarrow$  stercobilin  
Hepatomegaly (cat)  
Normal to microhepatica(dog)  
Pytalism (cat)  
Gastroduodenal ulceration  
If  $\downarrow$  albumin and portal hypertension  
Ascites  
Edema (rare in cat)  
Hepatic encephalopathy  
Stupor, lethargy, depression, pacing, head pressing, rarely coma, seizures  
Hyperammonemia  
Usually coincides with HE signs  
Ammonium biurate crystalluria  
Cystic/renal caculi  
Urinary tract obstruction

### CONGENITAL

#### Portosystemic Vascular Anomaly

Stunted body size  
Abnormal behavior : lethargic  
Diarrhea/constipation  
Weight loss  
Pyrexia  
No jaundice  
Polyuria/ polydipsia  
Clear urine, urobilinogen "+"  
Copper-colored iris (cat)  
Nomal coagulation  
Brown feces  
Melena : hookworms, coccidia  
Microhepatica  
"Plump" kidneys  
Clyptorchid (dog)  
Gastrointestinal ulceration (rare)  
Potal hypertension :  $\pm$  ligation, AV fistula  
Ascits rare unless hepatic AV fistula  
Edema does not occur  
Hepatic encephalopathy  
Amaurosis, stupor, depression, head pressing, pacing, aggression (esp, cat), ptyalism, seize with prolonged prodrome  
Hyperamminemia  
Usually coincides With HE signs  
Ammonium biurate crystalluria  
Cystic/renal calculi  
Urinary tract obstruction : pollakiuria, hematuri



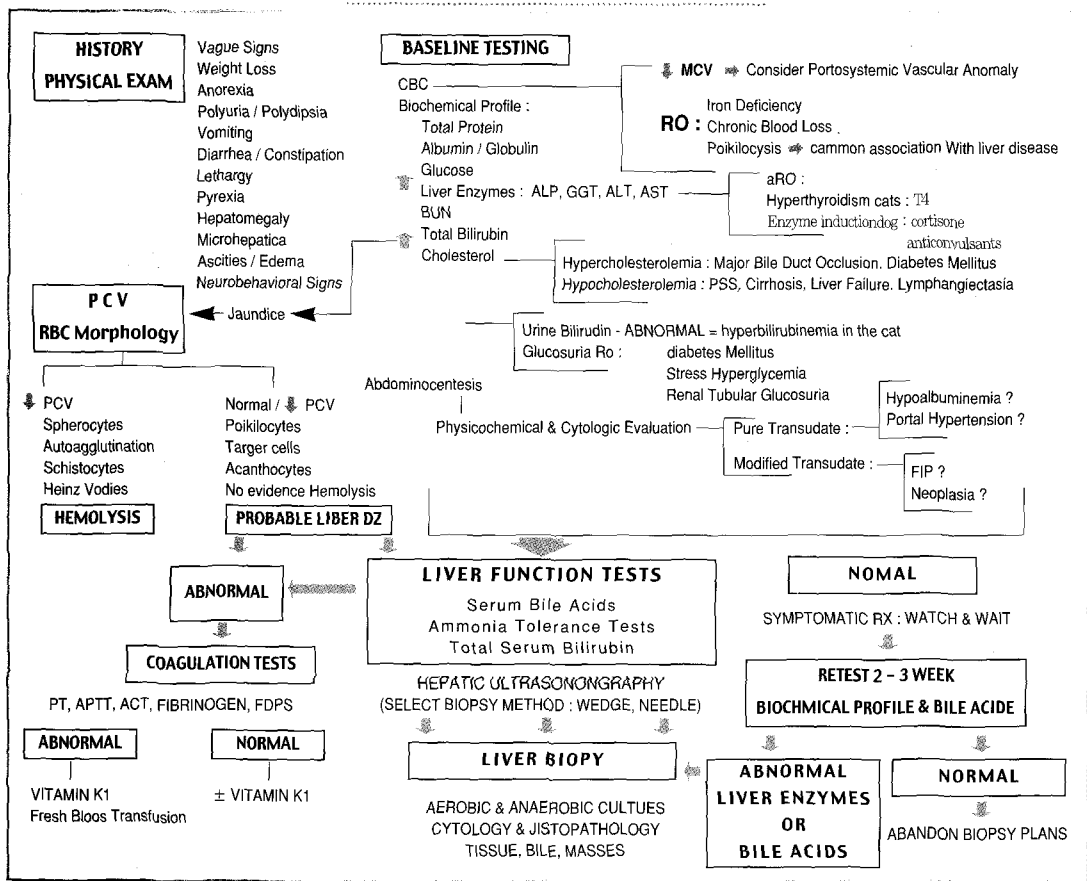
**VI. 간질환 환축에 대한 진단적 접근**

- A. 병력 및 신체검사
- B. 기초 검사
  - 1. 일반혈액검사(CBC)
  - 2. 혈액화학검사 간 효소: ALP, GGT, ALT, AST
  - 3. 노분석
  - 4. 고양이 백혈병 검사(FeLV)
  - 5. 복수 천자 검사
- C. 간 기능 검사:
  - 1. Serum bile acids
  - 2. Ammonia Tolerance Test
  - 3. Total serum bilirubin
- D. 방사선
- E. 간 초음파, MRI, CCT
- F. 간 생검

**VI. Approach to the patient with Liver Disease**

- A. History / Physical Exam
- B. Baseline Testing :
  - 1. CBC
  - 2. Biochemistry - Live Enzymes : ALP, GGT, ALT & AST
  - 3. Urinalysis
  - 4. FeL V
  - 5. Abdominalcentesis
- C. Liver Function Test :
  - 1. Serum bile acids
  - 2. Ammonia Tolerance Test
  - 3. Total serum bilirubin
- D. Radiology
- E. Hepatic Ultrasonography - Mri, CCT
- F. Liver Biopsy

### MAJOR HEPATOBILIARY FUNCTIONS



### VII 간 기초 검사

#### A. 기초 검사

1. 일반혈액검사(CBC)
2. 혈액화학검사

#### B. 간 기능검사

1. Serum bile acid
2. Ammonia Tolerance Test
3. Total Serum Bilirubin

#### C. 방사선, 초음파

#### Glossary and Abbreviations (for Table #1)

A. ALP: Alkaline Phosphatase

B. GGT: Gauma Geutamyl transferase

C. ALT: Alanine Amino transferase

D. AST: Asporate Amino transferase

E. Triglycerides: 혈액중의 지방량을 측정하는 검사

F. Glucose: 췌장과 간의 이상을 검사, 당뇨병

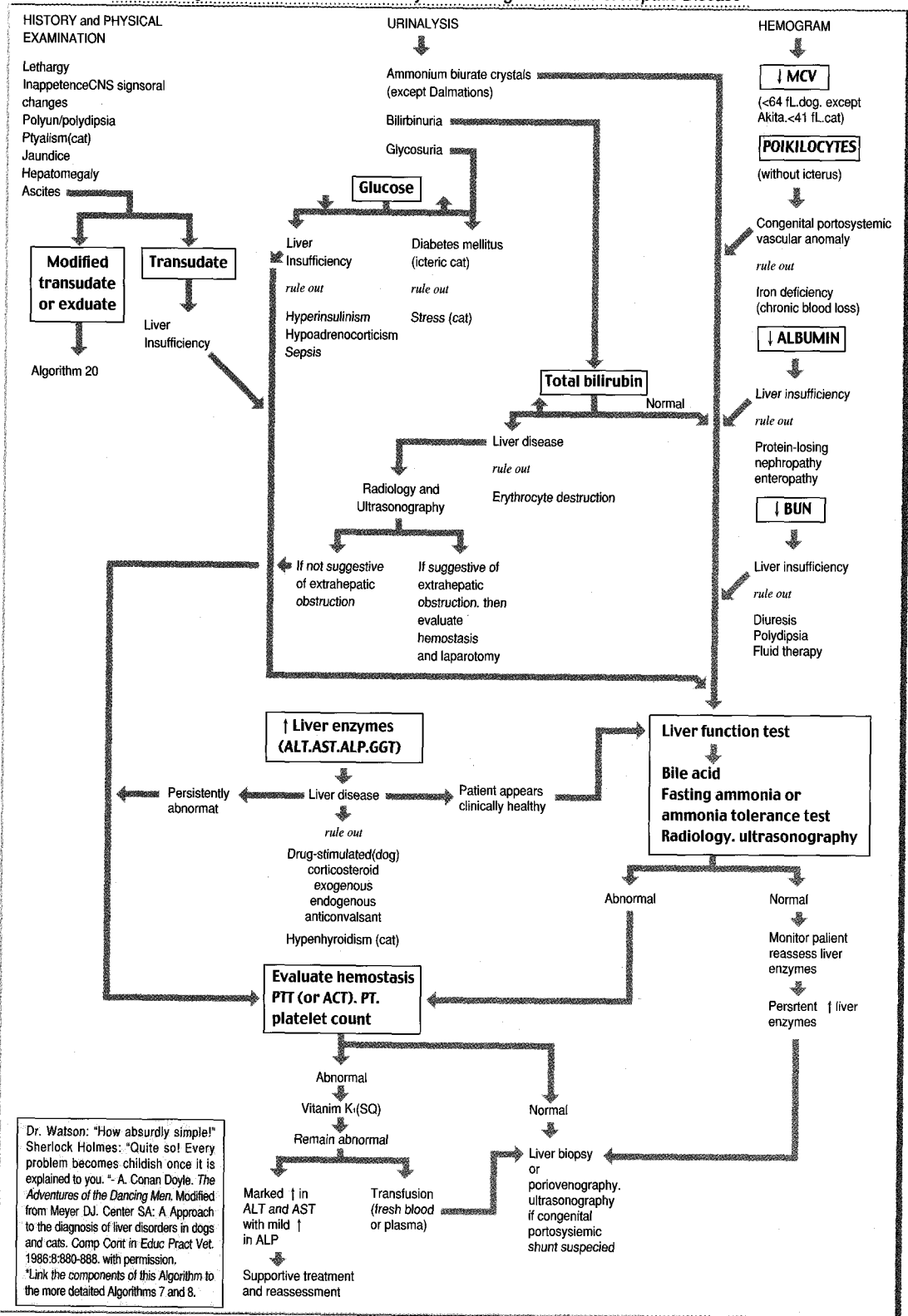
G. Uric Acid: 단백질 대사의 최종산물

H. BUN: 혈액 중 요소질소 농도

I. ATT: Ammonia Tolerance Test

J. LDH: Lactic Dehydrogenase

Hematologic, Biochemical, and Uroanalytical Findings Indicative of Hepatic Disease



Dr. Watson: "How absurdly simple!" Sherlock Holmes: "Quite so! Every problem becomes childish once it is explained to you." - A. Conan Doyle. *The Adventures of the Dancing Men*. Modified from Meyer DJ. Center SA: A Approach to the diagnosis of liver disorders in dogs and cats. Comp Cont in Educ Pract Vet. 1986;8:880-888. with permission. \*Link the components of this Algorithm to the more detailed Algorithms 7 and 8.





TABLE 3. Reference Intervals for Hematology Values of Adult Animals<sup>a,b</sup>

Test	Units	Canine	Feline	Equine	Bovine	Porcine	Ovine
RBC	$\times 10^9/\mu\text{l}$	5.4-7.8	5.8-10.7	6.4-10.0	5.0-10.0	5.0-8.0	8.0-15.0
Hemoglobin	g/dl	13-19	9-15	11-17	8-15	10-18	8-16
Hct	%	37-54	30-47	32-47	24-46	33-50	24-49
MCV	f	62-74	41-51	43-54	37-51	50-67	23-48
MCHC	g/dl	32-36	31-35	34-37	33-37	30-34	31-34
MCH	pg	22-27	13-18	15-19	13-18	17-21	8-12
RDW	%	12-15	14-19	18-22	16-24		
Platelets	$\times 10^9/\mu\text{l}$	1.6-4.3	3-8	1-2.7	2-7.3	2-8	3-8
MPV	f	6.7-11.1	ND	4.6-7.3	4.5-6.7		
Fibrinogen	mg/dl	100-400	100-300	100-500	200-700	100-500	100-500
Lcterus index	units	<5	<5	5-25	0-20	<5	<5
Plasma Protein	g/dl	6.0-7.8	6.2-8.0	6.1-8.0	7.0-8.5	6.0-8.0	6.0-7.5
Reticulocytes	$\times 10^3/\mu\text{l}$	<80	<30 agg <500 punc	0	0	<70	0
WBC	$\times 10^3/\mu\text{l}$	6.0-17.0	5.5-19.5	5.2-13.9	4.0-12.0	10-22	4.0-12.0
Bands	$\times 10^3/\mu\text{l}$	0-0.3	0-0.3	0-0.1	0-0.12		
Segmented	$\times 10^3/\mu\text{l}$	30-11.5	2.5-12.5	2.2-7.4	0.6-4.0	3.2-10.0	1.0-5.0
Lymphocytes	$\times 10^3/\mu\text{l}$	1.0-4.8	1.5-7.0	1.1-5.3	2.5-7.5	4.4-13.5	2.0-9.0
Monocytes	$\times 10^3/\mu\text{l}$	0.15-0.135	0-0.85	0-0.9	0.03-0.8	0.2-2.2	0-0.75
Eosinophils	$\times 10^3/\mu\text{l}$	0.1-1.25	0-1.5	0-0.6	0-2.4	0.2-2.0	0.1-0.75
Basophils	$\times 10^3/\mu\text{l}$	<0.1	<0.1	<0.3	<0.2	Rare	Rare

Erythrocyte morphology<sup>c</sup>

	1+	2+	3+	4+
Anisocytosis				
Canine	7-15d	16-20	21-29	>30
Feline	5-8	9-15	16-20	>20
Bovine	10-20	21-30	31-40	>40
Equine	1-3	4-6	7-10	>10
Polychromasia				
Canine	2-7	8-14	15-29	>30
Feline	1-2	3-8	9-15	>15
Bovine	2-5	6-10	11-20	>20
Equine	Rare	Rare	Rare	Rare
Hypochromasia (all species)	1-10	11-50	51-200	>200
Poikilocytosis (all species)	3-10	11-50	51-200	>200
Codocytes (canine only)	3-5	6-15	16-30	>30
Spherocytes (all species)	5-10	11-50	51-150	>150
Echinocytes (all species)	5-10	11-100	101-250	>250
Acanthocytes, schistocytes (all species)	1-2	3-8	9-20	>20

<sup>a</sup>From the Veterinary Teaching Hospital-University of Florida.

<sup>b</sup>Platelet counts determined electronically for all species except the cat. Reference range for canine platelet count determined by manual method is  $2 - 5 \times 10^9/\mu\text{l}$ .

<sup>c</sup>Weiss DJ : Uniform evaluation and semiquantitative reporting of hematologic data in veterinary laboratories. *vet Clin Pathol* 1984; 13:27

<sup>d</sup>Number of affected cells / 1000 x microscopic field.

TABLE 4. Reference Intervals for Serum Chemistry for Adult Animals<sup>a</sup>

Test	Units	Canine	Feline	Equine	Bovine	Porcine	Ovine
Ammonia	μmol/L	0-40	0-40	0-40			
ALP	U/L	10-73	15-92	102-257	29-99	26-362	68-387
ALP	U/L	15-58	30-100	4-12	17-37	32-84	60-84
AST	U/L	16-43	12-56	152-294	48-100	9-113	98-278
Amylase	U/L	510-1864	365-948	9-34	12-107		
Anion gap	mEq/L	11-26	13-24	7-16	12-22		
Bile acid-fast	μmol/L	<5	<2	<15	See text		
Postprandial	μmol/L	<15	<15				
Gilirubin(total)	mg/dL	0.1-0.3	0.1-0.2	0.5-2.1	0.1-0.3	0.1-0.2	0.1-0.4
Calcium	mg/dL	9.0-10.8	7.4-10.5	10.6-13.0	7.9-10.0	8-12	10.4-13
CO <sub>2</sub>	mEq/L	20-27	15-25	26-35	24-34	18-26	21-28
Chloride	mEq/L	110-118	116-125	97-104	94-104	100-105	98-115
Cholesterol	mg/dL	108-266	38-186	50-143	87-254	36-54	50-140
Cholinesterase	U/L	1347-2269	1000-2000				
Cortisol(basal)	μg/dL	1.0-6.8	0.3-2.6				
CK(CPK)	U/L	40-254	59-527	113-333	44-228		
Creatinine	mg/dL	0.5-1.4	0.7-1.8	1.0-1.9	0.7-1.1	1.0-2.7	1.2-1.9
Folate	μg/dL	7.5-17.5	13.4-38				
GGT	U/L	1-5	0-2	9-25	20-48		
Glucose	mg/dL	77-120	58-120	76-127	37-71	65-95	50-80
Iron	μg/dL	84-233	65-233	74-209	57-162	91-199	166-222
Lipase	U/L	13-200	0-83				
Magnesium	mEq/L	1.2-2.0	1.5-3.5	1.3-2.0	1.4-2.3		
Osmolality	mOsm/kg	291-315	292-356	282-302			
Phosphorus, inorganic	mg/dL	2.4-6.1	2.6-7.9	2.0-4.3	4.6-9.0	5.3-9.6	5.0-7.3
Potassium	mEq/L	4.2-5.6	4.0-5.3	2.4-5.2	4.0-5.3	4.9-7.1	4.0-6.0
Protein(total)	g/dL	5.4-7.1	5.7-7.9	5.5-7.3	5.9-7.7	7.0-8.9	6.0-7.9
Albumin	g/dL	2.5-3.6	2.3-3.4	2.7-4.2	2.7-4.3	1.9-3.3	2.4-3.9
Globulin	g/dL	2.4-4.0	2.6-4.5	2.1-3.8	2.5-4.1	5.3-6.4	3.5-5.7
Sodium	mEq/L	145-153	151-158	136-142	136-144	139-152	136-154
SD(SDH)	U/L	2.9-8.2	3.9-7.7	1.9-5.8	4.3-15.3	1-6	6-28
T1	ng/dL	85-250	85-250				
T2	μg/dL	1.2-3.0	1.2-3.0				
T4 (free)	ng/dL	0.7-3.3					
TLI	μg/dL	5-35					
Triglycerides	mg/dL	20-112	10-114	4-44	0-14		
Urea nitrogen	mg/dL	7-25	18-33	12-26	10-26	8-24	18-31

<sup>a</sup>From the Veterinary Teaching Hospital-University of Florida, with permission.



대한수의