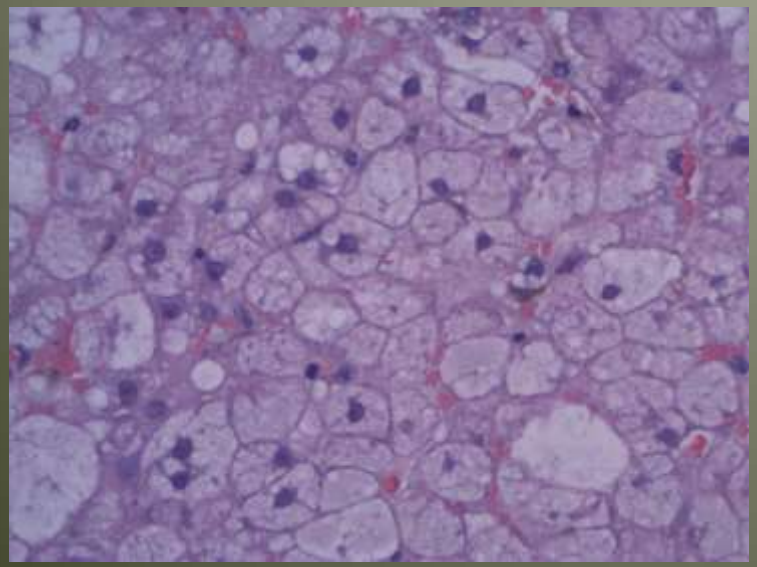
Liver Let Die

NIVA in association with the NEW NI YOUNG VET NETWORK

Craig Reilly BVM&S CertSAM MRCVS
Advanced practitioner (SAM)



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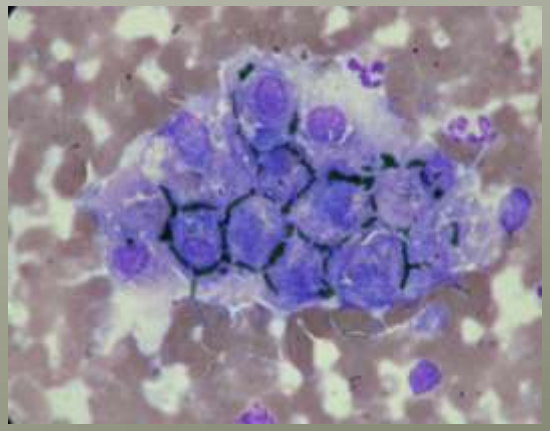

- Anatomy revision
- Signs
- Clinical exam
- Bloods/urine
- Xray

- Ultrasound
- Aspirate
- Biopsy
- Therapeutics
- Surgery tips

..and some cases!

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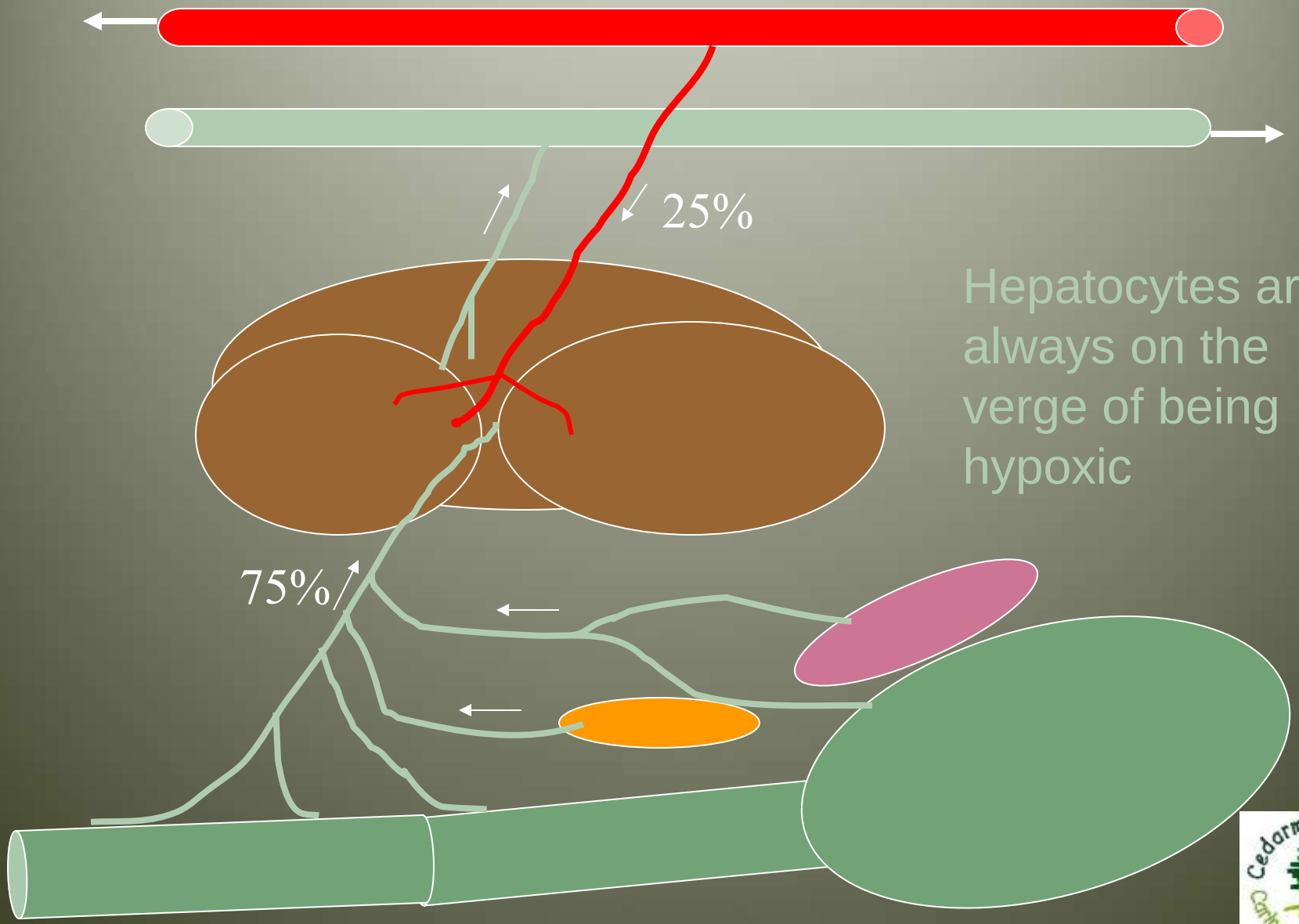
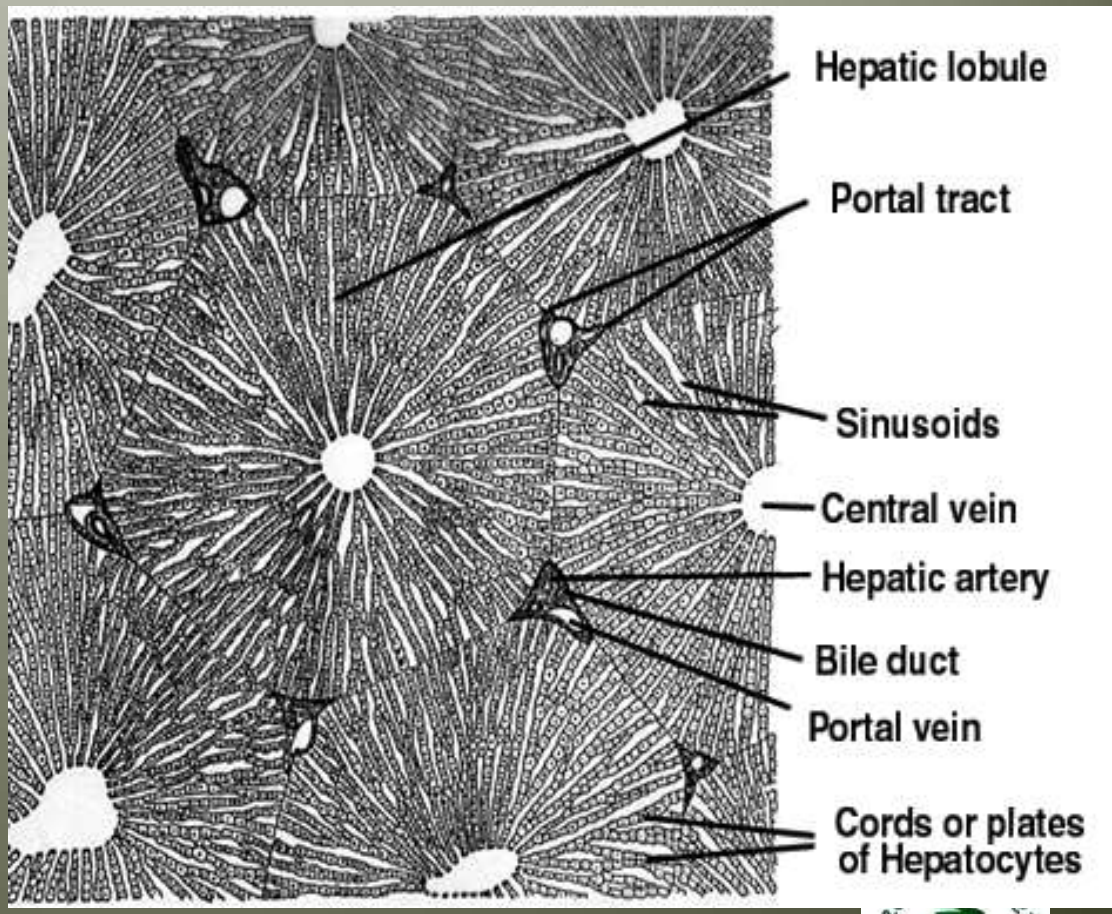
Liver : Blood supply



Hepatocytes are always on the verge of being hypoxic

Hepatic structure

- ‘Classic’ lobule
  - Central vein
  - Portal area
    - Bile duct
    - Portal vein
    - Hepatic artery
  - Cellular cords / sinusoids
  - Space of Disse
    - Kupffer cells
    - Stellate cells



/senior/metabolism/liver/

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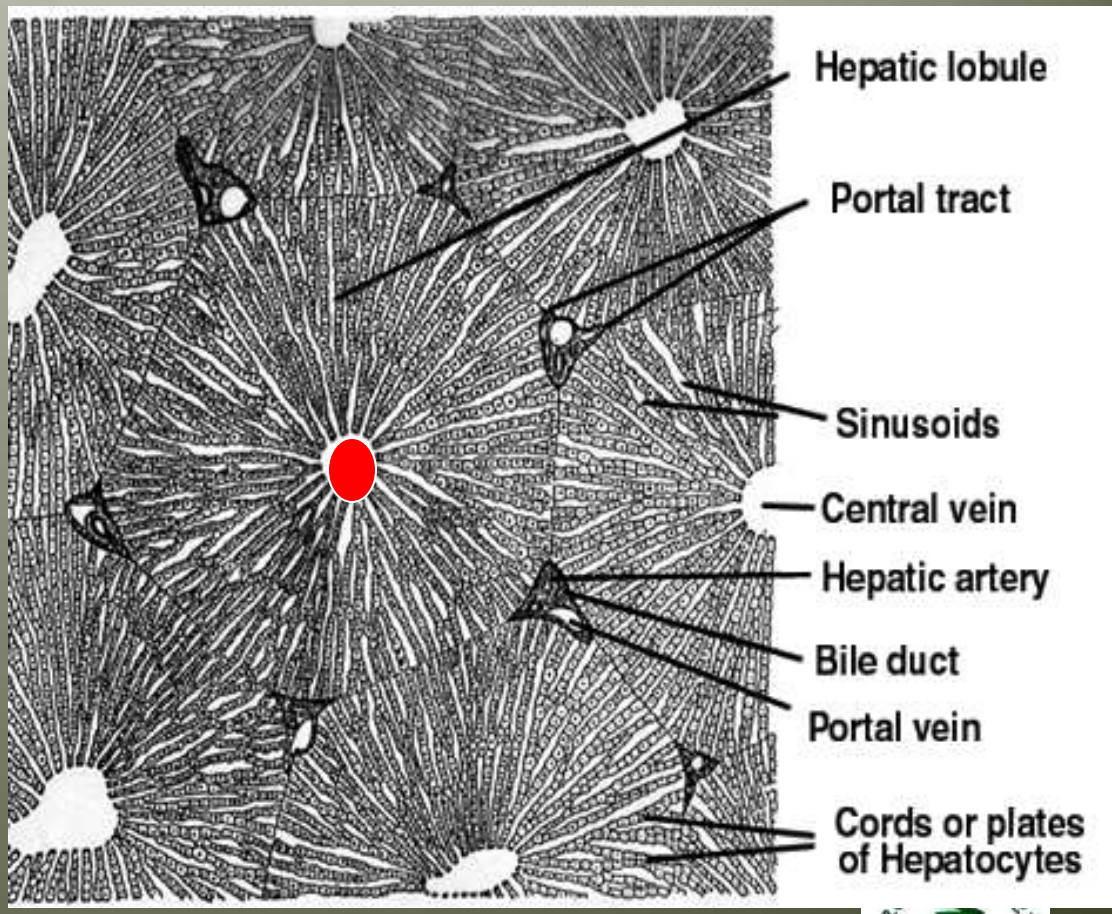

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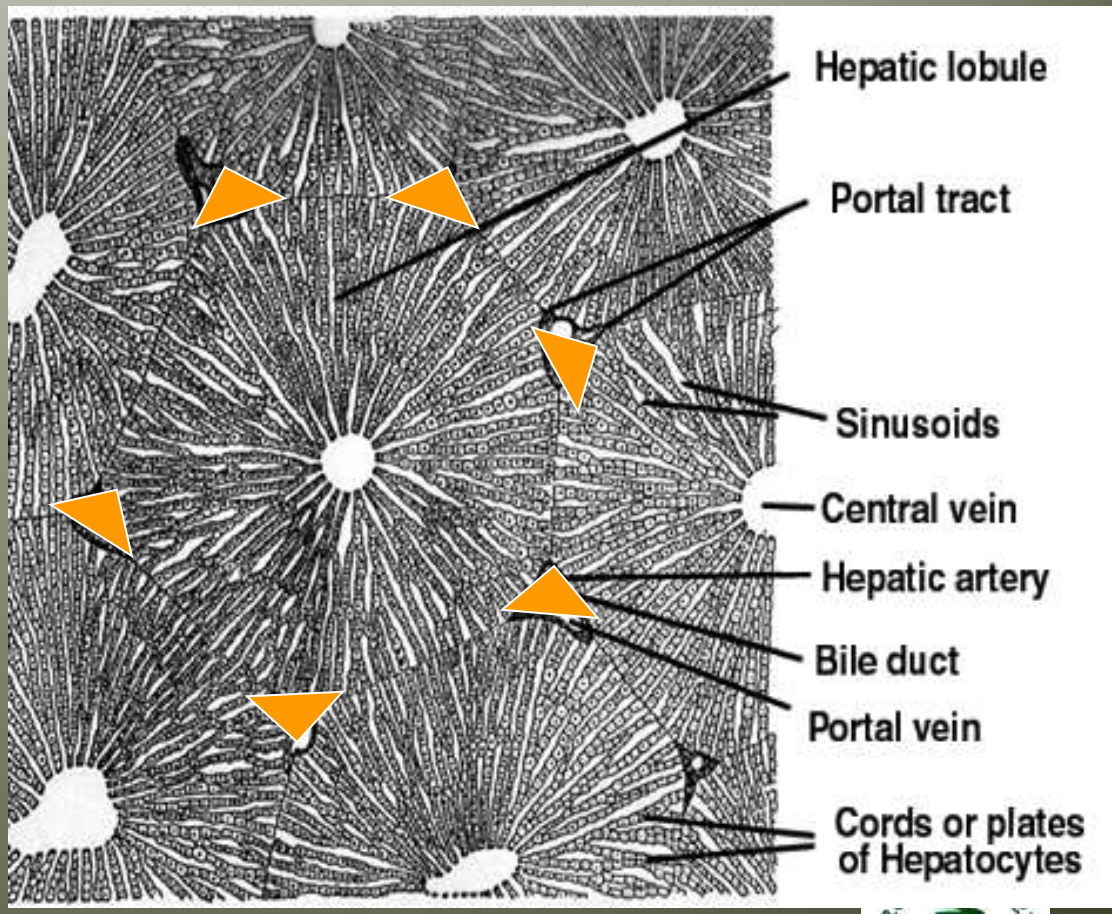

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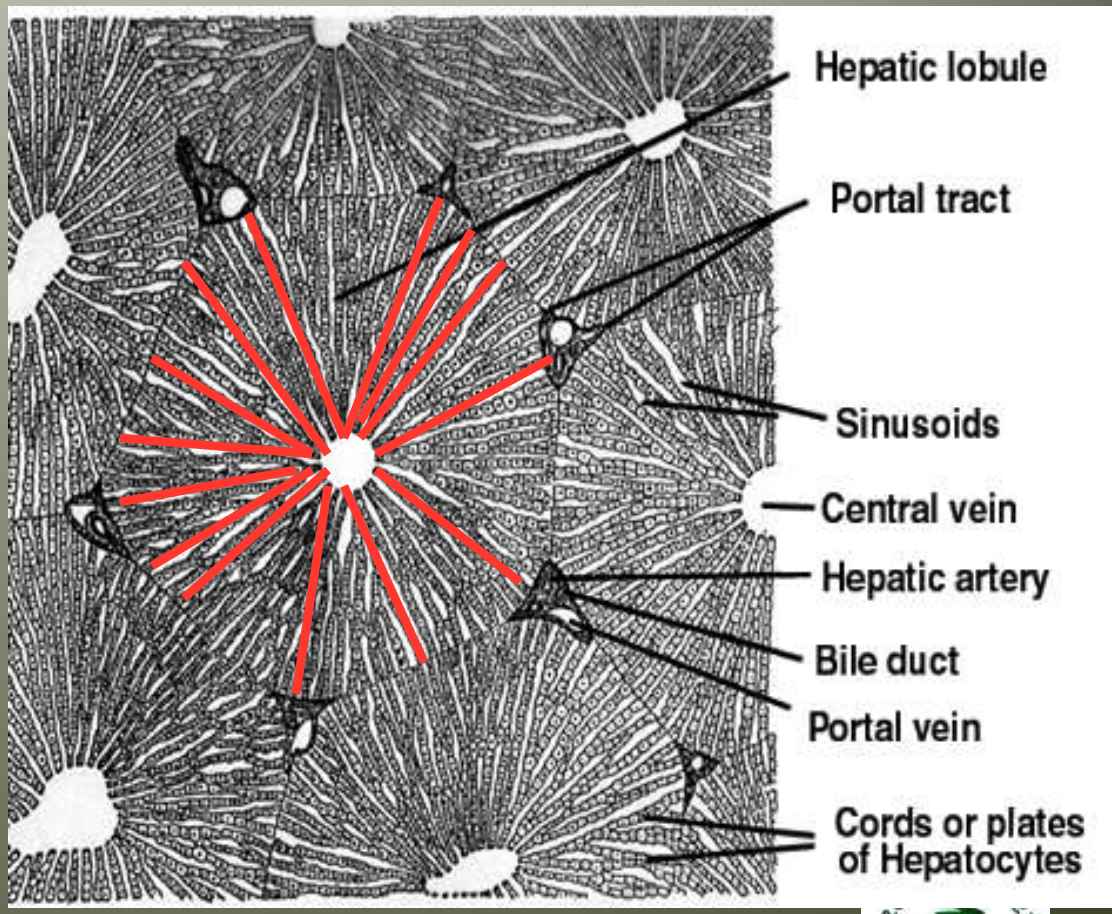

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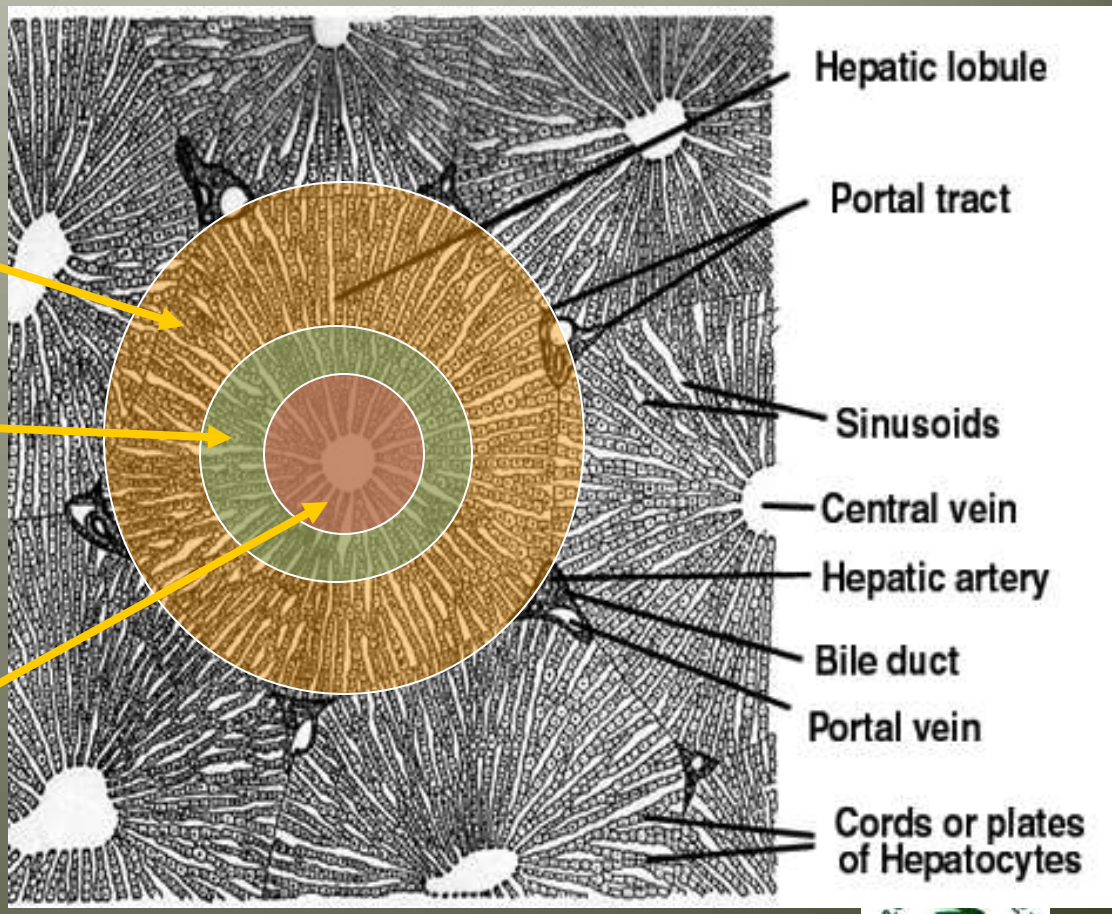
Hepatic structure

Periportal

Mid-zonal

Centrilobular



/senior/metabolism/liver/

Portal veins show as echogenic walls

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..none at all?

- Aids digestion (especially of fats)
- Synthesis of proteins and hormones
- Regulating energy and protein metabolism
- Metabolism and elimination of toxic and waste products
- Immune regulation

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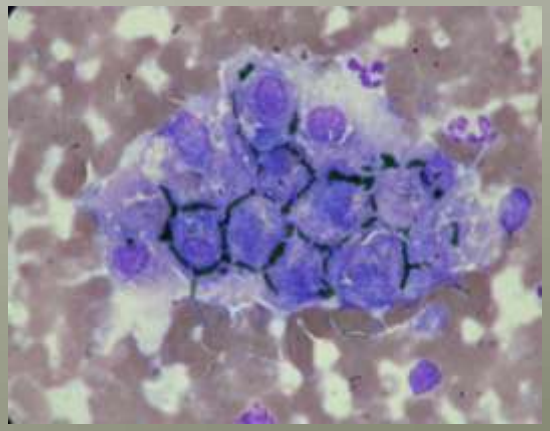

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..and some cases!

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Ascites?

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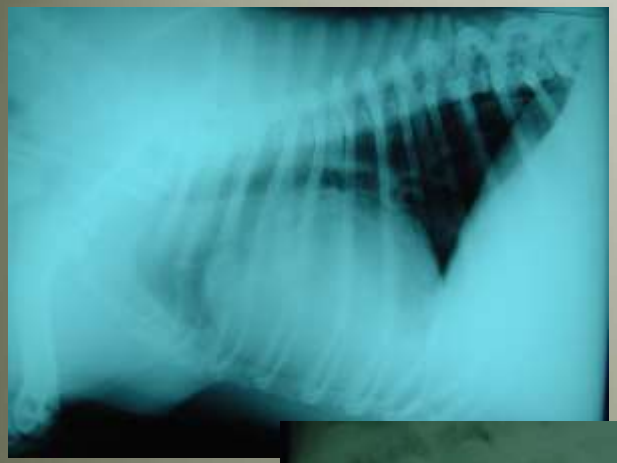
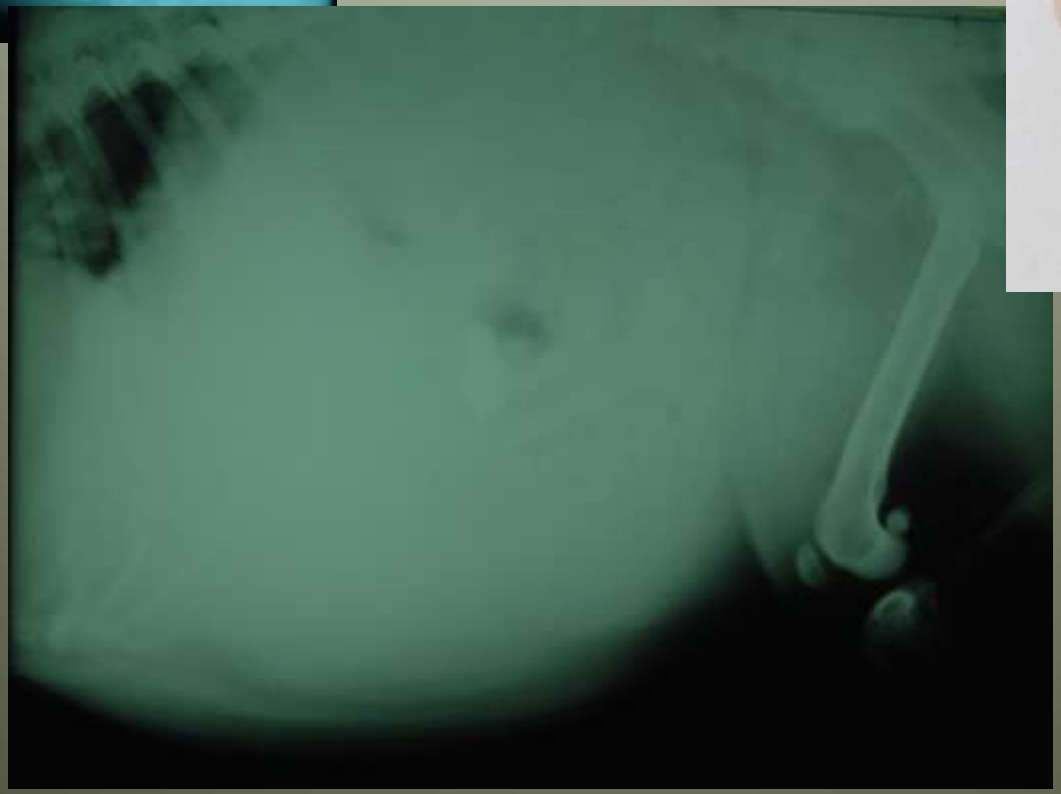


Alb ↓ ?
If not…portal hypertension?



?cardiac

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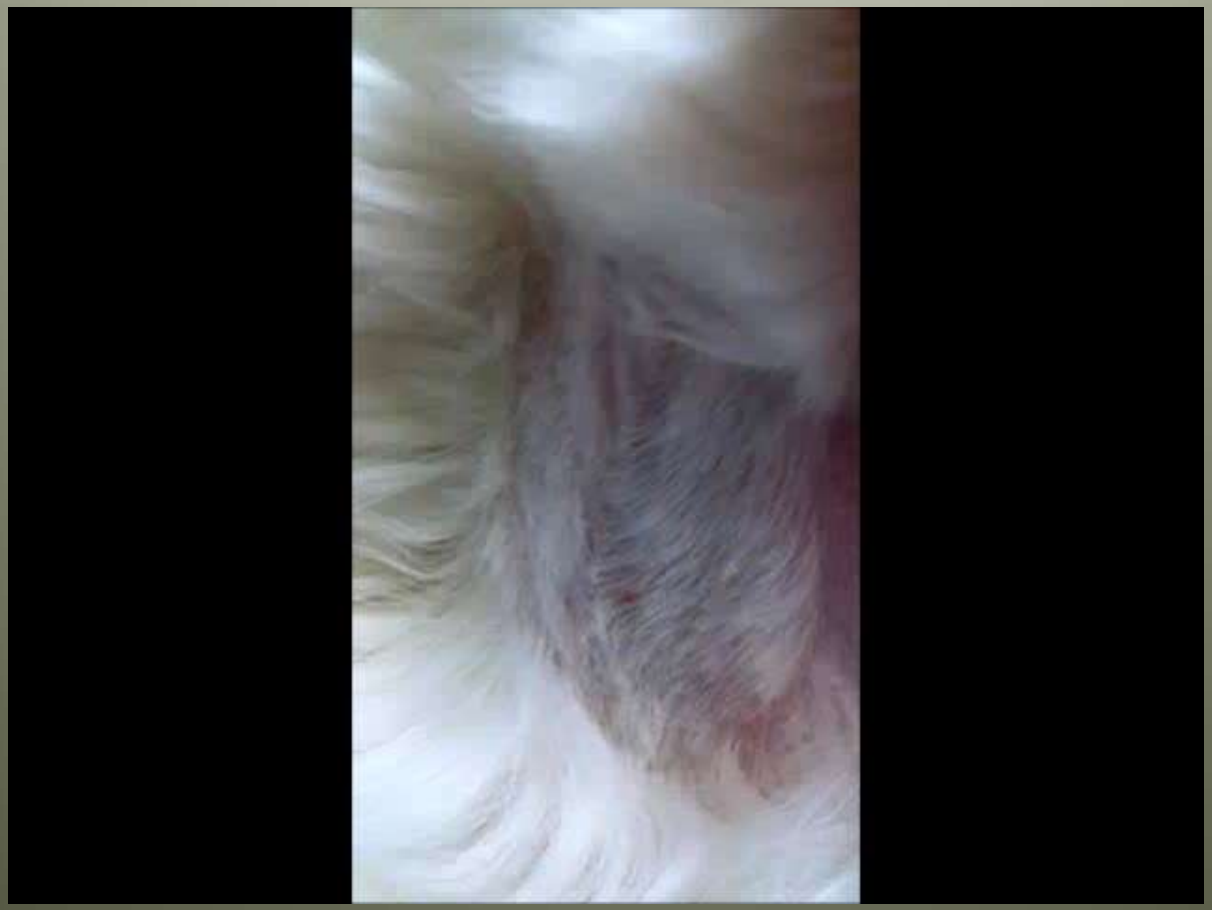
Abdominal distension + bilaterally distended jugulars = CHF (right-sided)

+/- Hepatojugular reflux (not pulsatile!!)



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- Cats also have an increased susceptibility because they lack some metabolic pathways in the liver that would be able to deal with some toxins

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But dogs too get liver poisoned!

Xylitol

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Do you have Anaemia?

4-5 mm

4-5 dd

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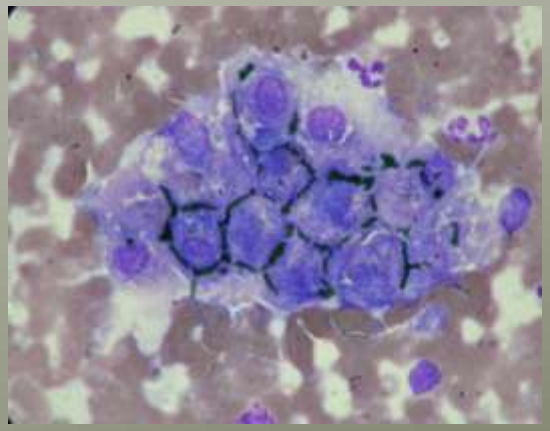

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COMMONLY MEASURED LIVER ENZYMES AND THEIR INTERPRETATION	
Enzyme	*Interpretation*
Alkaline phosphatase (ALP)	Induced enzyme released from canalicular parts of biliary tract; elevation therefore suggests cholestasis Non-specific liver enzyme: isoenzymes produced from other organs including bone and gut Usually the last enzyme to normalise after an acute insult Commonly elevated in older dogs as a result of secondary hepatopathies and benign hepatic hyperplastic nodules Also induced by certain drugs (eg, phenobarbitone and steroids)
Gamma glutamyl transferase (GGT)	Induced enzyme released from biliary tract epithelium further distally than ALP Induced by cholestasis, but exhibits less drug induction than ALP so is often a useful parameter to distinguish cases of suspected steroid hepatopathy
Alanine aminotransferase (ALT)	Hepatocellular enzyme – increased levels suggest leakage from hepatocytes Elevations also common in secondary hepatopathies Degree of elevation does not correlate with severity of liver damage Also released by regenerating hepatocytes, so elevation for days to weeks after an acute insult does not necessarily equate to a poor prognosis
Aspartate [illegible]sferase (AST)	Hepatocellular enzyme – increased activity indicates increased leakage from cells Not liver specific; also released in muscle damage (skeletal and cardiac)

Dog: often secondary

Beware rapid fall

SAP always signif in cats!

GGT normal in hepatic lipidotic cats!

ALT in cats often parallels T4

In Practice SEPTEMBER 2006

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Epilepsy

Haematology + serum biochemistry every 6 to 12 months

(for interpretation of liver parameters we use the following guidelines reproduced from Rusbridge (2013a), reference Webster and Cooper (2009))

- **Double ALT**
- **SAP X5**

Guidelines: Increases greater than these levels, or if the GGT, AST, bilirubin, bile acids, albumin or cholesterol are abnormal all suggest that there may be genuine liver damage happening, and will warrant further investigation/s.

Periodic thyroid function testing is advised in older breeds predisposed to hypothyroidism. A diagnosis of hypothyroidism cannot be made on the basis of thyroid hormone concentrations alone as epilepsy and phenobarbitone therapy can result in a euthyroid sick syndrome.

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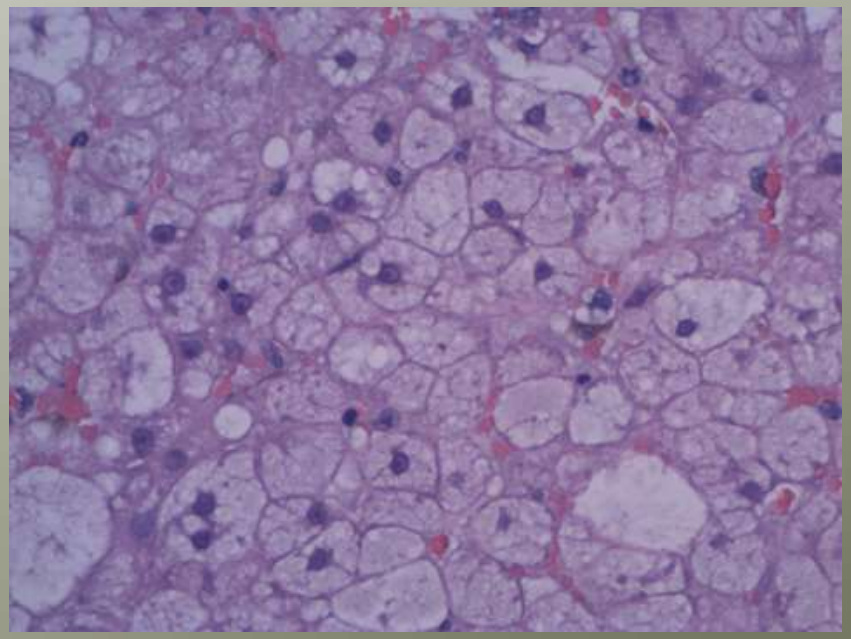
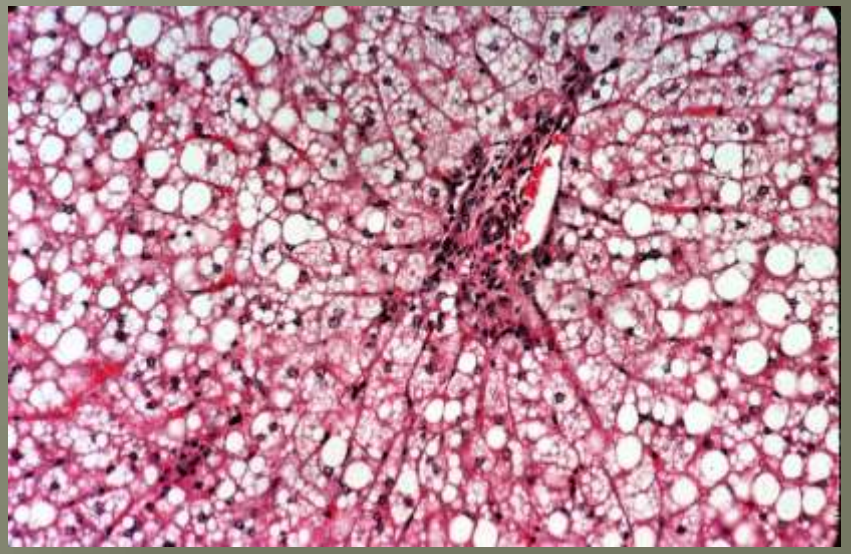
Secondary hepatopathies common!

- Hypoxia – anaemia/CHF
- GI disease
- Pancreatic disease
- DM
- Hypo/hyper thyroidism
- Cushings/Addisons
- Starvation/protein restriction
- Septicaemia/bacterial infections
- Shock





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Nodular hyperplasia is common – causes ALT and SAP elevation

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Other blood tests

Liver function tests

- Albumen (remember falls in acute phase of inflammation)
- Ammonia
- Bile acids (PPSBA) up to 50 may be non-specific, over 100 is liver!
- Cholesterol

Others

- Bilirubin – remember anorexic cats!
- Coagulation times esp if considering surgery
- PT/APTT prolongation in dogs very poor prognostic indicator

Never I/V in cats!

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Not unusual to detect liver shunt on urinalysis

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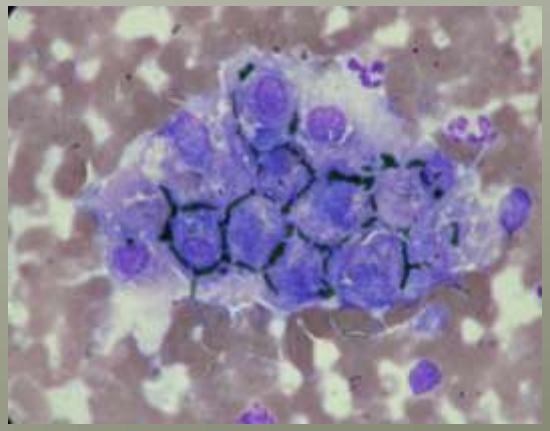

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- **Xray**

..and some cases!

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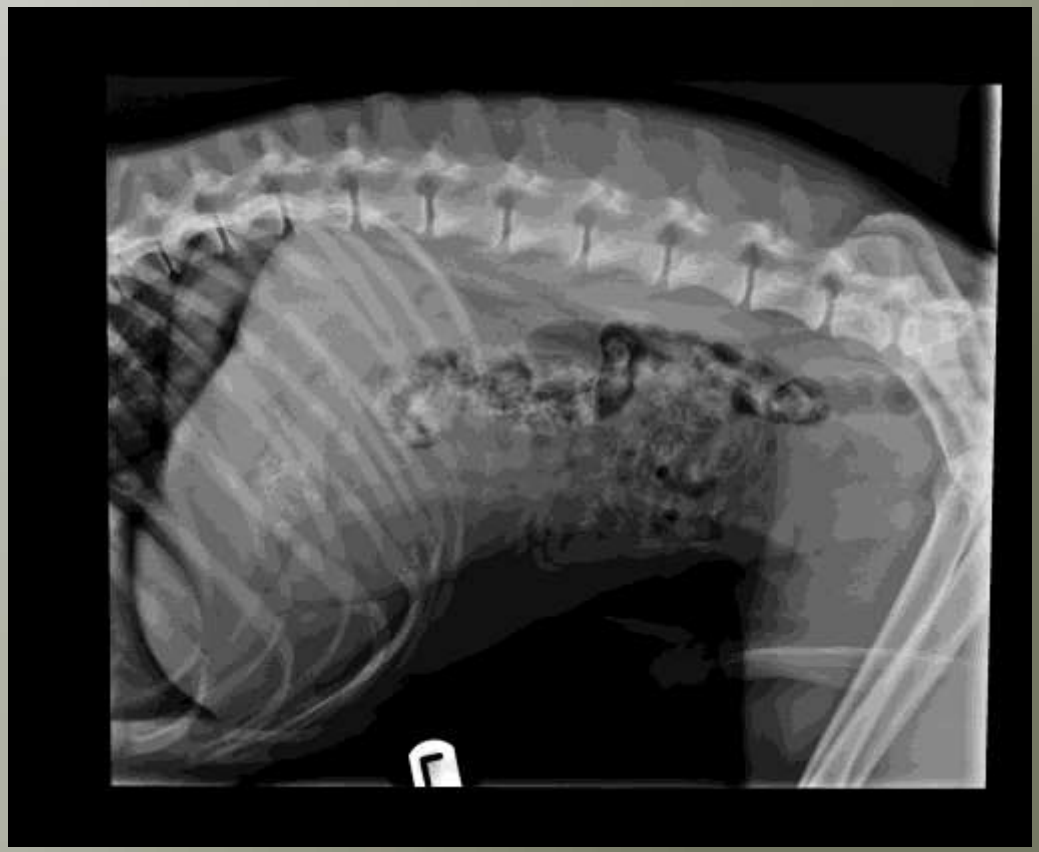
Radiography: great for general size and shape



Breed variation!

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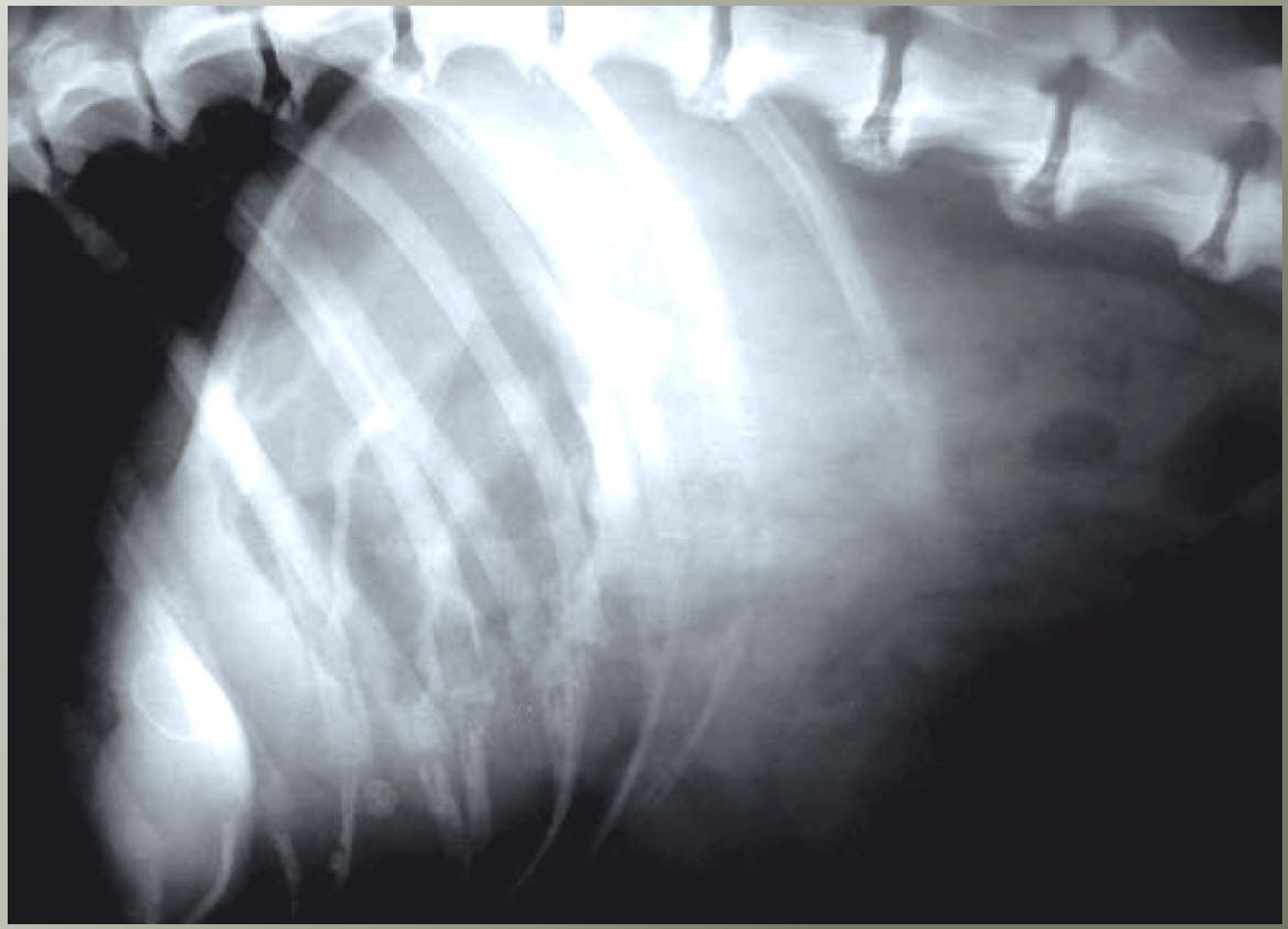
Microhepatica



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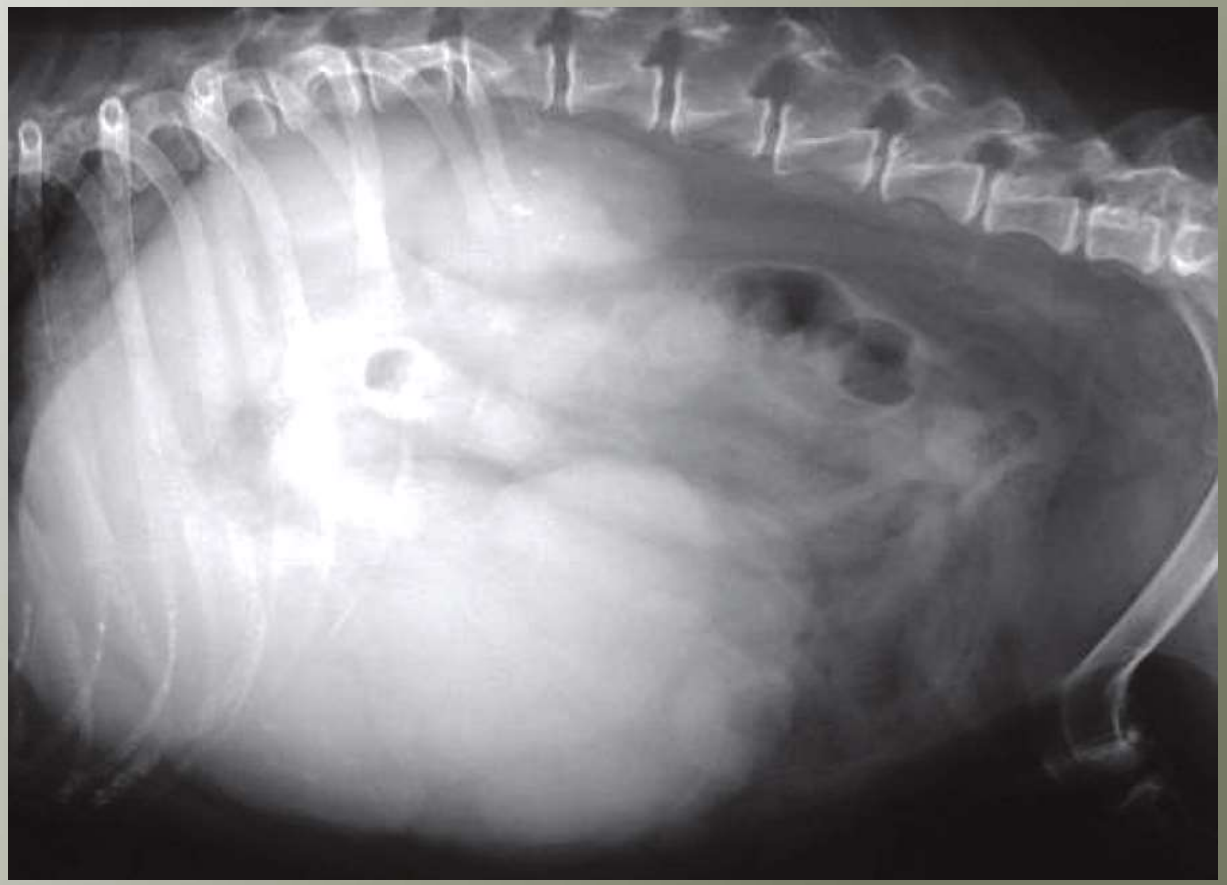
..the very opposite!



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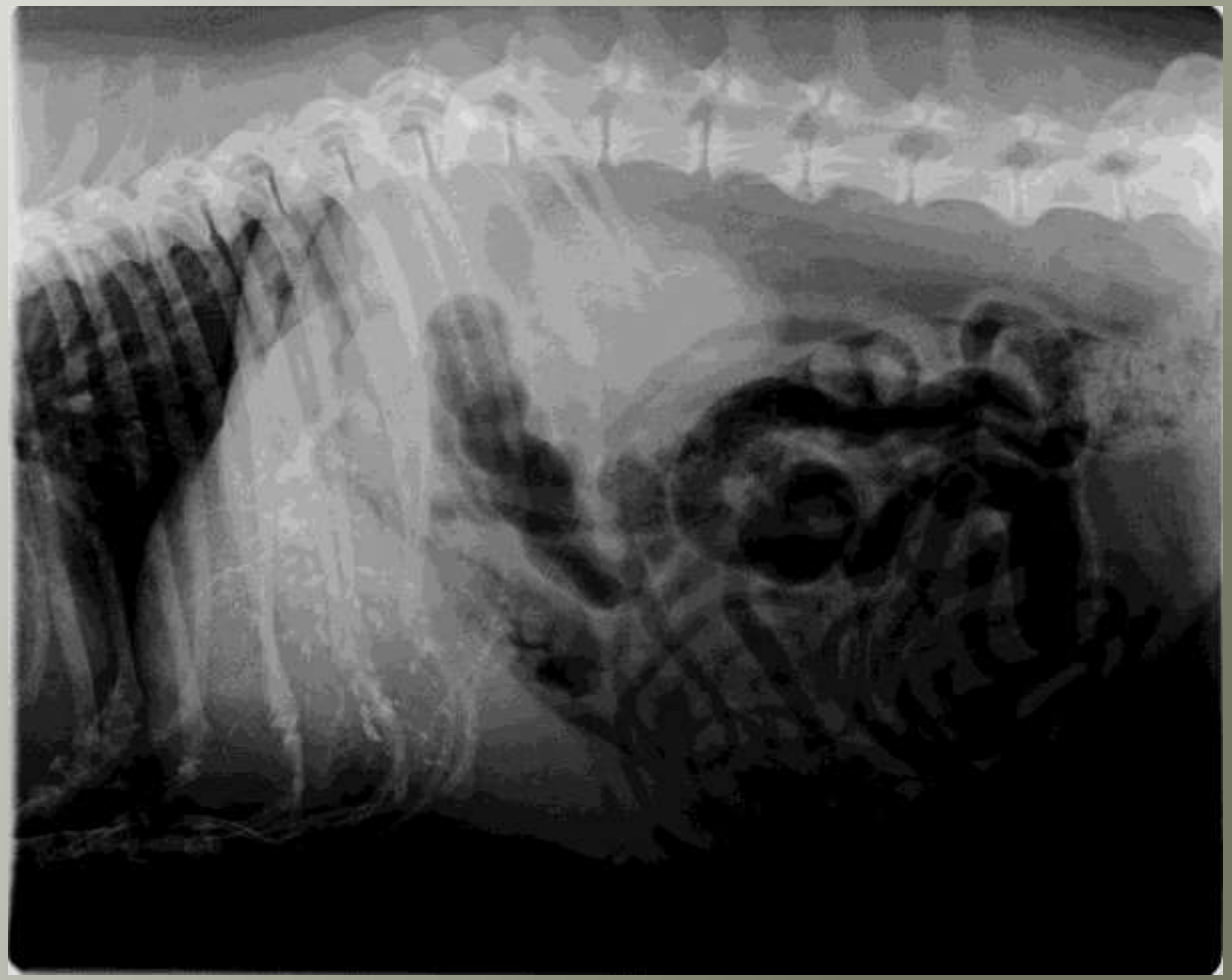
Sometimes incidental…



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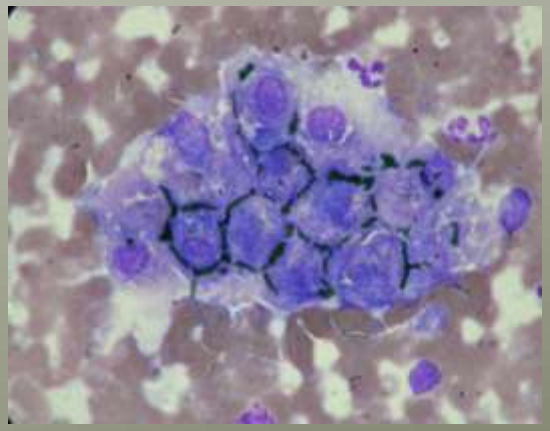

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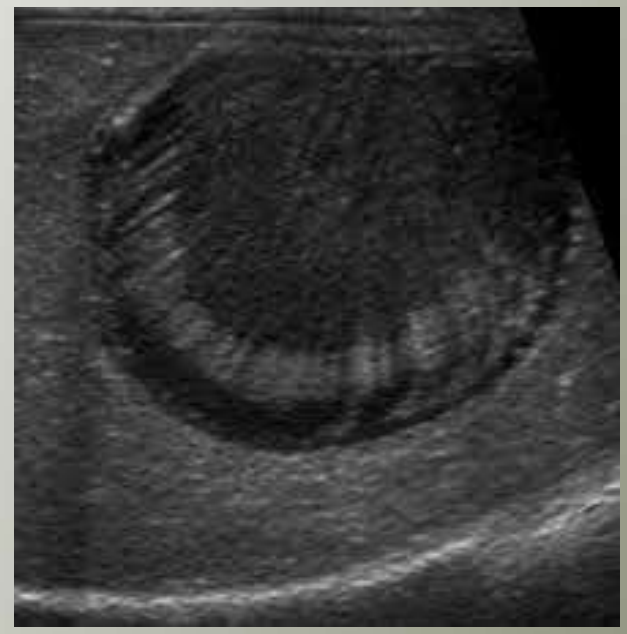
Mucocoele: emerging syndrome?



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Biliary Sludge – normal in dogs, less so in cats

..but if immobile?

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..immobile sludge strong marker for infection

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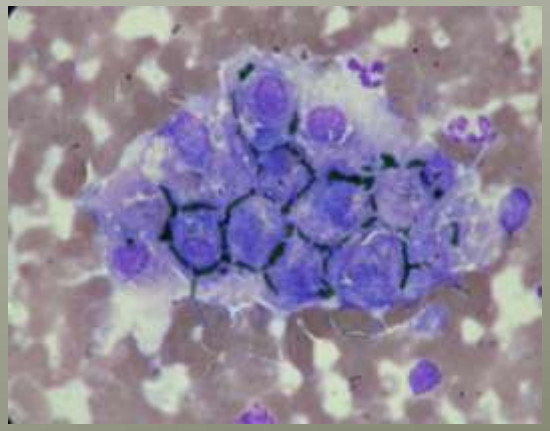

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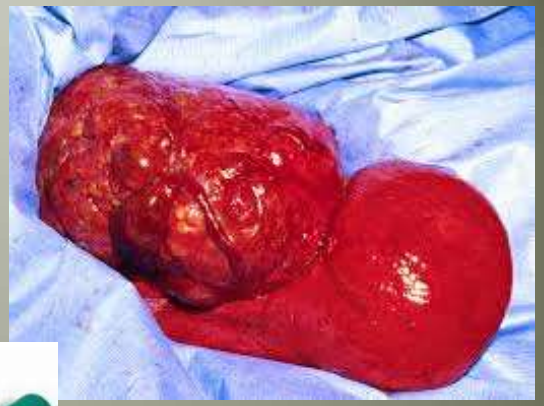

Don’t forget copper! ? Take fresh tissue, or biopsy for stain

Always culture the bile!

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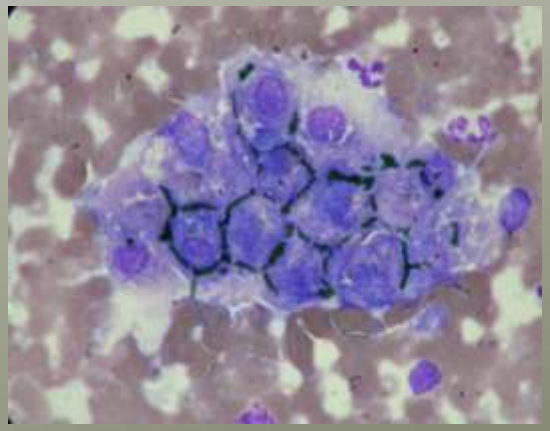

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A middle aged Boxer with reducing appetite and lethargy

- Species Canine
- Breed Boxer
- Age 7 years
- Sex Male neutered

- 4 week history of lethargy
- Weakness
- Icterus
- ALP 2000, Bile acids 150
- Abdo ultrasound normal

Haematology – blood film review

RBC	WNL		
Platelets	WNL		
WBC	14.31		6.0-15.0
Neutrophils	11.88	Hi	3.0-11.5
Bands	0.29		0.0–0.3
Lymphocytes	0.57	Lo	1.0-4.8
Monocytes	1.43	Hi	0.0-1.3
Eosinophils	0.14		0.0-1.25

- Leukocyte morphology - No significant left shift and no obvious toxic signs, low numbers of reactive lymphocytes
- Erythrocyte morphology - + polychromasia, low numbers of target cells, acanthocytes and occasional spherocytes
- Platelets – normal numbers and morphology

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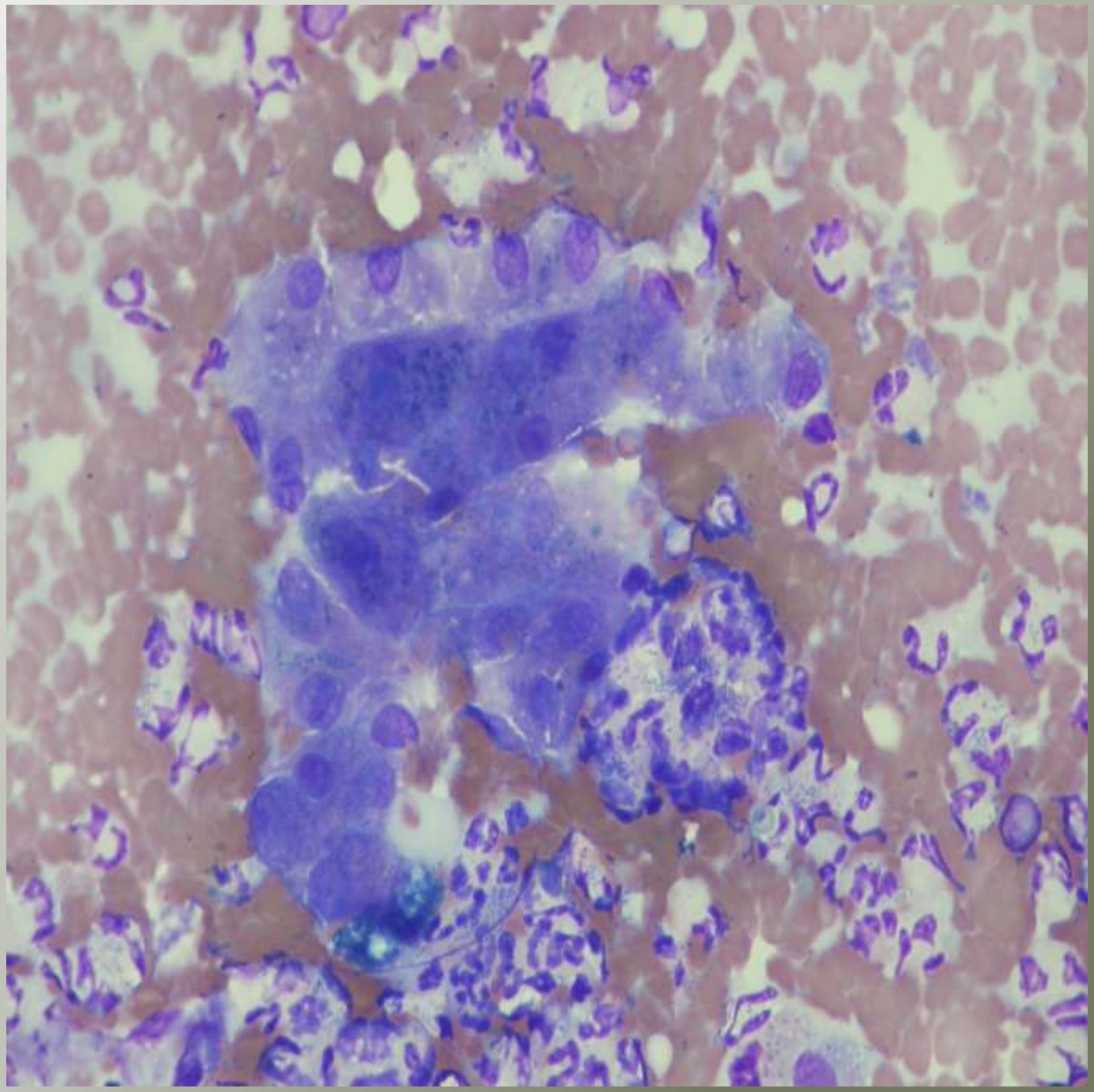
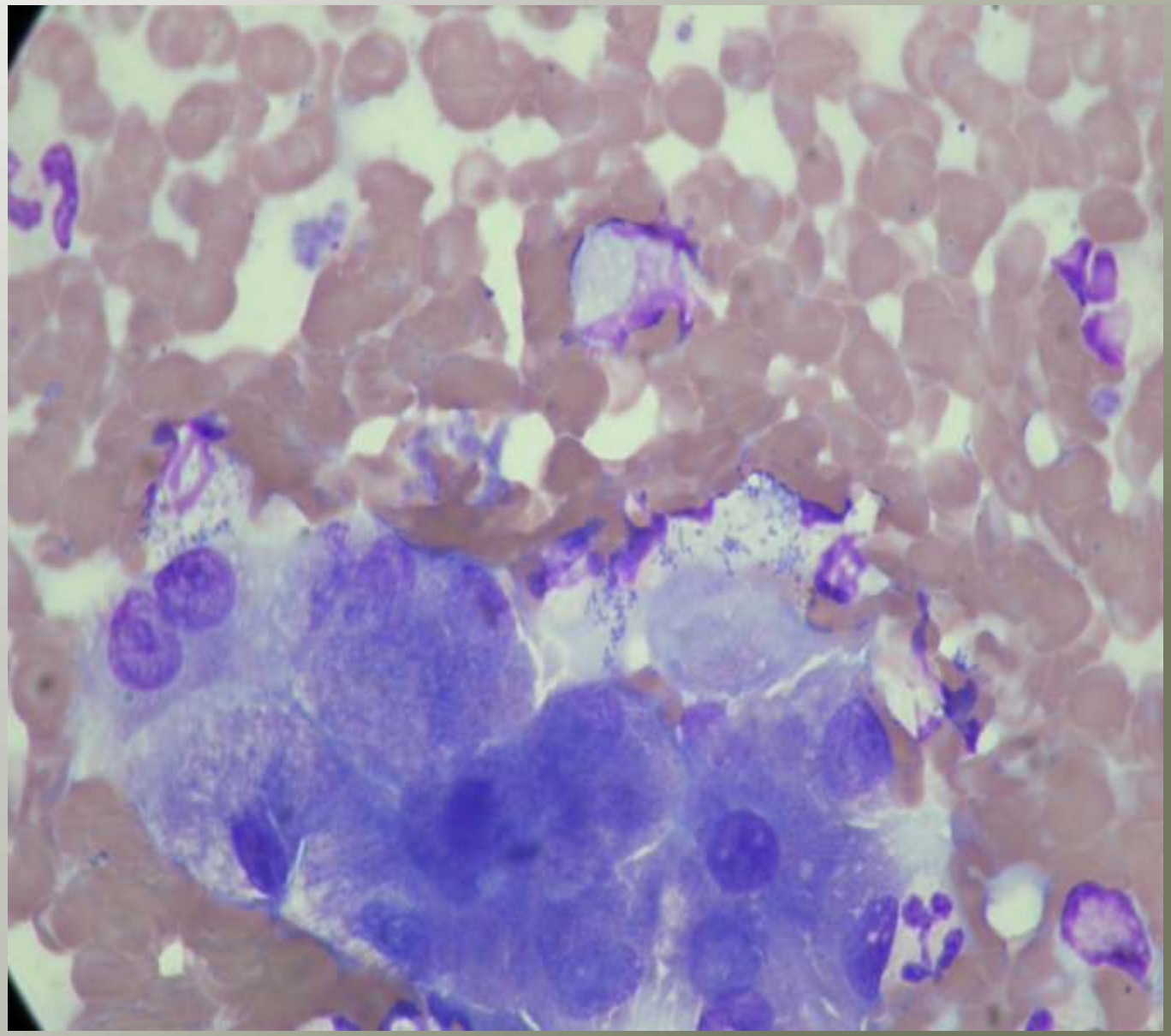


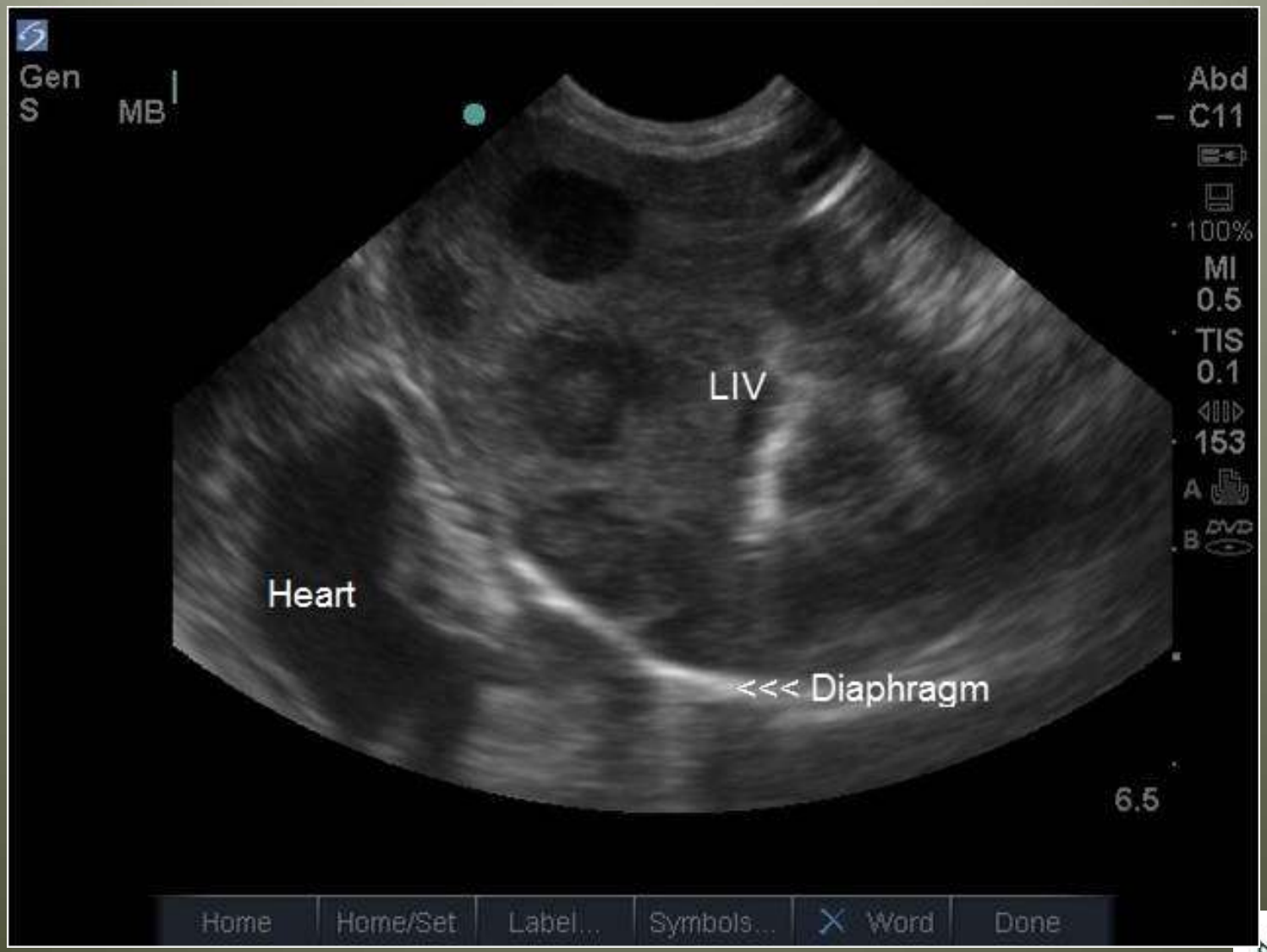


Heavy growth of E.coli – sens to amoxycillin, cephalexin, marbofloxacin

An aged Pointer with polyuria and polydipsia

- Species Canine
- Breed Pointer
- Age 11 years
- Sex Female

- PU/PD
- ALP 3000, ALT 513
- US – highly abnormal liver with multiple hyperechoic masses
- Large left adrenal mass



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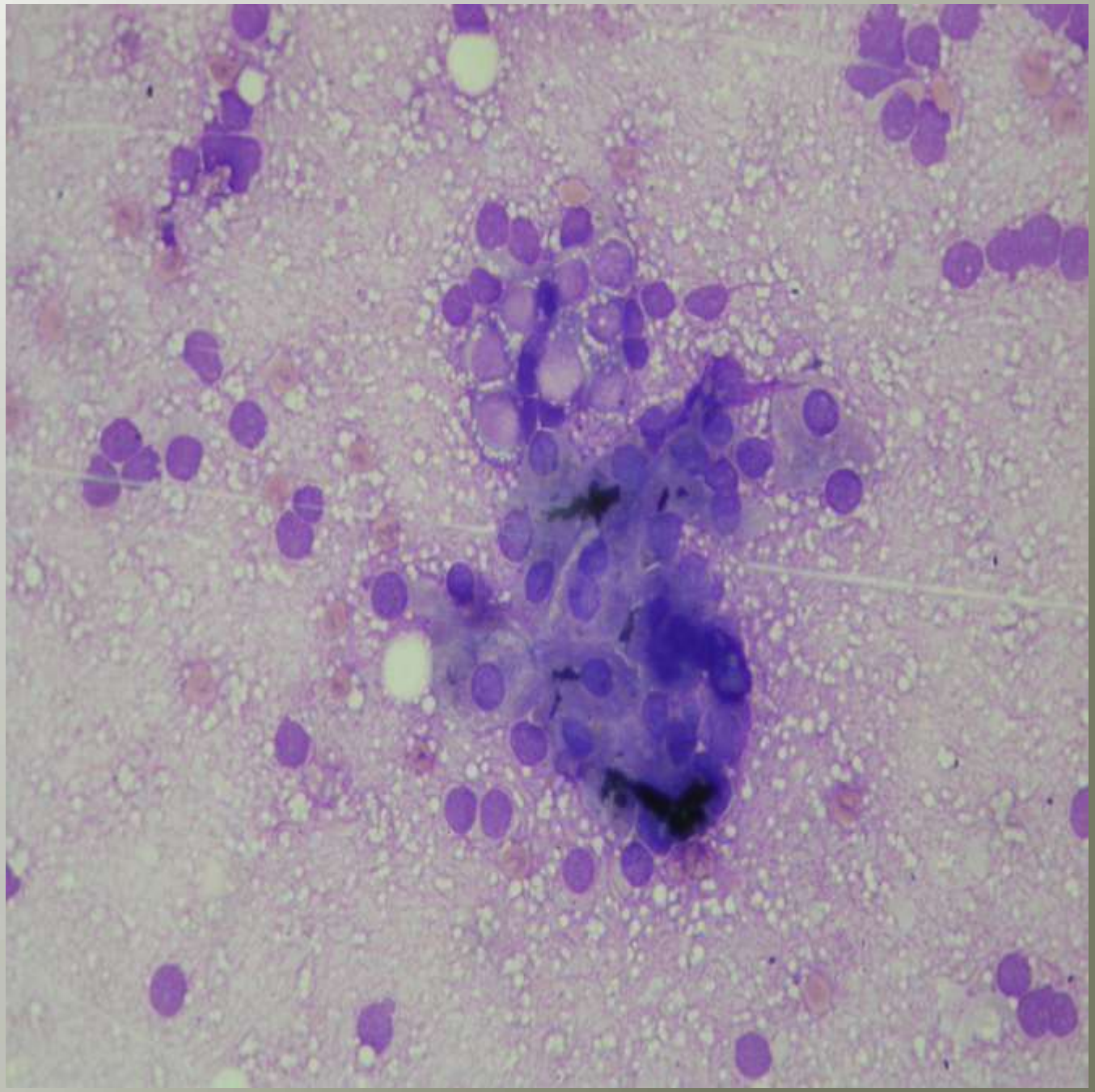

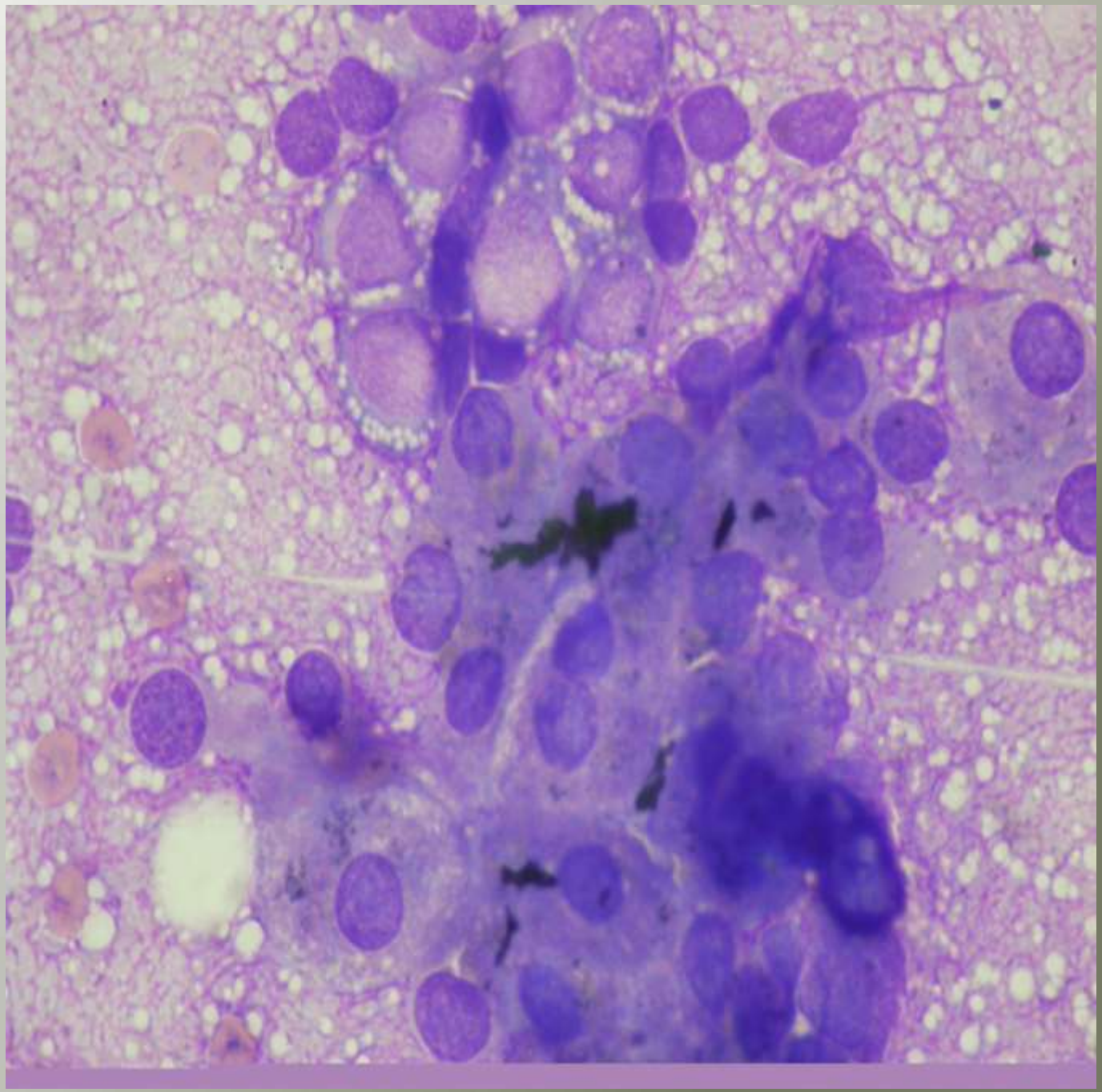

A young cat with anorexia, pyrexia and a peritoneal effusion

- Species Feline
- Breed DSH
- Age 4 years
- Sex Female neutered

- Pyrexia
- Jaundice
- Anorexia
- Treated with synulox and baytril

BIOCHEMISTRY AND HAEMATOLOGY

Total protein	42	Lo	54-80
Albumin	18	Lo	26-42
Globulin	24	Lo	25-45
Sodium	145		125-160
Potassium	3.1	Lo	3.6-6.0
Chloride	111		110-140
Total calcium	1.64	Lo	2.0-3.0
Phosphate	1.3		1.2-2.6
Urea	2.5	Lo	4.0-12.0
Creatinine	50	Lo	60-180
Alk Phos	30	Hi	0.0-25
ALT	133	Hi	0.0-40.0
GGT	2		0.0-10
Total bil	72	Hi	0.0-10
Bile acids	139	Hi	0.0-10
Glucose	8.7	Hi	3.5-6.6
GH	1476		0.0-152
Serum icteric			

Fluid TP 21, Albumin 10, Globulin 11, Alb:glob 0.91, WBC 60, RBC +

Modified transudate with haemorrhage

RBC	3.06	Lo	5.5-10.0
Hb	4.8	Lo	9.0-17.0
HCT	16.8	Lo	27-50
MCV	55		40-55
MCH	15.8		13.0-21
MCHC	28.8	Lo	31.0-36
Platelets	See comment		
WBC	1.85	Lo	4.0-15.0
Neutrophils	0.52	Lo	2.5-12.5
Bands	0.42	Hi	0.0-0.3
Lymphocytes	0.21	Lo	1.5-7.0
Monocytes	0.35		0.0-0.8
Eosinophils	0.0		0.0-1.5

Platelets clumped in film, actual count appears normal. Metamyelocytes, occ myelocyte, neutrophils show slight toxicity, occ dohle body, no polychromasia

FELV	Negative
FIV	Negative
Coronavirus	Negative <10

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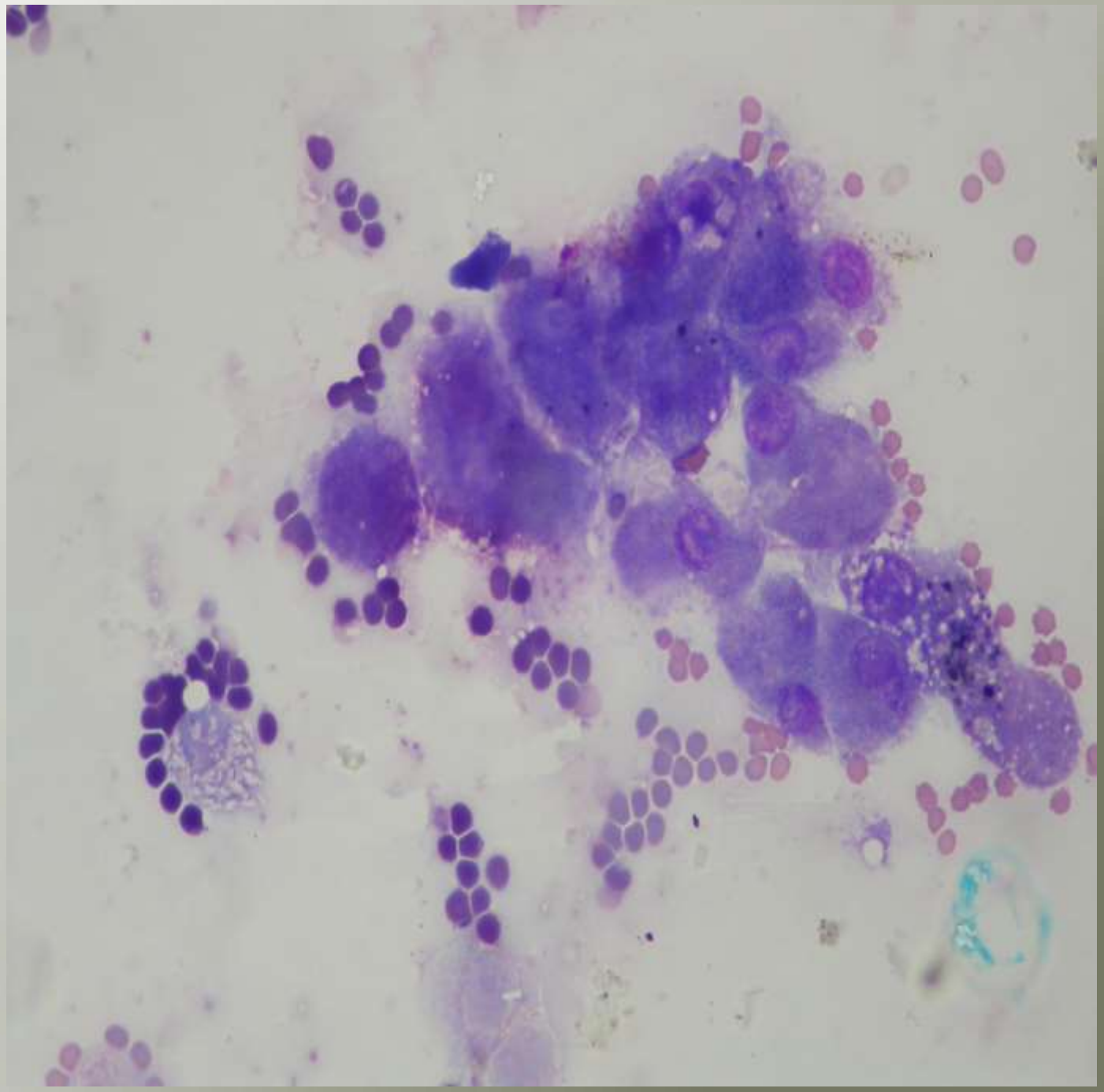
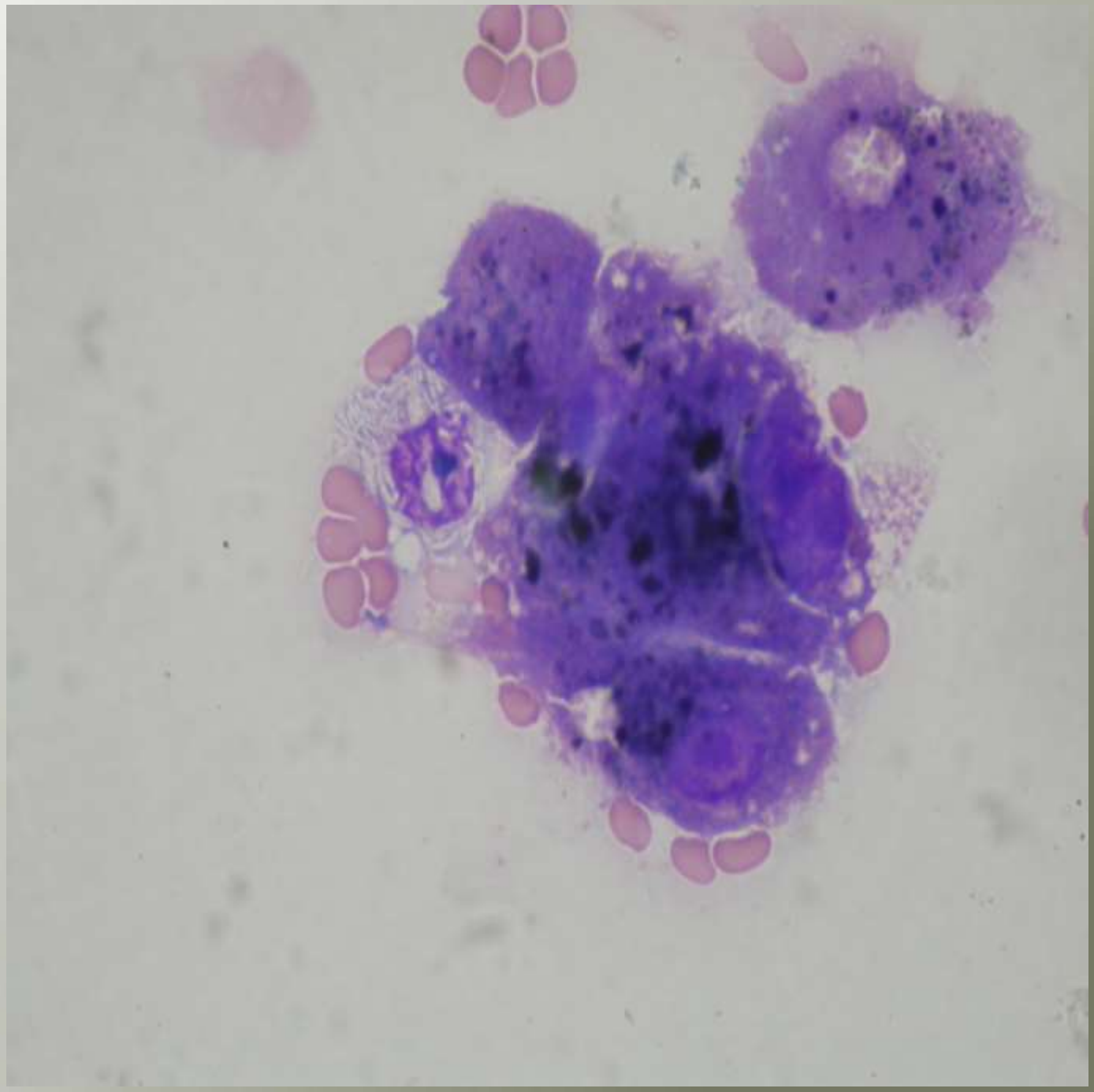
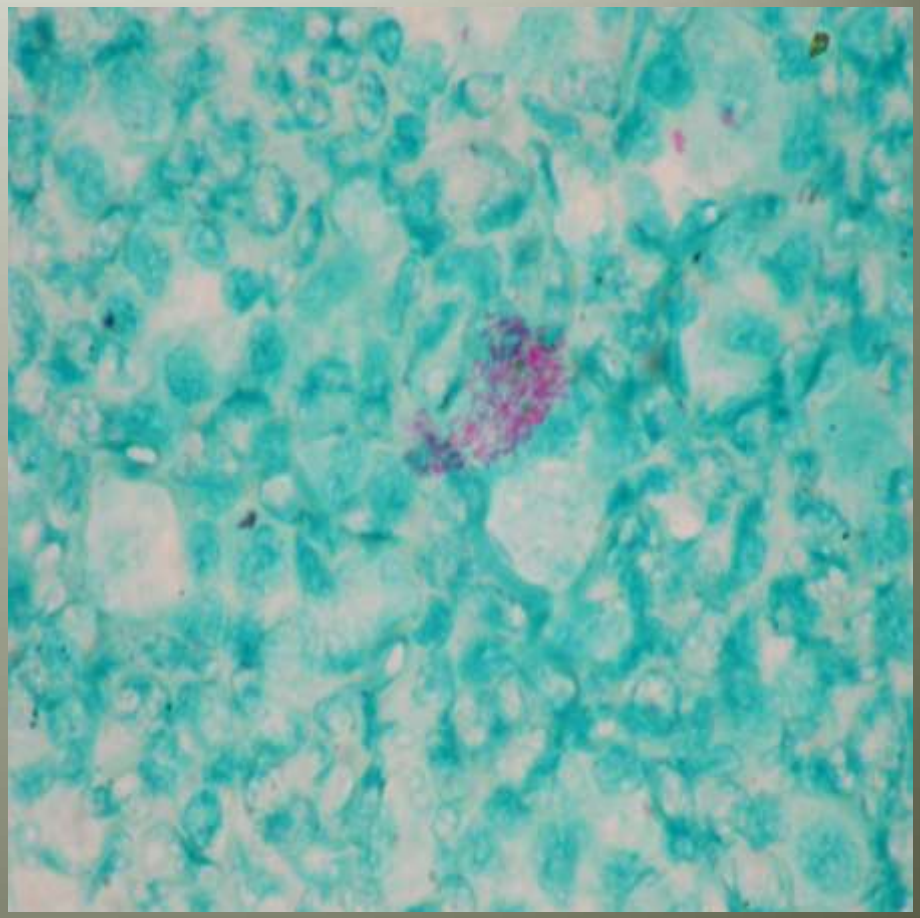




Blood Test for Suspect Feline TB

The interferon gamma test is intended to assist in the diagnosis of suspected feline TB cases. The interferon gamma test can be useful in categorising cats with suggestive lesions appropriately. This in turn can inform decisions as to whether treatment is appropriate and whether it is necessary to report the case to AHVLA (Suspected Bovine TB is a notifiable disease in all mammals). There is also some evidence that the test can be used to monitor treatment, with responses falling in cats in remission



biobest clinpath

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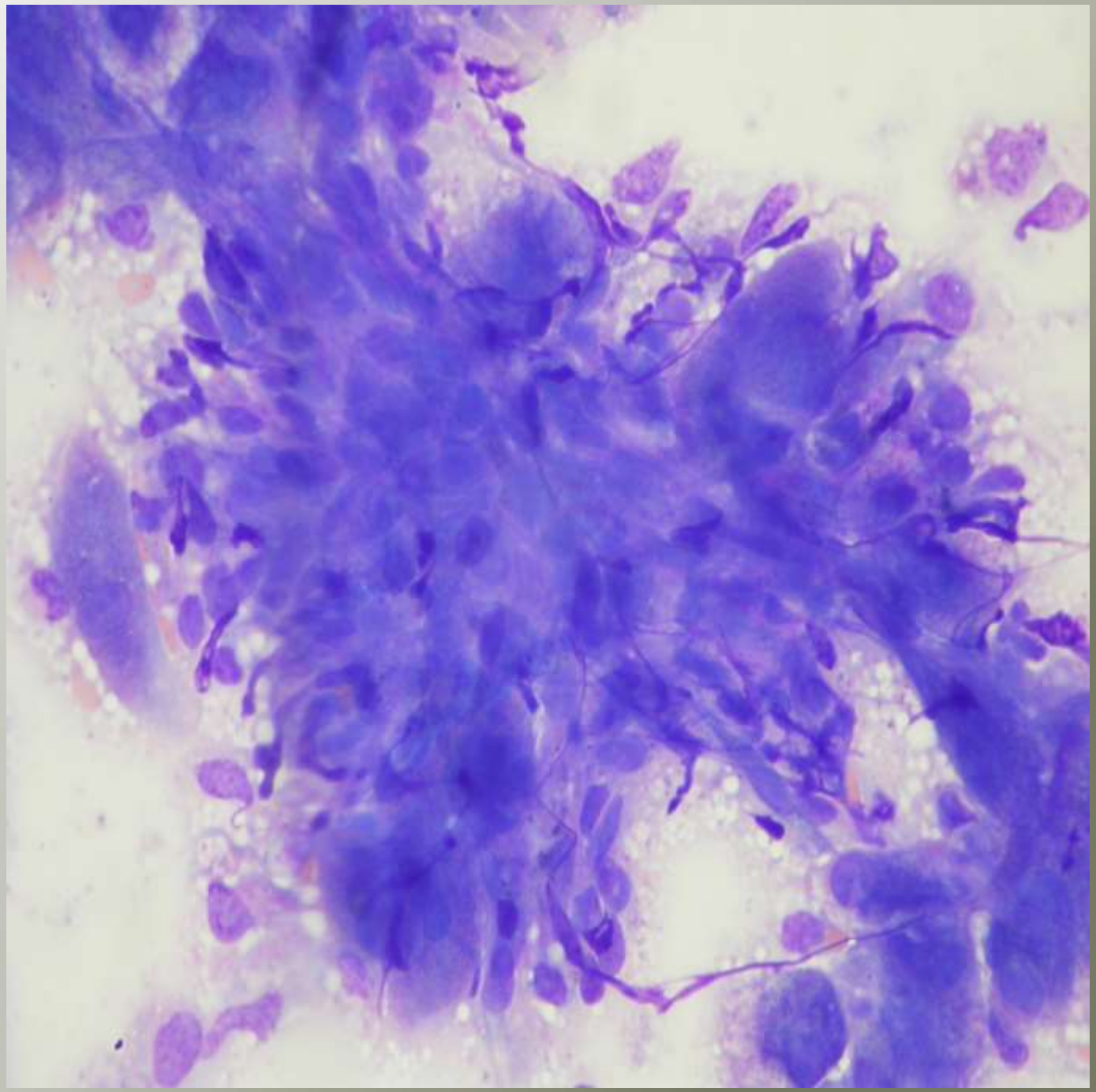
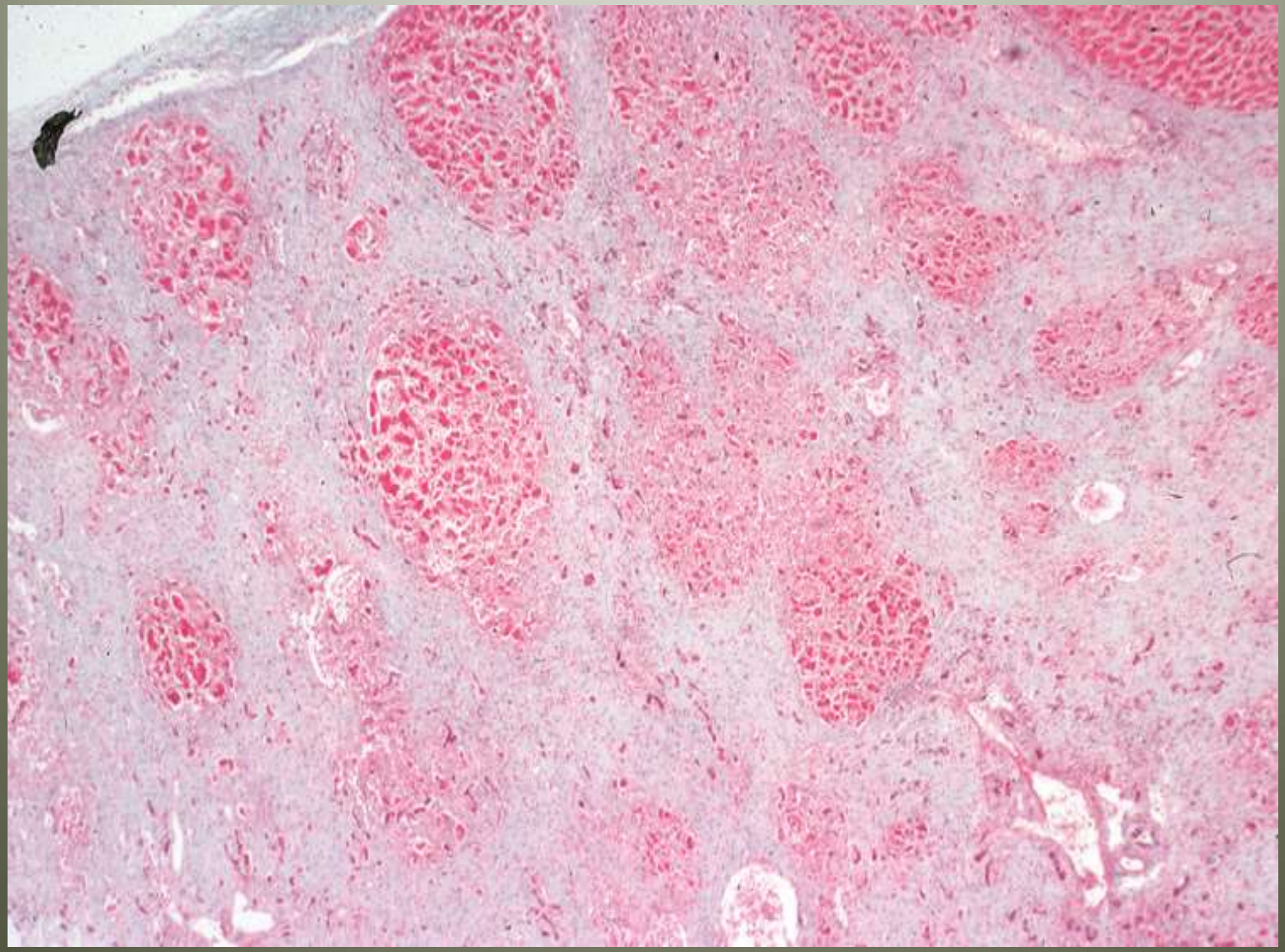
A young bitch with ascites

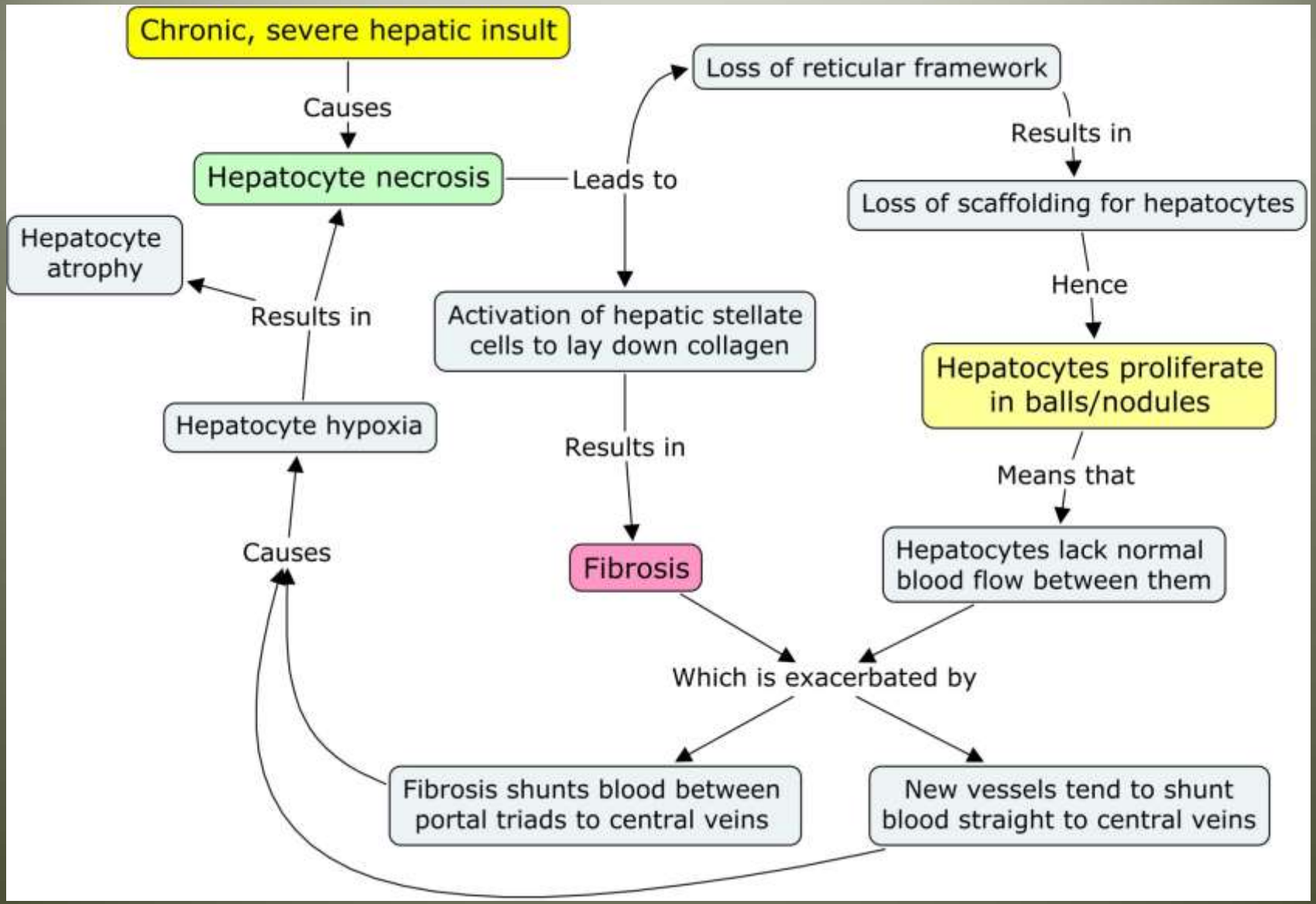
- Species Canine
- Breed Springer Spaniel
- Age 1 years
- Sex Female

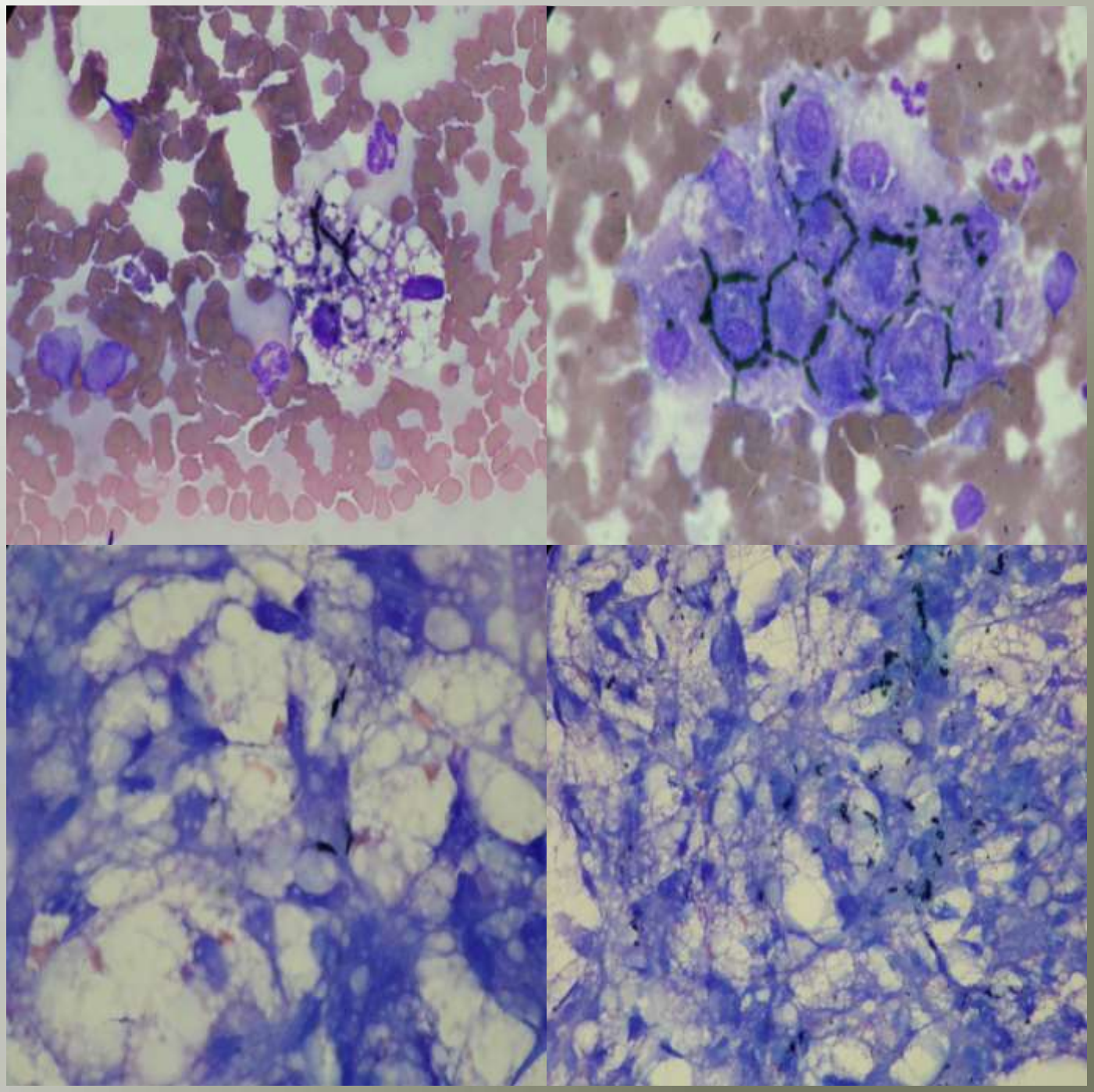
- Weight loss
- Reduced appetite
- Ascites – low protein modified transudate
- Low albumin, elevated ALT and ALP
- Bile acids pre 202, post 243

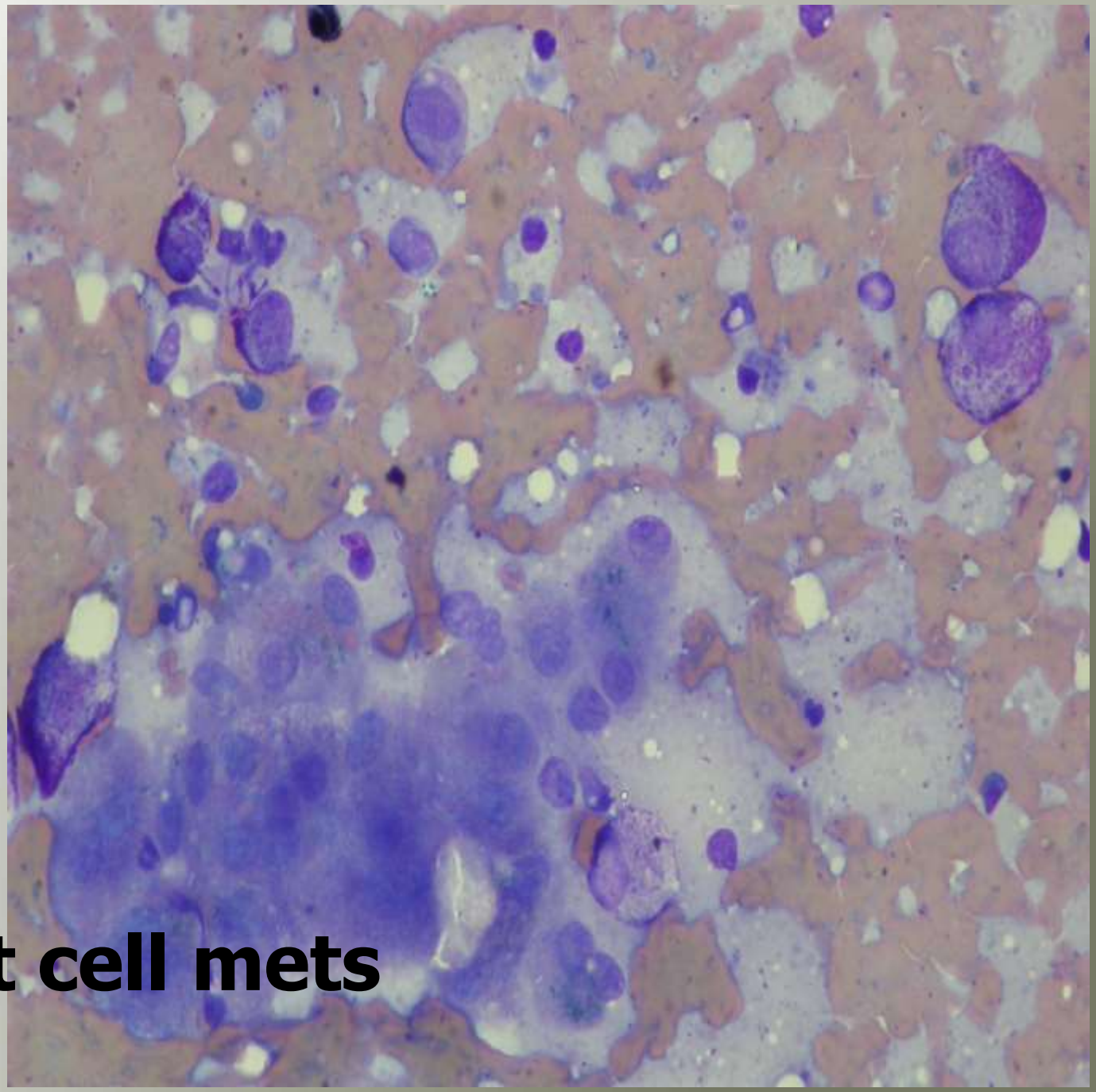


Cirrhosis = fibrosis + nodular regeneration + loss of hepatocytes




Chronic, severe hepatic insult
Causes
Hepatocyte necrosis
Leads to
Loss of reticular framework
Results in
Loss of scaffolding for hepatocytes
Hence
Hepatocytes proliferate in balls/nodules
Means that
Hepatocytes lack normal blood flow between them
Hepatocyte atrophy
Results in
Hepatocyte hypoxia
Causes
Activation of hepatic stellate cells to lay down collagen
Results in
Fibrosis
Which is exacerbated by
Fibrosis shunts blood between portal triads to central veins
New vessels tend to shunt blood straight to central veins





Mast cell mets

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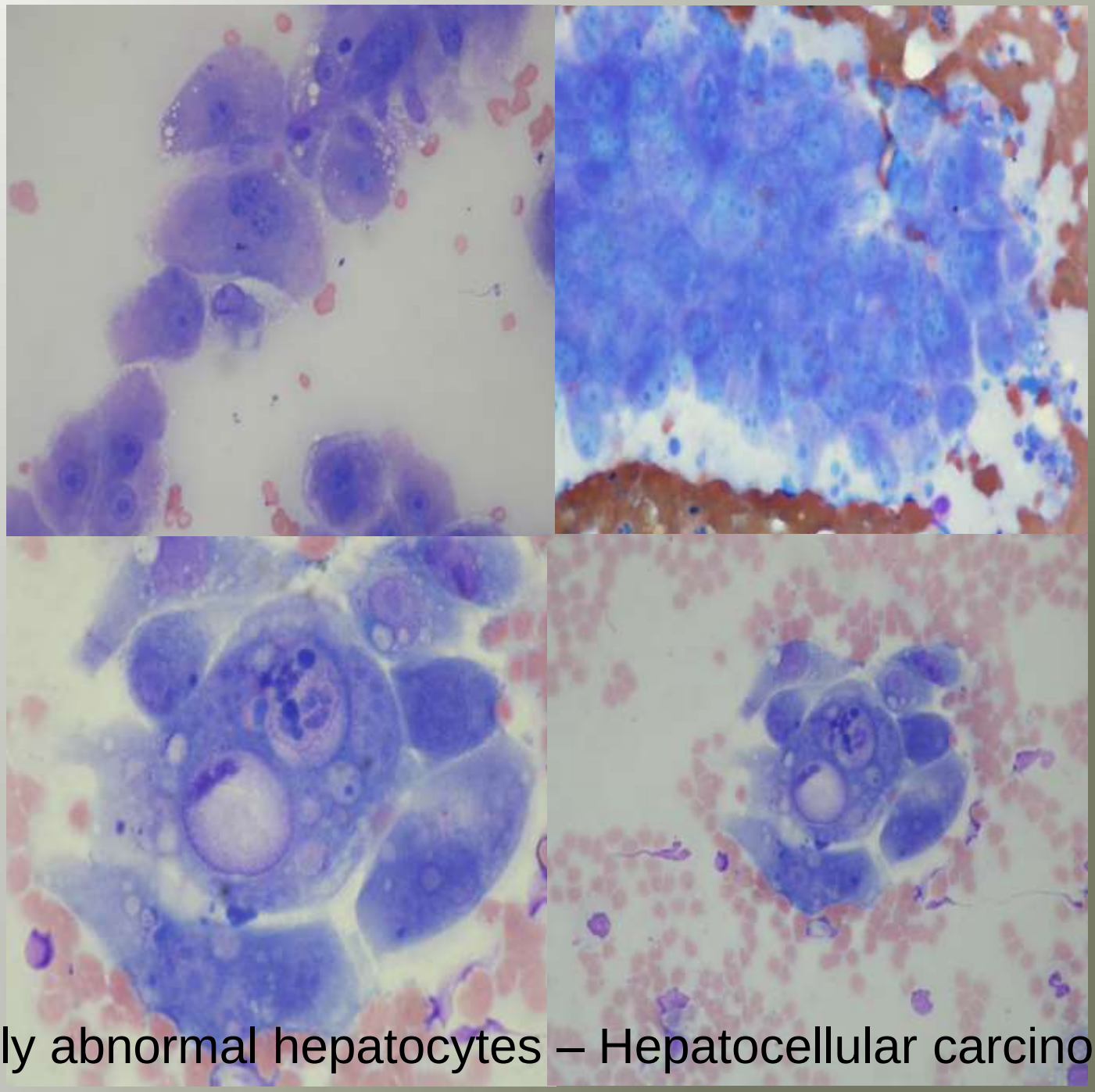
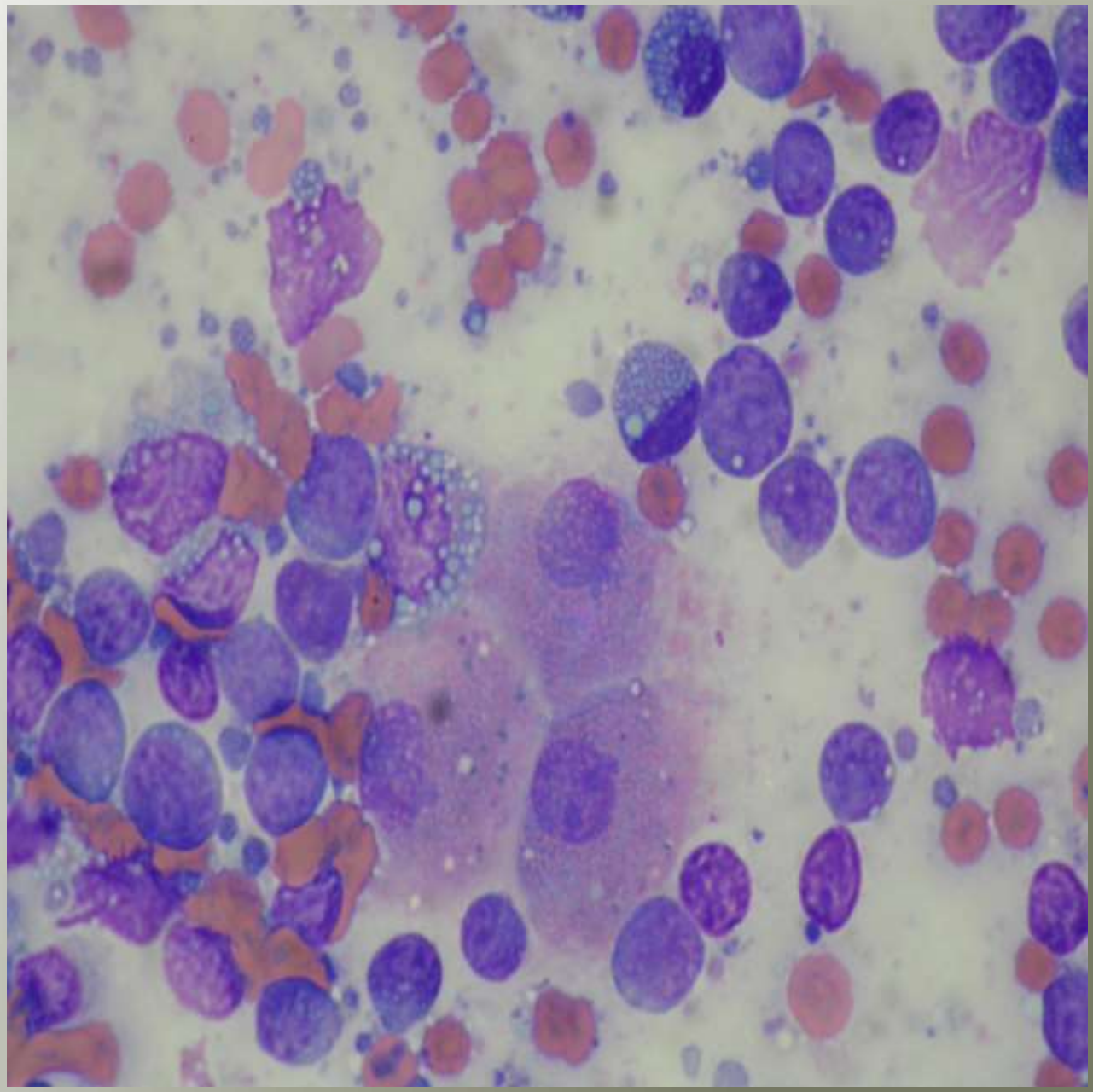
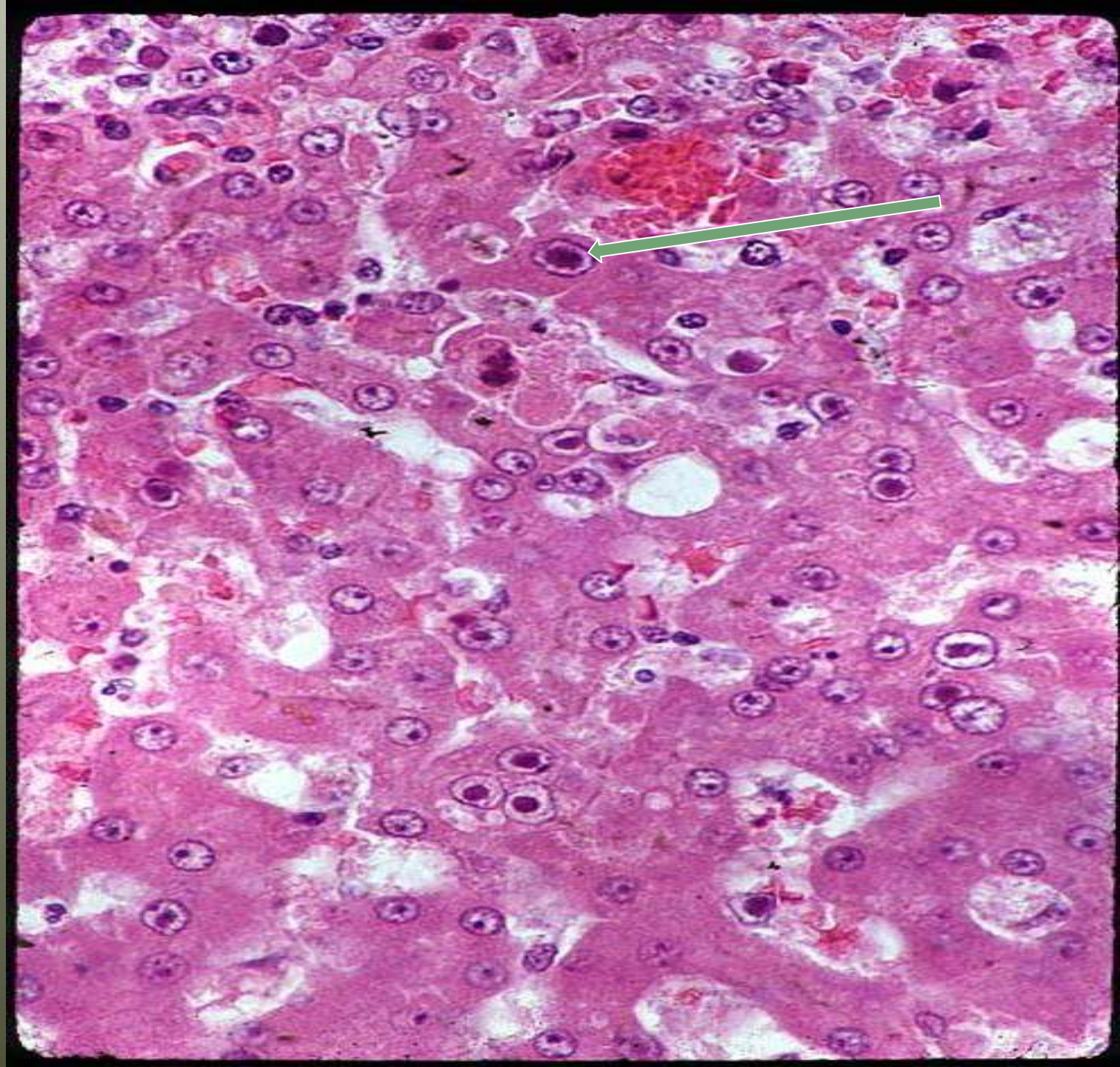


Severely abnormal hepatocytes – Hepatocellular carcinoma



Lymphoma with Mott cell differentiation in the liver

CAV-1



Therapy for liver disease

Diagnosis is vital - without it you are shooting in the dark!

Table 1: The commonest causes of chronic liver disease in dogs and cats

DOGS:

- Breed-related hepatitis: e.g. cocker hepatitis; doberman hepatitis; Westie hepatitis (some copper associated and some not copper associates)
- Copper toxicosis: Beddlington terriers
- Congenital or early developmental disease: e.g. lobular dissecting hepatitis in standard poodles; idiopathic non-inflammatory hepatic fibrosis in GSDs and others
- Chronic cholangiohepatitis: less common than in cats - cause unknown - ? relationship to pancreatitis and/or inflammatory bowel disease?
- Suppurative hepatitis ± cholestasis secondary to local or distant infection
- Chronic progression of acute hepatopathy e.g. toxic, idiosyncratic drug reaction, infectious, ischaemic, obstructive
- Neoplasia: lymphoma, hepatocellular carcinoma, metasases, others

CATS:

- Suppurative (acute) cholangitis: likely primary infection - ? extending up bile duct from GI tract?
- Chronic (lymphoplasmacytic) cholangiohepatitis complex: various histological forms. May be immune-mediated disease and/or some unknown cause (e.g. viral or hepatic helicobacter??). Divided in to:
- Chronic lymphocytic cholangitis (periportal + bile duct)
- Lymphocytic portal hepatitis (not involving bile duct)
- Lymphocytic cholangitis (mainly UK. High protein ascites)
- Sclerosing cholangitis: rare - severe fibrosis. May be end stage of chronic biliary obstruction
- Hepatic lipidosis: primary or secondary. Common in USA. Uncommon in UK but does occur - particularly the secondary form
- Infections: particularly FIP - associated hepatitis (major differential diagnosis for some forms of chronic cholangiohepatitis)
- Neoplasia: especially lymphosarcoma (- may be more acute liver failure)

University of Cambridge SAM Notes

Chronic Liver Disease Therapy

Aim to:

- Treat underlying cause where possible (?Copper/infection/immune-mediated)
- Slow progression (?corticosteroids/SAMe/Milk Thistle/Silymarin)
- Allow hepatic regeneration/rest

Manage clinical signs and complications:

- Hepatic encephalopathy
- Bowel Ulceration
- Inappetance (feeding tubes/mirtazapine)

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Therapy Chronic Liver Disease

- Diet diet, diet! (avoid renal diets – v high fat!)…then drugs – targeted therapy based on accurate diagnosis
- Dogs have anaerobes in liver – empirical antibiotic to cover those if liver traumatised or injured.

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Copper and hepatitis

Primary (?genetic)

- Bedlington, WHWT, Doberman, Labrador
- Characteristic copper distribution

Secondary in several breeds

- Still causes damage: chelation justified if raised levels irrespective of distribution

Lower intake (liver diets), add antioxidants, NI water low in copper, chelate with penicillamine for 6 months, then add Zinc to diet to compete with copper absorption

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Corticosteroids

- Useful anti-inflammatory, immune-modulating and anti-fibrotic effects – they slow progression esp. in cats
- NOT indicated in advanced bridging fibrosis or non-inflammatory fibrosis
- They decrease survival times if have ascites
- They can precipitate gastric ulceration!
- *If not safe, consider azathioprine or cyclosporin*

Ursodeoxycholic acid

- Contraindicated if biliary obstruction
- Modulates the toxic bile pool
- Especially useful in cholangiohepatitis (where there is a non-obstructive cholestasis)

50mg pills

SUMMIT VETERINARY PHARMACEUTICALS LIMITED
VETERINARY SPECIALS MANUFACTURER

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DRUG	DOGS	CATS	Main contraindications and notes
Prednisolone	1-2mg/kg/day po. Taper to 0.5mg/kg/day or eod	2-4 mg/kg/day po Taper to 0.5mg/kg/day or eod	Avoid in suppurative inflammation. Avoid in portal hypertension: ascites, potential GI ulceration. Avoid use of dexamethasone if possible as very ulcerogenic
Metronidazole	7.5 mg/kg po or slowly iv bid	7.5 mg/kg po bid	Avoid in severe hepatic insufficiency as hepatic metabolism
Ampicillin	15-20 mg/kg po or iv tid	15-20 mg/kg po or iv tid	Avoid in penicillin sensitivity
Neomycin	20 mg/kg tid to qid po or as retention enema	5.5-10 mg/kg bid po or as retention enema	Systemic absorption and oto- and nephrotoxicity may occur if GI ulceration - esp cats
Lactulose	5-15mls po tid	0.25-1ml po tid	Not licensed for use in small animals. Overdose results in diarrhoea - titrate to effect
Urso-deoxycholic acid	4 - 15 mg/kg total po daily - preferably divided bid	15 mg/kg po sid	Not licensed for use in small animals. Avoid in biliary obstruction. Not indicated in congenital PSS
SAM-e	20 mg/kg po sid or higher	20mg /kg or 200 to 400 mg total sid (*different sources of advice*)	Tablets must be given unbroken on empty stomach. 2 sizes available: 90mg and 225mg
Zinc acetate or sulphate	1-20 mg/kg/day of elemental zinc	7mg/cat/day elemental zinc	Not licensed for use in animals. Monitor blood levels every 1-2 weeks and keep 200-300 microg/dl
Colchicine	0.03 mg/kg/day po	Not recommended	Not licensed for use in animals. Monitor for bone marrow suppression. GI side-effects common
Penicillamine	10-15 mg/kg po bid	Not recommended	Not licensed for use in animals. Vomiting common. Immune-mediated disease possible
Spironolactone	2-4 mg/kg/day in divided doses	2-4 mgk/kg/day in divided doses	Gradual onset of action over 2-3 days.
Sucralfate	1g per 30kg qid	250mg/cat tid	Not licensed for use in animals
Ranitidine	2 mg/kg po bid	0.5-2 mg/kg po bid	May not be necessary if gastric pH high

CARE – quality!

Not cimetidine (consider omeprazole or famotidine)

Anti-fibrotic

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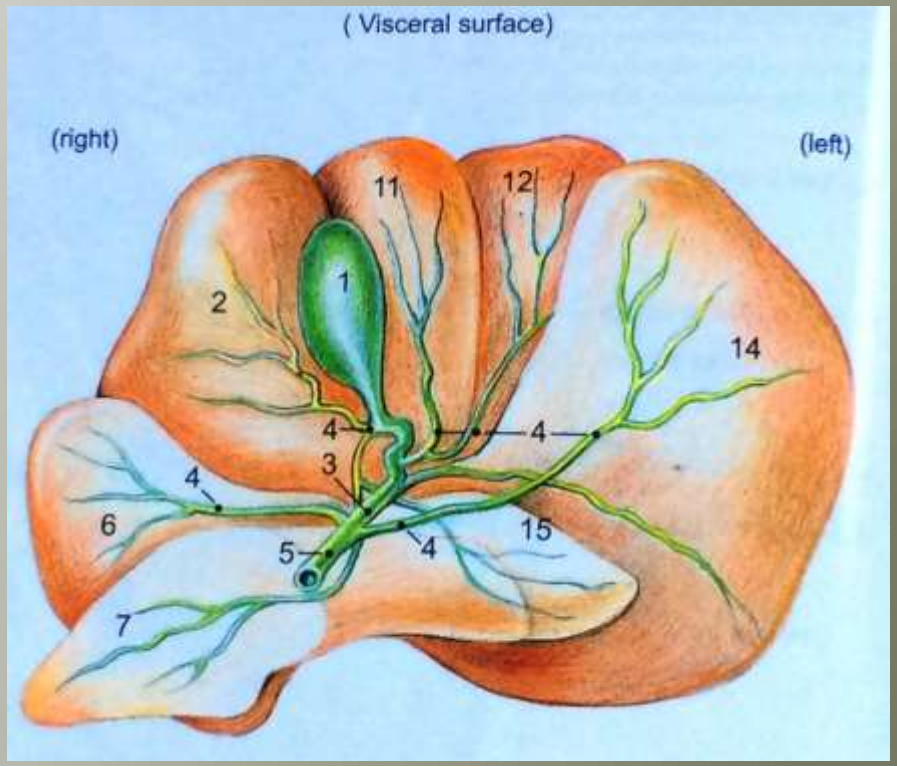
Surgery top tips!

- Don’t forget clotting (Vit K) 0.5-2.0mg/kg 12 hours before biopsy, rpt every 7-21 dd
- Don’t be frightened to remove gall bladder



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Fracture technique?

Surgitie™ Ligating Loop

Description

The Surgitie™ ligating loop consists of a narrow nylon carrier (3.9 mm O.D.) through which is threaded a 53 cm (21") length of absorbable Polysorb™ suture size 0 or 2-0 (3.5 or 3 metric). The suture is anchored at the proximal end of the carrier (marked by a black band) and the carrier is scored. The suture extends from the distal end of the carrier in the form of a loop, having a sliding knot which secures itself when tightened. A delivery system may be used (5 mm O.D. x 15.24 cm long) for the introduction of the loop and carrier into any appropriately sized trocar sleeve or larger sized trocar sleeve with the use of a converter.

Polysorb™ sutures are composed of Lactomer™ glycolide/lactide copolymer, which is a synthetic polyester derived from glycolic and lactic acids. Polysorb™ sutures are prepared by coating the suture with a caprolactone/glycolide copolymer mixture of caprolactone/glycolide copolymer and calcium stearoyl lactylate. Polysorb™ sutures are colored violet to increase visibility. Polysorb™ sutures meet all requirements established by the United States Pharmacopeia and the European Pharmacopeia (EP) except for minor variations in suture diameter.

Surgitie™ Loop with Polysorb™ Suture

Such Variations Are:

Maximum Suture Oversize in Diameter (mm) from U.S.P.

U.S.P. Size	U.S.P. Size Overage (mm)	Maximum Designation (mm)
2-0	0.30-0.339	0.050
0	0.339-0.35	0.050

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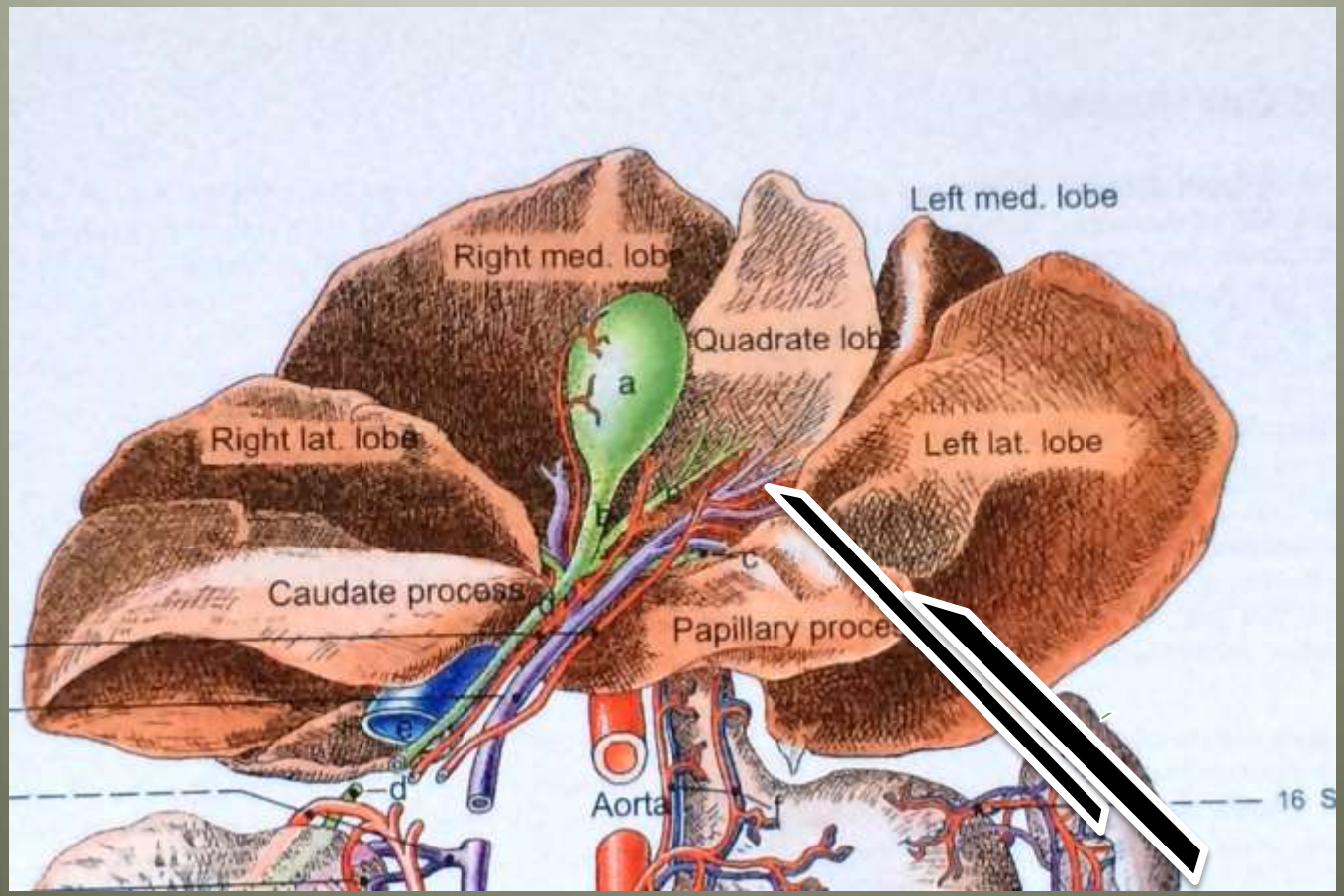

If lobe/mass too big for loop, use parallel bowel clamps (or tape loop) for temporary haemostasis and remove bulk before applying loop – **VERY EASY** and in my experience **VERY RELIABLE**!!

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Acknowledgements:

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