FREE WEBINAR

veteducation

ANALGESIA and ANAESTHESIA

OF THE PATIENT WITH LIVER DISEASE

SPEAKER:
DR. PHILIP JUDGE

08 APRIL
19:30 AEDT

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We have a patient!

- 3 yr. old MN Beagle
- Ate a cycad pot plant
- Vomiting/diarrhoea on presentation
- Obtunded

General Toxicity

- Cycad toxins are…
  - Intestinal irritants
  - Hepato-toxic
    - Interfere with cell protein synthesis
    - Cells slowly die
  - Neuro-toxic
  - Carcinogenic
  - Teratogenic

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Methyl-azoxy-methanol glycosides (MAM)

- Found throughout the plant
- Examples
  - Cycasin
  - Macrozamin
- MAM inhibits RNA polymerase
- Hydrolysed by plant glycosidases and gut enzymes to form aglycones
- Aglycones
  - Alkylate DNA
    - Cell necrosis
    - Carcinogenesis
    - Mutagenesis
    - Neuro-toxicity

Beta-N-methylamino-L-alanine (BMAA)

- Neuro-toxic amino acid
- Found in highest concentrations in plant seeds
- Prolonged exposure can cause neurological symptoms

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Symptoms of Toxicity

- Early symptoms
  - Gastrointestinal symptoms predominate early in toxicity
  - Anorexia
  - Tremors, ataxia, depression, seizures
- Later Symptoms
  - Jaundice
  - Ascites
  - Bleeding disorders
  - Polydipsia

Clinical Pathology

- Hyperbilirubinaemia
- Elevated transaminases
- Elevated alkaline phosphatase
- Hypoalbuminaemia
- Hypoglycaemia
- Prolonged clotting times
- +/- thrombocytopaenia
- +/- elevated amylase/lipase

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Treatment of Toxicity

- Intestinal decontamination
- Activated charcoal q 8-12 hrs. for 3-5 days
- Cholestyramine 200-300 mg/kg PO q 12 hrs.
- Supportive care
  - IV fluid therapy
  - Gastrointestinal and nutritional support
  - Renal support
  - Monitor cardiac rhythm
- Support hepatic function
  - Acetylcysteine; SAM-E
  - ? Ursodeoxycholic acid
  - Vitamin C
  - Ethanol?
- Symptoms of liver failure may appear 10 days to 3 months

Prognosis

- 32-50% survival in published literature
- ALT – non-survivors have higher ALT concentrations on presentation than survivors.
- Bilirubin – non-survivors have higher bilirubin concentration on presentation than survivors
- Albumin – non-survivors have a lower nadir serum albumin than survivors.
- Coagulation – non-survivors were more likely to have worse coagulopathy than survivors
- Activated charcoal – administration of activated charcoal on presentation was correlated with survival

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Back to the Patient…

- **Treatment**
  - **Gastrointestinal decontamination**
  - **Activated charcoal**
  - **Hepatic protectant drugs**
  - **Gastrointestinal support medications**
  - **IV fluid therapy**

The Patient

- **Day 3:**
  - **Tolerating nasogastric feeding, but inadequate calorie intake**
  - **Blood tests**
    - **ALT 1200 U/L**
    - **AST 88 U/L**
    - **ALP 1050 U/L**
    - **Urea 17.2 mmol/L**
    - **Creatinine 227 mmol/L**
    - **T Bilirubin 70 µmol/L**
    - **Albumin 17 g/L**
    - **ACT 198 seconds**
    - **Platelets 87 x 10/9/L**

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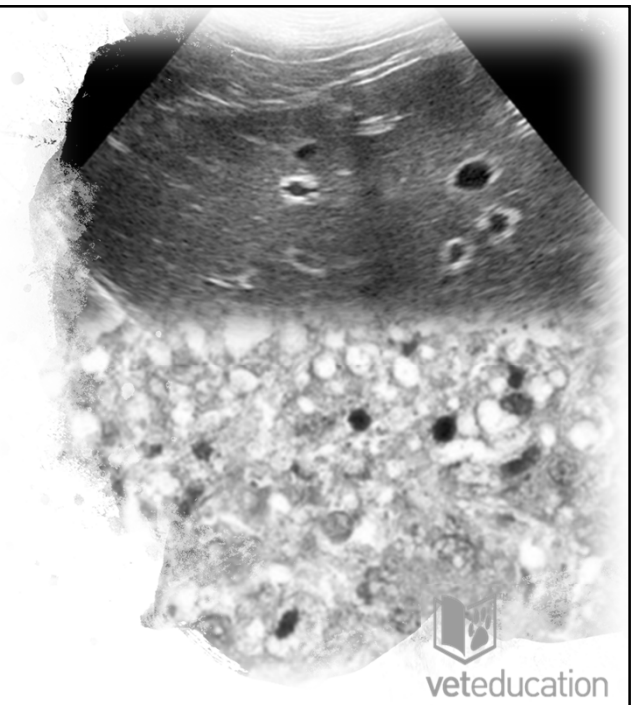
The Patient

- **Day 3:**
  - **Placement of oesophagostomy feeding tube is planned**

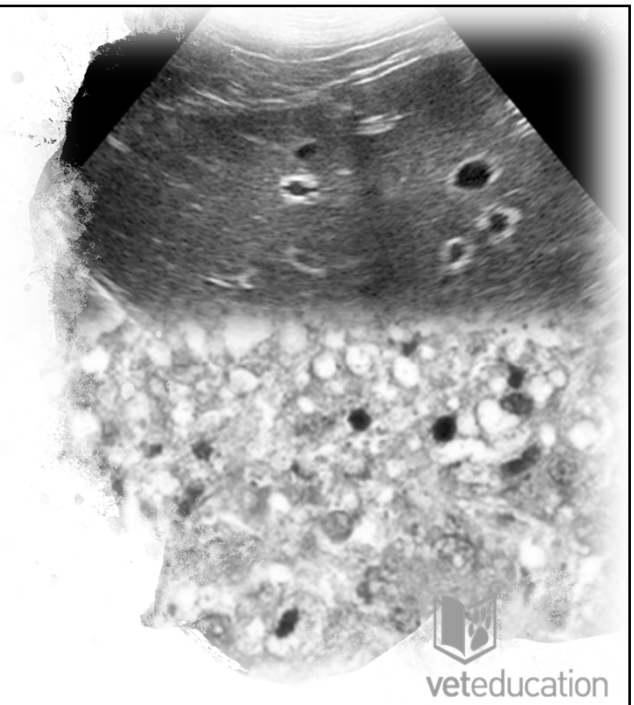
Anaesthetic Considerations

- **Biotransformation and metabolism of anaesthetic drugs**
- **Glucose**
- **Coagulation**
- **Albumin concentration**
- **Fluid balance**
- **CNS depression – query HE**
- **CO_2**



Anaesthetic Considerations

- **Vomiting/regurgitation**
- **Analgesia**



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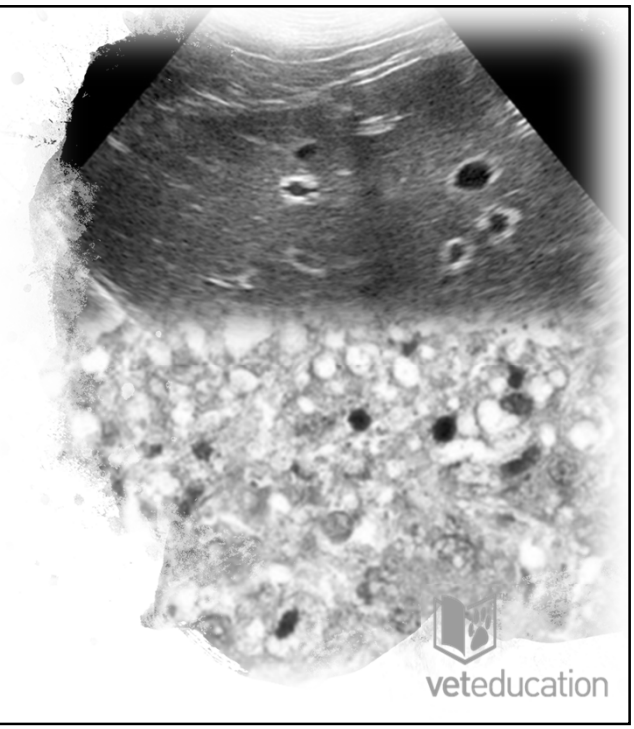
Anaesthetic Considerations

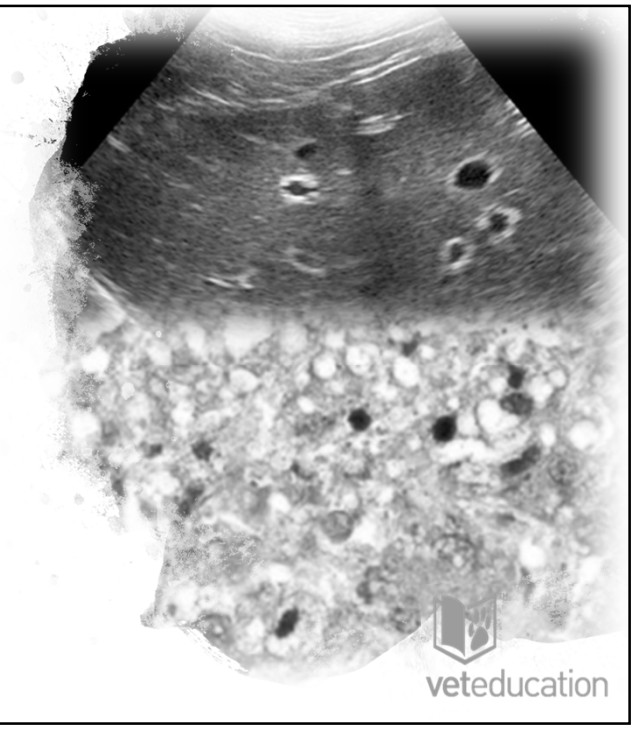
- **Reduced oxidation and glucuronidation = increase serum half-life**

Anaesthetic drugs affected by decreased liver metabolism
Barbiturates
Benzodiazepines
Opioids
Phenothiazines
NSAIDs
Ketamine
Alpha-2 agonists
Alfaxalone
Lidocaine



Premedication

- **Drugs to avoid**
  - **Acepromazine**
    - **Hepatic metabolism**
    - **No antidote**
    - **Long-acting**
    - **Reduced platelet aggregation (with atropine)**
  - **Alpha-2 agonists**
    - **Significant cardiovascular alteration**
    - **Liver protective?**
    - **Liver blood flow preserved**
    - **Reversible**
    - **Hepatic metabolism**



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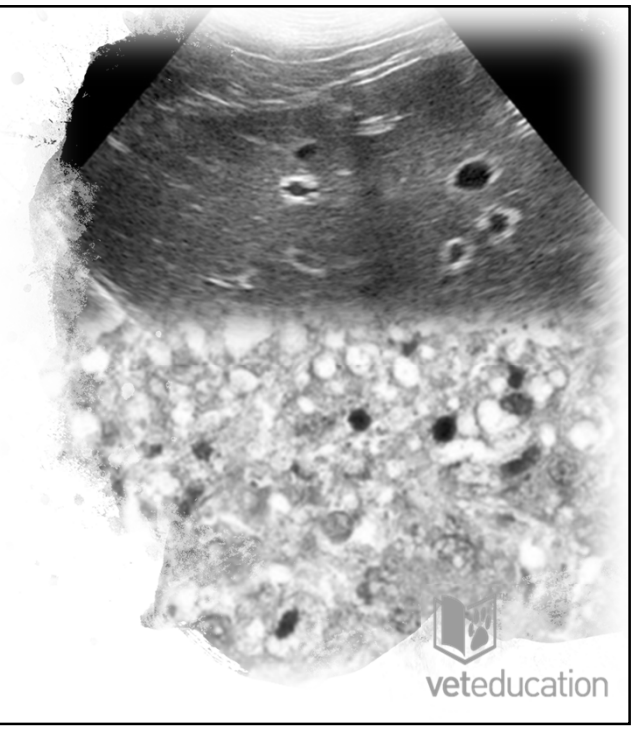
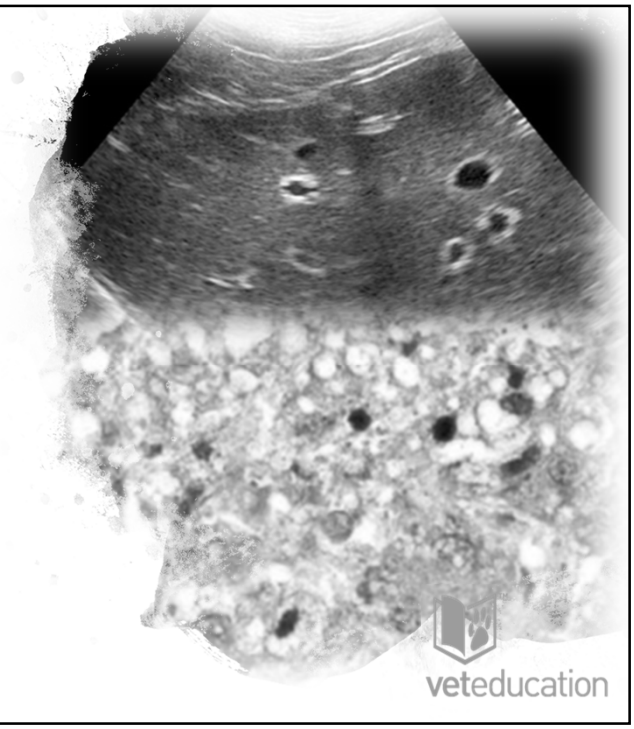
Premedication

- **Use with caution**
  - **Benzodiazepines**
    - **Minimal cardiovascular effects**
    - **Potentially reversible (flumazenil)**
    - **Extensive hepatic metabolism**
    - **Profound sedation in encephalopathic patients**



Premedication

- **Select**
  - **Opioids**
    - **Hepatic metabolism**
    - **Reversible (naloxone)**
    - **Sphincter of Oddi?**
    - **Remifentanil – extra-hepatic metabolism**
    - **MAC-sparing**
    - **CRI best**
    - **Consider ventilation support***



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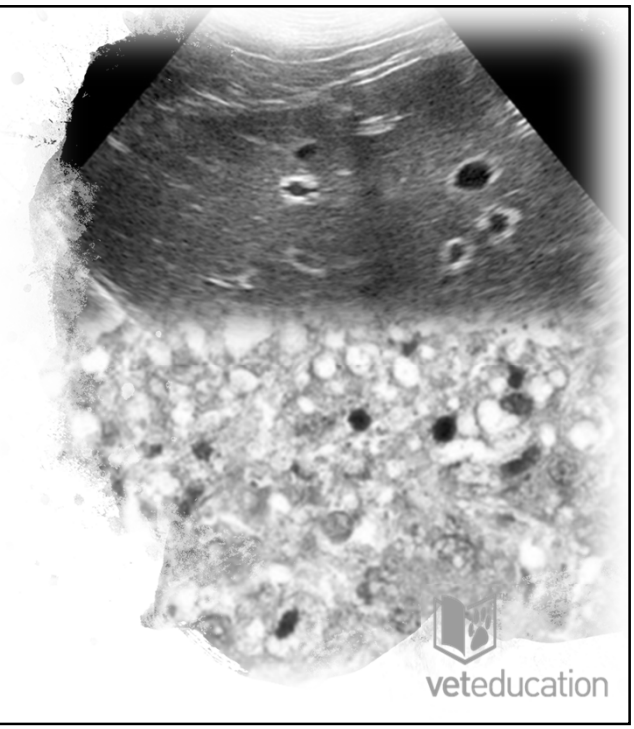
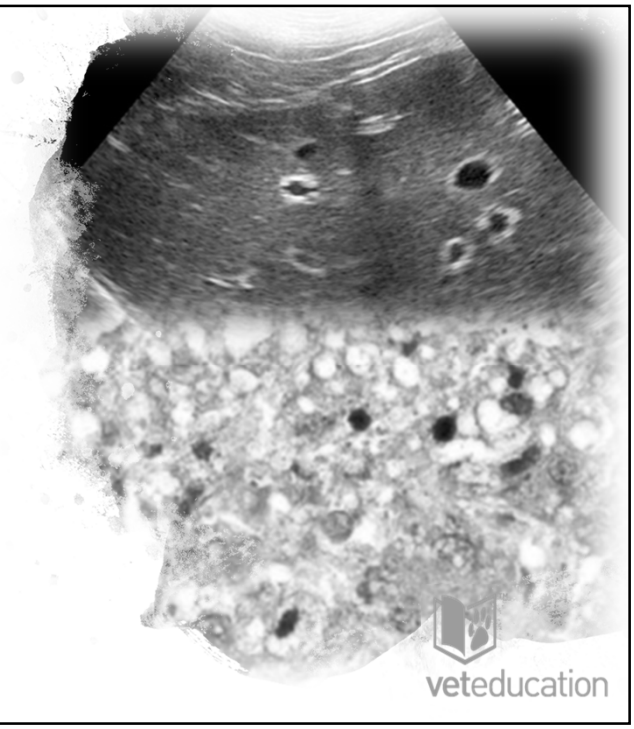
Induction

- **Avoid**
  - **Thiobarbiturates**
    - **Extensive hepatic metabolism**
    - **Prolonged duration of action**
    - **Arrhythmogenic**



Induction

- **Use with caution**
  - **Ketamine**
    - **Extensive liver metabolism**
    - **Stable liver blood flow**
    - **Slightly reduced hepatic oxygen delivery**



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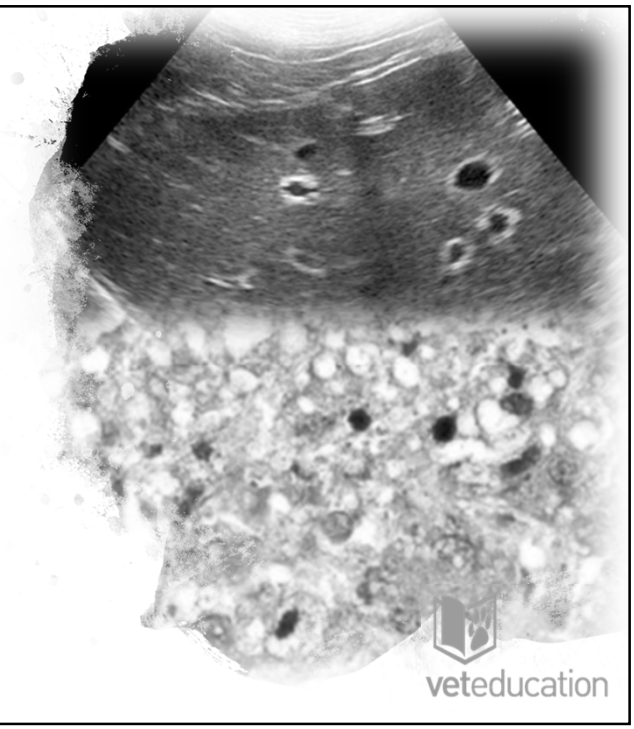
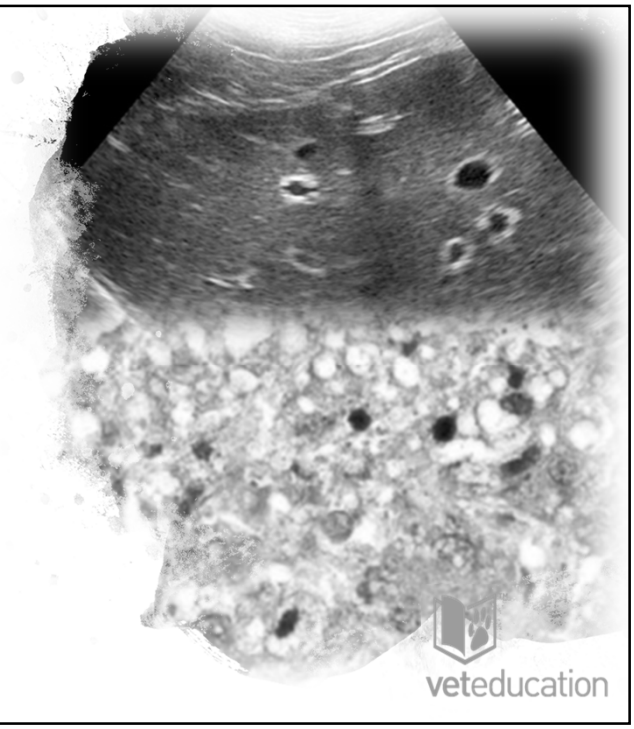
Induction

- **Use with caution**
  - **Alfaxalone**
    - **Increases channel activity at GABA-sub-type A receptor**
    - **Increases in GABA-ergic compounds in HE may increase sensitivity to Alfaxalone**
    - **Dose reduction required**
    - **Propofol safer**



Induction

- **Select**
  - **Propofol**
    - **Rapid acting**
    - **Short half-life**
    - **Rapid distribution**
    - **Hepatic and extra-hepatic clearance**
  - **Etomidate**
    - **Imidazole**
    - **Rapid distribution**
    - **Metabolism not significantly altered in liver disease (ester hydrolysis)**
    - **More rapid clearance than thiopentone**
    - **Cardiovascular stability vs. liver blood flow (decreased)**
    - **Haemolysis with propylene glycol carrier**



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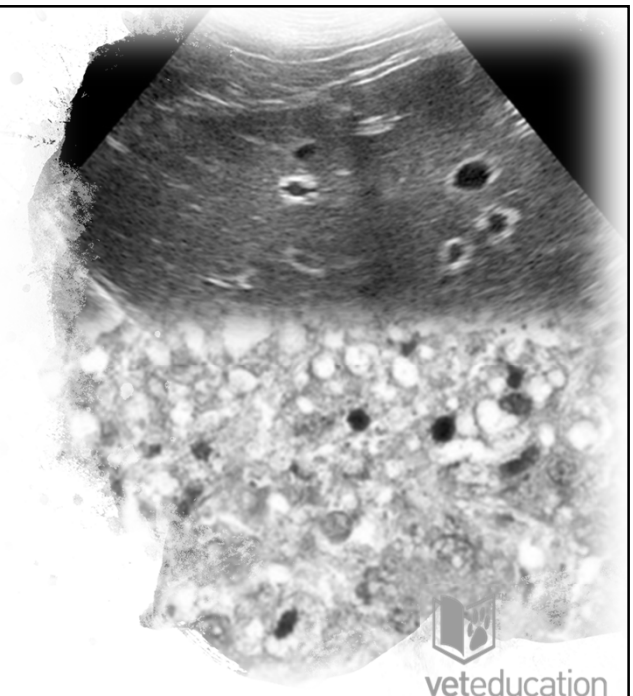
Maintenance

- **Inhalant**
  - **Minimal hepatic metabolism**
  - **Watch blood pressure**
  - **Watch hypoventilation**
- **Inhalant/CRI injectable**
  - **Reduce reliance on inhalant**
  - **Less hypotension**



RESEARCH ARTICLE

Isoflurane and Sevoflurane Induce Severe Hepatic Insulin Resistance in a Canine Model

Stella P. Kim, Josiane L. Broussard*, Cathryn M. Kolka*

Diabetes and Obesity Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA, 90048, United States of America

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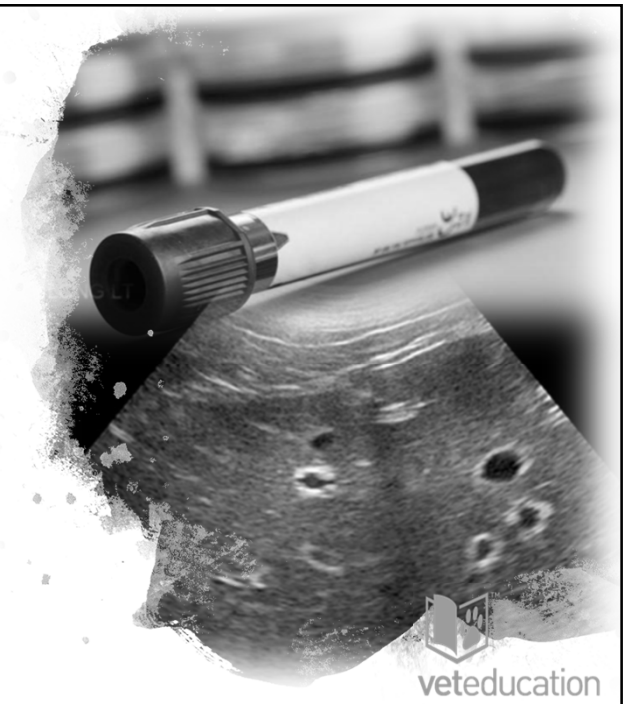
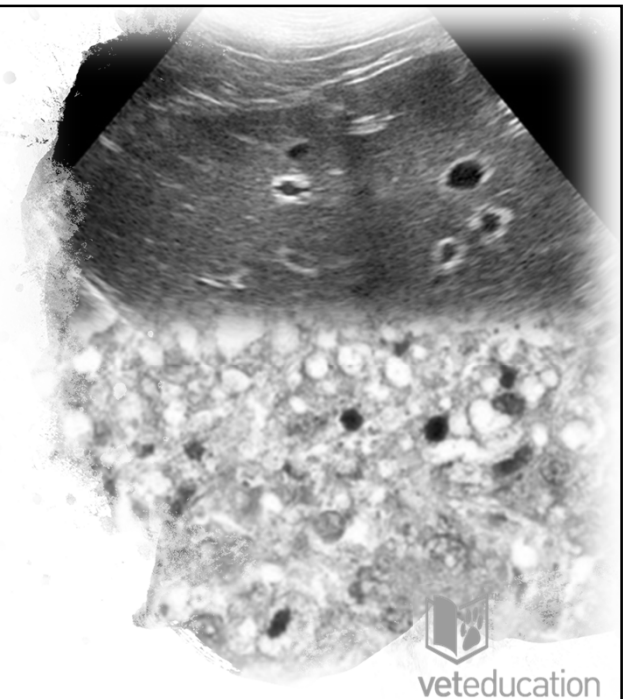
Pre-Anaesthetic Management

- **Hepatic encephalopathy**
- **Coagulopathy**
- **Hypoglycaemia**
- **Hypoalbuminaemia**
- **Hypotension**
- **Ascites**
- **Reduced drug metabolism**
- **Electrolyte abnormalities**



Pre-Anaesthetic Management

- **Reduced hepatic metabolism**
  - **Careful drug selection**
  - **Reduce dose rates**
  - **Ventilation therapy**
  - **Blood pressure support**



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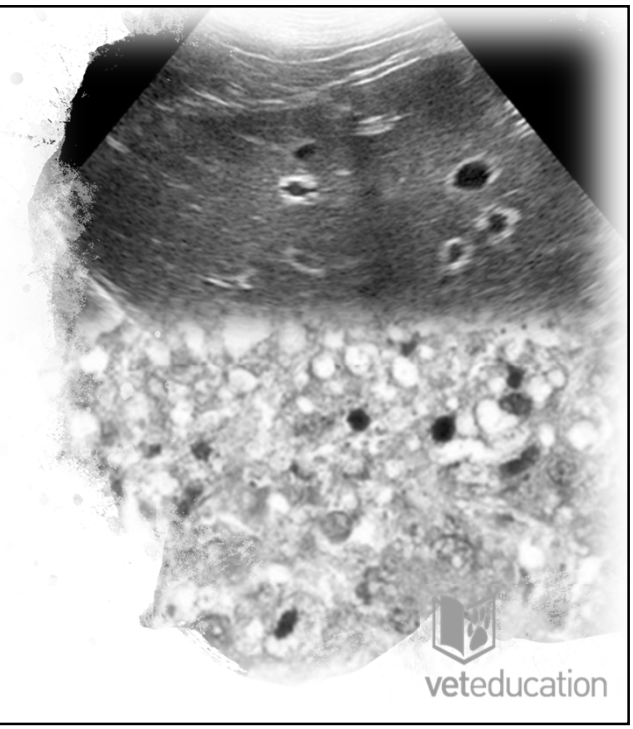
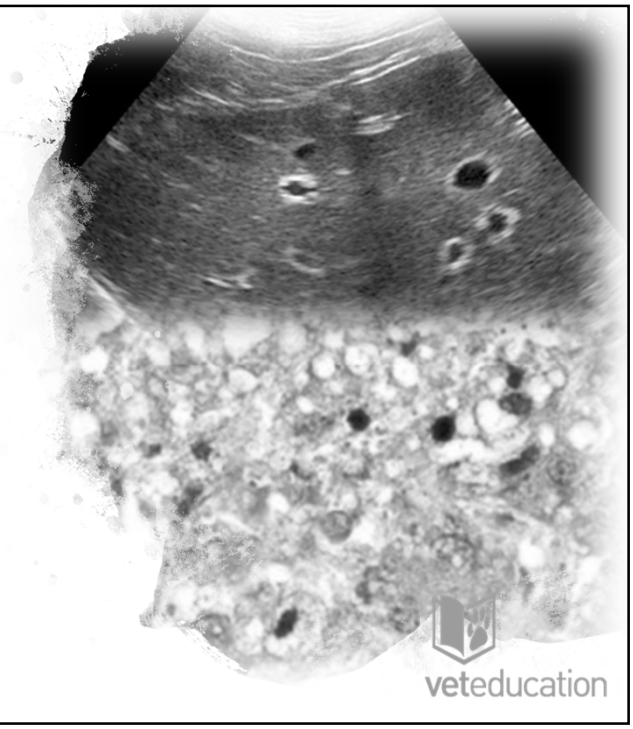
Pre-Anaesthetic Management

- **Hypoglycaemia**
  - **Monitor q 30-60 minutes**
  - **CRI 2.5-5% glucose**
  - **Remember glucose if anaesthetic recovery prolonged**



Pre-Anaesthetic Management

- **Hypoalbuminaemia**
  - **Increases free drug fraction**
  - **Reduced colloid oncotic pressure**
    - **Reduces blood volume**
    - **Increases volume of distribution – ascites etc.**
  - **Transfusion**



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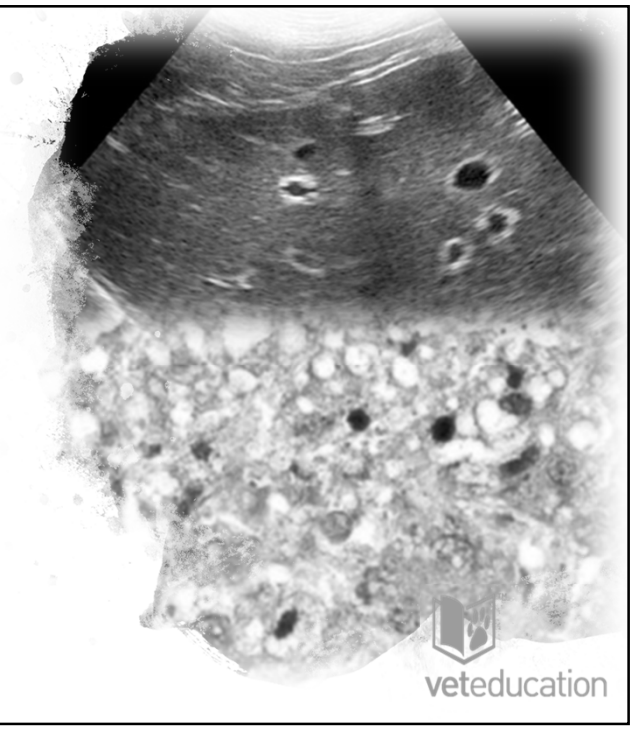
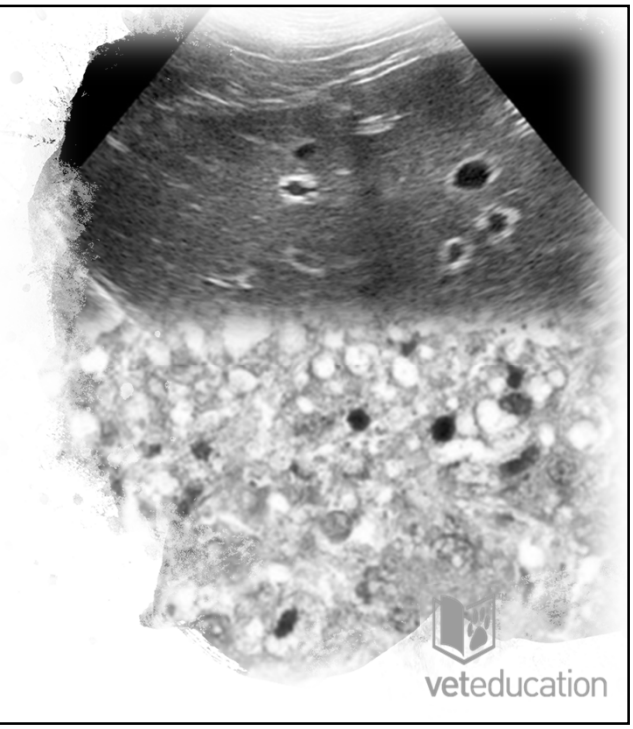
Pre-Anaesthetic Management

- **Hypotension**
  - **Causes**
    - **Hypovolaemia**
    - **Hypoalbuminaemia**
    - **Hypothermia**
  - **Treatment**
    - **Fluid therapy**
    - **Dobutamine (inotrope)**
    - **Noradrenaline (pressor)**
    - **Vasopressin (pressor)**



Pre-Anaesthetic Management

- **Coagulation**
  - **Check ACT/PT/APTT/Platelets**
  - **Plasma**
  - **Vitamin K_1**



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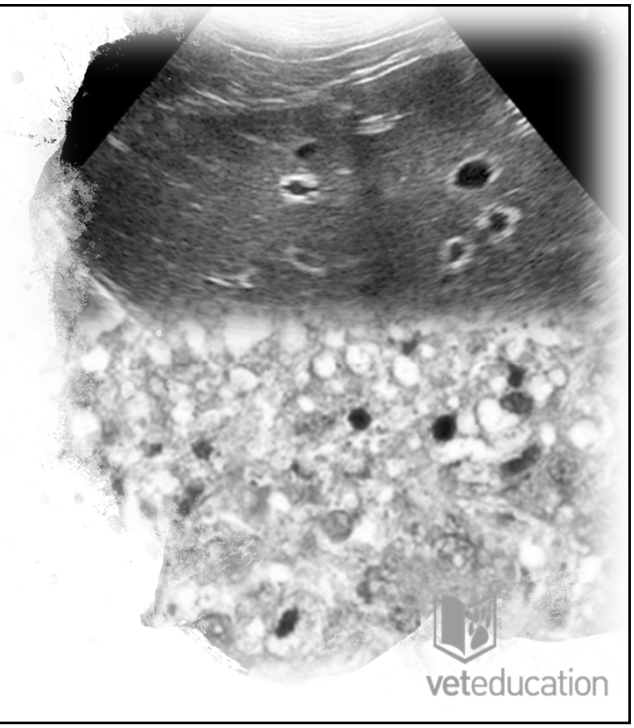
Pre-Anaesthetic Management

- **Hepatic Encephalopathy**
  - **Altered mentation**
  - **Seizures**
  - **Depression**
  - **Heightened sensitivity to sedatives**
    - **Benzodiazepines**
    - **Any drug with increased half-life**
  - **Adjust doses**
  - **Management of HE**



Suggested Protocols

- **Remifentanil**
  - **Propionic acid methyl ester link**
  - **Susceptible to metabolism by tissue and blood esterases**
  - **Minimal hepatic metabolism**
  - **Duration of action unaffected by hepatic or renal function/elimination (metabolites very weak (4,600 times less potent than remifentanil)**
  - **Short duration of action**
  - **Non-cumulative – rapid recovery**
  - **Bolus, followed by CRI**
  - **Dose: 2-4 micrograms/kg IV; 2-8 micrograms/kg/hr CRI**
- **Isoflurane and remifentanil CRI maintenance**

Suggested Protocols

CASE SERIES

Remifentanil/Isoflurane Anesthesia in Five Dogs with Liver Disease Undergoing Liver Biopsy

Tilemahos L. Anagnostou, PhD, DVM, George M. Kazakos, PhD, DVM, Ioannis Savvas, PhD, DVM, Lysimachos G. Papazoglou, PhD, DVM, MRCVS, Timoleon S. Rallis, PhD, DVM, Dimitris Raptopoulos, PhD, DVM, DVA, DECVAA

ABSTRACT

Remifentanil is a synthetic opioid with direct action on μ opioid receptors. It has an ultrashort duration of action, and its elimination is independent of hepatic or renal function. The anesthetic management of five dogs with nonuniform liver disease and requiring liver biopsy via celiotomy is described. Remifentanil and isoflurane were used for induction and maintenance of anesthesia. Intraoperative analgesia was provided by a constant rate infusion of remifentanil. Remifentanil, in combination with isoflurane, was safely and successfully used in five cases for the balanced anesthesia of dogs with hepatic diseases requiring liver biopsy via celiotomy. (*J Am Anim Hosp Assoc* 2011; 47:e103-e109. DOI 10.5326/JAAHA-MS-5613)

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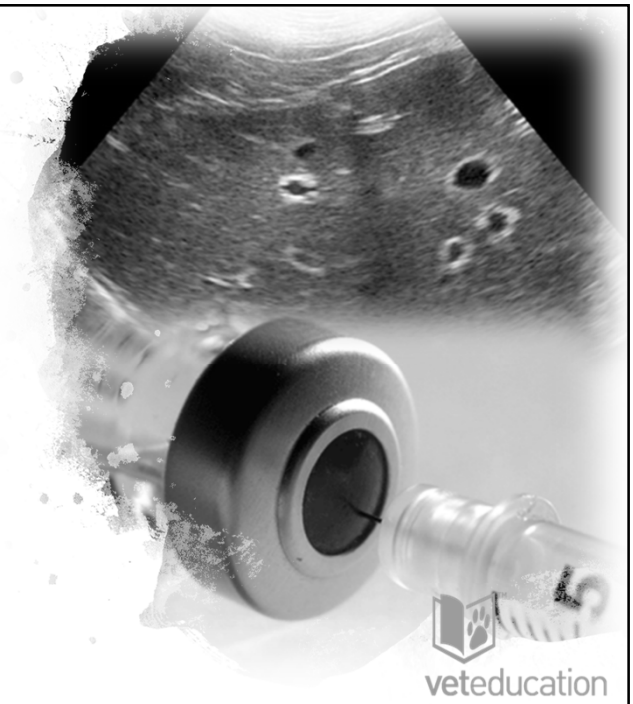
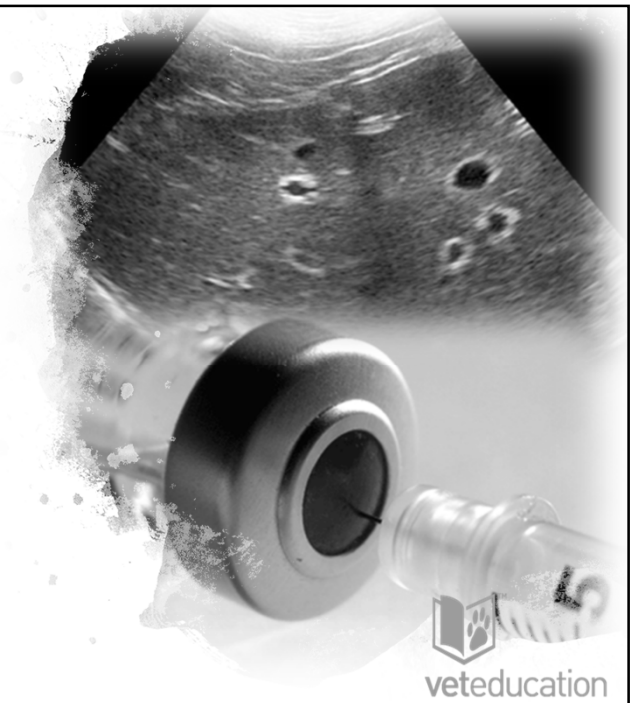
Suggested Protocols

- **Premedication**
  - **Fentanyl 2-4 micrograms/kg IV**
- **Induction**
  - **Propofol 4 mg/kg IV**
- **Maintenance**
  - **Fentanyl CRI +/-**
  - **Propofol CRI +/-**
  - **Isoflurane to effect**



Suggested Protocols

- **Premedication**
  - **Butorphanol 0.1 mg/kg IV**
- **Induction**
  - **Propofol 4 mg/kg IV**
- **Maintenance**
  - **Butorphanol CRI +/-**
  - **Propofol CRI +/-**
  - **Isoflurane to effect**



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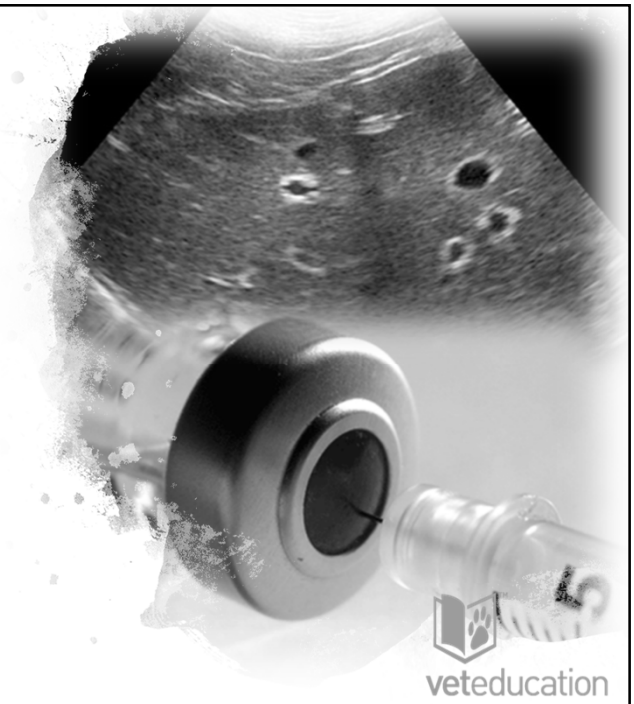
Suggested Protocols

- **Premedication**
  - **Fentanyl 2-4 micrograms/kg IV +/-**
  - **Ketamine 0.3 mg/kg/hr CRI**
- **Induction**
  - **Propofol 4 mg/kg IV**
- **Maintenance**
  - **Fentanyl CRI +/-**
  - **Ketamine CRI +/-**
  - **Isoflurane to effect**



Back to the Patient…

- **Before the anaesthetic**
  - **Fluid therapy**
  - **Fresh frozen plasma transfusion – 15 ml/kg IV**
  - **Prepare**
    - **Glucose 10% solution**
    - **Dobutamine**
    - **Noradrenaline**
  - **Active warming prior to anaesthesia**

Back to the Patient…

- **Anaesthetic protocol**
  - **Premedication**
    - **Fentanyl 2 micrograms/kg IV, then**
    - **CRI 2 micrograms/kg/hr**

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Back to the Patient…

- **Anaesthetic protocol**
  - **Induction**
    - **Propofol 4 mg/kg IV to effect**
    - **Fentanyl CRI increased to 4 micrograms/kg/hr**

Back to the Patient…

- **Anaesthetic protocol**
  - **Maintenance**
    - **Isoflurane**
    - **Fentanyl CRI**

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Check out...

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Selected References

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