

Slide Text

CL Davis 2007
Literature Review
Comparative Medicine
October 2006 vol 56 (5) slides 2-79
December 2006 vol 56 (6) slides 80-186
February 2007 vol 57 (1) slides 187-399



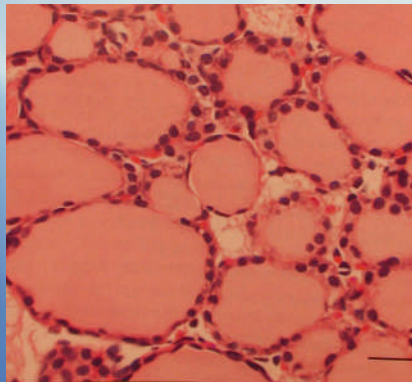
Comparative Medicine

October 2006

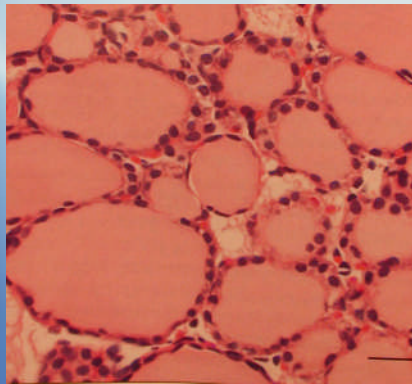
vol 56 (5) slides 2-79



Name the organ



Name the organ



thyroid



Altholtz, Lotus, et al. "Dose Dependent Hypothyroidism in Mice Induced by Commercial Trimethoprim-Sultamethoxazole (TMP-SMX) Rodent Feed" Comparative Medicine 56(5): 394-401, 2006

This study evaluated the induction of hypothyroidism of commercially available TMP-SMX feed. Which component of the antibiotic is suspected of causing the hypothyroidism?



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SMX



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- a) 120mg/kg
- b) 240 mg/kg
- c) 1200 mg/kg
- d) 2400 mg/kg
- e) Each induced hypothyroidism in a dose dependent manner

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How long did they have to feed the diet to see the hypothyroidism at the 2400mg/kg dose?



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How long did they have to feed the diet to see
hypothyroidism at the 2400mg/kg dose?

Saw reduction in hormone levels in two weeks



There was a dramatic reduction in the primary hormone released from the thyroid in the mice. Which hormone is that?

- a) T3
- b) Thyroxine
- c) Triiodothyronine
- d) TSH

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- a) T3
- b) **Thyroxine**
- c) Triiodothyronine
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Which of the following is true regarding the blood indices in mice fed the 2400mg/kg SMX

- a) Mice had low T4 and low TSH levels**
- b) Mice had high T4 and high TSH levels**
- c) Mice had low T4 and high TSH levels**
- d) Mice had high T4 and low TSH levels**

Which of the following is true regarding the blood indices in mice fed the 2400mg/kg SMX

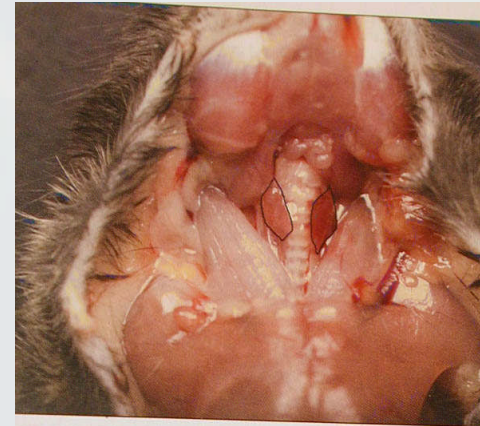
- a) Mice had low T4 and low TSH levels
- b) Mice had high T4 and high TSH levels
- c) **Mice had low T4 and high TSH levels**
- d) Mice had high T4 and low TSH levels



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Why do you see hyperplasia of the thyroid if animals are hypothyroid?

Diet B



Control



*Altholtz, Lotus, et al. "Dose Dependent Hypothyroidism in Mice Induced by Commercial Trimethoprim-Sultamethoxazole (TMP-SMX) Rodent Feed" Comparative Medicine 56(5): 394-401, 2006
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Why do you see hyperplasia of the thyroid if animals are hypothyroid?

Process is similar to iodine deficiency induced goiter. Inability to produce thyroid hormones leads to upregulation of TSH secretion and consequent hypertrophy and hyperplasia.



Genetically Epilepsy Prone Rats are prone to seizures induced by:

1. **Light**
2. **Sound**
3. **Movement**
4. **Touch**



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1. Light
2. **Sound**
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4. Touch



What hormone is associated with Rapid Eye Movement Sleep (REMS)?

- a) Aldosterone
- b) Melatonin
- c) Leptin
- d) Prolactin



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Toth, Linda, et al. Comparative Medicine 56 (5): 402-415, 2006
Sleep, Temperature, Activity, and Prolactin Phenotypes of Genetically
Epilepsy Prone Rats (GEPR)

Which animal strain/stock had lowest levels of prolactin?

1. SD
2. GEPR3
3. GEPR9
4. No differences were seen in prolactin levels



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What else did the authors speculate was associated with reduced prolactin availability in the GEPR9 rats?



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What else did the authors speculate was associated with reduced prolactin availability in the GEPR9 rats?

GEPR9 historically shown poor breeding performance and speculate may at least be due in part to reduced prolactin availability



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Seizures were induced at day onset and at night onset in this study. Which condition significantly altered sleep?

1. Day onset
2. Night onset
3. Both of them altered sleep
4. Neither altered sleep



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What type of altered sleep was seen?



Toth, Linda, et al. Comparative Medicine 56 (5): 402-415, 2006
Sleep, Temperature, Activity, and Prolactin Phenotypes of Genetically
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What type of altered sleep was seen?

Delayed sleep onset



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Sleep, Temperature, Activity, and Prolactin Phenotypes of Genetically
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Question for thought. I read the study did the following:

Induced sleep deprivation

One week or more later did day onset seizure induction

One week or more after that, did night seizure induction

Do think results might be different if the night seizure induction was done first
(one week after sleep deprivation) verses two weeks later?



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Which strain/stock had highest core body temperature?

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Sleep, Temperature, Activity, and Prolactin Phenotypes of Genetically
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Which strain/stock had lowest REMS (rapid eye movement sleep) time?

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Which strain/stock had lowest REMS (rapid eye movement sleep) time?

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2. **GEPR3**
3. GEPR9
4. There was no differences among/between the groups

Summary: GEPR3 had less SWS (small wave sleep) and REMS, higher core body temperature, higher prolactin



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Sleep, Temperature, Activity, and Prolactin Phenotypes of Genetically
Epilepsy Prone Rats (GEPR)**

Authors mention in the results section that both GEPR3 and GEPR9 rats are deficient in two neurotransmitters related to sleep and arousal which may also be playing a role? What are the two neurotransmitters?



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Sleep, Temperature, Activity, and Prolactin Phenotypes of Genetically
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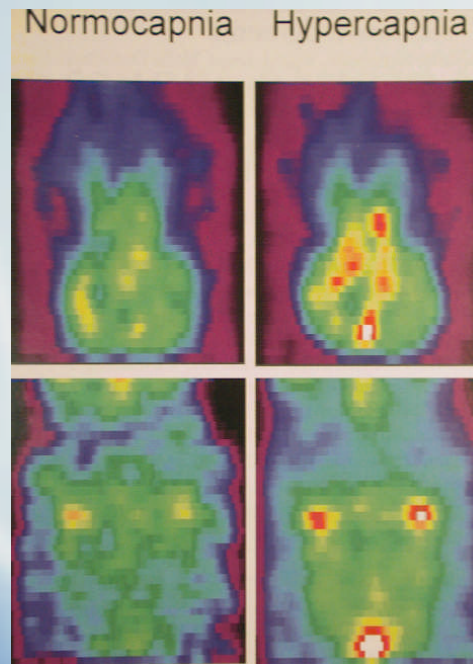
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Norepinephrine and serotonin



Olsen

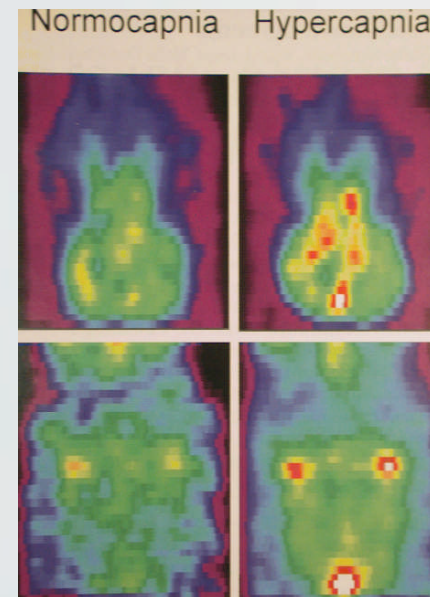
Name the diagnostic technique



Olsen, Keiding, and Munk. Comp Med 56(5): 416-420, 2006 "Effect of Hypercapnia on Cerebral Blood Flow (CBF) and Blood Volume (CBV) in Pigs Studied by Positron Emission Tomography" *Comp Med 56(5): 416-420, 2006*

Name the diagnostic technique

PET (positron Emission Tomography). This image shows how CBF and CBV measured pixel by pixel allowing evaluation for regional changes. This image demonstrates global effects on brain



Olsen, Keiding, and Munk. Comp Med 56(5): 416-420, 2006

What parameter was measured using the tracer
 $C^{15}O$?



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 $C^{15}O$?

Cerebral blood volume (CBV)



Olsen, Keiding, and Munk. Comp Med 56(5): 416-420, 2006

What is used to measure cerebral blood flow?



What is used to measure cerebral blood flow (CBF)?

$H_2^{15}O$ as a flow-determining diffusible tracer.

Olsen, Keiding, and Munk. Comp Med 56(5): 416-420, 2006

What happened to CBF and CBV as $p\text{CO}_2$ increased?



What happened to CBF and CBV as $p\text{CO}_2$ increased?

Tendency of both to increase.

- CBF increased 54% during hypercapnia (up to 25 kPa, partial pressure of CO_2)
- CBV increased 41%

Olsen, Keiding, and Munk. Comp Med 56(5): 416-420, 2006

Hypercapnia was induced by decreased tidal volume and number of breaths/minute on the respirator. How do you adjust your anesthesia parameters to maintain normal pO_2 ?



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Increase percent oxygen given. Pigs on O₂:nitrous oxide mix so percent oxygen in the mix increased.

Complete reference for previous questions:

Olsen, Keiding, and Munk. “Effect of Hypercapnia on Cerebral Blood Flow and Blood Volume in Pigs Studied by Positron Emission Tomography” Comp Med 56(5): 416-420, 2006



Mills and Tanumihardjo. "Vitamin A Toxicity in Wild-caught African Green Vervet Monkeys (*Chlorocebus aethiops*) after Two Years in Captivity" Comp Med 56(5): 421-425, 2006

How was Vitamin A toxicity diagnosed in the vervet monkeys?

- a) clinical signs and high retinol concentrations in serum**
- b) clinical signs and liver lesions consistent with Vitamin A toxicity**
- c) liver lesions consistent with Vitamin A toxicity and high serum levels of retinol**
- d) liver lesions consistent with Vitamin A toxicity, and high hepatic levels of Vitamin A**



Mills and Tanumihardjo. "Vitamin A Toxicity in Wild-caught African Green Vervet Monkeys (Chlorocebus aethiops) after Two Years in Captivity" Comp Med 56(5): 421-425, 2006

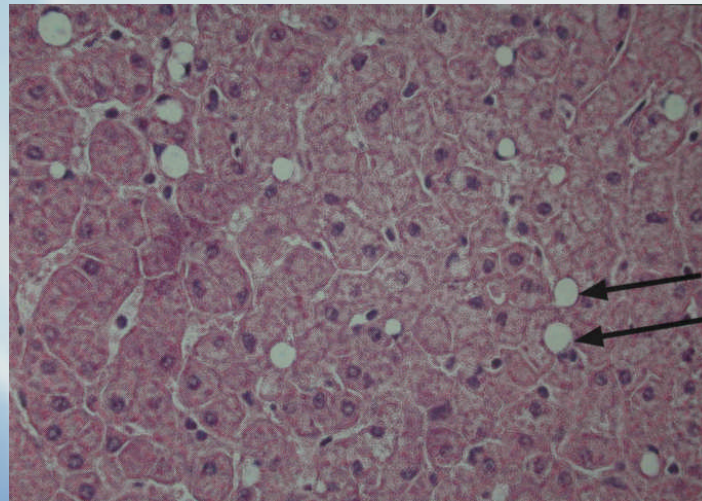
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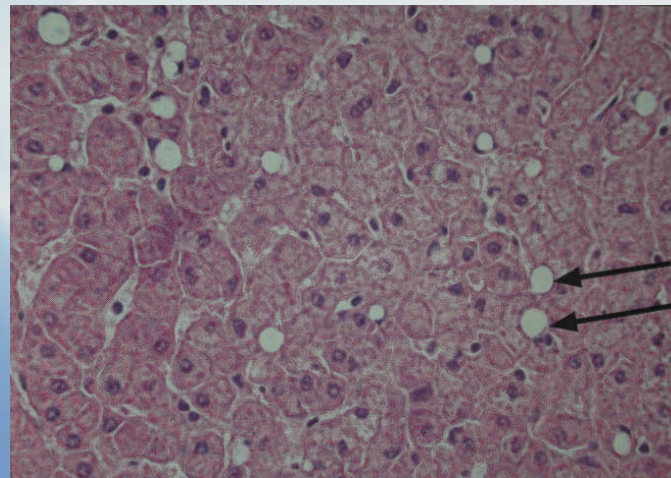
What are liver lesions consistent with Vitamin A toxicity as seen in this figure?



Mills and Tanumihardjo. "Vitamin A Toxicity in Wild-caught African Green Vervet Monkeys (Chlorocebus aethiops) after Two Years in Captivity" Comp Med 56(5): 421-425, 2006

What are liver lesions consistent with Vitamin A toxicity as seen in this figure?

hypertrophy and hyperplasia of Vit A storing stellate cells.



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Which retinyl ester was found in the highest percent in the liver?

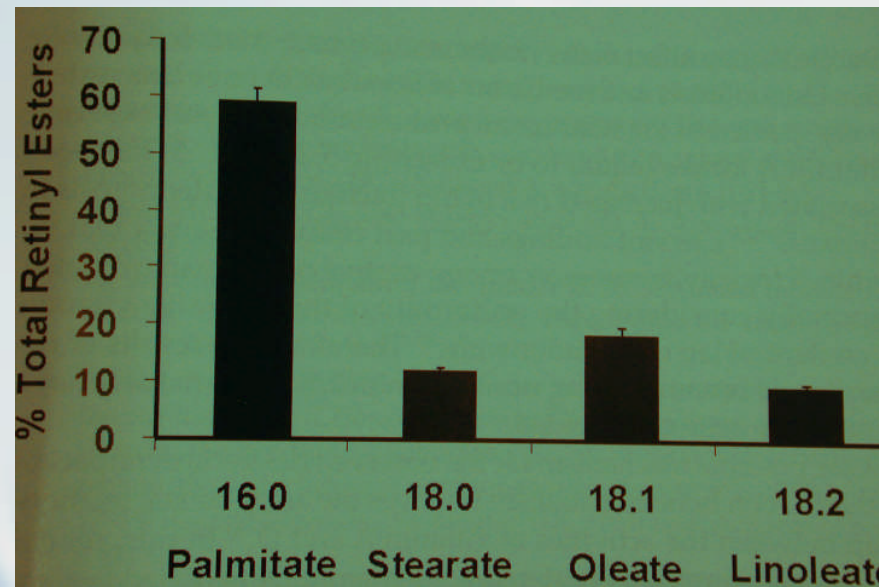
- a) palmitate**
- b) stearate**
- c) oleate**
- d) linoleate**



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Serum retinol levels were not elevated. How did the authors explain that?



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Species differences in Vitamin A transport and storage patterns or dietary behavior



Mills and Tanumihardjo. "Vitamin A Toxicity in Wild-caught African Green Vervet Monkeys (Chlorocebus aethiops) after Two Years in Captivity" Comp Med 56(5): 421-425, 2006

Animals were fed a standard primate chow. How did the authors explain the toxicity compared to primates in the wild?



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Vervets are primarily vegetarian in the wild, getting most of their Vitamin A from provitamin A carotenoid sources which are not absorbed as efficiently as the preformed Vitamin A in the commercial diet.



Trammell, et al. Comp Med 56(5): 426-434, 2006

What are the three broad components of blood coagulation?



Trammell, et al. Comp Med 56(5): 426-434, 2006

**What are the three broad components of
coagulation?**

initiation, amplification, propagation



Trammell, et al. Comp Med 56(5): 426-434, 2006

What are the two pathways that converge to a common pathway?



Trammell, et al. Comp Med 56(5): 426-434, 2006

What are the two pathways that converge to a common pathway?

intrinsic and extrinsic



Trammell, et al. Comp Med 56(5): 426-434, 2006

PL/J mice died post abdominal surgery and large volumes of unclotted blood was found in the abdomen. Which clotting time was found to be prolonged?

- a) activated prothrombin time
- b) activated fibrinogen time
- c) activated partial thromboplastin time
- d) activated thromboplastin time



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Trammell, et al. Comp Med 56(5): 426-434, 2006

What pathway did this indicate was defective?

Which factors?



What pathway did this indicate was defective?

Intrinsic

Which factors?

VIII, IX, XI, XII, prekallikrein, HK



Trammell, et al. Comp Med 56(5): 426-434, 2006

Which factor did the authors conclude was absent or reduced in these mice?



Trammell, et al. Comp Med 56(5): 426-434, 2006

Which factor did the authors conclude was absent or reduced in these mice?

IX



Trammell, et al. Comp Med 56(5): 426-434, 2006

True or False. Authors' experiments concluded that inhibitors to factor IX were involved in the reduced function of IX in these mice



True or False. Authors' experiments concluded that inhibitors to factor IX were involved in the reduced function of IX in these mice

False. Inhibition studies demonstrated that inhibitors were not responsible for the low factor IX activity

Trammell, et al. Comp Med 56(5): 426-434, 2006

One differential diagnosis for the clinical signs was ethylene glycol toxicity. Why?



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One differential diagnosis for the clinical signs was ethylene glycol toxicity. Why?

Ethylene glycol is produced as a byproduct of ethylene oxide sterilization and can deplete clotting factors



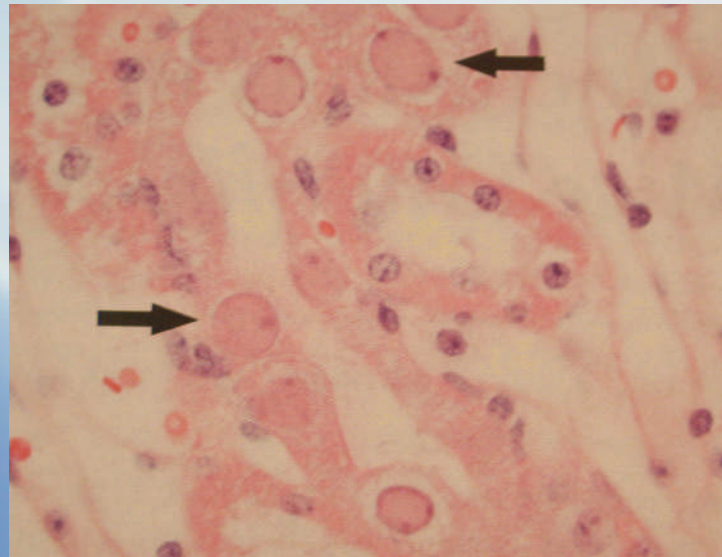
Complete Reference for previous questions:

Trammell, et al. "Fatal Hemorrhagic Diathesis Associated with Mild Factor IX Deficiency in PL/J Mice" *Comp Med* 56(5): 426-434, 2006

October 2006

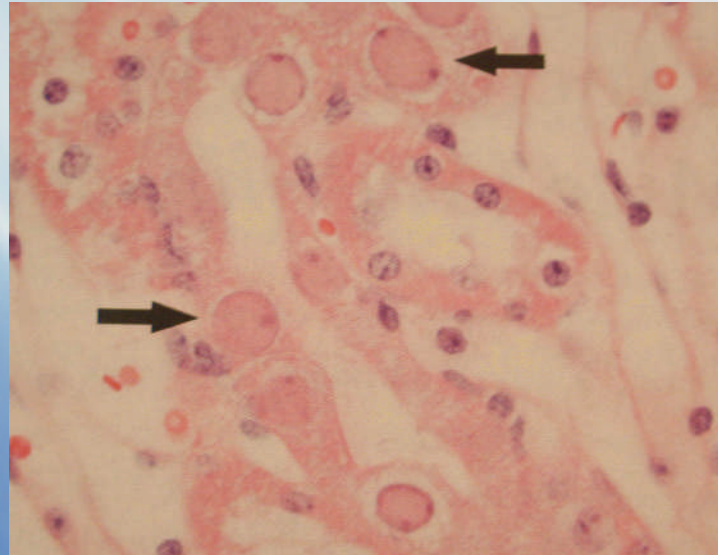


What are the arrows pointing to?



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Intranuclear Inclusion Bodies, eosinophilic



Baze, et al. "Karyomegaly and Intranuclear Inclusions in the Renal Tubules of Sentinel ICR Mice (*Mus musculus*)" *Comp Med* 56(5): 435-438, 2006

What viral agents were on the differential list for the INIB?



What viral agents were on the differential list?

polyoma virus

adenovirus

cytomegalovirus



Baze, Comp Med 56(5): 435-438, 2006

How did they rule these viruses out?



How did they rule these viruses out?

polyoma virus- on DNA extracted from paraffin-
embedded formalin fixed kidney tissue

adenovirus- immunohistochemistry

ultrastructural changes did not support a viral
etiology

Baze, Comp Med 56(5): 435-438, 2006

What was the final conclusion as to the cause of the lesions?



Baze, et al. "Karyomegaly and Intranuclear Inclusions in the Renal Tubules of Sentinel ICR Mice (*Mus musculus*)" *Comp Med* 56(5): 435-438, 2006

What was the final conclusion as to the cause of the lesions?

Lesions degenerative in nature rather than infective



Comparative Medicine
December 2006
Volume 56
Number 6
slides 80-185



What rat develops autochthonous hormone refractory prostate cancer (HRPC) spontaneously or after chemical induction?

- a) Noble-Wistar
- b) Fisher 344
- c) Brown Norway
- d) Lobund-Wistar



Morris and Suckow. "Dietary Prevention of Hormone Refractory Prostate Cancer in Lobund-Wistar Rats: A Review of Studies in a Relevant Animal Model"
Comparative Medicine 56(6):461-467, 2006 December

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What makes this rat model similar to human prostate cancer?

- a) Prostate shows early microscopic change of prostatic intraepithelial neoplasia similar to humans
- b) Tumors metastasize to bone similar to humans-mets more common to lung in rat model although respiratory distress not common
- c) Prostate tumors at later stage of development are sensitive to testosterone treatment similar to humans-later stages are NOT response to testosterone
- d) All the above are true



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Which is the biologically more active form of testosterone?

- a) Testosterone
- b) Testosterone propionate
- c) Dihydrotestosterone
- d) Testosterone monohydrate



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What chemical is commonly used to induce the prostate cancer?



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MNU (N-methyl-N-nitrosurea)



Morris and Suckow. "Dietary Prevention of Hormone Refractory Prostate Cancer in Lobund-Wistar Rats: A Review of Studies in a Relevant Animal Model"
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Which compound listed has NOT been shown to accelerate the MNU-induced PC?

- a) Testosterone
- b) Dihydrotestosterone
- c) Estrogen
- d) Phenobarbital



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The early pre-malignant stage of HRPC is clinically inapparent but testosterone dependent and promoted by endogenous testosterone. What is the incidence of prostate cancer in these LW rats when given MNU plus testosterone propionate pellets?

- a) 0%
- b) 30%
- c) 50%
- d) 90%



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Which form of dihydrotestosterone was found to prevent the development of prostate cancer in this model?

Esterified or nonesterified?



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Which form of dihydrotestosterone was found to prevent the development of prostate cancer in this model?

Esterified or nonesterified?

Nonesterified form of DHT prevents development whereas the esterified form promotes the development



Morris and Suckow. "Dietary Prevention of Hormone Refractory Prostate Cancer in Lobund-Wistar Rats: A Review of Studies in a Relevant Animal Model"
Comparative Medicine 56(6):461-467, 2006 December

What kind of diet prevented the occurrence of PC when fed the diet to rats 2-24 months of age?

- a) Natural soy-free diet containing 24% cornstarch
- b) Natural soy diet containing 59% soybean meal
- c) Soy protein isolate with high isoflavones containing 20% soy protein isolate



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- b) Natural soy diet containing 59% soybean meal
- c) Soy protein isolate with high isoflavones containing 20% soy protein isolate**



*Morris and Suckow. "Dietary Prevention of Hormone Refractory Prostate Cancer in Lobund-Wistar Rats: A Review of Studies in a Relevant Animal Model"
Comparative Medicine 56(6):461-467, 2006 December*

Summary:

Two stages to PC model:

- Stage 1 is premalignant-clinically inapparent and associated with high level of endogenous testosterone
- Stage 2 is testosterone independent, highly aggressive and not reversible by testosterone deprivation
- In rat-mets via lymphatics to lungs most common





Common name?

Genus/species?



Common name?

California deer mouse

Genus/species?

Peromyscus californicus

Peromyscus californicus

It is the largest species in its genus. Its total length is between 220-285 mm, with tail length ranging from approximately 117-156 mm. It is distinctly bicolored. Adults have a yellowish brown or gray mixed with black dorsal coloring, and a white underside, and feet. Many individuals have a distinctly fulvous throat patch and a fulvous lateral line separating dorsal from ventral pelage in the shoulder region, sometimes extending to the thigh. Juveniles are gray on top with a white underside. The tail matches the dorsal pelage and is not sharply bicolored. The ears are large, ranging from 20-25 mm



What disease develops
when fed a high fat diet?





What disease develops
when fed a high fat diet?

Type II Diabetes

Hyperlipidemia



What is seen clinically in these mice that develop type II diabetes when fed the high fat diet?

- a) Obesity**
- b) Polyphagia**
- c) Polyuria**
- d) None of the above**



What is seen clinically in these mice that develop type II diabetes when fed the high fat diet?

- a) Obesity
- b) Polyphagia
- c) Polyuria
- d) **None of the above**



The hyperlipidemia seen in these mice was found to be associated with oversecretion of which compound?

1. Low density lipoprotein
2. Very low density lipoprotein
3. High density lipoprotein
4. Lipoprotein lipase



The hyperlipidemia seen in these mice was found to be associated with oversecretion of which compound?

1. Low density lipoprotein
2. **Very low density lipoprotein**
3. High density lipoprotein
4. Lipoprotein lipase



Insulin resistance and type II diabetes is seen in humans with dyslipidemias such as familial combined hyperlipidemia. What serum compound increase is this associated with?

- a) Monoacylglycerol
- b) Diacylglycerol
- c) Triacylglycerol
- d) Triacylcholesterol



Insulin resistance and type II diabetes is seen in humans with dyslipidemias such as familial combined hyperlipidemia. What serum compound increase is this associated with?

- a) Monoacylglycerol
- b) Diacylglycerol
- c) **Triacylglycerol**
- d) Triacylcholesterol



*Reference to previous questions:
Kruger-Higby, Shelness, and Holler "Heritable, Diet-induced Hyperlipidemia in California Mice (*Peromyscus californicus*) is Due to Increased Hepatic Secretion of Very Low Density Lipoprotein Triacylglycerol" Comp Med 56(6): 468-475, December 2006*



Cho, Suh, et al "The Circling Mouse (C57BL/6J-cir) has a 40-kilobase Genomic Deletion that includes the Transmembrane Inner Ear (tmie) Gene" Comp Med 56(6): 476-481, 2006 December

What other phenotype does the circling mouse have in addition to circling?



Cho, Suh, et al "The Circling Mouse (C57BL/6J-cir) has a 40-kilobase Genomic Deletion that includes the Transmembrane Inner Ear (tmie) Gene" Comp Med 56(6): 476-481, 2006 December

What other phenotype does the circling mouse have in addition to circling?

Deafness

Hyperactive at 7 days of age

Degenerated cochlea



Cho, Suh, et al "The Circling Mouse (C57BL/6J-cir) has a 40-kilobase Genomic Deletion that includes the Transmembrane Inner Ear (tmie) Gene" Comp Med 56(6): 476-481, 2006 December

What gene has it been localized to?



Cho, Suh, et al "The Circling Mouse (C57BL/6J-cir) has a 40-kilobase Genomic Deletion that includes the Transmembrane Inner Ear (tmie) Gene" Comp Med 56(6): 476-481, 2006 December

What gene has it been localized to?

Chromosome 9

Autosomal recessive

100% penetrance



Cho, Suh, et al "The Circling Mouse (C57BL/6J-cir) has a 40-kilobase Genomic Deletion that includes the Transmembrane Inner Ear (tmie) Gene" Comp Med 56(6): 476-481, 2006 December

What gene has it been shown allelic to?



Cho, Suh, et al "The Circling Mouse (C57BL/6J-cir) has a 40-kilobase Genomic Deletion that includes the Transmembrane Inner Ear (tmie) Gene" Comp Med 56(6): 476-481, 2006 December

What gene has it been shown allelic to?

Sr



*Cho, Suh, et al "The Circling Mouse (C57BL/6J-cir) has a 40-kilobase Genomic Deletion that includes the Transmembrane Inner Ear (tmie) Gene" Comp Med 56(6): 476-481, 2006
December*

Summary:

Bred cir/cir mice to sr/sr to generate cir/sr mice

Cir/sr mice demonstrated behavior just like cir/cir mice in terms of circling and central area activity

Cir mice have deletion of two genes: tmie and mRn49018

Future studies would be to generate single gene KO to study



Grindle, et al "Validation of High-throughput methods for Measuring Blood Urea Nitrogen (BUN) and Urinary Albumin Concentrations in Mice" Comp Med 56(6): 482-486, December 2006

What has been shown to interfere with accurate measurements of mouse plasma creatinine using autoanalyzers?



Grindle, et al "Validation of High-throughput methods for Measuring Blood Urea Nitrogen (BUN) and Urinary Albumin Concentrations in Mice" Comp Med 56(6): 482-486, December 2006

What has been shown to interfere with accurate measurements of mouse plasma creatinine using autoanalyzers?

Plasma chromagens



Grindle, et al “Validation of High-throughput methods for Measuring Blood Urea Nitrogen (BUN) and Urinary Albumin Concentrations in Mice” Comp Med 56(6): 482-486, December 2006

- **Study showed the you could get accurate BUN concentrations with autoanalyzer**
- **Albumin measurement-good precision, but underestimated by 3.5-4 fold so will require linear regression using mouse albumin standards which are commercially available.**



Which of the following are lipophilic?

- a) Fentanyl and hydromorphone**
- b) Fentanyl and oxymorphone**
- c) Hydromorphone and morphine**
- d) Hydromorphone and oxymorphone**



Which of the following are lipophilic?

- a) Fentanyl and hydromorphone
- b) Fentanyl and oxymorphone
- c) Hydromorphone and morphine
- d) **Hydromorphone and oxymorphone**

Note: why authors have worked with these in liposomes.



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

How long was analgesia proven with a single dose of liposome-encapsulated hydromorphone was given preemptively in the model in this article?

- a) 1 day
- b) 2 days
- c) 5 days
- d) 7 days



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

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How long was analgesia proven with a single dose of liposome-encapsulated hydromorphone when given after the development of neuropathic pain?

- a) 1 day
- b) 2 days
- c) 5 days
- d) 7 days



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

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Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

True or false. The analgesic time provided by the high dose standard hydromorphone was equal to the single dose of liposome-encapsulated hydromorphone when given after the development of neuropathic pain?



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

True or false. The analgesic time provided by the high dose standard hydromorphone was equal to the single dose of liposome-encapsulated hydromorphone when given after the development of neuropathic pain?

FALSE. Both reversed hyperalgesia. Standard hydromorphone had no lasting effect.

Note: abstract stated standard lasted 90 minutes but didn't see in paper where showed that.



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

This model involves sciatic nerve ligation followed by analgesia test. What is the test?



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

This model involves sciatic nerve ligation followed by an analgesia test. What is the test?

Thermal hyperalgesia—thermal withdrawal latency measurements



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

How long does it take for the hyperalgesia to develop post the sciatic ligation?

- a) 1 day
- b) 3 days
- c) 5 days
- d) 7 days



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

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Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

True or False. In general, neuropathic pain is clinically difficult to treat and responds best to opioids.



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

True or False. In general, neuropathic pain is clinically difficult to treat and responds best to opioids.

False.



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

When are opioids most likely to be effective for neuropathic pain in animals?

- a) **As lesion gets closer to the CNS (central nervous system)**
- b) **As lesion gets further away from the CNS**
- c) **Neither**



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

When are opioids most likely to be effective for neuropathic pain in animals?

- a) As lesion gets closer to the CNS (central nervous system)—effectiveness decreases closer get
- b) **As lesion gets further away from the CNS**
- c) Neither



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

What drugs does neuropathic pain respond best to?



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

What drugs does neuropathic pain respond best to?

Sodium channel blockers such as lidocaine or mexilitine

Drugs inhibit spinal neurotransmission such as gabapentin



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

The response of an animal when given an opioid of crouched appearance of the body and the tail is characteristically rigid and erected (dorsiflexion) on an arched back (shown in picture) is called what?



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone (LEH) Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

The response of an animal when given an opioid of crouched appearance of the body and the tail is characteristically rigid and erected (dorsiflexion) on an arched back is called what?

Straub tail reflex

Animals given the LEH or standard displayed this typical sign that dissipated by 30 minutes. Classical behavior sign of neuroexcitation in rodents.



Smith, Valenzuela, et al "A Single Dose of Liposome-encapsulated Hydromorphone (LEH) Provides Extended Analgesia in a Rat Model of Neuropathic Pain" Comp Med 56(6): 487-492, December 2006

- LEH provided analgesia for at least 5 days when given before hyperalgesia develops
- LEH reversed thermal hyperalgesia for at least 2 days after development
- May be some bolus release of drug from liposomes as saw neuroexcitatory effects-transient (30 minutes)
- Standard hydromorphone did not provide extended analgesia even when given at the same mg/kg dose of the liposome encapsulated product



A study was done to evaluate the effectiveness of ascorbic acid and basic fibroblast growth factor (bFGF) in protecting muscle cells from oxidative stress.

True or False

Both ascorbic acid and bFGF were found effective



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True or False

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TRUE



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True or False

A synergistic effect was observed when both ascorbic acid and bFGF was used.

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True or False

A synergistic effect was observed when both ascorbic acid and bFGF was used.

FALSE therefore, think operate under same pathway

Burdzinska, et al "Sodium Ascorbate and Basic Fibroblast Growth Factor Protect Muscle-derived Cells from H₂O₂-induced oxidative Stress" Comp Med 56(6): 493-501, December 2006

Which protein did the authors suggest was increased or enhanced by ascorbate and bFGF?

- a) Akt kinase
- b) c-Jun protein



Burdzinska, et al "Sodium Ascorbate and Basic Fibroblast Growth Factor Protect Muscle-derived Cells from H₂O₂-induced oxidative Stress" Comp Med 56(6): 493-501, December 2006

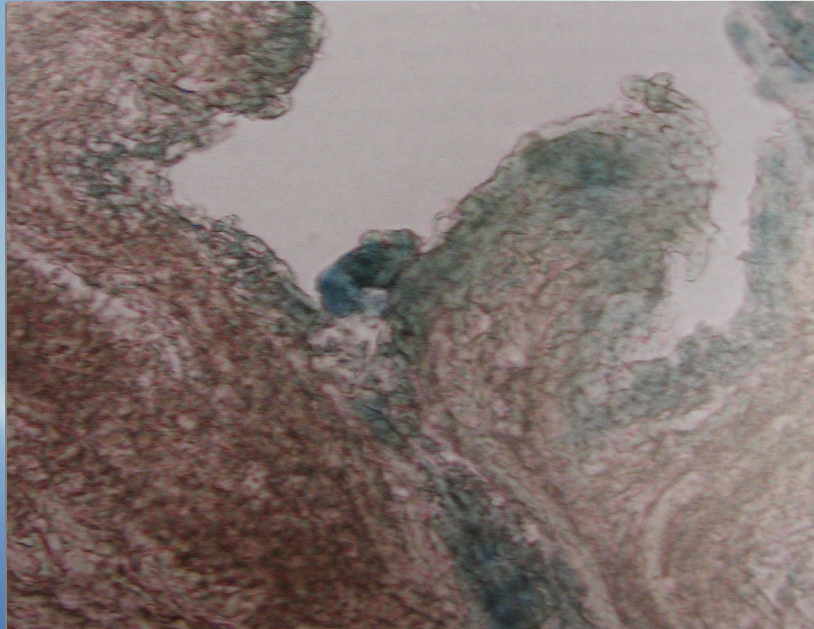
Which protein did the authors suggest was increased or enhanced by ascorbate and bFGF?

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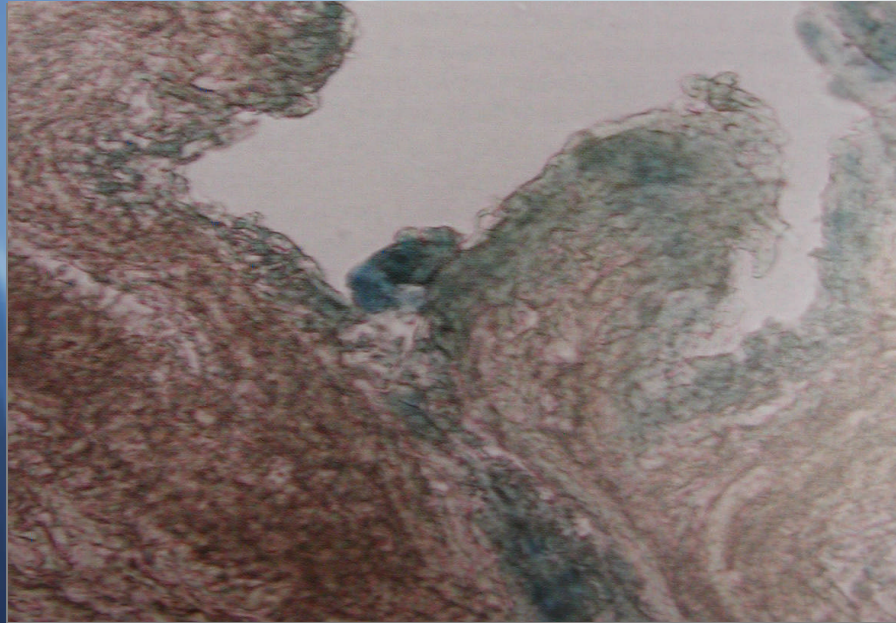


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This section contains muscle derived cells transfected with LacZ containing plasmid and stained with X-Gal. The blue staining indicates the presence of what compound?

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This section contains muscle derived cells transfected with LacZ containing plasmid and stained with X-Gal. The blue staining indicates the presence of what compound?

β-galactosidase



Burdzinska, et al "Sodium Ascorbate and Basic Fibroblast Growth Factor Protect Muscle-derived Cells from H₂O₂-induced oxidative Stress" Comp Med 56(6): 493-501, December 2006

Transfection of cells was done using lipofectamine rather than viral transfection. What is one advantage of doing the transfection this way?



Burdzinska, et al "Sodium Ascorbate and Basic Fibroblast Growth Factor Protect Muscle-derived Cells from H₂O₂-induced oxidative Stress" Comp Med 56(6): 493-501, December 2006

Transfection of cells was done using lipofectamine rather than viral transfection. What is one advantage of doing the transfection this way?

- **Easy to perform**
- **Effective in the presence of serum**
- **Does not affect viability of cells (adenovirus has been shown to enhance cell death post grafting)**



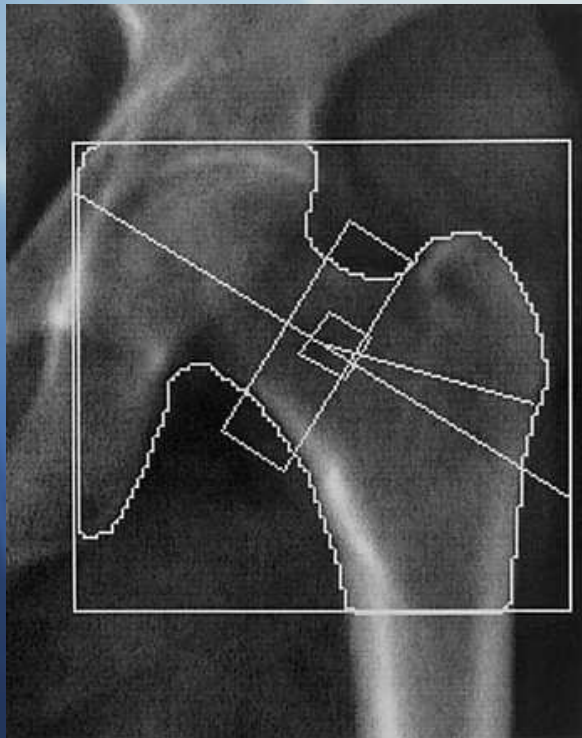
*Hotchkiss, Latendresse, and Ferguson Comp Med 56(6): 501-511, December
2006*

What is Ward's Triangle?



Hotchkiss, Latendresse, and Ferguson "Oral Treatment with Reinoic Acid Decreases Bone mass in Rats" Comp Med 56(6): 501-511, December 2006

- **Ward's triangle - an area in the top part of the femur or thigh bone, near the hip of least dense bone**



Outer rectangle defines global ROI (often described as "total hip"), narrow transverse rectangle orthogonal to the axis of symmetry constitutes the femoral neck, while the Ward "triangle" is the area of least density in a smaller area within a search area centered on the midline at the inferior edge of the femoral neck rectangle.

Rats were treated with all trans-retinoic acid or 13-cis-retinoic acid. What was seen in those treatment with 13-cis retinoic acid?

- a) Spontaneous fractures occurred in the long bones of all rats treated.**
- b) Serum alkaline phosphatase was significantly elevated.**
- c) Female rats demonstrated decreased bone mineral content at both doses used.**
- d) Male rats demonstrated decreased bone mineral content at both doses used.**

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- a) Spontaneous fractures occurred in the long bones of all rats treated.
- b) Serum alkaline phosphatase was significantly elevated.
- c) **Female rats demonstrated decreased bone mineral content at both doses used.**
- d) Male rats demonstrated decreased bone mineral content at both doses used.

Hotchkiss, Latendresse, and Ferguson

True or false

The femur and lumbar spine were equally affected by treatment with all-trans RA.



True or false

The femur and lumbar spine were equally affected by treatment with all-trans RA.

False. The lumbar spine was not affected.

True or false

The femurs of rats showed decreased bone mineral density at both doses of all-trans RA and both doses of 13-cis-RA.



True or false

The femurs of rats showed decreased bone mineral density at both doses of all-trans RA and both doses of 13-cis-RA.

False. Both doses of all-trans-RA and high dose of cis-RA

True or false

Both a decrease in bone area and reduced diaphyseal bone diameter in rats treated with all-trans-RA.

True or False

Both a decrease in bone area and reduced diaphyseal bone diameter in rats treated with all-trans-RA.

True. Retinoids alter modeling of cortical bone and these findings confirmed that retinoic acid inhibits cortical expansion.

Hotchkiss, Latendresse, and Ferguson

What is the technology used to measure bone mineral density and bone mineral content?



Hotchkiss, Latendresse, and Ferguson

What is the technology used to measure bone mineral density and bone mineral content?

Dual-energy X-ray absorptiometry (DXA, DEXA)



Hotchkiss, Latendresse, and Ferguson

Bone strength is a function of what two factors?



Bone strength is a function of what two factors?

bone composition

bone geometry

Hotchkiss, Latendresse, and Ferguson

Which group demonstrated spontaneous fractures?



Which group demonstrated spontaneous fractures?

all-trans-RA –both doses of 10 and 15mg/kg which is lower than previous studies have shown of 70 to 120 mg/kg

All-trans-RA treated rats demonstrated:

- a) decreased trabecular number and decreased trabecular separation
- b) decreased trabecular number and increased trabecular separation
- c) increased trabecular number and decreased trabecular separation
- d) increased trabecular number and increased trabecular separation

All-trans-RA treated rats demonstrated:

- a) decreased trabecular number and decreased trabecular separation
- b) decreased trabecular number and increased trabecular separation**
- c) increased trabecular number and decreased trabecular separation
- d) increased trabecular number and increased trabecular separation

Hotchkiss, Latendresse, and Ferguson

Bone loss may be due to an increase in bone resorption secondary to increase in osteoclasts. What urinary marker has been used to detect bone resorption with rats treated with retinyl palmitate?



Hotchkiss, Latendresse, and Ferguson

Bone loss may be due to an increase in bone resorption secondary to increase in osteoclasts. What urinary marker has been used to detect bone resorption with rats treated with retinyl palmitate?

hydroxyproline



Hotchkiss, Latendresse, and Ferguson

What is the serum marker used in this study that is similar to hydroxyproline to monitor bone resorption?



Hotchkiss, Latendresse, and Ferguson

**What is the serum marker used in this study
that is similar to hydroxyproline to
monitor bone resorption?**

pyridinoline



Hotchkiss, Latendresse, and Ferguson

What is the serum marker used in this study that is similar to hydroxyproline to monitor bone resorption? Pyridinoline

Was it increased in this study?



Hotchkiss, Latendresse, and Ferguson

What is the serum marker used in this study that is similar to hydroxyproline to monitor bone resorption? Pyridinoline

Was it increased in this study?

No. This finding then does not support the hypothesis of an overall increase in bone resorption. It was not possible to determine whether the alkaline phosphatase increase was related to bone formation associated with increase turnover or induction of liver enzyme as there was no difference among groups.



Hotchkiss, Latendresse, and Ferguson

The doses of 13-cis RA used in the rats on a mg/kg basis was significantly higher than mg/kg basis in humans. How did the authors explain the doses they used?



Hotchkiss, Latendresse, and Ferguson

The doses of 13-cis RA used in the rats on a mg/kg basis was significantly higher than mg/kg basis in humans. How did the authors explain the doses they used?

Used doses on mg/kg basis to generate serum concentrations in humans when given 0.5-1 mg/kg orally daily



Hotchkiss, Latendresse, and Ferguson “Oral Treatment with Retinoic Acid Decreases Bone Mass in Rats” Comp Med 56(6): 501-511, 2006

Summary:

- **Both all-trans-RA and 13-cis RA decreased BMC in rat femurs (not seen in spine)**
- **13-cis RA has significantly fewer detrimental effects**
- **13-cis RA used in humans orally**
- **Need further studies on impact**



Doane, Lee, and Sleeper "Electrocardiogram Abnormalities in Captive Chimpanzees (Pan troglodytes)" Comp Med 56(6): 512-518, December 2006

ECG's were examined in chimpanzees. The incidence of cardiac arrhythmia was higher in animals that:

- a) were male**
- b) had hypertension**
- c) had hyperlipidemia**
- d) had hepatitis C**



Doane, Lee, and Sleeper

ECG's were examined in chimpanzees. Incidence of cardiac arrhythmia was higher in chimpanzees that:

- a) **were male**
- b) had hypertension
- c) had hyperlipidemia
- d) had hepatitis C



Mortality was significantly higher in those chimps demonstrating what type of arrhythmia?

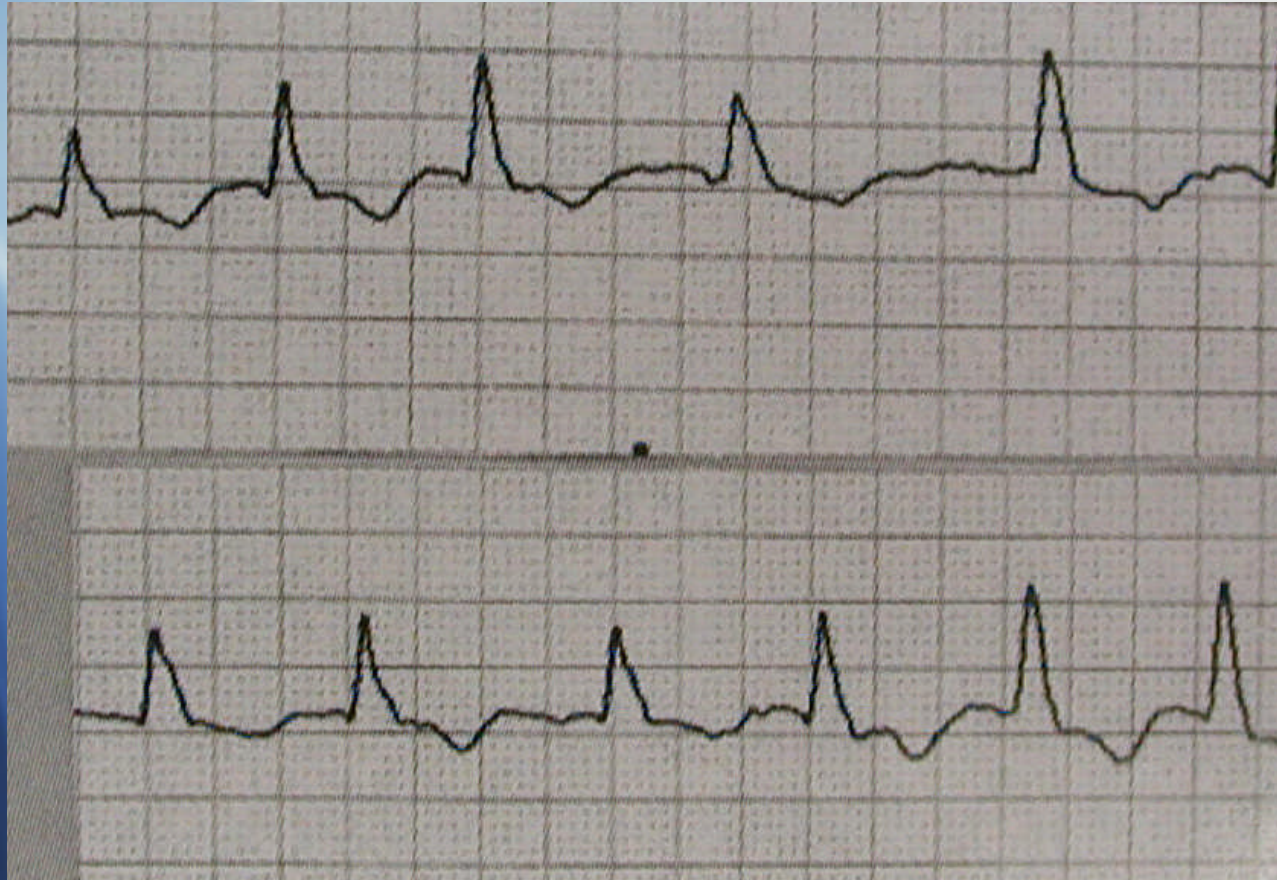
- a) atrial fibrillation**
- b) bradycardia**
- c) supraventricular arrhythmia**
- d) ventricular arrhythmia**

Mortality was significantly higher in those chimps demonstrating what type of arrhythmia?

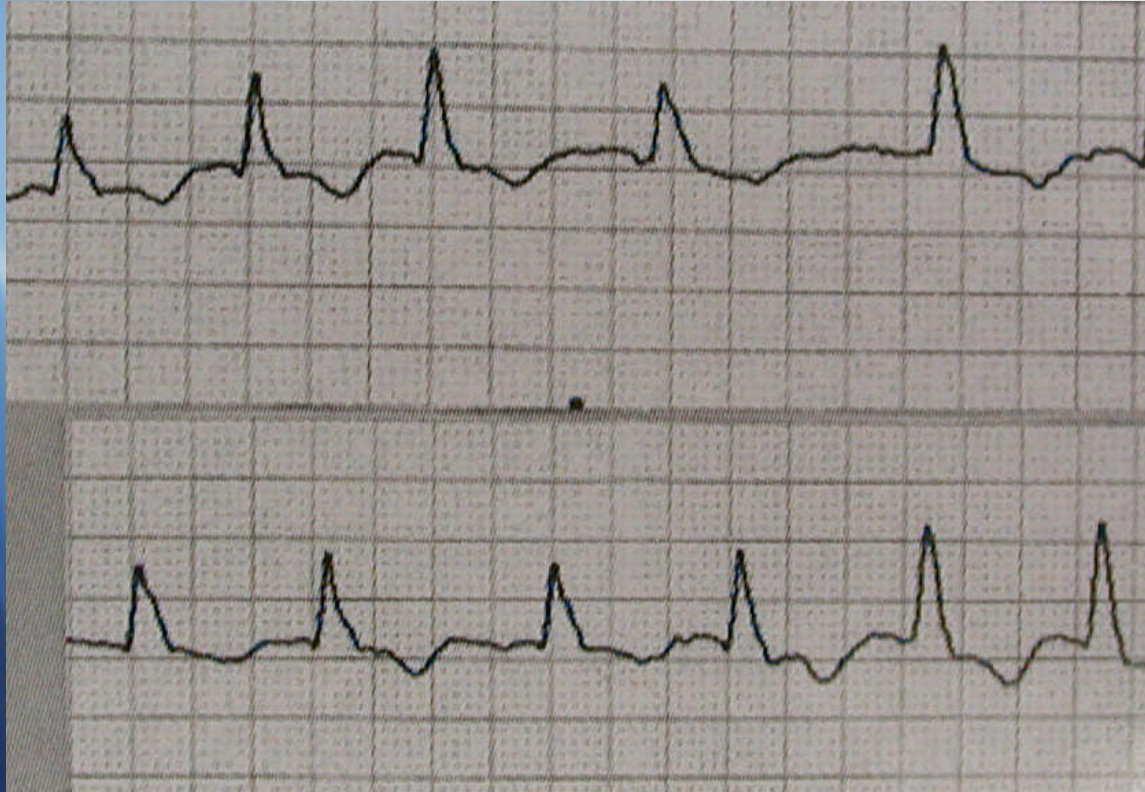
- a) atrial fibrillation
- b) bradycardia
- c) supraventricular arrhythmia
- d) **ventricular arrhythmia**

Doane, Lee, and Sleeper

What is the abnormality in this ECG?



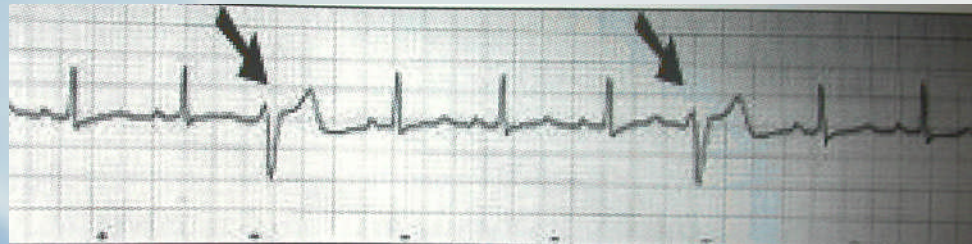
What is the abnormality in this ECG?



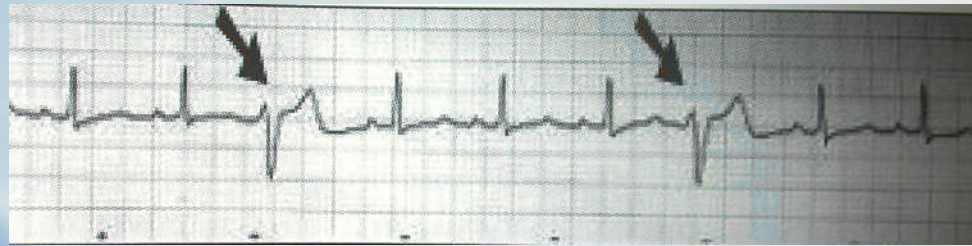
Atrial fibrillation, irregular R-R intervals (figure 7 of article)

Doane, Lee, and Sleeper

What is the abnormality in this ECG?



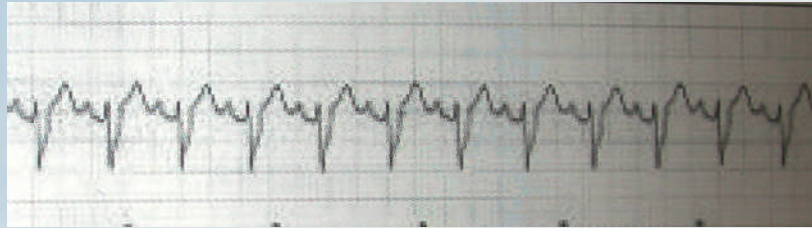
What is the abnormality in this ECG?



Premature ventricular contractions (figure 1)

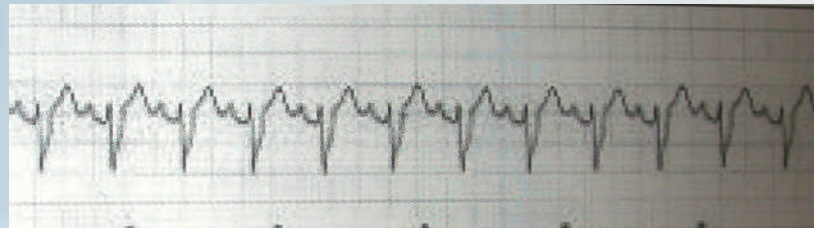
Doane, Lee, and Sleeper

What is the abnormality in this ECG?



Doane, Lee, and Sleeper "Electrocardiogram Abnormalities in Captive Chimpanzees (Pan troglodytes)" Comp Med 56(6): 512-518, December 2006

What is the abnormality in this ECG?



Right bundle branch block (notched and wide S waves) Figure 5

Comparative Medicine
57(1)

February 2007
slides 187-399



Carroll, Guillot, and Qureshi

*“Mammalian Model Hosts of Cryptococcal Infection” Comp Med 57(1): 9-17,
2007*

On the basis of biologic, morphologic, and phenotypic criteria, it is generally accepted that the genus *Cryptococcus* consists of two species. What are they?



On the basis of biologic, morphologic, and phenotypic criteria, it is generally accepted that the genus *Cryptococcus* consists of two species. What are they?

C. neoformans serotypes A, D and AD

C. gattii serotypes B and C

Cryptococcus spp is classified as what Biosafety Level?

- a) BSL-1
- b) BSL-2
- c) BSL-3
- d) BSL-4

Cryptococcus spp is classified as what Biosafety Level?

- a) BSL-1
- b) **BSL-2**
- c) BSL-3
- d) BSL-4

Carroll, Guillot, and Qureshi

*"Mammalian Model Hosts of Cryptococcal Infection" Comp Med 57(1): 9-17,
2007*

C. neoforms' pathogenesis is mediated by four main virulence factors. What are they?



C. neoforms' pathogenesis is mediated by four main virulence factors. What are they?

- Ability to grow at 37° C
- Synthesis of an extracellular capsule
- Production of melanin
- Secretion of degradative enzymes

What enzyme is involved in the production of melanin from diphenolic compounds?

- a) Laccase**
- b) Lactase**
- c) Melanase**
- d) Maltase**

What enzyme is involved in the production of melanin from diphenolic compounds?

- a) **Laccase**
- b) Lactase
- c) Melanase
- d) Maltase

**Which species listed is more naturally resistant to
C. neoforms infection?**

- a) **Mouse**
- b) **Rat**
- c) **Guinea pig**
- d) **Rabbit**

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- a) Mouse
- b) Rat
- c) Guinea pig
- d) **Rabbit**

Carroll, Guillot, and Qureshi

*"Mammalian Model Hosts of Cryptococcal Infection" Comp Med 57(1): 9-17,
2007*

What is one reason that is attributable to the rabbit's more natural resistance?



What is one reason that is attributable to the rabbit's more natural resistance?

**Relatively higher normal body temperature
(39.3 to 39.5°C)**

Carroll, Guillot, and Qureshi Comp Med 57(1): 9-17, 2007

What are some advantages of using the rabbit then?



What are some advantages of using the rabbit then?

Model of cryptococcal meningitis. Pathology similar to humans, larger animal to repeat CSF sampling on, docile nature, and fact most humans get meningitis are immunocompromised so in general humans have more natural resistance.

True/False

Transmission of *C. neoforms* to sentinel animals housed with infected mice has been documented.

True/False

Transmission of *C. neoforms* to sentinel animals housed with infected mice has been documented.

FALSE

True or False

Female guinea pigs have been shown to be more resistant to *C. neoforms* than males following intraperitoneal infection.

True or False

Female guinea pigs have been shown to be more resistant to *C. neoforms* than males following intraperitoneal infection.

True and this reflects what is observed in humans.

Carroll, Guillot, and Qureshi
"Mammalian Model Hosts of Cryptococcal Infection" Comp Med 57(1): 9-17,
2007

Three inbred strains of mice and rats were compared after *C. neoforms* infection. Alveolar macrophages were depleted three days before infection. Which was demonstrated?

- a) Mice demonstrated decreased fungal burden and rats demonstrated increased fungal burden in the lungs.
- b) Mice demonstrated increased fungal burden and rats demonstrated decreased fungal burden in the lungs
- c) All six strains demonstrated reduced fungal burden in the lungs
- d) All six strains demonstrated increased fungal burden in the lungs



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- b) Mice demonstrated increased fungal burden and rats demonstrated decreased fungal burden in the lungs
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The C57BL/6 mouse is a strain considered susceptible to *C. neoforms*. How does its immune response to infection differ from those strains considered resistant?

The C57BL/6 mouse is a strain considered susceptible to *C. neoforms*. How does its immune response to infection differ from those strains considered resistant?

Development of Interleukin-5 dependent immune response (more towards Th2 response?)

True/False.

**In contrast to inbred mouse strains,
immunocompetent rats do not predictably
disseminate a pulmonary infection after
intratracheal instillation.**

True/False.

**In contrast to inbred mouse strains,
immunocompetent rats do not predictably
disseminate a pulmonary infection after
intratracheal instillation.**

True

Which agent listed has been shown to promote Cryptococcal growth when given at the time of infection, but decreases fungal burden when administered to chronically infected rats?

- a) Transforming Growth Factor beta-1
- b) Tumor Necrosis Factor alpha
- c) Interleukin-12
- d) Interferon gamma

Which agent listed has been shown to promote Cryptococcal growth when given at the time of infection, but decreases fungal burden when administered to chronically infected rats?

- a) **Transforming Growth Factor beta-1**
- b) Tumor Necrosis Factor alpha
- c) Interleukin-12
- d) Interferon gamma

He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

What is the CDC Category A list?



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

What is the CDC Category A list?

Agents designated as having the greatest potential to induce significant negative impact on public health. All agents are also agents that pose a threat to animal and plant health and safety.



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
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**What two agencies regulate the possession, use
and transfer of these agents?**



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CDC and USDA



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Which bacterial agent is not on the list?

- a) Anthrax
- b) Botulism
- c) Brucellosis
- d) Plague
- e) Tularemia



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Which strain of mouse listed is the most resistant to *F. tularensis*?

- a) CBA
- b) C3H
- c) SM
- d) SJL



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

Which strain of mouse listed is the most resistant to *F. tularensis*?

- a) CBA
- b) C3H
- c) SM
- d) **SJL**

Note: Sex differences also reported and vary with strain. No differences between Balb/C and C57BL/6 strains, but differences seen in CBA and CB6F1 when mice vaccinated and later challenged



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

How do rat models differ from mouse models with regards to *Yersinia pestis* disease?



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

How do rat models differ from mouse models with regards to *Yersinia pestis* disease?

Brown Norway develops many clinical signs and pathological changes such as development of buboes not seen in mice.



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

Which agent listed in Category A is the mouse bioassay the most sensitive and specific measurement of toxin activity?

- a) Anthrax**
- b) Botulism**
- c) Tularemia**
- d) Plague**



He, Rush, Liepman, Xiang, and Colby
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Which agent listed in Category A is the mouse bioassay the most sensitive and specific measurement of toxin activity?

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He, Rush, Liepman, Xiang, and Colby
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What are the three basic elements of containing risk associated with hazardous agents?



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

**What are the three basic elements of containing
risk associated with hazardous agents?**

Facility design

Laboratory practice and technique

Safety equipment



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

Which category agent requires a 3-step decontamination process?

- a) **B. anthracis**
- b) **C. botulinum**
- c) **F. tularensis**
- d) **Y. pestis**



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
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- c) F. tularensis
- d) Y. pestis



He, Rush, Liepman, Xiang, and Colby
“Pathobiology and Management of Laboratory Rodents Administered CDC
Category A Agents” Comp Med 57(1): 18-32, 2007

Which two agents listed in Category A require BSL4 practices?

- a) **Vaccinia and Lassa viruses**
- b) **Vaccinia and Ebola viruses**
- c) **Lassa and Ebola viruses**
- d) **Lassa and B. anthracis**
- e) **Lassa and Y. pestis**



He, Rush, Liepman, Xiang, and Colby
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Which two agents listed in Category A require BSL4 practices?

- a) Vaccinia and Lassa viruses
- b) Vaccinia and Ebola viruses
- c) **Lassa and Ebola viruses**
- d) Lassa and B. anthracis
- e) Lassa and Y. pestis



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<http://helab.bioinformatics.med.umich.edu/hazard>

Internet based database designed to assist those who need information on animal studies with certain hazardous agents.



Stump and VandeWoude

*“Animal Models for HIV AIDS: A Comparative Review” Comp Med 57(1):33-43,
2007*

Which three genera of retroviridae are considered simple retroviruses and encode only gag, pro, pol, and env genes?



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Which three genera of retroviridae are considered simple retroviruses and encode only gag, pro, pol, and env genes?

Alpharetrovirus

Betaretrovirus

Gammaretrovirus



Which genera of retroviridae cause cytopathic effects in vitro and are clinically characterized by slowly progressing disease?

- a) Alpharetrovirus
- b) Deltaretrovirus
- c) Lentivirus
- d) Spumavirus

Which genera of retroviridae cause cytopathic effects in vitro and are clinically characterized by slowly progressing disease?

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Which virus is not in the lentivirus group?

- a) Human immunodeficiency virus**
- b) Simian immunodeficiency virus**
- c) Feline immunodeficiency virus**
- d) Feline leukemia virus**
- e) Equine infectious anemia virus**

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All lentiviruses infect what cell type?

- a) T-cells**
- b) B-cells**
- c) Neutrophils**
- d) Macrophages**



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- c) Neutrophils
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Stump and VandeWoude

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**Which lentivirus is the only one known to be
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2007*

**Which lentivirus is the only one known to be
vector-borne/transmitted?**

Equine Infectious Anemia Virus. Note: also
varies in that it causes acute, recurrent disease verses chronic



Stump and VandeWoude

*“Animal Models for HIV AIDS: A Comparative Review” Comp Med 57(1):33-43,
2007*

Which lentivirus is most similar to HIV in that it primarily targets CD4 cells?

- a) SIV
- b) FIV
- c) BIV
- d) MVV



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*“Animal Models for HIV AIDS: A Comparative Review” Comp Med 57(1):33-43,
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Which lentivirus is most similar to HIV in that it primarily targets CD4 cells?

- a) SIV
- b) **FIV**
- c) BIV
- d) MVV

Note: FIV uses CXCR4 as entry receptor and CD134/OX40L as binding receptor—which are all on CD4+T cells



Stump and VandeWoude

*“Animal Models for HIV AIDS: A Comparative Review” Comp Med 57(1):33-43,
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Which Simian Immunodeficiency virus (SIV) is considered the most important PRIMATE model of HIV disease?

- a) **SIV_{smm}**
- b) **SIV_{cpz}**
- c) **SIV_{mac}**
- d) **SIV_{bab}**



Stump and VandeWoude

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- c) **SIV_{mac}**
- d) SIV_{bab}

Results in clinical and immunological manifestations closely mirroring human AIDS



Olivadoti, Toth, Weinberg, and Opp Comp Med 57(1): 44-50, 2007

Gammaherpesvirus 68 of mice has been proposed as a model for what human virus?



Olivadoti, Toth, Weinberg, and Opp

Comp Med 57(1): 44-50, 2007

Gammaherpesvirus 68 of mice has been proposed as a model for what human virus?

Epstein-Barr Virus

Note: some differences. EBV is gamma-1-herpesvirus or lymphocryptovirus where MuGHV is gamma-2-herpesvirus or rhadinovirus.



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

What other group of primates can Epstein-Barr virus infect?

- a) **New world primates**
- b) **Old world African primates**
- c) **Old world Asian Primates**
- d) **All the above**



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Olivadoti, Toth, Weinberg, and Opp
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What cell type is infected?



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

What cell type is infected?

B-cells, primarily

**Initially alveolar epithelial and pulmonary
mononuclear cells**



Olivadoti, Toth, Weinberg, and Opp

“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

EBV can go latent in which viral gene expression is restricted and reduced. An important factor in this process is transformation of the linear viral genome into the circular form which is called _____?



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“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

EBV can go latent in which viral gene expression is restricted and reduced. An important factor in this process is transformation of the linear viral genome into the circular form which is called an episome



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

True/False.

**The natural route of infection of Murine
Gammaherpes Virus (MuGHV) is the respiratory
tract.**



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

True/False.

The natural route of infection of Murine Gammaherpes Virus (MuGHV) is the respiratory tract.

False. Not known



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

True/False.

**Virus transmission has been reported between
infected and uninfected mice.**



Olivadoti, Toth, Weinberg, and Opp
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True/False.

**Virus transmission has been reported between
infected and uninfected mice.**

False



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

In what organ is MuGHV latency studied?



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
~~Infections and Related Diseases” Comp Med 57(1): 44-50, 2007~~”

In what organ is MuGHV latency studied?

Spleen

**Latency associated with splenomegaly,
polyclonal B cell activation, autoantibody
production, and lymphocytosis (primarily
CD8+ Tcell)**



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

**What cytokine has been associated with the fatigue
in humans with EBV?**



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

**What cytokine has been associated with the fatigue
in humans with EBV?**

**IFN-gamma. B cells from patients with latent
infection express it where those from
noninfected people do not.**



Olivadoti, Toth, Weinberg, and Opp
“Murine Gammaherpesvirus 68: A Model for the Study of Epstein-Barr Virus
Infections and Related Diseases” Comp Med 57(1): 44-50, 2007

Which strain showed greater induction of chemokines and greater viral gene expression during the lytic phase of infection with MuGHV?

- a) A/J
- b) BALB/c
- c) C57BL/6
- d) C3H



Olivadoti, Toth, Weinberg, and Opp
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- c) C57BL/6
- d) C3H

Note: latent viral load was similar 15 day after infection suggesting establishment of latency was same in Balb/C and B6



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

What is a nested PCR?



What is a nested PCR?

Nested PCR means that **two pairs of PCR primers** were used for a single locus.

The first pair amplifies the locus as seen in any PCR experiment. The second pair of primers (nested primers) bind within the first PCR product and produce a second PCR product that will be shorter than the first one. The logic behind this strategy is that if the wrong locus were amplified by mistake, the probability is very low that it would also be amplified a second time by a second pair of primers.



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

Which PCR assay was found to detect more MPV?



Agca, et al

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Nested PCR



Agca, et al

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Embryos were collected from MPV infected mice. The mice were of various age ranges. Which age group was MPV **NOT** detected by nested PCR?

- a) 4-6 week old mice
- b) 4-8 week old mice
- c) 8-10 week old mice
- d) 10-12 week old mice



Agca, et al

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Agca, et al

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**Embryos were collected from MPV infected mice.
Was MPV detection (by nested PCR) eliminated
by extensively washing the embryos?**



Agca, et al

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**Embryos were collected from MPV infected mice.
Was MPV detection eliminated by extensively
washing the embryos?**

No, embryos were still positive by nested PCR



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

Sperm was collected from 10-12 week old MPV infected male mice. 50% of the mice had sperm positive by nested PCR for MPV. Did Percoll separation decrease this incidence?



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

Sperm was collected from 10-12 week old MPV infected male mice. 50% of the mice had sperm positive by nested PCR for MPV. Did Percoll separation decrease this incidence?

No—14/25 sperm positive



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

Oocytes were collected from 10-12 week old mice infected with MPV. 25% of the mice had MPV positive oocytes after standard washing was done of the oocytes (by nested PCR). Did extensive (extra) washing decrease the incidence?



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

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Yes-negative by both primary and nested PCR



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

**Standard washing of oocytes has been reported
NOT to be sufficient to remove what other
rodent virus from adhering to the zona
pullicida?**



Agca, et al

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**Standard washing of oocytes has been reported
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Sendai virus on mouse oocytes



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

Has vertical transmission of MPV been demonstrated?



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

Has vertical transmission of MPV been demonstrated?

Not yet, but feel potential is there



Agca, et al

“Detection of Mouse Parvovirus in Mus musculus Gametes, Embryos, and Ovarian Tissues by Polymerase Chain Reaction Assay” Comp Med 57(1): 51-56, 2007

Additional Notes:

- Ovarian tissue was also positive
- Detection of antigen, does not necessarily mean infection-further studies are ongoing
- Emphasize importance of testing offspring that are reconstituted (don't assume “clean”)



Eaton, et al. "A Reproducible Scoring System for Quantification of Histologic Lesions of Inflammatory Disease in Mouse Gastric Epithelium" Comp Med 57(1): 57-65, 2007

Summary:

Scoring system based on percent of microscopic fields (viewed at 200x) that they saw lesions.

Lesions counted: gastritis, neutrophilic infiltration, epithelial metaplasia

Agent: Helicobacter pylori



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

Study evaluated shedding time with MPV in Balb/C and SCID mice. Also looked at whether pregnancy and lactation affected viral load or transmission of MPV.



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

BALB/C and SCID mice were oronasally inoculated with MPV1 within 24 hours of birth, weaned at 4 weeks of age, and housed in same sex groups per cage. Some of the mice euthanized 12 weeks to look for viral DNA. Which is correct?

- a) Both BALB/C and SCID mice had high levels of viral DNA in lymphoid tissues
- b) BALB/C had high levels and SCID mice had low levels of viral DNA in lymphoid tissue
- c) BALB/C had low levels and SCID mice had high levels of viral DNA in lymphoid tissue
- d) Both BALB/C and SCID mice had low levels of viral DNA in lymphoid tissue



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Did not alter viral load in feces

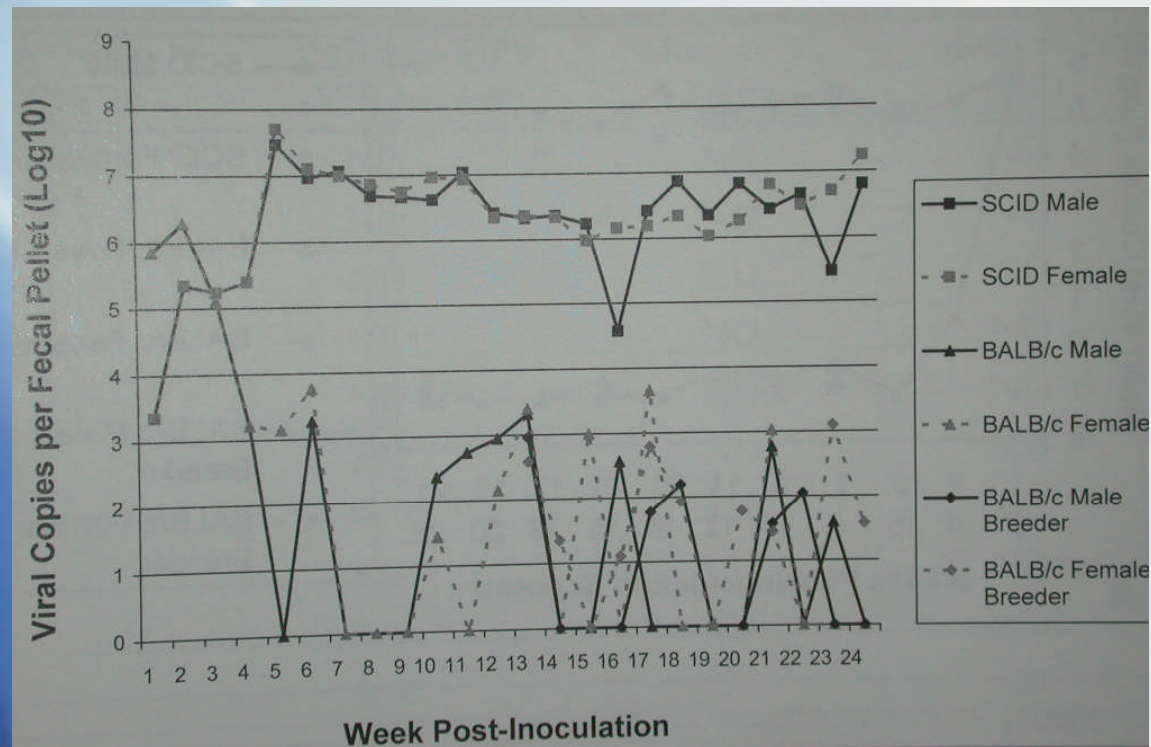


Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

Viral particle loads in feces: increased copies of viral DNA in SCID mice to week 6 and then held steady

BALB/c: highest levels detected in first 3 weeks then fell to 10³ copies or less for rest of the study



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

Sentinel mice were exposed to soiled bedding from infected male and female SCID mice from study start. How long was sero-conversion demonstrated?

- a) 2 weeks post infection
- b) 6 weeks post infection
- c) 18 weeks post infection
- d) Seroconversion of the sentinels did not take place



Besselsen, et al

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- a) **2 weeks post infection**
- b) 6 weeks post infection
- c) 18 weeks (duration of the study)
- d) Seroconversion of the sentinels did not take place

Note: low levels of viral DNA was intermittently detected in lymphoid tissues of sentinel mice post weeks 3-22.



Besselsen, et al
“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

Note:

Sentinels placed on soiled bedding of the breeding BALB/c mice did not seroconvert; however did see low levels viral DNA intermittently in lymphoid tissue



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

At 26 weeks post-inoculation, the naïve breeding partners which had been housed with previously infected mice were euthanized. Which is true?

1. High levels of viral DNA were detected in lymphoid tissue of all naïve SCID mice paired with previously infected SCID partner
2. High levels of viral DNA were detected in lymphoid tissue of all naïve BALB/c mice paired with previously infected BALB/c partner
3. Seroconversion was seen in the naïve BALB/c paired with previously infected BALB/c partner
4. All the above are correct



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

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2. High levels of viral DNA were detected in lymphoid tissue of all naïve BALB/c mice paired with previously infected BALB/c partner
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4. All the above are correct



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

An antibody response to which antigen suggests a productive infection with MPV because the response develops after virus entry and transcription?

1. rNS1
2. MPV rVP2
3. Both responses are required to suggest a productive infection
4. None of the above



Besselsen, et al

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“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

Summary:

- Transmission through soiled bedding to sentinels correlated well with viral fecal loads
- SCIDs infected as neonates persistently shed high levels of virus which was transmitted by both direct contact and soiled bedding



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

Summary:

- Sentinels exposed to BALB/c soiled bedding seroconverted only during the first 2 week inoculation exposure period
- Low levels of MPV DNA intermittently detected in lymphoid tissues of naïve mice exposed to infected BALB/c or soiled bedding suggesting adaptive immune response substantially reduces fecal shedding but does not eliminate it



Besselsen, et al

“Temporal Transmission Studies of Mouse Parvovirus 1 in BALB/c and C.B-17/Icr-Prkdc^{scid} Mice” Comp Med 57(1): 66-73, 2007

Summary:

- Changes with pregnancy and lactation do not alter fecal shedding in immunocompetent mice
- Seroconversion of several 6 week old progeny of infected male mice occurred, suggesting a productive infection in these mice
- Progeny of infected female BALB/c had high antibody levels consistent with transfer of maternal antibody.
- At 6 weeks, it was difficult to rule in/out the antibody from maternal vs productive infection



Thomas III, ML, et al
“Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute Virus” Comp Med 57(1): 74-81, 2007

Male and female B6NCr mice were housed 4/cage and infected with MMV. Blood and feces taken for analyses post inoculation. How many days did it take for all males to seroconvert?

- a) 8 days
- b) 16 days
- c) 28 days
- d) Not all seroconverted



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- a) 8 days
- b) 16 days
- c) 28 days
- d) **Not all seroconverted**-only 9/16 seroconverted by 28 days.



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9-12 days (note shorter than that reported for natural infection)



Thomas III, ML, et al
“Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute Virus” Comp Med 57(1): 74-81, 2007

Lactating dams were inoculated with MMV. What percent of the dams sero-converted by 28 days?

1. 0%
2. 25%
3. 50 %
4. 100%



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"Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute
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1. 0%
2. 25%
3. 50 %
4. **100%--by day 16**



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Lactating dams were inoculated with MMV. What percent of the **pups** seroconverted during the study?

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2. 25%
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Pups from lactating dams were inoculated with MMV. What percent of the dams seroconverted by 28 days?

- 0%
- 25%
- 50%
- **100% by day 28**



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Pups from lactating dams were inoculated with MMV. What percent of the pups seroconverted by the end of the study?

1. 0%
2. 25%
3. 50%
4. 100%



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Pups from lactating dams were inoculated with MMV. What percent of the pups seroconverted by the end of the study?

1. 0%
2. 25%
3. 50%
4. **100% by day 14**



Thomas III, ML, et al
“Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute Virus” Comp Med 57(1): 74-81, 2007

Males and females seropositive to MMV were paired 6 weeks after initial infection. Pups were periodically removed, euthanized, and tested serologically for MMV. What cumulative percent tested positive for the duration of the study?

- 1. 0%**
- 2. 25%**
- 3. 50%**
- 4. 100%**



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“Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute Virus” Comp Med 57(1): 74-81, 2007

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1. **0%**
2. 25%
3. 50%
4. 100%



Thomas III, ML, et al
“Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute Virus” Comp Med 57(1): 74-81, 2007

Sentinels were placed on dirty bedding 3 times a week for 12 days. How long did it take for sentinels to seroconvert?



Thomas III, ML, et al
“Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute Virus” Comp Med 57(1): 74-81, 2007

How long did it take for sentinels to seroconvert?

48 days and only males seroconverted

Reviewer TB note: Think stress of fighting is a factor?



Thomas III, ML, et al
“Gender Influences Infectivity in C57BL/6 Mice Exposed to Mouse Minute Virus” Comp Med 57(1): 74-81, 2007

Notes:

Study indicated that MMV is self limiting so stop breeding for 6-8 weeks, don't mix litters, etc

Be careful of strains that may be immunocompromised

Suggest using male mice for detection or use a strain known to be sensitive to MMV



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007

This study was undertaken to better define this fatal infection model of influenza. Where was the primary tissue pathology?

- a) Blood
- b) Brain
- c) Liver
- d) Lung

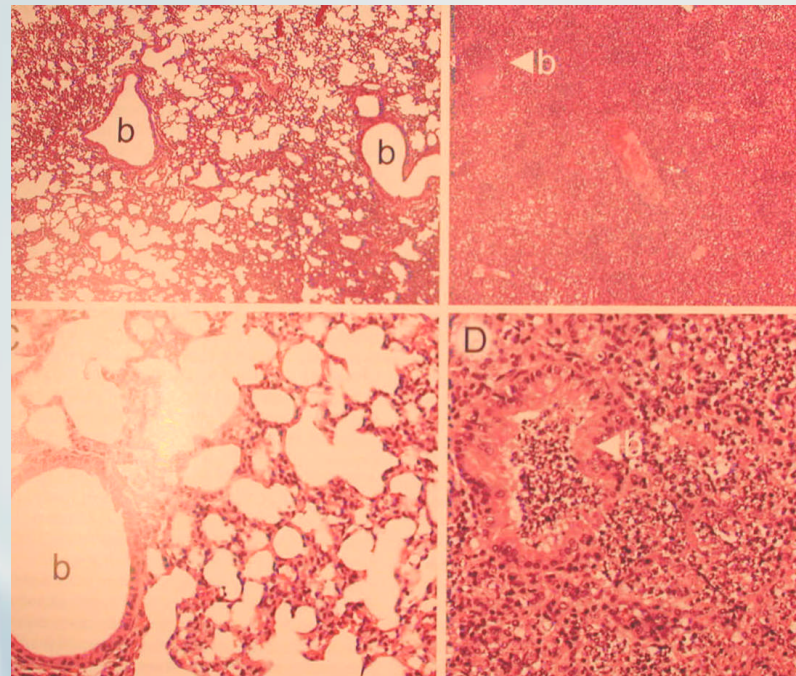


Smith, MW, et al

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control

infected



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007

Which molecules were elevated in both serum and lung in both groups of animals exposed to bacteria (PBS then bacteria or virus then bacteria)?

- a) IL1- β and TNF α
- b) IL1- β and IL-6
- c) IL1- β and KC
- d) TNF α and KC
- e) IL-6 and KC



Smith, MW, et al

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- d) TNF α and KC
- e) **IL-6 and KC**



Smith, MW, et al

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Which molecules were significantly elevated in the group given virus and bacteria over other groups?

- a) IL1- β and TNF α
- b) IL10 and MIP1 α
- c) IL1- β and IL-6
- d) IL-6 and IL10
- e) IL10 and KC



Smith, MW, et al

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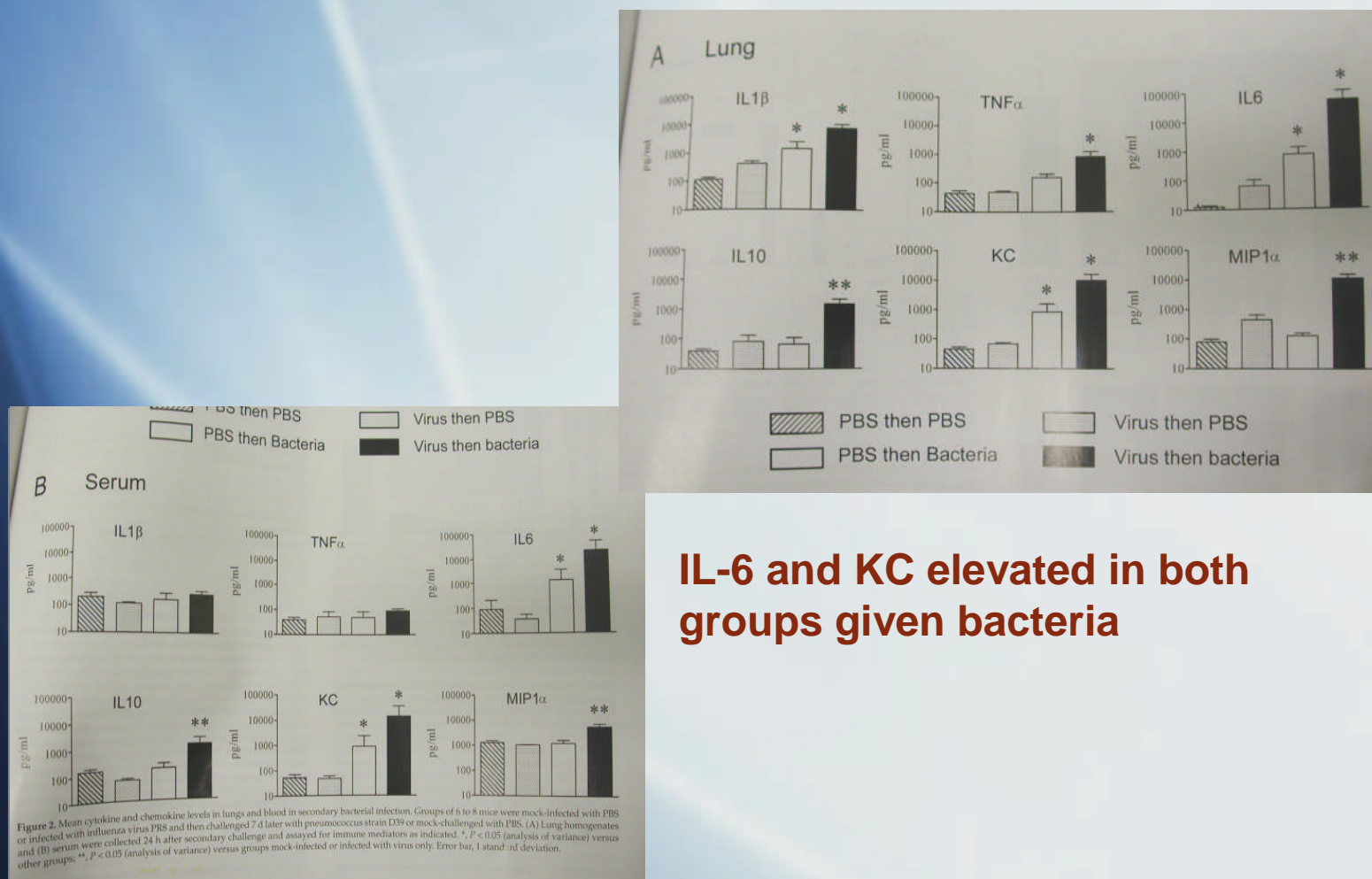
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- b) **IL10 and MIP1 α**
- c) IL1- β and IL-6
- d) IL-6 and IL10
- e) IL10 and KC



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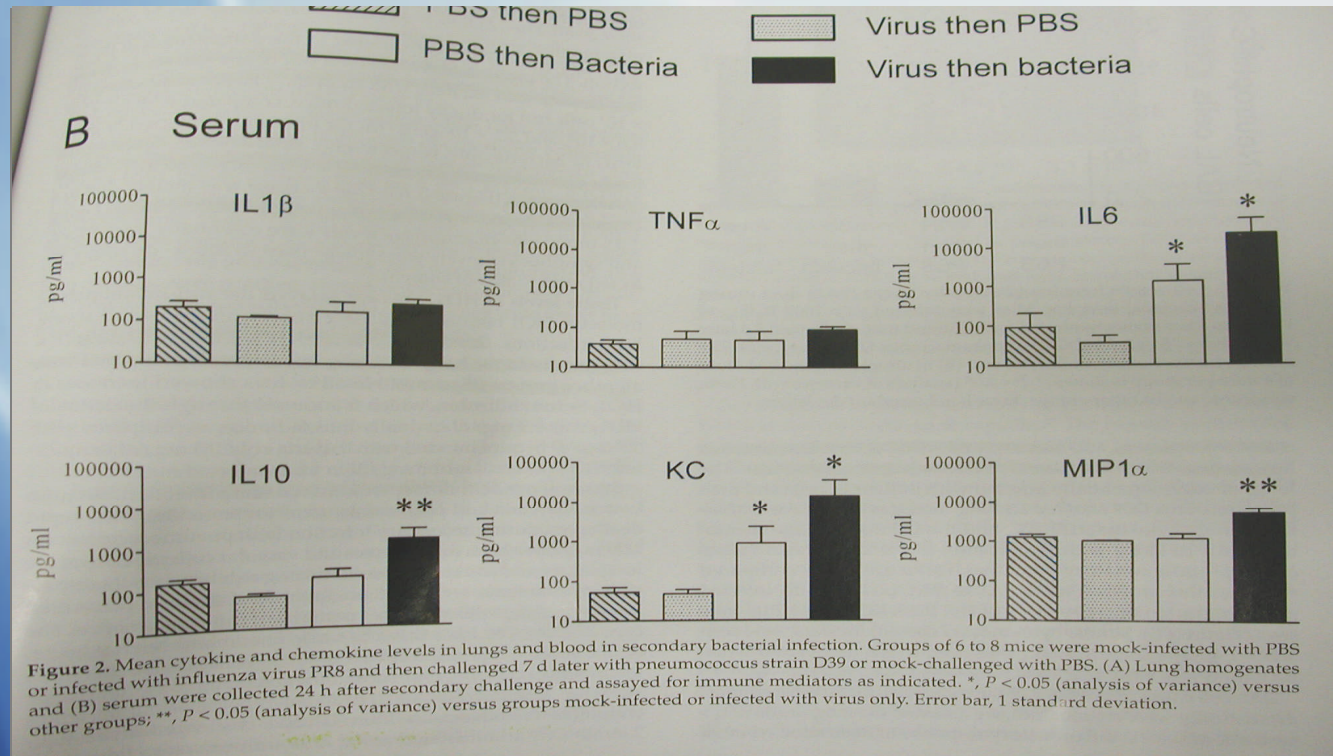


IL-6 and KC elevated in both groups given bacteria



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” *Comp Med* 57(1): 82-89, 2007



IL10 and MIP1 α elevated in group that received virus plus bacteria



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007

Which is true regarding the peripheral white blood cell count in influenza + bacteria infected mice?

- a) **Cell count was elevated and due to neutrophil increase**
- b) **Cell count was elevated and due to lymphocyte increase**
- c) **Cell count was decreased due to lymphopenia**
- d) **Cell count was not changed**



Smith, MW, et al

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Smith, MW, et al

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Which is true regarding the bronchial-alveolar lavage cell count in influenza + bacteria infected mice?

- a) Cell count was elevated and due to neutrophil increase
- b) Cell count was elevated and due to lymphocyte increase
- c) Cell count was decreased due to lymphopenia
- d) Cell count was not changed



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007

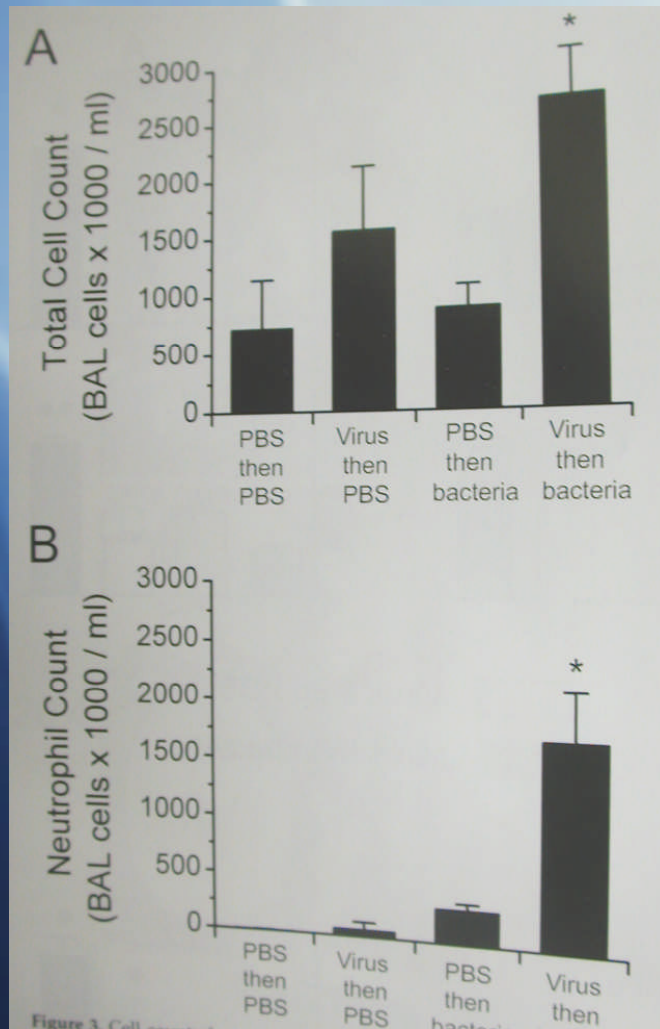
Which is true regarding the bronchial-alveolar lavage cell count in influenza + bacteria infected mice?

- a) **Cell count was elevated and due to neutrophil increase**
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Smith, MW, et al

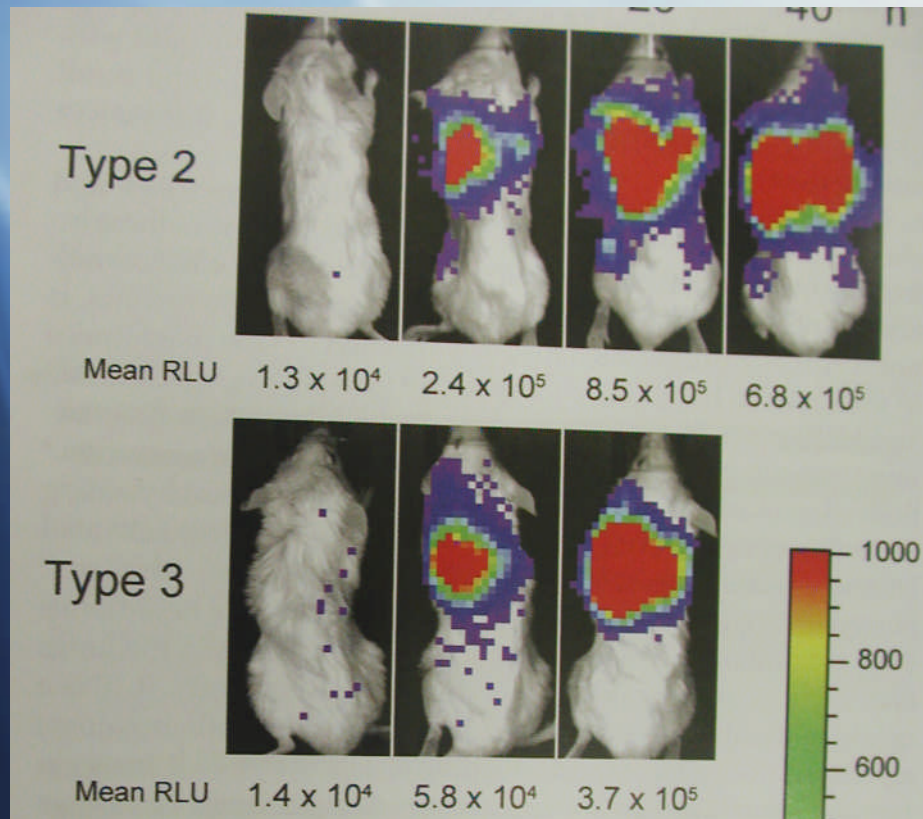
“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007



Cell counts in BAL increased due to neutrophil increase in those given influenza + bacteria

Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007

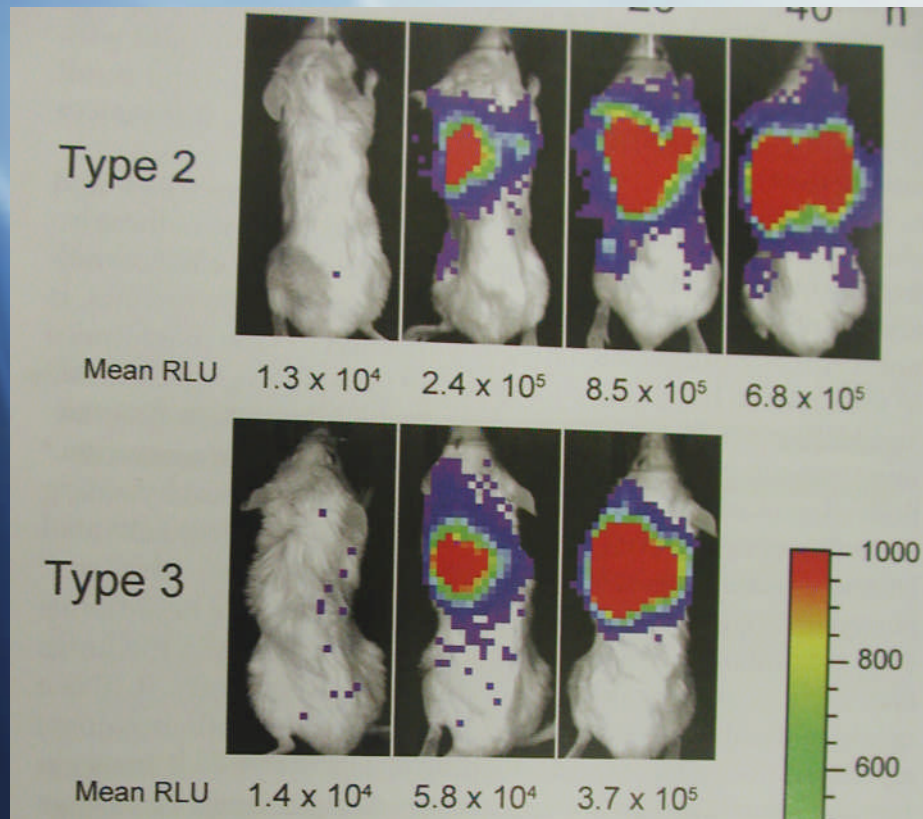


Why do these mice “light up”?



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007



Why do these mice “light up”?

Bacteria has been transformed with luciferase so that they would emit light



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007

Notes:

Pathogenesis of the fatal infection is massive pneumonia with local and systemic inflammation (not bacteremia)

TNF α and IL1 β increased in lung but not blood consistent with localization of inflammation to this site

KC and MIP1 α enhance recruitment of neutrophils and macrophages to site



Smith, MW, et al

“Induction of Pro- and Anti-inflammatory Molecules in a Mouse Model of Pneumococcal Pneumonia after Influenza” Comp Med 57(1): 82-89, 2007

Emerging concept is that there needs to be a balance of anti- and pro-inflammatory activity for resolution of infection and survival. In this case both anti- and pro-inflammatory molecules lead to problem of host not being able to clear organism.



Smith, PC et al

“Reliability of Soiled Bedding Transfer for Detection of Mouse Parvovirus and Mouse Hepatitis Virus”

Comp Med 57 (1): 90-96, 2007

In one study in this paper, MHV or MPV virus spiked feces was placed in 400 ml of autoclaved bedding. Sentinels were placed in these cages for 4 hours, 3 days or 7 days, then tested for antibodies 22 days after exposure.

At the highest MPV virus dose used; what percent of the sentinels converted at 4 hours?



Smith, PC et al

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100%



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At the highest MPV virus dose used; what percent of the sentinels converted at 3 days?



Smith, PC et al

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100%



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100%



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At the highest MHV virus dose used; what percent of the sentinels converted at 4 hours?



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50%



Smith, PC et al

*“Reliability of Soiled Bedding Transfer for Detection of Mouse Parvovirus and
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0% also true at 7 days

Virus	No. of ID ₅₀ added to bedding	No. of seropositive sentinels among the 4 animals placed on the bedding at the indicated time after adding virus		
		4 h	3 d	7 d
MPV	6	1	0	2
	30	2	4	2
	150	4	4	4
MHV	120	0	0	0
	600	0	0	0
	3000	2	0	0



Smith, PC et al

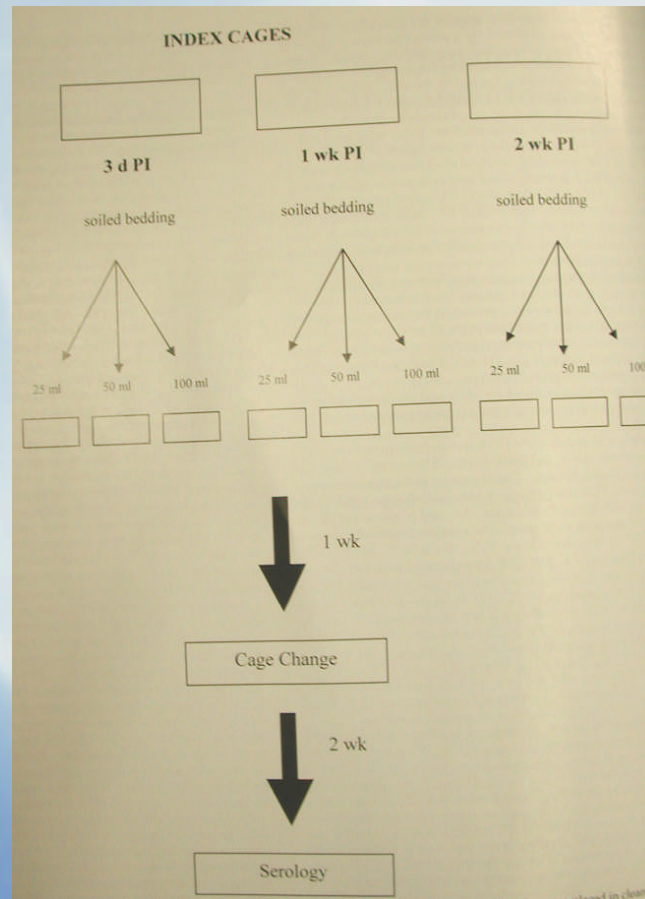
*“Reliability of Soiled Bedding Transfer for Detection of Mouse Parvovirus and
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Mice were inoculated with either MPV or MHV. Aliquots of dirty bedding from these animals were transferred to sentinel cages at 3 days, 1 week or 2 week post infection. See the next slide for schematic



Smith, PC et al
“Reliability of Soiled Bedding Transfer for Detection of Mouse Parvovirus and
Mouse Hepatitis Virus”
Comp Med 57 (1): 90-96, 2007



Smith, PC et al

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- a) 3 days
- b) 1 week
- c) 2 week
- d) Seroconversion in 100% not seen



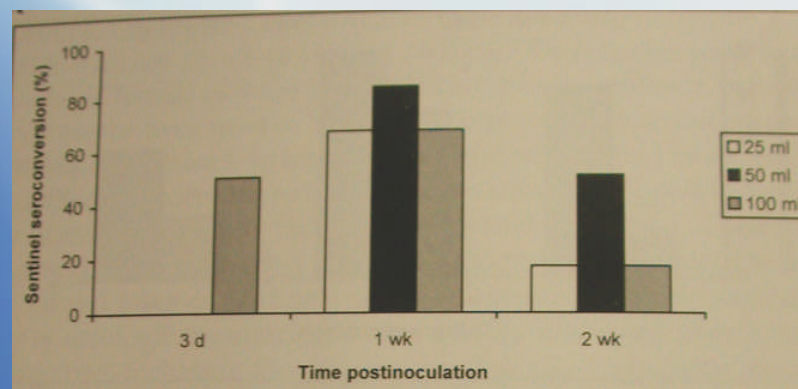
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Smith, PC et al

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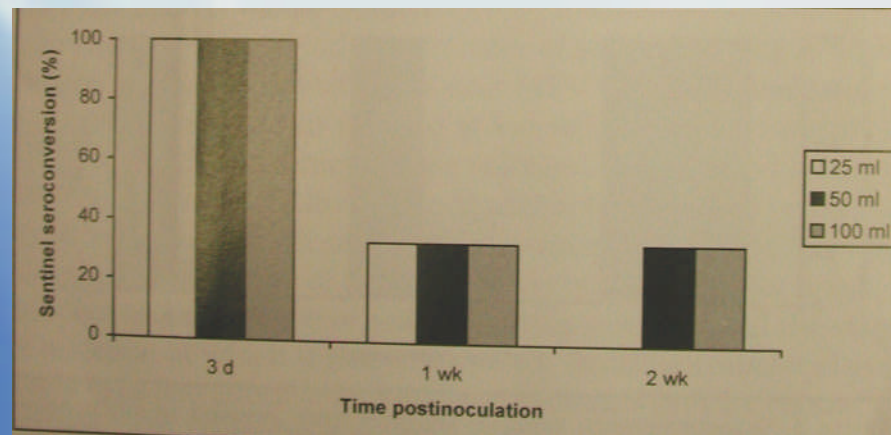
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“Reliability of Soiled Bedding Transfer for Detection of Mouse Parvovirus and Mouse Hepatitis Virus”

Comp Med 57 (1): 90-96, 2007

Mice were inoculated with either MPV or MHV. Aliquots of dirty bedding from these animals were transferred to sentinel cages at 3 days, 1 week or 2 week post infection. In which cages of sentinels was 100% sentinel seroconversion seen to MHV?

- a) **3 days**
- b) 1 week
- c) 2 week
- d) Seroconversion in 100% not seen



Smith, PC et al

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Mice were inoculated with either MPV or MHV. Aliquots of dirty bedding from these animals were transferred to sentinel cages at 3 days, 1 week or 2 week post infection. This study was done in both static microisolator cages and individually ventilated cages (IVC). Which cage set up demonstrated an overall higher percent of sentinel seroconversion?

- a) Static cage set up
- b) IVC set up
- c) Both setups had statistically equal seroconversion rates



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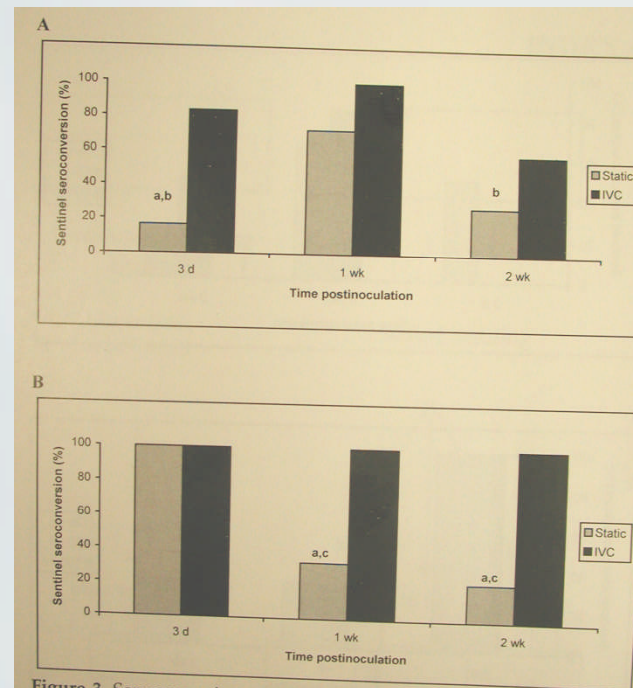


Figure 3. Seroconversion rates in sentinel mice housed in static cages compared with individually ventilated cages and exposed to soiled bedding from mice inoculated with (A) MPV or (B) MHV. Data are expressed as seroconversion rate (%) at each time point.

Smith, PC et al

*“Reliability of Soiled Bedding Transfer for Detection of Mouse Parvovirus and
Mouse Hepatitis Virus”*

Comp Med 57 (1): 90-96, 2007

Notes:

Soiled bedding effective under optimal conditions.

Rate of seroconversion varied with volume of soiled bedding and stage of infection

Bedding transfer also less likely to be effective for agents transmitted by direct contact or aerosol

Recommended a multi-faceted program including contact sentinels, soiled bedding, direct monitoring of principal animals

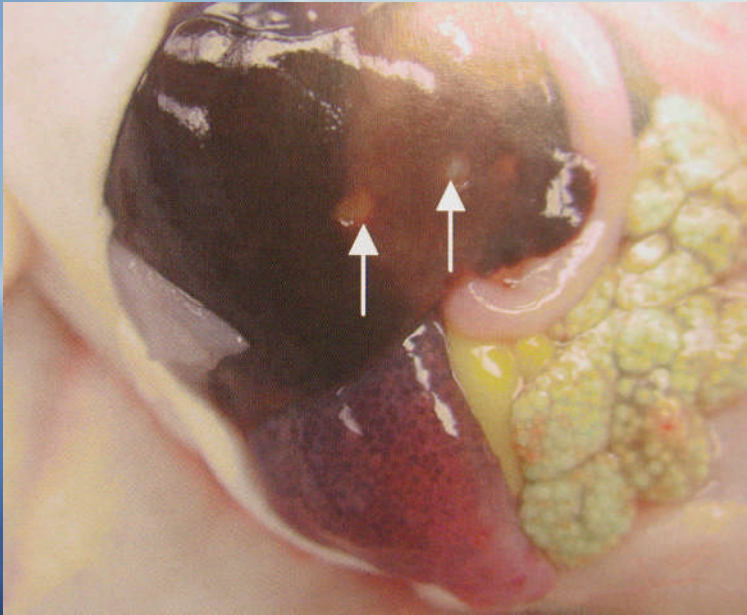




Raised red lesions

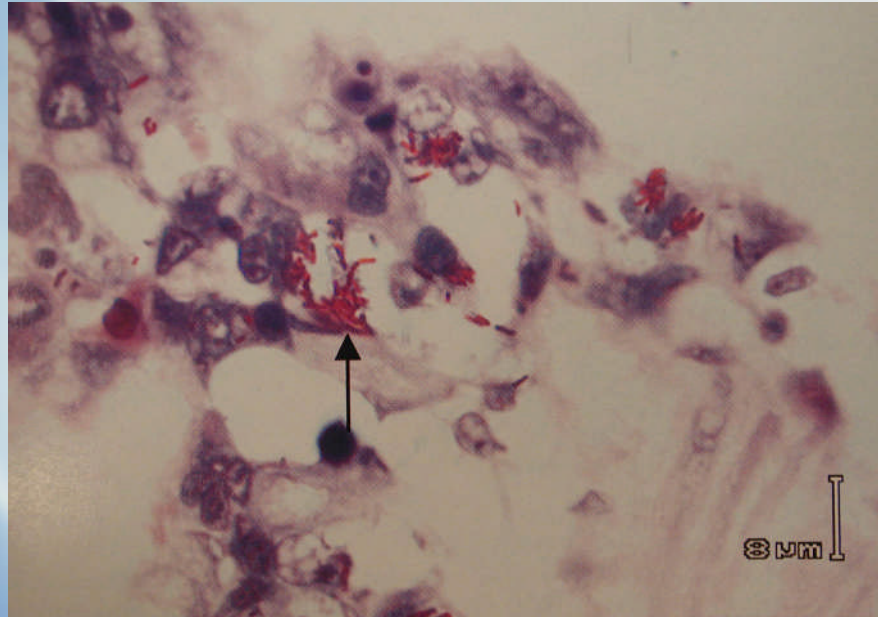


Bloated frog



Liver lesions

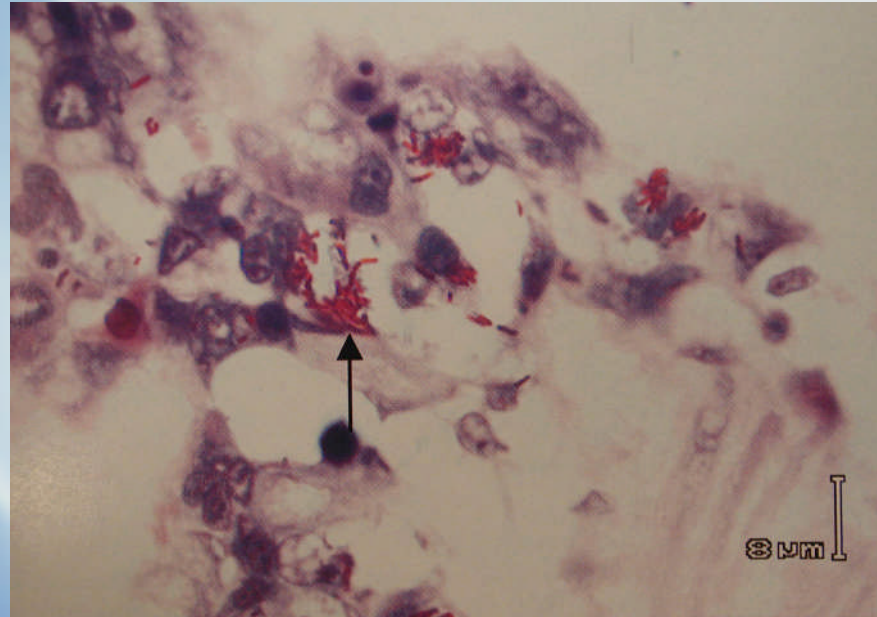




What's the stain?

What's the genus of organism?





What's the stain? **Acid fast**

What's the genus of organism? **Mycobacterium**



Godfrey, et al

How was the organism identified to species?



How as the organism identified to species?

PCR based on presence of MIsA which encodes for lactone core, presence of esxA and esxB

What is the species of Mycobacterium identified?



What is species of Mycobacterium identified?

Mycobacterium liflandii



Agent was identified in wild-caught *Xenopus laevis* with clinical signs. Did they find it in purpose bred frogs?



Agent was identified in wild-caught *Xenopus laevis* with clinical signs. Did they find it in purpose bred frogs?

Yes, at least one



Note: also cultured organism post UV light which was a concern. Think may be present in clumps where sensitivity would to UV would be decreased.



Godfrey, et al

What Mycobacterium species does it need to be differentiated from?



What mycobacterium species does it need to be differentiated from?

Mycobacterium ulcerans (which doesn't have *esxA* and *esxB* usually)

Godfrey, et al

What disease is associated with *Mycobacterium ulcerans*?



Godfrey, et al

What disease is associated with *Mycobacterium ulcerans*?

Buruli ulcers



**Reference for previous questions:
Godfrey, D, et al
“Newly Identified *Mycobacterium* Species in a
Xenopus laevis Colony”
Comp Med 57(1): 97-104, 2007**



Infection rate of STLV1 was studied in a baboon colony over the course of 4 years. Which sex to sex transmission predominated?

- a) Female to female**
- b) Male to male**
- c) Female to male**
- d) Male to female**

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- a) **Female to female**
- b) Male to male
- c) Female to male
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What percent represented the number of new adult male infections to STLV1?

- a) 0%
- b) 17%
- c) 50%
- d) 83%



What percent represented the number of new adult male infections to STLV1?

- a) **0%**
- b) 17%
- c) 50%
- d) 83%

41 new infections diagnosed over 4 year period, none in adult males although breeding to positive females

What percent represented the number of new adult female infections to STLV1?

- a) 0%
- b) 17%
- c) 50%
- d) 83%



What percent represented the number of new adult female infections to STLV1?

- a) 0%
- b) 17%
- c) 50%
- d) **83%**

Note: 50% new infections had occurred by time females were 5 years old (within 3 years of reaching sexual maturity)-suspect aggression which is the new part

d'Offay, JM, et al

**“Transmission Dynamics of Simian T-lymphotropic Virus Type
1 (STLV1) in a Baboon Breeding Colony: Predominance of
Female-to-female Transmission**

Comp Med 57(1):105-114, 2007



Primates at Yerkes and Tulane were surveyed serologically for antibodies to West Nile Virus. How did the incidence of West Nile antibodies in outdoor housed primates compare between Yerkes and Tulane?

- 1. The number of seropositive primates were low at both primate centers**
- 2. The number of seropositive primates were high at both primate centers**
- 3. Primates at Yerkes had a higher incidence than Tulane**
- 4. Primates at Tulane had a higher incidence than Yerkes**

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3. Primates at Yerkes had a higher incidence than Tulane
4. **Primates at Tulane had a higher incidence than Yerkes**

Cohen, JK, et al

How did the incidence of West Nile Virus antibody presence compare between nonhuman primates and humans?



Cohen, JK, et al

How did the incidence of West Nile Virus antibody presence compare between nonhuman primates and humans?

Incidence similar



Cohen, JK, et al

Mammal-feeding mosquito abundance was examined at Tulane and Yerkes primate centers. Which had the highest abundance of West Nile Virus infectious mammal-biting mosquitoes?



Cohen, JK, et al

Mammal-feeding mosquito abundance was examined at Tulane and Yerkes primate centers. Which had the highest abundance of West Nile Virus infectious mammal-biting mosquitoes?

Tulane 23X higher in 2003 and 33x higher 2004



Reference to previous questions

Cohen, JK, et al

**“Seroprevalence of West Nile Virus in Nonhuman
Primates as Related to Mosquito Abundance at
Two National Primate Research Centers”**

Comp Med 57(1): 115-119, 2007



Reference for next slide:

Mitsunaga, F, et al

**“Changes in the Titer of Anti-B Virus Antibody in
Captive Macaques (*Macaca fuscata*, *M. mulatta*, *M.
fascicularis*)”**

Comp Med 57(1): 120-124, 2007



Summary:

- **Found titers to B virus increased after shipped cynos overseas or transported rhesus from outdoor group housing to indoor single housing**
 - Two monkeys shipped overseas. One showed increased titer, one did not
 - Four rhesus brought in. One showed increased titer, 3 did not
- **Japanese macacque males but not females had increased titers during breeding season**
 - Looked at 3 males, 4 females. Two males increased titer. Females did not
- **Did not check for virus shedding but suggest warrants checking (antibody increase do to reactivation and possible shedding of virus)**



Common name?

Genus/species?





Common name? **Cotton-top tamarin**

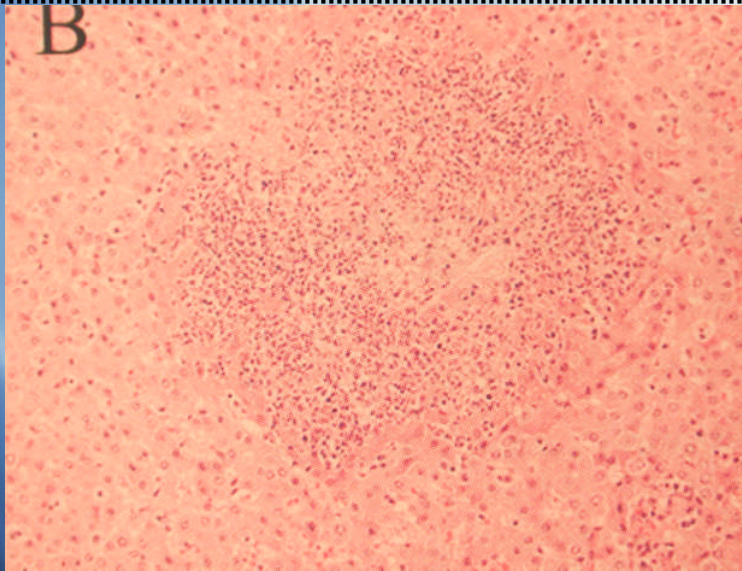
Genus/species? **Sanguinus oedipus**



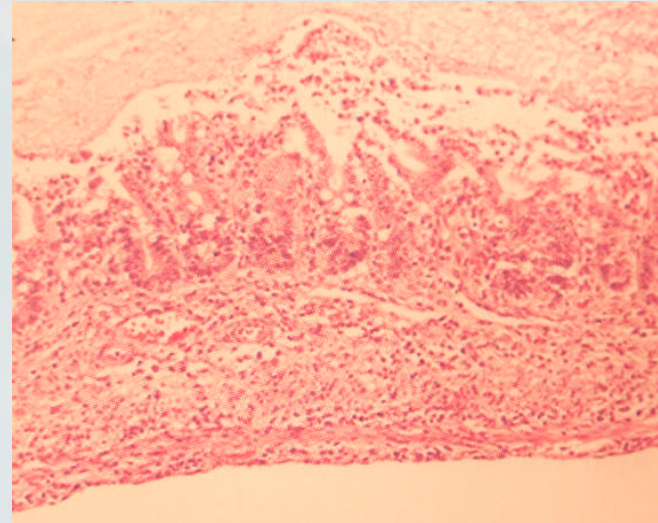
A cotton-top tamarin was found dead at a month of age. It had been rejected by its parents and was being nursery reared. Diarrhea preceded death.

Gross necropsy revealed watery contents in the gastrointestinal tract and multifocal pale areas up to 2.0 mm in the liver

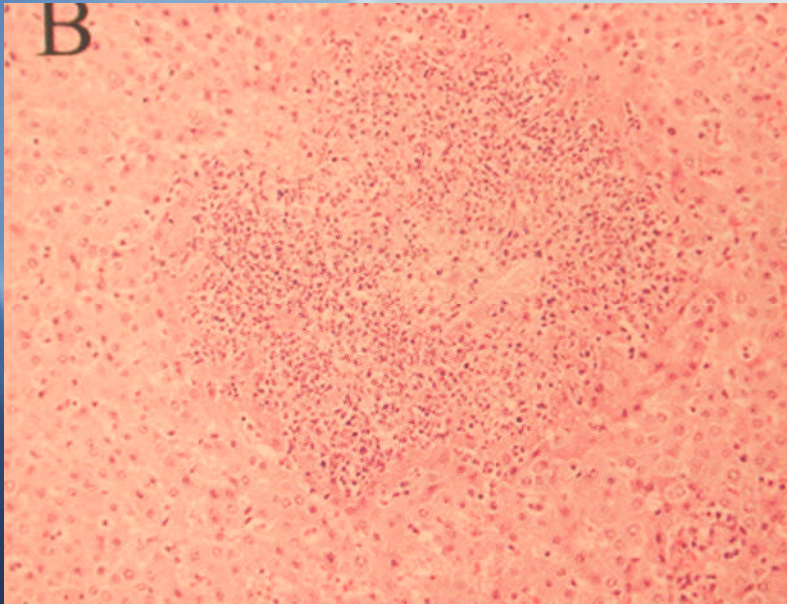




Name tissue
Name lesion?

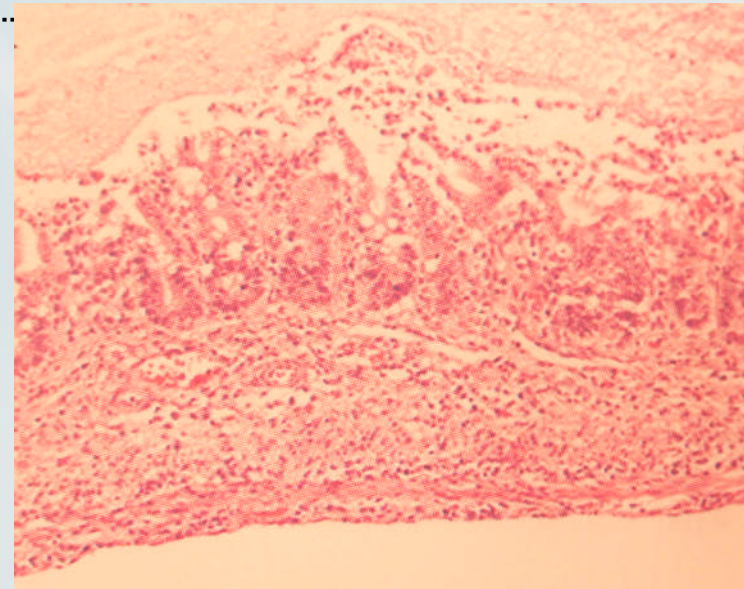


Name tissue
Histologic lesion?



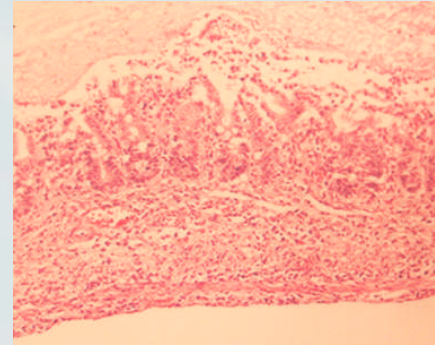
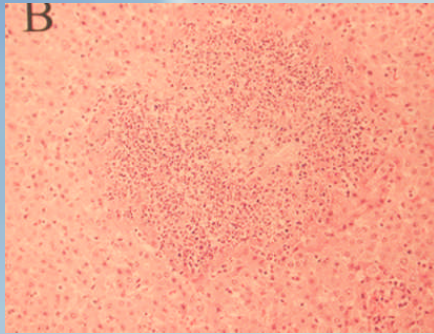
Name tissue--liver

Name lesion? Coagulative
necrosis surrounded by
rims of mononuclear cells--
hepatitis



Name tissue. colon

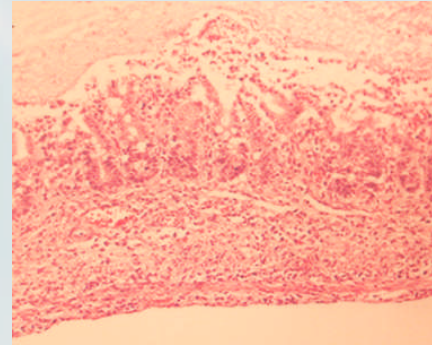
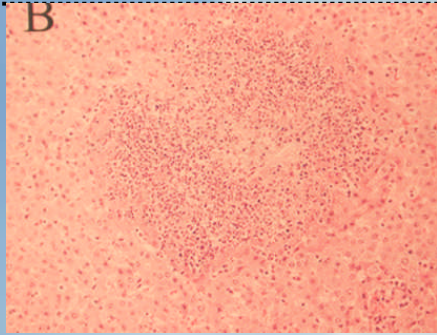
Histologic lesion? Colitis,
transmural



The heart, liver and colon were affected with these lesions of necrosis.

What disease might you be suspicious of?

What is the agent that causes that disease?



The heart, liver and colon were affected with these lesions of necrosis.

What disease might you be suspicious of?

Tyzzer's disease

What is the agent that causes that disease? ***Clostridium piliforme***



The heart, liver and colon were affected with these lesions of necrosis.

What stain do you want to use of the tissue sections?



The heart, liver and colon were affected with these lesions of necrosis.

What stain do you want to use of the tissue sections?

Some kind of silver stain (Steiner stain used in paper)



What condition must one always keep in mind with cotton top tamarins with diarrhea?



What condition must one always keep in mind with cotton top tamarins with diarrhea?

CTT idiopathic colitis

- occurs in animals as young as 19 days, increased incidence 24% 4 months to 52% at 48 months age
- Colon, cecum, rectum
- Linked to genetics, environment, bacterial infections

Focal ulcerative ileocolitis

4-12 months-separate disease causing discrete lesion confined to terminal ileum and colon



Reference:
Sasseville, VG, et al
**“Naturally Occurring Tyzzer’s Disease in Cotton-top
Tamarins (*Saguinus oedipus*)**
Comp Med 57(1):125-127, 2007



The End

