ALEUTIAN DISEASE
VIRUS OF FERRETS

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- TEXAS A&M 1991
- Private Practice
- Animal Clinic of Farmers Branch
- Dallas, Texas
- Owner of ferrets and former breeder
- Black-footed ferret
WHAT IS ADV?
ALEUTIAN DISEASE VIRUS

• ADV IS A PARVO VIRUS
• MINK AND FERRETS ARE THE MAIN ANIMALS THAT ARE AT RISK
• IMMUNE MEDIATED DISEASE WHICH IS
• SERIOUS AND CAN BE FATAL IN MINK AND FERRETS
ADV CAN ALSO INFECT

- SKUNKS
- MARTENS
- WEASELS
- FISHERS
- BADGERS
- OTTERS
- RACCOONS
- (PETS AND WILDLIFE)
CLINICAL SIGNS IN ADULT MINK

- CHRONIC WASTING DISEASE
- KIDNEY FAILURE (glomerulonephritis)
- PU/PD
- ANEMIA
- ANOREXIA
- MELENA
- WEIGHT LOSS
CLINICAL SIGNS IN ADULT MINK

- SPLENOMEGALY
- HEPATOMEGALY
- LETHARGY
- POOR PELTS
- INFERTILITY
- SMALL LITTERS
- STILLBORNS
- RESORBED FETUSES
CLINICAL SIGNS IN ADULT MINK

- UVEITIS (EYE)
- LYMPHADENOPATHY
- NEUROLOGICAL DYSFUNCTION
- HEMORRHAGE OF THE GI TRACT INCLUDING THE ORAL MUCOSA AND THE INTESTINES
CLINICAL SIGNS IN ADULT MINK

• BASED ON THE VIRUS STRAIN (6+ mink strains)
• GENETICS OF THE ANIMAL
• IMMUNE STATUS OF THE ANIMAL
• HUSBANDRY, AGE
ALEUTIAN MINK

- BLUE-GRAY COLOR
- CHEDIAK-HIGASHI syndrome
- Inherited immune system disorder
- Highly susceptible and usually FATAL
NON-ALEUTIAN MINK 3 DISEASE SYNDROMES:

- Progressive disease
- Persistent but non-progressive infection
- Non-persistent, non-progressive with clearance of the virus
CLINICAL SIGNS IN MINK KITS

• VIRAL REPLICATION IN THE LUNGS LEADS TO
• SEVERE AND USUALLY FATAL PNEUMONIA
ADV IN FERRETS HAS BEEN REPORTED IN:

• AMERICA
• CANADA
• ENGLAND
• JAPAN
• NEW ZEALAND
• SWEDEN
• BELGIUM + THE NETHERLANDS
CLINICAL SIGNS IN ADULT FERRETS

- CHRONIC WASTING DISEASE
- NEUROLOGICAL SIGNS (POSTERIOR PARESIS OR PARALYSIS; INCONTINENCE, TWITCHES/SEIZURES)
- RESPIRATORY: COUGH
- CARDIAC: ARTERITIS
- GI BLEEDING: MELENA
- GASTRITIS, ULCERS
- KIDNEY FAILURE
CLINICAL SIGNS IN ADULT FERRETS

• LIVER DAMAGE
• ANEMIA
• CLOTTING PROBLEMS
• PNEUMONIA
• UVEITIS (EYE)
• INFERTILITY
• SMALL LITTERS
• STILLBORN
CLINICAL SIGNS IN FERRET KITS

- SOME SEVERE AND USUALLY FATAL PNEUMONIA
- DEATH IN A FEW DAYS
- BUT SOME NORMAL
ADV IN LAB FERRETS HISTORICALLY

- 1960’S THRU 1980’S SOME ADV RESEARCH WITH LAB FERRETS
- CONSIDERED A MILD DISEASE
- SOME WITH CHRONIC WASTING
- NOT EASILY SPREAD FROM ONE FERRET TO ANOTHER FERRET
ADV IN PET FERRETS
HISTORICALLY

• 1980’S CHICAGO SHELTER
• DR SUSAN BROWN
• 10% POSITIVE (50 OUT OF 500)
• ONLY 2 OF THE 50 BECAME ILL (4% SICK)
ADV IN CANADA DIFFERENT FROM MOST

- 1976-1977 21 LAB FERRETS
- WESTERN COLLEGE OF VET MEDICINE, SASKATOON, SASKATCHEWAN, CANADA
- 9 OUT OF 21 (43%) DIED OF ADV
- SURVIVING 12: ALL POSITIVE BY CEP TEST (100% POSITIVE)
- WERE KEPT IN CAGES THAT HAD ADV+ MINK 2 YEARS AGO!
- CAN Vet Journal 1978 v19 p133-135
1990’s THINGS STARTED TO CHANGE FOR PETS

- **1990-1993 ENGLAND WESSEX FERRET CLUB:**
  446 FERRETS, **8.5% POSITIVE**

- **12 OF THE 38 BECAME SICK (32%)**
  NEUROLOGIC PROBLEMS:
  ATAXIA, POSTERIOR PARESIS, AND FECAL/URINARY INCONTINENCE

- *Vet Record v132 1993 p479-484*
ADV IN TEXAS, THINGS REALLY CHANGED!

• 2 OUTBREAKS:
• 1997 SAN ANTONIO SHELTER
• 2000 DALLAS/FT WORTH MULTIPLE FERRET HOMES
ADV IN PET FERRETS
SAN ANTONIO OUTBREAK

• SAN ANTONIO SHELTER
• 61 OF 65 BECAME POSITIVE (94% BECAME POSITIVE)
• 20 OUT OF 61 DIED OR WERE PUT DOWN BECAUSE OF ADV RELATED ILLNESS (33% FATAL)
• THE SHELTER REMAINED ADV POSITIVE TILL 2005
• IT WAS THE ADV-F STRAIN
ADV IN PET FERRETS
SAN ANTONIO OUTBREAK

- CLINICAL SIGNS IN THE SAN ANTONIO SHELTER OUTBREAK:
  - RESPIRATORY SIGNS: SNEEZING, COUGHING, PLEURAL EFFUSION, LUNG COLLAPSE, AND PNEUMONIA
  - POSTERIOR PARESIS/PARALYSIS
  - URINARY/FECAL INCONTINENCE
  - CHRONIC WASTING
  - KIDNEY FAILURE
  - HEART DISEASE AND UVEITIS
ADV IN PET FERRETS
D/FW OUTBREAK

• DALLAS/FT WORTH MULTIPLE FERRET HOMES 2000-2010
• SEVERAL ADV POSITIVE, INTACT FERRETS FROM MICHIGAN
• WENT TO 4 DIFFERENT HOMES
• THEN TO SEVERAL FERRET CLUB MEETINGS WITH MANY OTHER FERRETS
ADV IN PET FERRETS
DALLAS/FT WORTH

- HOUSE A
  - 11 OF 11 POSITIVE (100%)
  - 3 OF THE 11 DIED FROM ADV (27% FATAL)
  - ADV-F STRAIN

- HOUSE B
  - 6 OF 15 POSITIVE (40%) AT THE START
  - 9 OF 16 TESTED POSITIVE (56%) 7 MONTHS LATER
  - TITERS 4 TO 4096
  - NONE STILL ALIVE
ADV IN PET FERRETS
DALLAS/FT WORTH

- HOUSE C
  - 8 OF 16 TESTED POSITIVE (50%)
- ADV BREEDING: SMALL LITTERS, STILLBORNS, AND SOME KITS DYING FROM PNEUMONIA
- DFW FERRET CLUB
  - 22 OUT OF 86 POSITIVE (25.6%)
  - 7 OF THE 13 HOMES TESTED HAD POSITIVE FERRETS (54%)
ADV IN PET FERRETS
DALLAS/FT WORTH

• CLINICAL SIGNS IN THE DALLAS/FT WORTH OUTBREAK:
  • POSTERIOR PARESIS
  • MUSCLE TWITCHES, SEIZURES
  • HEPATITIS
  • GLOMERULONEPHRITIS
  • GASTRITIS, ANOREXIA
  • CHRONIC COUGH
  • DEATH
ALEUTIAN DISEASE VIRUS SEQUENCING:

• DR MARSHALL BLOOM NATIONAL INSTITUTES OF HEALTH (NIH, NIAID) ROCKY MOUNTAIN LABORATORIES HAMILTON, MONTANA
WHICH FERRET HAS ADV?
OTHER DISEASES WITH SIMILAR SIGNS:

- LYMPHOMA
- FIP-LIKE DISEASE
- INSULINOMA
- OTHER CANCERS
- CHRONIC ADRENAL DISEASE
- KIDNEY DISEASE (ARF OR CRF)
- DIM
- LIVER DISEASE
- INFLAMMATORY BOWEL DISEASE
- TRAUMA/DISC INJURY
- HEART/HW DISEASE
- MOD. TO SEVERE ANEMIA
- MOD. TO SEVERE GI ULCERS
- TOXICITY
IF YOU DON’T TEST EM, THEN YOU DO NOT KNOW!

ADV TESTS:

- GAMMA GLOBULIN
- CEP OR CIEP
- ELISA
- PCR
- DNA IN SITU HYBRIDIZATION
- HISTOPATHOLOGY: BIOPSY/NECROPSY
HYPERGAMMAGLOBULINEMIA

- HIGH GLOBULINS (>4.0 g/dL)
- PROTEIN ELECTROPHORESIS: GAMMA GLOBULINS >20% OF THE TOTAL SERUM PROTEIN IS CONSIDERED ELEVATED AND SUPPORTS A DIAGNOSIS OF ADV (ALSO ELEVATED IN FERRET FIP-LIKE DISEASE, which has a polyclonal gammopathy)
ADV Gammopathy: Monoclonal or Polyclonal
CEP OR CIEP TEST

- COUNTERIMMUNOELECTROPHORESIS
- TEST FOR ANTIBODIES TO THE ALEUTIAN DISEASE VIRUS
- GOOD SCREENING TEST!
- NO FALSE POSITIVE TESTS FROM OTHER PARVO VIRUSES OR FROM CANINE DISTEMPER
- LOW COST TEST!
CEP OR CIEP TEST
CEP OR CIEP TEST

- DR KENT BLAU
  BLUE CROSS ANIMAL HOSPITAL
  BURLEY, IDAHO, USA
  (208-678-5553) ($10)

- DR DAVOR OJKIC
  ONTARIO VETERINARY COLLEGE
  THE UNIVERSITY OF GUELPH
  GUELPH, ONTARIO, CANADA
  (519-824-4120 ext 54524) fecal PCR

- NO LONGER OFFERED BY
  UNITED VACCINES, INC. (2006)
  OR HARLAN LABS, UK.
THE UNIVERSITY OF GEORGIA

• NEW ELISA TEST FOR AB TO CAPSID PROTEINS: VP1 + VP2 (STRUCTURAL PROTEINS). TEST RESULTS WITH A TITER GOOD SCREENING TEST!

• PCR OF URINE, SALIVA, AND TISSUE SAMPLES FOR THE AD VIRUS ANTIGEN (SHEDDING)

• DNA IN SITU HYBRIDIZATION FROM TISSUE SAMPLES.
THE UNIVERSITY OF GEORGIA

• $45 FOR THE ADV PANEL: ELISA BLOOD + PCR ON URINE, SALIVA

• INFECTIOUS DISEASES LABORATORY- UGA

• DR PAULA CIEMBOR

• 706-542-8092 OR

• PCIEMBOR@UGA.EDU

• SHIP OVERNIGHT, ON ICE
MICHIGAN STATE UNIVERSITY

- PCR TEST FOR FECAL OR TISSUE SAMPLES ($37)
- DNA IN SITU HYBRIDIZATION FROM TISSUE SAMPLES
- WWW.FERRETTHEALTH.MSU.EDU
- DR ROGER MAES, VIROLOGIST
  DR MATTI KIUPEL, PATHOLOGIST
  517-432-2670
AVECON, INC

- **SEMI-NEW ELISA TEST FOR ANTIBODIES TO ADV**
- **AB AGAINST THE NONSTRUCTURAL PROTEIN (NS1) FROM WHEN THE AD VIRUS REPLICATES** (Similar to the mink ELISA test from Denmark)
- **MAY TAKE A LITTLE LONGER TIME WISE BEFORE THE TEST BECOMES POSITIVE AFTER EXPOSURE AND MAY BE NEGATIVE IF NOT REPLICATING.**
- **WWW.AVECON.COM**
AVECON, INC

- **3 ELISA TESTS OPTIONS:**
  - BLOOD SAMPLE THAT YOU SEND TO THEM ($15)
  - SALIVA SAMPLE THAT YOU SEND TO THEM ($15)
  - QUICKCHEK THAT YOU CAN RUN ON SALIVA (OR BLOOD)
BLOOD AND SALIVA ELISA TESTS THAT I SENT IN:
82 OUT OF 86 TESTS MATCHED UNITED’S CEP TEST

95+% AGREEMENT

BUT 4 WERE FALSE NEGATIVE ELISA TESTS (CEP POSITIVE BY UNITED AND U OF GEORGIA)

PRETTY GOOD SCREENING TEST!
THE QUICKCHEK TEST HAS NOT WORKED AS WELL FOR ME

2 FALSE NEGATIVE TESTS ON 2 CEP POSITIVE FERRETS (UNITED AND UGA: titers of 4 and 256)

No longer available?
HISTOPATHOLOGY

- BIOPSY OR NECROPSY:
- KIDNEY
- LIVER
- SPLEEN
- LYMPH NODES
- GI TRACT
- SPINAL CORD

Figure 2—(A) Normal mink kidney. (B) Lymphoplasmacytic cellular infiltrates are typical microscopic changes seen in the interstitium of the renal cortex of mink infected with pathogenic strains of Aleutian mink disease parvovirus (ADV). (C) Normal mink liver. (D) Cellular infiltrates are also commonly seen in the perportal areas of the liver of ADV-infected mink. Ferrets infected with ADV can have lesions similar to those shown here (original magnification, ×200).
TREATMENT OF ADV:
WHAT IS AN IMMUNE MEDIATED DISEASE?

- **AD VIRUS** IS THE ANTIGEN
- FERRET MAKES ANTIBODIES
- AG+AB → IMMUNE COMPLEXES
- IMMUNE COMPLEXES CAUSE THE DAMAGE TO THE ADULT FERRET
- DAMAGE TO THE VESSELS → ORGANS:
  - KIDNEY, LIVER, SPLEEN, GI TRACT
  - BONE MARROW
  - CNS/SPINAL CORD
  - HEART, LUNGS
  - EYES (UVEITIS)
  - ADRENALS
  - PANCREAS
TREATMENT GOALS

• DECREASE THE HUMORAL RESPONSE:
  • IMMUNE SUPPRESSION TO DECREASE ANTIBODY PRODUCTION
  • ↓ INFLAMMATION

• BOOST THE CELL-MEDIATED IMMUNE RESPONSE:
  • ↓ VIRAL REPLICATION
  • AND HOPEFULLY ELIMINATE THE PARVOVIRUS!
IMMUNE SUPPRESSION

- **PEDIAPRED™ (PREDNISOLONE)**
- **IMMUNE SUPPRESSION (↓AB)**
- **ANTI-INFLAMMATORY**
- **REDUCES THE MACROPHAGES UPTAKE OF THE VIRUS (VIA Fc Receptors)**
- **↑ APPETITE**
IMMUNE SUPPRESSION

- **IMURAN™ (AZATHIOPRINE)**
- IMMUNE SUPPRESSION (↓AB)
- Should be used with Pediapred
- Bone marrow suppression, liver toxicity; lymphoma
THE TWO NEW OPTIONS FOR CMI STIMULATION

• POLYPRENYL IMMUNOSTIMULANT
• ↑ mRNA EXPRESSION OF T-HELPER LYMPHOCYTES
• ↑ Th-1 CYTOKINES
• AND ENHANCES CMI THRU TOLL-LIKE RECEPTORS
• U of Tennessee

• LYMPHOCYTE T-CELL IMMUNE MODULATOR (LTCI)
• POTENT REGULATOR OF CD-4 LYMPHOCYTES AND IL-2 PRODUCTION
• conditional license
SUPPORTIVE CARE

• ANOREXIA:
  • SOFT FOODS
  • CIMETIDINE
  • CARAFATE
  • IV/SQ FLUIDS
  • CLAVAMOX OR AMOXI DROPS
  • AND BIAXIN
  • CERENIA/REGLAN

• ANEMIA:
  • EPOGEN/PROCRIT
  • MELATONIN
  • PET-TINIC (IRON)
  • IV/SQ FLUIDS
  • ? BLOOD TRANS.
  • ? BONE MARROW T.
  • ? LITHIUM CARB.
  • ? NEUPOGEN
VASCULITIS TREATMENT

• DOXYCYCLINE
• INHIBITION OF MATRIX METALLOPROTEINASES (MMP)
• INHIBITS TNF-α
• ↓ FIBROSIS
• ↓ WBC ADHESION TO ENDOTHELIAL CELLS

• TRENTAL™ (PENTOXIFYLLINE)
• PHOSPHODIESTERASE INHIBITOR
• ↑ TISSUE OXYGENATION
• INHIBITS TNF-α
• ↓ IL-1+6 LEVELS
• ↓ FIBROSIS
SUPPORTIVE TREATMENT

- ANOREXIA:
  - ANTACID
  - CARAFATE
  - SOFT FOODS
  - REGLAN/CERENIA
  - IV/SQ FLUIDS
  - CLAVAMOX OR
  - AMOXI DROPS
  - BIAXIN

- ANEMIA:
  - EPOGEN/PROCRIT
  - MELATONIN
  - PET-TINIC (IRON)
  - IV/SQ FLUIDS
  - BLOOD TRANS.
  - ? BONE MARROW T.
  - ? LITHIUM CARB.
  - ? NEUPOEGN

2011 Symposium International Ferret Congress
TREATMENT OF ADV

SUMMARY:

• IMMUNE SUPPRESSION
• IMMUNE MODULATION
• SQ, PO, OR IV FLUID THERAPY
• A/D, BABY FOOD, CARN. CARE
• ANTIBIOTICS (DOXYCYCLINE)
• VASCULITIS MEDICATIONS
• ANTIOXIDANTS: VIT A,B,C,E; SAMe/SILYBIN, MELATONIN, ZINC, AND SOD (OXSTRIN™)?
TRANSMISSION OF ADV

• ADV IS SHED IN BLOOD, URINE, AND FECES; ALSO IN SALIVA AND LIKELY IN RESPIRATORY SECRETIONS TOO, EVEN ASYMPTOMATIC FERRETS!
• VERTICALLY FROM JILL TO KITS
• FOMITES: CAGES, LITTER BOXES, BEDDING, HAMMOCKS, FOOD/WATER BOWLS; POSSIBLY CLOTHES, PEOPLE, CARPET, FURNITURE, ETC
• CANADIAN OUTBREAK FROM CAGES THAT HAD ADV MINK 2 YEARS PRIOR TO THE FERRETS BEING IN THEM!
PREVENTION OF ADV

• TEST ALL FERRETS BEFORE BRINGING THEM HOME OR INTO A FERRET SHELTER!
• ISOLATE POSITIVE FERRETS
• TEST BEFORE SHOWS, ETC.
• PARVOCIDAL CLEANING PRODUCTS (BLEACH, ETC)
• MINK: TEST AND CULL
SUGGESTED READING FOR VETERINARIANS

- **COMPENDIUM**
- **VOL23(2)178-185**
- **FEB 2001**
- **ALEUTIAN MINK DISEASE PARVOVIRUS: IMPLICATIONS FOR COMPANION FERRETS**
SUGGESTED READING FOR FERRET OWNERS

• *FERRETS MAGAZINE*
• MAY/JUNE 2006
• HEARTBREAK & HOPE: DESPITE PAST TRAGEDIES, HOPE IS SLOWLY EMERGING IN THE BATTLE AGAINST ALEUTIAN DISEASE VIRUS P 41-45
• BY DANEEL DEVORE
E-MAIL QUESTIONS:
AFERRETVET@CS.COM
I’ll answer questions for Pepsi!
THANK YOU VERY MUCH!
THAT’S ALL FOLKS!
PHOTO CREDITS:

- SHERLOCK: Jeanne Carley
- WILD MINK: Bob Walker
- PET MINK: Gail Elsey
- Ferrets, skunk, raccoon, mink kit, Pepsi, polar bears, etc: Jerry Murray