(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 12/8/2019 12:57 PM

To: Danielle Parks <dp546@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; smintner <smintner@uw.edu>

2 attachments (32 KB)

Nursery Schedule -December 9th 2019.xlsx; Week of December 9th 2019.xlsx;

Make sign for M09202 for biscuit count and EE by Vet Staff only (separate)

Caroline Off Friday
Schante Ship Tissue
104: Z17162 biofire
Mon/Tues Danielle B Bldg and 212/131 ultrasounds, if in B Bldg follow-up Schante can assist when available
Schante can bring T10118/T10174 upstairs 232 "c"

Nursery:
"253" train self-feeder and gruel mix, check if temp steady move to cage maybe
"221" cage, still might need warming blanket at night with cool night-time, depending if her temp stays stable, give soaked/dry biscuits
"201" same give soaked/dry biscuits, now on rubber sipper, BW daily 40 % dilution
Socialization w/221/201

104:006 & 178 EE, no water bottle, stuff toy might, will take away next week, BWs on Friday
Rm 104: humidifier on all day/night

Monday December 9th

Kelly 104: group house if we have connecting cages at top (or move Z18043, and Z17175 is returning to group) Z19020 and Z19059 pair w/Z19069 and Z19052- (they are same size as Z18199 in 152) so they get ready for 152 since couple more will move out.

B Bldg:

Z14138-rads (fast)

152: Z17175 BW

142: T10118/T10174 return to 232 confirm w/Vets-fecal results negative

212(6)/131(7) Quarterly Ultrasounds

131:

GR30/ L09006 recheck chem

Male/L09006/DJ72 cocci titers

Male/DJ72 chest rads

ATs separate 131 male into "C", dams lock inside A

Male will be sedated with dams as well

Start time 8AM (fast) groups 212/131

Start upstairs 1st (single trapping run, 2 squeeze cages, 2 recovery cages, couple white boxes)

Downstairs 2nd (single trapping run, 2 squeeze cages, 2 recovery cages, couple white boxes)

Vet Staff 241: separate male into "C" for overnight

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 5/26/2019 3:26 PM

To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>; Christopher M. Wozniak <chrisw36@uw.edu>

2 attachments (35 KB)

Week of the May 27th 2019.xlsx; Nursery Schedule May 27th 2019.xlsx;

Sherri initial -80 freezer
Schante fill out Protocyte decontamination sheet

Gallon Distilled water, should be written Not for Animal Use

103: 059 on sipper now
103: Thor starts formula dilution, we can now use powder formula (make sure this is indicated for night shift) and bowl once daily, but very, very small amount of food, don't over feed him
103: BWs on Fridays

104: Z18121 BW on Friday, start Friday bowl once daily, then hopefully next week will pair house

Schante will separate 241 and then she will help me with introductions

Sherri assist Vets with the two sedations

Tuesday May 28th

142: S11069, not sure if schedule to remove rest of sutures, keep checking to see if any remain

142: Z14063- not sure if returning back to 171

142: DH46 cbc/chem/fecal (fast)

104: Z16358 cocci titer (fast)

104: Z18121- fecal swab to Seattle

142: M06139 intro back to 242

142: K11143/infant intro back to 242

142: ET02/infant intro back to 231

142: Z14320/infant intro back into 112

241: M09202 & Z12034 BWs

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 2/3/2019 5:57 PM

To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>

2 attachments (33 KB)

Nursery Schedule Feb 4th 2019.xlsx; Week of the Feb 4th 2019.xlsx;

Monday February 4th

241: male K-9 removal (male to recover in group six in bay) make sure cage plate Vet staff to feed only

104: Z17139 -sedate to exam and cocci titer

111: Z17184 BW (check with Vet before letting back in group)

221: CV61 BW

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 11/3/2019 3:12 PM

To: Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>; smintner <smintner@uw.edu>

2 attachments (31 KB)

Week of November 4th 2019.xlsx; Nursery Schedule -November 4th 2019.xlsx;

Caroline Off Friday switch week/weekend. Thursday meeting with everybody since everyone will be here.
Day to day schedule changes, make sure to read emails for updates and changes

Need to get shipment 3 ID#s, so cbc/chem blood vials can be prepped, they arrive November 12th for following week exam
Next three days will be (3) Vets w/TB exams
Still trying to get a system down with new building, we will be busy between two building with follow-up and exams

Nursery:
"221" cage, temp BW daily AM. keep warming blanket if temp is below 99 if rectal temp has been steady for couple days. Once warming blanket removed and steady temp remove towel/absorbent pad, then she can three diapers and surrogate.
"201" same give soaked/dry biscuits (training on sipper when time permits), BW daily
"178" one diaper at night, BW daily, now at 20%
Comingle 178/201 on days we have time

Read assigned dates for TBs: 24/48/72 into Saturday.

009: humidifier on all day/night, make sure we have distilled water, let Jim know if out
Clean isolette after each nebulization use

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 11/10/2019 5:57 PM

To: Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>; smintner <smintner@uw.edu>

2 attachments (32 KB)

Nursery Schedule -November 11th 2019.xlsx; Week of November 11th 2019.xlsx;

Monday November 11th

Holiday
Dr M on-call, Dr Fuller ½ day
104: Z16283 (fast) suture removal
103: Z19178 suture removal

Wednesday off @2PM
Friday Danielle in later morning
Day to day schedule changes, make sure to read emails for updates and changes
New arrivals November 12th Sunday prep for semi-annual exams for that following Monday

Nursery:
"221" cage, temp BW daily AM. keep warming blanket if temp is below 99 if rectal temp. Once warming blanket removed and steady temp remove towel/absorbent pad, then she can three diapers and surrogate.
"201" same give soaked/dry biscuits (training on sipper when time permits), BW daily
"178" one diaper at night, BW daily, now at H20 (leave note for night shift)
Comingle 178/069 on days we have time

009: humidifier on all day/night, make sure we have distilled water, let Jim know if out
Clean isolette after each nebulization use

protatek to send out tomorrow

smintner <smintner@uw.edu>

Sun 12/8/2019 1:55 PM

To: cjmead2 <cjmead2@uw.edu>

1 attachments (2 MB)

protatek 12-6-2019.pdf;

Re: protatek requisition for 11/27/2019

smintner <smintner@uw.edu>

Wed 11/27/2019 2:27 PM

To: cjmead2 <cjmead2@uw.edu>

1 attachments (2 MB)

Prototek_Requisition_Form 7-31-19.pdf;

No! I put it on the form correctly (I checked....they haven't picked up yet.) Sorry for the confusion.

From: cjmead2 <cjmead2@uw.edu>
Sent: Wednesday, November 27, 2019 1:36 PM
To: smintner <smintner@uw.edu>
Subject: RE: protatek requisition for 11/27/2019

Is this the correct animal?

From: smintner <smintner@uw.edu>
Sent: Wednesday, November 27, 2019 9:41 AM
To: cjmead2 <cjmead2@uw.edu>
Subject: protatek requisition for 11/27/2019

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 12/1/2019 7:39 PM

To: Danielle Parks <dp546@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; smintner <smintner@uw.edu>

2 attachments (31 KB)

Nursery Schedule -December 2nd 2019.xlsx; Week of December 2nd 2019.xlsx;

Danielle send out tissue Monday (I will show you)
Caroline Off Friday
Tuesday Schante B Bldg and 222/232 ultrasounds

Nursery:
"221" cage, still might need warming blanket at night with cool night-time, depending if her temp stays stable, give soaked/dry biscuits
"201" same give soaked/dry biscuits, now on rubber sipper, BW daily 60 % dilution
Socialization w/221/201

104:
006 & 178 EE, remove water bottle if not using, (if hasn't been removed already) BWs on Friday
178: stuff toy day and diaper/stuff toy night
Rm 104: humidifier on all day/night

Monday December 2nd

142: T10118/T10174 follow-up fecal swab-mixed feces

B Bldg:

302: Z14244-check w/Vets first before return to group 317CD

320C: A09109 (fast) sedate for eye exam, then can return to group if cleared by Vet (319AB)

302: Z13247 intro back to 319AB

302: Z12353- (fast) suture removal, check if cleared to return Wednesday (319AB)

302: F02420 intro into 319CD

PROTATEK REFERENCE LABORATORY
540 WEST IRON AVENUE • SUITE 106 • MESA, AZ 85210
TEL: (480) 545-8499 • FAX: (480) 545-8409

PROTATEK INTERNATIONAL, INC.

REQUISITION FORM

PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC
Address PO Box 208336
Mesa, AZ 85215
Phone 206-685-6031
Fax N/A
Email Address th81@uw.edu, cjmead2@uw.edu
Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*
Name _____
Address _____
_____
Phone _____
Fax _____

Owner WaNPRC **Animal's Name / ID** See Attached
Species Macaca nemestrina **Breed** Pig Tailed Macaque **Sex** See Attached **Age** See Attached
Collection Date 12 / 6 / 2019
Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

Rickettsia

1. Ehrlichia canis (sst)
2. Feline Ehrlichia (E. canis + N. risticii) (sst)
3. Neorickettsia risticii (E. risticii) (sst)
4. Anaplasma phagocytophilum (E. equi) (sst)
5. Ehrlichia sennetsu (sst)
6. Rickettsia rickettsii (RMSF) (sst)
7. Chlamydia (sst)
8. Bartonella henselae (sst)

Viral

9. Canine parvovirus (IgM / IgG) (sst)
10. Canine distemper (IgM / IgG) (sst)
11. Canine distemper smears (DFA) (sl)
12. Feline leukemia (ELISA) (sst)
13. Feline leukemia (IFA) (ltt)
14. Feline infectious peritonitis (FIP) (sst)
15. Feline immunodeficiency syndrome (FIV) (sst)
16. Feline rhinotracheitis (sst)
17. Feline panleukopenia (sst)
18. Equine rhinopneumonitis (sst)

Bacterial

19. Borrelia burgdorferi (Lyme) (IFA) (sst)
20. Lyme Multiplex assay (sst)
21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

Microscopic Identification

42. Mycoplasma haemocanis (ltt) (Haemobartonella canis)
43. Mycoplasma haemofelis (ltt) (Haemobartonella felis)
44. Babesia spp. (sl, ltt)
45. Trypanosoma spp. (sl, ltt)
46. Brucella canis (sl,ltt)

DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
48. EHRLICHIA – FUNGAL PANEL
Ehrlichia canis, Coccidioides (sst)
49. FUNGAL PANEL
Cocci, Blasto, Histo (sst)
50. CANINE HEMOLYTIC ANEMIA PANEL
Babesia canis (sst), Coomb's test (ltt)
51. FELINE DISEASE PANEL
E. canis, N. risticii, FeLV, FIP, Toxo (sst)
52. CANINE EXPORT PROFILE I
B. gibsoni (IFA) (sst), Babesia spp. (sl)
53. CANINE EXPORT PROFILE II
E. canis, Leishmania, Lepto, Brucella canis (agglutination) (sst)

ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
55. Ketoconazole (sst)
56. Itraconazole (sst)
57. Voriconazole (sst)

HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
60. T4/ Cholesterol (sst)
61. Chemistry Profile 14 + CBC (sst, ltt)
62. Chemistry Profile 14 + CBC + T4 / Cholesterol (sst, ltt)
63. Ehrlichia canis + Chem Profile 14 + CBC (sst, ltt)
64. Coccidioides + Chem Profile 14 + CBC (sst, ltt)
65. E. canis + Cocci + Chem Profile 14 + CBC (sst, ltt)
66. Tick-borne Disease Panel + T4 / Cholesterol (sst)
67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z17161		F	2 yrs 6 mos	12/6/2019	10/28/2019 IgG positive 1:2, IgM negative
2	Z17142		F	2 yrs 6 mos	12/6/2019	10/28/2019 IgG positive 1:2, IgM negative
3	Z17150		F	2 yrs 6 mos	12/6/2019	10/28/2019 IgG positive 1:2, IgM negative
4						
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7						
8						
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20						

Re: RE:

smintner <smintner@uw.edu>
Fri 12/13/2019 9:49 AM
To: cjmead2 <cjmead2@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>

1 attachments (249 KB)
12-13-2019 protatek.pdf;

Protatek sent out. Paperwork is attached.

Thanks,
Sherri

From: cjmead2 <cjmead2@uw.edu>
Sent: Thursday, December 12, 2019 4:17 PM
To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>
Subject: RE:

Just let me know cocci titers are sent out and send me paperwork
Email update if any new changes

From: cjmead2
Sent: Thursday, December 12, 2019 4:17 PM
To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>
Subject:

Friday December 13th
104: case BWs
142: case BWs
142: EI33 fecal swab?
104: (fast) Z18043 rads w/o cast
B Bldg.: 302 case BWs
Vet Tech 1PM training

Week of October 28th 2019 *Schedule Subject To Change*

7am-3:30	Tues 10-28-2019	Tues 10-29-2019	Wed 10-30-2019	Thurs 10-31-2019	Fri 11-1-2019	Sat 11/2/2019	Sun 11/3/2019
Caroline	Tx 104/142 EE: 104/142 Obs: 104/142 TB exams Shipment Paperwork	Tx 104/142 EE: 104/142 Obs: 104/142 New Arrivals AB Building TB exams24 hr TB reads Shipment/paperwork	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean B Building Behav Obs 142: moves/intros	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean B Building Behav Obs 222/241 exams	Off	Off	Off
Sherri	Tx/Ob/EE Upstairs Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 10 TB Exams/tattoo 162: (2) male TB 142: 079 TB & rads 142: T10118 U/S 104: 7 TB exams Sweep/mop Nurs/ProcRm	Tx/Ob/EE Upstairs Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm 152:TB Exams/ tattoos Itule Order-celery	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm 142: multiple exams 142 intros back to group 104 intros back to group	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 change out nursery cage Sweep/mop Nurs/ProcRm 222: HK97- new birth ex 241: GR11 New birth ex 241: GP45 follow-up CBC	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Prep for TB Exams Bldg Organize stockProc B Bldg AftrLunc/endDayLaundry 221/112/104/142 BWs 104: Z15386 suture rem Sweep/mop Nurs/ProcRm	Off	Off
Schante	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean 10 TB Exams/tattoo 162: (2) male TB 142: 079 TB & rads 142: T10118 U/S 104: 7 TB exams Sweep/mop Nurs/ProcRm	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Sweep/mop Nurs/ProcRm AftrLunc/endDayLaundry 152:TB Exams/ tattoos 24hr TB Reads B Building	Off	Off	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 Obs Annex152 Sweep/mop Nurs/ProcRm 221/112/104/142 BWs 104: Z15386 suture rem	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs set-up SA B Bldg/Proc Rm	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs set-up SA B Bldg/Proc Rm Sweep/mop Nurs/ProcRm
Danielle	Off	Off	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs 48hr TB Reads 142: multiple exams 142 intros back to group 104 intros back to group	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs 72hr TB Reads entry 222: HK97- new birth ex 241: GR11 New birth ex 241: GP45 follow-up CBC	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs Sweep/mop Nurs/ProcRm 221/112/104/142 BWs 104: Z15386 suture rem	Tx 104/142 EE: 104/142 Obs: 104/142 Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm	Tx 104/142 EE: 104/142 Obs: 104/142 Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm
Dr Amber **Dr House** **Dr Malinowski**	On-Call	Off On-Call	Off On-Call	On-Call	1/2 day On-Call	**Malinowski** On-Call	**Malinowski** On-Call

Everyone is to assist in doing dishwasher and laundry duties, as well as, keep areas cleaned and organized. Sign Off Checklist Sheets Procedure/Surgery/Necropsy

Mon 10/28/19	Tues 10/29/2019	Wed 10/30/2019	Thurs 10/31/19	Friday 11/2/19
10 TB Exams/tattoo 162: (2) male TB 142: 079 TB & rads 142: T10118 U/S 104: 7 TB exams	(92) New Arrivals AB Building 152:11 TB Exams and 3 chest tattoos	142:331Rads/cocci 142:331infant chesttattoo 142: 340 infant Ex 142: HL83 Exam 104: 076 sut removal 104:intro 116,158,196 142: ET02 intro 231 142: ET63 intro 242 142:118 & 174 intro 232 104:004to122/122grpBWs	222: HK97- new birth exam 241: GR11 New birth exam 241: GP45 follow-up CBC	221: R10113 & CV61 BWs 112: M11094, Z14257, Z13082 Follow-up BWs 104: Z15386 (fast) suture removal 104: case BWs 142: case BWs

11/4/2019

Nursery Schedule

Infant #	DOB	Days in Age	What to Feed	Delivery Type	Frequency	Additional Information:
New	9/21/2019	Day 43	**See Note below	Self-Feeder 60mL	7am, 11am	Cage: hanging surrogate -EE toys, puffs
Z19221			60mL -increase by 5mL	Adjustments made daily	3pm, (430 AT check)	self-feeder, warming blanket PRN
Female	Dam K06231		self-feeder, puffs		7pm, 11pm	rectal temp in am (Vet staff), minimal diapers (3), stuffed toy
Cage	from 131		100% soy		3am, (6am AT check)	BW daily (Vet Staff), record feedings
New	8/12/2019	Day 82	**See Note below	Self feeder 80-90mL ONLY	7am, 11am	Cage: Surrogate - EE, teething toys
Z19201			increase by 5mL	Adjustments made daily	3pm, (430 AT check)	self bottle feeding, 2 soaked/6 dry biscuit BID, train on sipper
Female	Dam K06231		per Vet Staff ONLY	**4 soaked biscuits/6 dry biscuits**	7pm, 11pm	puffs/cherrios, minimal diapers (2), stuffed toy,
cage	from 131		Enfamil Neuro Pro	every feeding fresh food	3am, (6am AT check)	BW daily (Vet Staff), record feedings
New	7/2/2019	Day 124	20% formula	Self feeder 400mL ONLY	7am	Cage: No surrogate - EE, teething toys
Z19178			12 dry biscuits BID	Adjustments made PRN	3pm, (430 AT check)	self bottle feeding, 12 dry biscuits BID
Male	Dam A09110		80 formula/320 H20	**Self Feeder**	11pm	puffs, minimal diapers (1 night), NO stuffed toy, NO diaper during day
cage	from 231		4 scoops to 250ml H20	metal sipper	(6am AT check)	BW daily (Vet Staff), record feedings

Special Feeding Instruction:

<u>Note: Starting with 10mL will adjust daily, read notes on Infant Log Sheet if unclear ask Caroline</u>**

<u> Ready to Use formula, open/date and stored in refrigerator, good for 24 hrs once opened</u>**

If at any time the infant coughs, or expels fluid through their nose, discontinue feeding, Infants can easily inhale formula, which may lead to aspiration.

Aspiration is the inhalation or introduction of fluids into the lungs, which can cause pneumonia and even death.

To avoid aspiration, give the infant breaks when feeding and NEVER force formula down an infant, or squeeze the bottle while feeding

Normal rectal temp 97.5, if below contact Vet Staff and above 101.0 contact Vet Staff

Recording inside isolette temp very critical, especially our isolettes are very touchy, so DO NOT adjust without permission

Inside temp should be ideal 82-84F at this time, if it needs decrease/increased DO NOT touch the scrolls on left side (ask Caroline, before adjusting)

change temp with right side, only move up by .2 per Caroline, then monitor temp for over 30-60 minutes, make sure Isolette closed-up, takes time to adjust when door left open.

If alarms, press silence/reset on left side

Bottle make sure small hole in nipple, not large. Keep bottle rinsed and clean, wear clean, gloves & lab coat at feedings-keep up with laundry

Put infant in isolette propped up, not on back, or side.

11/11/2019

Nursery Schedule

Infant #	DOB	Days in Age	What to Feed	Delivery Type	Frequency	Additional Information:
New Z19221 Female Cage	9/21/2019 Dam K06231 from 131	Day 50	**See Note below 60mL -increase by 5mL self-feeder, puffs 100% soy	Self-Feeder 60mL Adjustments made daily 	7am, 11am 3pm, (430 AT check) 7pm, 11pm 3am, (6am AT check)	Cage: hanging surrogate -EE toys, puffs self-feeder, warming blanket PRN rectal temp in am (Vet staff), minimal diapers (3), stuffed toy BW daily (Vet Staff), record feedings
New Z19201 Female cage	8/12/2019 Dam K06231 from 131	Day 89	**See Note below increase by 5mL per Vet Staff ONLY Enfamil Neuro Pro	Self feeder 80-90mL ONLY Adjustments made daily **4 soaked biscuits/6 dry biscuits** every feeding fresh food	7am, 11am 3pm, (430 AT check) 7pm, 11pm 3am, (6am AT check)	Cage: Surrogate - EE, teething toys self bottle feeding, 2 soaked/6 dry biscuit BID, train on sipper puffs/cherrios, minimal diapers (2), stuffed toy, BW daily (Vet Staff), record feedings
New Z19178 Male cage	7/2/2019 Dam A09110 from 231	Day 131	400mL H20 12 dry biscuits BID 	Self feeder 400mL ONLY Adjustments made PRN **Self Feeder** metal sipper	7am 3pm, (430 AT check) 11pm (6am AT check)	Cage: No surrogate - EE, teething toys self bottle feeding, 12 dry biscuits BID puffs, minimal diapers (1 night), NO stuffed toy, NO diaper during day BW daily (Vet Staff), record feedings

Special Feeding Instruction:

****Note: Starting with 10mL will adjust daily, read notes on Infant Log Sheet if unclear ask Caroline**

**** Ready to Use formula, open/date and stored in refrigerator, good for 24 hrs once opened**

If at any time the infant coughs, or expels fluid through their nose, discontinue feeding, Infants can easily inhale formula, which may lead to aspiration.

Aspiration is the inhalation or introduction of fluids into the lungs, which can cause pneumonia and even death.

To avoid aspiration, give the infant breaks when feeding and NEVER force formula down an infant, or squeeze the bottle while feeding

Normal rectal temp 97.5, if below contact Vet Staff and above 101.0 contact Vet Staff, optimum 99.0

Recording inside isolette temp very critical, especially our isolettes are very touchy, so DO NOT adjust without permission

Inside temp should be ideal 82-84F at this time, if it needs decrease/increased DO NOT touch the scrolls on left side (ask Caroline, before adjusting)

change temp with right side, only move up by .2 per Caroline, then monitor temp for over 30-60 minutes, make sure Isolette closed-up, takes time to adjust when door left open.

If alarms, press silence/reset on left side

Bottle make sure small hole in nipple, not large. Keep bottle rinsed and clean, wear clean, gloves & lab coat at feedings-keep up with laundry

Put infant in isolette propped up, not on back, or side.

Week of November 11th 2019 *Schedule Subject To Change*

7am-3:30	Mon 11-11-2019	Tues 11-12-2019	Wed 11-13-2019	Thurs 11-14-2019	Fri 11-15-2019	Sat 11/16/2019	Sun 11/17/2019
Caroline	Off	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean	302:Z14298 Sut Removal 302:K04362 (fast) Sx Rm	AB302-GL14 (male) K-9 ext	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Schedule/Paperwork Meetings Moves	Off	Off
Sherri	Off	Off	Tx 104/142 EE: 104/142 Obs: 104/142 Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm 142:Z14331 F/U fecalswab 104/152: F/U chem Itule Order-squash	Nursery-cage change out AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs Sweep/mop Nurs/ProcRm Ckeckw/Schante PM Tx 103: Z19006 rads/cocci Moves: 162/221/181/142	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs ObsAnnex152 Sweep/mop Nurs/ProcRm AftrLunc/endDayLaundry 104/142: case BWs 212: Z14130 BW 112: moves	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs Sweep/mop Nurs/ProcRm	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs Sweep/mop Nurs/ProcRm Prep sem-annual Exams
Schante	Tx 104/142 EE: 104/142 Obs: 104/142 Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm 104:Z16283SutRem 103:Z19178SutRem	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm AftrLunc/endDayLaundry 232: ET40 new birth Ex	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs Sweep/mop Nurs/ProcRm 104/152: F/U chem 104: Z16281 intro 122 104: Z16283 intro to 122	Tx 104/142 EE: 104/142 Obs: 104/142 Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm 103: Z19006 rads/cocci Moves: 162/221/181/142 Off @2PM	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm 104/142: case BWs 212: Z14130 BW 112: moves B Bldg.: 302 case BWs	Off	Off
Danielle	Nursery AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs Sweep/mop Nurs/ProcRm 104:Z16283SutRem 103:Z19178SutRem	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs Run cbc/chem Sweep/mop Nurs/ProcRm 232: ET40 new birth Ex	Off	Off	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean 104/142: case BWs 212: Z14130 BW 112: moves B Bldg.: 302 case BWs In Late Morning	Tx 104/142 EE: 104/142 Obs: 104/142 Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm	Tx 104/142 EE: 104/142 Obs: 104/142 Tx: down/annex/152 EE: downstairs/anex/152 Obs: down/annex/152 Sweep/mop Nurs/ProcRm Prep sem-annual Exams
Dr Amber Dr House Dr Malinowski	1/2 day On-Call	Off On-Call	Off On-Call	 On-Call	1/2 day On-Call	House On-Call	House On-Call

Everyone is to assist in doing dishwasher and laundry duties, as well as, keep areas cleaned and organized. Sign Off Checklist Sheets Procedure/Surgery/Necropsy

Mon 11/11/19	Tues 11/12/2019	Wed 11/13/2019	Thurs 11/14/19	Friday 11/15/19
104:Z16283SutRem 103:Z19178SutRem	Ship DNA samples Separate 317AB EM80 for TB exam Separate 312CD K04362 to 302 232: ET40 new birth Ex DI60 cocci titer Shipment 3 arrival (86)	B Build 302:Z14298 Sut Removal 302:K04362 (fast) Sx Rm 142:Z14331 F/U fecalswab 104: Z16281 intro 122 104: Z17175 F/U chem 152: Z17253 F/U chem 104: Z16283 intro to 122 ATs: 121 BWs	103: Z19006 rads & follow-up cocci titer B Build AB302-GL14 (male) **fast** upper K-9s extractions, Sx 103: Z19006 rads/cocci 162C: Move over to 171A/B just A, B blocked Moves: 221/181/142 Nursery cage change out	104: case BWs 142: case BWs 212: Z14130 BW B Bldg.: 302 case BWs Moves: 112 moves and intro with other dam breeders 171

PROTATEK REFERENCE LABORATORY
540 WEST IRON AVENUE • SUITE 106 • MESA, AZ 85210
TEL: (480) 545-8499 • FAX: (480) 545-8409

PROTATEK INTERNATIONAL, INC.

REQUISITION FORM

PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC
Address PO Box 208336
Mesa, AZ 85215
Phone 206-685-6031
Fax N/A
Email Address th81@uw.edu, cjmead2@uw.edu
Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*
Name _____
Address _____
_____
Phone _____
Fax _____

Owner WaNPRC **Animal's Name / ID** See Attached
Species Macaca nemestrina **Breed** Pig Tailed Macaque **Sex** See Attached **Age** See Attached
Collection Date 7 / 30 / 2019
Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

Rickettsia

1. Ehrlichia canis (sst)
2. Feline Ehrlichia (E. canis + N. risticii) (sst)
3. Neorickettsia risticii (E. risticii) (sst)
4. Anaplasma phagocytophilum (E. equi) (sst)
5. Ehrlichia sennetsu (sst)
6. Rickettsia rickettsii (RMSF) (sst)
7. Chlamydia (sst)
8. Bartonella henselae (sst)

Viral

9. Canine parvovirus (IgM / IgG) (sst)
10. Canine distemper (IgM / IgG) (sst)
11. Canine distemper smears (DFA) (sl)
12. Feline leukemia (ELISA) (sst)
13. Feline leukemia (IFA) (ltt)
14. Feline infectious peritonitis (FIP) (sst)
15. Feline immunodeficiency syndrome (FIV) (sst)
16. Feline rhinotracheitis (sst)
17. Feline panleukopenia (sst)
18. Equine rhinopneumonitis (sst)

Bacterial

19. Borrelia burgdorferi (Lyme) (IFA) (sst)
20. Lyme Multiplex assay (sst)
21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

Microscopic Identification

42. Mycoplasma haemocanis (ltt) (Haemobartonella canis)
43. Mycoplasma haemofelis (ltt) (Haemobartonella felis)
44. Babesia spp. (sl, ltt)
45. Trypanosoma spp. (sl, ltt)
46. Brucella canis (sl,ltt)

DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
48. EHRLICHIA – FUNGAL PANEL
Ehrlichia canis, Coccidioides (sst)
49. FUNGAL PANEL
Cocci, Blasto, Histo (sst)
50. CANINE HEMOLYTIC ANEMIA PANEL
Babesia canis (sst), Coomb's test (ltt)
51. FELINE DISEASE PANEL
E. canis, N. risticii, FeLV, FIP, Toxo (sst)
52. CANINE EXPORT PROFILE I
B. gibsoni (IFA) (sst), Babesia spp. (sl)
53. CANINE EXPORT PROFILE II
E. canis, Leishmania, Lepto, Brucella canis (agglutination) (sst)

ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
55. Ketoconazole (sst)
56. Itraconazole (sst)
57. Voriconazole (sst)

HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
60. T4/ Cholesterol (sst)
61. Chemistry Profile 14 + CBC (sst, ltt)
62. Chemistry Profile 14 + CBC + T4 / Cholesterol (sst, ltt)
63. Ehrlichia canis + Chem Profile 14 + CBC (sst, ltt)
64. Coccidioides + Chem Profile 14 + CBC (sst, ltt)
65. E. canis + Cocci + Chem Profile 14 + CBC (sst, ltt)
66. Tick-borne Disease Panel + T4 / Cholesterol (sst)
67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z19039		F	10 mo	11/27/2019	
2						
3						
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12/2/2019

Nursery Schedule

Infant #	DOB	Days in Age	What to Feed	Delivery Type	Frequency	Additional Information:
New	9/21/2019	Day 71	**See Note below	Self-Feeder 60mL	7am, 11am	Cage: hanging surrogate -EE toys, puffs
Z19221			60mL -increase by 5mL	Adjustments made daily	3pm, (430 AT check)	self-feeder, warming blanket PRN
Female	Dam L08020		self-feeder, puffs	**2 soaked biscuit/ 6 dry**	7pm, 11pm	rectal temp in am (Vet staff), minimal diapers (3), stuffed toy, biscuits
Cage	from 222		100% soy	every feeding fresh food	3am, (6am AT check)	BW daily (Vet Staff), record feedings
New	8/12/2019	Day 110	60% formula	Self feeder 400mL ONLY	7am, 11am	Cage: Surrogate - EE, teething toys
Z19201			10 dry/2 soaked biscuits BID	Adjustments made PRN	3pm, (430 AT check)	self bottle feeding, 2 soaked/10 dry biscuit BID, rubber sipper
Female	Dam K06231		240 Enfamil/160 H20	**Self Feeder**	7pm, 11pm	puffs/cherrios, minimal diapers (2), stuffed toy,
cage	from 131		Enfamil Neuro Pro	rubber sipper	3am, (6am AT check)	BW daily (Vet Staff), record feedings

Special Feeding Instruction:

****Note: Starting with 10mL will adjust daily, read notes on Infant Log Sheet if unclear ask Caroline**

**** Ready to Use formula, open/date and stored in refrigerator, good for 24 hrs once opened**

Normal rectal temp 97.5, if below contact Vet Staff and above 101.0 contact Vet Staff, optimum 99.0

Recording inside isolette temp very critical, especially our isolettes are very touchy, so DO NOT adjust without permission

Week of December 2nd 2019 *Schedule Subject To Change*

7am-3:30	Mon 12-2-2019	Tues 12-3-2019	Wed 12-4-2019	Thurs 12-5-2019	Fri 12-6-2019	Sat 12/7/2019	Sun 12/8/2019
Caroline	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs B Bldg move male B Bldg dam moves	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs 222/232 Ultrasounds	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs schedule	Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs paperwork	Off	Off	Off
Sherri	Off	Off	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean 121: Cocci titer- Z17142, Z17150, Z16161 104: Z18178 intro 121 Itule Order	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean 142: M09202 Exam 111: f/u BW Z17250 152: Vet Tech BWs 104:Z17175 f/uchem/152	Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm 104all/142: case BWs 171:BW Z14066&Z14320 B Bldg.: 302 case BWs	Nursery Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs Tx/Obs/EE/annex/152 Sweep/mop Nurs/ProcRm	Nursery Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs Tx/Obs/EE/annex/152 Sweep/mop Nurs/ProcRm
Schante	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean B Bldg: 302: 244 to 317CD 302: 247 to 317AB 302:F02420-319CD 302: 353 sut rem 320C-A09109 Ex	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean A Bldg: Start time 8AM 222/232 Ultrasounds 142: Z14331 to 112 142: FL04- 131	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm 121: Cocci titer- Z17142, Z17150, Z16161 104: Z18178 intro 121	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm 142: M09202 Exam 111: f/u BW Z17250 152: Vet Tech BWs 104:Z17175 f/uchem/152	Nursery Tx 104/142 EE: 104/142 Obs: 104/142 Tx/Obs/EE: downstairs 104: case BWs (all) 142: case BWs 171: BWZ14066&Z14320 B Bldg.: 302 case BWs	Off	Off
Danielle	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm AftrLunc/endDayLaundry Ship Tissue	Nursery Tx/Obs/EE Upstairs Tx Annex/152 EE Annex/152 ObsAnnex152 Sweep/mop Nurs/ProcRm 142: Z14331 to 112 142: FL04- 131	Off	Off	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean 104/142: case BWs 171:BW Z14066&Z14320 B Bldg.: 302 case BWs 104all/142: case BWs 171:BW Z14066&Z14320 B Bldg.: 302 case BWs	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs	AM/PM: B building Tx/Obs:B building EE:B Bldg/Proc Rm Clean Tx/Ob/EE Upstairs
Dr Amber Dr House Dr Malinowski	On-Call	On-Call	Off On-Call	Off Off On-Call	1/2 day On-Call Off	House On-Call	House On-Call

Everyone is to assist in doing dishwasher and laundry duties, as well as, keep areas cleaned and organized. Sign Off Checklist Sheets Procedure/Surgery/Necropsy

Mon 12/2/19	Tues 12/3/2019	Wed 12/4/2019	Thurs 12/5/19	Friday 12/6/19
B Bldg: 302: 244 to 317CD 302: 247 to 317AB 302:F02420-319CD 302: 353 sut rem 320C-A09109 Ex and return to 319AB 142: fecal F/U	142: Z14331 to 112 142: FL04- 131 A Bldg: Start time 8AM 222/232 Ultrasounds	121: Cocci titer- Z17142, Z17150, Z16161 104: Z18178 intro 121 ATs: 121 BWs B Bldg: 302: Z12353- 319AB	142: M09202 Exam 111: f/u BW Z17250 152: Vet Tech BWs 104: Z17175 f/u chem- intro back 152	104: case BWs (all) 142: case BWs 171: BWs Z14066 & Z14320 B Bldg.: 302 case BWs

PROTATEK REFERENCE LABORATORY
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TEL: (480) 545-8499 • FAX: (480) 545-8409

PROTATEK INTERNATIONAL, INC.

REQUISITION FORM

PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC

Address PO Box 208336
Mesa, AZ 85215

Phone 206-685-6031

Fax N/A

Email Address th81@uw.edu, cjmead2@uw.edu

Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*

Name _____

Address _____

Phone _____

Fax _____

Owner WaNPRC

Animal's Name / ID See Attached

Species Macaca nemestrina

Breed Pig Tailed Macaque

Sex See Attached

Age See Attached

Collection Date 12 / 11 / 2019

Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

Rickettsia

1. Ehrlichia canis (sst)
2. Feline Ehrlichia (E. canis + N. risticii) (sst)
3. Neorickettsia risticii (E. risticii) (sst)
4. Anaplasma phagocytophilum (E. equi) (sst)
5. Ehrlichia sennetsu (sst)
6. Rickettsia rickettsii (RMSF) (sst)
7. Chlamydia (sst)
8. Bartonella henselae (sst)

Viral

9. Canine parvovirus (IgM / IgG) (sst)
10. Canine distemper (IgM / IgG) (sst)
11. Canine distemper smears (DFA) (sl)
12. Feline leukemia (ELISA) (sst)
13. Feline leukemia (IFA) (ltt)
14. Feline infectious peritonitis (FIP) (sst)
15. Feline immunodeficiency syndrome (FIV) (sst)
16. Feline rhinotracheitis (sst)
17. Feline panleukopenia (sst)
18. Equine rhinopneumonitis (sst)

Bacterial

19. Borrelia burgdorferi (Lyme) (IFA) (sst)
20. Lyme Multiplex assay (sst)
21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

Microscopic Identification

42. Mycoplasma haemocanis (ltt)
(Haemobartonella canis)
43. Mycoplasma haemofelis (ltt)
(Haemobartonella felis)
44. Babesia spp. (sl, ltt)
45. Trypanosoma spp. (sl, ltt)
46. Brucella canis (sl,ltt)

DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
48. EHRLICHIA – FUNGAL PANEL
Ehrlichia canis, Coccidioides (sst)
49. FUNGAL PANEL
Cocci, Blasto, Histo (sst)
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Babesia canis (sst), Coomb's test (ltt)
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B. gibsoni (IFA) (sst), Babesia spp. (sl)
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E. canis, Leishmania, Lepto, Brucella canis (agglutination) (sst)

ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
55. Ketoconazole (sst)
56. Itraconazole (sst)
57. Voriconazole (sst)

HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
60. T4/ Cholesterol (sst)
61. Chemistry Profile 14 + CBC (sst, ltt)
62. Chemistry Profile 14 + CBC + T4 / Cholesterol (sst, ltt)
63. Ehrlichia canis + Chem Profile 14 + CBC (sst, ltt)
64. Coccidioides + Chem Profile 14 + CBC (sst, ltt)
65. E. canis + Cocci + Chem Profile 14 + CBC (sst, ltt)
66. Tick-borne Disease Panel + T4 / Cholesterol (sst)
67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z16203		F	3yrs 5mos	12/11/2019	10/28/2019 IgG 1:32, IgM 1:2 positive
2	Z16053		F	3yrs 9mos	12/11/2019	10/28/2019 IgG 1:4, IgM 1:2 positive
3	Z16342		F	3yrs	12/11/2019	10/28/2019 IgG 1:2, IgM 1:2 positive
4	Z16068		F	3yrs 8m0s	12/11/2019	10/15/19 negative
5	L03132		F	16yrs 8mo	12/12/2019	9/3/2019 positive (+)1:2 negative (-)<1:1
6						
7						
8						
9						
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11						
12						
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14						
15						
16						
17						
18						
19						
20						

Re: protatek requisition for 11/27/2019

smintner <smintner@uw.edu>
Wed 11/27/2019 2:27 PM
To: cjmead2 <cjmead2@uw.edu>

1 attachments (2 MB)
Prototek_Requisition_Form 7-31-19.pdf;

No! I put it on the form correctly (I checked....they haven't picked up yet.) Sorry for the confusion.

From: cjmead2 <cjmead2@uw.edu>
Sent: Wednesday, November 27, 2019 1:36 PM
To: smintner <smintner@uw.edu>
Subject: RE: protatek requisition for 11/27/2019

Is this the correct animal?

From: smintner <smintner@uw.edu>
Sent: Wednesday, November 27, 2019 9:41 AM
To: cjmead2 <cjmead2@uw.edu>
Subject: protatek requisition for 11/27/2019

PROTATEK REFERENCE LABORATORY
540 WEST IRON AVENUE • SUITE 106 • MESA, AZ 85210
TEL: (480) 545-8499 • FAX: (480) 545-8409

PROTATEK INTERNATIONAL, INC.

REQUISITION FORM

PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC
Address PO Box 208336
Mesa, AZ 85215
Phone 206-685-6031
Fax N/A
Email Address th81@uw.edu, cjmead2@uw.edu
Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*
Name _____
Address _____
_____
Phone _____
Fax _____

Owner WaNPRC **Animal's Name / ID** See Attached
Species Macaca nemestrina **Breed** Pig Tailed Macaque **Sex** See Attached **Age** See Attached
Collection Date 7 / 30 / 2019
Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

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21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

Microscopic Identification

42. Mycoplasma haemocanis (ltt) (Haemobartonella canis)
43. Mycoplasma haemofelis (ltt) (Haemobartonella felis)
44. Babesia spp. (sl, ltt)
45. Trypanosoma spp. (sl, ltt)
46. Brucella canis (sl,ltt)

DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
48. EHRLICHIA – FUNGAL PANEL
Ehrlichia canis, Coccidioides (sst)
49. FUNGAL PANEL
Cocci, Blasto, Histo (sst)
50. CANINE HEMOLYTIC ANEMIA PANEL
Babesia canis (sst), Coomb's test (ltt)
51. FELINE DISEASE PANEL
E. canis, N. risticii, FeLV, FIP, Toxo (sst)
52. CANINE EXPORT PROFILE I
B. gibsoni (IFA) (sst), Babesia spp. (sl)
53. CANINE EXPORT PROFILE II
E. canis, Leishmania, Lepto, Brucella canis (agglutination) (sst)

ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
55. Ketoconazole (sst)
56. Itraconazole (sst)
57. Voriconazole (sst)

HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
60. T4/ Cholesterol (sst)
61. Chemistry Profile 14 + CBC (sst, ltt)
62. Chemistry Profile 14 + CBC + T4 / Cholesterol (sst, ltt)
63. Ehrlichia canis + Chem Profile 14 + CBC (sst, ltt)
64. Coccidioides + Chem Profile 14 + CBC (sst, ltt)
65. E. canis + Cocci + Chem Profile 14 + CBC (sst, ltt)
66. Tick-borne Disease Panel + T4 / Cholesterol (sst)
67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z19039		F	10 mo	11/27/2019	
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PROTATEK REFERENCE LABORATORY
540 WEST IRON AVENUE • SUITE 106 • MESA, AZ 85210
TEL: (480) 545-8499 • FAX: (480) 545-8409

PROTATEK INTERNATIONAL, INC.

REQUISITION FORM

PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC
Address PO Box 208336
Mesa, AZ 85215
Phone 206-685-6031
Fax N/A
Email Address th81@uw.edu, cjmead2@uw.edu
Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*
Name _____
Address _____
_____
Phone _____
Fax _____

Owner WaNPRC **Animal's Name / ID** See Attached
Species Macaca nemestrina **Breed** Pig Tailed Macaque **Sex** See Attached **Age** See Attached
Collection Date 7 / 30 / 2019
Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

Rickettsia

1. Ehrlichia canis (sst)
2. Feline Ehrlichia (E. canis + N. risticii) (sst)
3. Neorickettsia risticii (E. risticii) (sst)
4. Anaplasma phagocytophilum (E. equi) (sst)
5. Ehrlichia sennetsu (sst)
6. Rickettsia rickettsii (RMSF) (sst)
7. Chlamydia (sst)
8. Bartonella henselae (sst)

Viral

9. Canine parvovirus (IgM / IgG) (sst)
10. Canine distemper (IgM / IgG) (sst)
11. Canine distemper smears (DFA) (sl)
12. Feline leukemia (ELISA) (sst)
13. Feline leukemia (IFA) (ltt)
14. Feline infectious peritonitis (FIP) (sst)
15. Feline immunodeficiency syndrome (FIV) (sst)
16. Feline rhinotracheitis (sst)
17. Feline panleukopenia (sst)
18. Equine rhinopneumonitis (sst)

Bacterial

19. Borrelia burgdorferi (Lyme) (IFA) (sst)
20. Lyme Multiplex assay (sst)
21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

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42. Mycoplasma haemocanis (ltt) (Haemobartonella canis)
43. Mycoplasma haemofelis (ltt) (Haemobartonella felis)
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45. Trypanosoma spp. (sl, ltt)
46. Brucella canis (sl,ltt)

DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
48. EHRLICHIA – FUNGAL PANEL
Ehrlichia canis, Coccidioides (sst)
49. FUNGAL PANEL
Cocci, Blasto, Histo (sst)
50. CANINE HEMOLYTIC ANEMIA PANEL
Babesia canis (sst), Coomb's test (ltt)
51. FELINE DISEASE PANEL
E. canis, N. risticii, FeLV, FIP, Toxo (sst)
52. CANINE EXPORT PROFILE I
B. gibsoni (IFA) (sst), Babesia spp. (sl)
53. CANINE EXPORT PROFILE II
E. canis, Leishmania, Lepto, Brucella canis (agglutination) (sst)

ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
55. Ketoconazole (sst)
56. Itraconazole (sst)
57. Voriconazole (sst)

HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
60. T4/ Cholesterol (sst)
61. Chemistry Profile 14 + CBC (sst, ltt)
62. Chemistry Profile 14 + CBC + T4 / Cholesterol (sst, ltt)
63. Ehrlichia canis + Chem Profile 14 + CBC (sst, ltt)
64. Coccidioides + Chem Profile 14 + CBC (sst, ltt)
65. E. canis + Cocci + Chem Profile 14 + CBC (sst, ltt)
66. Tick-borne Disease Panel + T4 / Cholesterol (sst)
67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z17196		F	1 yrs 11 mo	7/30/2019	4/16/2019 IgG/IgM negative
2						
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212 222 231 Bloodwork- 2/25/2019

Date	Animal #	Alias	Sex	Cage	BW	Cocci Titer (1.0 mls)	Serology (4.0-8mLs)	CBC (0.5 mLs)	Chem (1.0 mLs)	Haplotypes (1-2.0 mLs)
2/25/2019	K07017	GV32	M	AA212	17.17kg	yes	yes x 2	yes	yes	yes
2/25/2019	K05143	GA42	M	AA222	18.07kg	yes	yes x 2	yes	yes	yes
2/25/2019	F01108	DH01	M	AA231	15.28kg	yes	yes x 2	yes	yes	

DNA (2.0 mLs)	Fecal Collection	Initial	ARMS

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PROTATEK INTERNATIONAL, INC.

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PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC
Address PO Box 208336
Mesa, AZ 85215
Phone 206-685-6031
Fax N/A
Email Address th81@uw.edu, cjmead2@uw.edu
Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*
Name _____
Address _____
_____
Phone _____
Fax _____

Owner WaNPRC **Animal's Name / ID** See Attached
Species Macaca nemestrina **Breed** Pig Tailed Macaque **Sex** See Attached **Age** See Attached
Collection Date 7 / 30 / 2019
Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

Rickettsia

1. Ehrlichia canis (sst)
2. Feline Ehrlichia (E. canis + N. risticii) (sst)
3. Neorickettsia risticii (E. risticii) (sst)
4. Anaplasma phagocytophilum (E. equi) (sst)
5. Ehrlichia sennetsu (sst)
6. Rickettsia rickettsii (RMSF) (sst)
7. Chlamydia (sst)
8. Bartonella henselae (sst)

Viral

9. Canine parvovirus (IgM / IgG) (sst)
10. Canine distemper (IgM / IgG) (sst)
11. Canine distemper smears (DFA) (sl)
12. Feline leukemia (ELISA) (sst)
13. Feline leukemia (IFA) (ltt)
14. Feline infectious peritonitis (FIP) (sst)
15. Feline immunodeficiency syndrome (FIV) (sst)
16. Feline rhinotracheitis (sst)
17. Feline panleukopenia (sst)
18. Equine rhinopneumonitis (sst)

Bacterial

19. Borrelia burgdorferi (Lyme) (IFA) (sst)
20. Lyme Multiplex assay (sst)
21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

Microscopic Identification

42. Mycoplasma haemocanis (ltt) (Haemobartonella canis)
43. Mycoplasma haemofelis (ltt) (Haemobartonella felis)
44. Babesia spp. (sl, ltt)
45. Trypanosoma spp. (sl, ltt)
46. Brucella canis (sl,ltt)

DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
48. EHRLICHIA – FUNGAL PANEL
Ehrlichia canis, Coccidioides (sst)
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Cocci, Blasto, Histo (sst)
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Babesia canis (sst), Coomb's test (ltt)
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B. gibsoni (IFA) (sst), Babesia spp. (sl)
53. CANINE EXPORT PROFILE II
E. canis, Leishmania, Lepto, Brucella canis (agglutination) (sst)

ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
55. Ketoconazole (sst)
56. Itraconazole (sst)
57. Voriconazole (sst)

HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
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61. Chemistry Profile 14 + CBC (sst, ltt)
62. Chemistry Profile 14 + CBC + T4 / Cholesterol (sst, ltt)
63. Ehrlichia canis + Chem Profile 14 + CBC (sst, ltt)
64. Coccidioides + Chem Profile 14 + CBC (sst, ltt)
65. E. canis + Cocci + Chem Profile 14 + CBC (sst, ltt)
66. Tick-borne Disease Panel + T4 / Cholesterol (sst)
67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z19006		M	10 mo	11/14/2019	10/24/2019 IgG/IgM positive
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Re: RE:

smintner <smintner@uw.edu>
Fri 12/13/2019 9:50 AM
To: cjmead2 <cjmead2@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>

1 attachments (249 KB)
12-13-2019 protatek.pdf;

Protatek sent out. Paperwork is attached.

Thanks,
Sherri

From: cjmead2 <cjmead2@uw.edu>
Sent: Thursday, December 12, 2019 4:17 PM
To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>
Subject: RE:

Just let me know cocci titers are sent out and send me paperwork
Email update if any new changes

From: cjmead2
Sent: Thursday, December 12, 2019 4:17 PM
To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>
Subject:

Friday December 13th
104: case BWs
142: case BWs
142: EI33 fecal swab?
104: (fast) Z18043 rads w/o cast
B Bldg.: 302 case BWs
Vet Tech 1PM training

PROTATEK REFERENCE LABORATORY
540 WEST IRON AVENUE • SUITE 106 • MESA, AZ 85210
TEL: (480) 545-8499 • FAX: (480) 545-8409

PROTATEK INTERNATIONAL, INC.

REQUISITION FORM

PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC

Address PO Box 208336
Mesa, AZ 85215

Phone 206-685-6031

Fax N/A

Email Address th81@uw.edu, cjmead2@uw.edu

Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*

Name _____

Address _____

Phone _____

Fax _____

Owner WaNPRC

Animal's Name / ID See Attached

Species Macaca nemestrina

Breed Pig Tailed Macaque

Sex See Attached

Age See Attached

Collection Date 12 / 11 / 2019

Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

Rickettsia

1. Ehrlichia canis (sst)
2. Feline Ehrlichia (E. canis + N. risticii) (sst)
3. Neorickettsia risticii (E. risticii) (sst)
4. Anaplasma phagocytophilum (E. equi) (sst)
5. Ehrlichia sennetsu (sst)
6. Rickettsia rickettsii (RMSF) (sst)
7. Chlamydia (sst)
8. Bartonella henselae (sst)

Viral

9. Canine parvovirus (IgM / IgG) (sst)
10. Canine distemper (IgM / IgG) (sst)
11. Canine distemper smears (DFA) (sl)
12. Feline leukemia (ELISA) (sst)
13. Feline leukemia (IFA) (ltt)
14. Feline infectious peritonitis (FIP) (sst)
15. Feline immunodeficiency syndrome (FIV) (sst)
16. Feline rhinotracheitis (sst)
17. Feline panleukopenia (sst)
18. Equine rhinopneumonitis (sst)

Bacterial

19. Borrelia burgdorferi (Lyme) (IFA) (sst)
20. Lyme Multiplex assay (sst)
21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

Microscopic Identification

42. Mycoplasma haemocanis (ltt)
(Haemobartonella canis)
43. Mycoplasma haemofelis (ltt)
(Haemobartonella felis)
44. Babesia spp. (sl, ltt)
45. Trypanosoma spp. (sl, ltt)
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DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
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Ehrlichia canis, Coccidioides (sst)
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ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
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HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
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61. Chemistry Profile 14 + CBC (sst, ltt)
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67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z16203		F	3yrs 5mos	12/11/2019	10/28/2019 IgG 1:32, IgM 1:2 positive
2	Z16053		F	3yrs 9mos	12/11/2019	10/28/2019 IgG 1:4, IgM 1:2 positive
3	Z16342		F	3yrs	12/11/2019	10/28/2019 IgG 1:2, IgM 1:2 positive
4	Z16068		F	3yrs 8m0s	12/11/2019	10/15/19 negative
5	L03132		F	16yrs 8mo	12/12/2019	9/3/2019 positive (+)1:2 negative (-)<1:1
6						
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15						
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17						
18						
19						
20						

Example to send to Protatek Lab

cjmead2 <cjmead2@uw.edu>

Sun 8/4/2019 5:21 PM

To: Danielle Parks <dp546@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; smintner <smintner@uw.edu>

1 attachments (2 MB)

Prototek_Requisition_Form 7-31-19.pdf;

If I am not hereto submit cocci titer.
Here is the form to use, you edit this form.

Get same information as this example indicates and you can find last cocci titer for individual animals under panel reports.
Collect sample/separate, make sure date ID label on tube, double bag small biohazard bag. Place paperwork in out bag, pocket sleeve.
Call 480# after (9am, but before 1130am cut off for pick-up)
Say, I am calling from Washington Primate Facility in Mesa Az, I have 1 sample for a pick-up.
Put in Idexx box with 2-3 ice packs, check later to ensure it is picked up.

Send me a copy of the paperwork, so I can track for billing and make sure results are downloaded.

If questions, let me know.
Caroline

PROTATEK REFERENCE LABORATORY
540 WEST IRON AVENUE • SUITE 106 • MESA, AZ 85210
TEL: (480) 545-8499 • FAX: (480) 545-8409

PROTATEK INTERNATIONAL, INC.

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PRL Reference # _____

Account Code UWPCAZ

Clinic Name WaNPRC-ABC

Address PO Box 208336
Mesa, AZ 85215

Phone 206-685-6031

Fax N/A

Email Address th81@uw.edu, cjmead2@uw.edu

Veterinarian Tess House, Caroline Mead

Billing Info *(if different)*

Name _____

Address _____

Phone _____

Fax _____

Owner WaNPRC

Animal's Name / ID See Attached

Species Macaca nemestrina

Breed Pig Tailed Macaque

Sex See Attached

Age See Attached

Collection Date 12 / 11 / 2019

Clinical History / DD

ANALYSIS REQUESTED (circle)

SEROLOGY

Rickettsia

1. Ehrlichia canis (sst)
2. Feline Ehrlichia (E. canis + N. risticii) (sst)
3. Neorickettsia risticii (E. risticii) (sst)
4. Anaplasma phagocytophilum (E. equi) (sst)
5. Ehrlichia sennetsu (sst)
6. Rickettsia rickettsii (RMSF) (sst)
7. Chlamydia (sst)
8. Bartonella henselae (sst)

Viral

9. Canine parvovirus (IgM / IgG) (sst)
10. Canine distemper (IgM / IgG) (sst)
11. Canine distemper smears (DFA) (sl)
12. Feline leukemia (ELISA) (sst)
13. Feline leukemia (IFA) (ltt)
14. Feline infectious peritonitis (FIP) (sst)
15. Feline immunodeficiency syndrome (FIV) (sst)
16. Feline rhinotracheitis (sst)
17. Feline panleukopenia (sst)
18. Equine rhinopneumonitis (sst)

Bacterial

19. Borrelia burgdorferi (Lyme) (IFA) (sst)
20. Lyme Multiplex assay (sst)
21. Brucella canis (IFA) (sst)
22. Brucella canis (EXPORT) (sst)
23. Leptospira (6 serovars) (sst)

Protozoan

24. Babesia canis (sst)
25. Babesia gibsoni (sst)
26. Babesia caballi (equine) (sst)
27. Babesia bigemina (bovine) (sst)
28. Toxoplasma gondii (IgM / IgG) (sst)
29. Neospora caninum (IgM / IgG) (sst)
30. Leishmania infantum (chagasi) (sst)

Fungal

31. Coccidioidomycosis (Cocci, Valley Fever) (sst)
32. Blastomycosis (sst)
33. Histoplasmosis (sst)
34. Aspergillosis (sst)
35. Cryptococcus antigen (sst)

Helminthic

36. Heartworm antigen (ELISA) (sst)
37a. Knott's microfilaria test (ltt)
37b. D. immitis microfilarial filtration test (ltt)

Hormonal/Autoimmune

38. Progesterone assay (sst)
39. Canine rheumatoid factor (sst)
40. Coomb's test (direct) (ltt)
41. Antinuclear antibodies (ANA) (sst)

Microscopic Identification

42. Mycoplasma haemocanis (ltt)
(Haemobartonella canis)
43. Mycoplasma haemofelis (ltt)
(Haemobartonella felis)
44. Babesia spp. (sl, ltt)
45. Trypanosoma spp. (sl, ltt)
46. Brucella canis (sl,ltt)

DISEASE PANELS

47. TICK-BORNE DISEASE PANEL
E. canis, B. canis, RMSF, Lyme (sst)
48. EHRLICHIA – FUNGAL PANEL
Ehrlichia canis, Coccidioides (sst)
49. FUNGAL PANEL
Cocci, Blasto, Histo (sst)
50. CANINE HEMOLYTIC ANEMIA PANEL
Babesia canis (sst), Coomb's test (ltt)
51. FELINE DISEASE PANEL
E. canis, N. risticii, FeLV, FIP, Toxo (sst)
52. CANINE EXPORT PROFILE I
B. gibsoni (IFA) (sst), Babesia spp. (sl)
53. CANINE EXPORT PROFILE II
E. canis, Leishmania, Lepto, Brucella canis (agglutination) (sst)

ANTI-FUNGAL DRUG LEVELS

54. Fluconazole (sst)
55. Ketoconazole (sst)
56. Itraconazole (sst)
57. Voriconazole (sst)

HEALTH PROFILES AND PANELS

58. CBC (ltt)
22 parameters with 5-part differential
59. Chemistry Profile 14 (sst): ALT, ALB, ALP, AMY, CA, PHOS, CRE, GLOB, GLU, K+, NA+, TBIL, TP, BUN
60. T4/ Cholesterol (sst)
61. Chemistry Profile 14 + CBC (sst, ltt)
62. Chemistry Profile 14 + CBC + T4 / Cholesterol (sst, ltt)
63. Ehrlichia canis + Chem Profile 14 + CBC (sst, ltt)
64. Coccidioides + Chem Profile 14 + CBC (sst, ltt)
65. E. canis + Cocci + Chem Profile 14 + CBC (sst, ltt)
66. Tick-borne Disease Panel + T4 / Cholesterol (sst)
67. Tick-borne Disease Panel + Chem Profile 14 + CBC (sst, ltt)

PCR PANELS (submit 1ml whole blood in ltt)

68. Ehrlichia / Anaplasma / Neorickettsia (ltt)
69. Rickettsia (ltt)
70. Bartonella (ltt)
71. Hemoplasma (Hemobartonella) (ltt)
72. Babesia (ltt)

OTHER TESTS: _____

_____

sst = serum separator tube • ltt = lavender top tube • sl = slides (unstained)

	Animal ID	Alias	Sex	Age	Collection Date	Clinical History
1	Z16203		F	3yrs 5mos	12/11/2019	10/28/2019 IgG 1:32, IgM 1:2 positive
2	Z16053		F	3yrs 9mos	12/11/2019	10/28/2019 IgG 1:4, IgM 1:2 positive
3	Z16342		F	3yrs	12/11/2019	10/28/2019 IgG 1:2, IgM 1:2 positive
4	Z16068		F	3yrs 8m0s	12/11/2019	10/15/19 negative
5	L03132		F	16yrs 8mo	12/12/2019	9/3/2019 positive (+)1:2 negative (-)<1:1
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 5/26/2019 3:26 PM

To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>; Christopher M. Wozniak <chrisw36@uw.edu>

2 attachments (35 KB)

Week of the May 27th 2019.xlsx; Nursery Schedule May 27th 2019.xlsx;

Sherri initial -80 freezer
Schante fill out Protocyte decontamination sheet

Gallon Distilled water, should be written Not for Animal Use

103: 059 on sipper now
103: Thor starts formula dilution, we can now use powder formula (make sure this is indicated for night shift) and bowl once daily, but very, very small amount of food, don't over feed him
103: BWs on Fridays

104: Z18121 BW on Friday, start Friday bowl once daily, then hopefully next week will pair house

Schante will separate 241 and then she will help me with introductions

Sherri assist Vets with the two sedations

Tuesday May 28th

142: S11069, not sure if schedule to remove rest of sutures, keep checking to see if any remain

142: Z14063- not sure if returning back to 171

142: DH46 cbc/chem/fecal (fast)

104: Z16358 cocci titer (fast)

104: Z18121- fecal swab to Seattle

142: M06139 intro back to 242

142: K11143/infant intro back to 242

142: ET02/infant intro back to 231

142: Z14320/infant intro back into 112

241: M09202 & Z12034 BWs

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 2/3/2019 5:57 PM

To: smintner <smintner@uw.edu>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>

2 attachments (33 KB)

Nursery Schedule Feb 4th 2019.xlsx; Week of the Feb 4th 2019.xlsx;

Monday February 4th

241: male K-9 removal (male to recover in group six in bay) make sure cage plate Vet staff to feed only

104: Z17139 -sedate to exam and cocci titer

111: Z17184 BW (check with Vet before letting back in group)

221: CV61 BW

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 1/20/2019 6:53 PM

To: Sherri Mintner <sherri.mintner@wanprc.org>; Schante M. Hodges <shodges3@uw.edu>; Danielle Parks <dp546@uw.edu>

2 attachments (32 KB)

Week of the Jan 20th 2019.xlsx; Nursery Schedule Week -Jan 21st 2019.xlsx;

I will send out cocci titers Wed, since might be more
Waiting if other NYU to process
Thurs Danielle starts
Sat Sherri works for Schante

Tuesday January 22nd

142: Z13337 follow-up fecal swab
241: male (K04170) follow-up fecal swab
142: K11143/Z19007 infant BW Exam (check ears if tattooed)
142: Z14320/Z19006 infant BW Exam (check ears if tattooed)

142: Z14345-intro back to 112 (wait on this one, I will reschedule)

(No subject)

cjmead2 <cjmead2@uw.edu>

Sun 1/13/2019 8:09 PM

To: Schante M. Hodges <shodges3@uw.edu>; smintner <smintner@uw.edu>

2 attachments (32 KB)

Week of the Jan 14th 2019.xlsx; Nursery Schedule Week -Jan 14th 2019.xlsx;

Kinda busy Monday, on top of nursery
One infant now to pull

Sherri Off Tues 3pm
Schante Off Wed 2pm

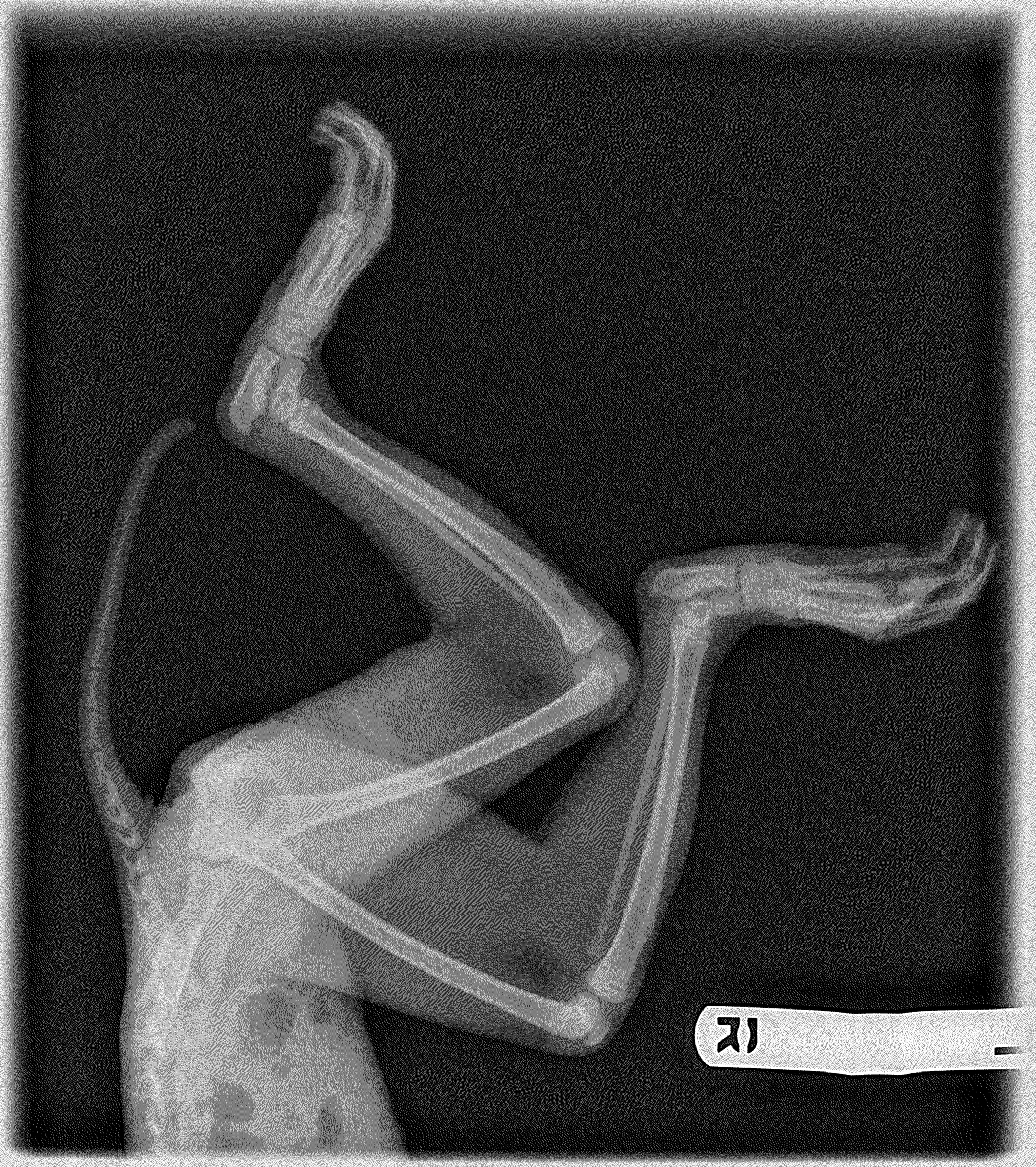
Week of switch and weekend

I supposed to leave at noon Mon & Tues, will see how day goes
Caroline Off Friday

Tuesday:

~~232: (2-4) juvenile chest tattoo~~
104: Z16005- follow-up cocci titer
142: M04326 intro back into 131

231: ET02 New birth Exam
231: F11079 BW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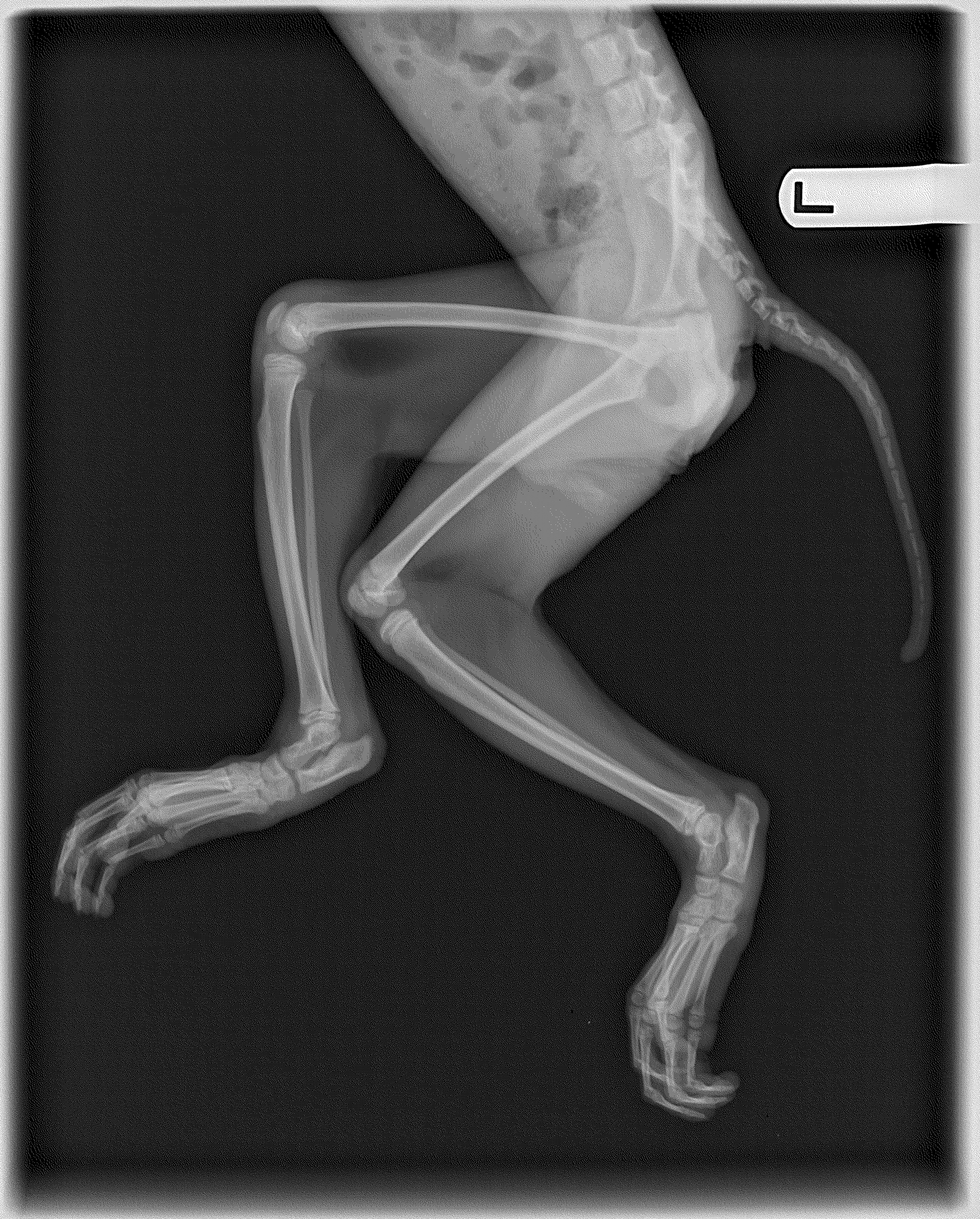
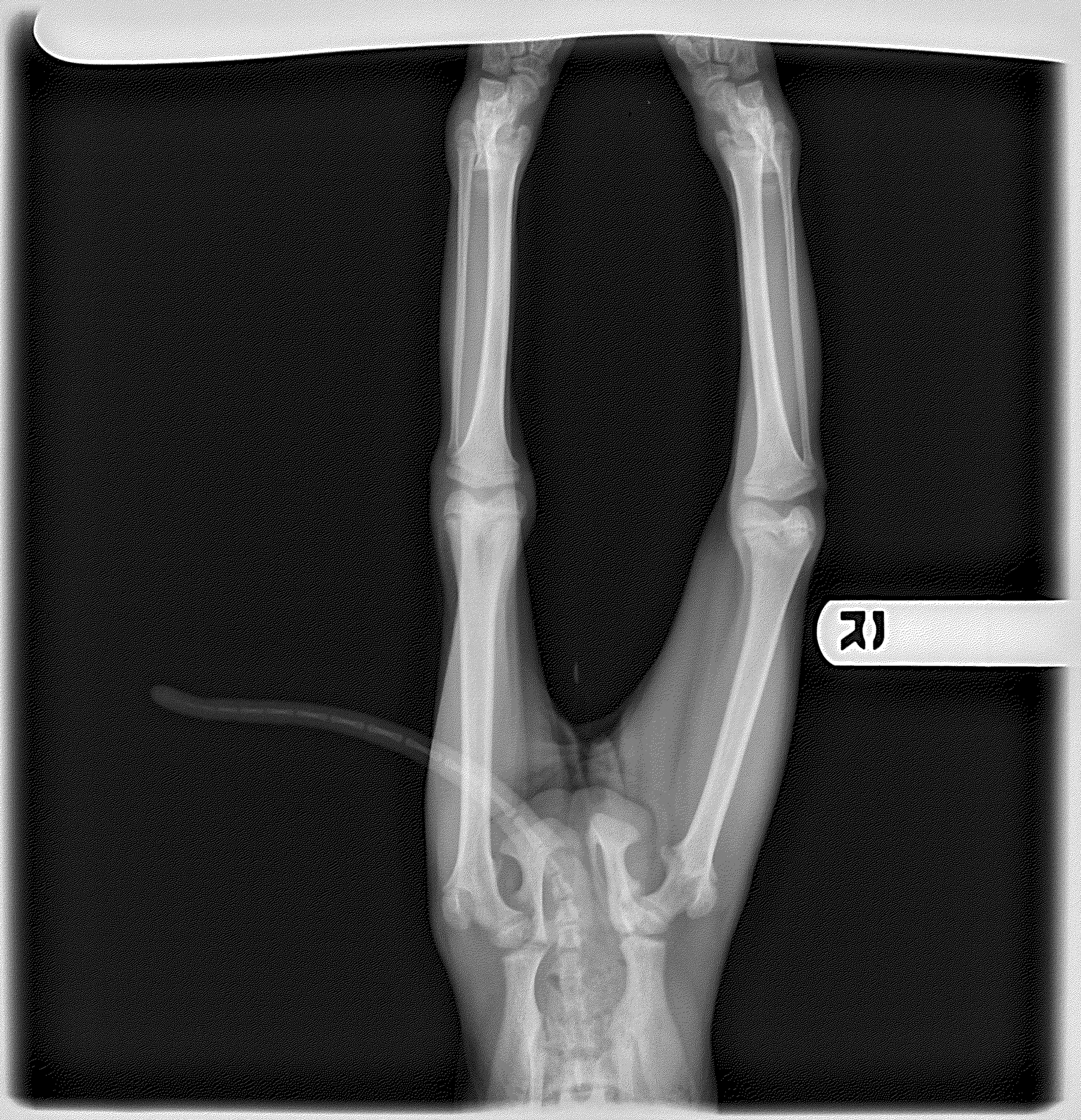
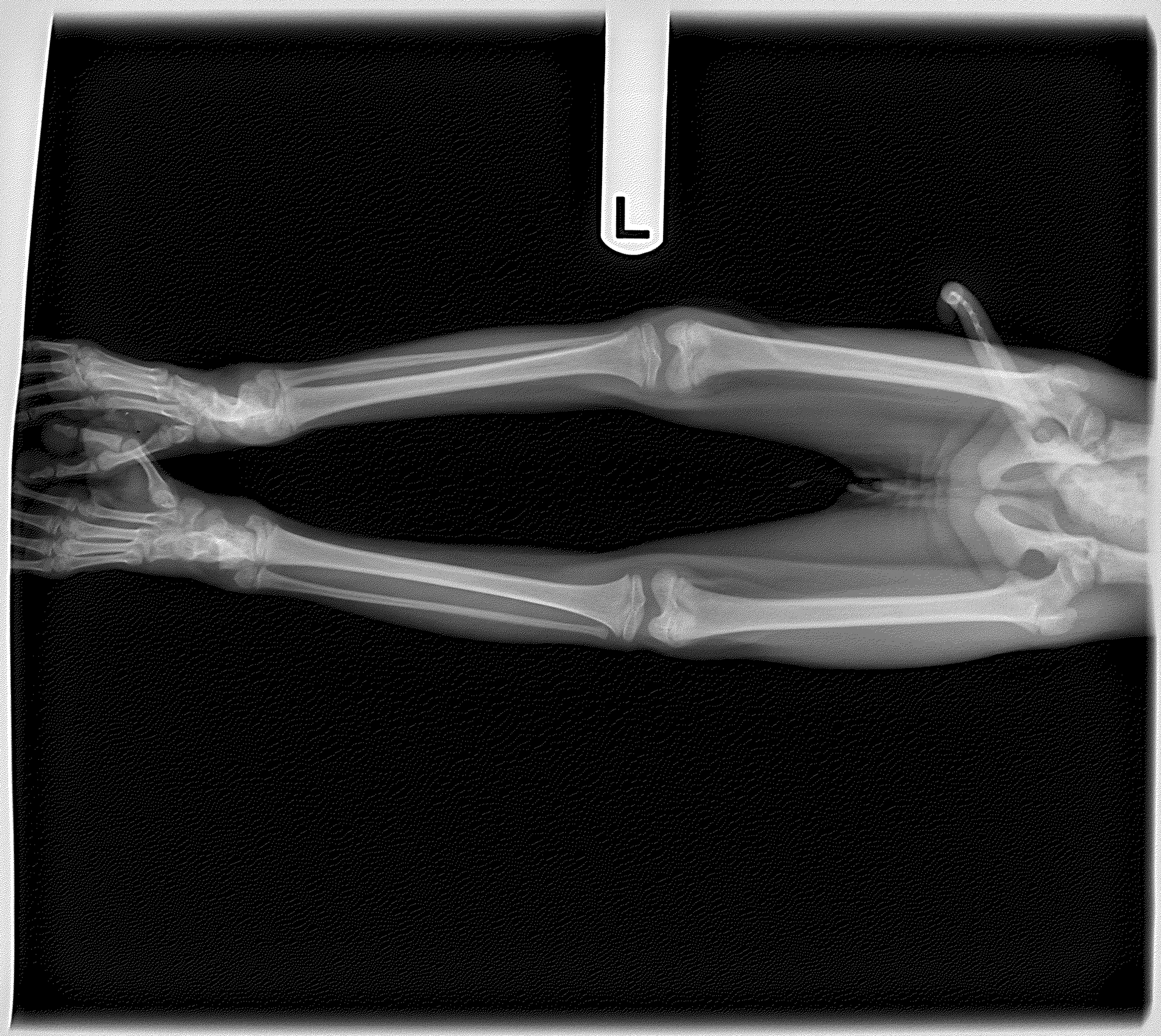

L


RT


L

Dean Jeffery

From: Dean Jeffery
Sent: Wednesday, February 27, 2019 5:22 PM
To: jasonl73 (jasonl73@uw.edu); Keith Vogel; Kate Guerriero
Cc: Carolyn Malinowski (cmali@uw.edu)
Subject: FW: Z17139 for Discussion
Attachments: 12022019-085025_EXTREMITY.jpg; 12022019-085207_EXTREMITY.jpg; 12022019-073001_EXTREMITY.jpg; 12022019-084931_EXTREMITY.jpg

I went back and looked at the original rads. Granted they were only 2 weeks ago but I see the same sort of mottling with the femoral and tibial epiphyses. I wonder if this is what immature cancellous bone looks like.

Also, just looking at the lateral aspect of the femoral condyles on the DV view, it shows just how much a little rotation can distort the image to create the appearance of differently sized joint spaces.

I can't wait to see what the Valley Fever titer shows! In the meantime, is it possible to reach out to the lab you sent the cytology too and ask for a re-read to look for Valley Fever spores? There's usually a small nominal fee associated with this. Also, it sounds like it's time for an antibiotic change in the event that this is some resistant bug. I'd go doxy or clindamycin (and just be prepared to manage the diarrhea, which sounds like the lesser of two evils).

DJ

From: cmali <cmali@uw.edu>
Sent: Tuesday, February 12, 2019 1:13 PM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>; Sally Thompson-Iritani <sti2@uw.edu>; Keith Vogel <vogelk@uw.edu>; Dean Jeffery <daj12@uw.edu>; Kathryn A. Guerriero <kag18@uw.edu>; Britni C. Curtis <britcurt@uw.edu>; Jason D. Laramore <jasonl73@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: Z17139 for Discussion

Hi All,

Case discussion for tomorrow (or via email if that works better)...

Z17137 presented on for toe-touching lameness and non-weight bearing on the rear left leg on 29 Jan. This animal was in an indoor/outdoor enclosure with ~20 other juvenile animals. On PE there was nothing remarkable (no soft tissue swellings) and ROM was normal for affected limb. X-rays revealed nothing unusual. He was prescribed Meloxicam and cage rest.

Since then, techs report intermittent weight bearing on the limb and also on the right limb. This morning he was scooting on the perch bars on his bottom and holding both feet up, and not grasping with the right. He was also swinging around a bit and holding both hind limbs tucked up (but there was a lot happening in the room so he may have been nervous/stressed and therefore behaving weirdly).

Further examination today revealed firm swelling/thickening on the medial aspect of the left stifle and decreased extension of the leg at the stifle (~90% extension) when compared to the contralateral limb. Cranial drawer, tibial thrust, and patellar laxity seemed comparable between limbs (but we aren't sure what normal

is, the stifles bilaterally seemed a little wiggly/loose subjectively). X-rays are attached. Right limb appears normal. Meloxicam and cage rest were extended.

Plan for now is to recheck with xrays in 2 weeks.

All input/suggestions are welcome!!!

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
Washington National Primate Research Center/University of Washington
Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care... | explore UW's Compassion Fatigue Program

Pregnancy outcomes following gabapentin use

Results of a prospective comparative cohort study

Hisaki Fujii, MD
Akash Goel, BSc
Nathalie Bernard, PhD
Alessandra Pistelli, MD
Laura M. Yates, MBCHB
Sally Stephens, PhD
Jungyeol Y. Han
Doreen Matsui, MD
Fatwa Etwell, BSc
Thomas R. Einarson, PhD
Gideon Koren, MD
Adrienne Einarson, RN

Correspondence to Ms. Einarson: einarson@sickkids.ca

ABSTRACT

Objectives: Our objectives were to 1) determine whether first-trimester use of gabapentin is associated with an increased risk for major malformations; 2) examine rates of spontaneous abortions, therapeutic abortions, stillbirths, mean birth weight and gestational age at delivery; and 3) examine rates of poor neonatal adaptation syndrome following late pregnancy exposure.

Methods: The study design was prospective. Women were included who initially contacted the services between 5 and 8 weeks with a comparison group of women exposed to nonteratogens, collected in a similar manner.

Results: We have data on 223 pregnancy outcomes exposed to gabapentin and 223 unexposed pregnancies. The rates of major malformations were similar in both groups ($p = 0.845$). There was a higher rate of preterm births ($p = 0.019$) and low birth weight <2,500 g ($p = 0.033$) in the gabapentin group. Among infants who were exposed to gabapentin up until delivery, 23 of 61 (38%) were admitted to either the neonatal intensive care unit or special care nursery for observation and/or treatment, vs 6 of 201 (2.9%) live births in the comparison group ($p < 0.001$). There were 2 cases of possible poor neonatal adaptation syndrome in neonates exposed to gabapentin close to delivery, compared with none in the comparison group, although it must be noted that these infants were concomitantly exposed to other psychotropic drugs. Among the women who took gabapentin, the major indications were pain (n = 90; 43%) and epilepsy (n = 71; 34%); the remainder were for other indications, mostly psychiatric.

Conclusion: Our results suggest that although this sample size is not large enough to make any definitive conclusions, and there was no comparator group treated with other antiepileptic drugs, gabapentin use in pregnancy does not appear to increase the risk for major malformations. This finding and the increased risk for low birth weight and preterm birth require further investigation. ***Neurology*® 2013;80:1565–1570**

GLOSSARY

NICU = neonatal intensive care unit; **SCN** = special care nursery; **TIS** = teratogen information service.

Gabapentin (Neurontin; Pfizer Canada Inc., Kirkland, QC) is an antiepileptic drug designed to treat partial seizures and is a γ-aminobutyric acid analog that differs both structurally and pharmacologically from other classes of antiepileptic drugs.[1]

The drug was approved by the US Food and Drug Administration for use in epilepsy in 1993 and subsequently for neuropathic pain in 2002.[2] However, despite the increasing number of patients receiving gabapentin, there is only limited information regarding the safety of this medication when used during pregnancy.

A study from the European Gabapentin Registry included prospective and retrospective data with a total of 51 outcomes and 44 live births of women with epilepsy and other disorders exposed to gabapentin during pregnancy. The researchers reported 2 major malformations in infants exposed to gabapentin in the first trimester of pregnancy.[3] In another group of 7 women

From The Motherisk Program (H.F., A.G., T.R.E., G.K., A.E.), Department of Pediatrics, The Hospital for Sick Children, The University of Toronto, Canada; Centre Régional de Pharmacovigilance (N.B.), Lyon, on behalf of the French Network of Pharmacovigilance Centers, France; Florence Teratogen Information Service (A.P.), Florence, Italy; UK Teratology Information Service (L.M.Y., S.S.), Newcastle-Upon-Tyne, England; Korean Motherisk Program (J.Y.H.), Seoul, Korea; Frame Program (D.M., F.E., G.K.), Children's Hospital, London Health Sciences Centre and Clinical Pharmacology, University of Western Ontario, London, Canada; and Leslie Dan Faculty of Pharmacy (T.R.E.), University of Toronto, Canada.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

with hyperemesis gravidarum, 2 congenital defects were reported.[4] A cohort study in Denmark reported on 59 fetuses exposed to gabapentin during pregnancy, and documented 1 major malformation and 6 spontaneous abortions.[5] Recently, the North American antiepileptic drug pregnancy registry reported on 145 fetuses (monotherapy), and documented 1 major malformation with no information on other outcomes.[6]

Considering the increasing number of pregnant women who may be taking gabapentin for other conditions during pregnancy, such as restless legs syndrome,[7] and paucity of information regarding the safety of this medication in pregnancy, more information regarding fetal safety is required.

The objectives of our study were 3-fold: 1) to determine whether gabapentin exposure during pregnancy increases the rate of major malformations above the baseline population rate of 1% to 3%; 2) to examine the rates of stillbirths, spontaneous abortions, therapeutic abortions, gestational age at birth, and mean birth weight in exposed infants; and 3) to determine whether neonates experienced poor neonatal adaptation syndrome, which includes symptoms such as jitteriness, tachycardia, hypothermia, vomiting, hypoglycemia, irritability, hypertonia, eating/sleeping difficulties, convulsion, and respiratory stress.

METHODS Data for this research were obtained from teratogen information services (TISs) as well as a pharmacovigilance center in several countries, which included Toronto (Canada), London (Canada), Lyon (France), Newcastle-Upon-Tyne (England), Florence (Italy), and Seoul (Korea). TISs provide evidence-based information regarding the safety and/or risks associated with exposure to drugs for pregnant and lactating women and their health care providers. French data were collected by one of the European TIS members from several French pharmacovigilance centers that use procedures similar to those of TISs, although requests are received mostly from physicians. The United Kingdom TIS does not currently routinely collect data from women, as it is their health provider who makes the initial inquiry. However, the same data are collected in the same manner in all centers, be it by a physician or an information specialist at a TIS. The services are run by various sources, such as universities, hospitals, and other academic centers.

During the initial contact, which was early on in pregnancy, most frequently between 5 and 8 weeks of pregnancy, demographics, medical and obstetrical histories, as well as details of exposure and concurrent exposures were recorded on a standardized questionnaire. Shortly after birth to approximately 2 to 3 months after delivery at most services, researchers contacted women who had taken gabapentin and received oral and/or written consent to complete the follow-up pregnancy outcome questionnaire. Outcomes of interest included live birth, spontaneous or therapeutic abortion, ectopic pregnancy, stillbirth, presence or absence of major malformation, defined as structural anomalies in the offspring that have serious medical effects or require surgery (genetic and cytogenetic anomalies were excluded), birth weight, gestational age at delivery, and presence or absence of neonatal distress in the newborn period up to 2 weeks postnatal. At some of the programs, but not all, following completion of the questionnaire, a letter was sent to the infant's physician asking for verification of the information obtained from the mother regarding the baby's health.

Each woman was compared with another woman who contacted the same TIS or pharmacovigilance center with exposure to a nonteratogenic substance, for example, acetaminophen or antibiotics. They were matched for maternal age (±2 years), alcohol consumption, and smoking, as well as for gestational age at time of initial contact (±2 weeks). The latter is critical when calculating the incidence of spontaneous abortion, because the observed proportion of pregnancies ending in loss is highly dependent on the gestational age at which pregnancies are recognized and how the losses are identified.

Statistical analysis. Maternal characteristics and pregnancy outcomes measured on a continuous scale were compared using unpaired Student t tests. Categorical variables were contrasted using χ^2 tests. The p values ≤ 0.05 were considered statistically significant.

Standard protocol approvals, registrations, and patient consents. Researchers, with the exception of the United Kingdom, contacted women who had taken gabapentin and obtained oral and/or written consent. This study was approved by the Research Ethics Board at The Hospital for Sick Children in Toronto, Canada, and at local research ethic boards at the other centers. In the United Kingdom, data collection is covered by Section 251 of the NHS Act, 2006.

RESULTS We completed data on the outcomes of 223 pregnancies exposed to gabapentin and compared them with 223 unexposed pregnancies. The maternal demographics were very similar on all characteristics, with the exception of the gabapentin group having significantly more women who consumed alcohol. However, the use of alcohol was minimal during pregnancy (mostly an occasional drink, or only prior to the woman finding out that she was pregnant) and was not associated with any adverse outcomes. Among the 223 women exposed to gabapentin, 207 (92.8%) reported the indication for use, and the major indication was pain (90, 43%); only 71 (34%) took it for the treatment of epilepsy. The psychiatric indications included 11% depression, 4% panic attacks/anxiety, 4% bipolar illness/psychosis, 2% obsessive-compulsive disorder, and 2% anorexia.

There were 182 women who reported dose and 173 who reported both dose and indication. Overall, the average dose was 1,000 mg (SD = 825 mg), with a range of 100 to 4,800 mg/d. The average dose among those taking it for epilepsy (n = 58) was 1,538 mg/d, 853 mg/d for pain (n = 73), and 538 mg/d for other indications (n = 42) (table 1).

Table 1 Maternal characteristics

Characteristic	Gabapentin	Nonteratogens	p Value
No.	223	223	
Maternal age, y (SD)	31.9 (5.9)	31.9 (5.7)	0.942[a]
Gravida, n (SD)	1.5 (1.6)	1.5 (1.3)	0.822[a]
Para, n (SD)	1.0 (1.1)	0.7 (0.8)	0.002[a]
Tobacco use, n	46	44	0.549[b]
Alcohol use, n	19	9	0.040[b]
Indication for gabapentin, n (%)			
Epilepsy	71 (34)	NA	NA
Pain	90 (43)	NA	NA
Psychiatric conditions	46 (22)	NA	NA
Average dose, mg/d (SD)	999 (825)	NA	NA
Minimum and maximum daily dose, mg	100, 4,800	NA	NA

Abbreviation: NA = not applicable.
[a] Tested using Student *t* test.
[b] Tested using χ^2.

The pregnancy outcomes are presented in table 2. Among the mothers of children with major malformations, in 3 of 7, the indication was epilepsy (average dose = 1,300 mg/d in 2 women; 1 dose not reported), and 4 took it for pain (average dose = 1,500 mg/d).

Rates of major malformations were similar in both groups, and in addition, none of the 36 women exposed only to gabapentin with no concomitant medications delivered a baby with a major malformation. The groups differed in rates of live births, therapeutic abortions, preterm births, low birth weight, and neonatal intensive care unit (NICU)/special care nursery (SCN). However, reported NICU/SCN admission rates included all exposed infants, regardless of time of exposure to gabapentin; consequently, some would have occurred long after maternal discontinuation of the drug. Of the 61 infants exposed up until delivery, 23 were admitted to either the NICU or SCN for observation and/or treatment vs 6 in the comparison group. The indications for admission included jaundice, low heart rate, hypotonia, hypoglycemia, respiratory distress, jitteriness, diarrhea, fever, and arrhythmia. All of these adverse events were self-limiting and resolved within a few days to a week. One infant was admitted for seizures in addition to respiratory distress syndrome, jaundice, seizures, and septicemia and was concomitantly exposed to trazodone, venlafaxine, eletriptan, and dimenhydrinate. Two of the neonates were described as having withdrawal symptoms. However, one of these infants was concomitantly exposed to vigabatrin, carbamazepine, and clobazam up until birth and the other was exposed to methadone throughout pregnancy. The symptoms were self-limiting and resolved within a few days to a week.

Birth weight and preterm birth. There were 18 infants with a low birth weight of <2,500 g in the gabapentin group and 9 in the comparison group. Among those with a birth weight <2,500 g, the average gestational age at birth was 35 weeks (range 29–40) in the gabapentin group compared with 35.1 weeks (29–40) in the comparison group ($p = 0.95$).

Table 3 lists the details of the malformations identified in 7 infants exposed to gabapentin, including doses taken, concomitant medications, and other factors possibly exerting an influence on outcomes. In the comparison unexposed group, 5 infants had malformations, which included 2 with ventricular septal defects, a dysplastic kidney (identified as requiring a transplant), bladder exstrophy, and bilateral hexadactyly

Table 2 Pregnancy outcomes

Outcome	Gabapentin	Nonteratogens	χ^2	p Value
No.	223	223	NA	NA
Live births	170 (76.2%)	201 (90%)	14.43	<0.001
Major malformations	7 (4.1%)	5 (2.5%)	0.04	0.555
Spontaneous abortions	22 (9.8%)	17 (7.6%)	0.45	0.502
Therapeutic abortions	29 (13%)	5 (2.2%)	18.54	<0.001
Stillbirth	2 (1.1%)	0 (0.0%)		NS
Preterm birth	18 (10.5%)	8 (3.9%)	5.47	0.019
NICU/SCN (late pregnancy exposure)	23/61 (38%)	6 (2.9%)	29.89	<0.001
Low birth weight <2,500 g	18 (10.5%)	9 (4.4%)	4.56	0.033
Intrauterine growth retardation	6 (3.5%)	4 (1.9%)	0.64	0.422
Mean birth weight, g (SD)	3,180 (605)	3,315 (545)	$t = 2.23$[a]	0.027
Mean gestational age at birth, wk (SD)	38.6 (2.1)	39.1 (1.9)	$t = 2.38$[a]	0.018

Abbreviations: NA = not applicable; NICU = neonatal intensive care unit; NS = not significant; SCN = special care nursery.
[a] Student *t* test used on continuous variables.

Table 3 Major malformations

Malformations	Gabapentin, mg/d	Trimester(s) exposed	Indication	Concomitant drugs	Other factors
VSD	2,400	1-2-3	Pain (Charcot-Marie-Tooth disease)	Alprazolam, levothyroxine, oxybutynin, paracetamol, codeine	IUGR, smoked 5–10 cigarettes/d, depression, hypothyroidism
VSD	Unknown	1-2-3	Epilepsy	Carbamazepine, diazepam	None reported
Anencephaly	600	1-2	Spastic paraparesis	Baclofen	None reported
Macrocephaly, microretrognathism, cutis marmorata	800	1-2-3	Brain tumor	Clobazam	Neonate severely hypotonic at birth
Pyloric stenosis	2,400	1	Pain (disk herniation)	Tetrazepam, oral morphine, paracetamol	Smoked 5–10 cigarettes/d
Bilateral varus clubfoot	600	1-2-3	Pain	Bromazepam, venlafaxine	Maternal multiple sclerosis, family history of clubfoot
Cryptorchidism	1,800	1-2-3	Seizure prophylaxis (brain abscess)	Acenocoumarol until 6 wk post-LMP, cotrimoxazole, hydrocortisone, ceftriaxone, heparin throughout pregnancy	Neonatal hypocalcemia, tremors, and irregular respiration; maternal myasthenia, smoked 10 cigarettes/d

Abbreviations: IUGR = intrauterine growth retardation; LMP = last menstrual period; VSD = ventricular septal defect.

plus bilateral colomba (in both optic nerves). Of the 223 women exposed to gabapentin, 142 were exposed in the first trimester only and had been taking it before becoming pregnant, 10 in the first and second trimesters only, 1 in the second trimester only, 1 in the third trimester only, 1 in the second and third trimesters only, and 59 before and throughout pregnancy. We did not have details of trimester exposure for the 9 remaining cases; however, none of these infants were noted as having a major malformation or any other adverse outcome.

DISCUSSION To our knowledge, this is the largest prospective comparative study to date reporting on a number of pregnancy and neonatal outcomes after exposure to gabapentin during pregnancy. However, this is a small number when considering the possibility that there are probably thousands of women of childbearing age taking this drug worldwide.

There was no increased risk for major malformations, which is consistent with data from previous studies.[3–6] There were 4 significant outcomes, one of which was live births, which correlated to the large number of therapeutic abortions in the gabapentin group compared with the comparison group. There were also higher rates of preterm births ($p = 0.019$) and low birth weight ($p = 0.033$) and this may have been attributable to a correlation between these 2 variables. An infant born weighing <2,500 g is considered low birth weight, and if the birth occurred before 37 weeks' gestation, preterm birth. Both outcomes involve an increased risk of morbidity and mortality of the newborn. A low-birth-weight infant can be born full term, and a preterm infant may not necessarily be low birth weight. A measure used to combine these aspects is intrauterine growth retardation, known as "small for gestational age" and is a baby whose birth weight is below the 10th percentile, based on birth weight reference curves and stratified by infant sex and gestational age.[8] There was no difference in the rates of small for gestational age in our cohort.

The other significant outcome was the number of admissions to the NICU/SCN, which included 23 of 61 (38%) neonates exposed to gabapentin in late pregnancy. However, not all of these neonates presented with symptoms, as some were admitted for observation, which is the policy for infants who have been exposed to psychotropic drugs throughout pregnancy in some institutions (anecdotal information). There were 2 cases in which it was noted that the infant had "withdrawal symptoms." However, one of these infants was concomitantly exposed to vigabatrin, carbamazepine, and clobazam up until birth and the other one was concomitantly exposed to methadone throughout pregnancy. There are several case reports in the literature in adults suggesting that gabapentin withdrawal can occur at doses ranging from 400 to 8,000 mg/d. Patients experienced symptoms similar to those that develop with benzodiazepine withdrawal and were taking gabapentin for as little as 3 weeks to as long as 5 years.[9] There is only 1 small study of 6 women who took gabapentin throughout pregnancy that reported neonatal outcomes. The authors suggested that there is probably an active transplacental transport of gabapentin, with accumulation in the fetus, which could be by the specific L-type amino acid transporter and is expressed in the placenta. The newborns appeared to have a slightly lower capacity to eliminate gabapentin than do adults. However, there were no reports of any

adverse effects in these 6 neonates.[10] In our study, the 2 infants were also exposed to other psychotropic drugs throughout pregnancy; consequently, it would be difficult to ascertain whether their symptoms were due to the gabapentin, the other drugs, or a combination of both.

As in all observational studies, there are strengths and limitations. The strengths of this type of study include a personal interview with the majority of the women, which involved detailed history-taking and included documentation of consumption of the drug during pregnancy. In addition, in many cases, details were verified with the child's physician. Using prospective comparative groups is considered Class II evidence because it allows comparisons between exposed and nonexposed groups. Because randomized controlled trials are unlikely to be conducted in pregnancy, this level of evidence is likely to be the highest available to physicians caring for women who require gabapentin pharmacotherapy during pregnancy. There were 2 main limitations that should be mentioned. First, we had a relatively small sample size, which has only 80% power to detect approximately a 3.5-fold increased risk for malformations above the baseline risk of 3%, with an α of 0.05. Typically, approximately 750 subjects in each group would be required to detect a 2-fold increase in major malformations and thousands would be required to detect rare malformations. The second limitation was that we did not have a comparative group of women who were treated for similar conditions with other medications (i.e., disease group) and therefore only had 1 comparison group of women who were unexposed to gabapentin.

Of interest was the low number of women (only one-third) taking gabapentin for epilepsy, and that number differed among countries. France had the largest number (61%), then the United Kingdom (28%), with the remaining countries ranging from 0% to 8%.

In our study, only 28% of the women continued taking gabapentin throughout pregnancy as two-thirds of the women (66%) discontinued in the first trimester, most following pregnancy confirmation between 6 and 8 weeks' gestation. This number of women discontinuing their medication early in pregnancy has remained consistent for many years, despite reassuring results from many studies that have been published on pregnancy outcomes following exposure to various medications. This is most likely attributable to alarming information received from various sources. At Motherisk, we recently conducted a study in which we evaluated the impact of negative information from friends, family, health care providers, and the media on women who had taken an antidepressant during pregnancy. Most of the women reported that negative information they received from these sources affected their decision-making as to whether they continued taking their medication during pregnancy.[11] Finally, there are no studies that have been conducted to examine possible long-term neurodevelopmental adverse effects of taking gabapentin in pregnancy and we did not attempt this in our study, as it requires more resources than we had available to us.

Our results suggest that although this sample size is not large enough to make a definitive conclusion, gabapentin does not appear to increase the rate of major malformations above baseline. The other significant findings require further investigation before coming to any definitive conclusions. Infants exposed to gabapentin close to delivery, especially if concomitantly exposed to other psychotropics, should be monitored after birth for poor neonatal adaptation syndrome.

AUTHOR CONTRIBUTIONS

Dr. Fujii, MD: study concept and design, acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content. Mr. Goel, BSc: acquisition of data, critical revision of the manuscript for important intellectual content. Dr. Bernard, PhD, Dr. Pistelli, MD, Dr. Yates, MBCHB, Dr. Stephens, PhD, Dr. Han, MD, Dr. Matsui, MD: acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content. Ms. Etwell, BSc: acquisition of data, critical revision of the manuscript for important intellectual content. Dr. Einarson, PhD, Dr. Koren, MD: study concept and design, analysis and interpretation, critical revision of the manuscript for important intellectual content. Ms. Einarson, RN: study concept and design, acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content, study supervision.

ACKNOWLEDGMENT

The participation of several French pharmacovigilance centers (in particular Dijon and Tours) is warmly acknowledged. Thanks to all of the women and/or their health care providers, without whom this study would not have been possible.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

H. Fujii, A. Goel, N. Bernard, A. Pistelli, L.M. Yates, S. Stephens, J.Y. Han, D. Matsui, F. Etwell, T.R. Einarson, and G. Koren report no disclosures. A. Einarson for The Motherisk Program received an unrestricted educational grant to study the safety of Cymbalta (duloxetine) in pregnancy from Eli Lilly Inc., Canada. Go to Neurology.org for full disclosures.

Received August 30, 2012. Accepted in final form January 24, 2013.

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Editor's Note to Authors and Readers: Levels of Evidence in *Neurology*®

Effective January 15, 2009, authors submitting Articles or Clinical/Scientific Notes to *Neurology*® that report on clinical therapeutic studies must state the study type, the primary research question(s), and the classification of level of evidence assigned to each question based on the classification scheme requirements shown below (left). While the authors will initially assign a level of evidence, the final level will be adjudicated by an independent team prior to publication. Ultimately, these levels can be translated into classes of recommendations for clinical care, as shown below (right). For more information, please access the articles and the editorial on the use of classification of levels of evidence published in *Neurology*.[1-3]

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Classification scheme requirements for therapeutic questions

Class I. A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class II. A randomized, controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criterion a-e in Class I or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b-e in Class I. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III. All other controlled trials (including well-defined natural history controls or patients serving as their own controls) in a representative population where outcome is independently assessed or independently derived by objective outcome measurements.

Class IV. Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

AAN classification of recommendations

A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specific population. (Level A rating requires at least two consistent Class I studies.)

B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specific population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specific population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Robert D. Murnane <rmurnane@uw.edu>
Sent: Thursday, September 5, 2019 11:39 AM
To: Audrey Baldessari; wanprc_vets@uw.edu
Subject: [Wanprc_vets] 19-146 and 158 (Z19182 and Z19199)
Attachments: 19-146 (Z19182) histo.docx; 19-158 (Z19199) histo.docx; ATT00001.txt

HI all:

Please find attached the final reports on the above 2 cases.

Please contact me with any questions, comments or concerns.

Cheers
Bob

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Robert D. Murnane <rmurnane@uw.edu>
Sent: Friday, November 1, 2019 1:26 PM
To: Audrey Baldessari; wanprc_vets@uw.edu
Subject: [Wanprc_vets] 19-218 (Z17170)
Attachments: 19-218 (Z17170) histo.docx; ATT00001.txt

Hi all:

Please find attached final report on the above cases. This animal breaks the previous record for extent of dissemination….!

Cheers
Bob

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Robert D. Murnane <rmurnane@uw.edu>
Sent: Tuesday, October 29, 2019 2:14 PM
To: wanprc_vets@uw.edu
Subject: [Wanprc_vets] Z17170
Attachments: ATT00001.txt

Hi all (especially ABC vets!)

Disseminated valley fever EVERYWHERE:

Hilar nodes, lungs, rib, bone above eye, sternum, liver, kidneys, lungs, multiple abscesses….

Final report to follow soon.
Cheers
Bob

University of Washington
National Primate Research Center

Accession #___19-040_
Submission Date_20 Mar 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester____TH_____ Investigator___Hotchkiss_____ Animal ID #___Z19068_
Species_____Mn____ Requester's Phone___5-1842_____

Date of Death__03/06/19_____ Date of Necropsy 03/06/19 Time_1300__Pathologist ____TH____

Nutritional Condition: ☐ Adequate X Marginal ☐ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other_____

Other Diagnostic Samples _____

Type of report: ☒ Final __9 May 19____ ☒ Preliminary _____ ☐ Amended _____

Clinical History:

Infant delivered overnight and found dead in the enclosure (181) when husbandry staff arrived in the morning. The dam (L03132) was sedated for her semi-annual exam on 03/04/19 and based on measurements at that time, the estimated due date was 03/22/19. The infant was positioned head down and the placenta appeared normal. Fetal heart rate at that time was normal as well (210 bpm). There were no significant abnormalities on the dam's exam that day other than a BCS of 4/5 and moderate dental calculus.

The dam has a history of a natural nonviable birth in 2013 and had viable births in 2014, 2015, and 2016. The dam was positive in the past for valley fever and had been on treatment until September 21st, 2018. She was discontinued from treatment after having a year of negative cocci titers. One of her previous births (infant born in 2014) is a current valley fever case.

The majority of the placenta could not be recovered from the group enclosure but very small portions of it observed in the bedding appeared normal.

Gross Description:

A 0.48 kg (BCS 2.5/5) female Macaca nemestrina is presented for necropsy.

Externally there are two abrasions on the ventral abdomen and inguinal region consistent with postmortem trauma. (When the infant was removed from the group enclosure, the dam reached through the mesh to grab at the infant's rear legs.) No other signs of bruising, bleeding, or trauma noted; no breaks in the skin were identified. A small amount of dark, fluid feces was present around the rectum and a rectal swab was collected and submitted. A small portion (about 2 cm) of the umbilicus was attached and appeared normal; this was submitted for histopathology.

Upon internal examination, the liver, gallbladder, stomach, kidneys, adrenal glands, intestines, bladder, and reproductive organs appeared normal. The spleen was of normal shape, consistency, and color but

subjectively appeared slightly smaller than expected. The heart appeared normal and no free fluid was found within the thoracic cavity. The cranial left lung lobe was mottled in appearance and had areas of dark red mixed with a light cream color. No exudate was noted on cut cross section and the lobe would partially float in formalin. The remaining lung lobes on the left side and the entirety of the right side were dark red in color and sank in formalin. These lung lobes did not have exudate on cross section.

A small area (about 1 cm in diameter) of hemorrhage was noted in the left occipital region of the brain. No fractures of the cranium were noted and the skull and brain appeared otherwise normal. The cerebellum and brain stem appeared normal. There was no hematoma or bruising noted in the skin overlying the occipital region. Animal husbandry did comment that the dam was on a perch in the enclosure and dropped the deceased infant when they went to shift her to a different enclosure.

Gross Diagnosis(es):

1. Stillbirth

Histological Findings:

Lungs are uninflated and have diffuse, moderate, deep aspiration of amniotic cells and debris. There also is extensive congestion.

Sections of brain, spleen, adipose (adequate), lymph node, pancreas, liver, heart, kidneys, skin with umbilicus, and umbilical cord are unremarkable.

Final Principal Diagnosis(es):

1. Moderate, diffuse, deep aspiration of amniotic cells and debris with uninflated lungs

Histology Comments:

Amniotic cells and debris within alveoli without inflammation and noninflation of the lungs are consistent with agonal aspiration due to fetal distress. This finding in concert with lack of other overt lesions suggests stillbirth due to dystocia.

Please contact either of us with any questions, comments or concerns.

Pathologist__TH(gross)/RM (histo)_____

University of Washington
National Primate Research Center

Accession # 19-041
Submission Date 20 Mar 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester TH/CM Investigator Hotchkiss Animal ID # Z14141
Species Mn Requester's Phone 5-1842

Date of Death 03/13/19 Date of Necropsy 03/13/19 Time 1100 Pathologist TH/CM

Nutritional Condition: ☒ Adequate ☐ Marginal ☐ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other_____

Other Diagnostic Samples ____CSF (cryovial)_____

Type of report: ☒ Final _9 May 19_____ ☒ Preliminary _____ ☐ Amended _____

Clinical History:

A 4 year, 10 month old, 8.23 kg female pigtail was presented for necropsy in good condition. She was negative for valley fever on cocci titers leading up until April 16th, 2018 when she was tested at the time of semi-annual exams. She had been noted around this time for coughing and radiographs showed a moderate bronchointerstitial pattern bilaterally. She was started on an oral dose (100 mg) of fluconazole. On May 8th, 2018 she was observed favoring her right hand and had superficial abrasions on D3 and D4 and a short course of NSAIDs were added to ther treatment plan. A week later, on May 15th, 2018 she was observed with bilateral epistaxis and did not want to turn her head side to side. She was removed from her social group and started on amoxicillin and a short course of prednisone. The epistaxis resolved but reluctance to turn her head was noted on May 17th, 2018. She was sedated again on May 23rd for a follow up cocci titer and full body radiographs. No evidence of compressed disc spaces, reactive bone, or spondylosis were noted, lungs appeared stable. On physical exam under sedation, there was normal ROM of the head and neck. She appeared to be improving and was returned to her social group on May 30th and continued on fluconazole. On June 21st, she was noted for audible breathing and albuterol was started as well as a short course of prednisone. A slight cough and audible breathing was noted on July 3rd, particularly when active or excited and a short course of prednisone given. On July 30th she would not come up to the front of the group enclosure to take her treatment and appeared ataxic and uncoordinated. She was sedated for an exam, blood work, and radiographs. Her lung sounds were slightly increased on inspiration on the left side but not the right and radiographic changes were mild on the left side. The CBC had a machine error and the chemistry showed a slightly decreased GGT that may have been a machine error and a low albumin (2.7). The cocci titer showed a decreased IgG (see table below). On August 27th, she was noted to be coughing again and a tapered course of prednisone was tried this time. Two days later, she was found seizing prior to receiving her morning dose of fluconazole. Leading up to the seizure, she was noted to be ataxic on the left side and tossing her left arm in a rhythmic pattern towards her chest. By the time that the vet tech had called the veterinarian, the seizure had stopped. She was given her fluconazole and a dose or oral diazepam for any refractory seizures and moved from her social group to a single cage. Shortly after being moved to the cage, she seized again and an injection of diazepam was given, which she responded to quickly. The following day (August 30th) she was sedated for another exam, blood work, cocci titer, and radiographs. Both lung fields had increased sounds on inspiration and a mild bronchointerstitial pattern

was noted (vertebrae appeared normal). There was a moderate hypoproteinemia and a mild neutrophilia. On September 25th, another seizure occurred and she was sedated for exam. There were bilateral increased lungs sounds on inspiration but no other abnormalities found on exam. A CBC showed a mild leukocytosis and the ALP was unremarkable. Pregnancy was discovered on ultrasound on this exam. The third observed seizure occurred on October 15th and long term antiepileptic medication was started. Initially daily oral diazepam was given until levitracetam and gabapentin could be acquired. A break through seizure was noted on November 9th and responded quickly to injectable diazepam. The animal had not yet received her doses of gabapentin, levitracetam, or fluconazole for the day when that occurred. Another break through seizure was observed on December 15th in the morning, when she had consumed about half of her morning medications and responded to an injection of diazepam. She was noted to be increasingly difficult to medicate (would try to pick out pills) so oral formulations of levitracetam and gabapentin were obtained from a compounding pharmacy. She seemed to do better with oral liquid medications but continued to have break through seizures, with another observed on January 4th which again responded to injectable diazepam. After discussion and concerns were raised with respect to seizures and the stress of the impending labor, a C-section was elected and performed on January 10th. The surgery went smoothly and additional pain meds and antibiotics were added to her treatment plan. The infant was reintroduced following recovery but the dam would hold the infant very tightly around the neck and would not allow the infant to nurse for very long so the infant was removed. The doses of oral levitracetam and gabapentin were adjusted as her weight changed following the pregnancy and she continued on 100 mg of fluconazole. A break through seizure was observed on March 6th which responded to injectable diazepam and endpoint set for March 13th.

Cocci	Panel Comments	IgG Titer Result	IgG Titer Value	IgM Titer Result	IgM Titer Value
1/10/19		positive (+)	1:4	negative (-)	<1:1
10/29/18		positive (+)	1:2	positive (+)	1:2
9/25/18		positive (+)	1:8	positive (+)	1:2
8/30/18		positive (+)	1:32	positive (+)	1:2
7/30/18		positive (+)	1:4	negative (-)	<1:1
5/23/18		positive (+)	1:32	positive (+)	1:2
4/16/18		positive (+)	1:16	positive (+)	1:4

Note that cocci titers were done in 2014-2016 and were negative. No titer was done in 2017.

Gross Description: There was a moderate amount of subcutaneous fat noted during necropsy and a significant amount of intrabdominal and pericardial fat. There were some mild adhesions of the subcutaneous fat over the linea alba from the previous C-section incision.

The liver had slightly rounded edges but appeared otherwise normal on gross appearance and there were no abnormalities of the gallbladder appreciated. Several sections of the liver were submitted including a section with a portion of the gallbladder attached.

The stomach, intestines, pancreas, kidneys, adrenals, spleen, and bladder appeared normal. There was a moderate amount of digesta within the stomach and intestines that was of normal consistency and appearance.

The uterus had several small adhesions over the previous C-section incision site and what appeared to be a small amount of suture material present. The ovaries and uterine horns appeared normal. Externally, mild to moderate tumescence was noted.

The lung lobes were mottled and of varying shades of pink and dark pink or red. There were numerous small (1-2 mm) multifocal white nodules throughout all lung fields. Several adhesions were present

between the right cranial lung lobe and the thoracic wall. No free fluid was present within the thorax and no exudate noted on cut cross section of the lungs. All sections of lung tissue floated in formalin. There were no gross abnormalities of the heart other than the pericardial fat previously mentioned.

The brain and a small portion of the spinal cord were removed from the skull. No gross abnormalities were appreciated.

Blood samples were collected for cocci titer and serum chemistry and complete blood count but, unfortunately, were severely clotted. Attempts to run the samples on in-house machines resulted in errors.

A small amount of CSF was collected and submitted in a cryovial. Attempts to collect joint fluid from both stifles were unsuccessful.

Gross Comments:

While no abnormalities of the CNS were identified, valley fever is suspected as the cause of the seizures and histopathology is pending.

Histological Findings:

In the cerebrum, there are regional, multifocal and coalescing pyogranulomas and granulomas with numerous giant cells, Mott cells and rare organisms consistent with *Coccidiodes* sp, and the lesions cause extensive, regional effacement of neuropil. There also is regional, chronic-active, leptomeningitis. Spinal cord is unremarkable.

Lungs have diffuse congestion and edema (agonal), and two, small, alveolar nodules of granulomatous and fibrosing inflammation, and also mild to moderate perivascular, peribronchial and peribronchiolar lymphohistiocytic aggregates and pneumoconiosis.

Stomach, small intestine and large intestine have mild to moderate lamina propria infiltrate of/increase in eosinophils, lymphocytes, plasma cells, and macrophages. The small intestine has moderate villar blunting and fusion, and some regions with moderate goblet cell hyperplasia.

Sectons of lymph nodes, spleen, liver (mild lobular collapse and scattered, mild lymphohistiocytic aggregates), gall bladder, heart (moderate steatosis of atria, and mild megalo- and dyskaryosis), kidneys (mild diffuse membranoproliferative change of glomeruli and focal minor interstitial lymphohistiocytic aggregate), skin with mammary gland, muscle, and pancreas are unremarkable besides stated minor changes.

Final Principal Diagnosis(es):

1. Severe, regional-multifocal-cerebral, pyogranulomas and granulomas with rare organisms consistent with *Coccidiodes* sp: **Cerebral coccidiodomycosis**
2. Mild, bi-focal, granulomatous and fibrosing pneumonia
3. Mild to moderate, diffuse, eosinophilic, lymphoplasmacytic and histiocytic gastro-entero-colitis with enteric villar blunting and fusion, and with near-diffuse, large intestinal spirochetosis

Histology Comments:

Clinical CNS signs and demise were due to cranial Valley Fever. Additionally, the chronic lung lesions were likely from past Valley Fever as well.

Diagnosis #3, which can cause diarrhea and potentially other sequelae thereof, represents typical changes in this species in this colony, and they have been previously discussed. Changes present are consistent with food allergy/hypersensitivity/dietary intolerance/IBD. Please contact me if you wish to discuss these changes further.

Please contact any of us with any questions, comments, or concerns.

Pathologist__TH/CM (gross)/RM (histo)___

From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Thursday, May 9, 2019 12:20 PM
To: Audrey Baldessari; Keith Vogel; Charlotte E. Hotchkiss; Kathryn A. Guerriero; Dean Jeffery; Jason D. Laramore; Tess House; cmali
Subject: 19-041 and 042 (Z19068 and Z14141)
Attachments: 19-040 (Z19068) histo.docx; 19-041 (Z14141) histo.docx

Hi all:

Please find attached final reports on the above 2 cases. Interestingly, Z14141 was cerebral Valley Fever, and both animals were from the same dam who also was diagnosed clinically with Valley Fever.

Please contact me with any questions, comments or concerns.

Cheers
Bob

University of Washington
National Primate Research Center

Accession # 19-056
Submission Date 5 Apr 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester TH Investigator Colony Animal ID # Z19076
Species Mn Requester's Phone 5-1842

Date of Death 03/31/19 Date of Necropsy 03/31/19 Time 1330 Pathologist TH

Nutritional Condition: ☐ Adequate ☒ Marginal ☐ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other

Other Diagnostic Samples

Type of report: ☒ Final 26 Apr 19 ☐ Preliminary ☐ Amended

Clinical History:

Infant delivered overnight and found dead in the enclosure (242) when husbandry staff arrived in the morning. The dam (M03312) was sedated for her semi-annual exam on 03/25/19 and based on measurements at that time, the estimated due date was 4/30/2019. The placenta appeared normal on ultrasound and fetal heart rate at that time was normal (180 bpm). There were no significant abnormalities on the dam's exam that day. The dam is currently on fluconazole for valley fever. She was in a portable cage for previous weight loss and diarrhea cases (Biofire was positive for EPEC) and returned to her social group at the time of semi-annual exam as the cases had resolved.

The dam has a history of a natural viable births in 2012, 2014, 2015, 2016, 2017, and a fetal loss (not recovered) in October 2018. The infants born in 2012 and 2016 were endpoint at two months and one month of age, respectively.

The placenta was not recovered or found within the social group by husbandry staff that morning or by veterinary services later that day.

Microbiology of a rectal swab identified 2+ growth of *Shigella* sp.

Gross Description:

A 0.40 kg (BCS 2/5) female Macaca nemestrina is presented for necropsy. The infant is in lean body condition with minimal subcutaneous and intrabdominal fat.

Externally the infant appears normal and there are no deformities or signs of trauma. A small portion (about 2 cm) of the umbilicus was attached and appeared normal; this was submitted for histopathology. A rectal swab was also collected.

Upon internal examination, the gallbladder, stomach, kidneys, adrenal glands, intestines, spleen, bladder, and reproductive organs appeared normal. The liver was slightly friable and dark red in color on

the right side, compatible with post-mortem changes (infant placed in right recumbency). The lungs were light pink to pale pink in color with darker areas noted on the right lung lobes and all lobes sank in formalin. The heart appeared normal and no free fluid was found within the thoracic cavity. The brain appeared normal on gross appearance but was mild to moderately friable.

Gross Diagnosis(es):

1. Stillbirth

Histological Findings:

Lungs are only slightly inflated and have near-diffuse, moderate, deep aspiration of amniotic cells and debris.

Sections of brain, lymph node, spleen, adipose (adequate), pancreas, liver, gall bladder, heart, kidneys, skin with umbilicus, umbilical cord, and muscle are unremarkable.

Final Principal Diagnosis(es):

1. Moderate, near-diffuse, deep aspiration of amniotic cells and debris with mostly uninflated lungs

Histology Comments:

Amniotic cells and debris within alveoli without inflammation and minimal inflation of the lungs are consistent with agonal aspiration due to fetal distress. This finding suggests stillbirth due to dystocia, while noting this dam has had numerous viable births suggesting dystocia is less likely.

The isolation of *Shigella* sp is surprising, and could be from fecal contamination from the dam or some other monkey, or possibly there may have been a placentitis/amnionitis that was not evident in sections examined (however in such case umbilical cord inflammation would be expected and was not present).

Please contact either of us with any questions, comments or concerns.

Pathologist__TH (gross)/RM (histo)_____

From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Friday, April 26, 2019 12:33 PM
To: Audrey Baldessari; Keith Vogel; Charlotte E. Hotchkiss; Tess House; cmali; Dean Jeffery; Kathryn A. Guerriero; Jason D. Laramore
Subject: 19-056 (Z19076)
Attachments: 19-056 (Z19076) histo.docx

Hi all:

Please find attached the final report on the above case.

I really don't have any good explanations why the rectal swab was positive for *Shigella* sp!!

Cheers
Bob

University of Washington
National Primate Research Center

Accession # 19-085
Submission Date 12 Apr 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester TH/CM Investigator Hotchkiss Animal ID # Z17139
Species Mn Requester's Phone 5-1842

Date of Death 04/12/19 Date of Necropsy 04/12/19 Time 0800 Pathologist TH/CM

Nutritional Condition: ☐ Adequate ☐ Marginal ☒ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other_____

Other Diagnostic Samples _____

Type of report: ☒ Final 19 Jun 19 ☐ Preliminary 24 May 19 ☐ Amended _____

Clinical History: The macaque first presented on 1/29/19 with left hind limb lameness while in his social group. He was observed toe touching and not fully weight bearing on this side when standing but would grasp the mesh with this foot and utilize it well. No trauma had been witnessed by veterinary services or animal husbandry staff. He was removed from the group and sedated for an exam and radiographs. On physical exam he was slightly dehydrated (3%) and had normal range of motion in the left leg with no wounds identified. No soft tissue swelling could be appreciated. He was moved to a portable cage for rest and started on oral meloxicam for pain relief. He continued to be intermittently lame over the course of the next few days despite NSAIDs and was hand caught for a cocci titer which came back negative.

He was sedated again on February 12th for follow up radiographs and exam. He was still non-weight bearing intermittently on the left side and had just begun to hold up his right foot at rest at times as well. On exam he was 5% dehydrated, had reduced extension of the left stifle (about 10% reduction) and moderate thickening of the stifle on the medial aspect. There was no crepitus palpated and no draining tracts present. The right leg was normal on examination with a normal range of motion. Both ankles and feet appeared normal and no abnormalities were noted on any of the toes, metatarsals, or tarsals. The dehydration was corrected, a dose of Vitamin B was given, and injectable NSAIDs were given. Arthrocentesis was scheduled for the following day after consulting with Seattle vets and the local diagnostic lab.

He was sedated on February 13th for left stifle arthrocentesis and the exam findings were similar to the previous day. After the sample was collected, he was started on oral clavamox, fiber bites, banatrol, probiotics, and continued NSAIDs for pain control with an additional injection of buprenorphine given. A cbc/chemistry was taken and revealed a mild monocytosis, thrombocytosis, elevated globulin (5.1), elevated cholesterol (189), and elevated ALP (1164). The arthrocentesis sample submitted came back as marked chronic neutrophilic inflammation but no etiology was seen. Based on the increased cellularity and the predominance of neutrophils, an underlying bacterial cause was suspected but rickettsial disease and immune-mediated causes were also possible. Unfortunately there was not enough sample collected to perform culture and sensitivity. A repeat arthrocentesis on both stifles was recommended after no improvement was noted with NSAIDs and oral antibiotics. He began to have mounding feces after starting the antibiotics and pepto-bismol was added to his treatments.

A second arthrocentesis was collected from both stifles on February 27th and a follow up cocci titer was also done. Radiographs were taken and a cbc/chemistry performed. Due to his size, additional blood for a rickettsial panel was not drawn but was planned to be done at the next follow up exam. The chemistry showed an elevated globulin (decreased slightly from before, was now at 4.9) and the ALP was normal. The cbc showed a mild neutrophilia (8.58) but no overall leukocytosis was present (normal at 12.21). While waiting for the cocci titer, the macaque was started on fluconazole and gabapentin, and NSAIDs, antibiotics, and GI supportive therapy were continued. The cocci titer came back negative. His clinical appearance and intermittent non-weight bearing lameness (both sides now but more frequently on the left side) was unchanged.

The results from the second arthrocentesis came back on March 5th and both stifles had neutrophilic inflammation noted. Based on the clinical history and treatment, the pathologist suspected an immune mediated cause and the fluconazole and antibiotics were discontinued. Immunosuppressive doses of prednisone were started. There was no improvement in clinical symptoms and redness of the left D1 was noted with an area of swelling along the proximal and medial aspect of the digit. The animal was sedated on March 17th when the swelling was first noted and an FNA was done. Blood drained from the site and the area was cleaned with chlorhexidine and topical antibiotic ointment applied. A few days later the opposite side was affected (same digit) but only uniform redness was noted, no swelling. It was suspected that the animal was sucking on the toes as no excoriations were found secondary to dragging the toes but the animal was not definitively observed toe sucking. A tick panel was run on March 26th and was negative for anaplasma, ehrlichia, and Rickettsia sp. On PCR. Follow up CBC and Chemistry on this date showed a monocytosis (1.08), hyperglobulinemia (now up to 5.6) and increased total bilirubin (2.2) and cholesterol (186).

He continued to show no improvement in clinical condition and was sedated for an immune panel (Coombs and ANA) and borrelia PCR on April 10th. The borrelia PCR was negative; Coombs and ANA were declined to be performed by the referring lab. He broke with fluid feces on April 10th and techs reported hematochezia. A biofire sample was collected and came back positive for EPEC and Shigella or EIEC. His appetite began to diminish along with his activity around April 10th and he was started on diazepam and azithromycin. He failed to improve and was determined endpoint on April 12th. That morning pieces of intestinal mucosa were noted in the pan along with fluid feces and blood.

A past diarrhea case in May of 2018 was noted for this animal. Biofire on that date was positive for Campylobacter, Shigella, and Giardia. That case responded to panacur and metronidazole and later a course of azithromycin. The past history of shigella suggests a chronic carrier that may have developed a polyarthritis secondary to this organism.

Gross Description:

A 2.48 kg (BCS 2/5) male *Macaca nemestrina* is presented for necropsy in good postmortem condition. The macaque is in lean body condition with minimal subcutaneous and intrabdominal fat present.

Externally there are no wounds, abrasions, or draining tracts present. No erosions or ulcers were identified in the oral cavity. A small amount of bloody fluid feces was present on the ventral aspect of the base of the tail. Multiple attempts were made to collect joint fluid from each stifle but were unsuccessful. Both stifles were submitted for analysis (right side has longer section of distal femur). The popliteal lymph nodes were moderately enlarged bilaterally and submitted for histopathology. The feet and toes appeared normal, with the previous redness of the D1 on both feet resolved and the previous left D1 swelling absent.

Upon internal examination, the intestinal loops were moderately thickened on palpation and the mesenteric lymph nodes were enlarged. Several clusters of mesenteric lymph nodes were collected for histopathology and the lymphadenopathy appeared present throughout the mesentery. Several sections of the intestines and stomach were submitted for histopathology. Both kidneys were normal on gross inspection (right kidney sectioned length-wise) and both were unremarkable on cut section. The

gallbladder appeared normal, however, the liver was mild to moderately friable and had areas of pallor on cut section. Some regions of the cut section appeared slightly yellow in color as well. The pancreas, spleen, bladder, and both testicles (bilaterally undescended) appeared normal. The lung lobes were mottled various shades of pink and were pale along the lobe margins, particularly on the left side. The right cranial and right middle lung lobes had a clear, frothy fluid noted on cut cross section. All sections of lung collected floated in formalin. No free fluid was noted in the thorax. The heart appeared of normal size but was diffusely pale in color; no abnormatlies were noted on cut cross section.

Gross Diagnosis(es):

- Moderate intestinal thickening with mesenteric lymphadenopathy
- Moderate popliteal lymphadenopathy

Histological Findings:

Sections of large intestine have multifocal, extensive abscessation of GALT, moderate to extensive, multifocal luminal suppuration/suppurative crusting, moderate, multifocal mucosal effacement and erosion and occasional ulceration by suppurative infiltrate, and scattered crypt abscesses. Stomach, small intestine, and large intestine also have moderate, diffuse, lamina propria infiltrate of/increase in lymphocytes, plasma cells, macrophages and eosinophils, and with small intestinal villar blunting and fusion and increase in mucosal cell turnover.

Sections of lymph nodes, spleen (reactive endothelium), heart, lungs (minimal perivascular, peribronchial and peribronchiolar lymphohistiocytic aggregates and pneumoconiosis), kidneys (minimal membranoproliferative change of glomeruli diffusely), liver (mild lymphohistiocytic aggregates), pancreas, muscle, and skin with mammary gland are unremarkable besides stated changes.

Final Principal Diagnosis(es):

1. Moderate to severe, multifocal, suppurative and multifocally ulcerative colitis
2. Moderate, diffuse, lymphocytic, plasmacytic, and histiocytic gastro-entero-colitis with enteric villar blunting and fusion

Histology Comments:

The suppurative colitis was likely bacterial with common etiologic agents including *Campylobacter, Yersina, Salmonella* and *Shigella* sp and others. This condition led to the GI clinical signs noted.

Decalcified sections of both stifles are pending and an addendum will follow.

Diagnosis #2, which can cause diarrhea and potentially other sequelae thereof, represents typical changes in this species in this colony, and they have been previously discussed. These changes are consistent with food allergy/hypersensitivity/dietary intolerance/IBD.

Please contact any of us with any questions, comments, concerns.

Pathologist__TH/CM(gross)/RM (histo)____

ADDENDUM/FINAL REPORT RM 19 JUN 19

Decalcified sections of both stifles across the joints reveals mild to moderate, synovial to subsynovial, multifocal infiltrate of lymphocytes, plasma cells and macrophages and associated with synovial proliferation. One section also has areas of minimal fibrin deposition and suppuration in the joint space. Growth plates are mostly unremarkable with mild irregularity and multifocal minor cartilage retention in maturing metaphyseal trabecular bone.

ADDITIONAL DIAGNOSIS:

Mild to moderate, multifocal, bilateral, proliferative and granulomatous synovitis/arthritis: stifle joints

Comment:

Considering the history and other findings, an immune-mediated arthritis is most suspect. Low grade infection is another possibility. Please contact RM with any questions, comments or concerns.

From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Wednesday, June 19, 2019 1:26 PM
To: Audrey Baldessari; Charlotte E. Hotchkiss; Keith Vogel; Jason D. Laramore; Dean Jeffery; Kathryn A. Guerriero; Tess House; cmali; wanprc_vets@uw.edu; Sally Thompson-Iritani
Subject: 19-085 (Z17139)
Attachments: 19-085 (Z17139) histo.docx

Hello all:

Please find attached the final report concerning decalcified sections of both stifles on the above case.

Please contact me with any questions, comments or concerns.

Cheers
Bob

University of Washington
National Primate Research Center

Accession # 19-146
Submission Date 16 Jul 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester TH Investigator Hotchkiss Animal ID # Z19182
Species Mn Requester's Phone 5-1842

Date of Death 07/12/19 Date of Necropsy 07/12/19 Time 0930 Pathologist TH

Nutritional Condition: ☐ Adequate X Marginal ☐ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other_____

Other Diagnostic Samples _____

Type of report: ☒ Final 5 Sep 19 ☒ Preliminary _____ ☐ Amended _____

Clinical History:

Infant delivered overnight and found dead in the enclosure (242) when husbandry staff arrived in the morning. Estimated due date was August 9th, 2019. The dam (R09036) was has a history of a non-viable fetus in 2013 and viable births in 2014, 2016, and 2018. She is currently on fluconazole for valley fever. She has been positive since 2014 and her most recent titer (3/25/19 during spring semi-annual exam) was IgG 1:2, IgM negative.

Gross Description:

A 0.39 kg (BCS 2/5) male Macaca nemestrina is presented for necropsy. The infant is in lean body condition with minimal subcutaneous and intrabdominal fat.

Externally the infant appears normal and there are no deformities or signs of trauma. The placenta was still attached to the infant and appeared normal on gross inspection. The umbilicus appeared normal and was submitted attached to the placenta.

Upon internal examination, the gallbladder, liver, stomach, kidneys, adrenal glands, intestines, spleen, bladder, and reproductive organs appeared normal. The lungs were light pink to pale pink in color and all lobes sank in formalin. The heart appeared normal and no free fluid was found within the thoracic cavity. The brain had a very small area of subdural hematoma in the caudal aspect but no damage was noted to the cranial bones prior to removal of the brain tissue.

Gross Diagnosis(es):

1. Spontaneous abortion

Histological Findings:

Sections of brain, lymph node, spleen, adipose (adequate), liver, gall bladder, pancreas, heart, kidneys, lungs (unexpanded and with moderately extensive, multifocal, deep aspiration of amniotic cells and debris), placenta, and umbilical cord are unremarkable besides stated changes.

Final Principal Diagnosis(es):

1. Aborted fetus – cause open
2. Moderately extensive, multifocal, deep aspiration of amniotic cells and debris
3. Otherwise unremarkable tissues/organs

Histology Comments:

Deep aspiration of amniotic cells and debris is due to agonal distress. A cause of abortion is not identified.

Please contact either of us with any questions, comments or concerns.

Pathologist__TH(gross)/RM (histo)____

University of Washington
National Primate Research Center

Accession # 19-158
Submission Date 7 Aug 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester TH Investigator Hotchkiss Animal ID # Z19199
Species Mn Requester's Phone 5-1842

Date of Death 08/4/19 Date of Necropsy 08/4/19 Time 1150 Pathologist TH

Nutritional Condition: ☐ Adequate ☒ Marginal ☐ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other

Other Diagnostic Samples

Type of report: ☒ Final 5 Sep 19 ☐ Preliminary ☐ Amended

Clinical History:

Infant delivered overnight and found dead in the enclosure (241) when husbandry staff arrived in the morning. Estimated due date was August 4th, 2019. The dam (Z12028) was has a history of a non-viable fetus in 2016, viable birth in 2017, and a nonviable breech infant in 2018. She is currently on fluconazole for valley fever. She has been positive since 2018 and her most recent titer (3/19/19 during spring semi-annual exam) was IgG 1:16, IgM 1:2.

Gross Description:

A 0.57 kg (BCS 3/5) female Macaca nemestrina is presented for necropsy. The infant is in good body condition with minimal subcutaneous and intrabdominal fat.

Externally the infant's skull is very conical and there are a few minor abrasions by the perineum. No significant dermal bruising was present. The placenta could not be recovered from the group enclosure and only a very small portion of the umbilicus was present, which appeared normal.

Upon internal examination, the gallbladder, stomach, kidneys, adrenal glands, pancreas, intestines, bladder, and reproductive organs appeared normal. The spleen was of normal size and color but moderately friable. The liver was dark red in color with some areas of light tan areas and mildly friable. The lungs were dark pink in color and all lobes sank in formalin. The heart appeared normal and no free fluid was found within the thoracic cavity. The thymus appeared normal and the diaphragm was intact. The brain had a significant amount of subdural hematoma along the caudal aspect with slight movement of the cranial bones in this region. The brain was moderately friable.

Gross Diagnosis(es):

1. Spontaneous stillbirth compatible with dystocia

Histological Findings:

Lungs are uninflated and have multifocal, mild to moderate, deep aspiration of amniotic cells and debris.

Sections of brain, spleen, thymus, adipose (adequate), lymph node, pancreas, liver, heart, and kidneys are unremarkable.

Final Principal Diagnosis(es):

1. Mild to moderate, multifocal, deep aspiration of amniotic cells and debris with uninflated lungs

Histology Comments:

Amniotic cells and debris within alveoli without inflammation and noninflation of the lungs are consistent with agonal aspiration due to fetal distress. This finding in concert with lack of other overt lesions and large size suggests stillbirth due to dystocia.

Please contact either of us with any questions, comments or concerns.

Pathologist__TH(gross)/RM (histo)_____

University of Washington
National Primate Research Center

Accession # 19-218
Submission Date 24 Oct 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester CMM/KG Investigator Hotchkiss Animal ID # Z17170
Species Mn Requester's Phone 60501

Date of Death 10/22/19 Date of Necropsy 10/22/19 Time 1300 Pathologist CMM/KG

Nutritional Condition: Adequate ☐ Marginal X Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other

Other Diagnostic Samples

Type of report: ☒ Final 1 Nov 19 ☐ Preliminary ☐ Amended

Clinical History:

A 2.23 kg 2.3 year old female macaca nemestrina was euthanized due to continued declining clinical condition despite aggressive veterinary treatment.

The original case for this animal was initiated on 9/11/19 when a weight loss case was opened due to decreasing body weights over the previous two weight checks during enclosure weights. The animal appeared otherwise healthy and was started on NS and vitamins with a weight recheck the following week.

On 9/20/19, the animal was sedated for a PE due to continued weight loss and favoring of the left hand. Radiographs and ROM revealed no abnormalities in the left hand. The animal was moved to 104 for monitoring of fecal output. Prescribed TX included meloxicam, cage rest, NS, and weight monitoring.

Cage side exams over the sequential 2 weeks revealed stable weight despite supportive care and improved use of the left hand.

On 10/09/19, a biscuit count was intitiated due to lack of weight gain despite supportive care and NS.

On 10/11/19, the animal was noted for additional weight loss (150g). Two days later on 10/13, the animal broke with fluid feces, a fecal was collected (positive for Campylobacter) and additional TX was implemented including Azithromycin, pepto, and other GI supportive care.

On 10/14/19, the animal underwent a semi-annual exam with survey xrays. The animal was 10-12% dehydrated (given IV and SQ LRS and Vitamin B Comp) and experienced a significant weight decrease of 600g (1.64 kg). Survey xrays appeared WNL on quick inspection. CBC revealed mild leukocytosis with mild neutrophilia, moderate monocytosis, and mild anemia. Iron was prescribed. CHM revealed slight hypocalcemia, moderate hypoproteinemia and hypoalbuminemia, and moderately increased ALKP. A TB test was placed in the right eyelid and was read negative at 72 hours.

Cage side exams over the next week revealed significant dehydration daily despite daily SQ fluid therapy and oral rehydration (ensure, Pedialyte fed via syringe). During this time, fecal consistency improved. Biscuit counts over this time revealed no appetite for biscuits, but the animal was consuming nutritional support.

On 10/18/19, mirtazapine was added as an appetite stimulant.

On 10/20/19, the cocci titer came back positive for coccidiomycosis with an IgG titer of 1:64. Treatment with fluconazole was started. At this same time, a flocculant swelling (~1cm) was noted over the right eyebrow.

Re-review of xrays from the 14th revealed a lytic lesion on right rib #2 on VD, and at sternabrae #3 on lateral views.

On 10/22/19, the animal was sedated for repeat xrays and examination of the flocculant swelling over the right eye. PE reveaed a BCS of 1/5, 10% dehydration, a ~1cm bony mass on the central right rib (#2) overlying the sternabrae, a ~1cm flocculant swelling over the right eyebrow with a palpable defect in the bone. Xrays revealed lytic lesions at the right rib and over thr ight eyebrow. Due to the presence of these lesions and the continued declining condition of the animal despite aggressive veterinary treatment, euthanasia was elected.

Gross Description:

The animal was in poor physical condition with no SQ or abdominal fat.

There was severe diffuse yellow-orange discoloration of the liver with multifocal white pinpoint spots present in all lobes. The liver was friable and there was an ~8mm piece of extrahepatic parenchymal tissue present on the right caudal liver lobe. The spleen had sporadic pinpoint white spots.

The left kidney was discolored and mottled tan and purple. There were multiple raised cream colored masses ~4-8mm in diameter on the cortical surface. On cut section, there was purulent discharge from one mass. The right kidney presented with similar color and 2 similar masses.

The GI tract appeared grossly normal with enlarged ileocecal lymph nodes. The reproductive tract and bladder appeared grossly normal.

There was a firm ~1cm mass present at the junction of the sternabrae and rib 2. The lungs were emphysematous and discolored with mottled purple/red/pink color with some rib impressions present in parenchymal tissue. There were occasional pinpoint military white spots in the lung parenchyma. There were multiple ~0.5-1.0 cm abscesses present along the mediastinum. The peri-bronchial lymph nodes were enlarged. There was an ~1cm mass along the upper left rib 2-3 that appeared to be an abscess with an adjacent ~0.5cm mass caudally. There was an ~8mm raised nodule at right rib 10. There was an ~0.5cm abscess in the middle of the diaphragm.

There was an ~8mm raised white lesion in the right atrium near the right auricle.

The submandibular lymph nodes were enlarged.

The flocculant mass above the right eye was an abscess with erosion of the underlying bone.

Gross Diagnosis(es) and Gross Comments:

Multifocal abscesses present throughout the liver, spleen, kidneys, lungs, and thoracic cavity. Single abscess above the right eye with erosion of the underlying bone. Suspect Coccidiomycosis as the cause of the abscesses. Histopathology is pending.

Histological Findings:

Sections/blocks labelled are as follows: 2 is axillary lymph node, 3 is inguinal lymph node, 4 is mesenteric lymph node, 5 is submandibular lymph node, 6 and 7 are pulmonary hilar, 8 is rib mass, 9 is sternal mass, and 10 is mass above the eye..

At the following locations and to the following degree there is abscessation to pyogranulomatous inflammation to pyogranuloma formation with numerous giant cells and numerous organisms consistent with *Coccidiodes* sp: pulmonary hilar node with extensive effacement and enlargement of the node, associated with the rib, sternum and bone above the eye with extensive boney destruction and invasion and remodeling and also with extension into adjacent soft tissue, multifocally and moderately extensively in the liver with effacement of parenchyma, severe and multifocally in the kidneys with effacement of parenchyma, multifocally and moderately extensively in the lungs with effacement of parenchyma, adjacent to an atrium of the heart and associated with an effaced lymph node, associated with striated musculature and connective tissue from undetermined sites, associated with subcutis and bone of an undetermined site, and adjacent to the aorta.

Small and large intestine have mild to moderate, multifocal lamina propria deposition of amyloid, and small intestine also has moderate villar blunting and fusion. GI tract also has moderate, diffuse, lamina propria infiltrate of/increase in lymphocytes, plasma cells with Mott cells, macrophages and eosinophils. The large intestine has extensive ciliate overgrowth (likely *B. coli* and others).

Spleen has moderate, multifocal, follicular amyloid deposition, and also reactive endothelium. Mesenteric lymph node has moderate amyloid deposition.

Pancreas has diffuse, moderate zymogen depletion.

Sectons of lymph nodes (besides mesenteric node), brain, liver (mild lobular collapse and scattered, mild lymphohistiocytic aggregates besides lesions stated above), gall bladder, heart, kidneys (moderate diffuse membranoproliferative change of glomeruli and multifocal moderate interstitial lymphohistiocytic aggregates in addition to lesions stated above), skin with mammary gland, and muscle are unremarkable besides stated changes.

Final Principal Diagnosis(es):

1. Severe, disseminated, abscesses and pyogranulomas associated with numerous organisms consistent with *Coccidiodes* sp: **Disseminated coccidiodomycosis**: lymph nodes, rib, sternum, frontal bone, liver, kidneys, and multiple other soft tissue sites
2. Moderate, multicentric and multifocal, small intestinal, large intestinal, mesenteric lymph node and splenic follicular amyloid deposition: **Systemic secondary amyloidosis**
3. Moderate, diffuse, eosinophilic, lymphoplasmacytic and histiocytic gastro-entero-colitis with enteric villar blunting and fusion, and with extensive large intestinal ciliate overgrowth

Histology Comments:

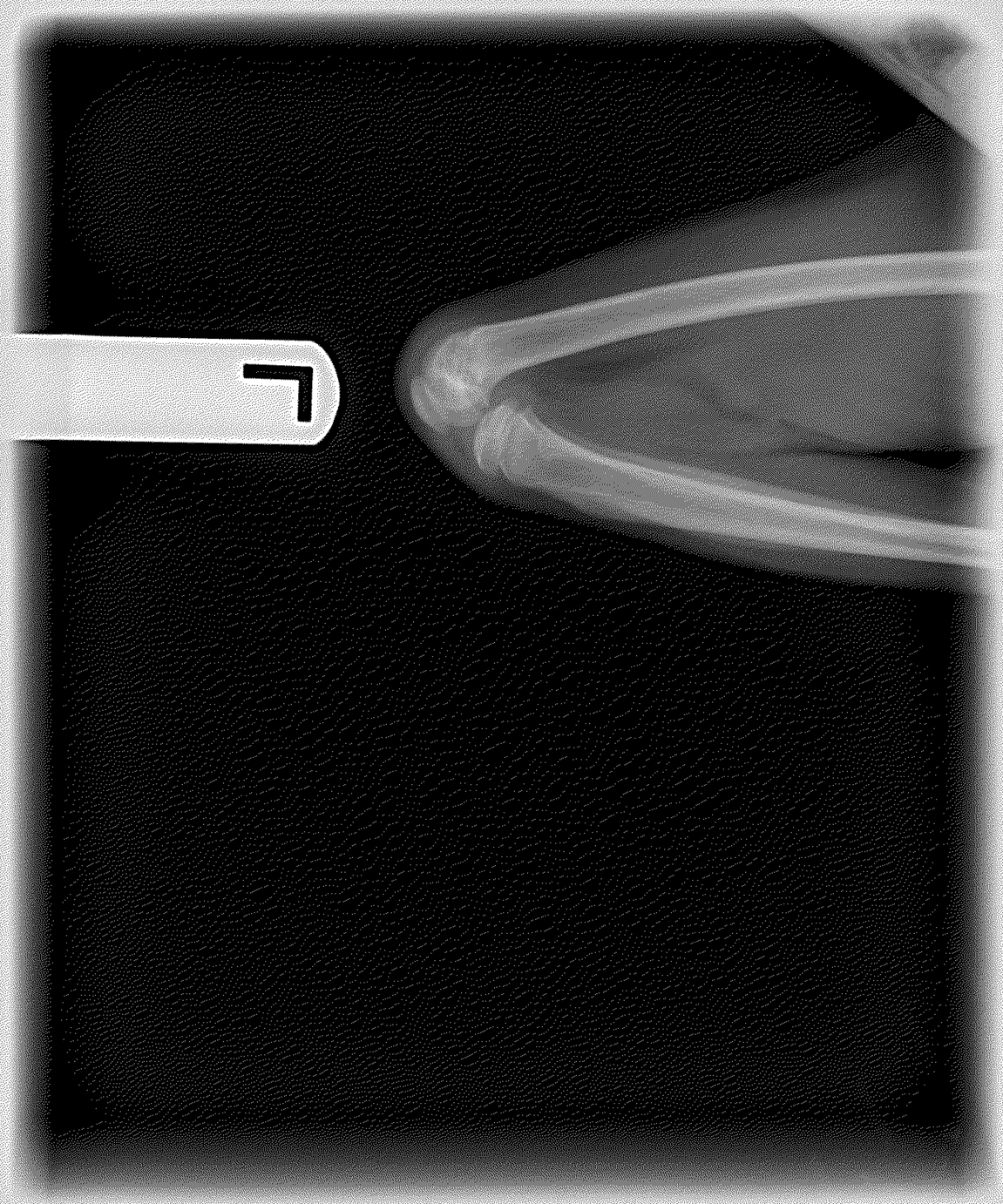
Clinical signs and demise were due to disseminated Valley Fever.

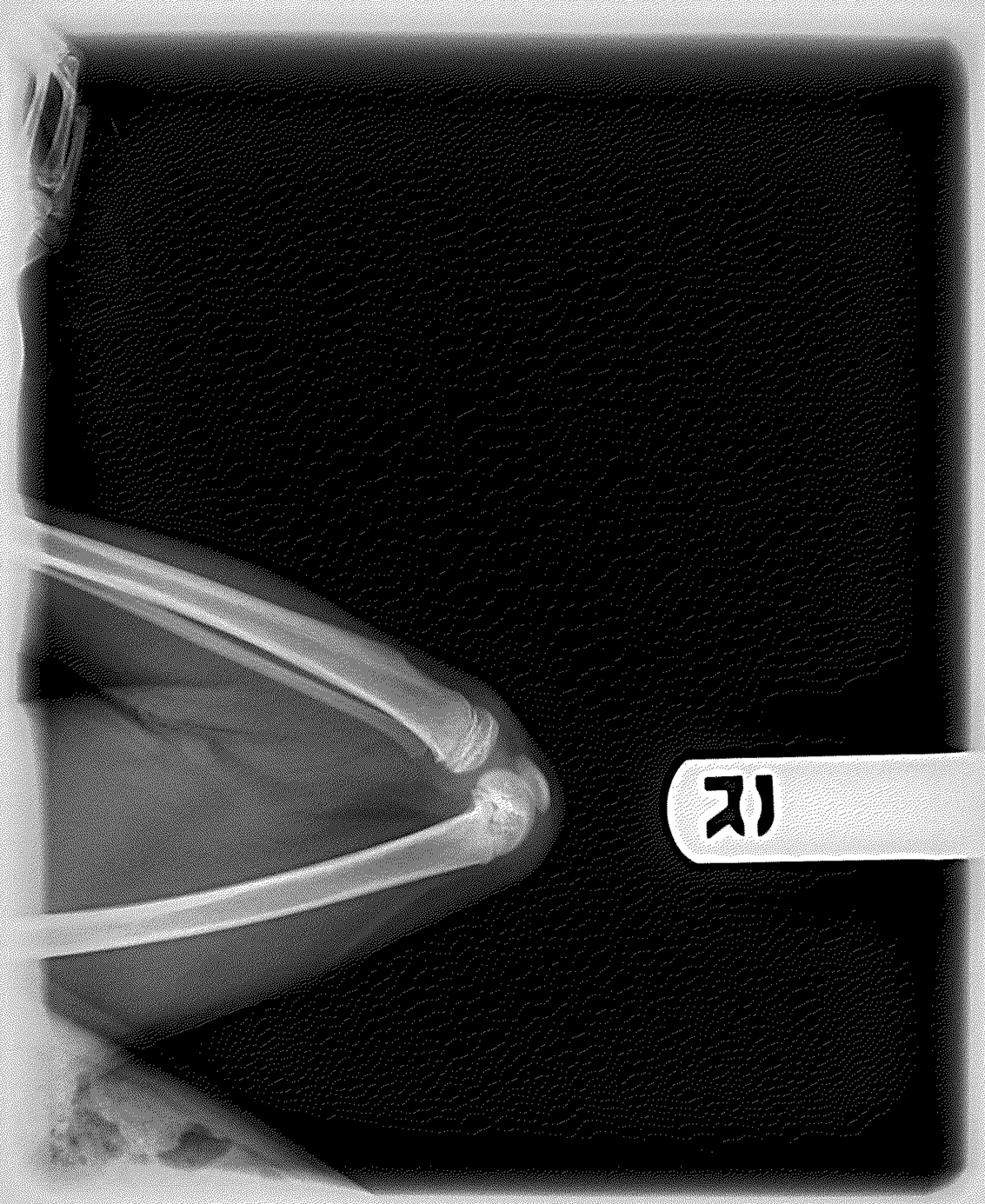
The amyloidosis is secondary amyloidosis: secondary to mis-metabolism of acute-phase reactive proteins from a sites of chronic inflammation. The sites of chronic inflammation inducing amyloidosis in this case was the disseminated Valley Fever and disseminated GI tract inflammation.

The inflammatory component of diagnosis #3, which can cause diarrhea and potentially other sequelae thereof, represents typical changes in this species in this colony, and they have been previously discussed. Changes present are consistent with food allergy/hypersensitivity/dietary intolerance/IBD. The ciliate overgrowth indicates dysbiosis which could be due to past antibiotic treatments. Please contact RM if you wish to discuss these changes further.

Please contact any of us with any questions, comments, or concerns.

Pathologist__CMM/KG(gross)/RM (histo)__

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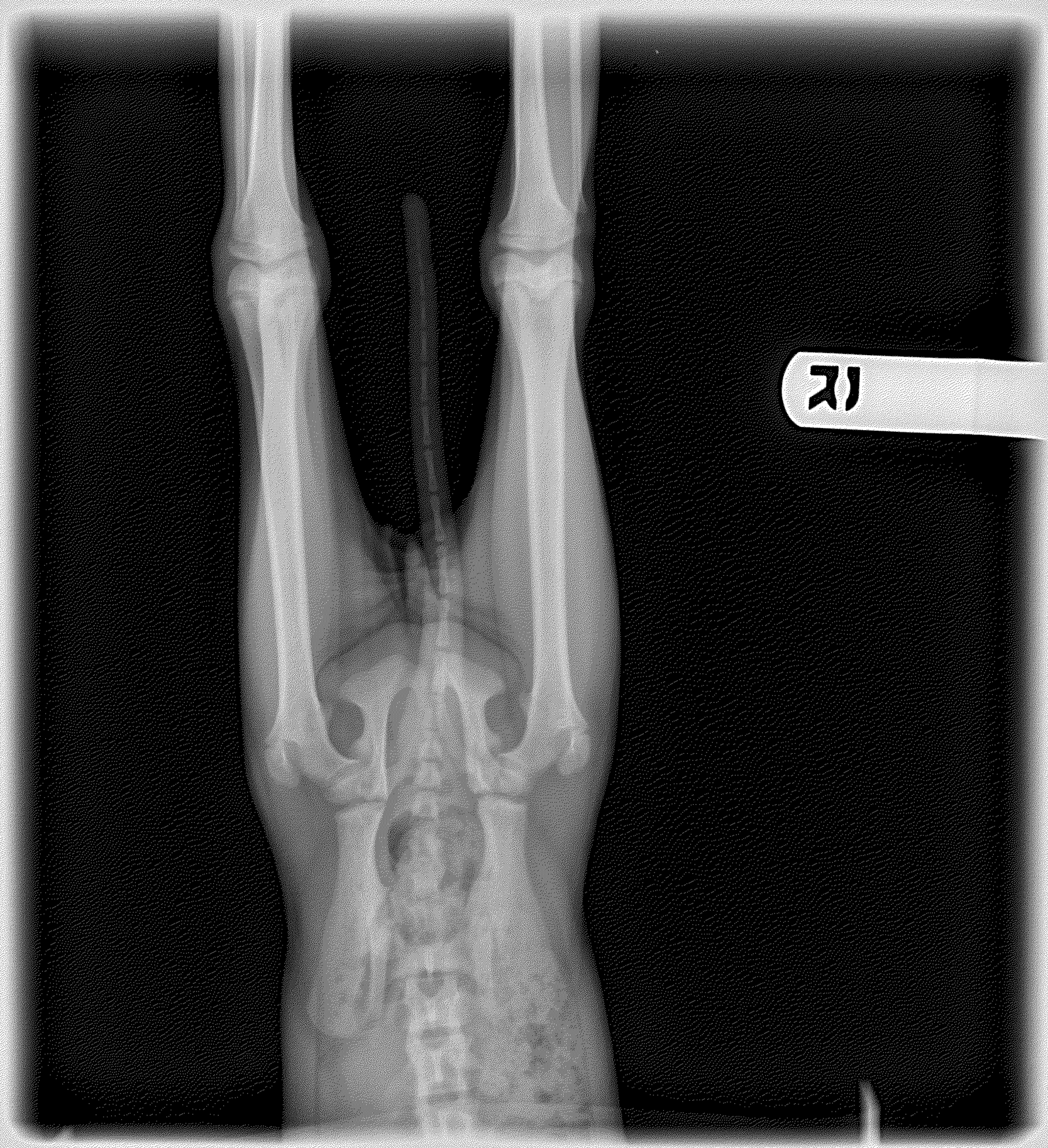
R

From: Tess House <th81@uw.edu>
Sent: Tuesday, December 24, 2019 10:45 AM
To: Sally Thompson-Iritani; Charlotte E. Hotchkiss; cjmead2; aw656; cmali
Subject: ABC Valley fever cases
Attachments: Valley Fever updated list 12.24.19.docx

Hi All-

I've updated our list of current cases and broken it down to titer negative and titer positive. I've also color coded those that came up positive at the fall semi-annual exams. I'm going to go back and also color code the spring cases so we can have that number as well so that should show up in Teams later today.

This document was uploaded to Teams but I've attached it for those not yet a part of the group or if you have any difficulties with it.

Thanks!

Theresa (Tess) House, DVM MPH
Supervisory Veterinarian
Washington National Primate Research Center
Arizona Breeding Colony
Office phone 206.685.1842
Mailing address- P.O. Box 20836/Mesa, AZ 85277

From: cmali <cmali@uw.edu>
Sent: Tuesday, January 29, 2019 1:55 PM
To: cjmead2
Subject: Animal Moves?
Attachments: Arizona Breeding Colony Spring Semi-Annual.pdf

Hi Caroline,

Just going back through my pinned (important emails) and noticed there are moves scheduled for the upcoming semi annuals.

Just wondering... what are these moves (new groups, rearranging breeding partners)? Do you coordinate these moves with Charlotte or get them approved by Charlotte? Still so many processes to learn....

Please let me know.

Thanks,
Dr M

Carolyn Malinowski, MS, DVM, CMAR, CPIA

Senior Veterinarian

Washington National Primate Research Center/University of Washington

Arizona Breeding Colony

PO Box 20836, Mesa, AZ 85277

Ph: 206.616.0501

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: cjmead2 <cjmead2@uw.edu>
Sent: Wednesday, January 9, 2019 3:49 PM

To: cmali; Tess House
Cc: Kelly L. Carbone; Jim Murphy
Subject:

This is what I compile each semi-annuals-waiting on DNA testing approval.

I write to each facility separately with dates of receivable shipments to ensure they are able to process on the dates scheduled.

Caroline

From: cmali <cmali@uw.edu>
Sent: Tuesday, February 12, 2019 10:13 AM
To: Tess House; Jim Murphy; cjmead2; Kelly L. Carbone
Subject: AZ VF Distribution
Attachments: Cocci.xls

Hi Team,

Here is the data that I pulled together for 2018 VF cases. Please see the attached document and tabs across the bottom.

The difference between new VF cases in the upstairs and downstairs enclosures looks like a big difference on the chart but in reality it is only a difference of 2 animals...

I don't know how useful this data is without doing statistics to see how significant the differences are but here it is.

Best,
Dr M

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Dare 2 Care... | explore UW's Compassion Fatigue Program

Animal	Sx	Result Date	Test Description
A03194	F	3/20/2018	IgG Titer Result,IgG Titer Value
A12255	F	1/4/2018	IgG Titer Result,IgG Titer Value
A12255	F	2/13/2018	IgG Titer Result,IgG Titer Value
A12262	F	9/24/2018	IgG Titer Result,IgG Titer Value
A12262	F	11/6/2018	IgG Titer Result,IgG Titer Value
A12264	F	3/27/2018	IgG Titer Result,IgG Titer Value
A12269	F	9/24/2018	IgG Titer Result,IgG Titer Value
F08047	F	2/13/2018	IgG Titer Result
F08047	F	2/13/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
F08047	F	4/30/2018	IgG Titer Result,IgG Titer Value
F08132	F	9/10/2018	IgG Titer Result,IgG Titer Value
K06192	F	10/1/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K06192	F	11/13/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K06192	F	12/11/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K06271	F	4/2/2018	IgG Titer Result,IgG Titer Value
K06271	F	6/18/2018	IgG Titer Result,IgG Titer Value
K06271	F	9/25/2018	IgG Titer Result,IgG Titer Value
K06271	F	12/26/2018	IgG Titer Result,IgG Titer Value
K07291	F	4/9/2018	IgG Titer Result,IgG Titer Value
K10112	F	10/2/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K10112	F	11/15/2018	IgG Titer Result,IgG Titer Value
K10112	F	12/26/2018	IgG Titer Result,IgG Titer Value
K11143	F	4/9/2018	IgG Titer Result,IgG Titer Value
K11143	F	10/8/2018	IgG Titer Result,IgG Titer Value
L02276	M	3/2/2018	IgG Titer Result,IgG Titer Value
L02276	M	8/28/2018	IgG Titer Result,IgG Titer Value
L06156	F	3/13/2018	IgG Titer Result,IgG Titer Value
L06156	F	9/10/2018	IgG Titer Result,IgG Titer Value
L10152	F	3/12/2018	IgG Titer Result,IgG Titer Value
L10152	F	9/10/2018	IgG Titer Result,IgG Titer Value
M10123	F	2/13/2018	IgG Titer Result,IgG Titer Value
M10123	F	5/9/2018	IgG Titer Result,IgG Titer Value
M10123	F	8/14/2018	IgG Titer Result,IgG Titer Value
M10123	F	12/17/2018	IgG Titer Result,IgG Titer Value
M11051	F	4/9/2018	IgG Titer Result,IgG Titer Value
M11051	F	10/8/2018	IgG Titer Result,IgG Titer Value
R09036	F	10/8/2018	IgG Titer Result,IgG Titer Value
R10113	F	3/26/2018	IgG Titer Result,IgG Titer Value
R10113	F	10/9/2018	IgG Titer Result,IgG Titer Value
R10151	F	3/26/2018	IgG Titer Result,IgG Titer Value
R10156	F	3/27/2018	IgG Titer Value
R10156	F	5/22/2018	IgG Titer Result,IgG Titer Value
R10156	F	7/30/2018	IgG Titer Value

Result
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positive (+),1:2
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positive (+),1:8
1:4

R10156	F	9/18/2018	IgG Titer Result,IgG Titer Value
R11037	F	3/13/2018	IgG Titer Result,IgG Titer Value
R11037	F	10/8/2018	IgG Titer Result,IgG Titer Value
S10114	F	4/2/2018	IgG Titer Result,IgG Titer Value
S10114	F	9/25/2018	IgG Titer Result,IgG Titer Value
S10185	F	3/13/2018	IgG Titer Result,IgG Titer Value
T06226	F	3/13/2018	IgG Titer Result,IgG Titer Value
T11135	F	4/9/2018	IgG Titer Result,IgG Titer Value
T11135	F	9/7/2018	IgG Titer Result,IgG Titer Value
Z07023	M	12/17/2018	IgG Titer Result,IgG Titer Value
Z11338	F	9/24/2018	IgG Titer Result,IgG Titer Value
Z12028	F	10/1/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z12028	F	11/13/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z12028	F	12/11/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z12342	F	3/12/2018	IgG Titer Result,IgG Titer Value
Z12342	F	9/10/2018	IgG Titer Result,IgG Titer Value
Z13022	F	2/13/2018	IgG Titer Result
Z13067	F	4/16/2018	IgG Titer Result,IgG Titer Value
Z13067	F	5/23/2018	IgG Titer Result,IgG Titer Value
Z13067	F	10/16/2018	IgG Titer Result,IgG Titer Value
Z13082	F	3/20/2018	IgG Titer Result,IgG Titer Value
Z13082	F	9/11/2018	IgG Titer Result,IgG Titer Value
Z13093	M	6/5/2018	IgG Titer Result,IgG Titer Value
Z13093	M	12/17/2018	IgG Titer Result,IgG Titer Value
Z13292	F	1/23/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z13292	F	4/16/2018	IgG Titer Result,IgG Titer Value
Z13292	F	6/4/2018	IgG Titer Result,IgG Titer Value
Z13292	F	10/16/2018	IgG Titer Result,IgG Titer Value
Z13337	F	12/24/2018	IgG Titer Result,IgG Titer Value
Z14001	F	1/22/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14001	F	4/16/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14001	F	6/4/2018	IgG Titer Result,IgG Titer Value
Z14001	F	10/29/2018	IgG Titer Result,IgG Titer Value
Z14027	M	10/22/2018	IgG Titer Result,IgG Titer Value
Z14130	F	1/30/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14130	F	4/16/2018	IgG Titer Result,IgG Titer Value
Z14130	F	6/4/2018	IgG Titer Result,IgG Titer Value
Z14130	F	10/22/2018	IgG Titer Result,IgG Titer Value
Z14141	F	4/16/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14141	F	5/23/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14141	F	7/30/2018	IgG Titer Result,IgG Titer Value

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positive (+),1:32,positive (+),1:2
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Z14141	F	8/30/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14141	F	9/25/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14141	F	10/29/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14251	M	12/17/2018	IgG Titer Result,IgG Titer Value
Z14323	F	7/3/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14323	F	7/31/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z14323	F	10/16/2018	IgG Titer Result,IgG Titer Value
Z14333	M	1/21/2018	IgG Titer Result,IgG Titer Value
Z14333	M	4/17/2018	IgG Titer Result,IgG Titer Value
Z16005	F	10/23/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z16005	F	12/5/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z16027	F	1/8/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z16341	F	10/15/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z16341	F	11/26/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z16358	M	10/15/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z16358	M	11/26/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z17135	F	10/15/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z17135	F	11/26/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
Z17137	M	10/15/2018	IgG Titer Result,IgG Titer Value
Z17137	M	11/26/2018	IgG Titer Result,IgG Titer Value

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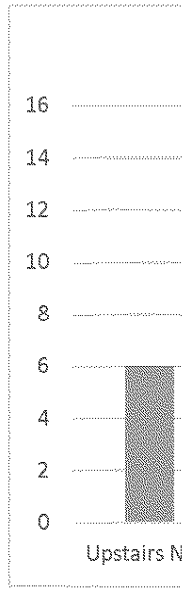
Animal	Location
Z17135	111
Z17137	111
Z16341*	111
Z16358*	111
Z13067	112
Z13292	112
Z14141*	112
Z13337**	112
Z14323**	112
Z16005	122
Z14333	162
Z14001	171
Z14027	171
Z14130	171
F08132	181
L06156	181
L10152	181
Z12342	181
A12264	212
R10156	212
R10113	221
R10151	221
A12262	222
A12269	222
Z11338	222
S10114	231
S10185	231
A03194	232
K06271	232
K10112	232
Z13082	232
K06192	241
Z12028	241
K07291	242
L02276	242
M11051	242
R09036	242
R11087	242
K11143**	242

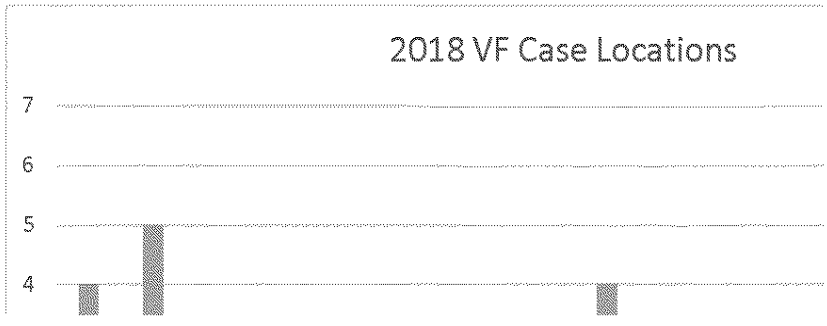
*= 104

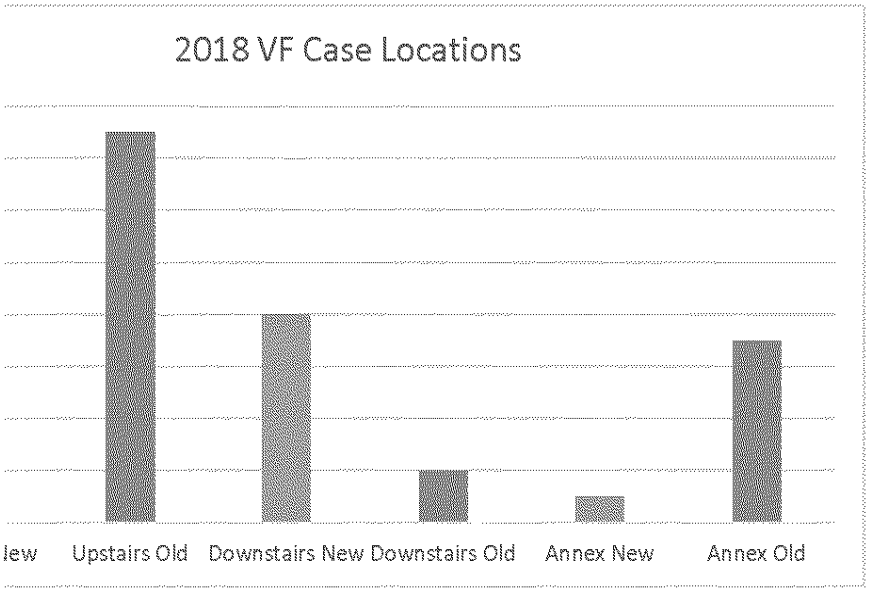
**=142

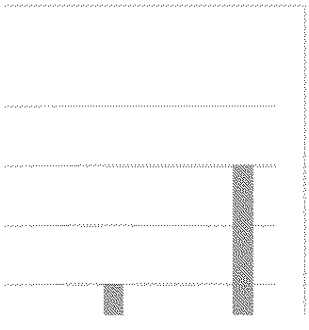
Upstairs New	6
Upstairs Old	15
Downstairs New	8
Downstairs Old	2
Annex New	1
Annex Old	7



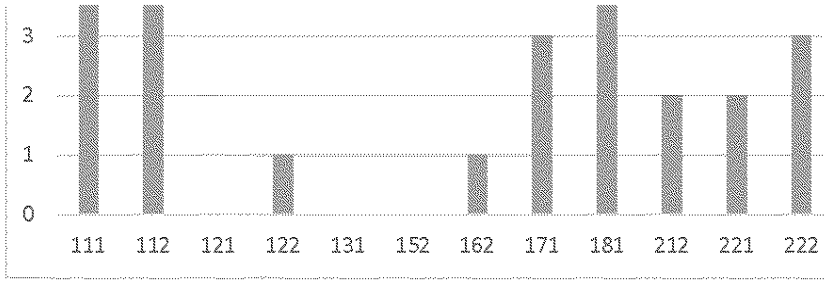
111	4
112	5
121	0
122	1
131	0
152	0
162	1
171	3
181	4



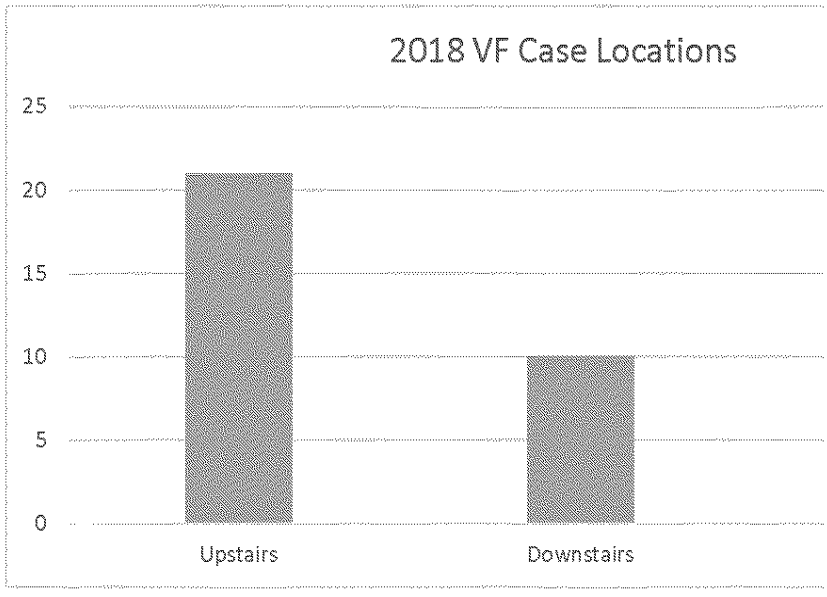

2018 VF Case Locations
lew
Upstairs Old
Downstairs New
Downstairs Old
Annex New
Annex Old

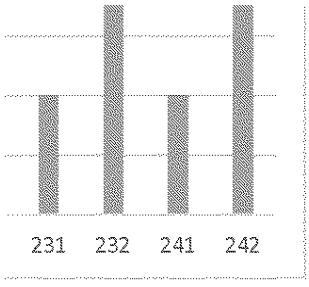


212	2
221	2
222	3
231	2
232	4
241	2
242	6



Upstairs	21
Downstairs	10
Annex	8

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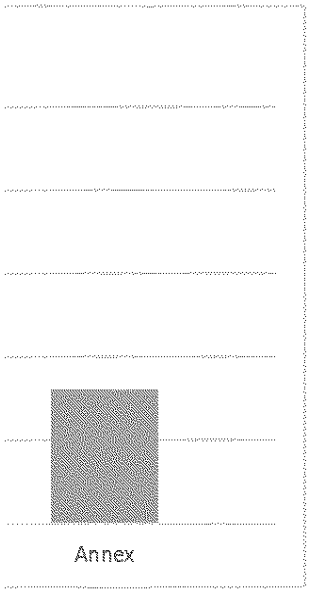
232
241
242


Annex

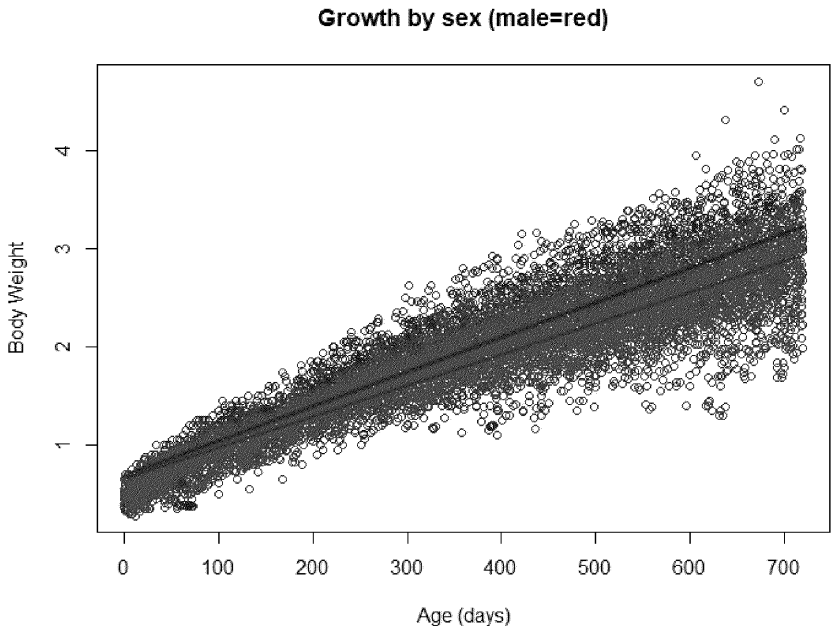
F08047	Seattle
M10123	Seattle
Z07023	Seattle
Z13022	Seattle
Z13093	Seattle
Z14251	Seattle

T06226	Euth
T11135	Euth
Z16027	EUTH

I couldn't figure out exactly what Rose did, but here's what I came up with. First, I put everything and every interaction into the model with the infant as a random effects, and here's what I got:

```
> Day_sex_fluc_model <- lmer(weight ~ Day + Sex + fluc + Day*fluc + Day*Sex +
(1 | Infant),data=fluc_data)
> Day_sex_fluc_model
Linear mixed model fit by REML ['lmerMod']
Formula: weight ~ Day + Sex + fluc + Day * fluc + Day * Sex + (1 | Infant)
   Data: fluc_data
REML criterion at convergence: -4255.703
Random effects:
 Groups   Name        Std.Dev.
 Infant   (Intercept) 0.2302
 Residual             0.1854
Number of obs: 10654, groups:  Infant, 389
Fixed Effects:
(Intercept)          Day         SexM      flucPos  Day:flucPos     Day:SexM
  0.7030858    0.0030465    0.0368791   -0.0402257    0.0001362    0.0003569
> anova(Day_sex_fluc_model)
Analysis of Variance Table
         Df Sum Sq Mean Sq    F value
Day       1 3569.9  3569.9 103897.776
Sex       1    1.5     1.5     44.661
fluc      1    0.0     0.0      0.002
Day:fluc  1    0.9     0.9     26.902
Day:Sex   1   10.7    10.7    312.546
```

This shows the effects of all the factors on body weight. Unfortunately, it doesn't give P values. Using an online calculator, the "Day" factor (age of the infant) is significant (P=0.002) and the "Day:Sex" (interaction of age and sex) is significant (P=0.036).



The data is similar if the infants without known gestation lengths are removed from the calculations:

```
Day_sex_fluc_diff_model <- lmer(weight ~ Day + Sex + fluc + Difference + Day*
fluc + Day*Sex + (1 | Infant),data=fluc_data_nopremNA)
> Day_sex_fluc_diff_model
Linear mixed model fit by REML ['lmerMod']
Formula: weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
(1 | Infant)
   Data: fluc_data_nopremNA
REML criterion at convergence: -3871.984
Random effects:
 Groups   Name        Std.Dev.
 Infant   (Intercept) 0.2318
 Residual             0.1869
Number of obs: 10137, groups:  Infant, 369
Fixed Effects:
(Intercept)          Day         SexM      flucPos   Difference  Day:flucPos
Day:SexM
  0.6990467    0.0030388    0.0367093   -0.0432946    0.0025982    0.0001426
0.0003596
> anova(Day_sex_fluc_diff_model)
Analysis of Variance Table
           Df Sum Sq Mean Sq    F value
Day         1 3433.5  3433.5 98274.7793
Sex         1    1.5     1.5    41.7191
fluc        1    0.0     0.0     0.0003
Difference  1    0.2     0.2     4.3563
Day:fluc    1    0.9     0.9    25.8495
Day:Sex     1   10.5    10.5   299.7611
```

Instead of just using the variable of fluconazole yes/no, I tried it with the days of fluconazole exposure as a variable (and excluding infants where it was not known whether or not they were premature):

```
> Day_sex_cont_diff_model <- lmer(weight ~ Day + Sex + Exptotal + Difference
+ Day*Exptotal + Day*Sex + (1 | Infant),data=fluc_data_nopremNA)
Warning message:
Some predictor variables are on very different scales: consider rescaling
> Day_sex_cont_diff_model
Linear mixed model fit by REML ['lmerMod']
Formula: weight ~ Day + Sex + Exptotal + Difference + Day * Exptotal +
    Day * Sex + (1 | Infant)
   Data: fluc_data_nopremNA
REML criterion at convergence: -4022.829
Random effects:
 Groups   Name        Std.Dev.
 Infant   (Intercept) 0.2308
 Residual             0.1853
Number of obs: 10137, groups:  Infant, 369
Fixed Effects:
 (Intercept)           Day          SexM      Exptotal    Difference  Day:Exp
total      Day:SexM
   7.059e-01     3.015e-03     4.364e-02    -9.509e-04     2.593e-03     3.36
5e-06     3.422e-04
fit warnings:
Some predictor variables are on very different scales: consider rescaling
> anova(Day_sex_cont_diff_model)
```

```
Analysis of Variance Table
             Df Sum Sq Mean Sq    F value
Day           1 3433.0  3433.0 99951.3647
Sex           1    1.4     1.4    42.0872
Exptotal      1    0.0     0.0     0.1041
Difference    1    0.1     0.1     4.3066
Day:Exptotal  1    7.8     7.8   226.1612
Day:Sex       1    9.5     9.5   276.2643
```

That gave a significant interaction for age by days of fluconazole exposure during pregnancy (P = 0.042), but threw an error message, so I don't know if I believe it.

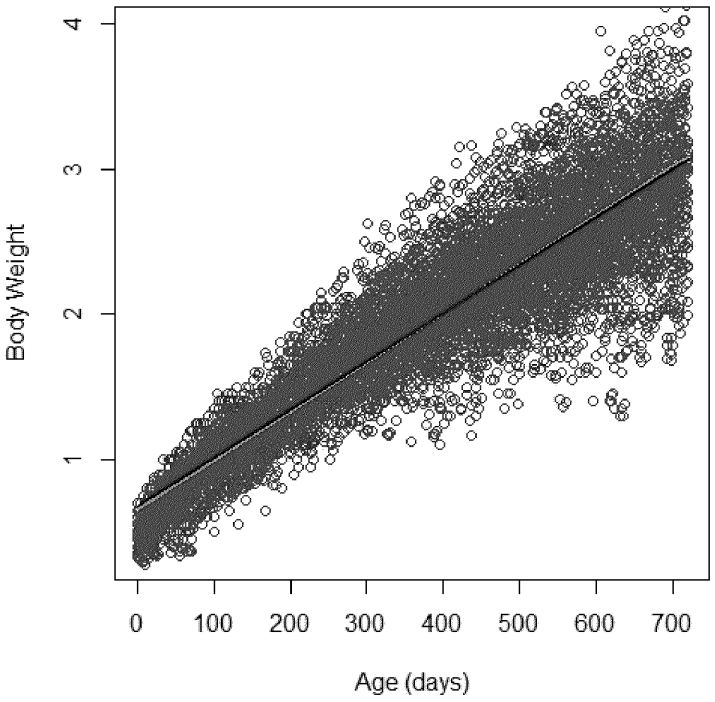
Then I tried the model again using a different R formula (lm instead of lmer), and using each infant as a fixed effect rather than a random effect, and got something where everything is significant, but I don't believe it:

```
Day_sex_cont_diff_model <- lm(weight ~ Day + Sex + Exptotal + Difference + Da
y*Exptotal + Day*Sex + Infant,data=fluc_data_nopremNA)
anova(Day_sex_cont_diff_model)
Analysis of Variance Table

Response: weight
               Df Sum Sq Mean Sq    F value  Pr(>F)
Day             1 4931.4  4931.4 1.4356e+05 < 2e-16 ***
Sex             1   68.1    68.1 1.9834e+03 < 2e-16 ***
Exptotal        1    4.8     4.8 1.4003e+02 < 2e-16 ***
Difference      1    0.2     0.2 6.4924e+00 0.01085 *
Infant        365  545.8     1.5 4.3533e+01 < 2e-16 ***
Day:Exptotal    1    7.6     7.6 2.2249e+02 < 2e-16 ***
Day:Sex         1    9.3     9.3 2.6962e+02 < 2e-16 ***
Residuals    9765  335.4     0.0
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

I got similar results with fluconazole yes/no instead of exposure days:

```
> lm_model <- lm(weight ~ Day + Sex + fluc + Difference + Day*fluc + Day*Sex
+ Infant,data=fluc_data_nopremNA)
> anova(lm_model)
Analysis of Variance Table

Response: weight
             Df Sum Sq Mean Sq    F value    Pr(>F)
Day           1 4931.4  4931.4 141135.072 < 2.2e-16 ***
Sex           1   68.1    68.1   1949.926 < 2.2e-16 ***
fluc          1    0.2     0.2      5.446  0.019633 *
Difference    1    0.3     0.3      8.187  0.004228 **
Infant      365  550.4     1.5     43.156 < 2.2e-16 ***
Day:fluc      1    0.9     0.9     26.066 3.362e-07 ***
Day:Sex       1   10.2    10.2    293.055 < 2.2e-16 ***
Residuals  9765  341.2     0.0
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

But, as I said, I don't really believe it is significant, because look at the graph.



The red dots and the orange line are the fluconazole-exposed infants; the blue dots and the black line are the untreated.

There's supposed to be a way to do a step test, where you add or subtract factors into and out of a linear regression model, and figure out whether the factor significantly affects the model. I think that is what Rose was doing. I ran something called a stepAIC and got results, but I don't know what they mean:

```
> step_test <- stepAIC(lm_model, direction="both")
Start:  AIC=-33635.47
weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
    Infant


Step:  AIC=-33635.47
weight ~ Day + Sex + fluc + Infant + Day:fluc + Day:Sex

            Df Sum of Sq    RSS    AIC
<none>                   341.20 -33635
- Day:fluc   1      1.22 342.42 -33601
- Day:Sex    1     10.24 351.44 -33338
- Infant   366    545.43 886.63 -24687
> step_test$anova
Stepwise Model Path
Analysis of Deviance Table
```

```
Initial Model:
weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
    Infant

Final Model:
weight ~ Day + Sex + fluc + Infant + Day:fluc + Day:Sex


          Step Df     Deviance Resid. Df Resid. Dev       AIC
1                                  9765   341.1984 -33635.47
2 - Difference  0 1.136868e-13      9765   341.1984 -33635.47
>
```

It looks like it wants to take out the Difference (that's the difference between due date and delivery date) but it doesn't change the AIC.

Then I tried to compare two models, one including fluconazole and one without it, and I got a significant P value, but again, I'm not sure whether or not I believe it:

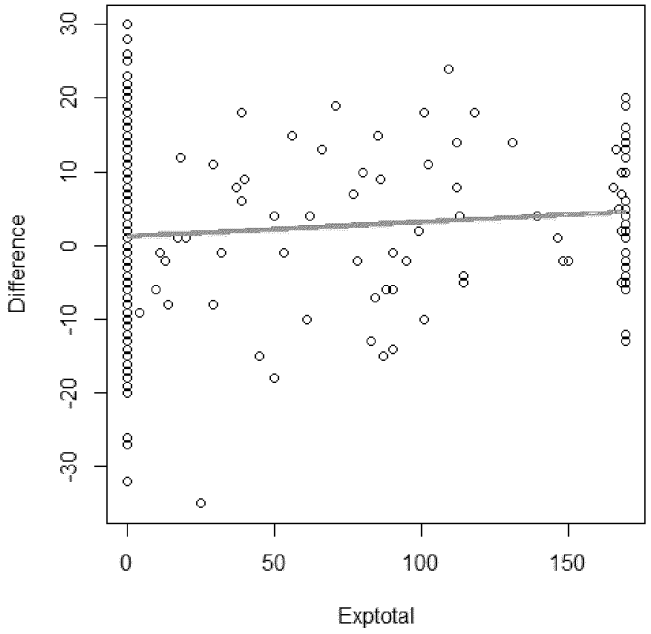
```
> lm_model_short <- lm(weight ~ Day + Sex + Difference + Day*Sex + Infant,dat
a=fluc_data_nopremNA)
> anova(lm_model_short)
Analysis of Variance Table

Response: weight
             Df Sum Sq Mean Sq    F value    Pr(>F)
Day           1 4931.4  4931.4 1.4065e+05 < 2.2e-16 ***
Sex           1   68.1    68.1 1.9432e+03 < 2.2e-16 ***
Difference    1    0.3     0.3 7.9665e+00  0.004775 **
Infant      366  550.6     1.5 4.2905e+01 < 2.2e-16 ***
Day:Sex       1    9.9     9.9 2.8317e+02 < 2.2e-16 ***
Residuals  9766  342.4     0.0
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
> anova(lm_model_short,lm_model)
Analysis of Variance Table

Model 1: weight ~ Day + Sex + Difference + Day * Sex + Infant
Model 2: weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
    Infant
  Res.Df    RSS Df Sum of Sq      F    Pr(>F)
1   9766 342.42
2   9765 341.20  1    1.2216 34.962 3.475e-09 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

Then I switched gears, and tried to see if there was an effect of fluconazole on length of gestation. It seems there is:

```
prem_fluc_model <- lm(Difference ~ Exptotal + Sex, data=prem_data)
> anova(prem_fluc_model)
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
```

```
Exptotal    1    460  459.58  4.6925 0.03094 *
Sex         1     14   13.98  0.1427 0.70578
Residuals 366  35846   97.94
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

And the graph shows that animals exposed to fluconazole were born later than those not exposed:



(Exptotal is the number of days fluconazole exposure, and Difference is the delivery date minus the due date.)

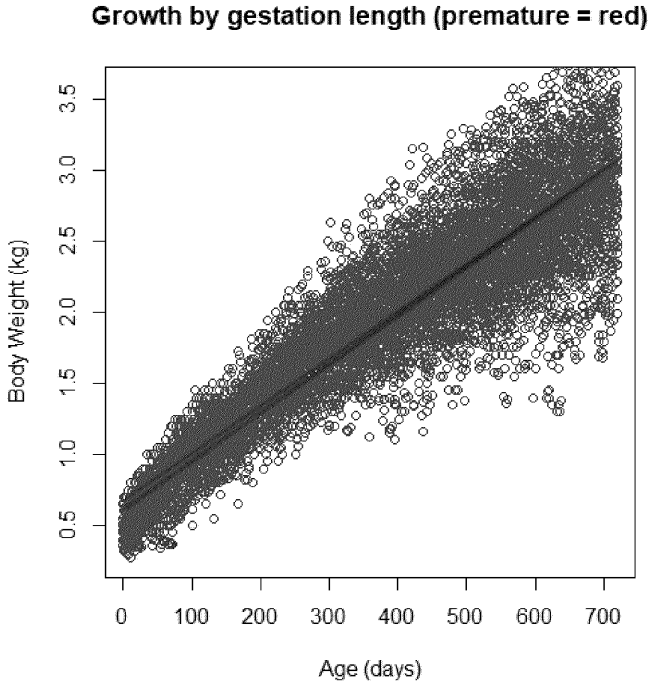
The effect on gestation length was significant based on the number of exposure days during the 1st trimester alone, but not for the 2nd or 3rd trimester:

```
prem_fluc_model1 <- lm(Difference ~ Expdayst1 + Sex, data=prem_data)
> anova(prem_fluc_model1)
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
Expdayst1   1    423  422.80  4.3129 0.03852 *
Sex         1     18   17.69  0.1804 0.67125
Residuals 366  35879   98.03
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1


prem_fluc_model2 <- lm(Difference ~ Expdayst2 + Sex, data=prem_data)
> anova(prem_fluc_model2)
```

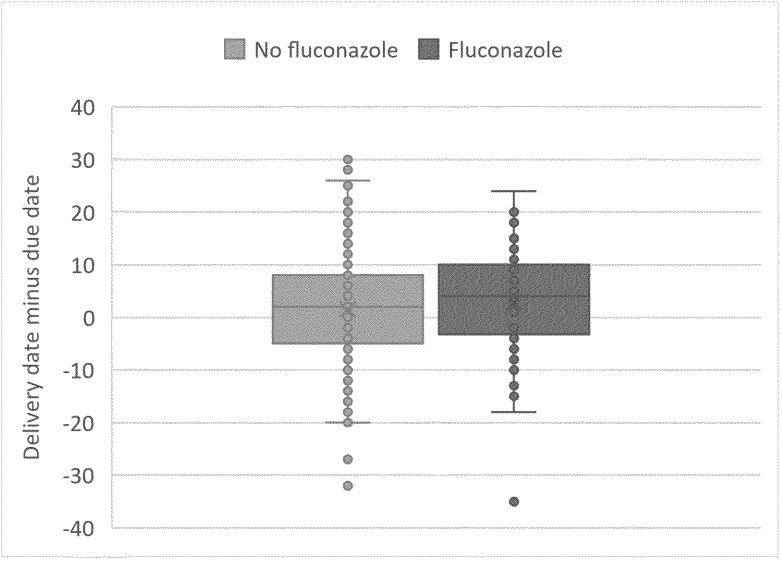
```
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
Expdayst2   1    396  395.83  4.0342 0.04532 *
Sex         1     13   12.87  0.1311 0.71746
Residuals 366  35911   98.12
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

```
prem_fluc_model3 <- lm(Difference ~ Expdayst3 + Sex, data=prem_data)
> anova(prem_fluc_model3)
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
Expdayst3   1    374  374.36   3.813 0.05162 .
Sex         1     11   11.19   0.114 0.73588
Residuals 366  35934   98.18
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

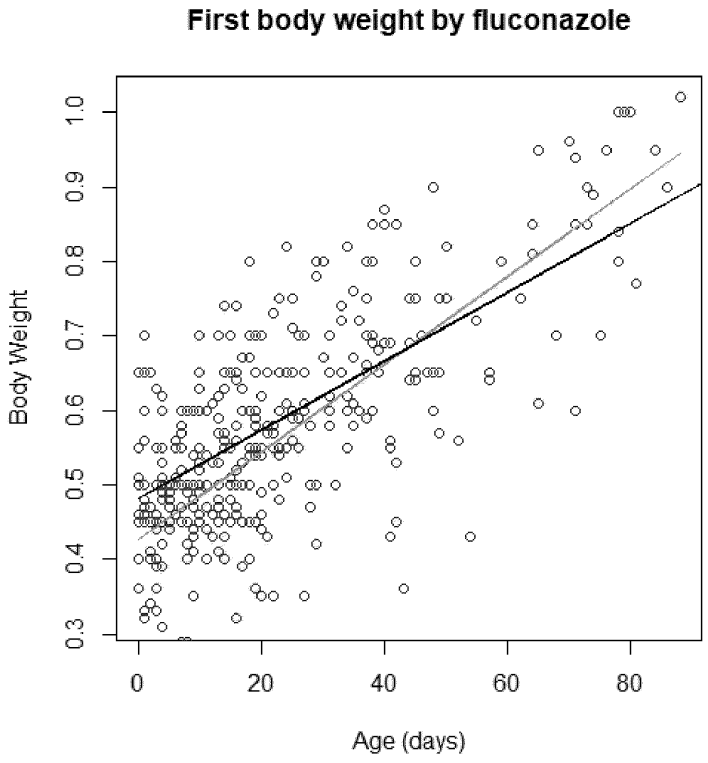
And then because I was playing with graphs, I was able to show that premature infants seem to be smaller at birth, but show catch up growth over time. Not sure how to run stats on it, but the graph is suggestive:



Then I realized something. If the fluconazole-treated animals are born later, and animals that are born later start out heavier, that could mask any fluconazole effect on birthweight. Although the graph is suggestive, a t-test comparing the gestation length between fluconazole treated and untreated was not significant (P = 0.23).



I tried to dig in anyway. Unfortunately, we do not have birthweights on most of the animals, and the age at which the first weight was taken varies significantly. Still, it looks like there could be something there when you graph it (red dots/orange line is positive for fluconazole):



Statistically, it looks like the first weight is significantly related to age, sex, fluconazole treatment, and gestational age at delivery:

```
firstwt_model <- lm(weight ~ Day + Sex + fluc + Difference + Day*fluc + Day*S
ex,data=fluc_data_first)
> anova(firstwt_model)
Analysis of Variance Table

Response: weight
            Df Sum Sq Mean Sq  F value    Pr(>F)
Day          1 3.9425  3.9425 472.8324 < 2.2e-16 ***
Sex          1 0.1736  0.1736  20.8251 6.902e-06 ***
fluc         1 0.0401  0.0401   4.8128   0.02888 *
Difference   1 0.3256  0.3256  39.0449 1.164e-09 ***
Day:fluc     1 0.0303  0.0303   3.6295   0.05756 .
Day:Sex      1 0.0129  0.0129   1.5526   0.21356
Residuals  362 3.0184  0.0083
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

In summary, the statistics aren't clear. Depending on which statistical test you use, fluconazole either does nothing, or else it delays delivery associated with lower birth weights, implying slower fetal growth in utero. But even if there is slower growth in utero, I think there's catch up growth, so that overall there's no difference in body weight after the first couple of months.

From: Charlotte E. Hotchkiss
Sent: Thursday, June 13, 2019 8:20 AM
To: Bob Murnane (rmurnane@uw.edu)
Subject: FW: Z14141
Attachments: 19-041 (Z14141) histo.docx

Bob –
We have to do Virtual Grand Rounds for the NPRC consortium next week, and we figure it's been long enough since we've done Valley Fever that we can do it again. Can you please take some pretty histo pictures of this animal?

The webinar is Thursday, so if I could get something early in the week it would be super.

Thanks!
Charlotte

From: cmali <cmali@uw.edu>
Sent: Wednesday, June 12, 2019 1:55 PM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: Z14141

Hi Charlotte,

Please see the path report for Z14141 (attached).
Tess wrote a VERY thorough case history.

Bob may be able to provide you with some histo pics...

Let us know what we can help with!

Best,
Carolyn

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
Washington National Primate Research Center/University of Washington
Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Thursday, May 9, 2019 12:19 PM
To: Audrey Baldessari; Keith Vogel; Charlotte E. Hotchkiss; Kathryn A. Guerriero; Dean Jeffery; Jason D. Laramore; Tess House; cmali
Subject: 19-041 and 042 (Z19068 and Z14141)

Hi all:

Please find attached final reports on the above 2 cases. Interestingly, Z14141 was cerebral Valley Fever, and both animals were from the same dam who also was diagnosed clinically with Valley Fever.

Please contact me with any questions, comments or concerns.

Cheers
Bob

From: Kelly Heffernan <ksh@uw.edu>
Sent: Friday, November 8, 2019 10:45 AM
To: Charlotte E. Hotchkiss; Rita U Bellanca
Subject: Notes from the WaNPRC Records Review
Attachments: WaNPRC Animal Observations.docx; WaNPRC Records Review - November 2019.docx

Hi Charlotte and Rita,

Can you look over my notes from the meeting and ensure I got all the information correct?

Thanks and Happy Friday! I hope you enjoy the long weekend!
Kelly

Kelly Heffernan
Reviewer and Scientific Liaison
Office of Animal Welfare

Health Sciences Building Box 357160
1705 NE Pacific Street Seattle, WA 98195-7160
206.616.3625
ksh@uw.edu / oaw.washington.edu

Breeding Management ()

1. Establish and maintain SPF *M. nemestrina* breeding colonies. Animals at both the NIRC and Arizona facilities remain free of SRV, STLV, and B virus. We continue semi-annual testing.
2. Consolidate breeding colony by moving animals from NIRC to Arizona and Seattle. The new animal housing building in Arizona was completed in September. 227 animals have been moved from NIRC to Arizona, leaving 151 animals at NIRC. There are requests for 122 animals in process, but not all are confirmed. Whenever possible, these orders will be filled with animals from NIRC, and any remaining animals will be transferred to Seattle. We anticipate that we will have all animals out of NIRC by June 2020.
3. Establish pool of *M. nemestrina* in Seattle for immediate assignment to project. We have received supplemental funding to construct pen housing for nonhuman primates in rooms formerly occupied by dogs, pigs, and sheep. Pen housing will provide a more enriched environment than cage housing, as well as reducing husbandry workload.
4. Supply animals to meet investigator needs as efficiently as possible. In 2019 ? *M. nemestrina* were assigned to on-site investigators, and ? were transferred to external investigators. The backlog of orders has been fulfilled, and new requests are processed in a timely manner following receipt of all paperwork.
5. Samples from 48 animals were shipped to Betsy Ferguson's lab in Oregon for genotyping by sequencing (GBS). From the GBS data, SNPs were identified for a 96-SNP panel to confirm parentage. 215 samples have now been processed, and where full trios are available the SNP data confirms the available pedigree information. Additional sample submission will begin in January 2020.

SPECIFIC UPDATES FOR ARIZONA BREEDING COLONY:

1. Staffing support: Staffing has been stable with two veterinarians and ~~three~~ four veterinary technicians. A part time veterinarian was contracted in October to assist with the increased number of animals on site. One full time veterinarian is leaving the program (1/3/20) for personal reasons and recruitment of a replacement is underway. The veterinary team is looking into hiring a full-time temporary technician in lieu of a part time veterinarian to aid with the increased clinical load. The husbandry staff consists of nine animal technicians and one supervisor. ~~In January 2019, an animal technician will be moving into a veterinary technician role and R~~recruiting is underway for additional animal technicians. ~~This increase in staffing will coincide with the completion of the new building and the increase in animal population~~
2. The ~~AD~~ Director is in regular, close communication with the staff in AZ. The personnel in AZ participate in multiple meetings, ~~s and~~ one on one phone calls with Seattle staff, and are involved in decision making regarding the AZ campus and Center as a whole.
3. AZ veterinarians participate in UW IACUC meetings. Dr. Tess House is a regular member, and Dr. Carolyn Malinowski serves as an alternate when Dr. House is not available.
4. AZ personnel participate in NPRC consortium working groups, and the combined BMC/BCMC face-to-face meeting is being hosted at the WaNPRC AZ facility in January 2019.

5. New building cConstruction has been completed and commissioned. 227 animals were moved into he facility from NIRC in October and November. ~~is progressing with the new building to increase capacity in AZ, which will result in lower per diem at that facility and eliminate cost for contract care of animals at NIRC. Extensive site preparation has been completed and the building slab is near completion.~~
6. Animal mortality is low - mortality at 5% (goal is below 10%).
7. Coccidioidomycosis is still present and being managed with Fluconazole treatment and environmental controls (wetting the areas regularly to decrease sporulation). Animals brought in from NIRC ~~will be~~are housed in the new building, inside and under HEPA filtration, thus protected from infection.
8. Fertility at 76% (goal is 60%) for animals in active breeding. Some breeding limited because of space and repair considerations.
9. We have made some progress in identifying an acceptable fix for paint chipping and peeling issues in the compounds. HDPE wall coverings with caulked edges. Good progress is being made in installing this solution within multiple enclosures in the facility.
10. We continue trying to be cost effective by completing (when possible and appropriate) repairs, upgrades, and grounds maintenance. Examples of repairs recently completed in-house, include: repairs to and re-installation of damaged CCTV tower and camera, replacement of worn stair treads, and weld repairs and wheel replacement on portable caging.

Veterinary Services

1. Veterinary staffing has been stable in Seattle since the last NSAB. One of the Arizona veterinarians is leaving in January, and that position has been posted. There are currently five veterinarians in Seattle available for clinical care (this include the breeding colony/compliance veterinarian) and two veterinarians in Arizona.
2. We are in the process of hiring a vet tech clinical supervisor to coordinate clinical support, improve processes to increase efficiency, and manage inventory to minimize waste.
3. We have developed new procedures to meet investigator needs. Specifically, we are performing surgical liver lobectomies for a project studying malaria infection, and have been supporting terminal neuroscience procedures using urethane to maintain animals under anesthesia while preserving specific neurologic signaling.
4. Veterinarians continue to have weekly meetings to discuss ways to improve equipment, procedures, and medications as well as develop standards to maintain consistency among the vivaria.
5. We are continuing to identify areas for improvement in our electronic Animal Research Management System and are working with IT to implement.
6. Continuing to provide clinical care, preventive medicine, pathogen screening, and surgical and anesthetic support for research projects.
7. Continuing to train residents, vet students, and undergrads.

WaNPRC Breeding Report 2018 – 4th Quarter

Macaca nemestrina Breeding Colonies

Commented [CH1]: This section cannot be updated until January because the final data for December is not available yet.

Both offsite colonies are producing SPF infants. There are no McHV-1 positive animals breeding off-site. However, colony production has been restricted in 2017 and 2018 via a decrease in the number of females in breeding situations. At the beginning of the 4nd quarter, there were 119 adult females at ABC, but only 71 were in active breeding situations. Similarly, at NIRC there were 208 adult females, but only 98 were in breeding situations. By the end of the quarter there were 87 females at NIRC and 76 females at ABC actively breeding.

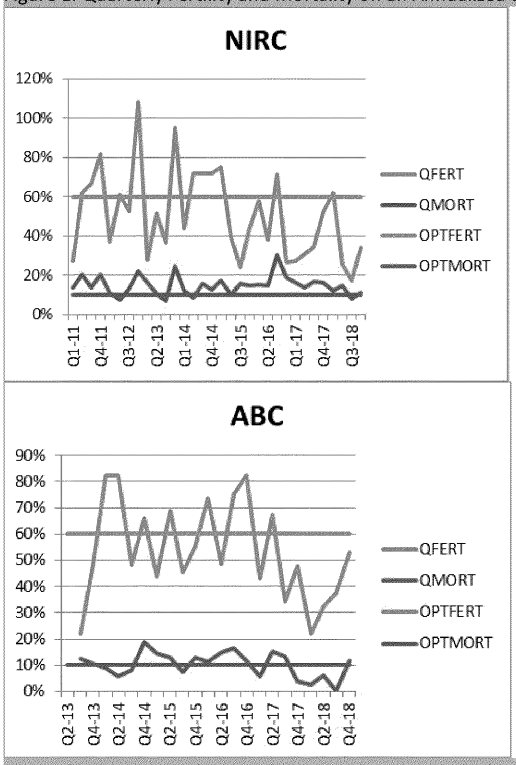
2019 Initial Census	Colony size	Juvenile replacements	Offspring < 1 yr	Breeding males	Breeding females	Adult breeding animals
	A	B	C	D	E	F
ABC MN	281	103	40	15	123	138
NIRC MN	432	188	57	17	170	187
Total MN	713	291	97	32	293	325

2018 Year (average colony size)	Colony size	Juvenile replacements	Offspring < 1 yr	Breeding males	Breeding females	Adult breeding animals	Colony production
	A	B	C	D	E	F	G
ABC MN	278	102	45	12	119	131	43
NIRC MN	500	188	74	30	208	238	73
Total MN	777	290	119	42	327	369	116

2017 Year	Colony size	Juvenile replacements	Offspring < 1 yr	Breeding males	Breeding females	Adult breeding animals	Colony production
	A	B	C	D	E	F	G
ABC MN	350	125	80	8	137	145	66
NIRC MN	576	200	82	62	232	294	85
Total MN	925.75	324.75	162	69.5	369.5	439	151

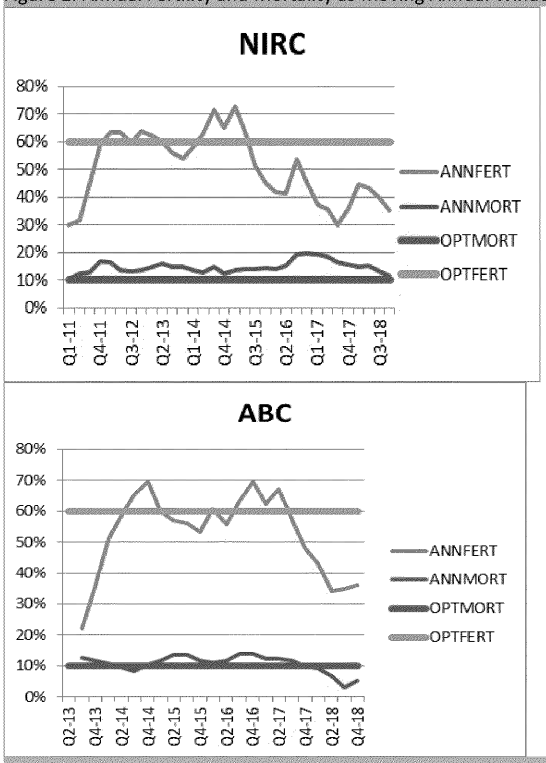
The following graphs compare the two facilities. Fertility tends to appear higher during the winter at NIRC because many animals are only in breeding situations when they are outdoors in the summer. Calculations are adjusted in the table below the graphs to account for animals not in breeding situations. At ABC, fertility has been decreasing. This is due to some animals not being in breeding situations, and some older infants remaining on dams, which reduces fertility. Mortality/culling is within acceptable limits.

Figure 1: Quarterly Fertility and Mortality on an Annualized Basis (data for the quarter multiplied by 4)



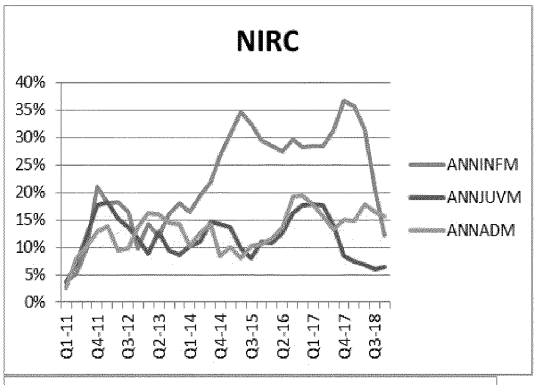
Legend: Blue = Fertility, Red = Mortality. Straight lines are standards to meet.

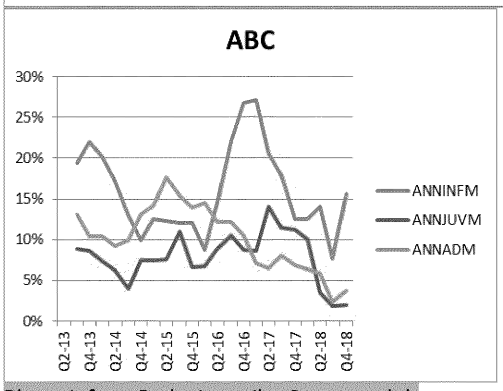
Figure 2: Annual Fertility and Mortality as Moving Annual Window (data from the preceding 12 months)



Legend: Blue = Fertility, Red = Mortality. Straight lines are standards to meet.

Figure 3: Annual Mortality as Moving Annual Window, By Age (Data from the preceding 12 months)



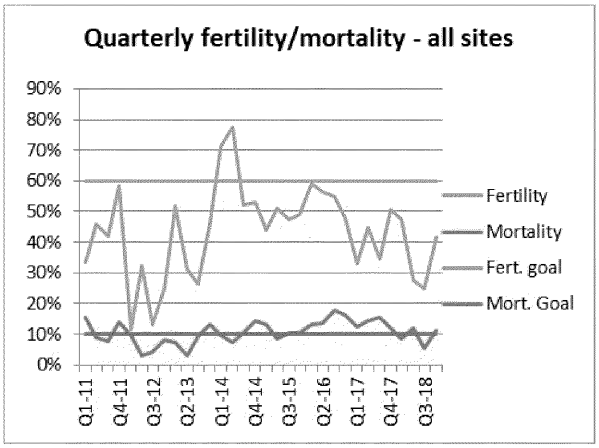


Blue = infant, Red = juvenile, Green = adult

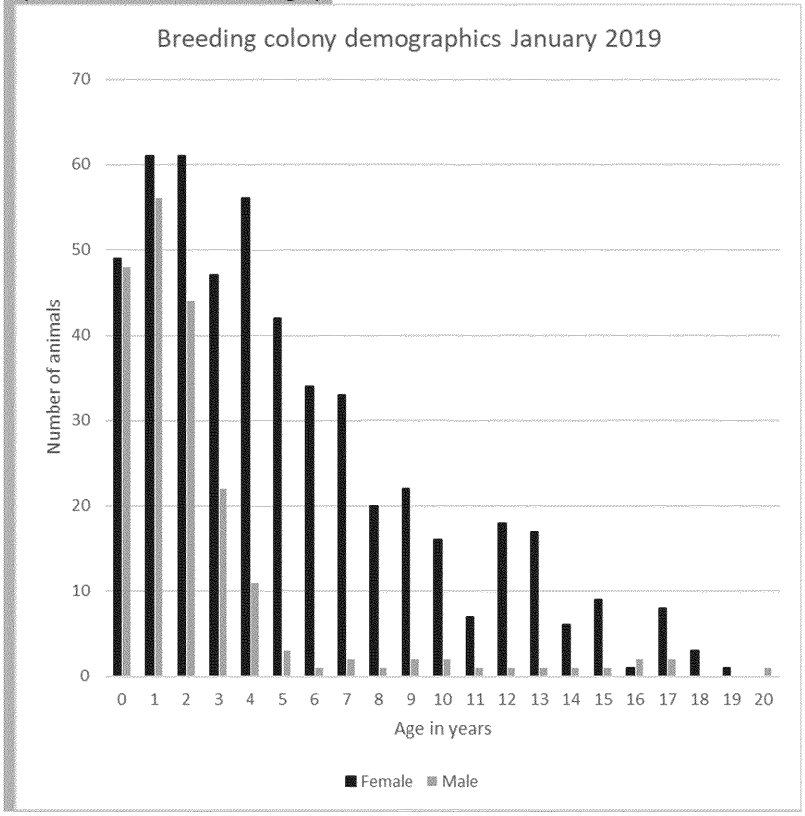
Looking at the off-site colonies combined, fertility has varied over the past few years, but was higher in 2015 and 2016 than in 2011-2013. Mortality had increased recently, but has now decreased dramatically at both facilities. Fertility has been low when all adult females are included in the equation, but good when only females in breeding situations at the beginning of the quarter are counted.

Year	Fertility (%)	Fertility (%) – active breeders only	Mortality (%)
2011	45		12
2012	21		7
2013	39		8
2014	64		10
Average '11-'14	40		9.25
2015	48		11
2016	55		15

2017	41		14
2018 q1	48		9
2018 q2	29	56	13
2018 q3	24	52	5
2018 q4	41	76	11



The age spread in the breeding colony shows few older animals, and a good number of replacement breeders coming up.



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8. Fertility at 76% (goal is 60%) for animals in active breeding. Some breeding limited because of space and repair considerations.
9. We have made some progress in identifying an acceptable fix for paint chipping and peeling issues in the compounds. HDPE wall coverings with caulked edges. Good progress is being made in installing this solution within multiple enclosures in the facility.
10. We continue trying to be cost effective by completing (when possible and appropriate) repairs, upgrades, and grounds maintenance. Examples of repairs recently completed in-house, include: repairs to and re-installation of damaged CCTV tower and camera, replacement of worn stair treads, and weld repairs and wheel replacement on portable caging.

Veterinary Services

1. Veterinary staffing has been stable in Seattle since the last NSAB. One of the Arizona veterinarians is leaving in January, and that position has been posted. There are currently five veterinarians in Seattle available for clinical care (this include the breeding colony/compliance veterinarian) and two veterinarians in Arizona.
2. We are in the process of hiring a vet tech clinical supervisor to coordinate clinical support, improve processes to increase efficiency, and manage inventory to minimize waste.
3. We have developed new procedures to meet investigator needs. Specifically, we are performing surgical liver lobectomies for a project studying malaria infection, and have been supporting terminal neuroscience procedures using urethane to maintain animals under anesthesia while preserving specific neurologic signaling.
4. Veterinarians continue to have weekly meetings to discuss ways to improve equipment, procedures, and medications as well as develop standards to maintain consistency among the vivaria.
5. We are continuing to identify areas for improvement in our electronic Animal Research Management System and are working with IT to implement.
6. Continuing to provide clinical care, preventive medicine, pathogen screening, and surgical and anesthetic support for research projects.
7. Continuing to train residents, vet students, and undergrads.

WaNPRC Breeding Report 2018 – 4th Quarter

Macaca nemestrina Breeding Colonies

Commented [CH1]: This section cannot be updated until January because the final data for December is not available yet.

Both offsite colonies are producing SPF infants. There are no McHV-1 positive animals breeding off-site. However, colony production has been restricted in 2017 and 2018 via a decrease in the number of females in breeding situations. At the beginning of the 4nd quarter, there were 119 adult females at ABC, but only 71 were in active breeding situations. Similarly, at NIRC there were 208 adult females, but only 98 were in breeding situations. By the end of the quarter there were 87 females at NIRC and 76 females at ABC actively breeding.

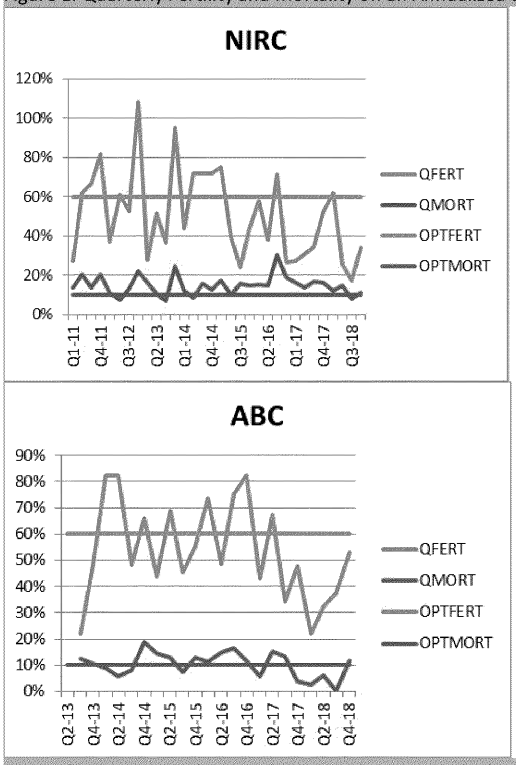
2019 Initial Census	Colony size	Juvenile replacements	Offspring < 1 yr	Breeding males	Breeding females	Adult breeding animals
	A	B	C	D	E	F
ABC MN	281	103	40	15	123	138
NIRC MN	432	188	57	17	170	187
Total MN	713	291	97	32	293	325

2018 Year (average colony size)	Colony size	Juvenile replacements	Offspring < 1 yr	Breeding males	Breeding females	Adult breeding animals	Colony production
	A	B	C	D	E	F	G
ABC MN	278	102	45	12	119	131	43
NIRC MN	500	188	74	30	208	238	73
Total MN	777	290	119	42	327	369	116

2017 Year	Colony size	Juvenile replacements	Offspring < 1 yr	Breeding males	Breeding females	Adult breeding animals	Colony production
	A	B	C	D	E	F	G
ABC MN	350	125	80	8	137	145	66
NIRC MN	576	200	82	62	232	294	85
Total MN	925.75	324.75	162	69.5	369.5	439	151

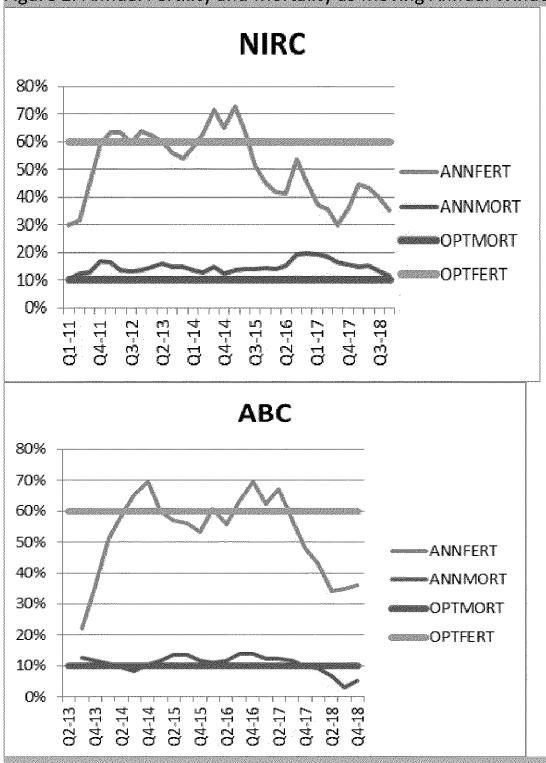
The following graphs compare the two facilities. Fertility tends to appear higher during the winter at NIRC because many animals are only in breeding situations when they are outdoors in the summer. Calculations are adjusted in the table below the graphs to account for animals not in breeding situations. At ABC, fertility has been decreasing. This is due to some animals not being in breeding situations, and some older infants remaining on dams, which reduces fertility. Mortality/culling is within acceptable limits.

Figure 1: Quarterly Fertility and Mortality on an Annualized Basis (data for the quarter multiplied by 4)



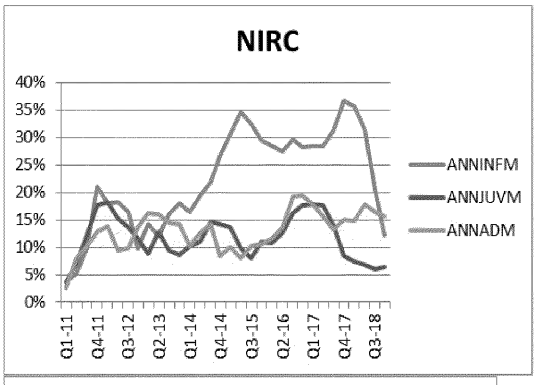
Legend: Blue = Fertility, Red = Mortality. Straight lines are standards to meet.

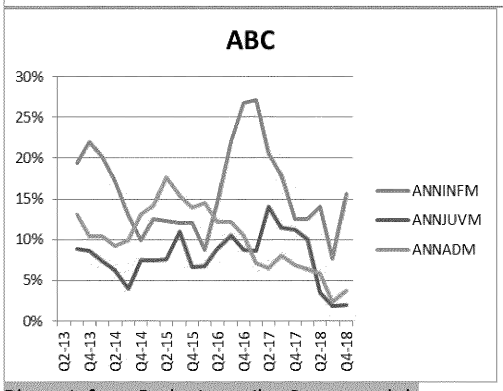
Figure 2: Annual Fertility and Mortality as Moving Annual Window (data from the preceding 12 months)



Legend: Blue = Fertility, Red = Mortality. Straight lines are standards to meet.

Figure 3: Annual Mortality as Moving Annual Window, By Age (Data from the preceding 12 months)



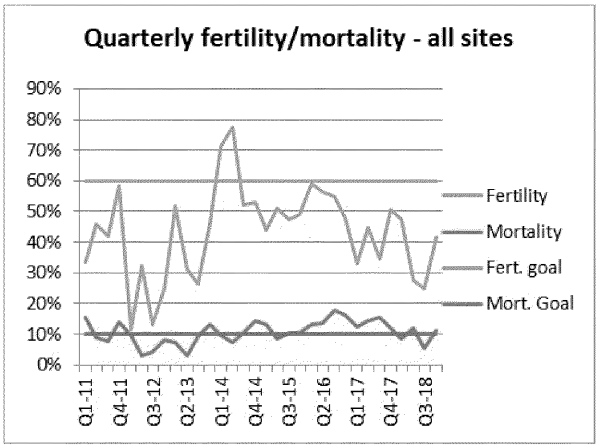


Blue = infant, Red = juvenile, Green = adult

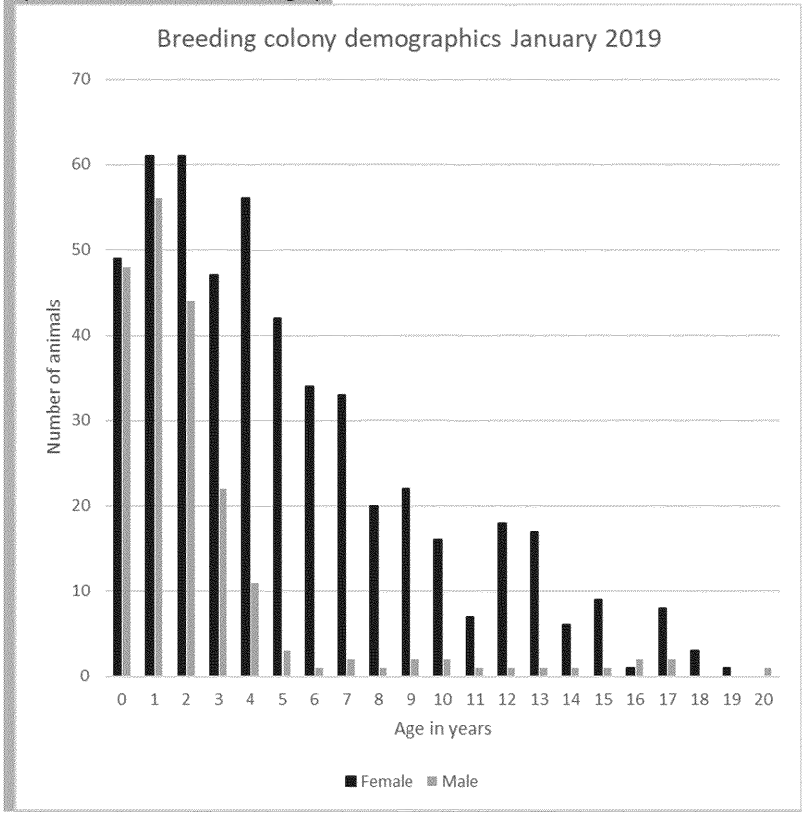
Looking at the off-site colonies combined, fertility has varied over the past few years, but was higher in 2015 and 2016 than in 2011-2013. Mortality had increased recently, but has now decreased dramatically at both facilities. Fertility has been low when all adult females are included in the equation, but good when only females in breeding situations at the beginning of the quarter are counted.

Year	Fertility (%)	Fertility (%) – active breeders only	Mortality (%)
2011	45		12
2012	21		7
2013	39		8
2014	64		10
Average '11-'14	40		9.25
2015	48		11
2016	55		15

2017	41		14
2018 q1	48		9
2018 q2	29	56	13
2018 q3	24	52	5
2018 q4	41	76	11



The age spread in the breeding colony shows few older animals, and a good number of replacement breeders coming up.



From: Charlotte E. Hotchkiss
Sent: Friday, December 20, 2019 9:33 AM
To: Jim Murphy
Subject: NSAB
Attachments: NSAB Jan 2020 Breeding and VS.docx

I've been working on the NSAB update, and in the past we had a section for Arizona in the Breeding Colony section. (I don't know if it really makes sense to have a separate Arizona section if we're trying to show that we're integrated, but that's the way it's been in the past.) Do you want to provide updates here? I know some of the stuff, but probably not everything.

Thanks!
Charlotte

Breeding Management

Accomplishments

- Both Arizona and NIRC completely SPF
- New building in Arizona completed and occupied
- Full integration of Arizona with Seattle personnel
- BCMC/BMC joint meeting successfully hosted in Arizona
- New U42 proposal submitted and scored
- Good fertility for actively breeding animals
- Low mortality in breeding colony
- 92 SNP panel based on GBS data validated and being used for parentage confirmation

Breeding production challenges

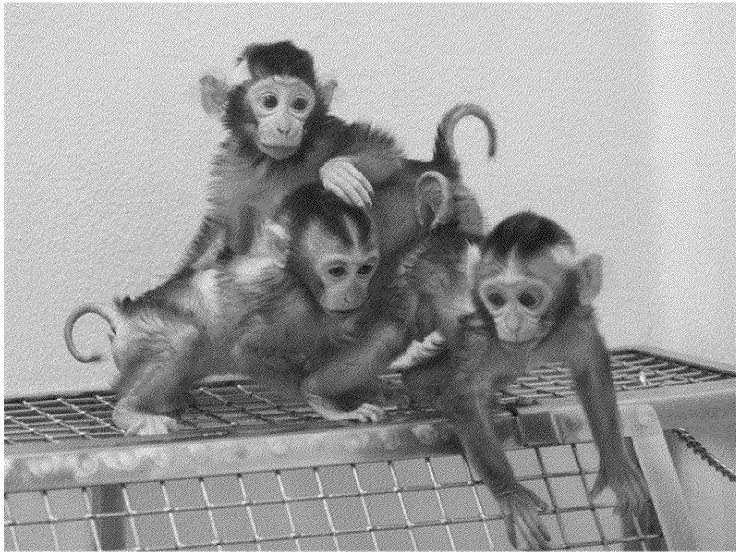
- Animals not in breeding due to moves and sales
- Increased demand for females
- Selecting males for genetics, behavior, clinical health, and productivity
- Limited options for breeding style in Arizona
  - Cage breeding is an option in Seattle for animals that don't do well in compounds
  - Shipping animals to Seattle only cost-effective in large groups

Goals – moving out of NIRC

- 227 animals moved to new building in Arizona
- 151 animals not moved
- Requests for 122 animals in process (not all confirmed)
- Installing pens in 6th floor G/H wing of HSB
  - Must be completed by April 2020
  - Plan to ship animals from NIRC to Seattle in spring

Whatever happened to eSPF colony?

- Survey of investigators who work with *M. nemestrina*
  - No specific demand for eSPF
- Requests for other characteristics
  - MHC typing
  - Behavioral characteristics
  - AAV serotype negative
  - MRSA, Chagas, flavivrus



From: Charlotte E. Hotchkiss
Sent: Thursday, June 20, 2019 11:49 AM
To: Bob Murnane (rmurnane@uw.edu)
Subject: powerpoint
Attachments: VGR Neuro cocci.pptx

Charlotte E. Hotchkiss, DVM, MS, PhD, DACLAM
Washington National Primate Research Center
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Box 357330
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Pager: 206-540-6615
chotchki@uw.edu
Work hours 8-5 M-F

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Tess House <th81@uw.edu>
Sent: Tuesday, October 29, 2019 2:23 PM
To: Kathryn A. Guerriero; Robert D. Murnane; wanprc_vets@uw.edu
Subject: Re: [Wanprc_vets] Z17170
Attachments: ATT00001.txt

A huge sigh of relief for us that it's VF and not TB-thank you Bob!!!

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Kathryn A. Guerriero
Sent: Tuesday, October 29, 2019 2:19 PM
To: Robert D. Murnane <rmurnane@uw.edu>; wanprc_vets@uw.edu
Subject: Re: [Wanprc_vets] Z17170

Glad that this was just valley fever (and not TB).

Kate

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Robert D. Murnane
Sent: Tuesday, October 29, 2019 2:14 PM
To: wanprc_vets@uw.edu
Subject: [Wanprc_vets] Z17170

Hi all (especially ABC vets!)

Disseminated valley fever EVERYWHERE:

Hilar nodes, lungs, rib, bone above eye, sternum, liver, kidneys, lungs, multiple abscesses….

Final report to follow soon.
Cheers
Bob

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Kathryn A. Guerriero <kag18@uw.edu>
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From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Robert D. Murnane <rmurnane@uw.edu>
Sent: Tuesday, October 29, 2019 2:32 PM
To: Tess House; Kathryn A. Guerriero; wanprc_vets@uw.edu; cmali
Subject: Re: [Wanprc_vets] Z17170
Attachments: ATT00001.txt

For sure a sigh of relief!!

Oh, it also had secondary amyloidosis and IBD…

Case report would work for sure, but what would be better is for someone/anyone to write up the case series to date!! Pretty easy to do and you could focus on just gross and histo of the cases we've had

Cheers
Bob

From: Tess House <th81@uw.edu>
Sent: Tuesday, October 29, 2019 2:23 PM
To: Kathryn A. Guerriero <kag18@uw.edu>; Robert D. Murnane <rmurnane@uw.edu>; wanprc_vets@uw.edu
Subject: RE: Z17170

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Subject: [Wanprc_vets] Z17170

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Final report to follow soon.
Cheers
Bob

From: Charlotte E. Hotchkiss
Sent: Tuesday, December 24, 2019 10:48 AM
To: Tess House; aw656
Subject: RE: Infant fluconazole and Serum fluconazole projects
Attachments: Fluconazole statistics.docx

I did try to run statistics on the infant data. Unfortunately, I got different results depending on how I set up the statistical model. Most of it I understand, but there are a few places I got really weird results and I don't know why. I've attached my summary.

Charlotte

From: Tess House <th81@uw.edu>
Sent: Wednesday, December 18, 2019 2:36 PM
To: aw656 <aw656@uw.edu>
Cc: cmali <cmali@uw.edu>; Charlotte E. Hotchkiss <chotchki@uw.edu>; Sally Thompson-Iritani <sti2@uw.edu>
Subject: Infant fluconazole and Serum fluconazole projects

Hi Amber,

The two VF related projects can be found below:

1) Infants exposed to fluconazole during pregnancy (comparison of body weights project that Adam and Rose also contributed a great deal on with respect to initial data organizing)

Z:\Arizona\Vet Services\Miscellaneous\Infant weight and fluconazole exposure

2) Serum fluconazole levels in animals on the fluconazole impregnated feed. There was a group of juveniles/young adults in 171 (at the time) on the feed that we looked at first and then later we looked at the 242 group (now the animals in 232) and compared them to other adults on fluconazole tablets. This project included the negotiation by John Hasenau to include Cyndi Holland of Protatek and Nathan Weiderhold from UT San Antonio Fungal Lab on as co-authors. The intention was for Rose and I to work on project 1 first and then tackle this project next.

Z:\Arizona\Vet Services\Miscellaneous\Serum Fluconazole Level Testing

Last contact information for Drs. Holland and Weiderhold are:

Cyndi Holland: cholland@pharmgate.com, phone is 480-545-8499, fax 480-545-8409 (note that even though these are Az numbers, she's based in Minneapolis/St. Paul)

Nathan Weiderhold: wiederholdn@uthscsa.edu, phone is 210-567-4086, fax 210-614-4250

I'm leaving John Hasenau's business card on your desk for you this afternoon. Let me know if you think of anything else. I'll try to hunt down the MoU for Drs. Holland and Weiderhold so you have that as well (finance should have it too).

Tess

Theresa (Tess) House, DVM MPH
Supervisory Veterinarian
Washington National Primate Research Center
Arizona Breeding Colony
Office phone 206.685.1842
Mailing address- P.O. Box 20836/Mesa, AZ 85277

From: Bridget Marie Barker <Bridget.Barker@nau.edu>
Sent: Thursday, November 21, 2019 8:15 AM
To: Charlotte E. Hotchkiss; Tess House; cmali
Subject: Re: Introductions
Attachments: PA-19-082 Novel approaches to understand, prevent, treat, and diagnose coccidioidomycosis (Valley F.pdf

Categories: Grants

Hi All!

While we don't know for sure what MHC alleles might be associated with asymptomatic vs. severe infection, I think these data might represent an opportunity to do this analysis and get out a nice paper.

I am currently putting an R01 together to investigate host genetic factors associated with differential disease. We propose to use naturally infected canines to address this, but I wonder if adding in the primate data might really give us a closer link to translation in humans. My other main interest is finding the organism in soil and air, and we are working on that part of the project already. Dan and I will complete our training and hope to get back out for a visit in January.

I understand that the animals are on a breeding protocol and not experimental, so we'd have to address that aspect if we wanted to draw blood for genotyping? I could envision a subcontract to UW for you to hold samples and do DNA extractions, and we could handle sequencing and analysis? The benefit I foresee for the colony is that we could define risk factors that might help understand which animals would be at higher risk for severe disease so they could be prioritized for removal to a safer location.

I did not discuss other ideas much, because they are projects with other PIs as lead, but they involve vaccine work and understanding correlates of protection. I am not sure where approval is for the current vaccine, but I believe the UA valley fever center (John Galgiani) is pursuing USDA license for use in veterinary setting (dogs mainly) so perhaps this would be helpful for your animals too? The rest of the group at NAU is interested in defining correlates of protection, so this could also be beneficial for your colony, especially if vaccination is considered.

I'm attaching the PA for NIH that is focused on Coccidioides research. I would also like to invite you to attend the annual Coccidioidomycosis Study Group meeting in Tucson, April 3-4.
http://coccistudygroup.com

Best,

Bridget

From: "Charlotte E. Hotchkiss" <chotchki@uw.edu>
Date: Tuesday, November 19, 2019 at 8:53 AM
To: Tess House <th81@uw.edu>, Bridget Marie Barker <Bridget.Barker@nau.edu>, cmali <cmali@uw.edu>
Subject: RE: Introductions

Hi!
It's good to virtually meet you! I would love it if you could learn things that would help us keep our animals healthy.

I do have MHC data on some of the animals (and expect to get more in the future) and am interested in looking for associations, but unfortunately it never seems to get to the top of my priority list. But I am ever hopeful.

Charlotte

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chotchki@uw.edu
Work hours 8-5 M-F

From: Tess House <th81@uw.edu>
Sent: Monday, November 18, 2019 1:48 PM
To: Bridget Marie Barker <Bridget.Barker@nau.edu>; cmali <cmali@uw.edu>; Charlotte E. Hotchkiss <chotchki@uw.edu>
Subject: Introductions

Hi everyone-

I just wanted to make virtual introductions after Bridget toured the Arizona site today. Bridget is an assistant professor and associate director of the ABSL3 at NAU in Flagstaff, Az and studies valley fever. Charlotte is our head veterinarian in Seattle and oversees the breeding and genetics of the colony.

Charlotte-I met Bridget at the Cocci Study Group meeting in California this year and set her up with Melinda for occ health clearance (which she has for a year) for a tour here. Bridget and her graduate student are interested in potential collaborations with us and the possibility of taking soil samples and trapping rodents at ABC to further characterize cocci here. She is also interested in the MHC typing and evaluating if there is a genetic susceptibility component in the colony. I have already provided Bridget

with the contact I have through Gail with the Community so she can reach out to them regarding how to obtain permissions for soil samples and trapping.

Bridget-thank you so much for visiting us today! We hope you enjoyed the visit as much as we did.

Tess and Carolyn

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Mailing address- P.O. Box 20836/Mesa, AZ 85277

From: Charlotte E. Hotchkiss
Sent: Tuesday, November 26, 2019 10:21 AM
To: Bridget Marie Barker; Tess House; cmali
Subject: RE: Introductions
Attachments: App13 SemlerIG18combined.pdf; Oleary pigtail 2009.pdf

With regard to genotyping, we do some genotyping as part of our colony characterization; I'm not sure if it's similar to what you're doing in dogs. We do genotyping for parentage – in the past we did microsatellite (STR) analysis of 20-some loci across the genome to verify parentage, but now we're in the process of switching to SNP analysis. We collaborate with a group in Oregon, and they're supposed to be running the first batch of samples on our brand new 96 locus SNP chip even as we speak. But that wouldn't help with figuring out factors related to infection.

We also do testing for MHC expressed alleles. We send blood samples with an RNA preservative to our Oregon collaborator who then makes cDNA and comes up with lots of complicated data about alleles, lineages, and haplotypes. I can't explain it very well, so I'm attaching articles about it. Is that the sort of MHC genotyping you're interested in? We have results on some animals, and are working towards getting MHC on all the animals. Of course, we'd love additional support to complete the process….

We would definitely be interested in a vaccine. I know there was some work done with a vaccine a few years back, but it didn't work.

Glad we've opened up communication – hope we can work together going forward!

Charlotte

From: Bridget Marie Barker <Bridget.Barker@nau.edu>
Sent: Thursday, November 21, 2019 8:15 AM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>; Tess House <th81@uw.edu>; cmali <cmali@uw.edu>
Subject: Re: Introductions

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Subject: RE: Introductions

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Mailing address- P.O. Box 20836/Mesa, AZ 85277

From: Charlotte E. Hotchkiss
Sent: Friday, December 20, 2019 11:52 AM
To: cmali; Sally Thompson-Iritani
Subject: RE: NSAB for AZ
Attachments: NSAB2020 - Breeding Management.pptx; NSAB Jan 2020 Breeding and VS.docx

We have both a Word document to give the NSAB people ahead of time as well as a Powerpoint to show when they're here. They say essentially the same thing. We won't have much time at NSAB, so I haven't been putting in much detail, but we should mention VF in both.

In contrast, we'll have to do the progress report (RPPR) in January, and there we will want more detail. We will definitely want to refer there to the information that Tess sent yesterday about how this year has been particularly bad for VF to put our numbers in context. But I haven't thought that far ahead yet.

Thanks,
Charlotte

From: cmali <cmali@uw.edu>
Sent: Friday, December 20, 2019 10:45 AM
To: Sally Thompson-Iritani <sti2@uw.edu>; Charlotte E. Hotchkiss <chotchki@uw.edu>
Cc: Jim Murphy <murphyjm@uw.edu>
Subject: NSAB for AZ

Hi Sally and Charlotte,

Tess mentioned that you want an update on VF cases for AZ for the NSAB as well as updates on the new building.

Would you like this in powerpoint form or does it need ot be written up ahead of time (similar to what Charlotte sent Him and I for NSAB updates)?

Please let me know what you expect/want and I will get it done!

Best,
Carolyn

Carolyn Malinowski, MS, DVM, CMAR, CPIA, DACLAM
Supervisory Veterinarian
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Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

DARE 2 CARE

UNIVERSITY *of* WASHINGTON

Compassion in Science

http://sites.uw.edu/d2c

From: cmali <cmali@uw.edu>
Sent: Friday, December 20, 2019 9:55 AM
To: Charlotte E. Hotchkiss; Jim Murphy
Subject: Re: NSAB
Attachments: NSAB Jan 2020 Breeding and VS CMM Edits.docx

Here you go Charlotte- see edits for AZ vet section in attached document

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DARE 2 CARE
UNIVERSITY *of* WASHINGTON
Compassion in Science
http://sites.uw.edu/d2c

From: Charlotte E. Hotchkiss <chotchki@uw.edu>
Sent: Friday, December 20, 2019 10:32 AM
To: Jim Murphy <murphyjm@uw.edu>
Cc: cmali <cmali@uw.edu>
Subject: NSAB

I've been working on the NSAB update, and in the past we had a section for Arizona in the Breeding Colony section. (I don't know if it really makes sense to have a separate Arizona section if we're trying to show that we're integrated, but that's the way it's been in the past.) Do you want to provide updates here? I know some of the stuff, but probably not everything.

Thanks!
Charlotte

From: cmali <cmali@uw.edu>
Sent: Wednesday, February 27, 2019 1:30 PM
To: Britni C. Curtis; Charlotte E. Hotchkiss; Sally Thompson-Iritani; backward_vets
Subject: Re: Vet meeting today
Attachments: 27022019-101145_STIFLE.jpg; 27022019-101433_STIFLE.jpg; 27022019-101526_STIFLE.jpg

Hi All,

this is Z17139, the kid who turned up lame that we did an arthrocentesis on....

We're thinking osteomyeltitis likely due to valley fever...

Would like to discuss...

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Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Britni C. Curtis <britcurt@uw.edu>
Sent: Wednesday, February 27, 2019 1:46 PM
To: Charlotte E. Hotchkiss; Sally Thompson-Iritani; backward_vets
Subject: Re: [Wanprc_vets] Vet meeting today

Hi,
I am closing the apheresis, so I will attend what I can, but it is likely that I will need to leave. Here is the agenda (attached). Most of the items for follow up are in red. Can someone please take notes, if I don't make it?
Thank you,

Britni

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Charlotte E. Hotchkiss
Sent: Wednesday, February 27, 2019 12:38 PM
To: Sally Thompson-Iritani <sti2@uw.edu>; backward_vets <wanprc_vets@uw.edu>
Subject: Re: [Wanprc_vets] Vet meeting today

I'm probably going to be late – I have a New Model Development Working Group conference call at 1:00, and expect it will go until 2:00.
Charlotte

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Sally Thompson-Iritani
Sent: Wednesday, February 27, 2019 12:36 PM
To: backward_vets <wanprc_vets@uw.edu>
Subject: [Wanprc_vets] Vet meeting today

I won't be able to call in.

Shout out to Dean for doing a nice job at the D2C meeting. He was very informative and helpful.

Also - some people need to update holiday hours in workday - if you need help let me know.

Thank you ~

Sally Thompson-Iritani, DVM/PhD, CPIA
~ *Certified Compassion Fatigue and Human-Animal Bond Practitioner* ~
Director, AWRS, WaNPRC; 206.661.6294
University of Washington,Seattle,WA
All typos courtesy of iPhone autocorrect

From: Charlotte E. Hotchkiss
Sent: Thursday, May 9, 2019 8:33 AM
To: Kelly Heffernan
Subject: RE: WaNPRC Records Review
Attachments: WaNPRC Records Review Notes- 04-29-19.docx

I put in the whole write up for the Murry animal because it was easier than trying to summarize it. But feel free to shorten it.
Charlotte

From: Kelly Heffernan <ksh@uw.edu>
Sent: Wednesday, May 8, 2019 1:36 PM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>
Subject: WaNPRC Records Review

Hi Charlotte,

Sorry for the additional email, but I need clarification on the highlighted items in the document. My notes are a little incomplete and/or confusing to me now.

Appreciate your help.
Kelly

KELLY HEFFERNAN
Reviewer and Scientific Liaison
Office of Animal Welfare

Health Sciences Building Box 357160
1705 NE Pacific Street Seattle, WA 98195-7160
206.616.3625 / fax 206.616.5664
ksh@uw.edu / oaw.washington.edu

From: Tess House <th81@uw.edu>
Sent: Thursday, June 13, 2019 9:03 AM
To: Charlotte E. Hotchkiss; cmali
Subject: RE: Z14141
Attachments: VF BCMC.pptx

Categories: Task listed

Hi Charlotte,

Here's the PP from the presentation I gave in January for the BCMC meeting. It includes Bob and Audrey's data on the necropsies from AZ over the years.

Anything else you need, let me know! A GI bug hit my daughter so I'm home today while Adam studies for his COMLEX exam on Monday but I'm checking emails when she's distracted with toys.

Tess

From: Charlotte E. Hotchkiss <chotchki@uw.edu>
Sent: Thursday, June 13, 2019 7:58 AM
To: cmali <cmali@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: RE: Z14141

Thanks!

Do you by any chance have:
Any data on the cocci vaccine study that Lee and Jeremy did?
Any old presentations by Lee or Cathy on Valley Fever? (Tess – did you do one? I have a memory of one, but I don't think you did it for a working group so I'm not sure what I'm remembering.) Lee did one in January 2016 – I hope that's long enough ago to get away with.

I promise to give credit where it is due, but I don't have time to reinvent the wheel.

Thanks!
Charlotte

From: cmali <cmali@uw.edu>
Sent: Wednesday, June 12, 2019 1:55 PM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: Z14141

Hi Charlotte,

Please see the path report for Z14141 (attached).

Tess wrote a VERY thorough case history.

Bob may be able to provide you with some histo pics...

Let us know what we can help with!

Best,
Carolyn

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
Washington National Primate Research Center/University of Washington
Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Thursday, May 9, 2019 12:19 PM
To: Audrey Baldessari; Keith Vogel; Charlotte E. Hotchkiss; Kathryn A. Guerriero; Dean Jeffery; Jason D. Laramore; Tess House; cmali
Subject: 19-041 and 042 (Z19068 and Z14141)

Hi all:

Please find attached final reports on the above 2 cases. Interestingly, Z14141 was cerebral Valley Fever, and both animals were from the same dam who also was diagnosed clinically with Valley Fever.

Please contact me with any questions, comments or concerns.

Cheers
Bob

From: cmali <cmali@uw.edu>
Sent: Thursday, June 13, 2019 8:07 AM
To: Charlotte E. Hotchkiss
Subject: Re: Z14141
Attachments: Valley Fever ABC Intro presentation.pptx

Categories: Task listed

I do have some data from the VX study but I don't think you want to report it... We can talk offline about that...

I've attached the powerpoint that Tess made for our new husbandry staff about VF.

Tess did give a presentation at the BCMC in January on VF but I'm not sure where she has it saved- she's out sick today and can send it along tomorrow.

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
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PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Charlotte E. Hotchkiss <chotchki@uw.edu>
Sent: Thursday, June 13, 2019 7:58 AM
To: cmali
Cc: Tess House
Subject: RE: Z14141

Thanks!

Do you by any chance have:
Any data on the cocci vaccine study that Lee and Jeremy did?

Any old presentations by Lee or Cathy on Valley Fever? (Tess – did you do one? I have a memory of one, but I don't think you did it for a working group so I'm not sure what I'm remembering.) Lee did one in January 2016 – I hope that's long enough ago to get away with.

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Charlotte

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Sent: Wednesday, June 12, 2019 1:55 PM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: Z14141

Hi Charlotte,

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Tess wrote a VERY thorough case history.

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Subject: 19-041 and 042 (Z19068 and Z14141)

Hi all:

Please find attached final reports on the above 2 cases. Interestingly, Z14141 was cerebral Valley Fever, and both animals were from the same dam who also was diagnosed clinically with Valley Fever.

Please contact me with any questions, comments or concerns.

Cheers
Bob

From: Kelly Heffernan <ksh@uw.edu>
Sent: Tuesday, March 12, 2019 10:33 AM
To: Charlotte E. Hotchkiss
Subject: Surgical facility info
Attachments: Appendix XX Surgical Facilities_03-12-19.DOCX

Hi Charlotte,

Can you (or a designee) update the surgery equipment information for WaNPRC spaces in the attached document? For the ARCF, I've filled in the DCM information, so please add any additional WaNPRC info.

Thank you!
Kelly

KELLY HEFFERNAN
Reviewer and Scientific Liaison
Office of Animal Welfare

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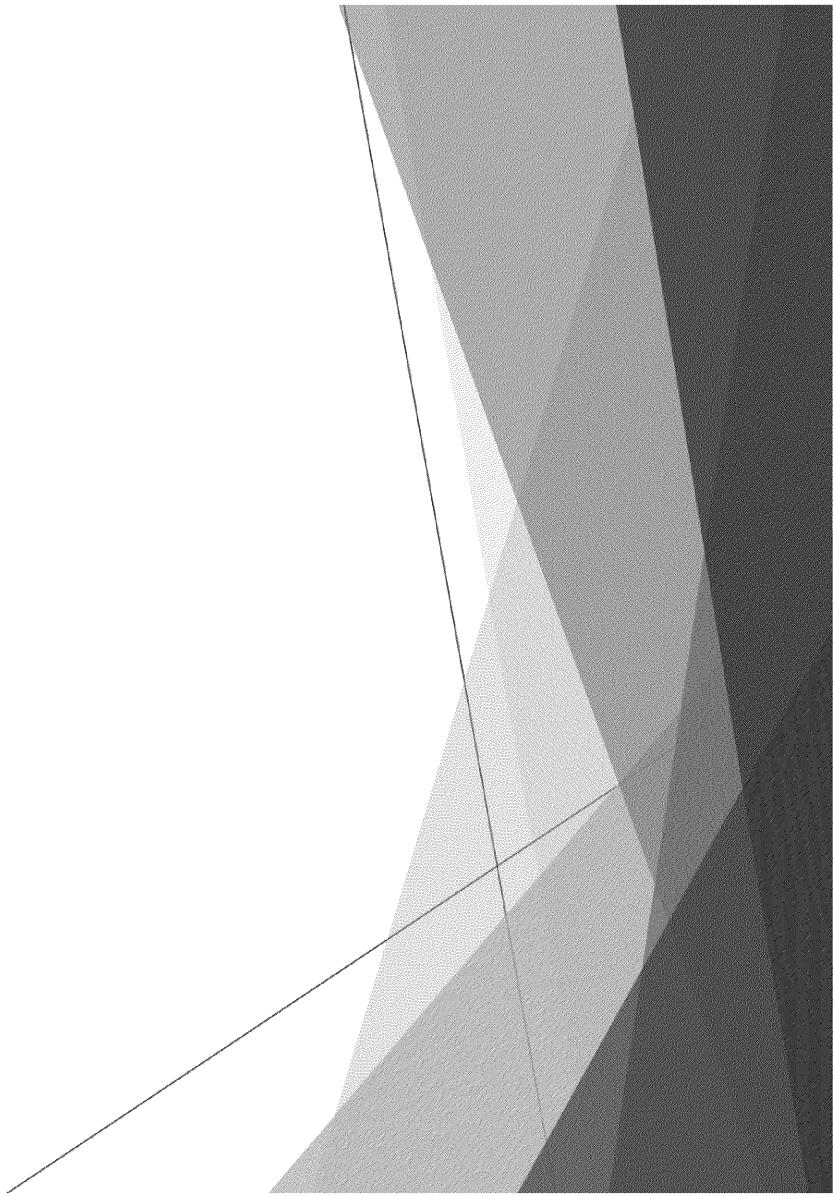
1705 NE Pacific Street Seattle, WA 98195-7160
206.616.3625
ksh@uw.edu / oaw.washington.edu

Valley Fever

An introduction

What material will we cover?

- What causes valley fever
- Sources of infection
- Symptoms of valley fever
- Diagnosis and testing
- Treatment
- Risk and prevention
- Additional resources



What causes valley fever?

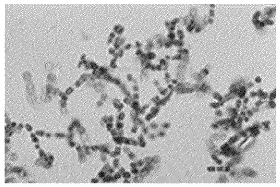


Image from CDC

- Valley fever is a fungal infection caused by spores of the genus Coccidioides.
- These spores are found in the soil in the Southwestern United States, Mexico, and throughout portions of Central and South America.
- More recently, the spores have been found in soil samples in southeastern Washington and cases of valley fever have been discovered in humans and animals in this area.
- Valley fever is sometimes called “San Joaquin Valley fever” or “desert rheumatism.”

Sources of infection

- The majority of cases are from inhalation of spores.
- Spores can be found in higher levels when dust storms or monsoons occur, during wildfires in endemic areas, and after earthquakes.
- Less commonly, infection can occur through a wound that is exposed to dirt or dust containing valley fever spores, receiving an organ from a donor that had valley fever, and inhaling spores from an infected wound.
- Many people (60%) are exposed but don't become ill.

(Chiller et al, 2003)

- Not contagious like the flu or a cold.

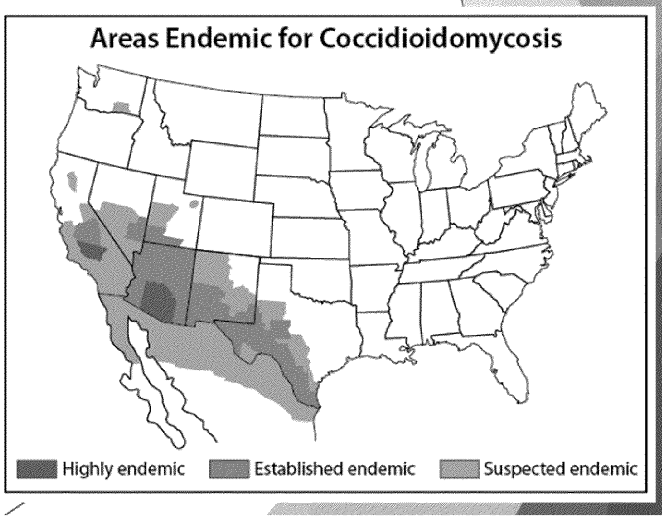


Image from CDC

Symptoms of valley fever

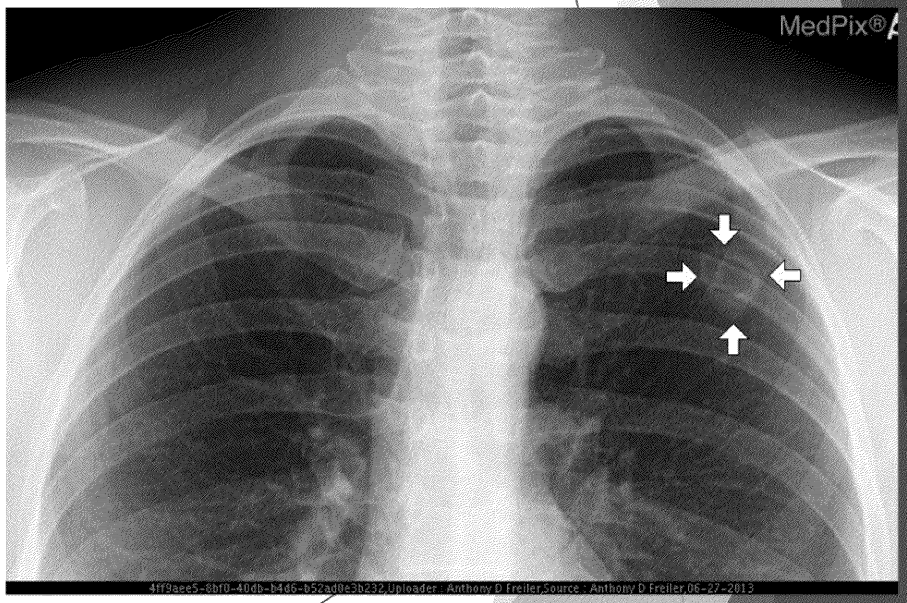
- Typically appear between 1 to 3 weeks after exposed.
- FATIGUE
- Cough
- Fever
- Shortness of breath
- Headache
- Night sweats
- Myalgia and/or joint pain
- Rash on upper body or legs

Symptoms, continued

- Symptoms usually last for a few weeks but can be up to several months or longer.
- A small portion (5-10%) will have long-term problems, typically in the lungs.
- Another portion of those exposed (about 1%) will have infection spread to other parts of the body. The skin, bone, joints, and central nervous system (CNS) can be affected.

Diagnosis and Testing

- Most common testing method is submitting a blood (serum) sample that looks for antibodies to valley fever
- Imaging (CT, x-rays) may also be performed
- Biopsy of nodules (found on imaging or skin lesions)
- Culture from body fluids or tissues
- Skin test
  - Commonly done leading up to the late 1990's
  - Became available in 2014



Treatment

- Antifungal medication
  - Fluconazole, amphotericin B most common for disseminated form
- No OTC medications

Risk and Prevention

- Anyone living in an endemic area is at risk
- Occupational exposure increased for:
  - Agricultural work
  - Construction work
  - Archeological dig sites
  - Military personnel/trainees
  - Wildland firefighters
  - Mining/gas/oil extraction
  - Prison employees and prisoners

https://inhabitat.com/firefighters-say-drones-are-getting-in-the-way-of-battling-californias-wildfires/

Risk and Prevention, continued

- Certain populations are at greater risk for developing disseminated form
  - People of Asian (esp. Filipino) or African American descent
  - Pregnant women during their third trimester
  - Immunocompromised persons
  - Comorbidities (ex: diabetes)

- Prevention
  - Avoid being outdoors during dust storms/monsoons and keep windows closed.
  - Use dust mitigation when possible (construction, archeology, gardening).
  - Clean air filters in your home on a regular basis.
  - Clean skin injuries exposed to dirt with soap and water.

Additional Resources

- CDC website https://www.cdc.gov/fungal/diseases/coccidioidomycosis/index.html
- Mayo Clinic https://www.mayoclinic.org/diseases-conditions/valley-fever/symptoms-causes/syc-20378761
- Valley Fever Center for Excellence (U of A, College of Medicine Tucson) https://vfce.arizona.edu/
- 2016 IDSA Clinical Practice Guideline for the Treatment of Coccidioidomycosis https://academic.oup.com/cid/article/63/6/e112/2389093

Questions?

Valley Fever updated list (12/24/19)

Current census 483 animals. 44 (9%) are on fluconazole treatment and 33 (7%) have cocci titer positive status.

Animals on treatment and titer negative:

- A12264
- Z17135
- Z16005
- L03132
- Z12342
- Z14027
- A12262
- A12269
- Z11338
- F08132
- R10156

Animals on treatment and titer positive:

- Z19006
- Z16358
- Z16342
- Z13067
- Z13292
- Z17142
- Z17150
- Z17161
- Z16053
- Z16203
- Z16283
- Z16341
- A10229
- L01151
- L09006
- Z14331
- K06271
- K10112
- Z13082
- L06156
- L10152
- R11037
- Z14130
- R10113

- S10114
- K07291
- K11143
- L02276
- L05311
- M11051
- R09036
- K06192
- Z12028

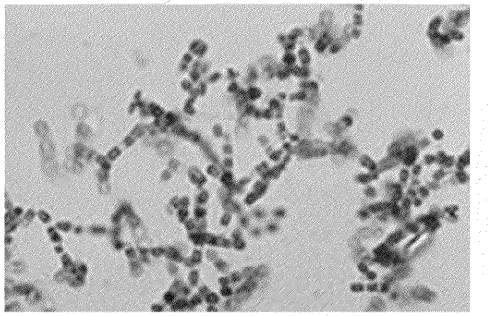
Cases in red were newly diagnosed Fall 2019

Coccidioidomycosis

Tess House

Coccidioidomycosis

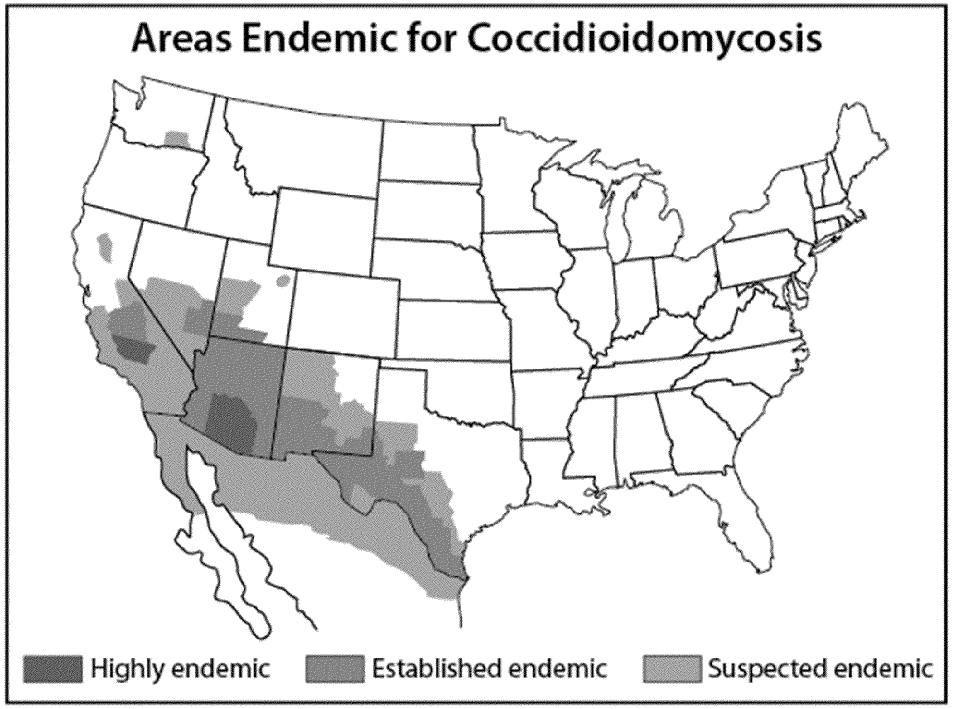
- Fungal infection caused by the genus Coccidioides
  - C. immitis
  - C. posadasii



CDC image

  - More commonly known as Valley Fever or Cocci
  - Able to infect humans and a wide range of animal species
    - NHP species with cases reported include baboons, capuchins, chimpanzees, geladas, guenons, gorillas, lemurs, mandrills, macaques, mangabeys, spider monkeys, squirrel monkeys, woolly monkeys

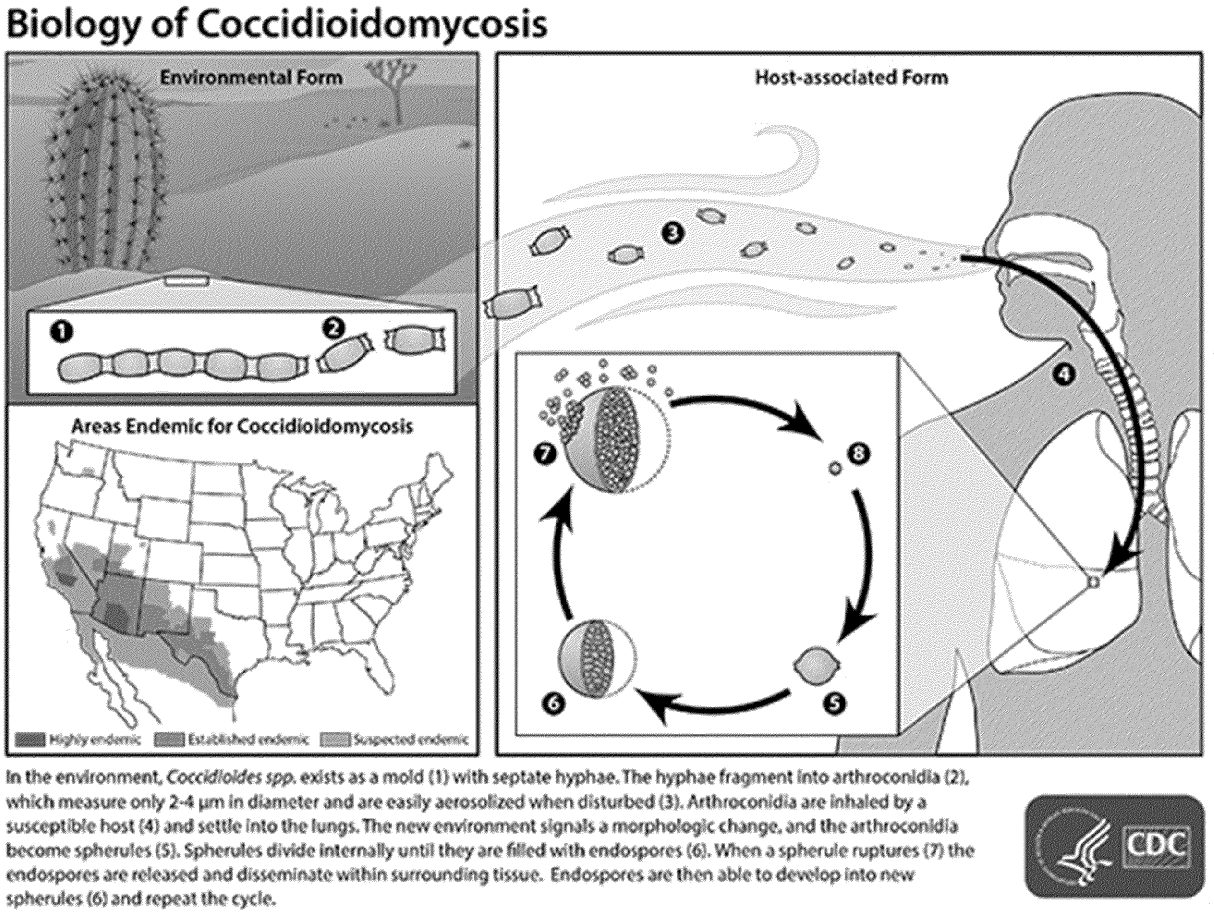
Endemic regions



www.cdc.gov/fungal/diseases/coccidioidomycosis/causes.html

- Found in portions of North, South, and Central America
- Highly endemic regions found in Arizona and California
- Newer region found in Washington state

Life cycle


Biology of Coccidioidomycosis
Environmental Form
Host-associated Form
Areas Endemic for Coccidioidomycosis
Highly endemic
Established endemic
Suspected endemic
1
2
3
4
5
6
7
8
In the environment, *Coccidioides spp.* exists as a mold (1) with septate hyphae. The hyphae fragment into arthroconidia (2), which measure only 2-4 µm in diameter and are easily aerosolized when disturbed (3). Arthroconidia are inhaled by a susceptible host (4) and settle into the lungs. The new environment signals a morphologic change, and the arthroconidia become spherules (5). Spherules divide internally until they are filled with endospores (6). When a spherule ruptures (7) the endospores are released and disseminate within surrounding tissue. Endospores are then able to develop into new spherules (6) and repeat the cycle.
CDC

Routes of Infection

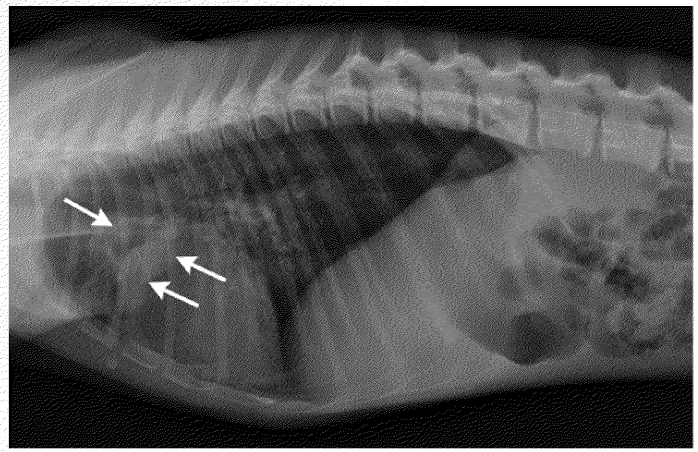
- Primary route of infection is inhalation
- Not contagious or zoonotic
- Less frequent routes of infection can include:
  - Break in the skin such as a cut, wound, or splinter
  - Aspiration of amniotic fluid during parturition
  - Organ transplantation
- Low infectious dose

Symptoms

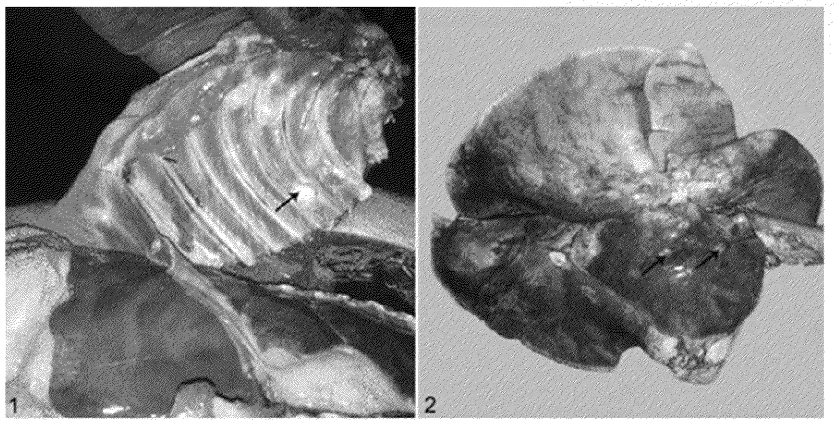
- Diverse clinical presentation (average 7-28 days after exposure)
- Clinical illness in NHP similar to humans
- Lethargy
- Coughing
- Shortness of breath
- Fever
- Inappetence and/or weight loss
- Joint pain or lameness
- Skin rash or nodules
- Neurological symptoms

Clinical and Pathological Findings

- Eosinophilia, mild lymphocytosis, monocytosis
- Hyperglobulinemia
- Radiographic changes
- Tan to white nodules particularly within lung tissue and thoracic wall



Kundu et al, 2017



Koistinen et al, 2018

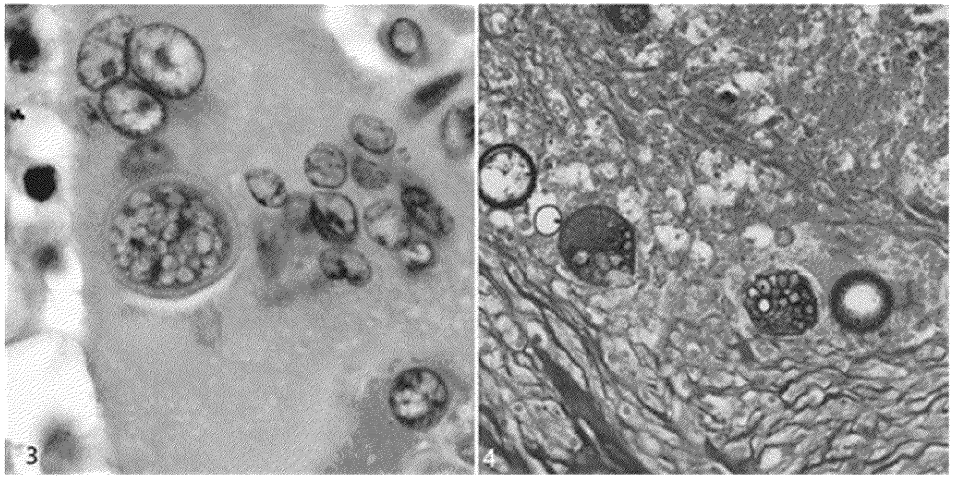
Necropsy Data from Arizona

Year	Cases	Gender	Location
2013	N=3	3 female	2 pulmonary, 1 disseminated
2014	N=18	17 female, 1 male	2 pulmonary, 16 disseminated
2015	N=13	12 female, 1 male	3 pulmonary, 10 disseminated
2016	N=8	7 female, 1 male	4 pulmonary, 4 disseminated
2017	N=2	2 female	1 pulmonary, 1 disseminated
2018	N=1	1 female	1 disseminated

Pathogen Detection

- Direct detection
  - Microscopy
  - Molecular detection
- Culture (safety concerns)
- Serology (EIA, IMDF, CF)

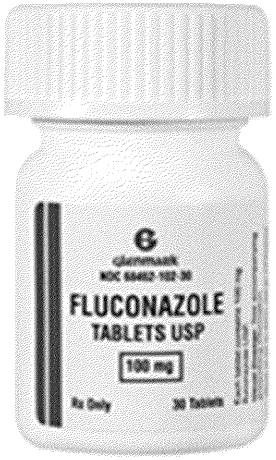
Hematoxylin and eosin (left), Periodic acid-Schiff



Koistinen et al, 2018

Treatment

- Triazoles or Amphotericin B
  - Fluconazole, Itraconazole, Voriconazole, Posaconazole
  - Fluconazole most frequently used
    - Tablet, liquid, fluconazole impregnated feed
    - Currently 18% of the colony at Arizona is on Fluconzaole
      - 20 of 52 animals (6.9% of colony) cocci negative
      - 32 animals (11.1% colony) are cocci positive



Prevention and Surveillance

- Dust mitigation/limiting exposure
  - Future growth to focus on indoor only animal enclosures with HEPA filtration
  - Construction site using dust mitigation practices
  - Minimizing animal exposure time outdoors when high wind/dust storms expected
  - Spray down of enclosures before having access to outdoor portion
- Routine serological surveillance captured at semi-annuals
  - Twice a year (+) clinical indication or suspicion (weight loss, coughing)

Vaccination

- No commercial vaccine available
- A human vaccine trial was conducted in the 1980's but no difference was found in the number of cases of the severity of disease between vaccine and placebo groups
- Challenging in terms of antigen expression, cost of production
- Interest in Delta-CPS1
  - U of A created mutant strain that does not cause disease in mice strains including those with no lymphocytes and those with bone marrow suppression
    - Good survival statistics in those vaccinated
    - Working on replacing the antibiotic resistance marker with one that does not involve antibiotics

Acknowledgements

- Dr. Sally Thompson-Iritani
- Drs. Charlotte Hotchkiss, Keith Vogel, Kate Guerriero, Dean Jeffrey, Carolyn Malinowski, Bob Murnane, Audrey Baldessari
- Veterinary Services and Animal Husbandry Staff at Arizona Breeding Colony
- Drs. Paul Barrass, Lee Chichester, Cathy Carrier
- Dr. Nathan Weiderhold (UT Fungal Lab)
- Dr. John Hasenau (Lab Animal Consultants)
- Dr. Cynthia Holland (Protatek International, LLC)
- Dr. Lisa Shubitz (University of Arizona)
- Salt River Pima-Maricopa Indian Community
- BCMC and John Nylander

SEIZURES IN A PIGTAILED MACAQUE

Tess House, DVM, MPH
Carolyn Malinowski, DVM, RLATG, CMAR, CPIA
Charlotte Hotchkiss, DVM, MS, PhD, DACLAM

PRESENTATION

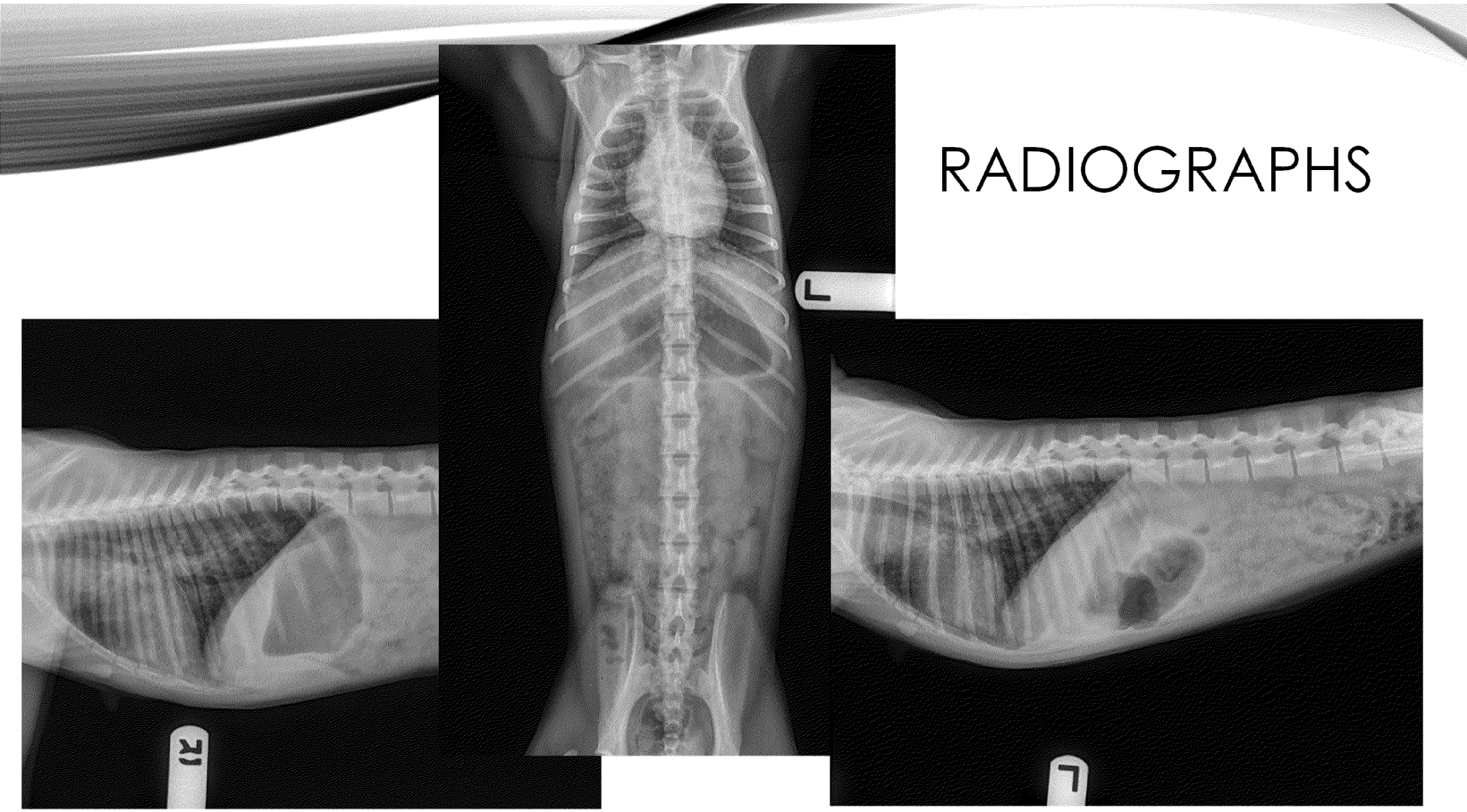
- 4-year old female *Macaca nemestrina*
- Assigned to SPF breeding colony
- Housed in indoor/outdoor compound in Arizona
- Coughing noted at time of routine semiannual exam

CBC/CHEMISTRY

WBC (Thou/ul)	**21.9**
RBC (mil/ul)	5.3
HGB (g/dl)	10.1
HCT (%)	36.5
MCV (fL)	68.7
MCH (pg)	19.0
MCHC (g/dL)	27.7
PLT (Thou/ul)	614
Neut (Thou/ul)	**13.6**
Lymph (Thou/ul)	6.1
Mono (Thou/ul)	**2.0**
Eos (Thou/ul)	0.3
Baso (Thou/ul)	0.0

Glucose (mg/dL)	**112**
Blood Urea Nitrogen (mg/dL)	11
Creatinine (mg/dL)	1
Total Protein (g/dL)	**8.2**
Albumin (g/dL)	3.1
Globulin (g/dL)	**5.1**
A:G Ratio	0.61
Total Bilirubin (mg/dL)	0.5
Calcium (mg/dL)	8.9
Phosphate (mg/dL)	6.8
Cholesterol (mg/dL)	82
Alkaline Phosphatase (U/L)	621
ALT (SGPT;U/L)	22
GGT (U/L)	49

RADIOGRAPHS



DIFFERENTIAL DIAGNOSIS

- Pneumonia
  - Bacterial
  - Viral
  - Fungal
  - Aspiration
- Pulmonary fibrosis

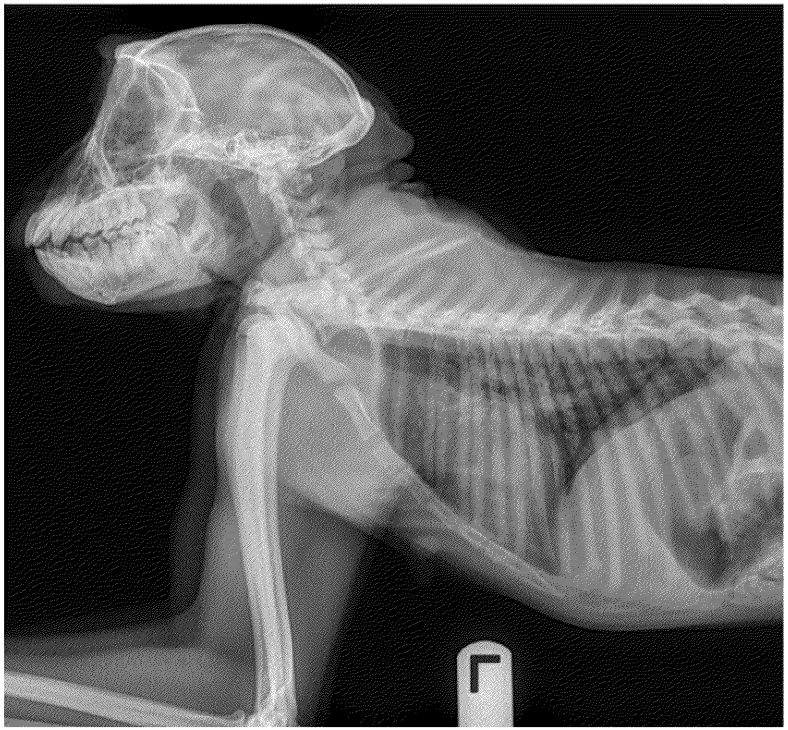
Presumptive diagnosis:
Coccidioidomycosis

Coccidioides titer positive
(1:4 IgM, 1:16 IgG)

Treatment:
Fluconazole
Albuterol

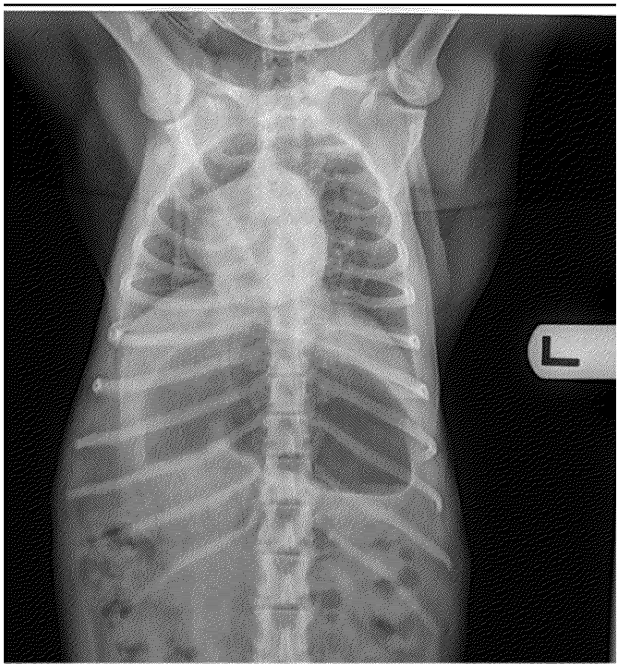
MAY 2018

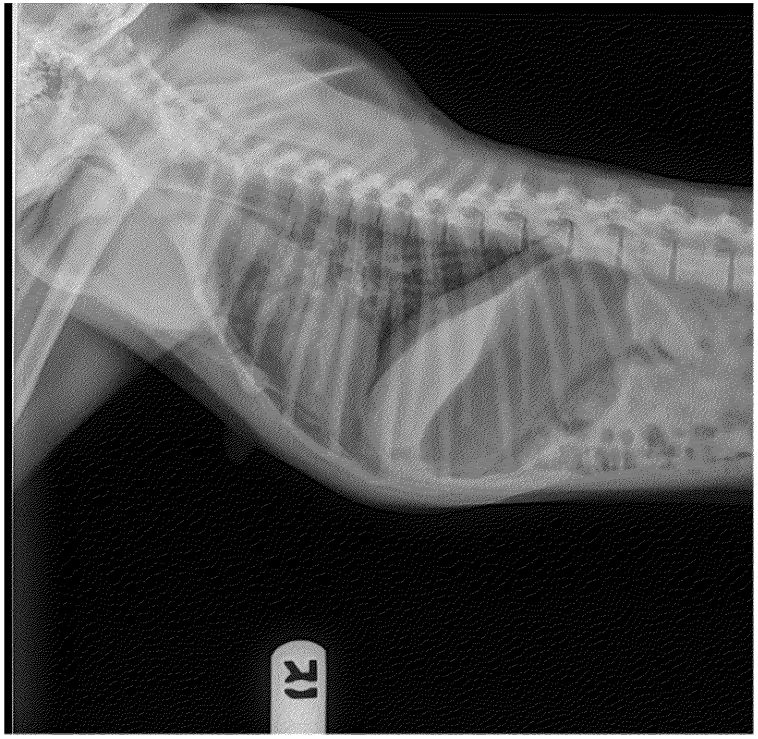
- May 15, 2018 – noted to be less active with stiff neck and bilateral epistaxis
- Radiographs May 23, 2018
- Cocci titer: IgM 1:2, IgG 1:32
- Treatments
  - Continue fluconazole
  - Amoxicillin
  - Prednisone
  - Meloxicam



JULY 2018

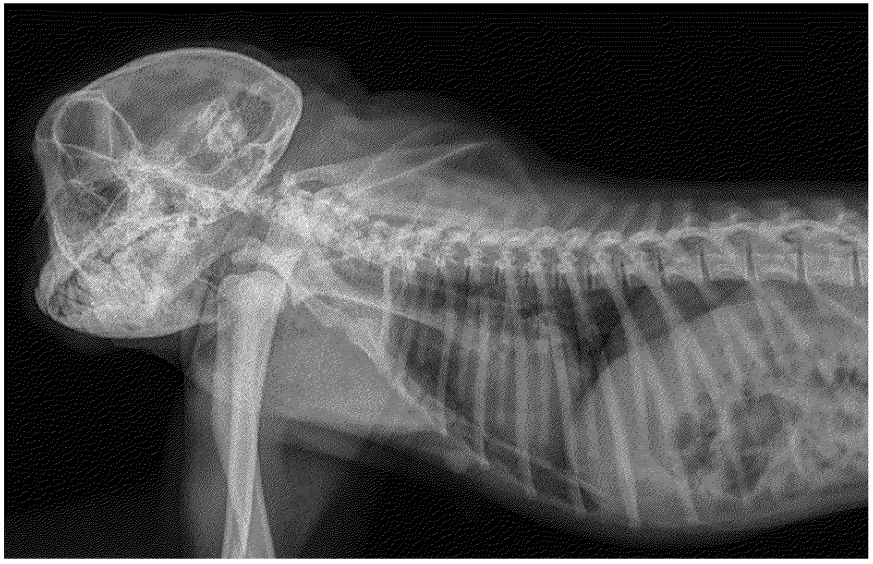
- Continuous fluconazole treatment
- Stable for a few months
- July 30, 2018
  - Lowered activity
  - Ataxia
- Cocci titer IgM negative, IgG 1:4
- Ataxia resolved with prednisone treatment

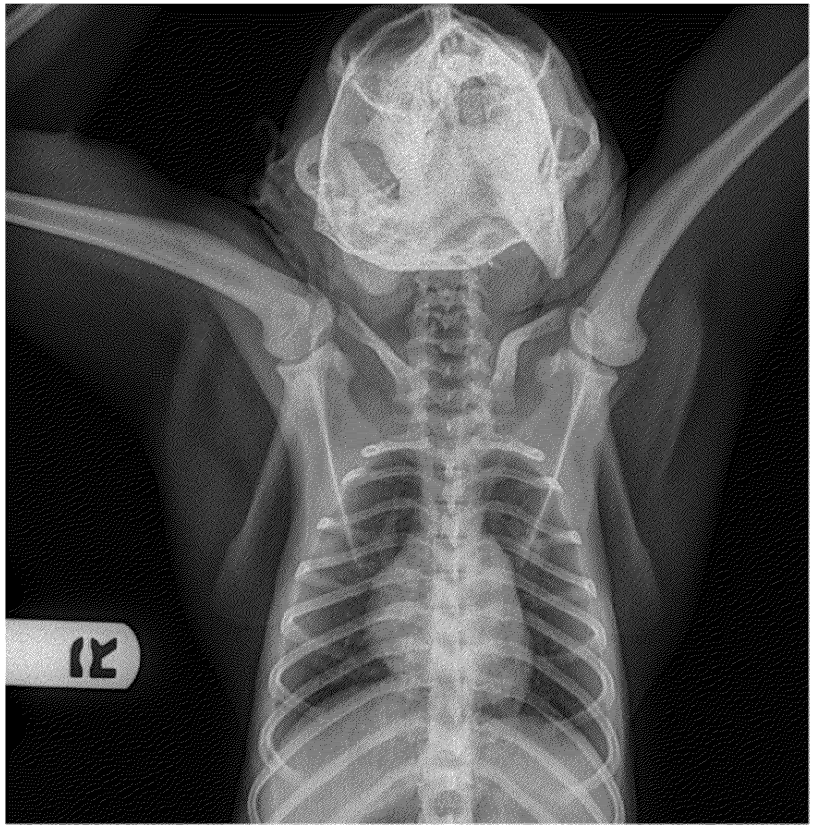




AUGUST 2018

- August 29, 2018
  - Seizure in a.m.
  - Ataxia and stereotypies in p.m.
  - Treated with diazepam
  - Neuro signs resolved next day





FALL 2018

- Returned to group 9/12/18
- 9/25/18 – seizure in compound – permanently moved to cage
- Determined to be pregnant
- Treated with diazepam
- Seizures 10/15/18, 10/19/18
- Started gabapentin and Keppra (levetiracetam) 10/19/18
- Decreased gabapentin dose 10/26/18 due to sedation
- Seizure 11/9/18 prior to medication
- Cocci IgM 1:2, IgG 1:2
- Seizure 12/15/18
- Order compounded levetiracetam for more accurate dosing
- Seizure 1/4/19

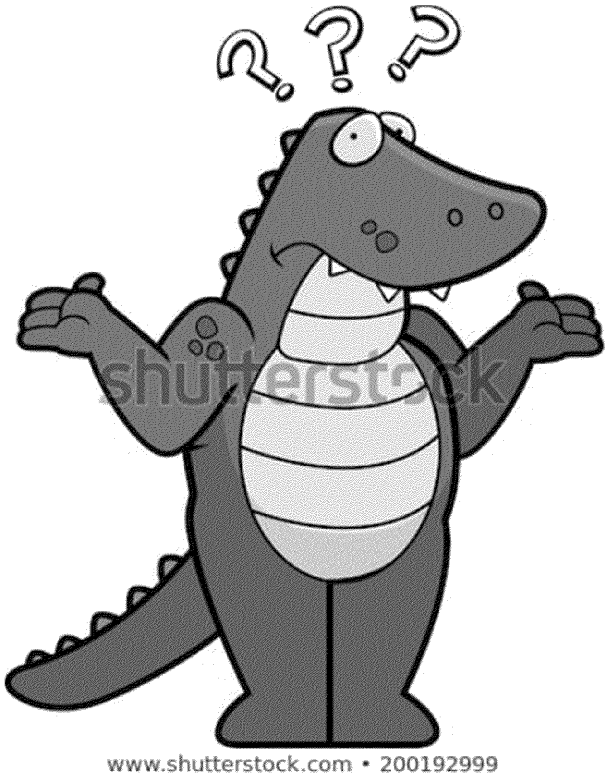
PREGNANCY CONCERNS

- Due date 1/23/19
  - What would happen if there were seizure during parturition?
  - What would happen to infant if there were seizure after birth?
  - Coccidioides can (rarely) be transmitted during vaginal delivery

PREGNANCY OUTCOME

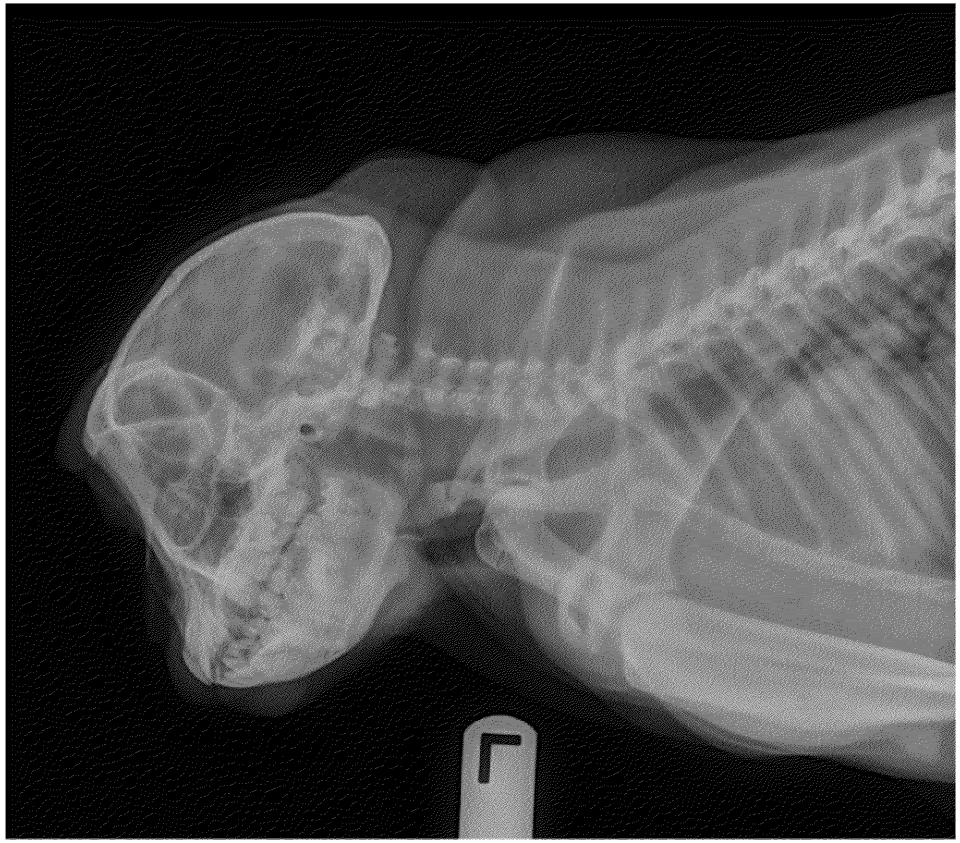
- C-section 1/10/19
- Routine surgery
- Collected amniotic fluid for potential dam-infant introduction
- 580 g healthy male infant
- Re-introduction not successful
- Infant fostered successfully

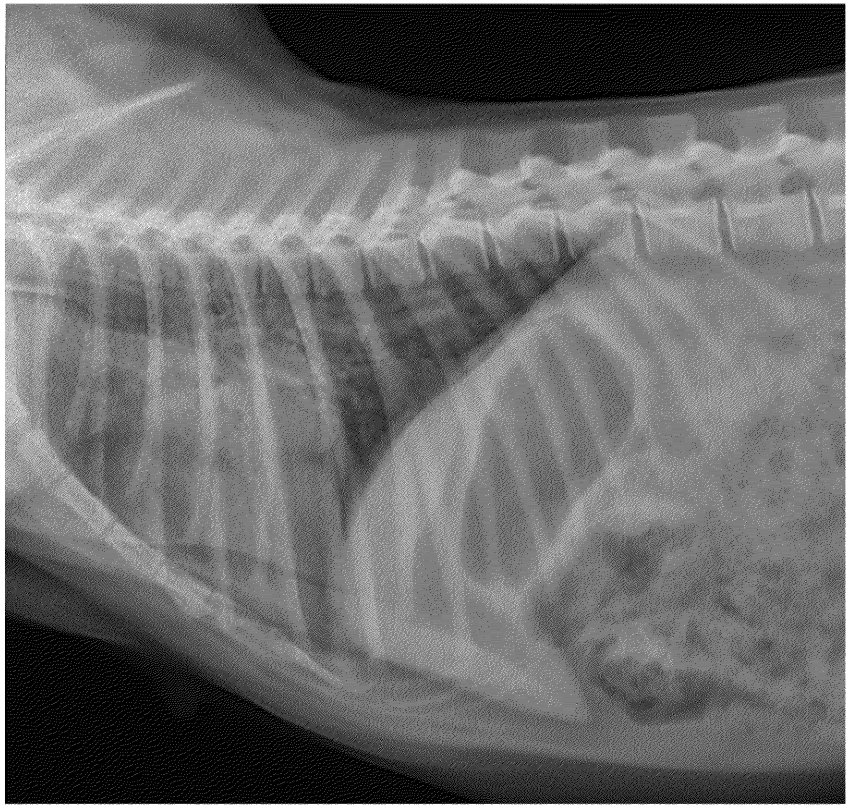
WHAT TO DO?



Continued seizures (3/6/19)
Continued positive cocci titers
Otherwise healthy with good BCS

FINAL RADIOGRAPHS

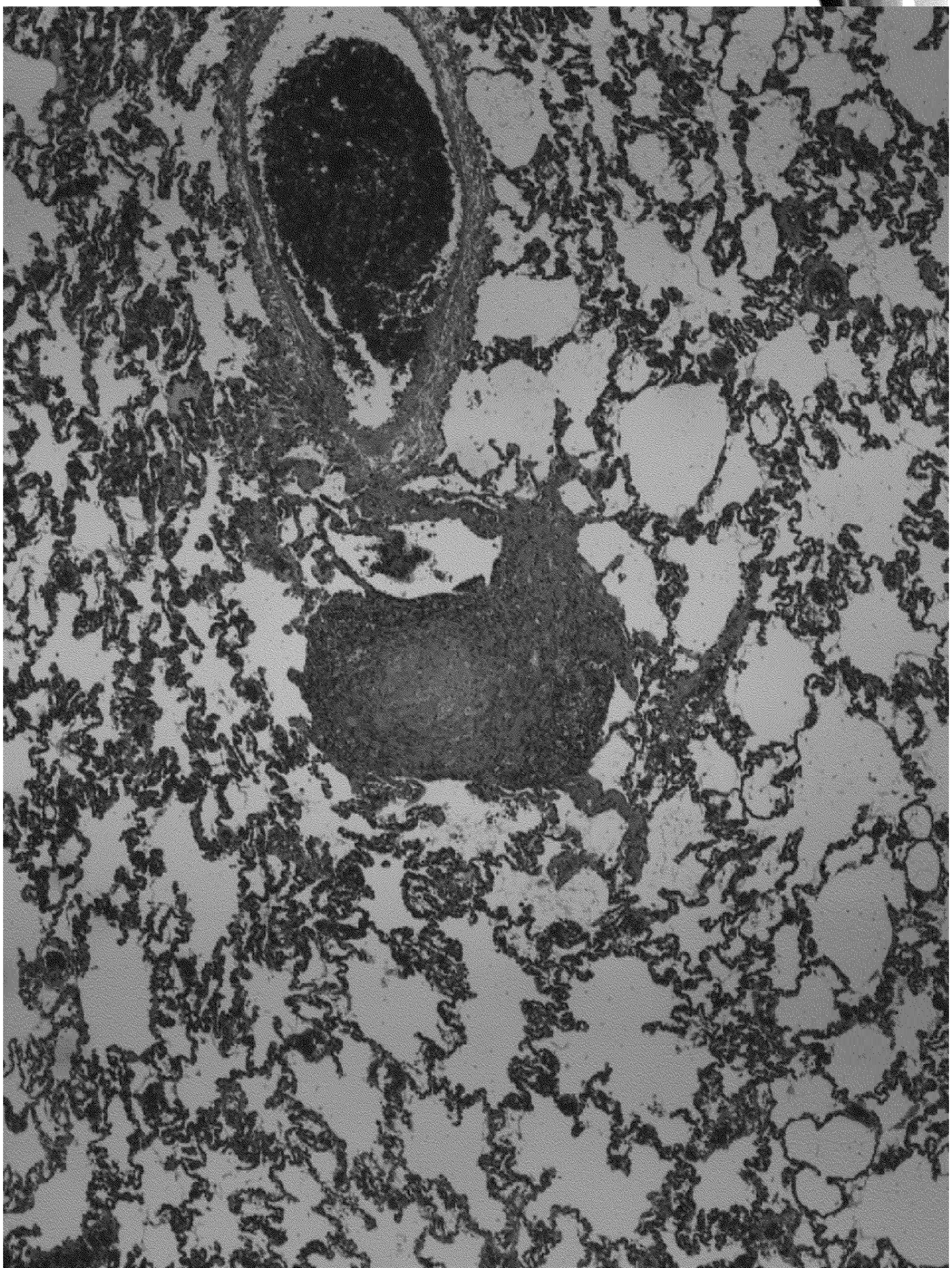




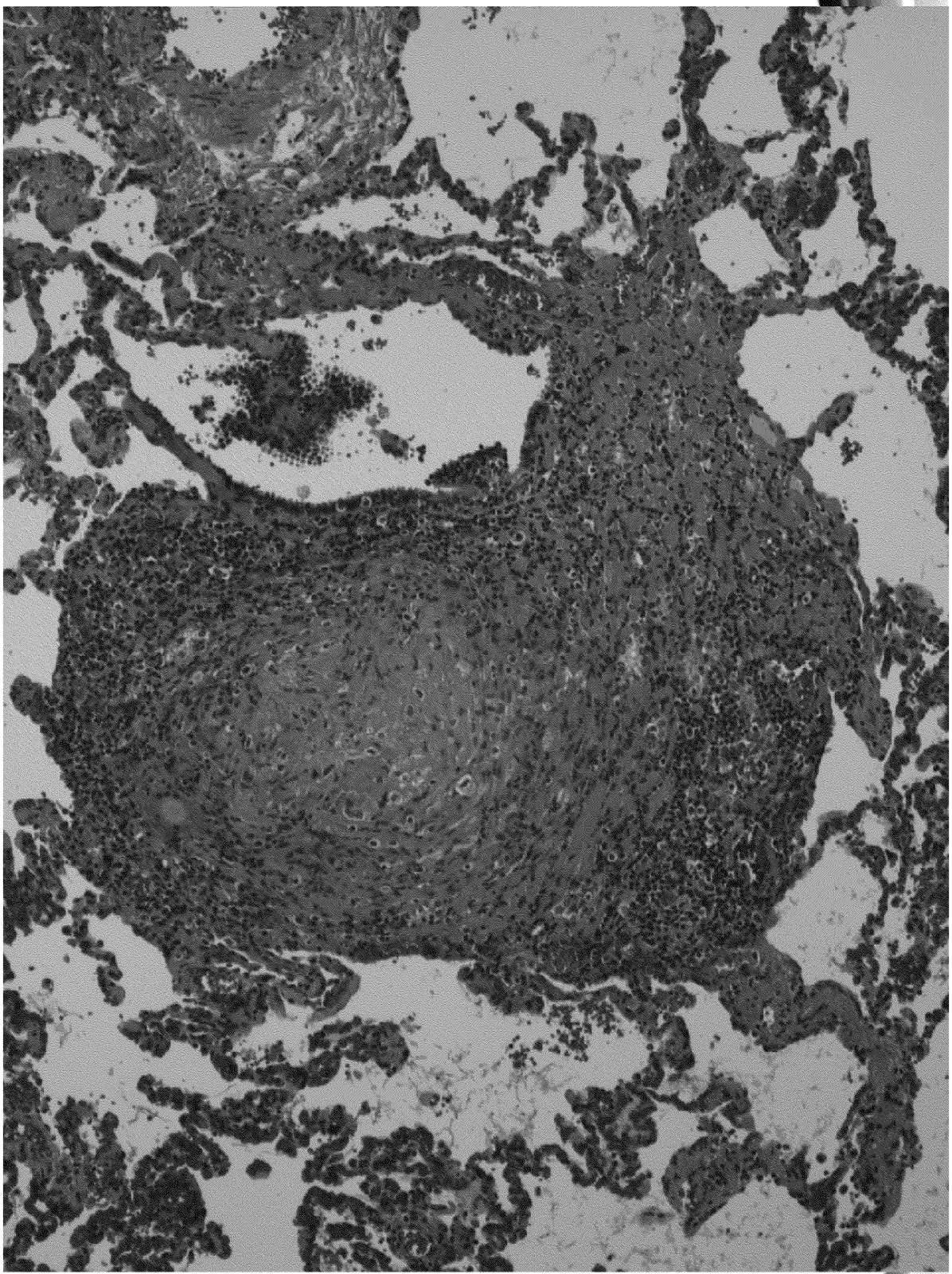
ENDPOINT

- Euthanasia 3/13/19
- Necropsy:
  - Lungs – mottled with multifocal 1-2 mm white nodules and adhesions
  - Brain fixed whole

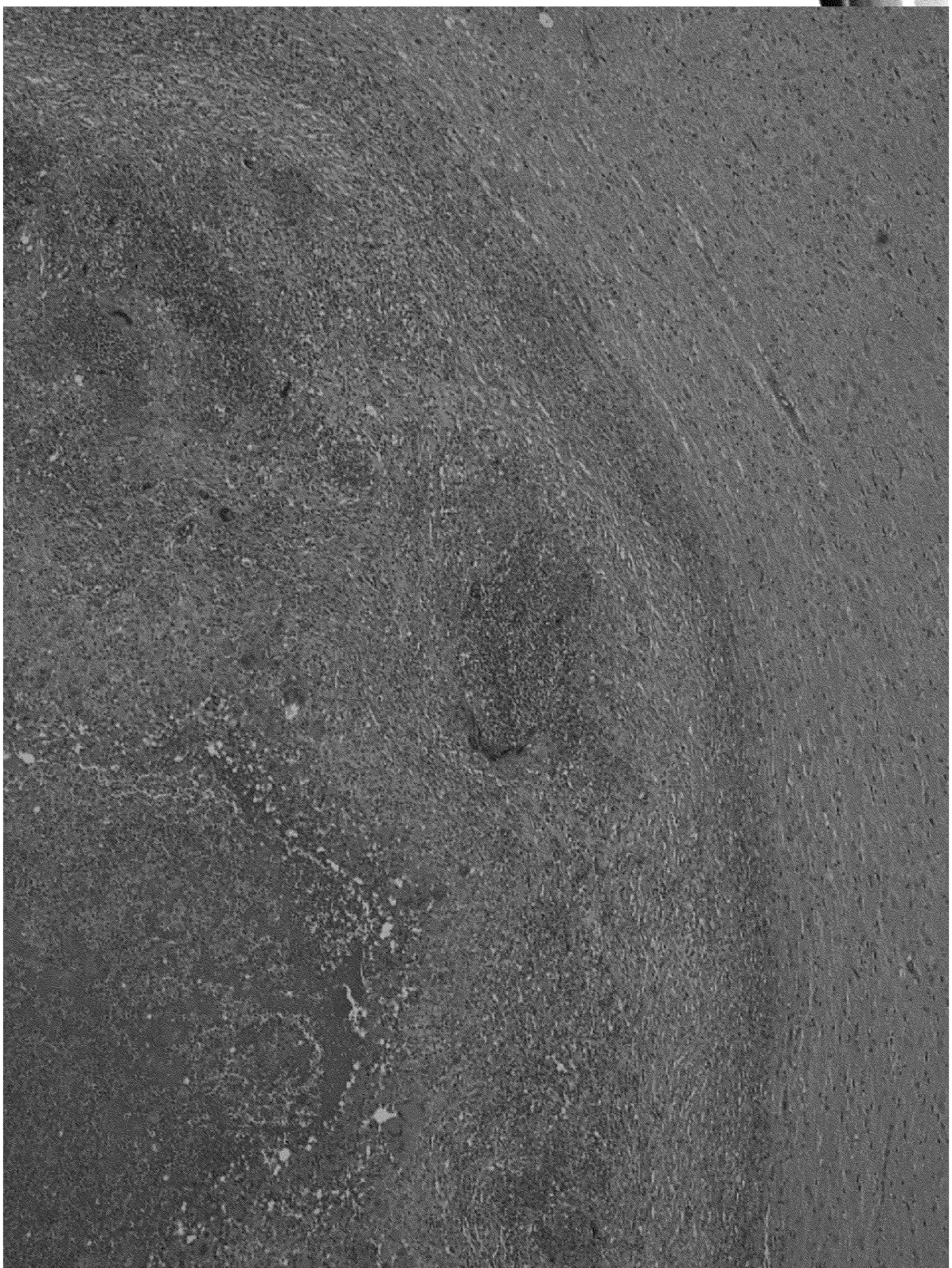
HISTOPATHOLOGY - LUNG



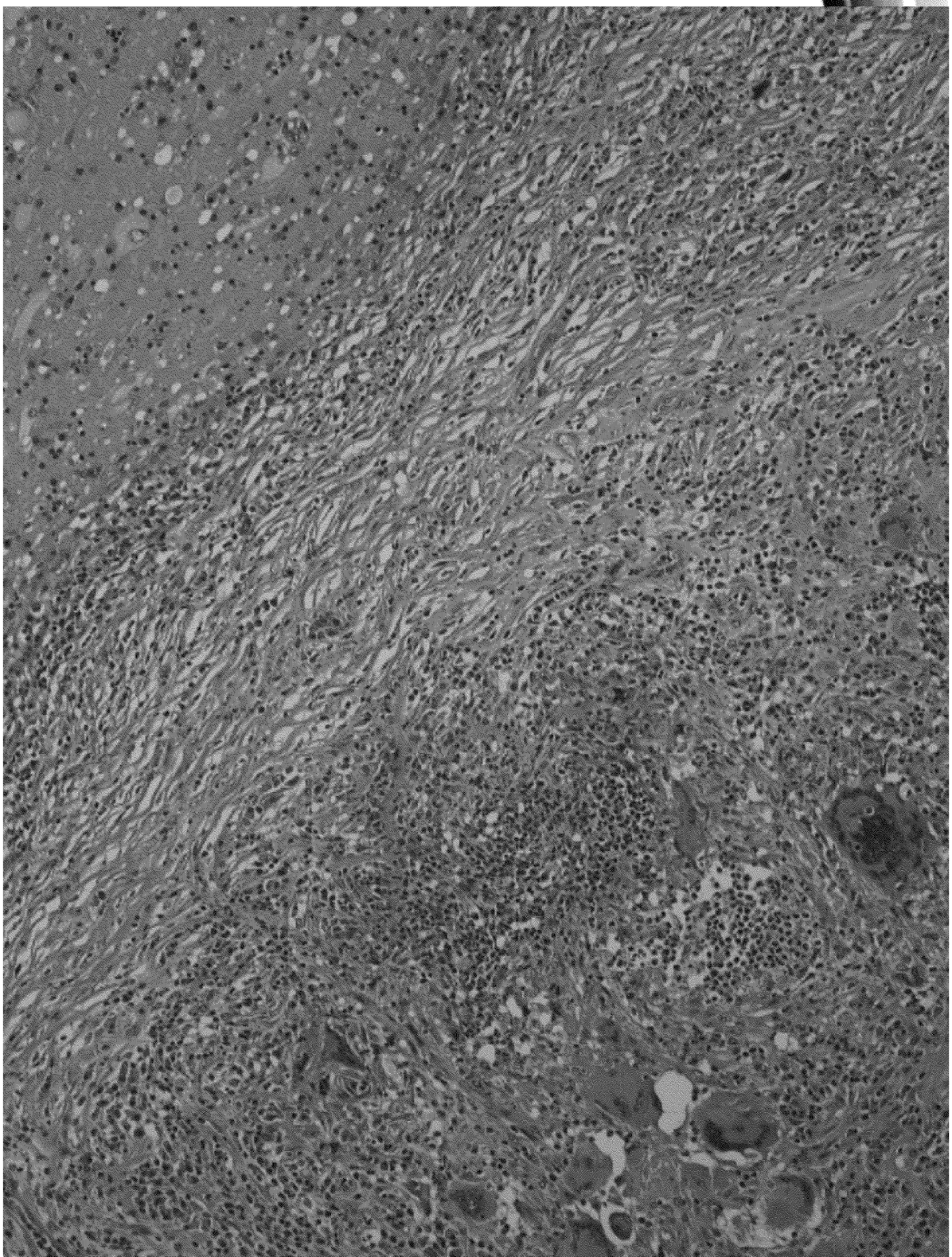
HISTOPATHOLOGY - LUNG



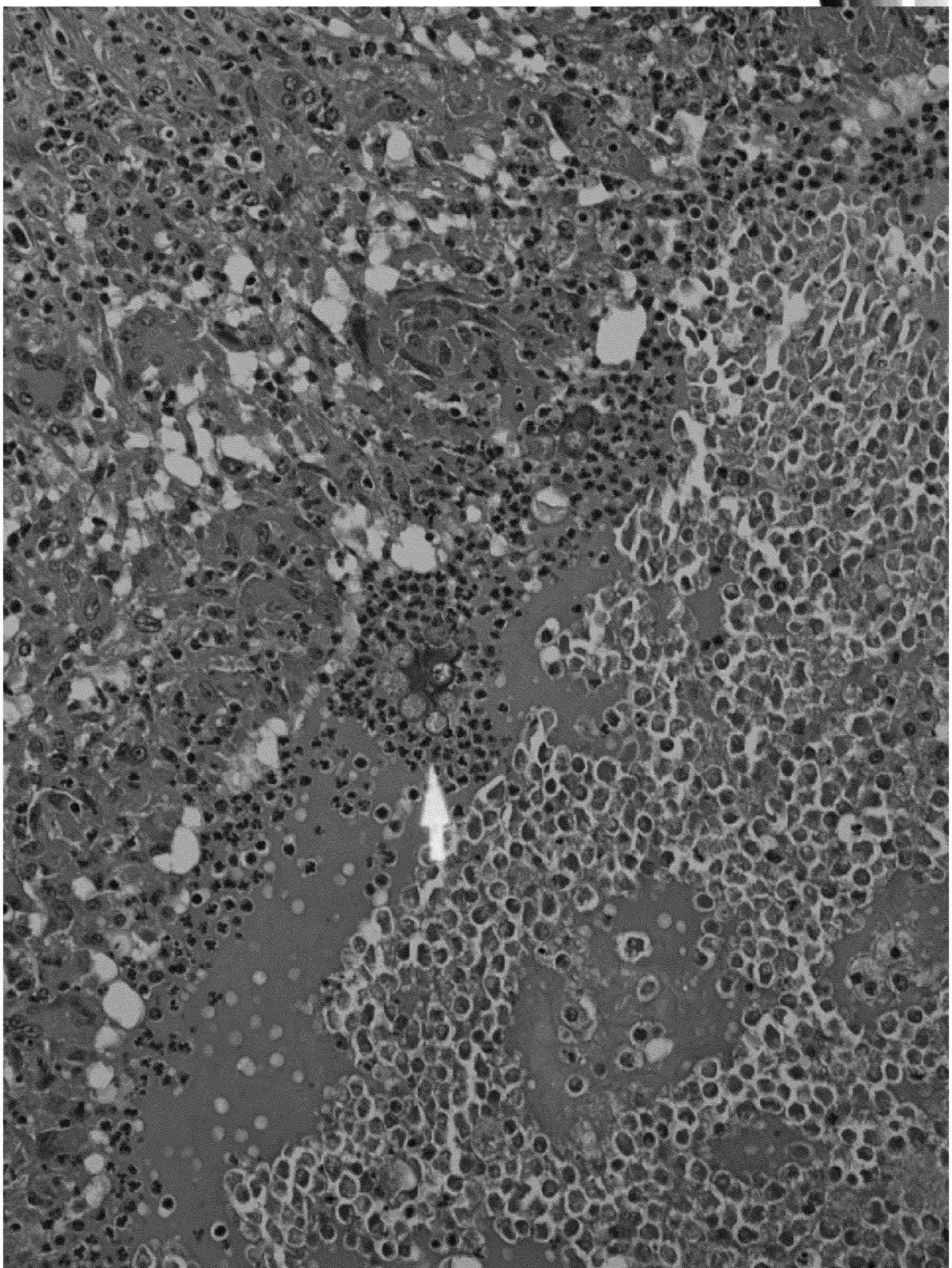
HISTOPATHOLOGY - BRAIN



HISTOPATHOLOGY - BRAIN



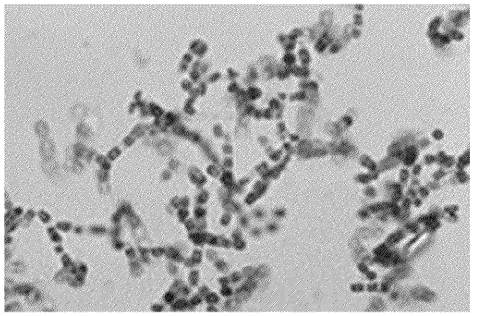
HISTOPATHOLOGY - BRAIN



COCCIDIOIDOMYCOSIS SUMMARY

Cocci	IgG Titer Result	IgG Titer Value	IgM Titer Result	IgM Titer Value
1/10/19	positive (+)	1:4	negative (-)	<1:1
10/29/18	positive (+)	1:2	positive (+)	1:2
9/25/18	positive (+)	1:8	positive (+)	1:2
8/30/18	positive (+)	1:32	positive (+)	1:2
7/30/18	positive (+)	1:4	negative (-)	<1:1
5/23/18	positive (+)	1:32	positive (+)	1:2
4/16/18	positive (+)	1:16	positive (+)	1:4
Note that cocci titers were done in 2014-2016 and were negative. No titer was done in 2017.				

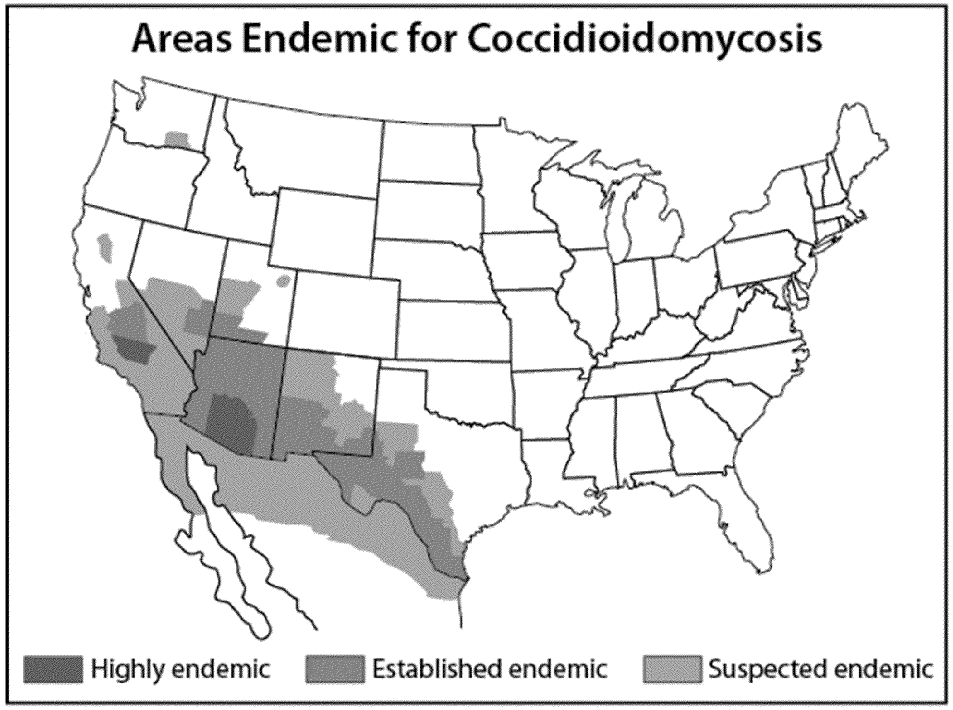
COCCIDIOIDOMYCOSIS



CDC image

- Fungal infection caused by the genus Coccidioides
  - C. immitis
  - C. posadasii
  - More commonly known as Valley Fever or Cocci
  - Able to infect humans and a wide range of animal species
    - NHP species with cases reported include baboons, capuchins, chimpanzees, geladas, guenons, gorillas, lemurs, mandrills, macaques, mangabeys, spider monkeys, squirrel monkeys, woolly monkeys

ENDEMIC REGIONS

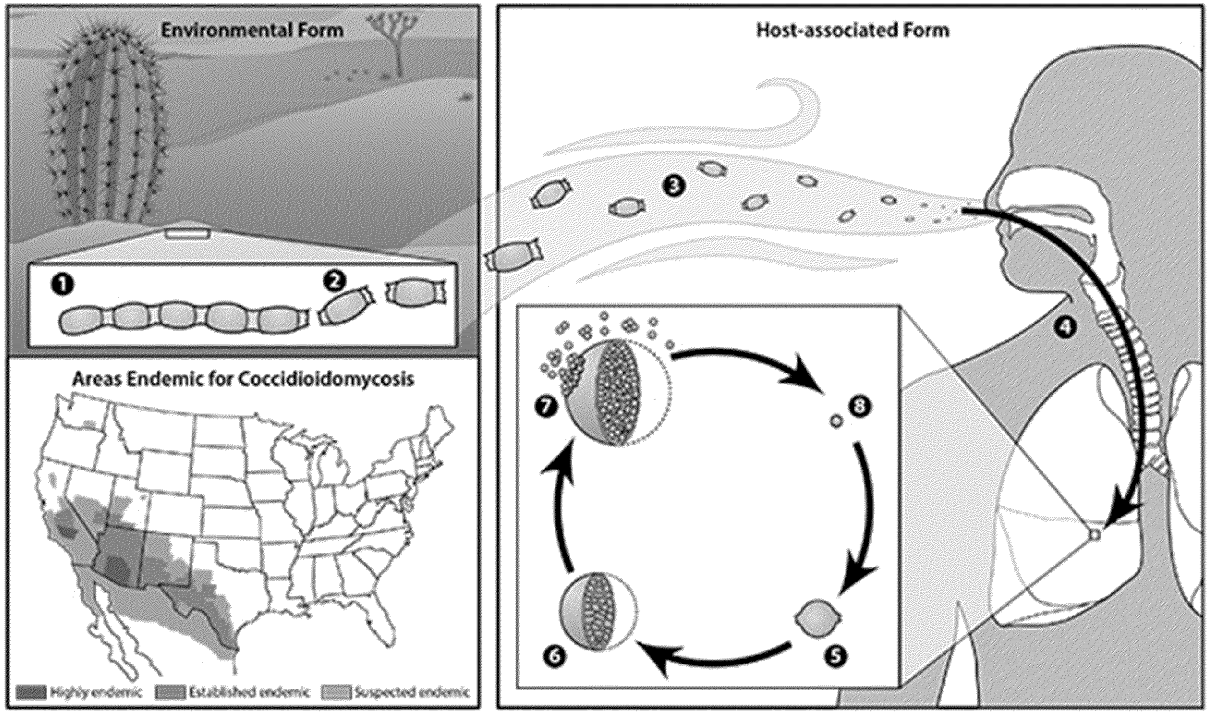


www.cdc.gov/fungal/diseases/coccidioidomycosis/causes.html

- Found in portions of North, South, and Central America
- Highly endemic regions found in Arizona and California
- Newer region found in Washington state

LIFE CYCLE

Biology of Coccidioidomycosis



In the environment, *Coccidioides spp.* exists as a mold (1) with septate hyphae. The hyphae fragment into arthroconidia (2), which measure only 2-4 µm in diameter and are easily aerosolized when disturbed (3). Arthroconidia are inhaled by a susceptible host (4) and settle into the lungs. The new environment signals a morphologic change, and the arthroconidia become spherules (5). Spherules divide internally until they are filled with endospores (6). When a spherule ruptures (7) the endospores are released and disseminate within surrounding tissue. Endospores are then able to develop into new spherules (6) and repeat the cycle.

CDC

ROUTES OF INFECTION

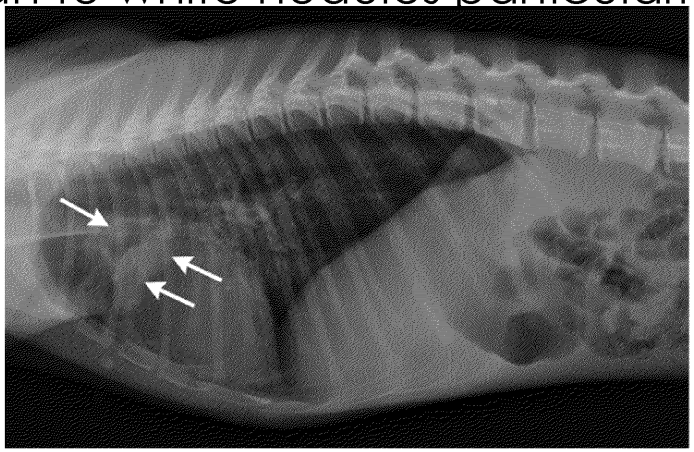
- Primary route of infection is inhalation
- Not contagious or zoonotic
- Less frequent routes of infection can include:
  - Break in the skin such as a cut, wound, or splinter
  - Aspiration of amniotic fluid during parturition
  - Organ transplantation
- Low infectious dose

SYMPTOMS

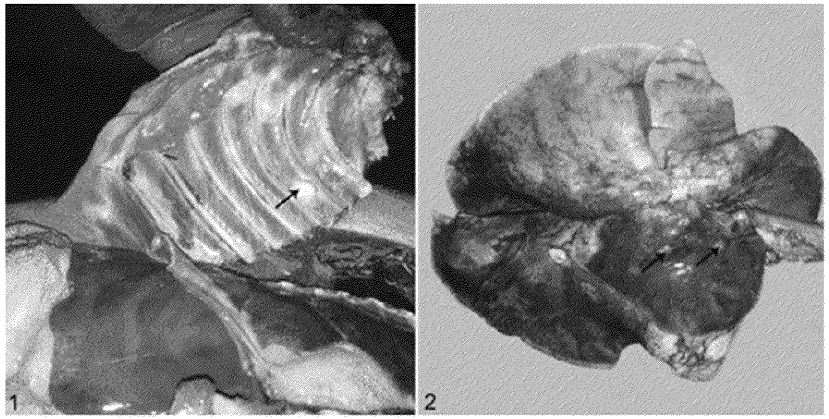
- Diverse clinical presentation (average 7-28 days after exposure)
- Clinical illness in NHP similar to humans
- Lethargy
- Coughing
- Shortness of breath
- Fever
- Inappetence and/or weight loss
- Joint pain or lameness
- Skin rash or nodules
- Neurological symptoms

CLINICAL AND PATHOLOGICAL FINDINGS

- Eosinophilia, mild lymphocytosis, monocytosis
- Hyperglobulinemia
- Radiographic changes
- Tan to white nodules particularly within lung tissue and thoracic wall



Kundu et al, 2017

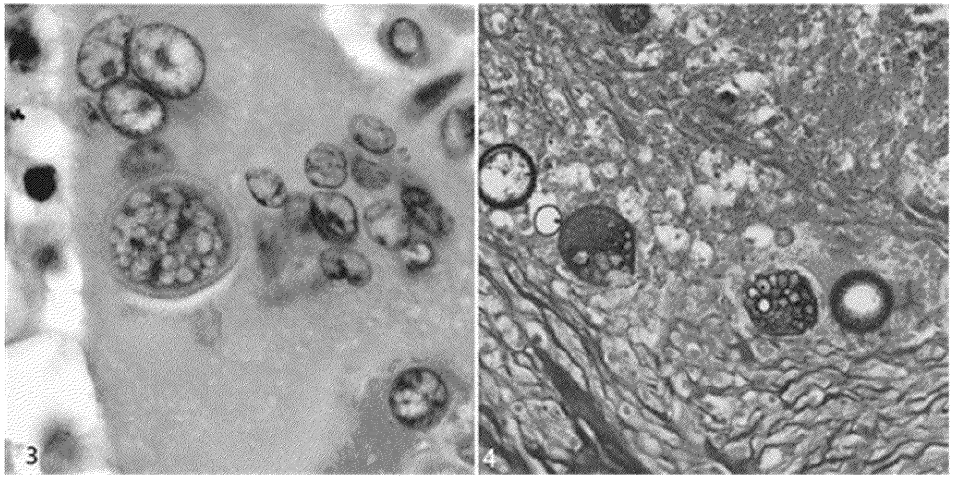


Koistinen et al, 2018

PATHOGEN DETECTION

- Direct detection
  - Microscopy
  - Molecular detection
- Culture (safety concerns – BSL3)
- Serology (EIA, IMDF, CF)

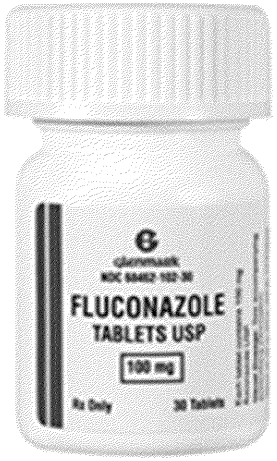
Hematoxylin and eosin (left), Periodic acid-Schiff



Koistinen et al, 2018

TREATMENT

- Triazoles or Amphotericin B
  - Fluconazole, Itraconazole, Voriconazole, Posaconazole
  - Fluconazole most frequently used
    - Tablet, liquid, fluconazole impregnated feed
    - Currently 13% of the colony at Arizona is on Fluconzaole
      - 16 of 40 animals (5.2% of colony) cocci negative – treatment continues for one year of negative titers
      - 24 animals (7.8% colony) are cocci positive



CEREBRAL COCCIDIOIDOMYCOSIS

- 95% fatal within two years in humans if untreated
- Most common presentation in humans is headache; very few reports of seizures
- Most common presentation in dogs is seizures
- Diagnosis: serology, CSF (exam, culture, PCR), neuroimaging
- Pathology – humans primarily meningitis; dogs primarily granulomas
- Treatment: antifungals, supportive care, surgery (CSF shunt)

ANTI-SEIZURE MEDICATIONS

- Diazepam
  - Enhances GABA activity
- Gabapentin
  - Interacts with voltage-sensitive Ca channels
- Levetiracetam
  - Binds to synaptic vesicle protein SV2A

PREVENTION AND SURVEILLANCE

- Dust mitigation/limiting exposure
  - Future growth to focus on indoor only animal enclosures with HEPA filtration
  - Construction site using dust mitigation practices
  - Minimizing animal exposure time outdoors when high wind/dust storms expected
  - Spray down of enclosures before having access to outdoor portion
- Routine serological surveillance captured at semi-annuals
  - Twice a year (+) clinical indication or suspicion (weight loss, coughing)

NECROPSY DATA FROM ARIZONA

Year	Cases	Gender	Location
2013	N=3	3 female	2 pulmonary, 1 disseminated
2014	N=18	17 female, 1 male	2 pulmonary, 16 disseminated
2015	N=13	12 female, 1 male	3 pulmonary, 10 disseminated
2016	N=8	7 female, 1 male	4 pulmonary, 4 disseminated
2017	N=2	2 female	1 pulmonary, 1 disseminated
2018	N=1	1 female	1 disseminated

VACCINATION

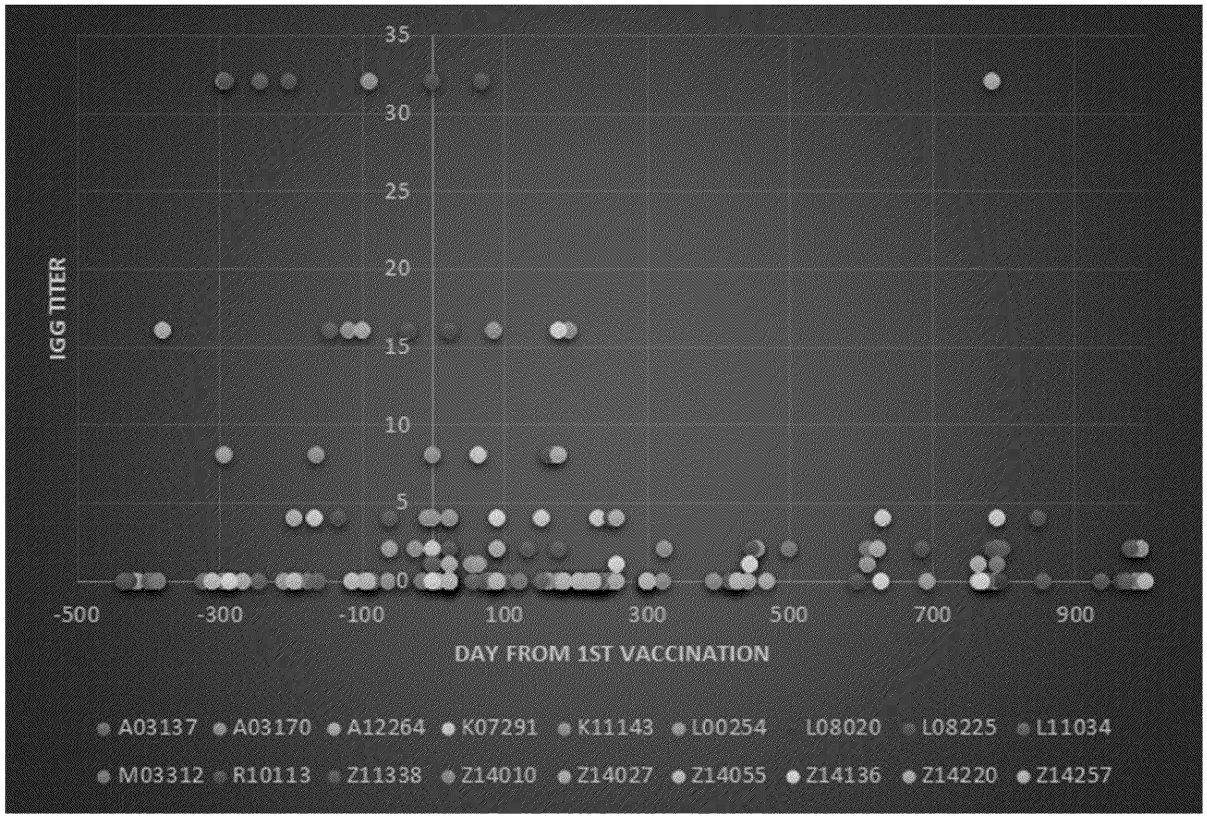
- No commercial vaccine available
- A human vaccine trial was conducted in the 1980's with spherules but no difference was found in the number of cases of the severity of disease between vaccine and placebo groups
- Challenging in terms of antigen expression, cost of production
- Interest in Delta-CPS1
  - U of A created mutant strain that does not cause disease in mice strains including those with no lymphocytes and those with bone marrow suppression
  - Good survival statistics in those vaccinated
  - Working on replacing the antibiotic resistance marker with one that does not involve antibiotics
- Mazen Animal Health developing maize-based subunit vaccine

VACCINATION IN NHP

Day 1, 8, and 45

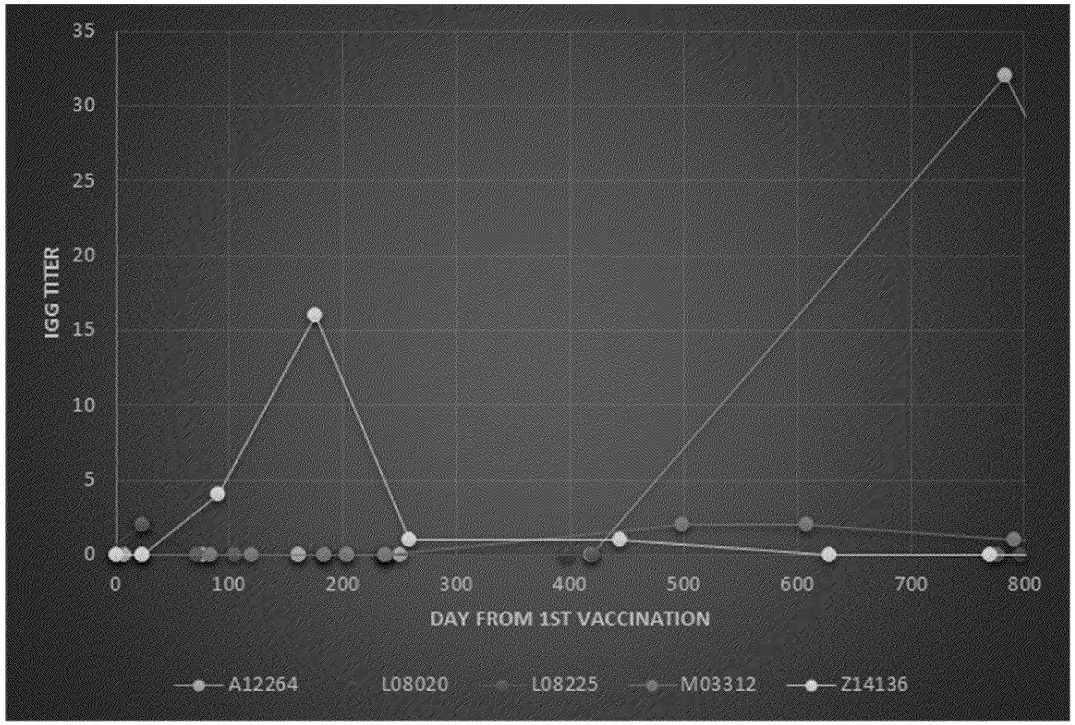
2 – 4 mg whole spherules

Some animals naïve; some history of prior cocci titers



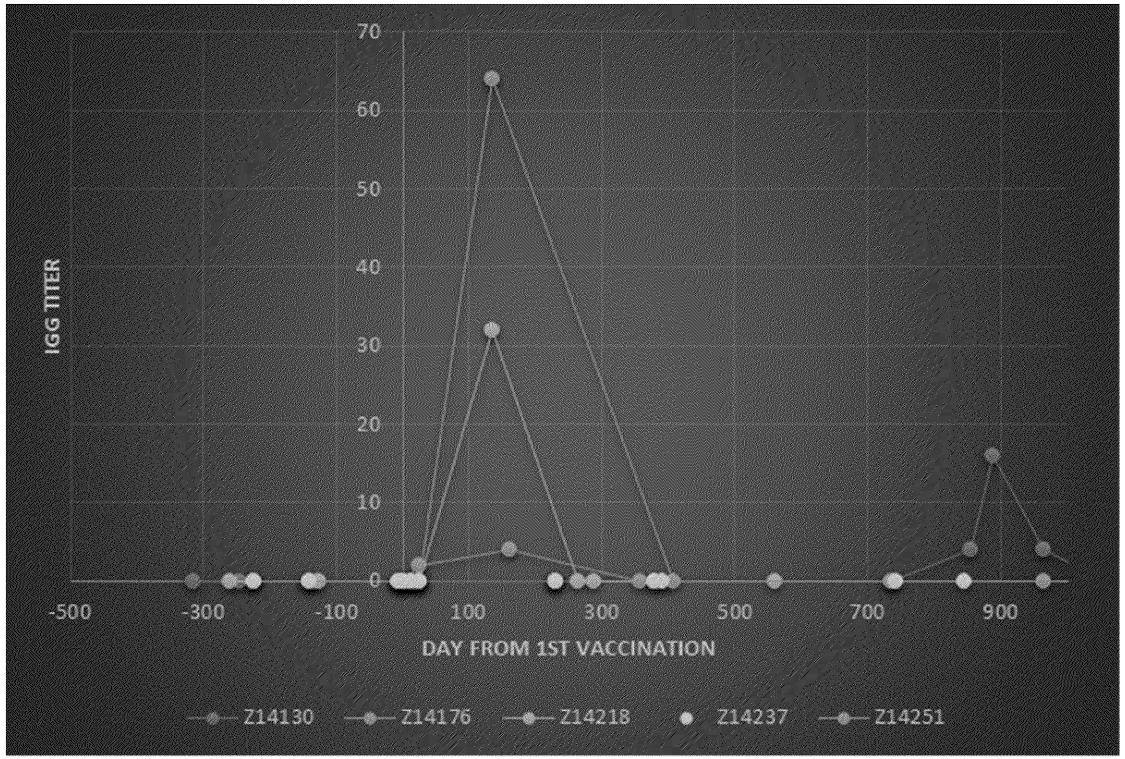
ANIMALS SERONEGATIVE PRIOR TO VACCINE

- 6 animals did not seroconvert
- 2 animals seroconverted after vaccination
- 3 animals became infected later



COHORT 2

- Day 1, 8, and 45
- 6 mg whole spherules
- All animals naïve
- 1 animal did not seroconvert
- 2-3 animals responded to vaccine
- 1-2 animals became infected later



COHORT 3

Day 1, 8, and 45

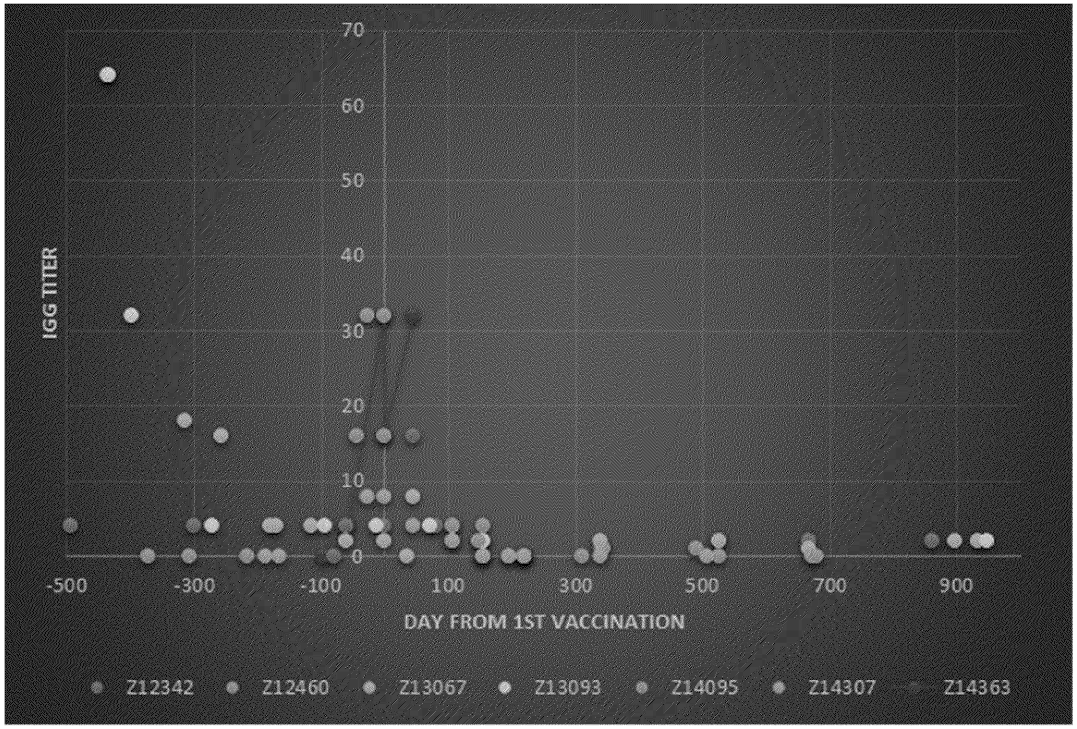
3 animals received 2 mg whole spherules

4 animals receive subunit vaccine with adjuvant

No animals naïve

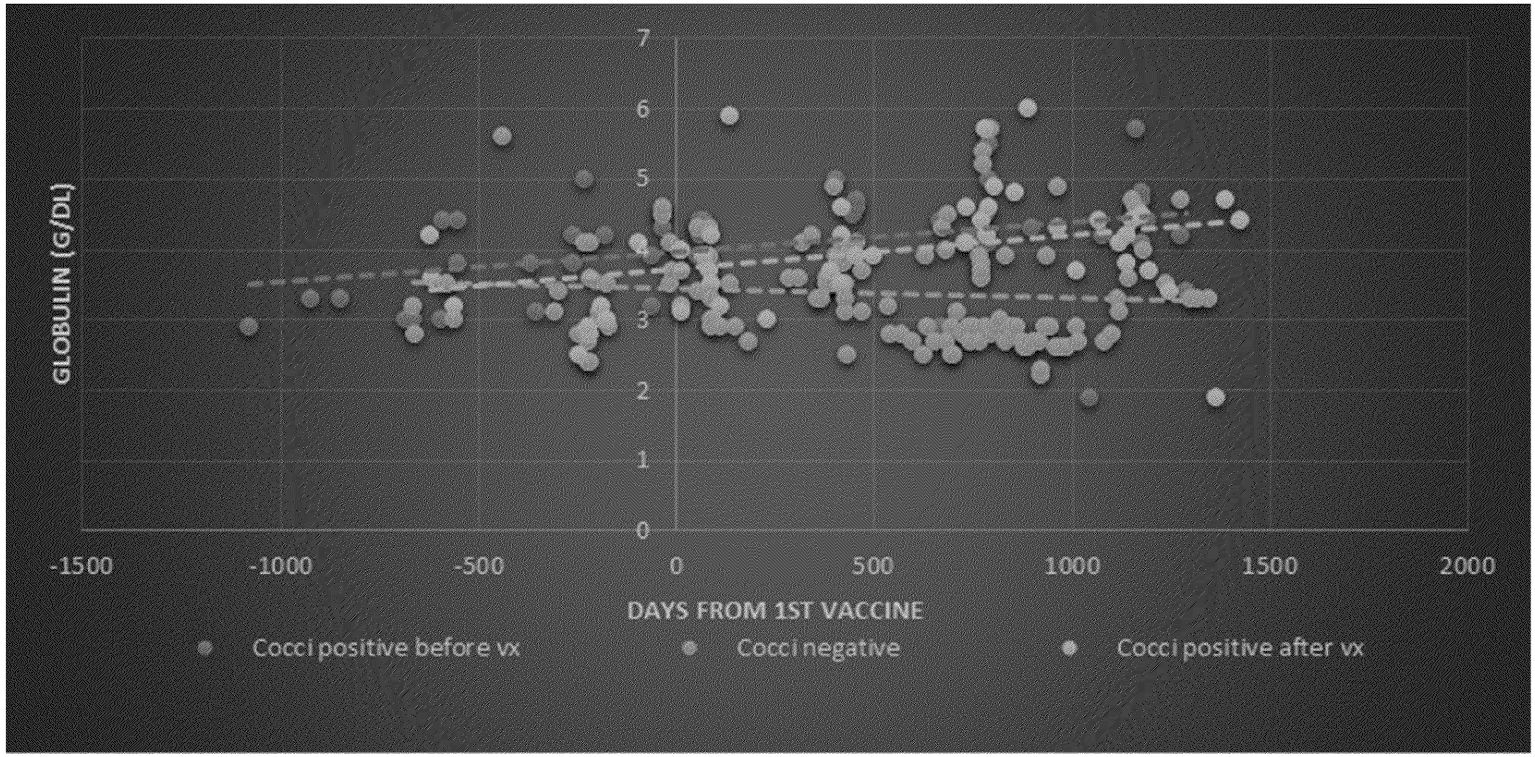
Two animals in subunit group developed persistent site reactions

One animals in subunit group developed disseminated disease



CLINICAL BIOMARKER

- Globulin most consistent biomarker in M. nemestrina
- Increase in globulin same in animals infected before or after vaccination



SUMMARY

- Coccidioidomycosis can usually be controlled, but elimination is more difficult
- Even non-severe infections can spread to CNS
- Medications can decrease seizure frequency and appear to be safe in pregnancy
- Levels of seizure activity that are manageable in pet animals may be problematic in research animals
- A vaccine is needed, but not currently available for this species

ACKNOWLEDGMENTS

- Lee Chichester
- Caroline Mead
- Robert Murnane
- Sally Thompson-Iritani
- Kate Guerriero
- Dean Jeffery
- Keith Vogel
- Jason Laramore
- Demosthenes Pappagianis
- Jeremy Smedley

From: Charlotte E. Hotchkiss
Sent: Sunday, June 16, 2019 6:52 PM
To: Tess House; cmali
Subject: Virtual grand rounds
Attachments: VGR Neuro cocci.pptx

Here's what I have so far for the virtual grand rounds on Thursday. Comments welcome.
Charlotte

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WaNPRC Records Review
Animal Observations noted during site visits

WaNPRC Western
Inspection date: 9/4/19

- Animal A11240: Health and behavioral records checked. Female with alopecia and lacerations on left side (healing well). Lacerations were from her partner (Z13035). Run through in cage was open. Per BMS, this level of social contact between the pair is currently not allowed due to fighting. Was corrected during visit.
    - A11240 currently has a new partner – A11242 and is doing well.

- 228: Health records checked for Z15284. This animal had two small lacerations from getting her arm stuck in between the caging earlier in the day. Was seen by a vet shortly after. Animal is recovering well, and techs plan to switch out type of caging in this space to minimize likelihood of recurrence.
    - Run through with another monkey, new cage and all is well.

- 310: Animal Z16339 had a small bare spot on shoulder, checked records to see if this was a behavioral/health issue, but it turned out to have been shaved for closer observation (no issues).
    - No clinical or behavior issues. Currently in Run-Through housing.

- 227: All the animals in this room were in various stages of recovery from anesthesia (for TB testing). Talked with vet/vet tech re: how animals are monitored following anesthesia and how this is documented. Monitoring records looked good.

- 307: Health and behavioral records checked for two animals in this room, Z13288 and Z14020. These two animals were not in social housing during visit. Health records show that these animals needed to be kept separate until a negative test came back for Z13288. The negative test arrived very recently, animals will be socialized very soon. There were no notable behavioral issues for Z13288, one concern about locomotor stereotypy in Sept 2018 for Z14020, but nothing notable since then.
    - Both animals are being introduced to new animals on Nov 6.

- Z15377 and Z14237 (AT observation sheet stated they were on treatment). Reviewed medical records. Both animals being treated for chronic diarrhea – suspected IBS.
    - All is well as long as they are on fiber and probiotics.

- 233: Health records checked for L10197 (enucleation following inflammation/infection).
    - Eye infection, maybe something splashed into her eye. Her eye was removed a few months ago. She's in Run-Through housing with J09022 and has mild alopecia.

WaNPRC I-Wing
Inspection date: 9/6/19

Clinical records reviewed:

- A19086, squirrel monkey that recently had an intravitreal injection.
    - After treatment by the 11th the eye looked normal. The animal is back in its social group.

- L09103, Animal on Zika project.
    - This animal is gone.

WaNPRC ARCF

Inspection date: 10/21/19

- Z15302 (Bonnie) – Bruising/rash observed on left flank. Animal was scratching the affected site. This was also noted by AT on daily log. Vet took a look at animal during visit. Appeared to be clipper burn. Reviewed typical treatment for this condition.
    - Not quite healed yet, but still on treatment. She's in Run-Through housing and has moderate to severe alopecia.

- Z16009 – Animal has cast on left (?) arm. Bright and alert. Reviewed case with vets.
    - Allentown cage. Animal got stuck behind the squeeze. Vet staff did x-rays today and put the cast back on. The animal in back in social housing.

- Z15032 – Animal observed to be sluggish and laying on bottom of cage. Animal was recovering from sedation event. Discussed how anesthetic recovery is performed and documented with site visit hosts and vet. Monitoring records for this animal had not yet been entered in to ARMS.
    - Animal had been sedated. This monkey is in Grooming-Contact housing and has minor alopecia. She displayed locomotor stereotypies when she was individually housed. BMS is checking to see if she still does this now that she has a social partner.

- T02319 – Daily observation log noted that this animal could use some extra TLC due to fight wounds sustained over the weekend from her partner. Observation of animal suggests that she is recovering well. Reviewed case with site visit hosts/vet.
    - Suffered injuries from her partner, and she is fine now. She has alopecia and will be introduced to a new social partner tomorrow.

WaNPRC RR-Wing

Inspection date: 9/23/19

- Did not review the log of biological indicator testing for the autoclave (located on the Z drive) so that should be covered at the WaNPRC records review.
    - These were reviewed.

WaNPRC Arizona

Inspection date: 9/30/19

- Z17162: prolapse that self-corrected
- M11094: Thin with alopecia, currently group housed. Her weight is back up after treatment.
- T09176: high globulen, not valley fever though
- Z18043: This youngster had a broken arm (radius), and it's not healing well. WaNPRC is looking into orthopedic equipment so they can pin the bone.
- Z17280: This youngster had a broken arm (radius and ulna). The animal messed with its cast, and it got so bad they had to euthanize the animal on 10-17-19.
- Z16358: On treatment for valley fever, was doing some coughing at the time of the inspection.

New Behavior person starts later in November at AZ.

WaNPRC Records Review

November 4, 2019 at 11am
Location: HSB I-421
Members present:
WaNPRC: CH, RB, STI, JD, AA
IACUC: JE, KS
Support: KSH, JFI, LI

Protocol Reassignments:
17 animals have been reassigned since the last records review.

Adverse Events and Spontaneous Deaths:

- A16231: On 04-17-19 this Buffalo animal developed a brain bleed and ended up dying while under clinical care.
- Z19106 (in AZ) in May this one week old was found dead in its enclosure. Its mom got sick and infant died. Failure to thrive.
- Z19260 (in AZ) in October this ~one week old, small infant was placed into the nursery for care. The animal did well that night and in the morning when they were working on it, it went agonal.
- In July four Kiem animals (Z16225, Z15342, Z15300 and Z15213) were given too many C-ART cells. Three of the four animals developed ARDS and one recovered. Changes have been made to prevent this from happening in the future.
- On October 7 a Murry animal (K04065) had surgery and recovered well but was found dead in its cate two days later. The group will increase post-op EKG monitoring. (Animal was given a stem cell injection and was assigned to Cardiomyocyte graft evaluation. They had not done an infarct, only cells. Animal was probably dead 8-12 hours before it was found.)
- On October 9 a Murry animal (A19191) died. Animal went into cardiac arrest and was euthanized on the table. Discussions about who is responsible for what in an instance like this was discussed. Communication, and “Code Blue” team were discussed.

Animal Observations noted during site visits:

- See IACUC site visit notes

WaNPRC Records Review

April 29, 2019 at 1pm
Location: HSB I-421
Members present:

- **WaNPRC:** Charlotte, Sally, Jesse, Rita
- **IACUC:** Jane S., Lisa, Kim, Jane E.
- **Support:** Kelly

Disaster Preparedness:

- Red box, inside is the green notebook with emergency plan in it.

Protocol Reassignments:

- 15 re-assignments

Adverse Events and Spontaneous Deaths:

- Last fall a male pigtail born in AZ on Oct 29, 2018. Z18198 ~~or Z18123~~. Discovered dead the next day. Necropsy revealed a skull fracture and post-mortem trauma.
- Murry A16164: Infarct surgery Nov 28, 2018. He was shocked multiple times during surgery. Then went into ventricular arrhythmia when back in the cage and died. Limits to shocks put in protocol as a result.
- Z18197: AZ infant had diarrhea, treated and returned to the dam. Still not doing well, so went back to the nursery, went back to mom, then back to nursery and then back to mom. Died. Pneumonia and pancreatitis
- Kiem Z12189: Apheresis, difficult recovery, treated with fluids, blood transfusion, developed respiratory distress. Looked like transfusion reaction at necropsy.
- R11007 in AZ, tested positive for cholera in Sept, treated and recovered. Anesthetic event for clinical exam and it died.
- Kiem A18096: Apheresis and catheter placed, 3 doses of TBI and before the 4th dose, it was found lying in its cage. It looked bloated, treated, problems continued and the animal was euthanized. Histology didn't show anything. Anesthesia death, or reaction to study drugs.
- Az Z19005 Jan 12, Z19049 Feb 26: first infant was 3 days old, second 2+ weeks old. New breeding group set up with inexperienced male. NO deep punctures, so unclear if male or females caused trauma. Compound has been split, male is on his way to Seattle.
- Murry animal in March: This female 14.8-year-old *Macaca mulatta* was assigned to the project "Cardiomyocyte Graft Evaluation", protocol # 2225-06. A coronary artery infarction surgery was scheduled for 3/6/19. On the morning of the surgery it was found that the animal had not been fasted. The veterinary and surgical teams discussed the situation and agreed to delay the procedure > 1 hour and proceed, in accordance with the WaNPRC fasting SOP in effect at that time. Following the procedure the animal was seen to cough or retch; it is not clear whether any vomition occurred at that time. The animal then went into respiratory arrest and CPR was performed. During CPR, the animal was seen to vomit, and ingesta was aspirated, based on observation of the endotracheal

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tube. Ondansetron was administered to prevent additional vomiting, and antibiotic coverage was increased. The animal recovered from anesthesia, and was returned to home cage.

In the home cage, the animal developed open mouth breathing, and the heart rate decreased rapidly. CPR was attempted, but intubation was not successful, and the animal expired.

Necropsy findings revealed experimental myocardial infarction, with multifocal areas of myofiber fibrosis. Ingesta with bacteria and neutrophilic inflammation was seen in one out of three lung sections. There was mild mixed inflammation with mild edema and congestion in the trachea and larynx.

Based on the clinical course, laryngospasm is postulated as the cause of death, but cannot be definitively proven.

- ~~Animal was not properly fasted for prior to planned surgery, but they went forward with surgery after withholding food for a little longer. The surgery went fine, but afterward the animal vomited and was re-intubated, animal received and heartrate dropped very quickly. Airway problem but couldn't re-intubate and animal died. Histology not informative but some aspiration in lungs.~~ Reported at last IACUC meeting.
- April 13, breeding male acutely looked lethargic, vet examined, kidney was enlarged, started meds, kidney size decreased, put animal back in cage and it died. Several years ago he had an inguinal hernia surgery with~~,~~ hemi castration, and since then BUN and creatinine have been mildly elevated but stable~~blood values were a little off of this.~~ Histology indicated nephritis due to E.~~e~~ coli, and evidence of infection in other organs (pneumonia) suggesting sepsis and hematogenous infection.~~, etc. Animal went septic.~~

Clinical Cases:
- See IACUC site visit notes below

Behavior Management:
- McGuire animals are in pairs, Amendment in process for experiment, they'll be put in groups eventually.
- See IACU site visit notes below

IACUC Non-compliances:
- Fentanyl issue already reported.

Animal Observations noted during site visits:
- See IACUC site visit notes below

Animal Observations noted during site visits

WaNPRC AZ
Inspection date: 03-08-19

- The following animal records were reviewed and the cases discussed:
    - Z16358: Valley fever animal in AZ, Starting mucinex (pair-housed)
    - Z14141: Animal developed seizures while pregnant and infant given to another dam after it was born. She kept having seizures and was euthanized
    - Z19055: Infant had scabs on ischial pads, healed and fine (group housed in a compound)
    - A10181: She had a wound and was in the hospital, healed and wounded again last week. Doesn't do well in a compound. She's due to come to WA in the next couple of months.
    - Z19020: Still in nursery, he had aspiration pneumonia and he's doing well.
    - Z13090: Campylobacter positive, treated, was positive for Valley Fever, fecal recheck on May 6 and return to social group.

WaNPRC I-Wing
Inspection date: 03-18-19

- I023: Animal A07101 is noted to have significant alopecia. She is currently scored as a '3'. Are there any additional treatments/enrichment that can be provided?
    - This animal is in social housing with another female, she regularly gets extra enrichment.
    - Our student Zhu is doing a project with her- on whether overgrooming behavior is associated with temperament.
    - Was part of our leafy greens project
    - Other therapies tried have included wood, paint roller, extra foraging, extra EE, moving within room, moving to another room, social contact, and as mentioned, extra leafy greens

- I089U: Squirrel monkey in this cage has significant alopecia on his tail and is also MRSA+. Please check with Vet Services and confirm whether these two conditions are related.

    - Probably not related. This animal is not MRSA+, so the sign needs to be changed.

- I359: Animals Z13027, Z13093, Z11295. 3 nemestrina in this room that are singly housed. When inspectors looked at the records there is a note that they have been singly housed since Dec 2018. Please clarify this situation for me. Is there a record of Z13093 engaging in sterotopies?
    - Z11295 and Z13093 have been tried as a social pair but were aggressive - their play turns to aggression so BMS intervened.
    - Z13027 injured his male partner and would likely do better with a female- waiting for a single female from RR-wing/Western to move over to I-wing. BMS is hoping to get them socialized asap- Might consider him for compound breeding.
    - Would like females for each of these three males. It took a little while to identify available females that could be long-term partners with any of these males, i.e. those that weren't needed for breeding, weren't going on project or being shipped to the CDC, etc. There was also the possibility of Z13093 going to the TDP at one point.

- Z11295-prior 2017 case for GOG + ALO 3. Discharged when ALO reduced to 2.
- Z13093- currently flagged/being monitored for possibly picking at sex skin/ischial callosity; extra EE as therapy incl. foraging. Engages in Infrequent LS (reported 6x since 2015). Currently being re-evaluated for LS based on this referral.
- Z13027- Flagged for SAN- prior SAN case was in 2016; LS 0% in Oct/Nov 2018.

- I463: Animal A10256's right eye was red and squinty and there was evidence of a recent surgery. Please confirm that this animal's eye is okay.
  - Had surgery on 03-11-19. Resoved by 03-22-19 and post-op case closed
  - This animal is currently in long-term pair housing with another male, and will likely be departing this summer.

- Animal A13003 was noted on a form outside the room as being "back on full water". Please report back why this is the case. Was this a vet decision or is the monkey no longer on study?
  - This was a clinical decision.
  - He has been tried with all available partners in the room, but will be tried with another monkey when one of Dr. Horwitz's animals goes to necropsy soon, leaving behind a single monkey to try him with.
  - Flagged for LS 2019. Social is the treatment plan for this animal
  - Was a former ALO case in 2018. ALO improved. As of March 2019, ALO starting to increase again. BMS is monitoring

- Animal A15381 had red and puffy eyes. Please follow up with Vet Services.
  - She had also lost a lot of weight and everyone was giving her all kinds of treats. Probably allergic to something, so she was put on benedryl over the weekend and foods have been limited.
  - No social plans- animal permanently exempt
  - On limited treats- due to possible allergies

- I565: Animal Z10217: The external area of his chamber is encrusted with either dried blood/exudate/feces. The margins of the chamber are also encrusted and irritated looking.
  - Lab cleans the chamber once a week. Site visit on a Monday so it hadn't been done yet. Otherwise fine

- I029: Animals A17009 and A17007 are housed in adjacent cages, but have no physical access. When inspectors looked at the records it was noted that there is a 'cage safety concern' for these monkeys. Please get more information on this.
  - Have tried these two in G-C contact and they were neutral. They have been tried with multiple partners with no success. Will continue to monitor current G-C pairing.
  - A17009- prior GOG + ALO 3 cases in 2017 and 2018/2019. Flagged for GOG + ALO 3 now.
  - A17007- ALO 3- flagged- not a current behavior case. GOG not confirmed.
  - A17009 was labeled as a "cage buster". When BMS was doing an intro in the room he busted out the side-gate.

- I565: Animals Z14343 and Z15061, please indicate why animals are separated by an opaque barrier. Inspectors believe that they are listed on the wall as being in run through contact.
    - They are pair housed. They must have been separated for feeding and treating.

WaNPRC Western
Inspection date: 03-20-19

- 226: Animal A09096, noted soft stools and alopecia. Both issues had been identified by veterinary and behavioral management staff, respectively. Reviewed behavioral case record with Behavioral Management Staff.
    - Soft stool on and off for a while treated and stool is normal. Pregnant, and assigned to Adams. Uterine implants are scheduled for this week.
    - She was singly caged because she was pregnant so she was closed off from the male prior to birth. She went on jacket/tether training in April and moved to I089S on 4/16 for Adams.
    - Arrived in Seattle Aug 2018- came in with ALO 4. Has fluctuated between 3 and 4. Currently flagged for ALO 4.
    - ALO improved when she was in breeding social contact with a male in Jan.

- Animal Z15195, in compound showing some locomotor stereotypy. BMS to follow up.
    - Animal is housed in a compound with a group of females.
    - History of recurring rectal **prolapse**
    - LS 0% - March 2019 observations
    - Flagged in ARMS for GOG + ALO 4. Social, extra EE, foraging implemented.

- Animals Z15217 and Z15220, showing some locomotor stereotypy while in the room. BMS to follow up.
    - Both are in run-through, pair housing together.
    - Z15217- not a behavior case; LS observed Feb/March 0.56% (< 1%) LS
    - Z15220 flagged for ALO 3- not a case; GOG not confirmed; LS obs 0% April 2019

WaNPRC RR-Wing
Inspection date: 03-29-19

- Checked records of Animal A11250, notes outside door had commented on chronic diarrhea and meds left in cage. Clinical record indicated that, in addition to GI issues, this breeder female was not getting pregnant after multiple attempts. Recently transferred to Tissue Distribution Program.
    - Euthanized on April 9

WaNPRC ARCF
Inspection date: 04-15-19

- B282A (Housing): Animal A15112 on agenda for NHP Records Review at the end of the month (animal looks fine, but want to follow up on some notes that were posted about this animal).

- Many cases on this animals. Long term AIDS project. Had some injuries from partner during site visit. Chronic dermatitis so it's on benedryl. Nutritional support, as well.
- Animal is in run-through, pair housing with A15106. This pair is closed several times per day for NS and ART treatments, meds, etc.
- Dermatitis.
- Minor Wounds but no aggression witnessed; wounds healing; being monitored by BMS for possible self-directed behavior as well as social aggression.
- Flagged for ALO 3- GOG not confirmed.

- B289: Animal A10066 had scratch on nose and blood on cage bars; AG noted on observation log and notified vet for follow up.
  - Examined and it was superficial and a case wasn't open. He was in a run-through with female, so they were put in G-C and seems better.

From: Kelly Heffernan <ksh@uw.edu>
Sent: Wednesday, May 8, 2019 1:36 PM
To: Charlotte E. Hotchkiss
Subject: WaNPRC Records Review
Attachments: WaNPRC Records Review Notes- 04-29-19.docx

Hi Charlotte,

Sorry for the additional email, but I need clarification on the highlighted items in the document. My notes are a little incomplete and/or confusing to me now.

Appreciate your help.
Kelly

KELLY HEFFERNAN
Reviewer and Scientific Liaison
Office of Animal Welfare

Health Sciences Building Box 357160
1705 NE Pacific Street Seattle, WA 98195-7160
206.616.3625 / fax 206.616.5664
ksh@uw.edu / oaw.washington.edu

Dare 2 Care... | explore **UW's Compassion Fatigue Program**

From: cmali <cmali@uw.edu>
Sent: Wednesday, June 12, 2019 1:55 PM
To: Charlotte E. Hotchkiss
Subject: Z14141
Attachments: 19-041 (Z14141) histo.docx

Categories: Task listed

Hi Charlotte,

Please see the path report for Z14141 (attached).
Tess wrote a VERY thorough case history.

Bob may be able to provide you with some histo pics...

Let us know what we can help with!

Best,
Carolyn

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
Washington National Primate Research Center/University of Washington
Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Thursday, May 9, 2019 12:19 PM
To: Audrey Baldessari; Keith Vogel; Charlotte E. Hotchkiss; Kathryn A. Guerriero; Dean Jeffery; Jason D. Laramore; Tess House; cmali
Subject: 19-041 and 042 (Z19068 and Z14141)

Hi all:

Please find attached final reports on the above 2 cases. Interestingly, Z14141 was cerebral Valley Fever, and both animals were from the same dam who also was diagnosed clinically with Valley Fever.

Please contact me with any questions, comments or concerns.

Cheers
Bob

From: Jim Murphy <murphyjm@uw.edu>
Sent: Thursday, February 27, 2020 5:50 PM
To: rgrant
Subject: Re: Cocci tests

Hi Richard, I'll follow up with Carolyn and Amber tomorrow.

Jim

Get Outlook for Android <https://aka.ms/ghei36>

From: rgrant <rgrant@uw.edu>
Sent: Thursday, February 27, 2020 4:29:45 PM
To: Jim Murphy <murphyjm@uw.edu>
Subject: RE: Cocci tests

Hi Jim,

Have you all had a chance to think about this and decide if it will serve your purposes to have us run the Cocci ELISA here?

--Richard

From: Jim Murphy <murphyjm@uw.edu>
Sent: Tuesday, February 18, 2020 10:13 AM
To: rgrant <rgrant@uw.edu>; cmali <cmali@uw.edu>; aw656 <aw656@uw.edu>
Subject: FW: Cocci tests

Richard,

Thank you for all the well thought out and detailed information. Interesting article too. As you probably know, Lisa Shubitz has consulted with veterinarians and others here in the past. I am sharing this with the veterinarians here so they can decide what best fits their needs.

Jim

From: rgrant <rgrant@uw.edu <mailto:rgrant@uw.edu> >
Sent: Friday, February 14, 2020 3:51 PM
To: Jim Murphy <murphyjm@uw.edu <mailto:murphyjm@uw.edu> >
Subject: Cocci tests

Hi Jim

I calculated the cost per sample for the battery of tests we would use to screen the colony animals for cocci, if that is what you decide to do . It would be about $9.70 per sample. Your people and our people already do the work of drawing blood and sending it up here. We would use the same samples for the cocci tests . All we need is to buy the supplies for cocci.

As we discussed the other day, if we run cocci ELISA on all of the healthy colony AZ animals we would report a POS/NEG result. Is that acceptable to you and the veterinarians? It would no longer be a titer but in our experience this ELISA picks up >94% of the Protatek positives and it sometimes detects positives that Protatek calls negative. Those numbers will improve now that we have the confirmatory assay. The ELISA kit is about $700 per plate which allows us to run 90 samples, which is a little less than $8 per sample just to run the ELISA. BUT to help us solve any indeterminate results we would use a blot test that compares well to the tests run at Protatek (see attached paper). So if a sample comes up low reactive or indeterminate by ELISA we would run the confirmatory blot test (additional $19 per sample) . If we assume that about 10% of animals will require the confirmatory test it would increase the cost of 90 samples by $171. That would make the average cost per sample about $9.70 with those assumptions. Then you should always get a POS/NEG result and you would only need to send the same sample you are already sending to us anyway. Seems like a no-brainer for the regular colony screens if we save $20 per samples.

The ELISA has the capability of giving us IgM and IgG results too. If that is of interest to you all then it would cost another $8 per sample to get IgM. I am thinking that it might be good to run IgM and IgG on animals when they arrive in Seattle or right before you ship out in cases where the investigators need to exclude cocci exposed animals. I think our P51 and U42 budgets should cover the cost of running these as it’s an SPF type testing .

I’ll let you decide who else needs to be in the loop to make the decision on whether or not we should run these tests. For your clinical cases or suspected cases your veterinarians might be interested in this blot test, described in the paper, which give a rapid result in only about 30 minutes. Probably too expensive

to run on every animal but when you need a result fast it might be very helpful. I attached a paper comparing the lateral flow (blot test) to the immunodiffusion test they run at Protatek labs.

Data we have on the ELISA plates in our hands is shown below . These numbers should be even better with the addition of the confirmatory blot test but these numbers are using only the ELISA with the Protatek results from animal records as the gold standard.

N= 693

Meridian Cocci ELISA

Sensitivity

94.02%

Specificity

97.60%

Positive predictive value

95.24%

Negative predictive value

96.97%

Richard Grant

Primate Pathogen Detection Services Laboratory

WaNPRC

University of Washington

Seattle, WA 98195

206-543-1437

From: Jim Murphy <murphyjm@uw.edu>

Sent: Tuesday, February 18, 2020 10:13 AM
To: rgrant; cmali; aw656
Subject: FW: Cocci tests
Attachments: Cocci lateral flow test vs immunodiffision tests.pdf

Richard,

Thank you for all the well thought out and detailed information. Interesting article too. As you probably know, Lisa Shubitz has consulted with veterinarians and others here in the past. I am sharing this with the veterinarians here so they can decide what best fits their needs.

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96.97%

Richard Grant

Primate Pathogen Detection Services Laboratory

WaNPRC

University of Washington

Seattle, WA 98195

206-543-1437

From: Tess House <th81@uw.edu>
Sent: Tuesday, October 22, 2019 10:57 AM
To: rgrant
Subject: RE: Cocci tests and grant application

Hi Richard,

Sorry for the delay in response, we've been pretty busy with semiannual exams and the new animals! Kate is here this week and it has been so helpful to have an extra vet around as we navigate the new building and new animals.

Thanks so much for reaching out. I'm actually going to be leaving the center in January so Carolyn and Dr. Amber Fuller, our current part time vet that started, will be taking over what projects I've worked on. Long story short, my husband is a third year medical student and wants to do audition rotations during the end of 3rd year and the majority of 4th year to be more competitive for residency match. My daughter and I are going to go with him as he travels and we are focusing on areas with programs that are close to extended family so I have some help on the parenting front and will have the flexibility of doing relief work. I'm saddened to leave the center and working with NHPs yet simultaneously excited for my husband and seeing some of the potential places we could land for residency.

I think there is so much potential here for PCR on tissues and further evaluation of valley fever in the colony and will pass your message on to Carolyn and Amber.

Best,

Tess

From: rgrant <rgrant@uw.edu>
Sent: Thursday, October 17, 2019 9:28 AM
To: Tess House <th81@uw.edu>
Subject: Cocci tests and grant application

Hi Tess

I wanted to follow up on our previous discussion about cocci serology testing and the grants you have considered submitting. I would like our lab to be involved if you think there is a place for us, even if it's just serology of other detection methods. We could possibly generate some preliminary results by doing some PCR on tissues. We have worked out a method for t cruzi detection in tissues by PCR and I'm sure we could do the same for cocci if you thought that could add to the strength of a grant application.

Of course we can also run standard or custom antibody and antigen detection too.

-Richard

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

Medical Mycology, 2019, 0, 1–5
doi: 10.1093/mmy/myz067
Advance Access Publication Date: 0 2019
Original Article

Original Article

Evaluation of a commercially available, point-of-care *Coccidioides* antibody lateral flow assay to aid in rapid diagnosis of coccidioidomycosis in dogs

Sallianne Schlacks[1,*], Polina Vishkautsan[1], Christine Butkiewicz[2] and Lisa Shubitz[2]

[1]Department of Internal Medicine, Veterinary Specialty Center of Tucson, Arizona, USA and [2]Valley Fever Center for Excellence, University of Arizona, Tucson, Arizona, USA

*To whom correspondence should be addressed. Sallianne J Schlacks, DVM, Veterinary Specialty Center of Tucson, Arizona, USA. Tel: +520-795-9955; Fax: +520-795-9960; E-mail: saschlacks@gmail.com

Received 19 March 2019; Revised 19 May 2019; Accepted 29 May 2019; Editorial Decision 22 May 2019

Abstract

Coccidioidomycosis in dogs can range from mild respiratory disease or vague, chronic malaise to acute, severe life-threatening illness. The diagnosis of coccidioidomycosis in dogs is based on clinical presentation and serology. Spherule identification is not typical because of low numbers of organisms in specimens, and the invasive nature of sampling tissues and lungs. Conventional serological assays require samples to be submitted to a reference laboratory and results take several days to one week. The sōna *Coccidioides* Antibody Lateral Flow Assay (LFA) (IMMY Diagnostics) is a rapid, bench-side test used for detection of *Coccidioides* antibodies that is available and FDA-cleared for use in humans but has not been evaluated in dogs. The goal of this study was to compare the LFA to conventional agar gel immunodiffusion (AGID). Paired serum samples were collected for screening by the LFA and submitted to a commercial reference laboratory for AGID screen and titer. Of 56 paired serum samples analyzed, 30 were positive and 26 were negative on the sōna *Coccidioides* antibody LFA. The overall percentage agreement plus 95% confidence interval (CI) was 87.5% (76.20–93.99). Positive percent agreement was 89.7% (73.38–96.65) and negative percent agreement was 85.2% (67.25–94.36). The kappa coefficient to assess agreement was 0.749 (95% CI, 0.576–0.923), which is interpreted as good agreement between the tests (>70%). The sōna *Coccidioides* antibody LFA provided rapid, point-of-care results with a high level of agreement to standard AGID serology in dogs clinically suspected to have coccidioidomycosis, and may aid in diagnosis of coccidioidomycosis in dogs.

Key words: antibody detection, lateral flow assay, coccidioidomycosis, canine, Valley fever.

Introduction

Coccidioidomycosis is a fungal infection caused by the dimorphic, soil-dwelling fungi *Coccidioides immitis* or *Coccidioides posadasii*. The organism is endemic to the semiarid desert regions of southern and centraI California, southern Arizona, southern New Mexico, western Texas, southern Nevada and Utah, northern Mexico, parts of Central and South America[1] and more recently discovered in the soil of Washington state.[2,3] The infection is most typically acquired by inhalation of aerosolized arthroconidia from the soil. The organism transforms into spherules then endosporulates in the lungs.[1,4] The fungus may remain localized to the respiratory system causing pulmonary infection, or it can disseminate via the blood and lymphatics to virtually any other tissue in the body.[1,5]

Disease manifestation in dogs varies widely from subclinical infection or mild respiratory illness to acute, severe pulmonary infection, or fatally progressive disseminated disease.[1,6,7] Acute and critical illness can result from several different clinical scenarios, requiring rapid diagnosis, aggressive treatment and resolution. For example, respiratory compromise can occur

secondary to acute, fulminant fungal pneumonia, or pleural effusion secondary to fungal pleuritis.[5] Dyspnea and respiratory obstruction can also occur secondary to hilar lymph node enlargement, which is a hallmark feature of coccidioidomycosis in canine patients.[6,8] Dissemination of the organism to the pericardium can result in restrictive pericarditis with secondary right-sided heart failure exhibited as either pleural effusion or ascites.[1,6,8] Coccidioidomycosis of the central nervous system can result in seizures and changes in mentation, paresis, and paralysis.[6–8] In all of the above case manifestations, rapid diagnosis of the disease would be beneficial to help guide initial treatment and a diagnostic plan for the patient.

Diagnosis of coccidioidomycosis in dogs can be challenging due to the variety of clinical manifestations and lack of pathognomonic signs. Some of the clinical findings, such as hilar lymph node enlargement and presence of pulmonary nodules can mimic other disease processes such as neoplasia or other fungal infections. The gold-standard method of diagnosis is *Coccidioides* spherule identification by cytology or histopathology, or culture of the organism from tissues or fluids. Spherule identification and culture are not always feasible because of low presence of *Coccidioides* organisms in active lesions. In humans, the organism can be isolated and cultured from sputum or bronchoalveolar lavage sampling,[9,10] but recovery of the organism in this manner in dogs is rare.[1] Unless superficial lesions are present for sampling, both culture and cytology require invasive techniques including biopsy or fine needle aspiration of lungs, thoracic lymph nodes, and other internal lesions. Culture is also costly and turn-around time takes several weeks.

The presumptive diagnosis of coccidioidomycosis in dogs relies heavily on clinical signs, diagnostic imaging, and anti-coccidioidal serology. Agar gel immunodiffusion (AGID) is the most common method used for serological diagnosis of coccidioidomycosis in dogs. The AGID assay utilizes two antigens, complement fixation (CF) or tube precipitin (TP).[11] Previous studies in humans and dogs suggest that immunodiffusion of CF primarily detects immunoglobulin G (IgG) and immunodiffusion of TP detects immunoglobulin M (IgM).[5,11] The test is highly specific and can detect both IgM and IgG antibodies against *Coccidioides* spp. in a variety of host species.[12] The disadvantage of this method is that it requires submission to a laboratory, with a turnaround time of at least three days and up to a week, dependent on the laboratory and specimen transport times. It is also well-accepted that AGID titer results are variable among labs and laboratorians, making comparison of results between different commercial labs difficult.

MiraVista Diagnostics Laboratory (Indianapolis, IN, USA) has a recently validated proprietary enzyme immunoassay (EIA) that they perform to detect *Coccidioides* IgG antibody in dogs.[13] When evaluated in patients with proven or probable coccidioidomycosis it showed a sensitivity and specificity for IgG of 89.2% and 97.2%, respectively.[13] While this assay can be completed faster and is comparable to the sensitivity of the AGID, transport time for specimens to the laboratory from the most endemic areas for *Coccidioides* spp. could negate the advantages from more rapid running of the assay.

Recently, the sōna *Coccidioides* antibody lateral flow assay (IMMY Inc., Norman, OK, USA) was approved for use in humans by the Food and Drug Administration. This test uses a proprietary mixture of recombinant and native *Coccidioides* antigens, including CF and TP antigens, adsorbed to a nitrocellulose strip. Therefore, it should detect both IgM and IgG antibodies in serum. According to the developers of the test, the assay is not specific to humans nor does it rely on an anti-human antibody, so would not require modification for anti-coccidioidal antibody detection in dogs. The test can be easily performed in a veterinary clinic setting and results are available within 30 minutes. Data provided by the manufacturer showed good antibody detection agreement with both immunodiffusion and enzyme immunoassay results in humans.[14] A study performed by an outside institution showed specificity of 93.8% when serum from an endemic and non-endemic human population was tested.[15] While this test shows promise for increasing the speed of diagnosis of coccidioidomycosis in people, it has not been evaluated for use in dogs.

A rapid screening tool for canine patients for use in a critical care setting would be beneficial in providing early direction of treatment and additional diagnostics. The objective was to evaluate the potential of the sōna *Coccidioides* antibody lateral flow assay (Ab LFA) performance in dogs by comparing in-clinic LFA test results to AGID results performed by commercial laboratories in this novel study in dogs.

Methods

Serum was collected from canine patients who were presented to the Veterinary Specialty Center of Tucson (Tucson, AZ, USA) who were either previously diagnosed with active coccidioidomycosis or were naïve to diagnosis and coccidioidomycosis was a differential after clinical evaluation. For all patients, either submission of an AGID screen and titer to a reference lab was submitted at the same time, or a titer had been performed within six weeks prior to collection of serum for the LFA. There were four commercial laboratories used to perform the AGID titers, including Idexx Laboratories, Inc. (Westbrook, ME, USA), Protatek Reference Laboratory International Inc. (Mesa, AZ, USA), Antech Diagnostics (Fountain Valley, CA, USA) and the Arizona Veterinary Diagnostic Laboratory (The University of Arizona, Tucson, AZ, USA). For Antech and Idexx, the physical locations where the tests are performed are in the Phoenix, AZ, metropolitan area, or Irvine, CA, for Antech weekend submissions. The commercial laboratory where the AGID test was performed was chosen based on preference of the clinician submitting the test. Written consent was procured from pet owners to allow for

additional serum to be obtained for performance of both tests, and the test was performed at no cost to the owner.

The sōna *Coccidioides* Ab LFA test was performed either directly after collection, or serum was stored at 2–5°C and performed within five days, per manufacturer instructions.[14] The test was performed and interpreted by a single technician who was blinded to the AGID test results. Briefly, diluent provided by the manufacturer was used to prepare a solution of 1:441 diluted serum. A 100 μl aliquot of diluted serum was then transferred to a flat bottom tube. The test strip was inserted into the tube and results were read after 30 minutes incubation at room temperature. The presence of a red control line only was considered a negative result, and the presence of two red or pink lines was considered a positive result. The LFA results were recorded as either negative or positive. In addition, if the test line was a dark red, the result was recorded as a strong positive, and if a faint red or pink line, it was recorded as a weak positive. The AGID results for IgG or IgM were either collected from the patient record if ≤6 weeks since testing, or serum collected for LFA was split and submitted to a commercial laboratory for AGID serology. The results were recorded as either positive or negative for presence of IgM and IgG. If IgG antibody test was positive, the titer was recorded.

The results of the AGID and LFA were compared by agreement analysis. Data were analyzed in Microsoft Excel (2016) by calculation of overall, positive, and negative percent agreements to compare diagnostic tests.[16,17] Confidence intervals were determined using techniques appropriate for analysis of binomial data.[18] Data were migrated to GraphPad Prism 8.0 (GraphPad Software, San Diego, CA, USA). To further evaluate agreement between the tests, a kappa coefficient was determined.[19] The null hypothesis was that the test results would not agree.

Results

A total of 56 serum samples were collected and analyzed. Clinical and clinicopathologic presentations were similar among all the dogs in this study. Seizures and neurological signs were the most common reasons for testing, followed by fever, clinicopathological changes (leukocytosis, monocytosis, neutrophilia, hyperglobulinemia), osteomyelitis, arthropathy or musculoskeletal pain, cough and/or pulmonary changes on radiography, pleural or pericardial effusion, and peritonitis. Twenty-one dogs had been previously diagnosed with coccidioidomycosis and of those, 20 were currently taking antifungal medication, while the remaining dog had stopped three months prior to testing. For the other 35 dogs, clinical signs at the time of evaluation led to testing due to suspicion of coccidioidomycosis.

The sōna *Coccidioides* Ab LFA yielded 30 positive and 26 negative results, while the AGID yielded 29 positive and 27 negative results (Table 1). A majority of the samples were submitted to either Protatek ($n = 29$) or Idexx ($n = 24$), while two were submitted to Antech and one to the Arizona Veterinary Diagnostic Laboratory for performance of AGID testing. The overall percentage agreement was 87.5% (95% confidence interval [CI], 76.20–93.99). Positive percent agreement was 89.7% (95% CI, 73.38–96.65) and negative percent agreement was 85.2% (95% CI, 67.25–94.36). The kappa coefficient to assess agreement was 0.749 (95% CI, 0.576–0.923). This is interpreted as good agreement between the tests (>70%).

Table 1. Summary of results.

sōna *Coccidioides* Ab LFA	Agar immunodiffusion results	
	Positive	Negative
Positive	26	4
Negative	3	23

All numbers represent number of samples. Ab LFA, antibody lateral flow assay.

There were three samples that showed negative results on the LFA test and positive results on the AGID. Table 2 summarizes the discrepant results for the AGID IgG results and the LFA. The AGID IgM results for all patients were negative. Case 1 presented for acute febrile illness and an elevated white blood cell count was identified on lab work. Chest radiographs were unremarkable. Ultrasound showed an enlarged, cystic prostate. Fine needle aspiration cytology and culture of the prostate revealed bacterial prostatitis infection with *Escherichia coli*. Therefore, the weak positive titer result was likely indicative of previous exposure and not relevant to the patient's illness. Case 2 presented for follow-up investigation after discontinuation of fluconazole for previous infection. The patient was treated with fluconazole for 12 months, at which time it was clinically normal and fluconazole was discontinued. Three months post-treatment, the dog was not showing any clinical signs suggestive of coccidioidomycosis when serum for routine monitoring was tested by both LFA and AGID, so based on these test results, no changes to therapy were made. Case 3 had a serum titer checked for follow-up investigation of chronic coccidioidomycosis. The patient was taking itraconazole and had been receiving the medication for

Table 2. Summary of cases with discrepant results.

Case	sōna *Coccidioides* Ab LFA	AGID IgG titer	Clinical findings
1	Negative	<1:2	Acute fever, lethargy, anorexia
2	Negative	<1:2	F/U previous CM
3	Negative	1:4	F/U previous CM
4	Weak positive	Negative	F/U previous CM
5	Weak positive	Negative	F/U previous CM
6	Weak positive	Negative	Acute fever, lethargy, cough
7	Weak Positive	Negative	Weight loss, anorexia

Ab LFA, antibody lateral flow assay; AGID, agar immunodiffusion; CM, coccidioidomycosis; F/U, follow up; IgG, immunoglobulin G.

several years due to previously diagnosed disseminated disease (pulmonary and osteomyelitis lesion). The patient was clinically doing well with previous problems of neutrophilia, hyperglobulinemia, and lameness resolved. Based on radiographic findings, clinicopathological data, and physical exam, neither of these patients had signs of active coccidioidomycosis infection.

Four samples showed a positive result on the LFA but were negative on the AGID assay. All four of the samples were read as a "weak positive" on the LFA. Cases 4 and 5 were patients with a previous diagnosis of coccidioidomycosis and both were receiving antifungals at the time of blood draw. Neither patient had clinical signs of active coccidioidomycosis. They had both been taking medication for six months or longer. Case 6 was presented for acute, febrile illness, and coughing. Lab work showed neutrophilia, monocytosis, and hyperglobulinemia, highly suggestive of acute coccidioidomycosis. Case 7 was presented for acute pain around the muzzle and mild weight loss. Blood work showed mild neutrophilia and was otherwise normal. A convalescent titer measurement was recommended for both patients but was not pursued and the patients were lost to follow-up.

There were six samples that were noted as a strong positive on the LFA. A majority of the samples ($n = 5$) had titers ranging from 1:16 to >1:256. There was only one sample that had a correlating AGID titer of 1:4, and this sample was also positive for IgM. All of these cases had clinical signs and clinicopathologic data to support a diagnosis of active coccidiomycosis. There were 13 samples that were noted to be weakly positive—showed a faint red or pink line—on the LFA. Four of these samples were negative on the AGID and previously mentioned (see Table 2). Of the remaining nine samples, a majority correlated with titer result range of <1:2 to 1:4 ($n = 6$). Two samples were 1:16 and one sample was 1:8.

Discussion

The sōna *Coccidioides* antibody lateral flow assay showed good agreement with agar immunodiffusion results and was useful in providing a rapid screening assessment for patients suspected to have coccidioidomycosis. The assay procedure was easily taught and performed in the clinical veterinary setting.

It is noteworthy that all of the samples with discrepant positive LFA results correlated with a faint or weak red line, while a majority of the tests that showed a dark red line correlated with positive AGID titers that were at least ≥1:16, which is commonly accepted to indicate active disease.[20] The only sample that had a titer below 1:16 was also positive for IgM, typically associated with active disease when found in combination with a positive IgG result in dogs, and was possibly the cause of the strong color band. This suggests that when using the LFA as a screening tool in a critical care situation, a strong positive result could be interpreted with more confidence that a pending AGID titer will be positive and cocciodioidomycosis should be highly suspected. A negative result cannot be used to rule out the disease, but this is true of any serology test for coccidioidomycosis, including the AGID. It is widely accepted that negative serology does not rule out coccidioidomycosis in dogs, but the percentage of seronegative dogs with clinically important coccidioidomycosis is not currently known.[5]

Due to the design of this study, the cause of the discrepant test results for the seven samples cannot be ascertained from the available information. It is possible that the LFA may be more sensitive than the AGID, especially considering two patients who presented for acute illness had a positive result on the LFA. It would have been beneficial to recheck commercial serology later in these patients, or perform additional testing such as immunoglobulin EIA, but the recommended follow-up was not pursued by either client, so the true disease status remains unknown. The incongruent results could also be secondary to inherent imperfection of the test and nonspecific reaction of the LFA. In the data provided by the manufacturer, there was cross-reactivity among humans to *Histoplasma* spp., and we can assume the same would be true in canine patients (manufacturer pamphlet, unpublished data). Although the endemic regions of these two fungal diseases do not overlap in the United States, it must also be considered that there is a substantial amount of seasonal travel to the southwestern United States, so cross-reactivity to other endemic fungi should not be dismissed.[21] This can be easily assessed in a future study by testing serum from dogs diagnosed with histoplasmosis.

This study had several limitations, including a small sample size and lack of control groups. The data were also collected from one referral center in Tucson, Arizona, and therefore does not represent a wide endemic region. Because of these limitations, sensitivity and specificity of the test cannot be determined. A larger, prospective study to include confirmation of disease, as well as negative control groups from endemic and nonendemic regions would be necessary to determine the overall sensitivity and specificity of this test in dogs. Our patient population in this study was also highly variable with some patients having the test performed for follow up purposes and others who were highly suspected to have acute, active infection, which could have affected the specificity of the test. It would be beneficial to design a study to assess the performance of the LFA in a controlled population, strictly assessing patients in a critical care setting that are suspected to have acute coccidioidomycosis. Finally, because AGID titer results can vary between commercial laboratories, controlling submission of samples to one single commercial lab would also eliminate some data variability and improve the study design.

Coccidioidomycosis continues to be a diagnostic challenge for clinicians, and in a critical care setting when a patient is acutely, severely ill, the ability to differentiate this disease from neoplastic disease, which carries a poorer prognosis, is vital. While we

believe assessment of agar gel immunodiffusion in the acute and convalescent time frame should, for the time being, remain the standard diagnostic of choice, these data suggest sōna *Coccidioides* antibody lateral flow assay to be a valuable diagnostic tool for rapid detection of *Coccidioides* antibodies in sera of clinically suspected dogs, and showed good agreement with AGID results. It requires no specialized equipment and can be performed in veterinary clinics with relative operator ease. However, as with any tool used for diagnosis of coccidioidomycosis, the result must be interpreted within the context of history, clinical signs and other diagnostic findings. Future studies that evaluate sensitivity and specificity of this test with a larger sample size in various clinical settings would be useful to further characterize the diagnostic utility of this rapid, in-clinic test.

Acknowledgments

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and the writing of the paper.

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From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Friday, May 24, 2019 9:21 AM
To: Sally Thompson-Iritani
Subject: FW: 19-041 and 042 (Z19068 and Z14141)
Attachments: 19-040 (Z19068) histo.docx; 19-041 (Z14141) histo.docx

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From: Robert D. Murnane
Sent: Thursday, May 9, 2019 12:20 PM
To: Audrey Baldessari <aeb4@uw.edu>; Keith Vogel <vogelk@uw.edu>; Charlotte E. Hotchkiss <chotchki@uw.edu>; Kathryn A. Guerriero <kag18@uw.edu>; Dean Jeffery <daj12@uw.edu>; Jason D. Laramore <jasonl73@uw.edu>; Tess House (th81@uw.edu) <th81@uw.edu>; Carolyn Malinowski <cmali@uw.edu>
Subject: 19-041 and 042 (Z19068 and Z14141)

Hi all:

Please find attached final reports on the above 2 cases. Interestingly, Z14141 was cerebral Valley Fever, and both animals were from the same dam who also was diagnosed clinically with Valley Fever.

Please contact me with any questions, comments or concerns.

Cheers
Bob

University of Washington
National Primate Research Center

Accession #___19-040_
Submission Date_20 Mar 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester____TH_____ Investigator___Hotchkiss_____ Animal ID #___Z19068_
Species_____Mn____ Requester's Phone___5-1842_____

Date of Death__03/06/19_____ Date of Necropsy 03/06/19 Time_1300__Pathologist ____TH____

Nutritional Condition: ☐ Adequate X Marginal ☐ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other_____

Other Diagnostic Samples _____

Type of report: ☒ Final __9 May 19____ ☒ Preliminary _____ ☐ Amended _____

Clinical History:

Infant delivered overnight and found dead in the enclosure (181) when husbandry staff arrived in the morning. The dam (L03132) was sedated for her semi-annual exam on 03/04/19 and based on measurements at that time, the estimated due date was 03/22/19. The infant was positioned head down and the placenta appeared normal. Fetal heart rate at that time was normal as well (210 bpm). There were no significant abnormalities on the dam's exam that day other than a BCS of 4/5 and moderate dental calculus.

The dam has a history of a natural nonviable birth in 2013 and had viable births in 2014, 2015, and 2016. The dam was positive in the past for valley fever and had been on treatment until September 21st, 2018. She was discontinued from treatment after having a year of negative cocci titers. One of her previous births (infant born in 2014) is a current valley fever case.

The majority of the placenta could not be recovered from the group enclosure but very small portions of it observed in the bedding appeared normal.

Gross Description:

A 0.48 kg (BCS 2.5/5) female Macaca nemestrina is presented for necropsy.

Externally there are two abrasions on the ventral abdomen and inguinal region consistent with postmortem trauma. (When the infant was removed from the group enclosure, the dam reached through the mesh to grab at the infant's rear legs.) No other signs of bruising, bleeding, or trauma noted; no breaks in the skin were identified. A small amount of dark, fluid feces was present around the rectum and a rectal swab was collected and submitted. A small portion (about 2 cm) of the umbilicus was attached and appeared normal; this was submitted for histopathology.

Upon internal examination, the liver, gallbladder, stomach, kidneys, adrenal glands, intestines, bladder, and reproductive organs appeared normal. The spleen was of normal shape, consistency, and color but

subjectively appeared slightly smaller than expected. The heart appeared normal and no free fluid was found within the thoracic cavity. The cranial left lung lobe was mottled in appearance and had areas of dark red mixed with a light cream color. No exudate was noted on cut cross section and the lobe would partially float in formalin. The remaining lung lobes on the left side and the entirety of the right side were dark red in color and sank in formalin. These lung lobes did not have exudate on cross section.

A small area (about 1 cm in diameter) of hemorrhage was noted in the left occipital region of the brain. No fractures of the cranium were noted and the skull and brain appeared otherwise normal. The cerebellum and brain stem appeared normal. There was no hematoma or bruising noted in the skin overlying the occipital region. Animal husbandry did comment that the dam was on a perch in the enclosure and dropped the deceased infant when they went to shift her to a different enclosure.

Gross Diagnosis(es):

1. Stillbirth

Histological Findings:

Lungs are uninflated and have diffuse, moderate, deep aspiration of amniotic cells and debris. There also is extensive congestion.

Sections of brain, spleen, adipose (adequate), lymph node, pancreas, liver, heart, kidneys, skin with umbilicus, and umbilical cord are unremarkable.

Final Principal Diagnosis(es):

1. Moderate, diffuse, deep aspiration of amniotic cells and debris with uninflated lungs

Histology Comments:

Amniotic cells and debris within alveoli without inflammation and noninflation of the lungs are consistent with agonal aspiration due to fetal distress. This finding in concert with lack of other overt lesions suggests stillbirth due to dystocia.

Please contact either of us with any questions, comments or concerns.

Pathologist__TH(gross)/RM (histo)_____

University of Washington
National Primate Research Center

Accession # 19-041
Submission Date 20 Mar 19

DIAGNOSTIC LABORATORY NECROPSY REPORT

Requester TH/CM Investigator Hotchkiss Animal ID # Z14141
Species Mn Requester's Phone 5-1842

Date of Death 03/13/19 Date of Necropsy 03/13/19 Time 1100 Pathologist TH/CM

Nutritional Condition: ☒ Adequate ☐ Marginal ☐ Poor ☐ Obese

Other Tests Required: ☐ Sero ☐ Micro ☐ Parasit ☐ Other_____

Other Diagnostic Samples ____CSF (cryovial)_____

Type of report: ☒ Final _9 May 19_____ ☒ Preliminary _____ ☐ Amended _____

Clinical History:

A 4 year, 10 month old, 8.23 kg female pigtail was presented for necropsy in good condition. She was negative for valley fever on cocci titers leading up until April 16th, 2018 when she was tested at the time of semi-annual exams. She had been noted around this time for coughing and radiographs showed a moderate bronchointerstitial pattern bilaterally. She was started on an oral dose (100 mg) of fluconazole. On May 8th, 2018 she was observed favoring her right hand and had superficial abrasions on D3 and D4 and a short course of NSAIDs were added to ther treatment plan. A week later, on May 15th, 2018 she was observed with bilateral epistaxis and did not want to turn her head side to side. She was removed from her social group and started on amoxicillin and a short course of prednisone. The epistaxis resolved but reluctance to turn her head was noted on May 17th, 2018. She was sedated again on May 23rd for a follow up cocci titer and full body radiographs. No evidence of compressed disc spaces, reactive bone, or spondylosis were noted, lungs appeared stable. On physical exam under sedation, there was normal ROM of the head and neck. She appeared to be improving and was returned to her social group on May 30th and continued on fluconazole. On June 21st, she was noted for audible breathing and albuterol was started as well as a short course of prednisone. A slight cough and audible breathing was noted on July 3rd, particularly when active or excited and a short course of prednisone given. On July 30th she would not come up to the front of the group enclosure to take her treatment and appeared ataxic and uncoordinated. She was sedated for an exam, blood work, and radiographs. Her lung sounds were slightly increased on inspiration on the left side but not the right and radiographic changes were mild on the left side. The CBC had a machine error and the chemistry showed a slightly decreased GGT that may have been a machine error and a low albumin (2.7). The cocci titer showed a decreased IgG (see table below). On August 27th, she was noted to be coughing again and a tapered course of prednisone was tried this time. Two days later, she was found seizing prior to receiving her morning dose of fluconazole. Leading up to the seizure, she was noted to be ataxic on the left side and tossing her left arm in a rhythmic pattern towards her chest. By the time that the vet tech had called the veterinarian, the seizure had stopped. She was given her fluconazole and a dose or oral diazepam for any refractory seizures and moved from her social group to a single cage. Shortly after being moved to the cage, she seized again and an injection of diazepam was given, which she responded to quickly. The following day (August 30th) she was sedated for another exam, blood work, cocci titer, and radiographs. Both lung fields had increased sounds on inspiration and a mild bronchointerstitial pattern

was noted (vertebrae appeared normal). There was a moderate hypoproteinemia and a mild neutrophilia. On September 25th, another seizure occurred and she was sedated for exam. There were bilateral increased lungs sounds on inspiration but no other abnormalities found on exam. A CBC showed a mild leukocytosis and the ALP was unremarkable. Pregnancy was discovered on ultrasound on this exam. The third observed seizure occurred on October 15th and long term antiepileptic medication was started. Initially daily oral diazepam was given until levitracetam and gabapentin could be acquired. A break through seizure was noted on November 9th and responded quickly to injectable diazepam. The animal had not yet received her doses of gabapentin, levitracetam, or fluconazole for the day when that occurred. Another break through seizure was observed on December 15th in the morning, when she had consumed about half of her morning medications and responded to an injection of diazepam. She was noted to be increasingly difficult to medicate (would try to pick out pills) so oral formulations of levitracetam and gabapentin were obtained from a compounding pharmacy. She seemed to do better with oral liquid medications but continued to have break through seizures, with another observed on January 4th which again responded to injectable diazepam. After discussion and concerns were raised with respect to seizures and the stress of the impending labor, a C-section was elected and performed on January 10th. The surgery went smoothly and additional pain meds and antibiotics were added to her treatment plan. The infant was reintroduced following recovery but the dam would hold the infant very tightly around the neck and would not allow the infant to nurse for very long so the infant was removed. The doses of oral levitracetam and gabapentin were adjusted as her weight changed following the pregnancy and she continued on 100 mg of fluconazole. A break through seizure was observed on March 6th which responded to injectable diazepam and endpoint set for March 13th.

Cocci	Panel Comments	IgG Titer Result	IgG Titer Value	IgM Titer Result	IgM Titer Value
1/10/19		positive (+)	1:4	negative (-)	<1:1
10/29/18		positive (+)	1:2	positive (+)	1:2
9/25/18		positive (+)	1:8	positive (+)	1:2
8/30/18		positive (+)	1:32	positive (+)	1:2
7/30/18		positive (+)	1:4	negative (-)	<1:1
5/23/18		positive (+)	1:32	positive (+)	1:2
4/16/18		positive (+)	1:16	positive (+)	1:4

Note that cocci titers were done in 2014-2016 and were negative. No titer was done in 2017.

Gross Description: There was a moderate amount of subcutaneous fat noted during necropsy and a significant amount of intrabdominal and pericardial fat. There were some mild adhesions of the subcutaneous fat over the linea alba from the previous C-section incision.

The liver had slightly rounded edges but appeared otherwise normal on gross appearance and there were no abnormalities of the gallbladder appreciated. Several sections of the liver were submitted including a section with a portion of the gallbladder attached.

The stomach, intestines, pancreas, kidneys, adrenals, spleen, and bladder appeared normal. There was a moderate amount of digesta within the stomach and intestines that was of normal consistency and appearance.

The uterus had several small adhesions over the previous C-section incision site and what appeared to be a small amount of suture material present. The ovaries and uterine horns appeared normal. Externally, mild to moderate tumescence was noted.

The lung lobes were mottled and of varying shades of pink and dark pink or red. There were numerous small (1-2 mm) multifocal white nodules throughout all lung fields. Several adhesions were present

between the right cranial lung lobe and the thoracic wall. No free fluid was present within the thorax and no exudate noted on cut cross section of the lungs. All sections of lung tissue floated in formalin. There were no gross abnormalities of the heart other than the pericardial fat previously mentioned.

The brain and a small portion of the spinal cord were removed from the skull. No gross abnormalities were appreciated.

Blood samples were collected for cocci titer and serum chemistry and complete blood count but, unfortunately, were severely clotted. Attempts to run the samples on in-house machines resulted in errors.

A small amount of CSF was collected and submitted in a cryovial. Attempts to collect joint fluid from both stifles were unsuccessful.

Gross Comments:

While no abnormalities of the CNS were identified, valley fever is suspected as the cause of the seizures and histopathology is pending.

Histological Findings:

In the cerebrum, there are regional, multifocal and coalescing pyogranulomas and granulomas with numerous giant cells, Mott cells and rare organisms consistent with *Coccidiodes* sp, and the lesions cause extensive, regional effacement of neuropil. There also is regional, chronic-active, leptomeningitis. Spinal cord is unremarkable.

Lungs have diffuse congestion and edema (agonal), and two, small, alveolar nodules of granulomatous and fibrosing inflammation, and also mild to moderate perivascular, peribronchial and peribronchiolar lymphohistiocytic aggregates and pneumoconiosis.

Stomach, small intestine and large intestine have mild to moderate lamina propria infiltrate of/increase in eosinophils, lymphocytes, plasma cells, and macrophages. The small intestine has moderate villar blunting and fusion, and some regions with moderate goblet cell hyperplasia.

Sectons of lymph nodes, spleen, liver (mild lobular collapse and scattered, mild lymphohistiocytic aggregates), gall bladder, heart (moderate steatosis of atria, and mild megalo- and dyskaryosis), kidneys (mild diffuse membranoproliferative change of glomeruli and focal minor interstitial lymphohistiocytic aggregate), skin with mammary gland, muscle, and pancreas are unremarkable besides stated minor changes.

Final Principal Diagnosis(es):

1. Severe, regional-multifocal-cerebral, pyogranulomas and granulomas with rare organisms consistent with *Coccidiodes* sp: **Cerebral coccidiodomycosis**
2. Mild, bi-focal, granulomatous and fibrosing pneumonia
3. Mild to moderate, diffuse, eosinophilic, lymphoplasmacytic and histiocytic gastro-entero-colitis with enteric villar blunting and fusion, and with near-diffuse, large intestinal spirochetosis

Histology Comments:

Clinical CNS signs and demise were due to cranial Valley Fever. Additionally, the chronic lung lesions were likely from past Valley Fever as well.

Diagnosis #3, which can cause diarrhea and potentially other sequelae thereof, represents typical changes in this species in this colony, and they have been previously discussed. Changes present are consistent with food allergy/hypersensitivity/dietary intolerance/IBD. Please contact me if you wish to discuss these changes further.

Please contact any of us with any questions, comments, or concerns.

Pathologist__TH/CM (gross)/RM (histo)___

From: Robert D. Murnane
Sent: Tuesday, October 29, 2019 2:32 PM
To: Tess House; Kathryn A. Guerriero; wanprc_vets@uw.edu; Carolyn Malinowski
Subject: RE: Z17170

For sure a sigh of relief!!

Oh, it also had secondary amyloidosis and IBD…

Case report would work for sure, but what would be better is for someone/anyone to write up the case series to date!! Pretty easy to do and you could focus on just gross and histo of the cases we've had

Cheers
Bob

From: Tess House <th81@uw.edu>
Sent: Tuesday, October 29, 2019 2:23 PM
To: Kathryn A. Guerriero <kag18@uw.edu>; Robert D. Murnane <rmurnane@uw.edu>; wanprc_vets@uw.edu
Subject: RE: Z17170

A huge sigh of relief for us that it's VF and not TB-thank you Bob!!!

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Kathryn A. Guerriero
Sent: Tuesday, October 29, 2019 2:19 PM
To: Robert D. Murnane <rmurnane@uw.edu>; wanprc_vets@uw.edu
Subject: Re: [Wanprc_vets] Z17170

Glad that this was just valley fever (and not TB).

Kate

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Robert D. Murnane
Sent: Tuesday, October 29, 2019 2:14 PM
To: wanprc_vets@uw.edu
Subject: [Wanprc_vets] Z17170

Hi all (especially ABC vets!)

Disseminated valley fever EVERYWHERE:

Hilar nodes, lungs, rib, bone above eye, sternum, liver, kidneys, lungs, multiple abscesses….

Final report to follow soon.
Cheers
Bob

From: Robert D. Murnane
Sent: Tuesday, October 29, 2019 2:14 PM
To: wanprc_vets@uw.edu
Subject: Z17170

Hi all (especially ABC vets!)

Disseminated valley fever EVERYWHERE:

Hilar nodes, lungs, rib, bone above eye, sternum, liver, kidneys, lungs, multiple abscesses….

Final report to follow soon.
Cheers
Bob

RE: Infant fluconazole and Serum fluconazole projects

Tuesday, March 10, 2020 11:52 AM

Subject	**RE: Infant fluconazole and Serum fluconazole projects**
From	Charlotte E. Hotchkiss
To	Tess House; aw656
Cc	cmali; Sally Thompson-Iritani
Sent	Tuesday, December 24, 2019 11:48 AM
Attachments	 Fluconazole statistics

I did try to run statistics on the infant data. Unfortunately, I got different results depending on how I set up the statistical model. Most of it I understand, but there are a few places I got really weird results and I don't know why. I've attached my summary.

Charlotte

From: Tess House <th81@uw.edu>
Sent: Wednesday, December 18, 2019 2:36 PM
To: aw656 <aw656@uw.edu>
Cc: cmali <cmali@uw.edu>; Charlotte E. Hotchkiss <chotchki@uw.edu>; Sally Thompson-Iritani <sti2@uw.edu>
Subject: Infant fluconazole and Serum fluconazole projects

Hi Amber,

The two VF related projects can be found below:

1) Infants exposed to fluconazole during pregnancy (comparison of body weights project that Adam and Rose also contributed a great deal on with respect to initial data organizing)

   Z:\Arizona\Vet Services\Miscellaneous\Infant weight and fluconazole exposure

2) Serum fluconazole levels in animals on the fluconazole impregnated feed. There was a group of juveniles/young adults in 171 (at the time) on the feed that we looked at first and then later we looked at the 242 group (now the animals in 232) and compared them to other adults on fluconazole tablets. This project included the negotiation by John Hasenau to include Cyndi Holland of Protatek and Nathan Weiderhold from UT San Antonio Fungal Lab on as co-authors. The intention was for Rose and I to work on project 1 first and then tackle this project next.

   Z:\Arizona\Vet Services\Miscellaneous\Serum Fluconazole Level Testing

   Last contact information for Drs. Holland and Weiderhold are:

   Cyndi Holland: cholland@pharmgate.com, phone is 480-545-8499, fax 480-545-8409 (note that even though these are Az numbers, she's based in Minneapolis/St. Paul)

Nathan Weiderhold: wiederholdn@uthscsa.edu, phone is 210-567-4086, fax 210-614-4250

I'm leaving John Hasenau's business card on your desk for you this afternoon. Let me know if you think of anything else. I'll try to hunt down the MoU for Drs. Holland and Weiderhold so you have that as well (finance should have it too).

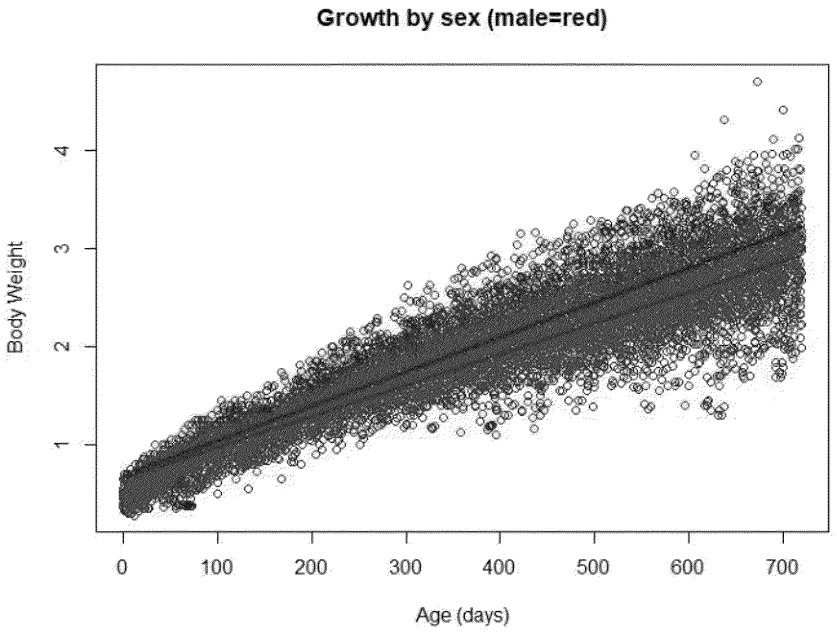
Tess

Theresa (Tess) House, DVM MPH
Supervisory Veterinarian
Washington National Primate Research Center
Arizona Breeding Colony
Office phone 206.685.1842
Mailing address- P.O. Box 20836/Mesa, AZ 85277

I couldn't figure out exactly what Rose did, but here's what I came up with. First, I put everything and every interaction into the model with the infant as a random effects, and here's what I got:

```
> Day_sex_fluc_model <- lmer(weight ~ Day + Sex + fluc + Day*fluc + Day*Sex +
(1 | Infant),data=fluc_data)
> Day_sex_fluc_model
Linear mixed model fit by REML ['lmerMod']
Formula: weight ~ Day + Sex + fluc + Day * fluc + Day * Sex + (1 | Infant)
   Data: fluc_data
REML criterion at convergence: -4255.703
Random effects:
 Groups   Name        Std.Dev.
 Infant   (Intercept) 0.2302
 Residual             0.1854
Number of obs: 10654, groups:  Infant, 389
Fixed Effects:
(Intercept)          Day         SexM      flucPos  Day:flucPos     Day:SexM
  0.7030858    0.0030465    0.0368791   -0.0402257    0.0001362    0.0003569
> anova(Day_sex_fluc_model)
Analysis of Variance Table
         Df Sum Sq Mean Sq    F value
Day       1 3569.9  3569.9 103897.776
Sex       1    1.5     1.5     44.661
fluc      1    0.0     0.0      0.002
Day:fluc  1    0.9     0.9     26.902
Day:Sex   1   10.7    10.7    312.546
```

This shows the effects of all the factors on body weight. Unfortunately, it doesn't give P values. Using an online calculator, the "Day" factor (age of the infant) is significant (P=0.002) and the "Day:Sex" (interaction of age and sex) is significant (P=0.036).



The data is similar if the infants without known gestation lengths are removed from the calculations:

```
Day_sex_fluc_diff_model <- lmer(weight ~ Day + Sex + fluc + Difference + Day*
fluc + Day*Sex + (1 | Infant),data=fluc_data_nopremNA)
> Day_sex_fluc_diff_model
Linear mixed model fit by REML ['lmerMod']
Formula: weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
(1 | Infant)
   Data: fluc_data_nopremNA
REML criterion at convergence: -3871.984
Random effects:
 Groups   Name        Std.Dev.
 Infant   (Intercept) 0.2318
 Residual             0.1869
Number of obs: 10137, groups:  Infant, 369
Fixed Effects:
(Intercept)          Day         SexM      flucPos   Difference  Day:flucPos
Day:SexM
  0.6990467    0.0030388    0.0367093   -0.0432946    0.0025982    0.0001426
0.0003596
> anova(Day_sex_fluc_diff_model)
Analysis of Variance Table
           Df Sum Sq Mean Sq    F value
Day         1 3433.5  3433.5 98274.7793
Sex         1    1.5     1.5    41.7191
fluc        1    0.0     0.0     0.0003
Difference  1    0.2     0.2     4.3563
Day:fluc    1    0.9     0.9    25.8495
Day:Sex     1   10.5    10.5   299.7611
```

Instead of just using the variable of fluconazole yes/no, I tried it with the days of fluconazole exposure as a variable (and excluding infants where it was not known whether or not they were premature):

```
> Day_sex_cont_diff_model <- lmer(weight ~ Day + Sex + Exptotal + Difference
+ Day*Exptotal + Day*Sex + (1 | Infant),data=fluc_data_nopremNA)
Warning message:
Some predictor variables are on very different scales: consider rescaling
> Day_sex_cont_diff_model
Linear mixed model fit by REML ['lmerMod']
Formula: weight ~ Day + Sex + Exptotal + Difference + Day * Exptotal +
    Day * Sex + (1 | Infant)
   Data: fluc_data_nopremNA
REML criterion at convergence: -4022.829
Random effects:
 Groups   Name        Std.Dev.
 Infant   (Intercept) 0.2308
 Residual             0.1853
Number of obs: 10137, groups:  Infant, 369
Fixed Effects:
 (Intercept)           Day          SexM      Exptotal    Difference  Day:Exp
total      Day:SexM
   7.059e-01     3.015e-03     4.364e-02    -9.509e-04     2.593e-03     3.36
5e-06     3.422e-04
fit warnings:
Some predictor variables are on very different scales: consider rescaling
> anova(Day_sex_cont_diff_model)
```

```
Analysis of Variance Table
             Df Sum Sq Mean Sq    F value
Day           1 3433.0  3433.0 99951.3647
Sex           1    1.4     1.4    42.0872
Exptotal      1    0.0     0.0     0.1041
Difference    1    0.1     0.1     4.3066
Day:Exptotal  1    7.8     7.8   226.1612
Day:Sex       1    9.5     9.5   276.2643
```

That gave a significant interaction for age by days of fluconazole exposure during pregnancy (P = 0.042), but threw an error message, so I don't know if I believe it.

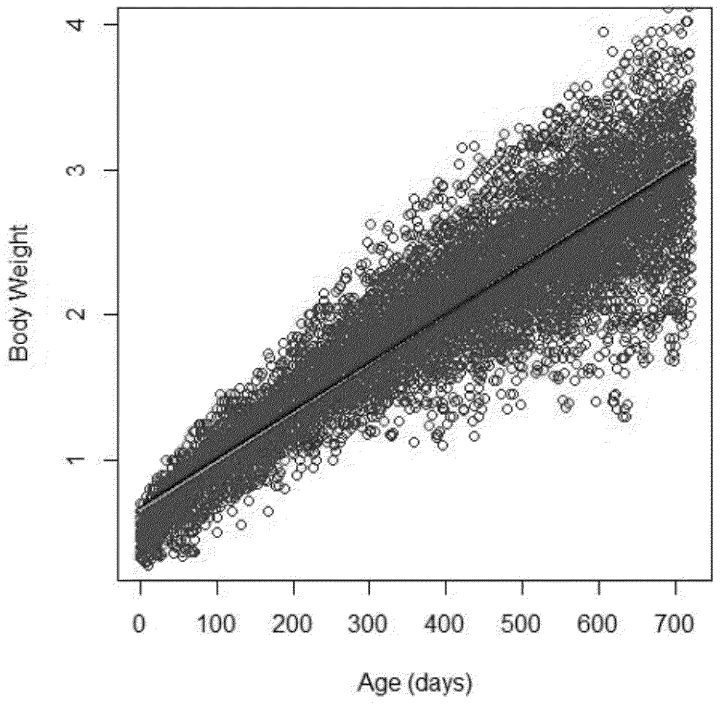
Then I tried the model again using a different R formula (lm instead of lmer), and using each infant as a fixed effect rather than a random effect, and got something where everything is significant, but I don't believe it:

```
Day_sex_cont_diff_model <- lm(weight ~ Day + Sex + Exptotal + Difference + Da
y*Exptotal + Day*Sex + Infant,data=fluc_data_nopremNA)
anova(Day_sex_cont_diff_model)
Analysis of Variance Table

Response: weight
               Df Sum Sq Mean Sq    F value  Pr(>F)
Day             1 4931.4  4931.4 1.4356e+05 < 2e-16 ***
Sex             1   68.1    68.1 1.9834e+03 < 2e-16 ***
Exptotal        1    4.8     4.8 1.4003e+02 < 2e-16 ***
Difference      1    0.2     0.2 6.4924e+00 0.01085 *
Infant        365  545.8     1.5 4.3533e+01 < 2e-16 ***
Day:Exptotal    1    7.6     7.6 2.2249e+02 < 2e-16 ***
Day:Sex         1    9.3     9.3 2.6962e+02 < 2e-16 ***
Residuals    9765  335.4     0.0
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

I got similar results with fluconazole yes/no instead of exposure days:

```
> lm_model <- lm(weight ~ Day + Sex + fluc + Difference + Day*fluc + Day*Sex
+ Infant,data=fluc_data_nopremNA)
> anova(lm_model)
Analysis of Variance Table

Response: weight
             Df Sum Sq Mean Sq    F value    Pr(>F)
Day           1 4931.4  4931.4 141135.072 < 2.2e-16 ***
Sex           1   68.1    68.1   1949.926 < 2.2e-16 ***
fluc          1    0.2     0.2      5.446  0.019633 *
Difference    1    0.3     0.3      8.187  0.004228 **
Infant      365  550.4     1.5     43.156 < 2.2e-16 ***
Day:fluc      1    0.9     0.9     26.066 3.362e-07 ***
Day:Sex       1   10.2    10.2    293.055 < 2.2e-16 ***
Residuals  9765  341.2     0.0
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

But, as I said, I don't really believe it is significant, because look at the graph.



The red dots and the orange line are the fluconazole-exposed infants; the blue dots and the black line are the untreated.

There's supposed to be a way to do a step test, where you add or subtract factors into and out of a linear regression model, and figure out whether the factor significantly affects the model. I think that is what Rose was doing. I ran something called a stepAIC and got results, but I don't know what they mean:

```
> step_test <- stepAIC(lm_model, direction="both")
Start:  AIC=-33635.47
weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
    Infant


Step:  AIC=-33635.47
weight ~ Day + Sex + fluc + Infant + Day:fluc + Day:Sex

            Df Sum of Sq    RSS    AIC
<none>                   341.20 -33635
- Day:fluc   1      1.22 342.42 -33601
- Day:Sex    1     10.24 351.44 -33338
- Infant   366    545.43 886.63 -24687
> step_test$anova
Stepwise Model Path
Analysis of Deviance Table
```

```
Initial Model:
weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
    Infant

Final Model:
weight ~ Day + Sex + fluc + Infant + Day:fluc + Day:Sex


          Step Df     Deviance Resid. Df Resid. Dev       AIC
1                                  9765   341.1984 -33635.47
2 - Difference  0 1.136868e-13      9765   341.1984 -33635.47
>
```

It looks like it wants to take out the Difference (that's the difference between due date and delivery date) but it doesn't change the AIC.

Then I tried to compare two models, one including fluconazole and one without it, and I got a significant P value, but again, I'm not sure whether or not I believe it:

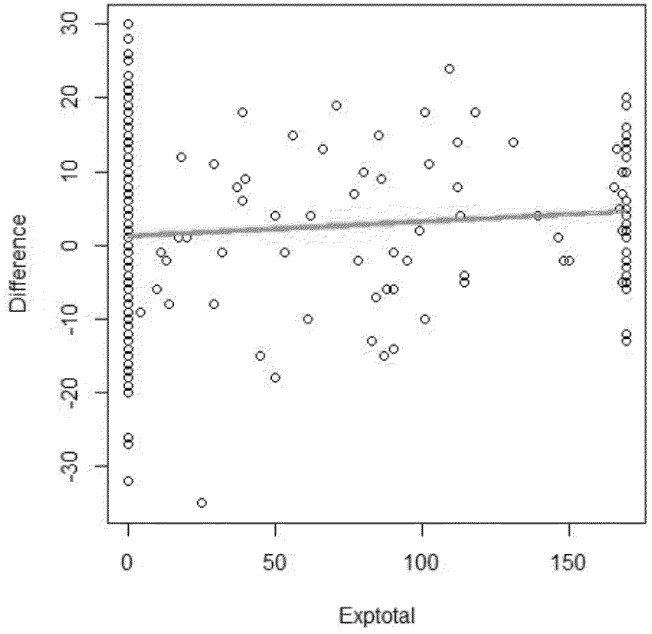
```
> lm_model_short <- lm(weight ~ Day + Sex + Difference + Day*Sex + Infant,dat
a=fluc_data_nopremNA)
> anova(lm_model_short)
Analysis of Variance Table

Response: weight
             Df Sum Sq Mean Sq    F value    Pr(>F)
Day           1 4931.4  4931.4 1.4065e+05 < 2.2e-16 ***
Sex           1   68.1    68.1 1.9432e+03 < 2.2e-16 ***
Difference    1    0.3     0.3 7.9665e+00  0.004775 **
Infant      366  550.6     1.5 4.2905e+01 < 2.2e-16 ***
Day:Sex       1    9.9     9.9 2.8317e+02 < 2.2e-16 ***
Residuals  9766  342.4     0.0
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
> anova(lm_model_short,lm_model)
Analysis of Variance Table

Model 1: weight ~ Day + Sex + Difference + Day * Sex + Infant
Model 2: weight ~ Day + Sex + fluc + Difference + Day * fluc + Day * Sex +
    Infant
  Res.Df    RSS Df Sum of Sq      F    Pr(>F)
1   9766 342.42
2   9765 341.20  1    1.2216 34.962 3.475e-09 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Then I switched gears, and tried to see if there was an effect of fluconazole on length of gestation. It seems there is:

```
prem_fluc_model <- lm(Difference ~ Exptotal + Sex, data=prem_data)
> anova(prem_fluc_model)
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
```

```
Exptotal    1    460  459.58  4.6925 0.03094 *
Sex         1     14   13.98  0.1427 0.70578
Residuals 366  35846   97.94
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

And the graph shows that animals exposed to fluconazole were born later than those not exposed:



(Exptotal is the number of days fluconazole exposure, and Difference is the delivery date minus the due date.)

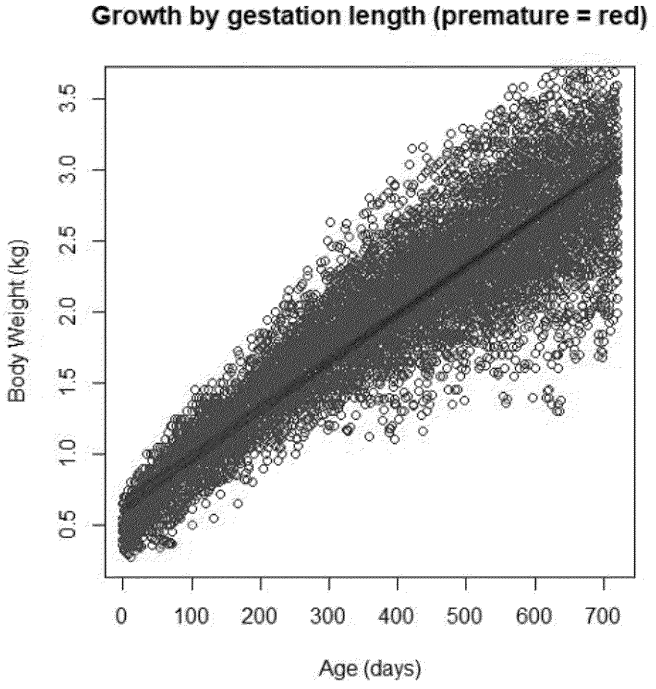
The effect on gestation length was significant based on the number of exposure days during the 1st trimester alone, but not for the 2nd or 3rd trimester:

```
prem_fluc_model1 <- lm(Difference ~ Expdayst1 + Sex, data=prem_data)
> anova(prem_fluc_model1)
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
Expdayst1   1    423  422.80  4.3129 0.03852 *
Sex         1     18   17.69  0.1804 0.67125
Residuals 366  35879   98.03
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1


prem_fluc_model2 <- lm(Difference ~ Expdayst2 + Sex, data=prem_data)
> anova(prem_fluc_model2)
```

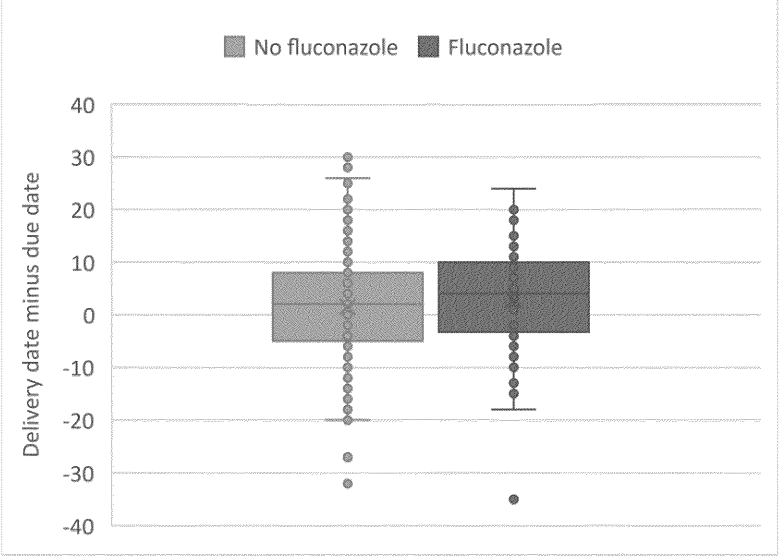
```
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
Expdayst2   1    396  395.83  4.0342 0.04532 *
Sex         1     13   12.87  0.1311 0.71746
Residuals 366  35911   98.12
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

```
prem_fluc_model3 <- lm(Difference ~ Expdayst3 + Sex, data=prem_data)
> anova(prem_fluc_model3)
Analysis of Variance Table

Response: Difference
           Df Sum Sq Mean Sq F value  Pr(>F)
Expdayst3   1    374  374.36   3.813 0.05162 .
Sex         1     11   11.19   0.114 0.73588
Residuals 366  35934   98.18
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

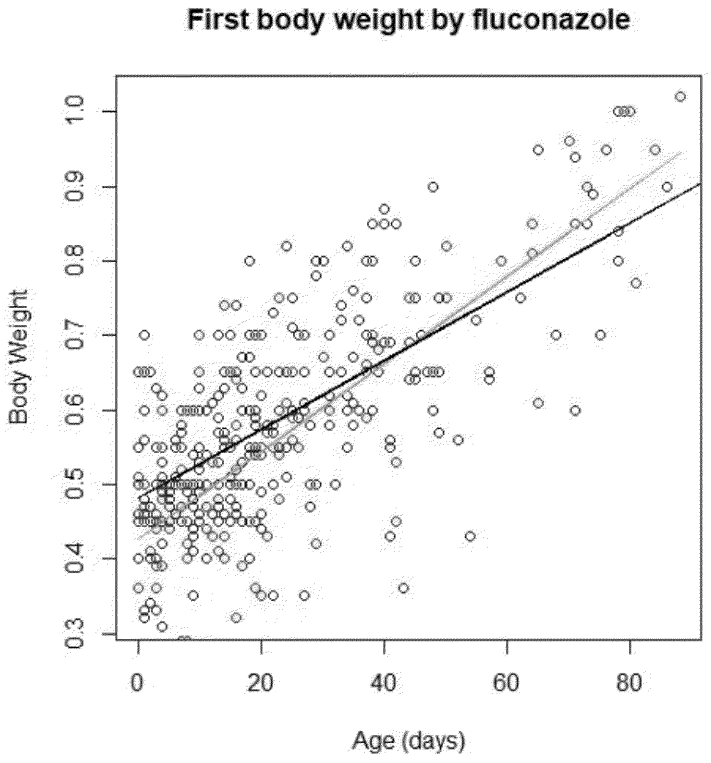
And then because I was playing with graphs, I was able to show that premature infants seem to be smaller at birth, but show catch up growth over time. Not sure how to run stats on it, but the graph is suggestive:



Then I realized something. If the fluconazole-treated animals are born later, and animals that are born later start out heavier, that could mask any fluconazole effect on birthweight. Although the graph is suggestive, a t-test comparing the gestation length between fluconazole treated and untreated was not significant (P = 0.23).



I tried to dig in anyway. Unfortunately, we do not have birthweights on most of the animals, and the age at which the first weight was taken varies significantly. Still, it looks like there could be something there when you graph it (red dots/orange line is positive for fluconazole):



Statistically, it looks like the first weight is significantly related to age, sex, fluconazole treatment, and gestational age at delivery:

```
firstwt_model <- lm(weight ~ Day + Sex + fluc + Difference + Day*fluc + Day*S
ex,data=fluc_data_first)
> anova(firstwt_model)
Analysis of Variance Table

Response: weight
            Df Sum Sq Mean Sq  F value    Pr(>F)
Day          1 3.9425  3.9425 472.8324 < 2.2e-16 ***
Sex          1 0.1736  0.1736  20.8251 6.902e-06 ***
fluc         1 0.0401  0.0401   4.8128   0.02888 *
Difference   1 0.3256  0.3256  39.0449 1.164e-09 ***
Day:fluc     1 0.0303  0.0303   3.6295   0.05756 .
Day:Sex      1 0.0129  0.0129   1.5526   0.21356
Residuals  362 3.0184  0.0083
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

In summary, the statistics aren’t clear. Depending on which statistical test you use, fluconazole either does nothing, or else it delays delivery associated with lower birth weights, implying slower fetal growth in utero. But even if there is slower growth in utero, I think there’s catch up growth, so that overall there’s no difference in body weight after the first couple of months.

Updated Pregnancy Sheet

Tuesday, March 10, 2020 11:53 AM

Subject	**Updated Pregnancy Sheet**
From	cjmead2
To	Kelly L. Carbone; Jim Murphy; Jessica Toscano; Tess House; cmali; aw656
Sent	Tuesday, December 24, 2019 12:24 PM
Attachments	 AZ Current Pregnanci...

Updated Pregnancy- two for follow-up dates next week to be determined. That's it till next Exams

Thanks,
Caroline

Tuesday, March 10, 2020 11:38 AM

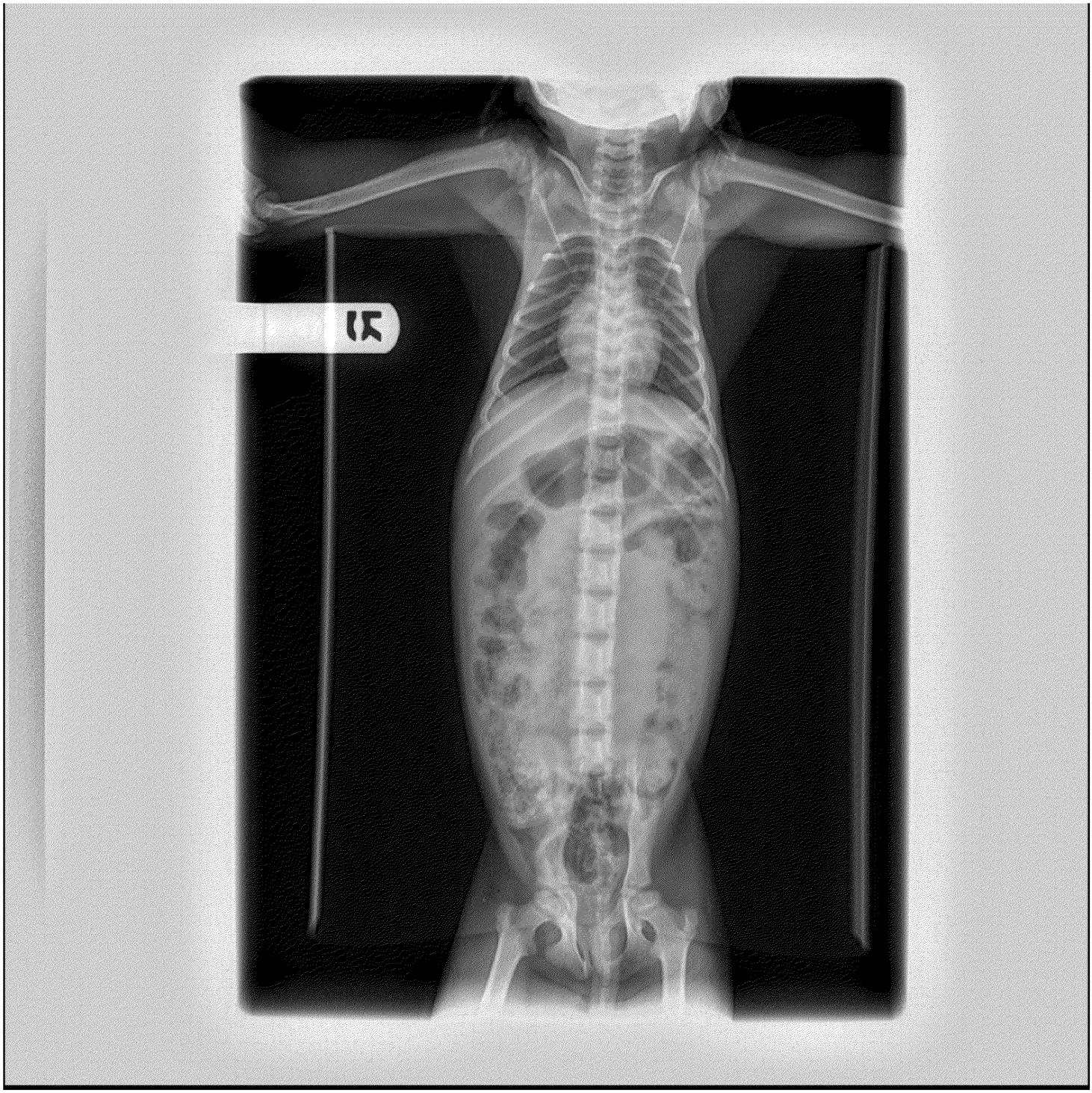
Subject	
From	cjmead2
To	Kelly L. Carbone; Jim Murphy; cmali; Tess House; aw656
Sent	Tuesday, October 29, 2019 10:59 AM
Attachments	 AZ Current Pregnanci...

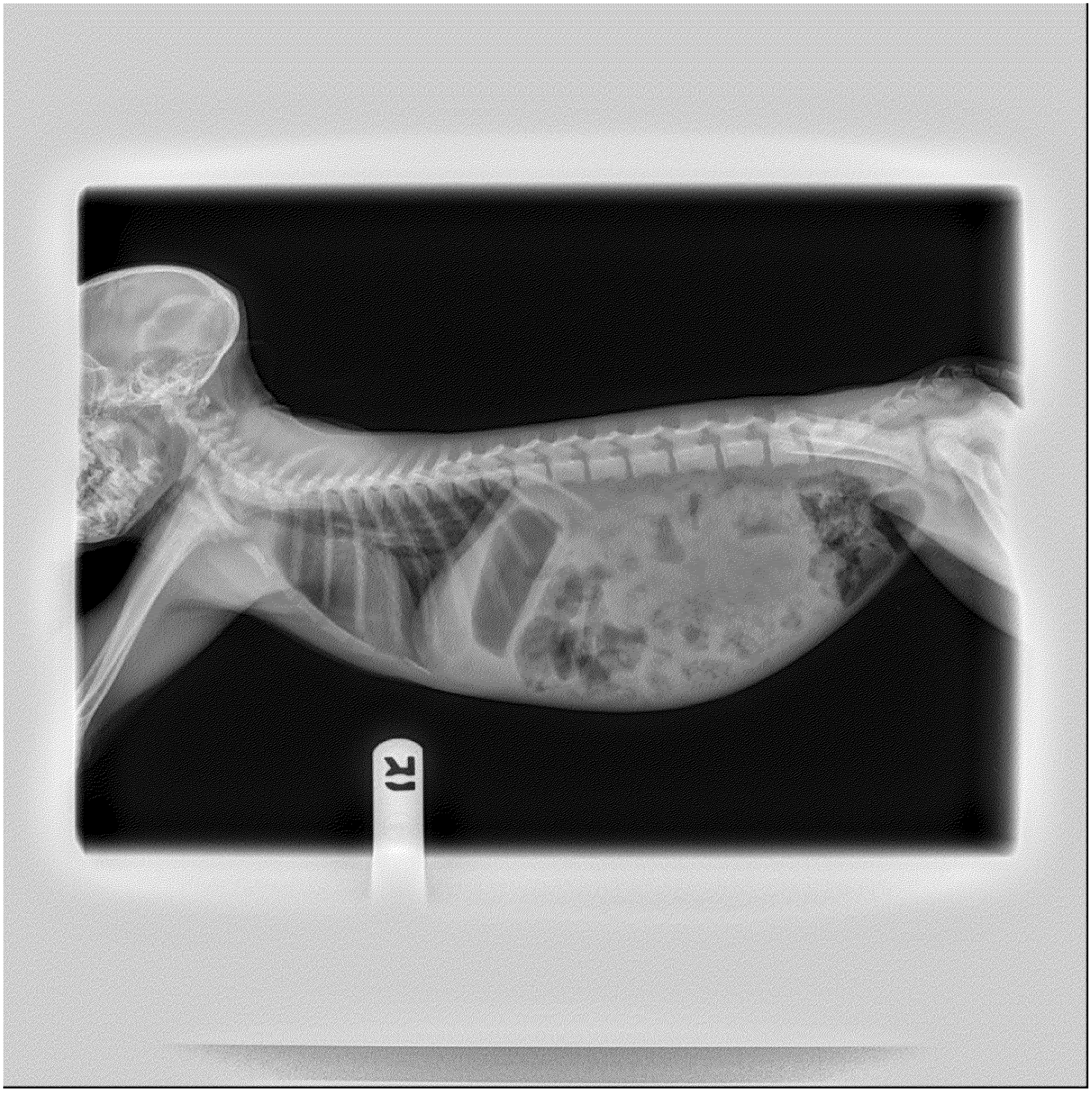
Current pregnancy sheet with A & B building

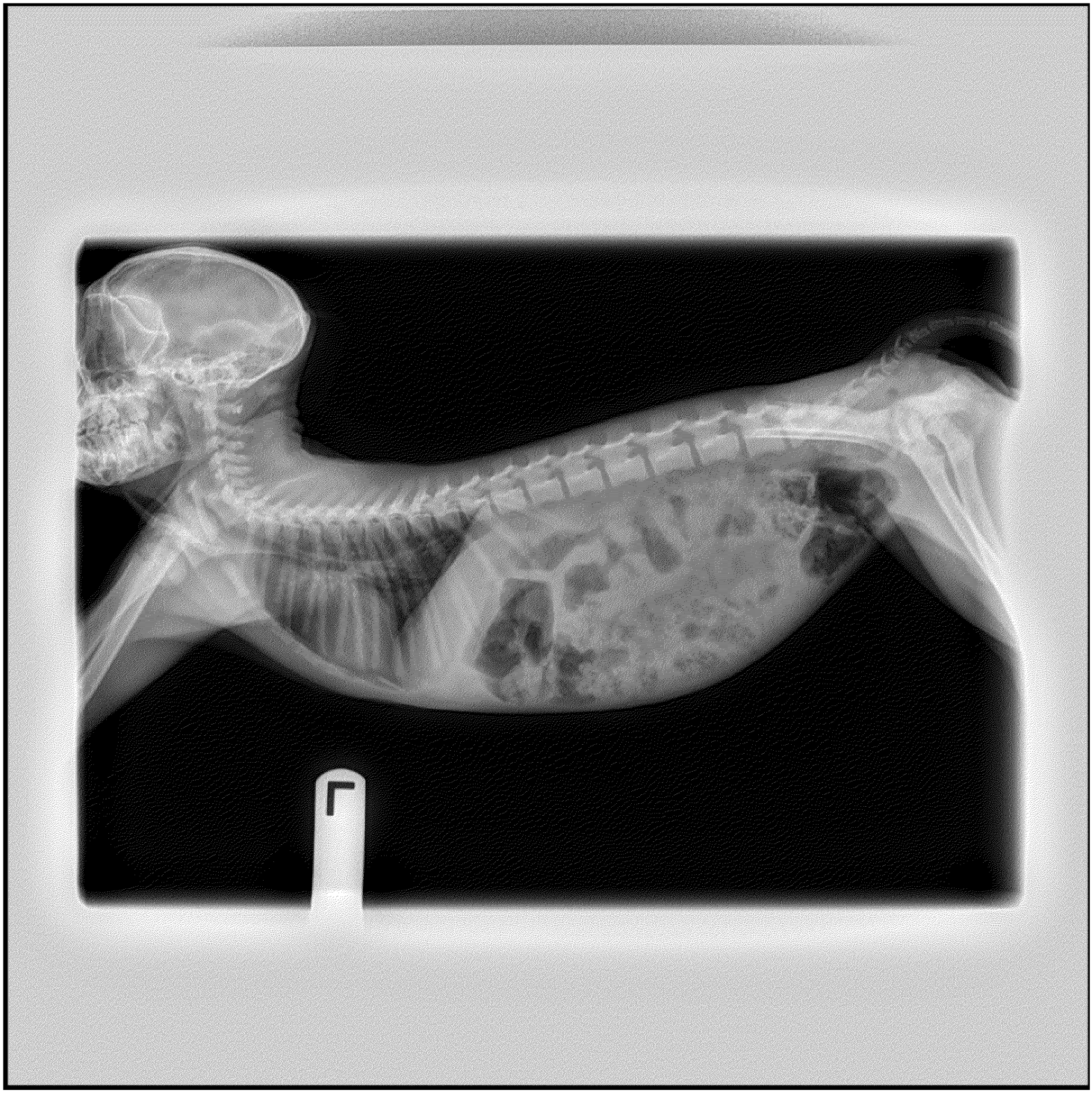
Still three from B building yet to be determined.

Thanks,
Caroline

Dam Information				Pregnancy Information		
Dam (links to Breeding Summary)	Alias	Current Location (links to Move Hx)	Potential Sire	Conception Date	Due Date	Comments
Z09114	A9W022	AB317A-B	M03185	20/Jun/19	09/Dec/19	no pregnancy Hx from NIRC
A03177	CW46, ET40	AA232A-B-C	L02276	24/Jun/19	13/Dec/19	2016 early non-viable, later 2016 viable infant, 2018-viable birth
Z14135	G-M	AA112A-B-C	Z13090	02/Jul/19	21/Dec/19	1st time pregnancy 2019 viable birth (18 days old FD-trauma, newly established breeder group)
A12268	B090607	AA231A-B-C	F01108	04/Jul/19	23/Dec/19	2014, 2015, 2016, 2017 and 2018-viable births
J03371	EV87	AA222A-B-C	K05143	08/Jul/19	27/Dec/19	2014, 2015, 2017 viable births, spring 2019 non-viable birth
L01151	DJ72	AA131A-B-C	A10229	18/Jul/19	06/Jan/20	2013, 2014, 2016, 2017 and 2918 viable births
M06139	GM35	AA232A-B-C	L02276	26/Jul/19	14/Jan/20	viable birth 2014, 2015, 2017 and 2018
Z12072		AA241A-B-C	K04170	26/Jul/19	14/Jan/20	2016 viable birth, 2017 stillborn full term and early 2018 dystocia full term fall 2018 viable birth
Z11098	A11W023	AB317A-B	M03185	10/Aug/19	29/Jan/20	2017 viable birth
L08144	ID14	AA231A-B-C	F01108	15/Aug/19	03/Feb/20	2019 viable birth- hand reared, due to premature, 2018 stillborn, 2017 infant couple days old FD, 2016 & 2014 viable births, valley fever Tx
R10195		AA241A-B-C	K04170	02/Sep/19	21/Feb/20	2016 and 2017 viable births
Z14374	A14W052	AB317C-D	Z12214	10/Sep/19	29/Feb/20	Hx from NIRC first time pregnancy




R



RE: Z14141

Tess House <th81@uw.edu>
Thu 6/13/2019 9:03 AM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>; cmali <cmali@uwedu>

1 attachments (5 MB)
VF BCMC.pptx;

Hi Charlotte,

Here's the PP from the presentation I gave in January for the BCMC meeting. It includes Bob and Audrey's data on the necropsies from AZ over the years.

Anything else you need, let me know! A GI bug hit my daughter so I'm home today while Adam studies for his COMLEX exam on Monday but I'm checking emails when she's distracted with toys.

Tess

From: Charlotte E. Hotchkiss <chotchki@uw.edu>
Sent: Thursday, June 13, 2019 7:58 AM
To: cmali <cmali@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: RE: Z14141

Thanks!

Do you by any chance have:
Any data on the cocci vaccine study that Lee and Jeremy did?
Any old presentations by Lee or Cathy on Valley Fever? (Tess – did you do one? I have a memory of one, but I don't think you did it for a working group so I'm not sure what I'm remembering.) Lee did one in January 2016 – I hope that's long enough ago to get away with.

I promise to give credit where it is due, but I don't have time to reinvent the wheel.

Thanks!
Charlotte

From: cmali <cmali@uw.edu>
Sent: Wednesday, June 12, 2019 1:55 PM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: Z14141

Hi Charlotte,

Please see the path report for Z14141 (attached).
Tess wrote a VERY thorough case history.

Bob may be able to provide you with some histo pics...

Let us know what we can help with!

Best,
Carolyn

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
Washington National Primate Research Center/University of Washington
Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care… | explore UW's Compassion Fatigue Program

From: Robert D. Murnane <rmurnane@uw.edu>
Sent: Thursday, May 9, 2019 12:19 PM
To: Audrey Baldessari; Keith Vogel; Charlotte E. Hotchkiss; Kathryn A. Guerriero; Dean Jeffery; Jason D. Laramore; Tess House; cmali
Subject: 19-041 and 042 (Z19068 and Z14141)

Hi all:

Please find attached final reports on the above 2 cases. Interestingly, Z14141 was cerebral Valley Fever, and both animals were from the same dam who also was diagnosed clinically with Valley Fever.

Please contact me with any questions, comments or concerns.

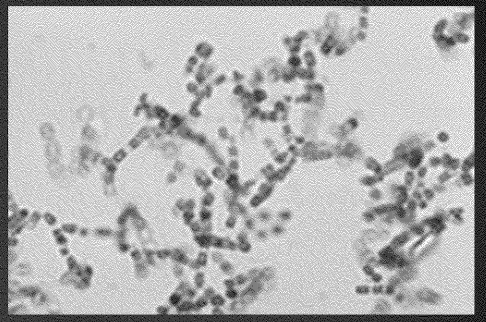
Cheers
Bob

Coccidioidomycosis

Tess House

Coccidioidomycosis

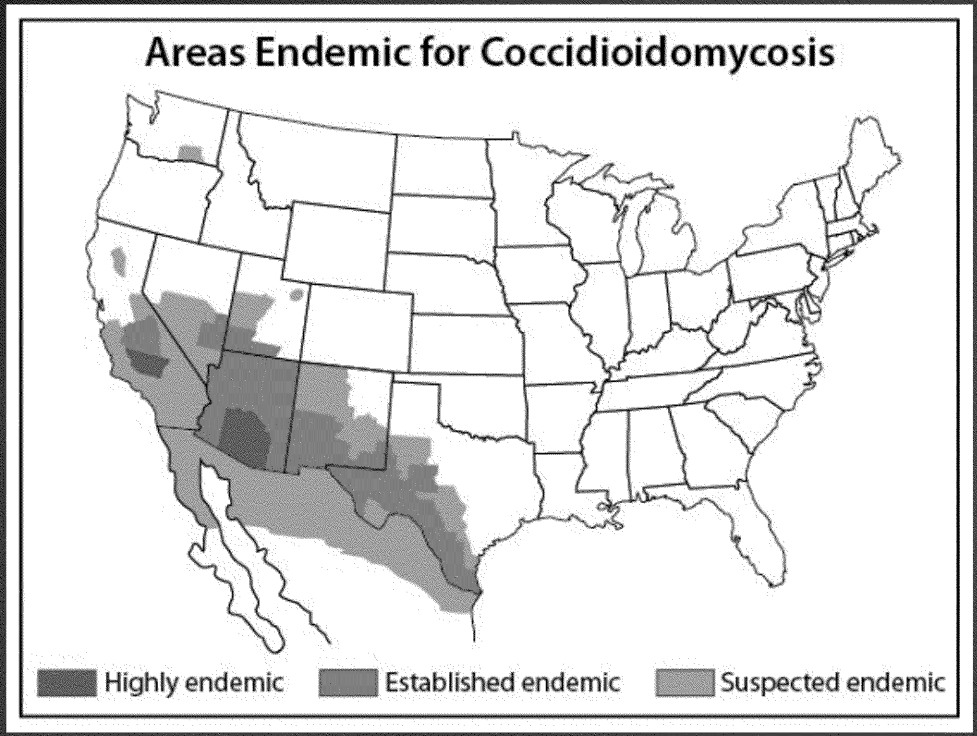
- Fungal infection caused by the genus Coccidioides
  - C. immitis
  - C. posadasii



CDC image

  - More commonly known as Valley Fever or Cocci
  - Able to infect humans and a wide range of animal species
    - NHP species with cases reported include baboons, capuchins, chimpanzees, geladas, guenons, gorillas, lemurs, mandrills, macaques, mangabeys, spider monkeys, squirrel monkeys, woolly monkeys

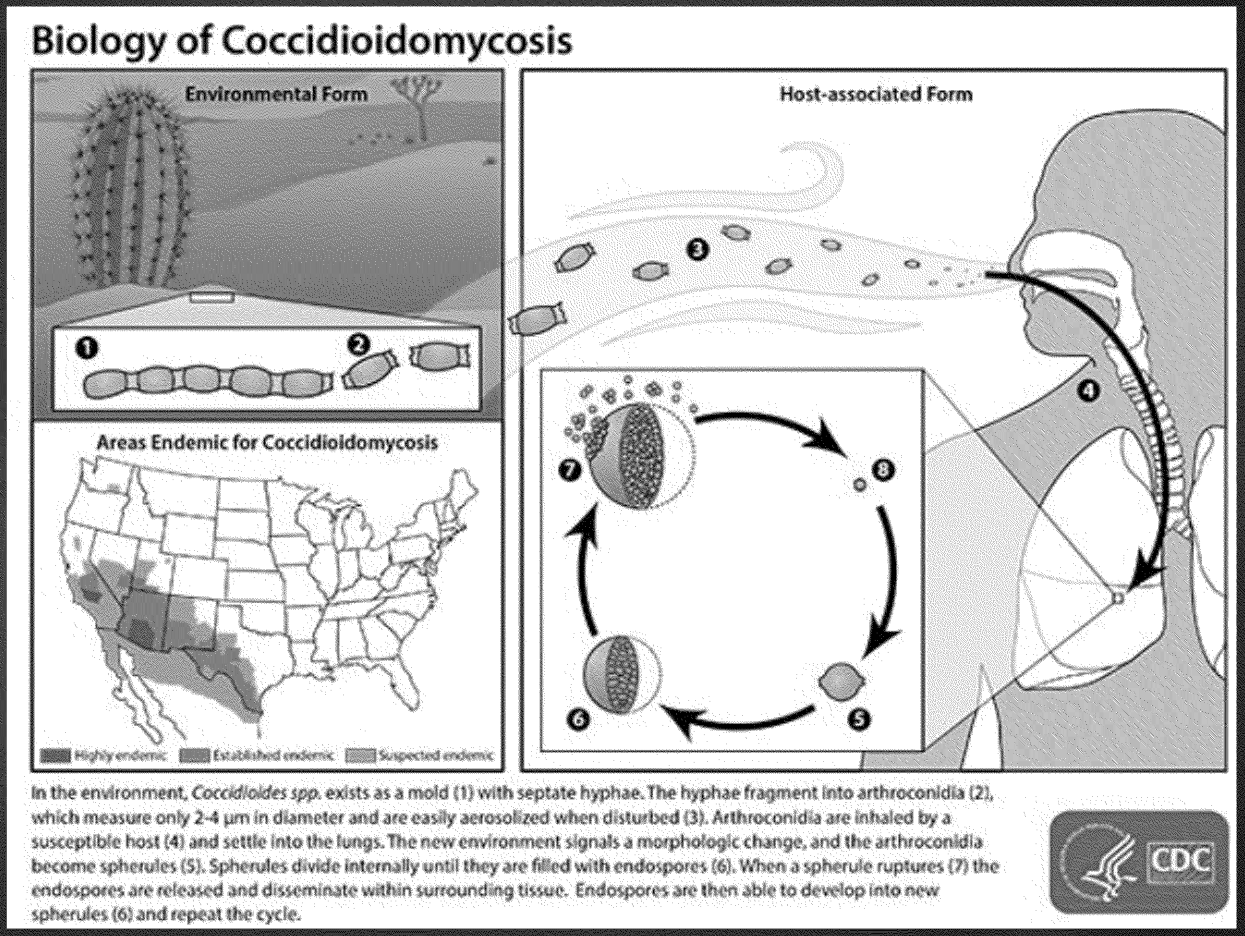
Endemic regions



www.cdc.gov/fungal/diseases/coccidioidomycosis/causes.html

- Found in portions of North, South, and Central America
- Highly endemic regions found in Arizona and California
- Newer region found in Washington state

Life cycle


Biology of Coccidioidomycosis
Environmental Form
Host-associated Form
Areas Endemic for Coccidioidomycosis
Highly endemic
Established endemic
Suspected endemic
In the environment, Coccidioides spp. exists as a mold (1) with septate hyphae. The hyphae fragment into arthroconidia (2), which measure only 2-4 µm in diameter and are easily aerosolized when disturbed (3). Arthroconidia are inhaled by a susceptible host (4) and settle into the lungs. The new environment signals a morphologic change, and the arthroconidia become spherules (5). Spherules divide internally until they are filled with endospores (6). When a spherule ruptures (7) the endospores are released and disseminate within surrounding tissue. Endospores are then able to develop into new spherules (6) and repeat the cycle.
CDC

Routes of Infection

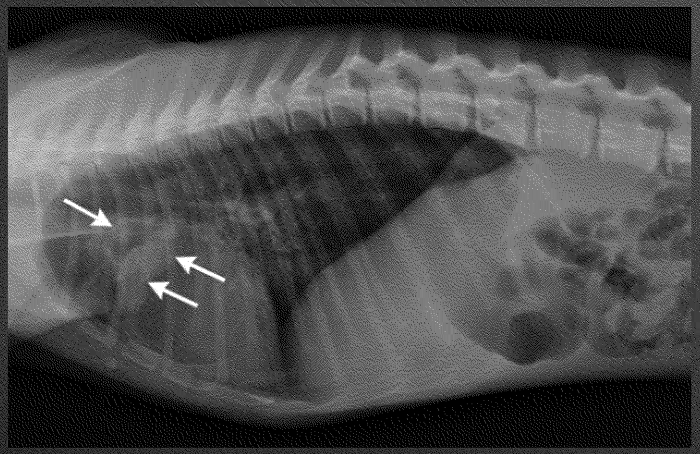
- Primary route of infection is inhalation
- Not contagious or zoonotic
- Less frequent routes of infection can include:
  - Break in the skin such as a cut, wound, or splinter
  - Aspiration of amniotic fluid during parturition
  - Organ transplantation
- Low infectious dose

Symptoms

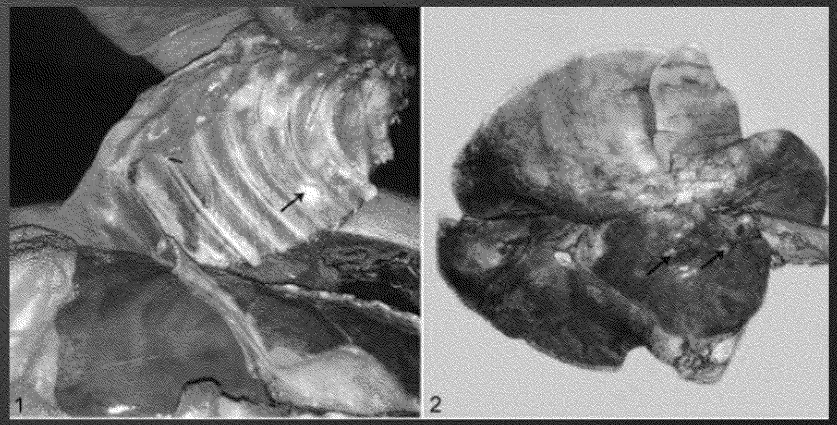
- Diverse clinical presentation (average 7-28 days after exposure)
- Clinical illness in NHP similar to humans
- Lethargy
- Coughing
- Shortness of breath
- Fever
- Inappetence and/or weight loss
- Joint pain or lameness
- Skin rash or nodules
- Neurological symptoms

Clinical and Pathological Findings

- Eosinophilia, mild lymphocytosis, monocytosis
- Hyperglobulinemia
- Radiographic changes
- Tan to white nodules particularly within lung tissue and thoracic wall



Kundu et al, 2017



Koistinen et al, 2018

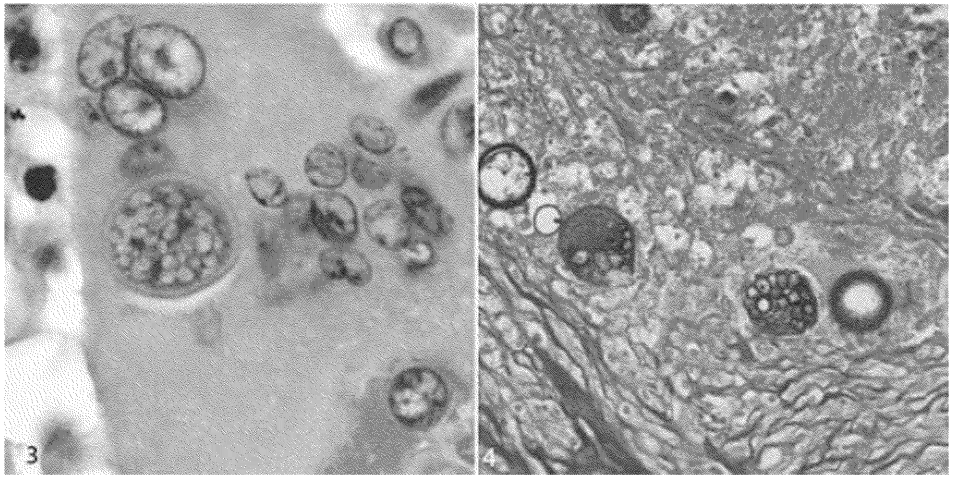
Necropsy Data from Arizona

Year	Cases	Gender	Location
2013	N=3	3 female	2 pulmonary, 1 disseminated
2014	N=18	17 female, 1 male	2 pulmonary, 16 disseminated
2015	N=13	12 female, 1 male	3 pulmonary, 10 disseminated
2016	N=8	7 female, 1 male	4 pulmonary, 4 disseminated
2017	N=2	2 female	1 pulmonary, 1 disseminated
2018	N=1	1 female	1 disseminated

Pathogen Detection

- Direct detection
  - Microscopy
  - Molecular detection
- Culture (safety concerns)
- Serology (EIA, IMDF, CF)

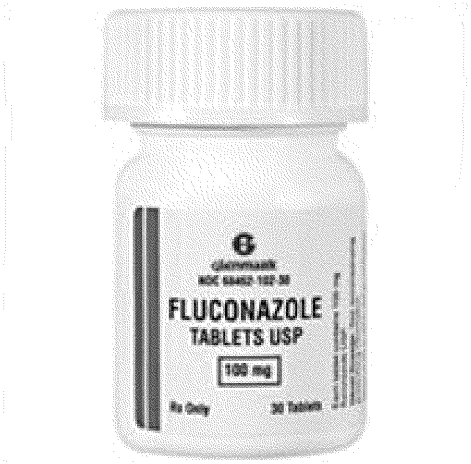
Hematoxylin and eosin (left), Periodic acid-Schiff



Koistinen et al, 2018

Treatment

- Triazoles or Amphotericin B
  - Fluconazole, Itraconazole, Voriconazole, Posaconazole
  - Fluconazole most frequently used
    - Tablet, liquid, fluconazole impregnated feed
    - Currently 18% of the colony at Arizona is on Fluconzaole
      - 20 of 52 animals (6.9% of colony) cocci negative
      - 32 animals (11.1% colony) are cocci positive



Prevention and Surveillance

- Dust mitigation/limiting exposure
  - Future growth to focus on indoor only animal enclosures with HEPA filtration
  - Construction site using dust mitigation practices
  - Minimizing animal exposure time outdoors when high wind/dust storms expected
  - Spray down of enclosures before having access to outdoor portion
- Routine serological surveillance captured at semi-annuals
  - Twice a year (+) clinical indication or suspicion (weight loss, coughing)

Vaccination

- No commercial vaccine available
- A human vaccine trial was conducted in the 1980's but no difference was found in the number of cases of the severity of disease between vaccine and placebo groups
- Challenging in terms of antigen expression, cost of production
- Interest in Delta-CPS1
  - U of A created mutant strain that does not cause disease in mice strains including those with no lymphocytes and those with bone marrow suppression
  - Good survival statistics in those vaccinated
  - Working on replacing the antibiotic resistance marker with one that does not involve antibiotics

Acknowledgements

- Dr. Sally Thompson-Iritani
- Drs. Charlotte Hotchkiss, Keith Vogel, Kate Guerriero, Dean Jeffrey, Carolyn Malinowski, Bob Murnane, Audrey Baldessari
- Veterinary Services and Animal Husbandry Staff at Arizona Breeding Colony
- Drs. Paul Barrass, Lee Chichester, Cathy Carrier
- Dr. Nathan Weiderhold (UT Fungal Lab)
- Dr. John Hasenau (Lab Animal Consultants)
- Dr. Cynthia Holland (Protatek International, LLC)
- Dr. Lisa Shubitz (University of Arizona)
- Salt River Pima-Maricopa Indian Community
- BCMC and John Nylander

Valley Fever

An introduction

What material will we cover?

- What causes valley fever
- Sources of infection
- Symptoms of valley fever
- Diagnosis and testing
- Treatment
- Risk and prevention
- Additional resources

What causes valley fever?

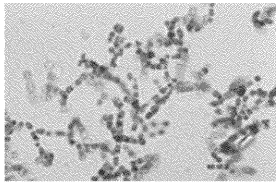


Image from CDC

- Valley fever is a fungal infection caused by spores of the genus Coccidioides.
- These spores are found in the soil in the Southwestern United States, Mexico, and throughout portions of Central and South America.
- More recently, the spores have been found in soil samples in southeastern Washington and cases of valley fever have been discovered in humans and animals in this area.
- Valley fever is sometimes called “San Joaquin Valley fever” or “desert rheumatism.”

Sources of infection

- The majority of cases are from inhalation of spores.
- Spores can be found in higher levels when dust storms or monsoons occur, during wildfires in endemic areas, and after earthquakes.
- Less commonly, infection can occur through a wound that is exposed to dirt or dust containing valley fever spores, receiving an organ from a donor that had valley fever, and inhaling spores from an infected wound.
- Many people (60%) are exposed but don't become ill.

(Chiller et al, 2003)

- Not contagious like the flu or a cold.

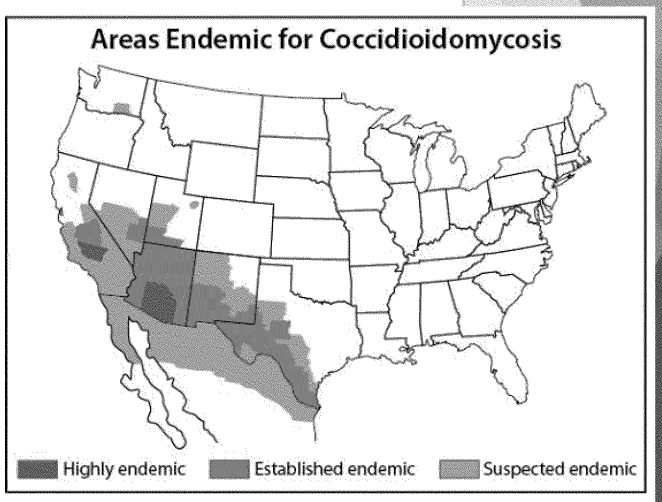


Image from CDC

Symptoms of valley fever

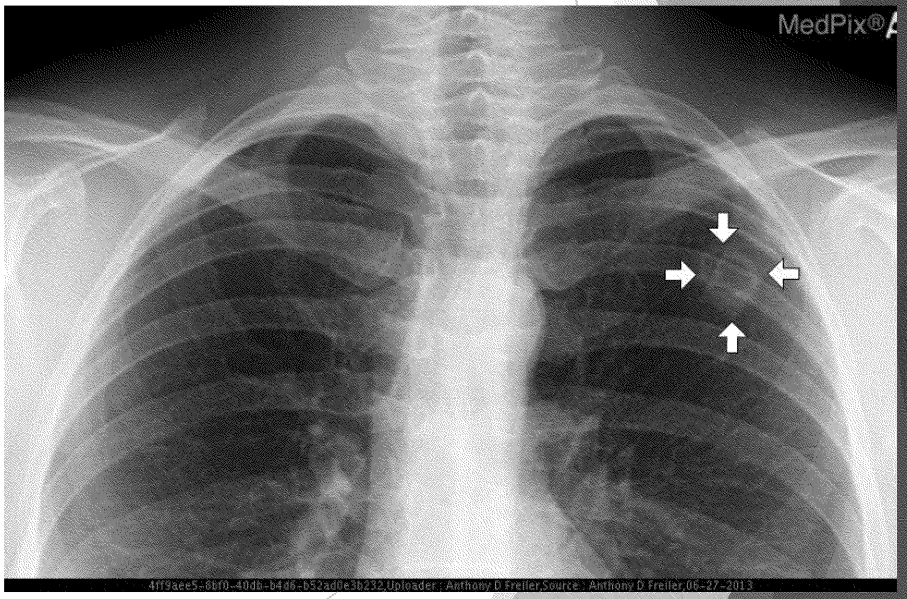
- Typically appear between 1 to 3 weeks after exposed.
- FATIGUE
- Cough
- Fever
- Shortness of breath
- Headache
- Night sweats
- Myalgia and/or joint pain
- Rash on upper body or legs

Symptoms, continued

- Symptoms usually last for a few weeks but can be up to several months or longer.
- A small portion (5-10%) will have long-term problems, typically in the lungs.
- Another portion of those exposed (about 1%) will have infection spread to other parts of the body. The skin, bone, joints, and central nervous system (CNS) can be affected.

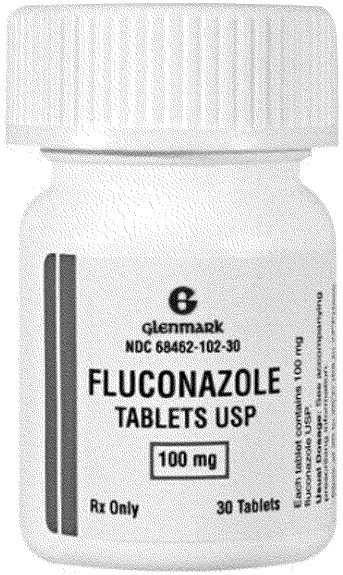
Diagnosis and Testing

- Most common testing method is submitting a blood (serum) sample that looks for antibodies to valley fever
- Imaging (CT, x-rays) may also be performed
- Biopsy of nodules (found on imaging or skin lesions)
- Culture from body fluids or tissues
- Skin test
  - Commonly done leading up to the late 1990's
  - Became available in 2014



Treatment

- Antifungal medication
  - Fluconazole, amphotericin B most common for disseminated form
- No OTC medications



Risk and Prevention

- Anyone living in an endemic area is at risk
- Occupational exposure increased for:
  - Agricultural work
  - Construction work
  - Archeological dig sites
  - Military personnel/trainees
  - Wildland firefighters
  - Mining/gas/oil extraction
  - Prison employees and prisoners

https://inhabitat.com/firefighters-say-drones-are-getting-in-the-way-of-battling-californias-wildfires/

Risk and Prevention, continued

- Certain populations are at greater risk for developing disseminated form
  - People of Asian (esp. Filipino) or African American descent
  - Pregnant women during their third trimester
  - Immunocompromised persons
  - Comorbidities (ex: diabetes)

- Prevention
  - Avoid being outdoors during dust storms/monsoons and keep windows closed.
  - Use dust mitigation when possible (construction, archeology, gardening).
  - Clean air filters in your home on a regular basis.
  - Clean skin injuries exposed to dirt with soap and water.

Additional Resources

- CDC website https://www.cdc.gov/fungal/diseases/coccidioidomycosis/index.html
- Mayo Clinic https://www.mayoclinic.org/diseases-conditions/valley-fever/symptoms-causes/syc-20378761
- Valley Fever Center for Excellence (U of A, College of Medicine Tucson) https://vfce.arizona.edu/
- 2016 IDSA Clinical Practice Guideline for the Treatment of Coccidioidomycosis https://academic.oup.com/cid/article/63/6/e112/2389093

Questions?

Animal	Sx	Result Date	Test Description
A03194	F	3/20/2018	IgG Titer Result,IgG Titer Value
A12255	F	1/4/2018	IgG Titer Result,IgG Titer Value
A12255	F	2/13/2018	IgG Titer Result,IgG Titer Value
A12262	F	9/24/2018	IgG Titer Result,IgG Titer Value
A12262	F	11/6/2018	IgG Titer Result,IgG Titer Value
A12264	F	3/27/2018	IgG Titer Result,IgG Titer Value
A12269	F	9/24/2018	IgG Titer Result,IgG Titer Value
F08047	F	2/13/2018	IgG Titer Result
F08047	F	2/13/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
F08047	F	4/30/2018	IgG Titer Result,IgG Titer Value
F08132	F	9/10/2018	IgG Titer Result,IgG Titer Value
K06192	F	10/1/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K06192	F	11/13/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K06192	F	12/11/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K06271	F	4/2/2018	IgG Titer Result,IgG Titer Value
K06271	F	6/18/2018	IgG Titer Result,IgG Titer Value
K06271	F	9/25/2018	IgG Titer Result,IgG Titer Value
K06271	F	12/26/2018	IgG Titer Result,IgG Titer Value
K07291	F	4/9/2018	IgG Titer Result,IgG Titer Value
K10112	F	10/2/2018	IgG Titer Result,IgG Titer Value,IgM Titer Result,IgM Titer Value
K10112	F	11/15/2018	IgG Titer Result,IgG Titer Value
K10112	F	12/26/2018	IgG Titer Result,IgG Titer Value
K11143	F	4/9/2018	IgG Titer Result,IgG Titer Value
K11143	F	10/8/2018	IgG Titer Result,IgG Titer Value
L02276	M	3/2/2018	IgG Titer Result,IgG Titer Value
L02276	M	8/28/2018	IgG Titer Result,IgG Titer Value
L06156	F	3/13/2018	IgG Titer Result,IgG Titer Value
L06156	F	9/10/2018	IgG Titer Result,IgG Titer Value
L10152	F	3/12/2018	IgG Titer Result,IgG Titer Value
L10152	F	9/10/2018	IgG Titer Result,IgG Titer Value
M10123	F	2/13/2018	IgG Titer Result,IgG Titer Value
M10123	F	5/9/2018	IgG Titer Result,IgG Titer Value
M10123	F	8/14/2018	IgG Titer Result,IgG Titer Value
M10123	F	12/17/2018	IgG Titer Result,IgG Titer Value
M11051	F	4/9/2018	IgG Titer Result,IgG Titer Value
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Animal	Location
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Z17137	111
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Z16358*	111
Z13067	112
Z13292	112
Z14141*	112
Z13337**	112
Z14323**	112
Z16005	122
Z14333	162
Z14001	171
Z14027	171
Z14130	171
F08132	181
L06156	181
L10152	181
Z12342	181
A12264	212
R10156	212
R10113	221
R10151	221
A12262	222
A12269	222
Z11338	222
S10114	231
S10185	231
A03194	232
K06271	232
K10112	232
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K06192	241
Z12028	241
K07291	242
L02276	242
M11051	242
R09036	242
R11037	242
K11143**	242

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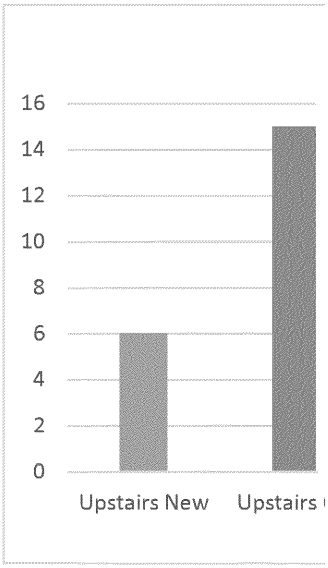
**=142

Upstairs New	6
Upstairs Old	15
Downstairs New	8
Downstairs Old	2
Annex New	1
Annex Old	7



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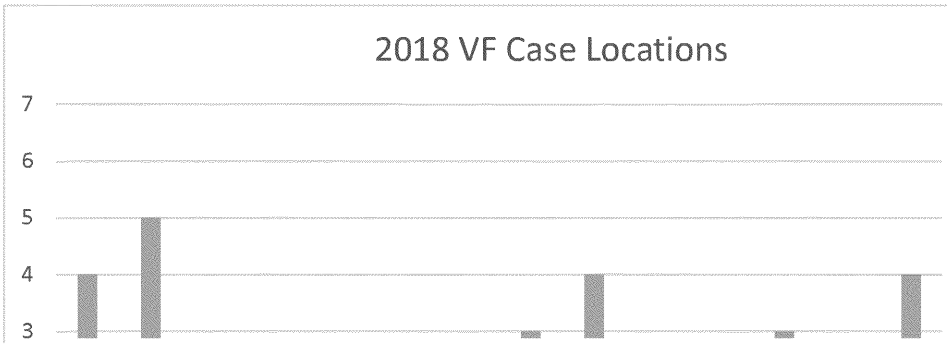

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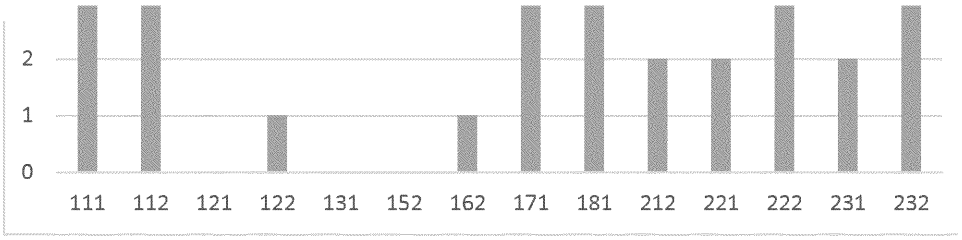
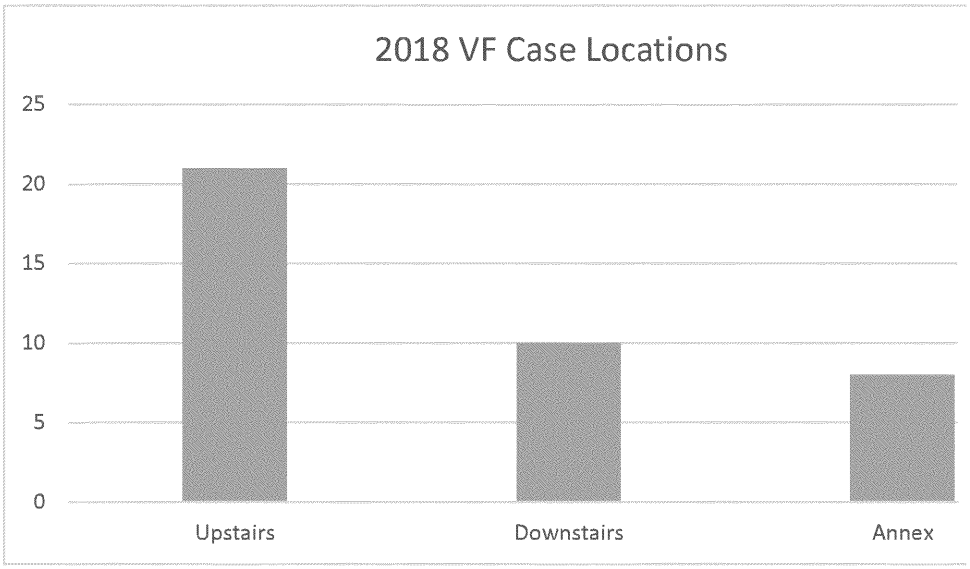
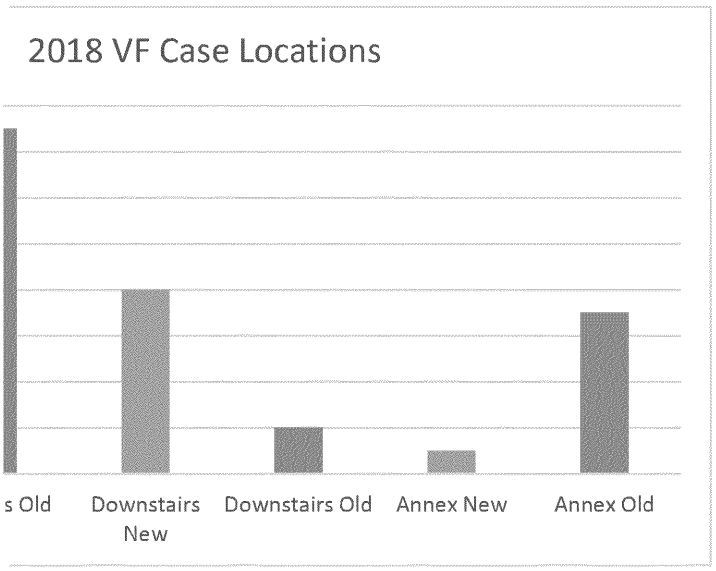
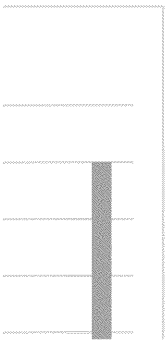
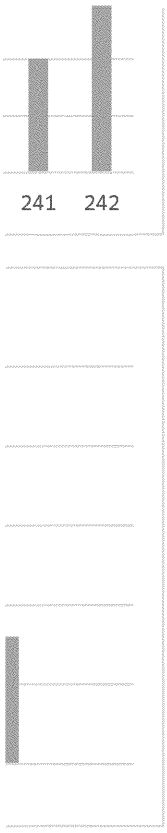


Upstairs	21
Downstairs	10
Annex	8




2018 VF Case Locations
s Old
Downstairs New
Downstairs Old
Annex New
Annex Old

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F08047	Seattle
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Z07023	Seattle
Z13022	Seattle
Z13093	Seattle
Z14251	Seattle

T06226	Euth
T11135	Euth
Z16027	EUTH

RE: Introductions

Charlotte E. Hotchkiss <chotchki@uw.edu>

Tue 11/26/2019 11:21 AM

To: Bridget Marie Barker <Bridget.Barker@nau.edu>; Tess House <th81@uw.edu>; cmali <cmali@uw.edu>

2 attachments (5 MB)

App13 SemlerIG18combined.pdf; Oleary pigtail 2009.pdf;

With regard to genotyping, we do some genotyping as part of our colony characterization; I'm not sure if it's similar to what you're doing in dogs. We do genotyping for parentage – in the past we did microsatellite (STR) analysis of 20-some loci across the genome to verify parentage, but now we're in the process of switching to SNP analysis. We collaborate with a group in Oregon, and they're supposed to be running the first batch of samples on our brand new 96 locus SNP chip even as we speak. But that wouldn't help with figuring out factors related to infection.

We also do testing for MHC expressed alleles. We send blood samples with an RNA preservative to our Oregon collaborator who then makes cDNA and comes up with lots of complicated data about alleles, lineages, and haplotypes. I can't explain it very well, so I'm attaching articles about it. Is that the sort of MHC genotyping you're interested in? We have results on some animals, and are working towards getting MHC on all the animals. Of course, we'd love additional support to complete the process….

We would definitely be interested in a vaccine. I know there was some work done with a vaccine a few years back, but it didn't work.

Glad we've opened up communication – hope we can work together going forward!

Charlotte

From: Bridget Marie Barker <Bridget.Barker@nau.edu>
Sent: Thursday, November 21, 2019 8:15 AM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>; Tess House <th81@uw.edu>; cmali <cmali@uw.edu>
Subject: Re: Introductions

Hi All!

While we don't know for sure what MHC alleles might be associated with asymptomatic vs. severe infection, I think these data might represent an opportunity to do this analysis and get out a nice paper.

I am currently putting an R01 together to investigate host genetic factors associated with differential disease. We propose to use naturally infected canines to address this, but I wonder if adding in the primate data might really give us a closer link to translation in humans. My other main interest is finding the organism in soil and air, and we are working on that part of the project already. Dan and I will complete our training and hope to get back out for a visit in January.

I understand that the animals are on a breeding protocol and not experimental, so we'd have to address that aspect if we wanted to draw blood for genotyping? I could envision a subcontract to UW for you to hold samples and do DNA extractions, and we could handle sequencing and analysis? The benefit I foresee for the colony is that we could define risk factors that might help understand which animals would be at higher risk for severe disease so they could be prioritized for removal to a safer location.

I did not discuss other ideas much, because they are projects with other PIs as lead, but they involve vaccine work and understanding correlates of protection. I am not sure where approval is for the current vaccine, but I believe the UA valley fever center (John Galgiani) is pursuing USDA license for use in veterinary setting (dogs mainly) so perhaps this would be helpful for your animals too? The rest of the group at NAU is interested in defining correlates of protection, so this could also be beneficial for your colony, especially if vaccination is considered.

I'm attaching the PA for NIH that is focused on Coccidioides research. I would also like to invite you to attend the annual Coccidioidomycosis Study Group meeting in Tucson, April 3-4.
http://coccistudygroup.com

Best,

Bridget

From: "Charlotte E. Hotchkiss" <chotchki@uw.edu>
Date: Tuesday, November 19, 2019 at 8:53 AM
To: Tess House <th81@uw.edu>, Bridget Marie Barker <Bridget.Barker@nau.edu>, cmali <cmali@uw.edu>
Subject: RE: Introductions

Hi!
It's good to virtually meet you! I would love it if you could learn things that would help us keep our animals healthy.

I do have MHC data on some of the animals (and expect to get more in the future) and am interested in looking for associations, but unfortunately it never seems to get to the top of my priority list. But I am ever hopeful.

Charlotte

Charlotte E. Hotchkiss, DVM, MS, PhD, DACLAM
Washington National Primate Research Center
University of Washington
Box 357330
Seattle, WA 98195-7330
Office phone: 206-685-2881
Cell phone: 206-496-4471
Pager: 206-540-6615
chotchki@uw.edu
Work hours 8-5 M-F

From: Tess House <th81@uw.edu>
Sent: Monday, November 18, 2019 1:48 PM
To: Bridget Marie Barker <Bridget.Barker@nau.edu>; cmali <cmali@uw.edu>; Charlotte E. Hotchkiss <chotchki@uw.edu>
Subject: Introductions

Hi everyone-

I just wanted to make virtual introductions after Bridget toured the Arizona site today. Bridget is an assistant professor and associate director of the ABSL3 at NAU in Flagstaff, Az and studies valley fever. Charlotte is our head veterinarian in Seattle and oversees the breeding and genetics of the colony.

Charlotte-I met Bridget at the Cocci Study Group meeting in California this year and set her up with Melinda for occ health clearance (which she has for a year) for a tour here. Bridget and her graduate student are interested in potential collaborations with us and the possibility of taking soil samples and

trapping rodents at ABC to further characterize cocci here. She is also interested in the MHC typing and evaluating if there is a genetic susceptibility component in the colony. I have already provided Bridget with the contact I have through Gail with the Community so she can reach out to them regarding how to obtain permissions for soil samples and trapping.

Bridget-thank you so much for visiting us today! We hope you enjoyed the visit as much as we did.

Tess and Carolyn

Theresa (Tess) House, DVM MPH
Supervisory Veterinarian
Washington National Primate Research Center
Arizona Breeding Colony
Office phone 206.685.1842
Mailing address- P.O. Box 20836/Mesa, AZ 85277

FW: Z17139 for Discussion

Dean Jeffery <daj12@uw.edu>
Wed 2/27/2019 6:21 PM

To: Jason D. Laramore <jasonl73@uw.edu>; Keith Vogel <vogelk@uw.edu>; Kathryn A. Guerriero <kag18@uw.edu>
Cc: cmali <cmali@uw.edu>

4 attachments (2 MB)
12022019-085025_EXTREMITY.jpg; 12022019-085207_EXTREMITY.jpg; 12022019-073001_EXTREMITY.jpg; 12022019-084931_EXTREMITY.jpg;

I went back and looked at the original rads. Granted they were only 2 weeks ago but I see the same sort of mottling with the femoral and tibial epiphyses. I wonder if this is what immature cancellous bone looks like.

Also, just looking at the lateral aspect of the femoral condyles on the DV view, it shows just how much a little rotation can distort the image to create the appearance of differently sized joint spaces.

I can't wait to see what the Valley Fever titer shows! In the meantime, is it possible to reach out to the lab you sent the cytology too and ask for a re-read to look for Valley Fever spores? There's usually a small nominal fee associated with this. Also, it sounds like it's time for an antibiotic change in the event that this is some resistant bug. I'd go doxy or clindamycin (and just be prepared to manage the diarrhea, which sounds like the lesser of two evils).

DJ

From: cmali <cmali@uw.edu>
Sent: Tuesday, February 12, 2019 1:13 PM
To: Charlotte E. Hotchkiss <chotchki@uw.edu>; Sally Thompson-Iritani <sti2@uw.edu>; Keith Vogel <vogelk@uw.edu>; Dean Jeffery <daj12@uw.edu>; Kathryn A. Guerriero <kag18@uw.edu>; Britni C. Curtis <britcurt@uw.edu>; Jason D. Laramore <jasonl73@uw.edu>
Cc: Tess House <th81@uw.edu>
Subject: Z17139 for Discussion

Hi All,

Case discussion for tomorrow (or via email if that works better)...

Z17137 presented on for toe-touching lameness and non-weight bearing on the rear left leg on 29 Jan. This animal was in an indoor/outdoor enclosure with ~20 other juvenile animals. On PE there was nothing remarkable (no soft tissue swellings) and ROM was normal for affected limb. X-rays revealed nothing unusual. He was prescribed Meloxicam and cage rest.

Since then, techs report intermittent weight bearing on the limb and also on the right limb. This morning he was scooting on the perch bars on his bottom and holding both feet up, and not grasping with the right. He was also swinging around a bit and holding both hind limbs tucked up (but there was a lot happening in the room so he may have been nervous/stressed and therefore behaving weirdly).

Further examination today revealed firm swelling/thickening on the medial aspect of the left stifle and decreased extension of the leg at the stifle (~90% extension) when compared to the contralateral limb. Cranial drawer, tibial thrust, and patellar laxity seemed comparable between limbs (but we aren't sure what normal is, the stifles bilaterally seemed a little wiggly/loose

subjectively). X-rays are attached. Right limb appears normal. Meloxicam and cage rest were extended.

Plan for now is to recheck with xrays in 2 weeks.

All input/suggestions are welcome!!!

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
Washington National Primate Research Center/University of Washington
Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care… | explore UW's Compassion Fatigue Program

Re: Vet meeting today

cmali <cmali@uw.edu>
Wed 2/27/2019 2:30 PM

To: Britni C. Curtis <britcurt@uw.edu>; Charlotte E. Hotchkiss <chotchki@uw.edu>; Sally Thompson-Iritani <sti2@uw.edu>; backward_vets <wanprc_vets@uw.edu>

3 attachments (957 KB)
27022019-101145_STIFLE.jpg; 27022019-101433_STIFLE.jpg; 27022019-101526_STIFLE.jpg;

Hi All,

this is Z17139, the kid who turned up lame that we did an arthrocentesis on....

We're thinking osteomyeltitis likely due to valley fever...

Would like to discuss...

Carolyn Malinowski, MS, DVM, CMAR, CPIA
Senior Veterinarian
Washington National Primate Research Center/University of Washington
Arizona Breeding Colony
PO Box 20836, Mesa, AZ 85277
Ph: 206.616.0501

Dare 2 Care... | explore UW's Compassion Fatigue Program

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> on behalf of Britni C. Curtis <britcurt@uw.edu>
Sent: Wednesday, February 27, 2019 1:46 PM
To: Charlotte E. Hotchkiss; Sally Thompson-Iritani; backward_vets
Subject: Re: [Wanprc_vets] Vet meeting today

Hi,
I am closing the apheresis, so I will attend what I can, but it is likely that I will need to leave. Here is the agenda (attached). Most of the items for follow up are in red. Can someone please take notes, if I don't make it?
Thank you,
Britni

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Charlotte E. Hotchkiss

Sent: Wednesday, February 27, 2019 12:38 PM
To: Sally Thompson-Iritani <sti2@uw.edu>; backward_vets <wanprc_vets@uw.edu>
Subject: Re: [Wanprc_vets] Vet meeting today

I'm probably going to be late – I have a New Model Development Working Group conference call at 1:00, and expect it will go until 2:00.
Charlotte

From: Wanprc_vets <wanprc_vets-bounces@mailman11.u.washington.edu> **On Behalf Of** Sally Thompson-Iritani
Sent: Wednesday, February 27, 2019 12:36 PM
To: backward_vets <wanprc_vets@uw.edu>
Subject: [Wanprc_vets] Vet meeting today

I won't be able to call in.

Shout out to Dean for doing a nice job at the D2C meeting. He was very informative and helpful.

Also - some people need to update holiday hours in workday - if you need help let me know.

Thank you ~

Sally Thompson-Iritani, DVM/PhD, CPIA
~ Certified Compassion Fatigue and Human-Animal Bond Practitioner ~
Director, AWRS, WaNPRC; 206.661.6294
University of Washington,Seattle,WA
All typos courtesy of iPhone autocorrect

FW: IDEXX Results (Final): (Clt)WANPRC (Pt)Z17139 (Ord)02/14/2019

Tess House <th81@uw.edu>
Fri 2/22/2019 10:38 AM
To: cjmead2 <cjmead2@uw.edu>; cmali <cmali@uwedu>

1 attachments (51 KB)
IDEXX Results_Z17139_02142019.pdf;

I just got off the phone with Dr. Jay and she is recommending the following:

1) Try to submit both slides/smears and fluid from the stifle-if it's enough to do C and S we can check that, otherwise she will look at the slides and compare it to the previous ones
2) Tap the opposite knee as well and submit slides on that knee
3) Do a cocci PCR test in case this is cocci but too localized or too early for the titer to go up (we may want to just send out a cocci titer on him to protatek anyways, she didn't know cost and availability of the PCR test for cocci-Caroline can you check the Idexx book you have to see if they have it or if we need to look elsewhere?)

She did comment that in some cases of CCL tears, she has seen neutrophilic inflammation like this but we still discussed the possibility of immune-mediated, localized valley fever, and bacterial infection not responding to therapy. She also threw out the idea of tickborne illness.

From: cjmead2 <cjmead2@uw.edu>
Sent: Thursday, February 14, 2019 11:11 AM
To: Tess House <th81@uw.edu>; cmali <cmali@uw.edu>
Subject: IDEXX Results (Final): (Clt)WANPRC (Pt)Z17139 (Ord)02/14/2019

Z16358

Tess House <th81@uw.edu>

Fri 1/18/2019 1:35 PM

To: Charlotte E. Hotchkiss <chotchki@uw.edu>; Sally Thompson-Iritani <sti2@uw.edu>
Cc: cmali <cmali@uw.edu>

7 attachments (4 MB)

02012019-083758_WHOLE BODY.jpg; 02012019-100019_WHOLE BODY.jpg; 02012019-100135_WHOLE BODY.jpg; 18012019-094429_WHOLE BODY.jpg; 18012019-100701_WHOLE BODY.jpg; 18012019-100754_WHOLE BODY.jpg; 18012019-100901_WHOLE BODY.jpg;

Hi Charlotte and Sally,

We sedated Z16358 for an exam, blood work, and follow up radiographs on coughing for this case. I have radiographs attached from today (4 views) as well as from the last set of radiographs on 1/2/19 (3 views). Last week on Thursday night Schante had commented that he was coughing a lot and over the weekend Sherri noted coughing as well as earlier in the week. Coughing was not noted today. On exam, I'm hearing increased lung sounds bilaterally but no crackles (these were noted on exam on 1/4/19). I have the radiographs attached. It appears radiographically and clinically we are heading in the right direction but I'm going to continue antibiotics (currently on Clavamox and started Azithromycin yesterday after ending a one week course of gentamicin) and recheck radiographs in 2 weeks.

I pulled cbc/chem today (pending right now) to see where we are at. At the last exam, a sample was pulled for a cocci titer and past titer history listed below. Currently this animal is receiving fluconazole, antibiotics (above), probiotics, fiber bites, multivitamins, and Dextromethorphan (ends Monday).

PANELS - Valley Fever

Animal:	Z16358	**Age:**	2 y 0 m	**Project:**	ABC Mn Breeding
Sex:	Male	**Weight:**		**Investigator:**	Breeding 75 01
Species:	Macaca nemestrina	**Location:**		**IACUC:**	4202-02

3.95 on 1/11/19
AA104-K2

Cocci	Panel Comments	IgG Titer Result	IgG Titer Value	IgM Titer Result	IgM Titer Value
1/2/19		positive (+)	1:32	positive (+)	1:4
11/26/18		positive (+)	1:64	positive (+)	1:16
10/15/18		positive (+)	1:32	positive (+)	1:16
3/12/18		negative (-)	<1:1	negative (-)	<1:1

Let me know your thoughts-
Thank you!

Theresa (Tess) House, DVM MPH
Supervisory Veterinarian
Washington National Primate Research Center
Arizona Breeding Colony
Office phone 206.685.1842
Mailing address- P.O. Box 20836/Mesa, AZ 85277

Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH (http://www.nih.gov))

Components of Participating Organizations

National Institute of Allergy and Infectious Diseases (NIAID (http://www.niaid.nih.gov/))

Funding Opportunity Title

Novel approaches to understand, prevent, treat, and diagnose coccidioidomycosis (Valley Fever) and other select endemic fungal infections (R01 Clinical Trial Not Allowed)

Activity Code

R01 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r01&Search.x=0&Search.y=0&Search_Type=Activity) Research Project Grant

Announcement Type

New

Related Notices

- **August 23, 2019** - Clarifying Competing Application Instructions and Notice of Publication of Frequently Asked Questions (FAQs) Regarding Proposed Human Fetal Tissue Research. See Notice NOT-OD-19-137 (/grants/guide/notice-files/NOT-OD-19-137.html).
- **July 26, 2019** - Changes to NIH Requirements Regarding Proposed Human Fetal Tissue Research. See Notice NOT-OD-19-128 (/grants/guide/notice-files/NOT-OD-19-128.html).

- **December 19, 2018** - Notice of Changes to PA-19-082. See Notice NOT-AI-19-026 (//grants.nih.gov/grants/guide/notice-files/NOT-AI-19-026.html).

Funding Opportunity Announcement (FOA) Number

PA-19-082

Companion Funding Opportunity

PA-19-083 (https://grants.nih.gov/grants/guide/pa-files/PA-19-083.html), R21 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r21&Search.x=0&Search.y=0&Search_Type=Activity) Exploratory/Developmental Grant

Number of Applications

See Section III. 3. Additional Information on Eligibility.

Catalog of Federal Domestic Assistance (CFDA) Number(s)

93.855

Funding Opportunity Purpose

The purpose of this Funding Opportunity Announcement is to support research activities that will contribute to the overall understanding of coccidioidomycosis, commonly known as Valley Fever, and other select endemic fungal diseases including histoplasmosis and blastomycosis. This research opportunity encourages studies that address diverse scientific areas such as: 1) pathogenesis; 2) host response; 3) disease transmission; 4) natural history and environmental factors contributing to disease; 5) vaccines; 6) diagnostics; and 7) therapeutics; with the ultimate goal of advancing the field towards solutions for the improved detection, prevention and treatment of select endemic mycoses.

Key Dates

Posted Date

November 26, 2018

Open Date (Earliest Submission Date)

January 05, 2019

Letter of Intent Due Date(s)

Not Applicable

Application Due Date(s)

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11111) apply, by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on these dates.

The first standard application due date for this FOA is February 5, 2019.

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

AIDS Application Due Date(s)

New Dates Standard AIDS dates apply, by 5:00 PM local time of applicant organization. All types of AIDS and AIDS-related applications allowed for this funding opportunity announcement are due on these dates.
The first AIDS application due date for this FOA is May 7, 2019.
Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

Scientific Merit Review

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) apply

Advisory Council Review

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) apply

Earliest Start Date

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) apply

Expiration Date

January 08, 2022

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000),except where instructed to do otherwise (in this FOA or in a Notice from NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/)).

Conformance to all requirements (both in the Application Guide and the FOA) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Applications that do not comply with these instructions may be delayed or not accepted for review.

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the NIH ASSIST system to prepare, submit and track your application online.

   Apply Online Using ASSIST

2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and eRA Commons (http://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.

3. Use Grants.gov (http://www.grants.gov/web/grants/applicants/download-application-package.html#search=true&oppNum=PA-19-082) Workspace to prepare and submit your application and eRA Commons (http://public.era.nih.gov/commons/) to track your application.

Table of Contents

Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Purpose

The purpose of this Funding Opportunity Announcement is to support research activities that will contribute to the overall understanding of coccidioidomycosis, commonly known as Valley Fever, and other select endemic fungal diseases including histoplasmosis and blastomycosis. This research opportunity encourages studies that address diverse scientific areas such as: 1) pathogenesis; 2) host response; 3) disease transmission; 4) natural history and environmental factors contributing to disease; 5) vaccines; 6) diagnostics; and 7) therapeutics; with the ultimate goal of advancing the field towards solutions for the improved detection, prevention and treatment of select endemic mycoses.

Background

The most common endemic mycoses in the United States are coccidioidomycosis (Valley Fever), histoplasmosis, and blastomycosis. These important regional fungal diseases are caused by dimorphic fungi that occupy a specific ecological niche, are generally acquired through inhalation and unlike most fungal pathogens, can cause disease in healthy individuals. Coccidioidomycosis (Valley Fever) is a systemic infection caused by dimorphic fungi *Coccidioides immitis* and *C. posadasii* . Clinical manifestations range from mild flu-like disease to severe disseminated infection that can require life-long therapy. These soil-dwelling fungi are found in arid, desert-like conditions throughout the southwestern United States (primarily Arizona, California, Nevada, New Mexico, Texas and Utah), Mexico, Central and South America. The incidence of infection has risen over the last several years; Valley Fever is endemic to California and Arizona where greater than 11,000 cases were reported in 2016. However, the disease is widely underdiagnosed, and these cases likely represent a

fraction of the true number.

Specific areas of research interest

Specific areas of research interest are focused on coccidioidomycosis, histoplasmosis and blastomycosis and include, but are not limited to:

- **Improve understanding of biology, transmission and pathogenesis of infection:**
  - Improve understanding of pathogenesis
  - Expand understanding of the pathogen life cycle, including the role of climate and geography, host factors, physical and environmental factors that contribute to disease
  - Improve genotypic and phenotypic characterization associated with adverse clinical outcomes, and host immunity
  - Expand understanding of speciation and impact on clinical outcome
- **Identify/characterize host responses required for protection:**
  - Determine the interaction of innate and adaptive immunity in response to infection
  - Identify immune markers associated with reduced disease severity
  - Elucidate mechanisms of protective immunity vs. those that ameliorate symptomatic disease
- **Support rational design of Coccidioides and other select endemic fungal pathogen vaccines:**
  - Identify immunogens that elicit broad protection
  - Advance new vaccine approaches into preclinical models that exploit emerging antigen design strategies, novel technologies, and/or platforms
  - Define mechanisms and correlates of vaccine-induced protection
  - Test adjuvants and alternative delivery methods to enhance breadth and durability of immunity
- **Develop novel therapeutics to clear infection**
- **Identify biomarkers that could inform disease progression and contribute to rapid diagnostics**

This FOA will not support projects focused on HIV/AIDS.

Note: This FOA uses the R01 grant mechanism, while the companion FOA, PA-19- 083 (//grants.nih.gov/grants/guide/pa-files/PA-19-083.html), uses the R21 mechanism. Applicants with preliminary data and/or planning longer-term studies may wish to apply using the R01 mechanism. High risk/high payoff projects that lack preliminary data or utilize existing data may be most appropriate for the R21 mechanism.

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Grant: A support mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity.

Application Types Allowed

New
Resubmission

The OER Glossary (//grants.nih.gov/grants/guide/url_redirect.htm?id=11116) and the SF424 (R&R) Application Guide provide details on these application types.

Clinical Trial?

Not Allowed: Only accepting applications that do not propose clinical trials
Need help determining whether you are doing a clinical trial? (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

Award Budget

Application budgets are not limited but need to reflect the actual needs of the proposed project.

Award Project Period

The maximum project period is 5 years.

NIH grants policies as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this FOA.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

  The following types of Higher Education Institutions are always encouraged to apply for NIH support as Public or Private Institutions of Higher Education:

  - Hispanic-serving Institutions
  - Historically Black Colleges and Universities (HBCUs)
  - Tribally Controlled Colleges and Universities (TCCUs)
  - Alaska Native and Native Hawaiian Serving Institutions
  - Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)
- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other

- Independent School Districts

- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Institutions)

Foreign Institutions

Non-domestic (non-U.S.) Entities (Foreign Institutions) **are** eligible to apply

Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

Foreign components, as defined in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are** allowed.

Required Registrations

Applicant organizations

Applicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications (//grants.nih.gov/grants/guide/notice-files/NOT-OD-15-039.html) states that failure to complete registrations in advance of a due date is not a valid reason for a late submission.

- Dun and Bradstreet Universal Numbering System (DUNS) (http://fedgov.dnb.com/webform) - All registrations require that applicants be issued a DUNS number. After obtaining a DUNS number, applicants can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- System for Award Management (SAM) (https://www.sam.gov/portal/public/SAM/) (formerly CCR) – Applicants must complete and maintain an active registration, which requires renewal at least annually. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
    - NATO Commercial and Government Entity (NCAGE) Code (//grants.nih.gov/grants/guide/url_redirect.htm?id=11176) – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in

order to register in SAM.

- eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Applicants must have an active DUNS number and SAM registration in order to complete the eRA Commons registration. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- Grants.gov – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF424 (R&R) Application Guide.

2. Cost Sharing

This FOA does not require cost sharing as defined in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11126)

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see NOT-OD-11-101 (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-101.html))

Section IV. Application and Submission Information

1. Requesting an Application Package

Buttons to access the online ASSIST system or to download application forms are available in Part 1 of this FOA. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000) except where instructed in this funding opportunity announcement to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.
For information on Application Submission and Receipt, visit Frequently Asked Questions – Application Guide, Electronic Submission of Grant Applications (//grants.nih.gov/grants/guide/url_redirect.htm?id=41137).

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits (//grants.nih.gov/grants/guide/url_redirect.htm?id=11133) must be followed

Instructions for Application Submission

The following section supplements the instructions found in the SF424 (R&R) Application Guide and should be used for preparing an application to this FOA.

SF424(R&R) Cover

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Project/Performance Site Locations

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Other Project Information

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Senior/Key Person Profile

All instructions in the SF424 (R&R) Application Guide must be followed.

R&R or Modular Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

R&R Subaward Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Cover Page Supplement

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Research Plan

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide.

The following modifications also apply:

- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

Appendix:

Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

PHS Human Subjects and Clinical Trials Information

When involving NIH-defined human subjects research, clinical research, and/or clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the SF424 (R&R) Application Guide must be followed.

Delayed Onset Study

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS Assignment Request Form

All instructions in the SF424 (R&R) Application Guide must be followed.

Foreign Institutions

Foreign (non-U.S.) institutions must follow policies described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11137), and procedures for foreign institutions described throughout the SF424 (R&R) Application Guide.

3. Unique Entity Identifier and System for Award Management (SAM)

See Part 1. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov

4. Submission Dates and Times

Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or Federal holiday (https://grants.nih.gov/grants/guide/url_redirect.html?id=82380) , the application deadline is automatically extended to the next business day.

Organizations must submit applications to Grants.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the NIH Policy on Late Application Submission.

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the SF424 (R&R) Application Guide.

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11142)

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) .

Pre-award costs are allowable only as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11143).

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the SF424 (R&R) Application Guide. Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically (//grants.nih.gov/grants/guide/url_redirect.htm?id=11144). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Guidelines for Applicants Experiencing System Issues (//grants.nih.gov/grants/ElectronicReceipt/support.htm#guidelines). For assistance with application submission, contact the Application Submission Contacts in Section VII.

> **Important reminders:**
>
> All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this FOA for information on registration requirements.
>
> The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the SF424 (R&R) Application Guide.
>
> See more tips (//grants.nih.gov/grants/guide/url_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review, NIH. Applications that are

incomplete or non-compliant will not be reviewed.

Requests of $500,000 or more for direct costs in any year

Applicants requesting $500,000 or more in direct costs in any year (excluding consortium F&A) must contact a Scientific/ Research Contact at least 6 weeks before submitting the application and follow the Policy on the Acceptance for Review of Unsolicited Applications that Request $500,000 or More in Direct Costs as described in the SF424 (R&R) Application Guide.

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in the policy (//grants.nih.gov/grants/guide/url_redirect.htm?id=82299). Any instructions provided here are in addition to the instructions in the policy.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. As part of the NIH mission (//grants.nih.gov/grants/guide/url_redirect.htm?id=11149), all applications submitted to the NIH in support of biomedical and behavioral research are evaluated for scientific and technical merit through the NIH peer review system.

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the project proposed).

Scored Review Criteria

Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance

Does the project address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific

environment, subject populations, or collaborative arrangements?

Additional Review Criteria

As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the Guidelines for the Review of Human Subjects (//grants.nih.gov/grants/guide/url_redirect.htm?id=11175).

Inclusion of Women, Minorities, and Individuals Across the Lifespan

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research (//grants.nih.gov/grants/guide/url_redirect.htm?id=11174).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines

for the Euthanasia of Animals. Reviewers will assess the use of chimpanzees as they would any other application proposing the use of vertebrate animals. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (//grants.nih.gov/grants/guide/url_redirect.htm?id=11150).

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmissions

For Resubmissions, the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewals

Not Applicable

Revisions

Not Applicable

Additional Review Considerations

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Applications from Foreign Organizations

Reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4)

plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: (1) Data Sharing Plan (//grants.nih.gov/grants/guide/url_redirect.htm?id=11151); (2) Sharing Model Organisms (//grants.nih.gov/grants/guide/url_redirect.htm?id=11152); and (3) Genomic Data Sharing Plan (GDS) (//grants.nih.gov/grants/guide/url_redirect.htm?id=11153).

Authentication of Key Biological and/or Chemical Resources:

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by the Center for Scientific Review, in accordance with NIH peer review policy and procedures (//grants.nih.gov/grants/guide/url_redirect.htm?id=11154), using the stated review criteria. Assignment to a Scientific Review Group will be shown in the eRA Commons. As part of the scientific peer review, all applications:

- May undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.
- Will receive a written critique.

Applications will be assigned on the basis of established PHS referral guidelines to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications. Following initial peer review, recommended applications will receive a second level of review by the appropriate national Advisory Council or Board. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.

- Relevance of the proposed project to program priorities.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.
Information regarding the disposition of applications is available in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11156).

Section VI. Award Administration Information

1. Award Notices

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157).
A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the grants management officer is the authorizing document and will be sent via email to the grantee's business official.

Awardees must comply with any funding restrictions described in Section IV.5. Funding Restrictions. Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

Any application awarded in response to this FOA will be subject to terms and conditions found on the Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158) website. This includes any recent legislation and policy applicable to awards that is highlighted on this website.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) as part of the NoA. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157) and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (//grants.nih.gov/grants/guide/url_redirect.htm?

id=11159). More information is provided at Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158).
Recipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights law. This means that recipients of HHS funds must ensure equal access to their programs without regard to a person's race, color, national origin, disability, age and, in some circumstances, sex and religion. This includes ensuring your programs are accessible to persons with limited English proficiency. HHS recognizes that research projects are often limited in scope for many reasons that are nondiscriminatory, such as the principal investigator's scientific interest, funding limitations, recruitment requirements, and other considerations. Thus, criteria in research protocols that target or exclude certain populations are warranted where nondiscriminatory justifications establish that such criteria are appropriate with respect to the health or safety of the subjects, the scientific study design, or the purpose of the research.

In accordance with the statutory provisions contained in Section 872 of the Duncan Hunter National Defense Authorization Act of Fiscal Year 2009 (Public Law 110-417), NIH awards will be subject to the Federal Awardee Performance and Integrity Information System (FAPIIS) requirements. FAPIIS requires Federal award making officials to review and consider information about an applicant in the designated integrity and performance system (currently FAPIIS) prior to making an award. An applicant, at its option, may review information in the designated integrity and performance systems accessible through FAPIIS and comment on any information about itself that a Federal agency previously entered and is currently in FAPIIS. The Federal awarding agency will consider any comments by the applicant, in addition to other information in FAPIIS, in making a judgement about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review of risk posed by applicants as described in 45 CFR Part 75.205 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

For additional guidance regarding how the provisions apply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA. HHS provides general guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see http://www.hhs.gov/ocr/civilrights/resources/laws/revisedlep.html. The HHS Office for Civil Rights also provides guidance on complying with civil rights laws enforced by HHS. Please see
http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html

(http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html); and http://www.hhs.gov/ocr/civilrights/understanding/index.html (http://www.hhs.gov/ocr/civilrights/understanding/index.html). Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html (http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html). Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at http://www.hhs.gov/ocr/office/about/rgn-hqaddresses.html (http://www.hhs.gov/ocr/office/about/rgn-hqaddresses.html) or call 1-800-368-1019 or TDD 1-800-537-7697. Also note it is an HHS Departmental goal to ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations. For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53 (http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53).

Cooperative Agreement Terms and Conditions of Award

Not Applicable

3. Reporting

When multiple years are involved, awardees will be required to submit the Research Performance Progress Report (RPPR) (//grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161)
A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161).

The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for awardees of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All awardees of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11170) on all subawards over $25,000. See the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11171) for additional information on this reporting requirement.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and

Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value greater than $10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of information reported in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). As required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 2011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts

eRA Service Desk (Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten on-time submission, and post-submission issues)

Finding Help Online: http://grants.nih.gov/support/ (//grants.nih.gov/support/) (preferred method of contact)
Telephone: 301-402-7469 or 866-504-9552 (Toll Free)

General Grants Information (Questions regarding application processes and NIH grant resources)
Email: GrantsInfo@nih.gov (mailto:GrantsInfo@nih.gov) (preferred method of contact)
Telephone: 301-945-7573

Grants.gov Customer Support (Questions regarding Grants.gov registration and Workspace)
Contact Center Telephone: 800-518-4726
Email: support@grants.gov (mailto:support@grants.gov)

Scientific/Research Contact(s)

Dona Love, Ph.D.
National Institute of Allergy and Infectious Diseases (NIAID)
Telephone: 301-761-7788
Email: dona.love@nih.gov (mailto:dona.love@nih.gov)

Peer Review Contact(s)

Examine your eRA Commons account for review assignment and contact information (information appears two weeks after the submission due date).

Financial/Grants Management Contact(s)

Vandhana Khurana
National Institute of Allergy and Infectious Diseases (NIAID)
Telephone: 240-669-2966
Email: vandhana.khurana@nih.gov (mailto:vandhana.khurana@nih.gov)

Section VIII. Other Information

Recently issued trans-NIH policy notices (//grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 45 CFR Part 75.

Weekly TOC for this Announcement (/grants/guide/WeeklyIndex.cfm?11-30-18)
NIH Funding Opportunities and Notices (/grants/guide/index.html)

SEIZURES IN A PIGTAILED MACAQUE

Tess House, DVM, MPH
Carolyn Malinowski, DVM, RLATG, CMAR, CPIA
Charlotte Hotchkiss, DVM, MS, PhD, DACLAM

PRESENTATION

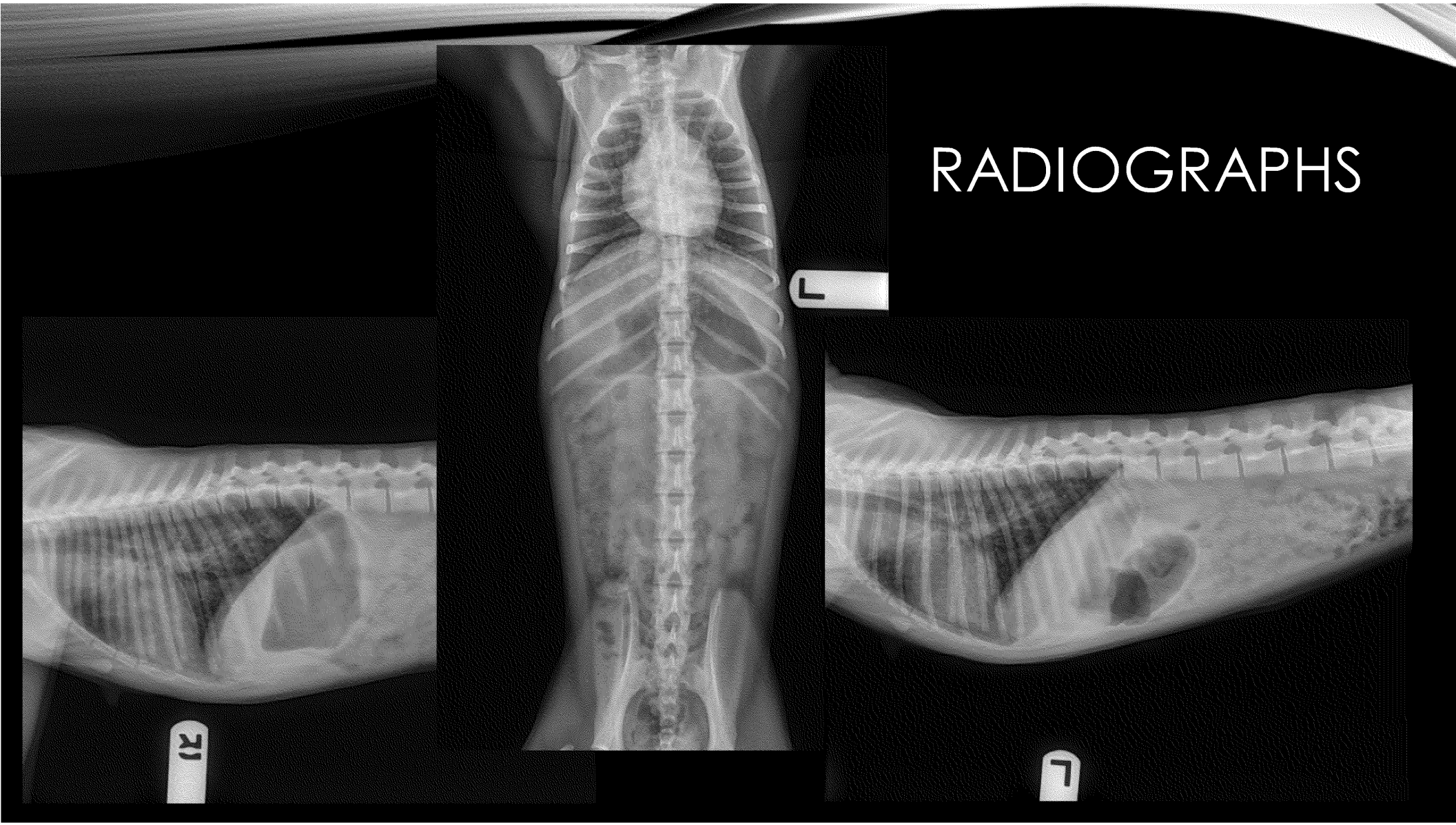
- 4-year old female *Macaca nemestrina*
- Assigned to SPF breeding colony
- Housed in indoor/outdoor compound in Arizona
- Coughing noted at time of routine semiannual exam

CBC/CHEMISTRY

WBC (Thou/ul)	**21.9**
RBC (mil/ul)	5.3
HGB (g/dl)	10.1
HCT (%)	36.5
MCV (fL)	68.7
MCH (pg)	19.0
MCHC (g/dL)	27.7
PLT (Thou/ul)	614
Neut (Thou/ul)	**13.6**
Lymph (Thou/ul)	6.1
Mono (Thou/ul)	**2.0**
Eos (Thou/ul)	0.3
Baso (Thou/ul)	0.0

Glucose (mg/dL)	**112**
Blood Urea Nitrogen (mg/dL)	11
Creatinine (mg/dL)	1
Total Protein (g/dL)	**8.2**
Albumin (g/dL)	3.1
Globulin (g/dL)	**5.1**
A:G Ratio	0.61
Total Bilirubin (mg/dL)	0.5
Calcium (mg/dL)	8.9
Phosphate (mg/dL)	6.8
Cholesterol (mg/dL)	82
Alkaline Phosphatase (U/L)	621
ALT (SGPT;U/L)	22
GGT (U/L)	49

RADIOGRAPHS



DIFFERENTIAL DIAGNOSIS

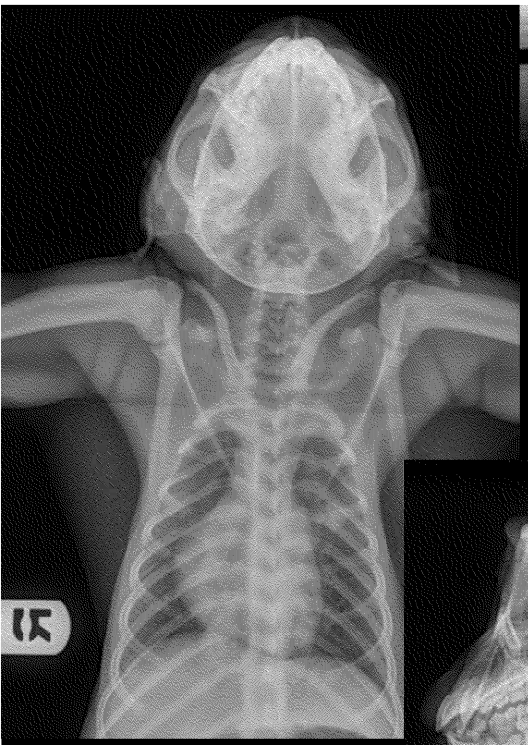
- Pneumonia
  - Bacterial
  - Viral
  - Fungal
  - Aspiration
- Pulmonary fibrosis

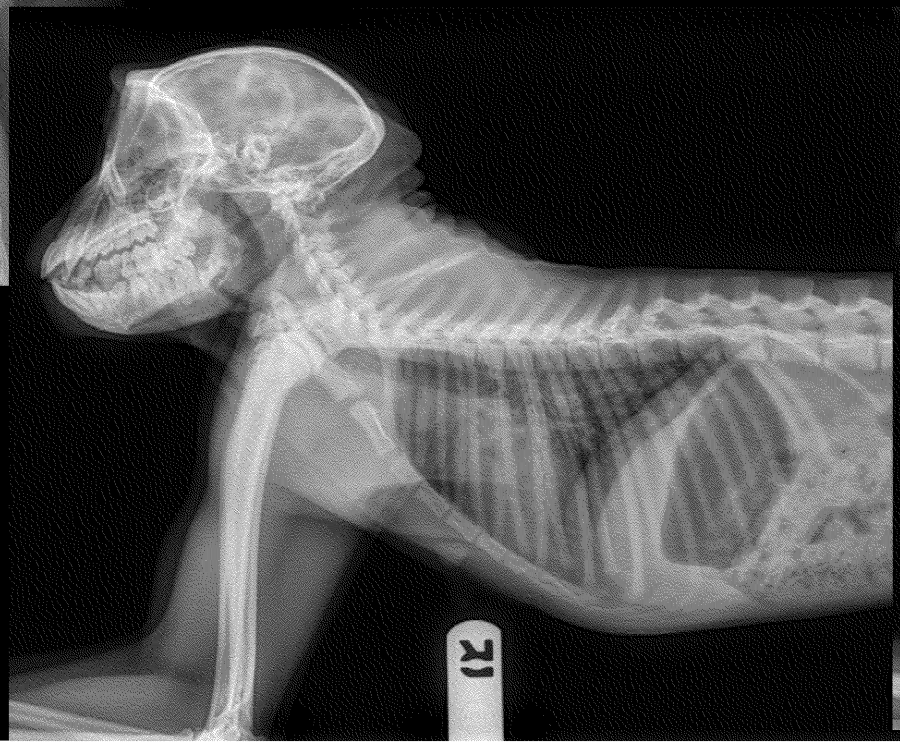
Presumptive diagnosis:
Coccidioidomycosis

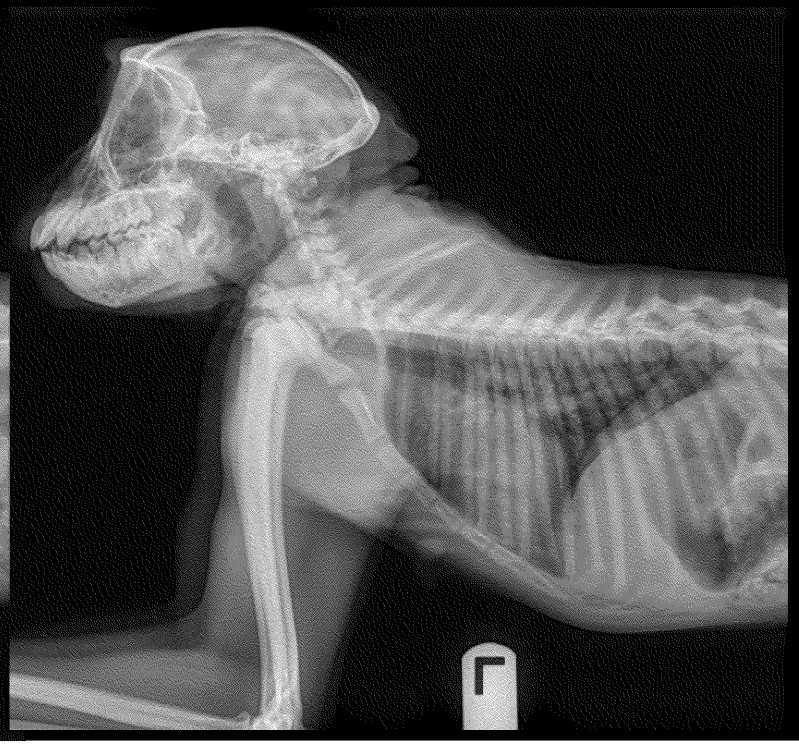
TREATMENT

- Initial (April 2018):
  - Fluconazole
  - Albuterol
- May 15, 2018 – noted to be less active with stiff neck and bilateral epistaxis
  - Amoxicillin
  - Prednisone
  - Meloxicam

RADIOGRAPHS 5/23/18



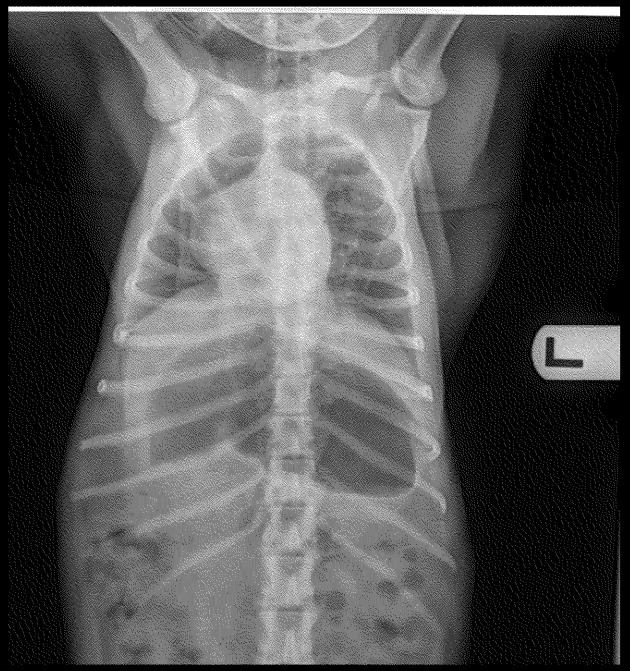


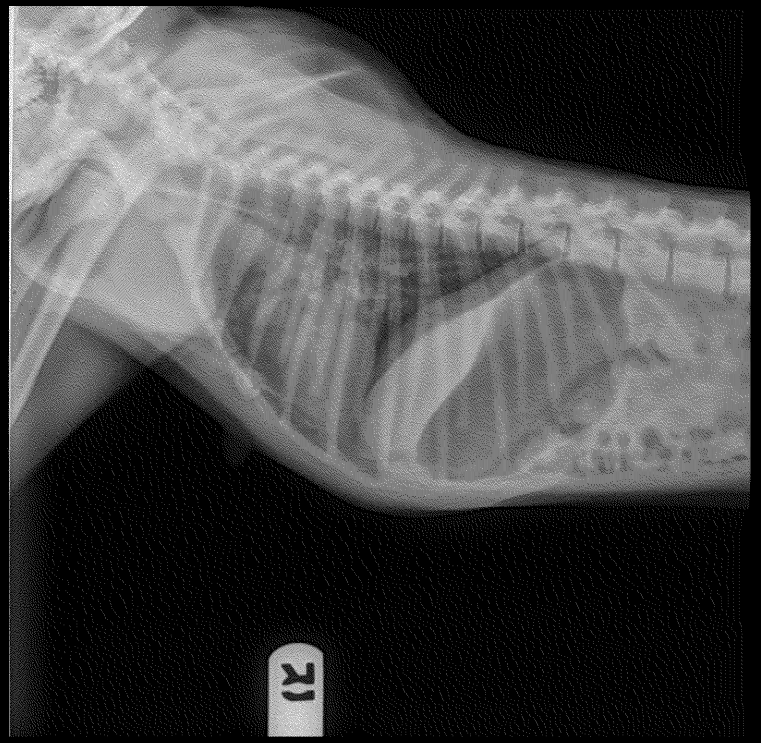


Cocci titer:
IgM 1:2
IgG 1:32

PROGRESSION

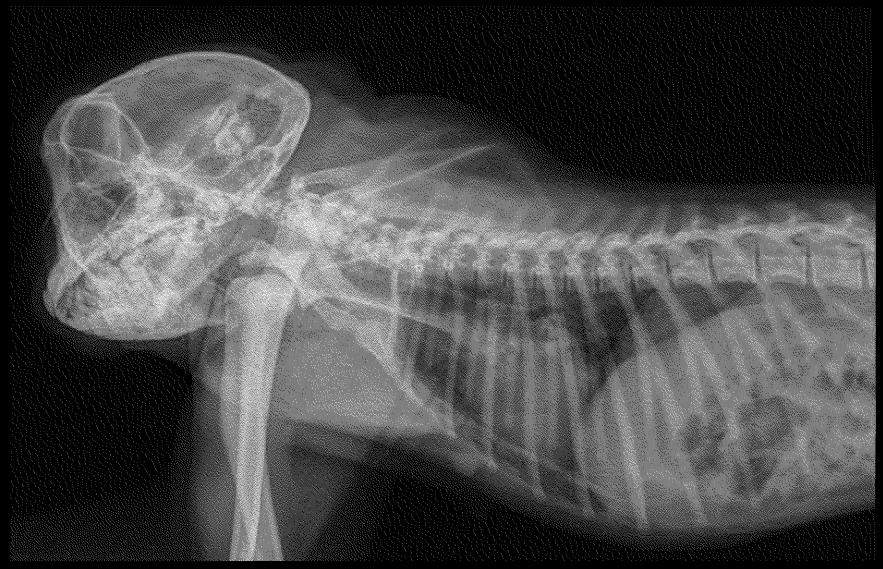
- Continuous fluconazole treatment
- Stable for a few months
- July 30, 2018
  - Lowered activity
  - Ataxia
- Cocci titer IgM negative, IgG 1:4
- Ataxia resolved with prednisone treatment

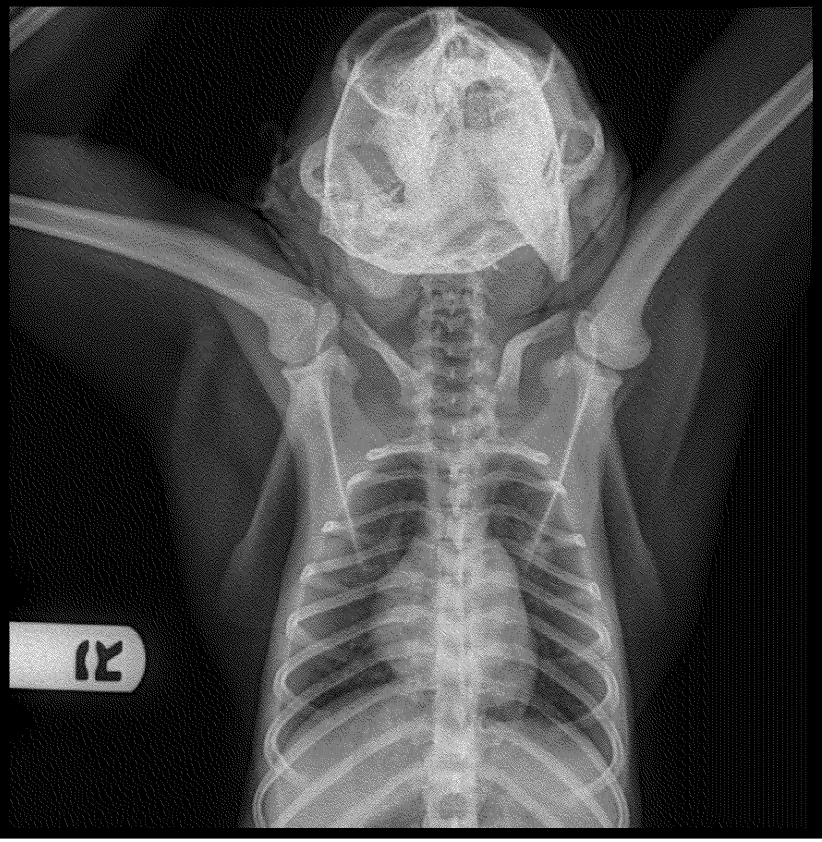




PROGRESSION

- August 29, 2018
  - Seizure in a.m.
  - Ataxia and stereotypies in p.m.
  - Treated with diazepam
  - Neuro signs resolved next day





PROGRESSION

- Returned to group
- 9/25/18 – seizure in compound
- Determined to be pregnant
- Treated with diazepam
- Kept in cage for seizure watch
- Seizures 10/15/18, 10/19/18
- Started gabapentin and Keppra (levetiracetam) 10/19/18
- Decreased gabapentin dose 10/26/18 due to sedation
- Seizure 11/9/18 prior to medication
- Cocci IgM 1:2, IgG 1:2

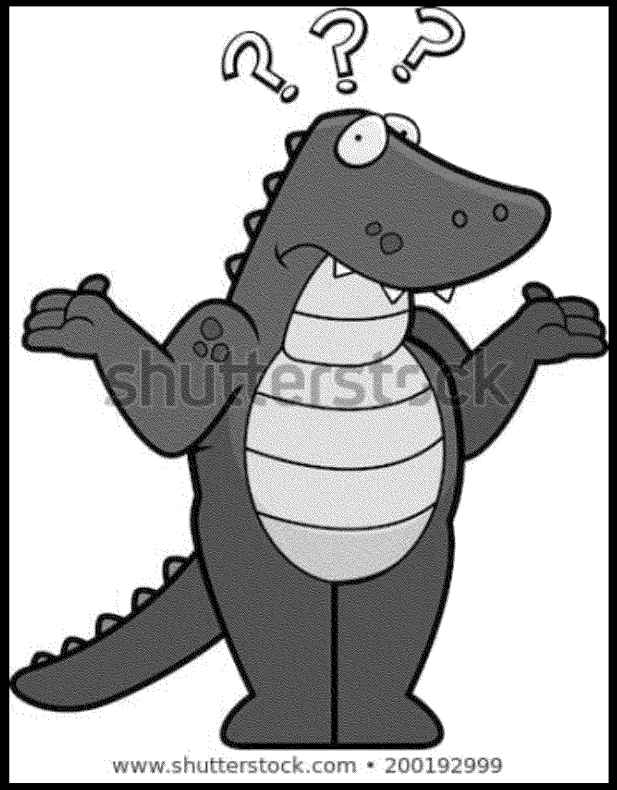
PROGRESSION

- Seizure 12/15/18
- Order compounded levetiracetam for more accurate dosing
- Seizure 1/4/19
- Due date 1/23/19
  - What would happen if there were seizure during parturition?
  - What would happen to infant if there were seizure after birth?

PREGNANCY OUTCOME

- C-section 1/10/19
- Routine surgery
- Collected amniotic fluid for potential dam-infant introduction
- 580 g healthy male infant
- Re-introduction not successful
- Infant fostered successfully

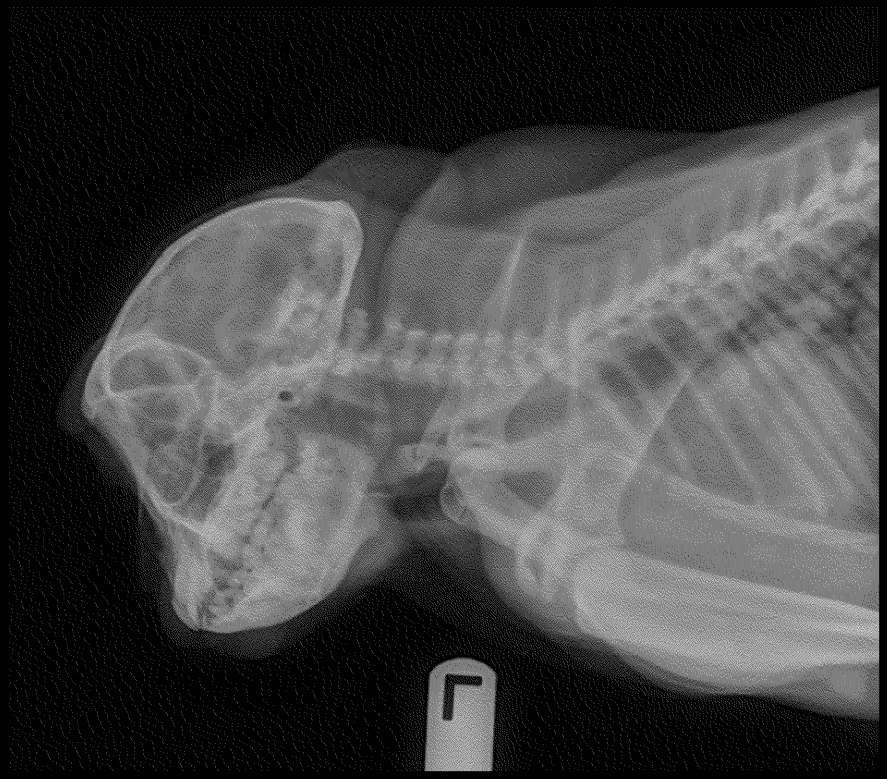
WHAT TO DO?

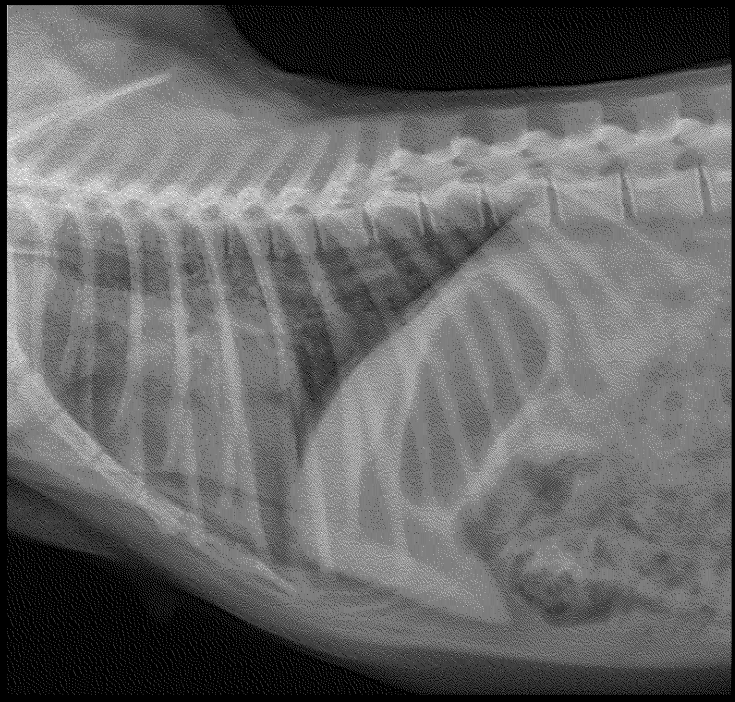


COCCIDIOIDOMYCOSIS SUMMARY

Cocci	IgG Titer Result	IgG Titer Value	IgM Titer Result	IgM Titer Value
1/10/19	positive (+)	1:4	negative (-)	<1:1
10/29/18	positive (+)	1:2	positive (+)	1:2
9/25/18	positive (+)	1:8	positive (+)	1:2
8/30/18	positive (+)	1:32	positive (+)	1:2
7/30/18	positive (+)	1:4	negative (-)	<1:1
5/23/18	positive (+)	1:32	positive (+)	1:2
4/16/18	positive (+)	1:16	positive (+)	1:4
Note that cocci titers were done in 2014-2016 and were negative. No titer was done in 2017.				

FINAL RADIOGRAPHS





ENDPOINT

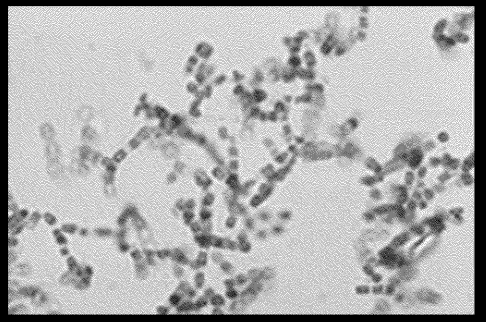
- Continued seizures (3/6/19)
- Euthanasia 3/13/19
- Necropsy:
  - Lungs – mottled with multifocal 1-2 mm white nodules and adhesions
  - Brain fixed whole

HISTOPATHOLOGY - LUNGS

HISTOPATHOLOGY - BRAIN

COCCIDIOIDOMYCOSIS

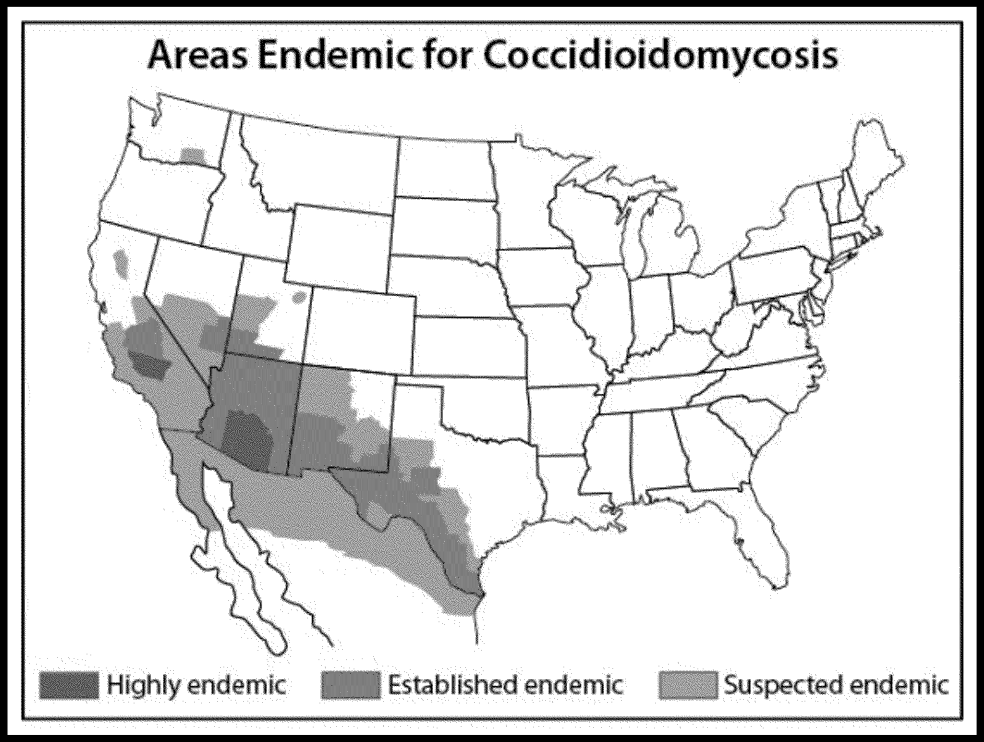
- Fungal infection caused by the genus Coccidioides
  - C. immitis
  - C. posadasii



CDC image

  - More commonly known as Valley Fever or Cocci
  - Able to infect humans and a wide range of animal species
    - NHP species with cases reported include baboons, capuchins, chimpanzees, geladas, guenons, gorillas, lemurs, mandrills, macaques, mangabeys, spider monkeys, squirrel monkeys, woolly monkeys

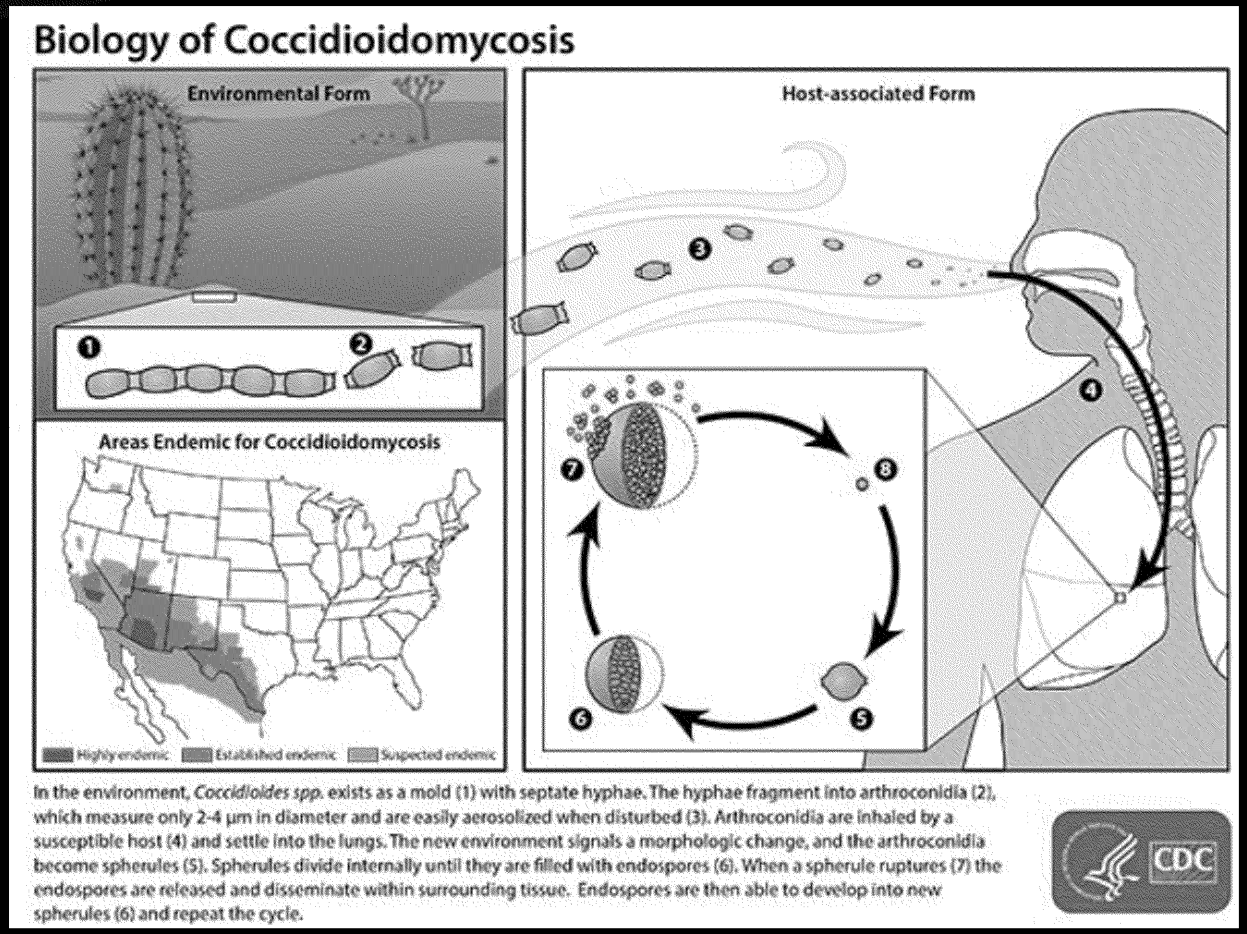
ENDEMIC REGIONS



www.cdc.gov/fungal/diseases/coccidioidomycosis/causes.html

- Found in portions of North, South, and Central America
- Highly endemic regions found in Arizona and California
- Newer region found in Washington state

LIFE CYCLE


Biology of Coccidioidomycosis
Environmental Form
Host-associated Form
Areas Endemic for Coccidioidomycosis
Highly endemic
Established endemic
Suspected endemic
In the environment, *Coccidioides spp.* exists as a mold (1) with septate hyphae. The hyphae fragment into arthroconidia (2), which measure only 2-4 µm in diameter and are easily aerosolized when disturbed (3). Arthroconidia are inhaled by a susceptible host (4) and settle into the lungs. The new environment signals a morphologic change, and the arthroconidia become spherules (5). Spherules divide internally until they are filled with endospores (6). When a spherule ruptures (7) the endospores are released and disseminate within surrounding tissue. Endospores are then able to develop into new spherules (6) and repeat the cycle.
CDC

ROUTES OF INFECTION

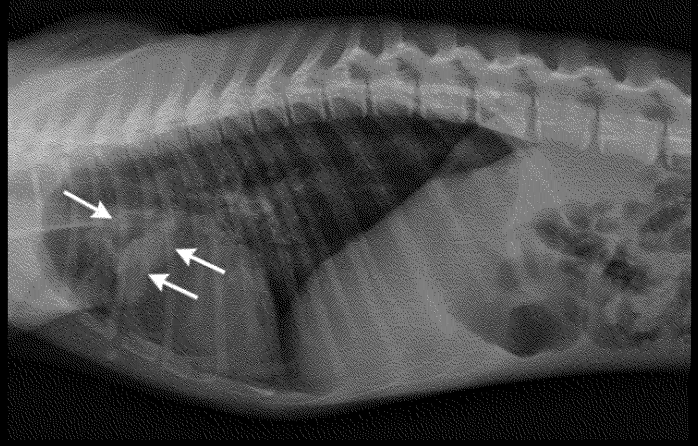
- Primary route of infection is inhalation
- Not contagious or zoonotic
- Less frequent routes of infection can include:
  - Break in the skin such as a cut, wound, or splinter
  - Aspiration of amniotic fluid during parturition
  - Organ transplantation
- Low infectious dose

SYMPTOMS

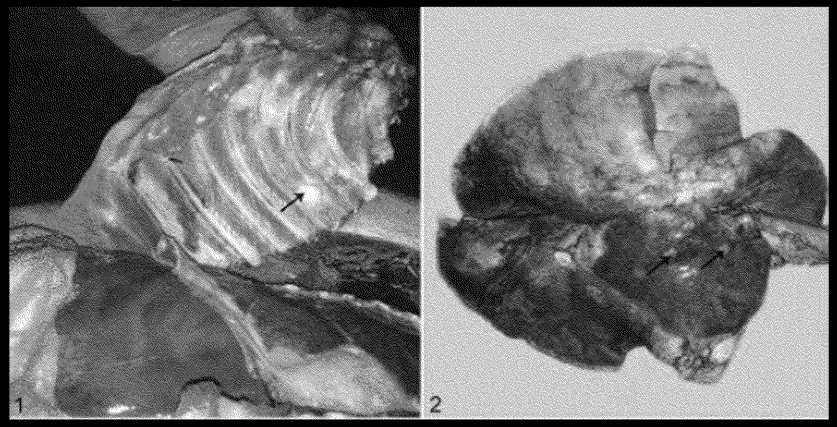
- Diverse clinical presentation (average 7-28 days after exposure)
- Clinical illness in NHP similar to humans
- Lethargy
- Coughing
- Shortness of breath
- Fever
- Inappetence and/or weight loss
- Joint pain or lameness
- Skin rash or nodules
- Neurological symptoms

CLINICAL AND PATHOLOGICAL FINDINGS

- Eosinophilia, mild lymphocytosis, monocytosis
- Hyperglobulinemia
- Radiographic changes
- Tan to white nodules particularly within lung tissue and thoracic wall



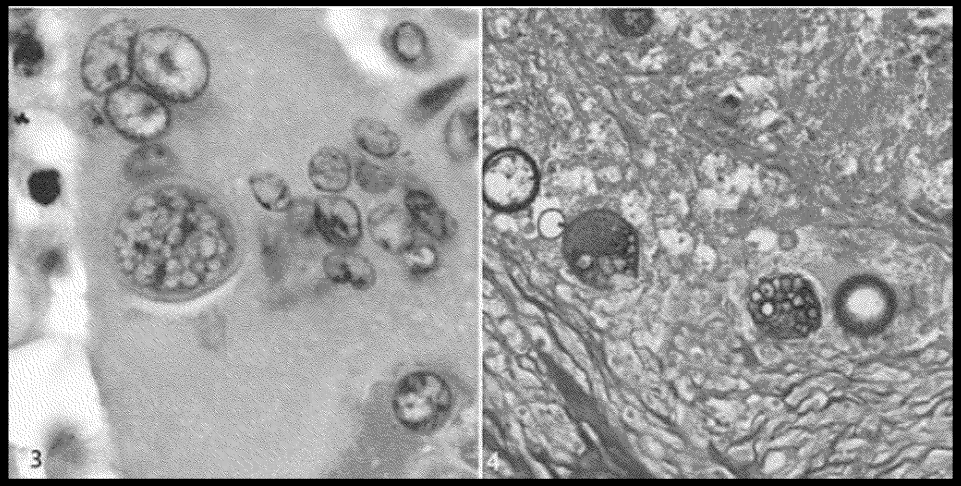
Kundu et al, 2017



Koistinen et al, 2018

PATHOGEN DETECTION

- Direct detection
  - Microscopy
  - Molecular detection
- Culture (safety concerns)
- Serology (EIA, IMDF, CF)



CEREBRAL COCCIDIOIDOMYCOSIS

- 95% fatal within two years in humans if untreated
- Most common presentation in humans is headache; very few reports of seizures
- Most common presentation in dogs is seizures
- Diagnosis: serology, CSF (exam, culture, PCR), neuroimaging
- Treatment: antifungals, supportive care, surgery (CSF shunt)

ANTI-SEIZURE MEDICATIONS

- Diazepam
  - Enhances GABA activity
- Gabapentin
  - Interacts with voltage-sensitive Ca channels
- Levetiracetam
  - Binds to synaptic vesicle protein SV2A

PREVENTION AND SURVEILLANCE

- Dust mitigation/limiting exposure
  - Future growth to focus on indoor only animal enclosures with HEPA filtration
  - Construction site using dust mitigation practices
  - Minimizing animal exposure time outdoors when high wind/dust storms expected
  - Spray down of enclosures before having access to outdoor portion
- Routine serological surveillance captured at semi-annuals
  - Twice a year (+) clinical indication or suspicion (weight loss, coughing)

TREATMENT

- Triazoles or Amphotericin B
  - Fluconazole, Itraconazole, Voriconazole, Posaconazole
  - Fluconazole most frequently used
    - Tablet, liquid, fluconazole impregnated feed
    - Currently 18% of the colony at Arizona is on Fluconzaole
      - 20 of 52 animals (6.9% of colony) cocci negative
      - 32 animals (11.1% colony) are cocci positive

NECROPSY DATA FROM ARIZONA

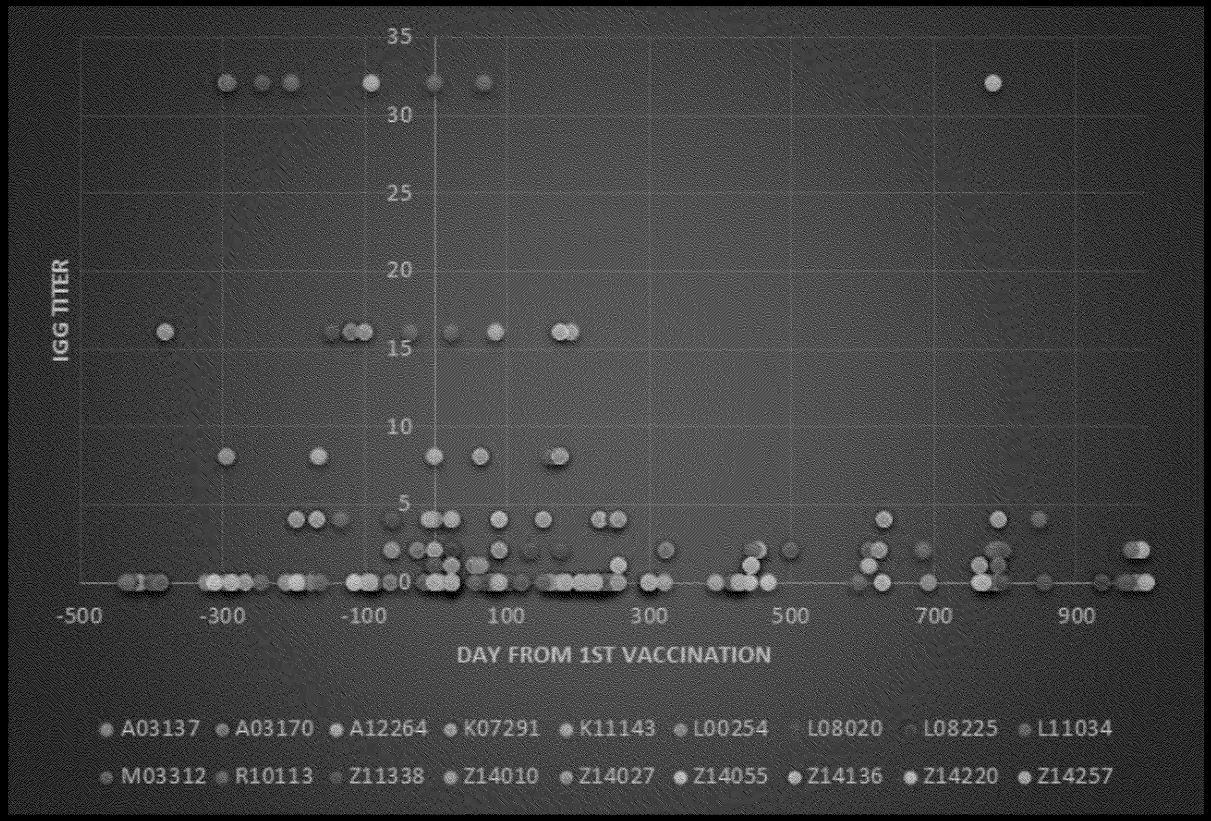
Year	Cases	Gender	Location
2013	N=3	3 female	2 pulmonary, 1 disseminated
2014	N=18	17 female, 1 male	2 pulmonary, 16 disseminated
2015	N=13	12 female, 1 male	3 pulmonary, 10 disseminated
2016	N=8	7 female, 1 male	4 pulmonary, 4 disseminated
2017	N=2	2 female	1 pulmonary, 1 disseminated
2018	N=1	1 female	1 disseminated

VACCINATION

- No commercial vaccine available
- A human vaccine trial was conducted in the 1980's but no difference was found in the number of cases of the severity of disease between vaccine and placebo groups
- Challenging in terms of antigen expression, cost of production
- Interest in Delta-CPS1
  - U of A created mutant strain that does not cause disease in mice strains including those with no lymphocytes and those with bone marrow suppression
  - Good survival statistics in those vaccinated
  - Working on replacing the antibiotic resistance marker with one that does not involve antibiotics

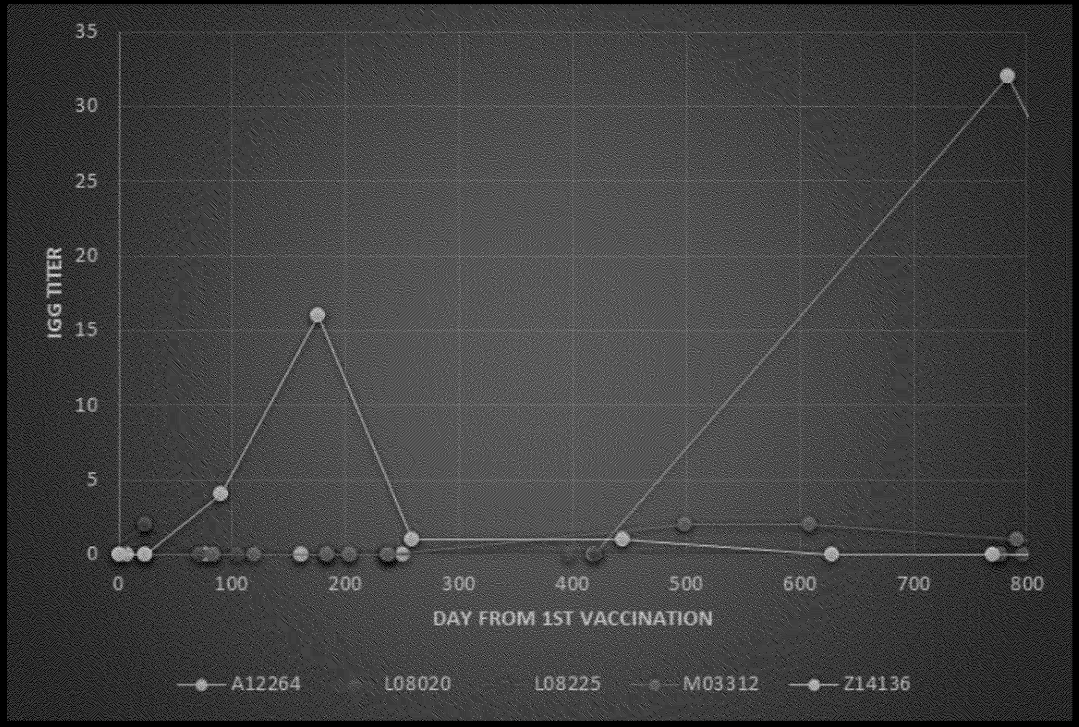
VACCINATION IN NHP

- Day 1, 8, and 45
- 2 – 4 mg whole spherules
- Some animals naïve; some history of prior cocci titers



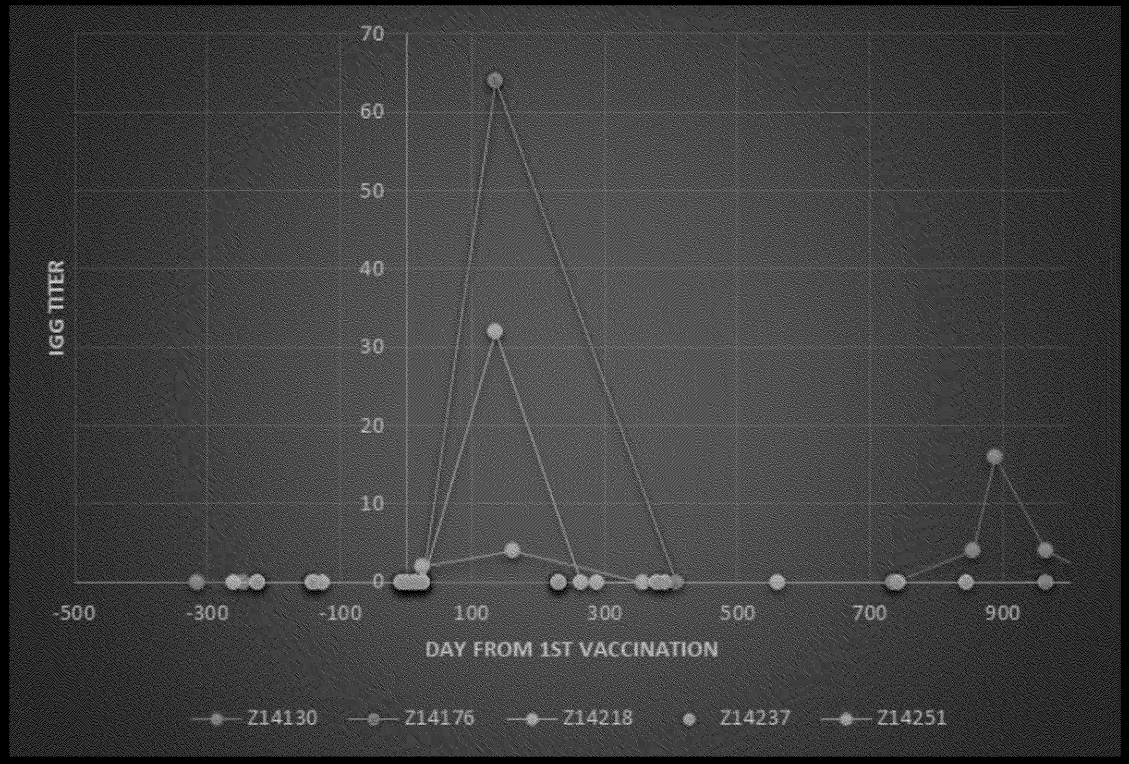
ANIMALS SERONEGATIVE PRIOR TO VACCINE

- 6 animals did not seroconvert
- 2 animals seroconverted after vaccination
- 3 animals became infected later



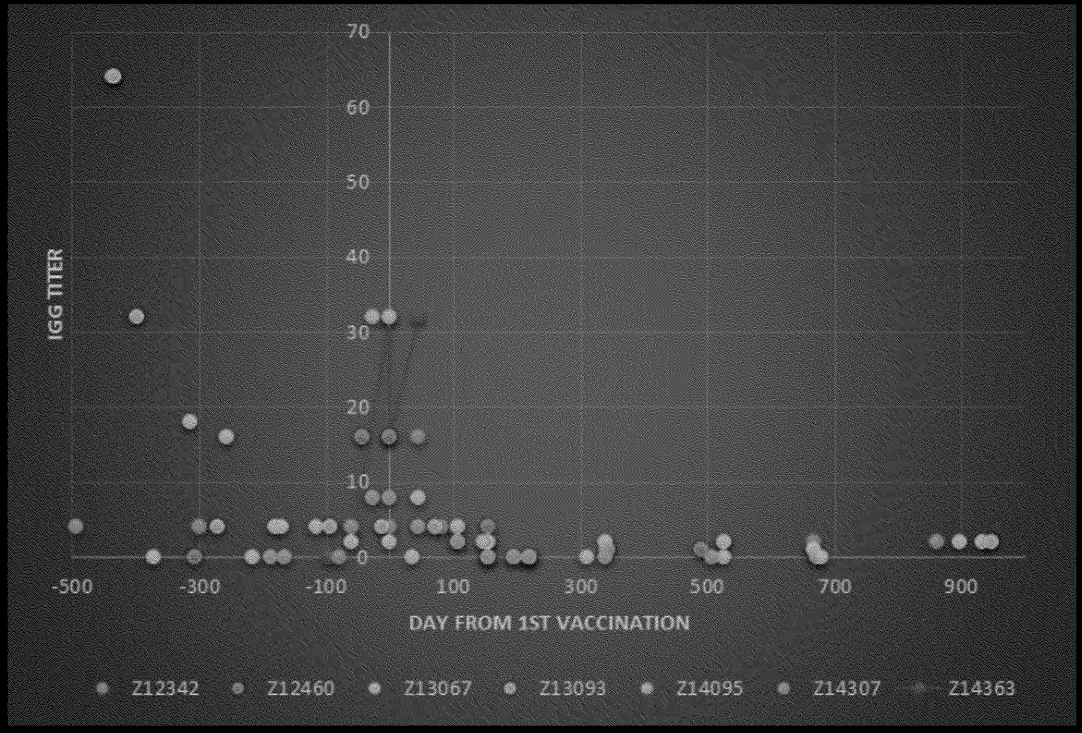
COHORT 2

- Day 1, 8, and 45
- 6 mg whole spherules
- All animals naïve
- 1 animal did not seroconvert
- 2-3 animals responded to vaccine
- 1-2 animals became infected later



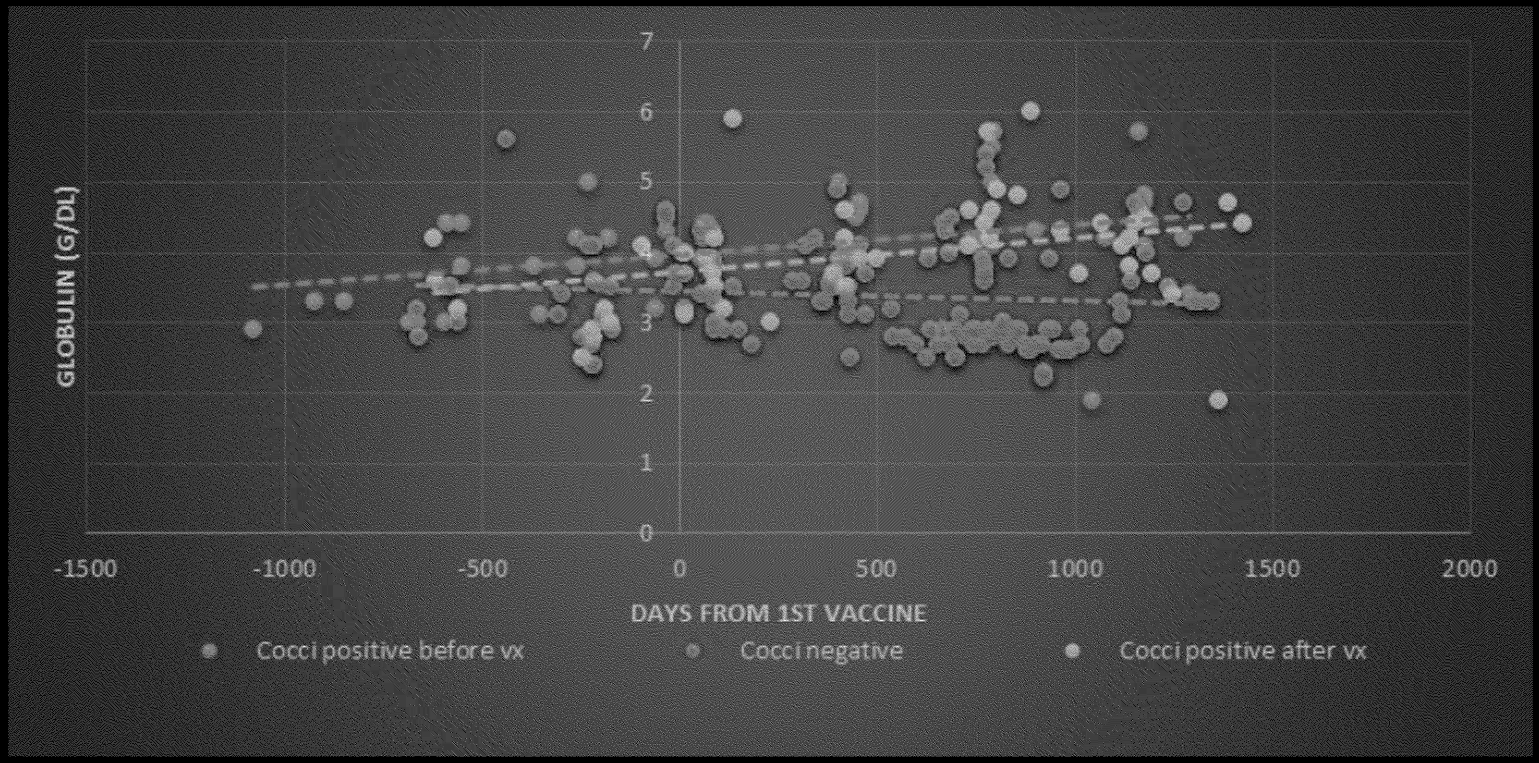
COHORT 3

- Day 1, 8, and 45
- 3 animals received 2 mg whole spherules
- 4 animals receive subunit vaccine
- No animals naïve
- Two animals in subunit group developed persistent site reactions
- One animals in subunit group developed disseminated disease



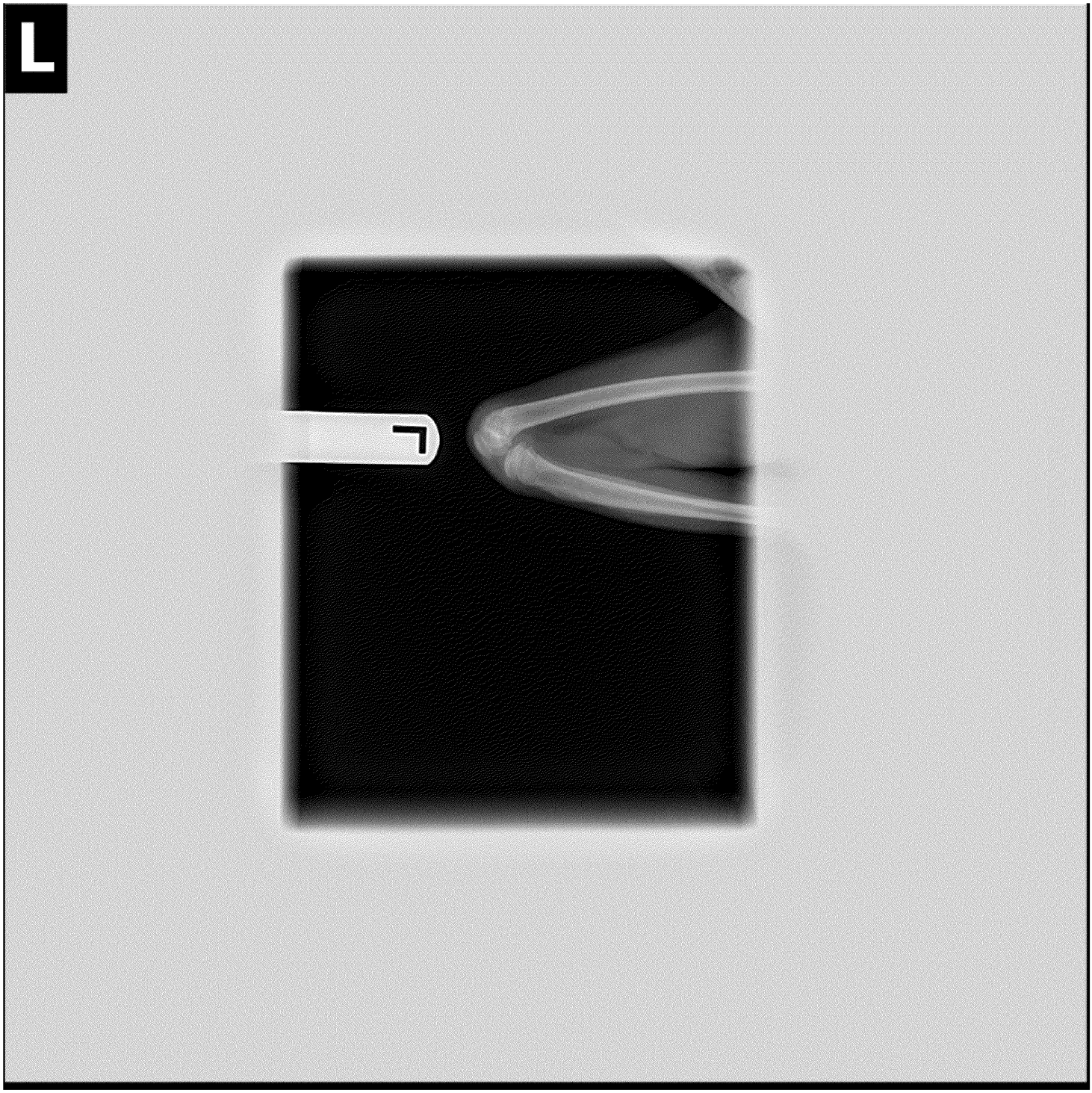
CLINICAL BIOMARKER

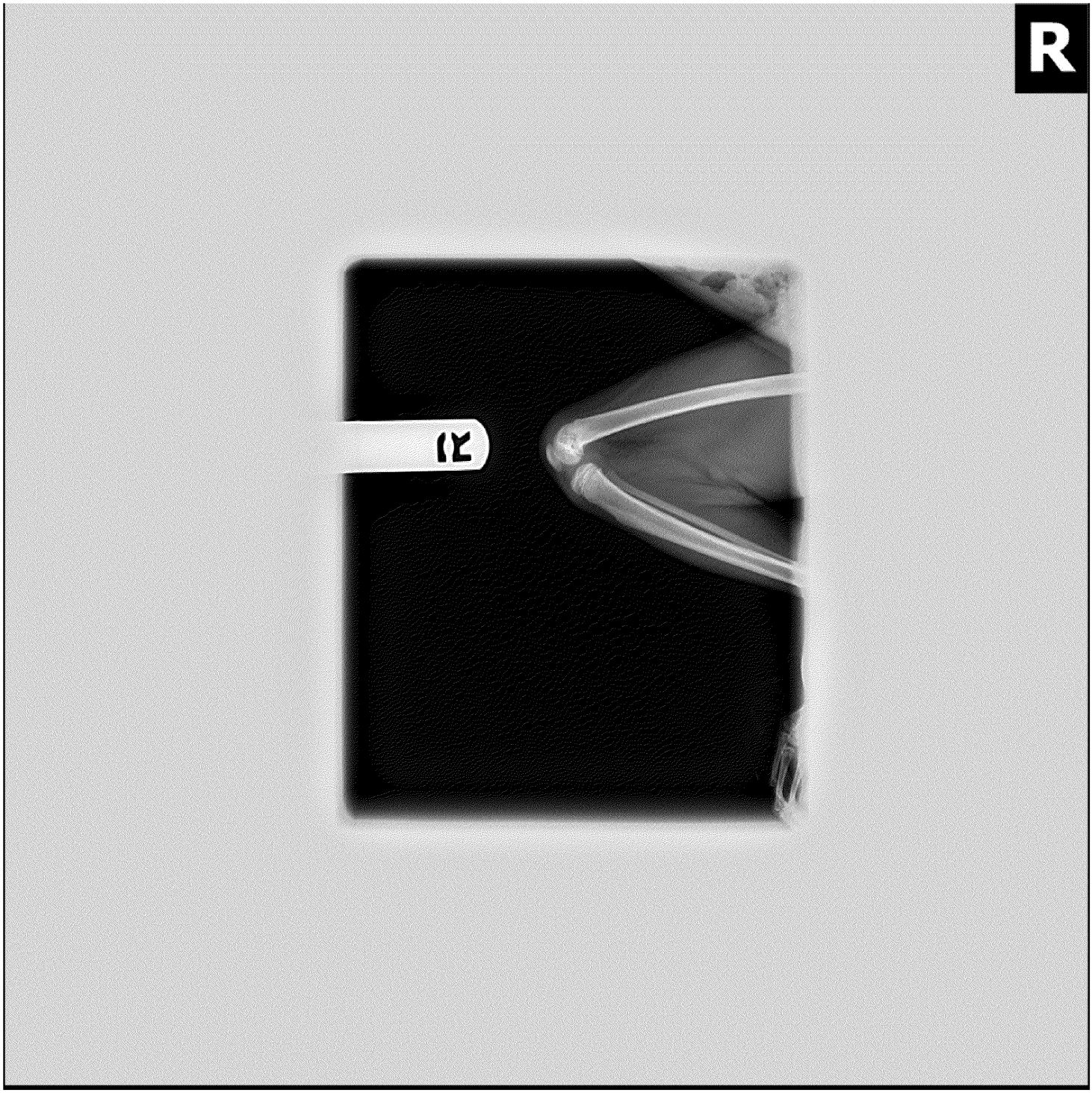
- Globulin most consistent biomarker in M. nemestrina
- Increase in globulin same in animals infected before or after vaccination



SUMMARY

- Coccidioidomycosis can usually be controlled, but elimination is more difficult
- Even non-severe infections can spread to CNS
- Medications can decrease seizure frequency and appear to be safe in pregnancy
- Levels of seizure activity that are manageable in pet animals may be problematic in research animals
- A vaccine is needed, but not currently available for this species

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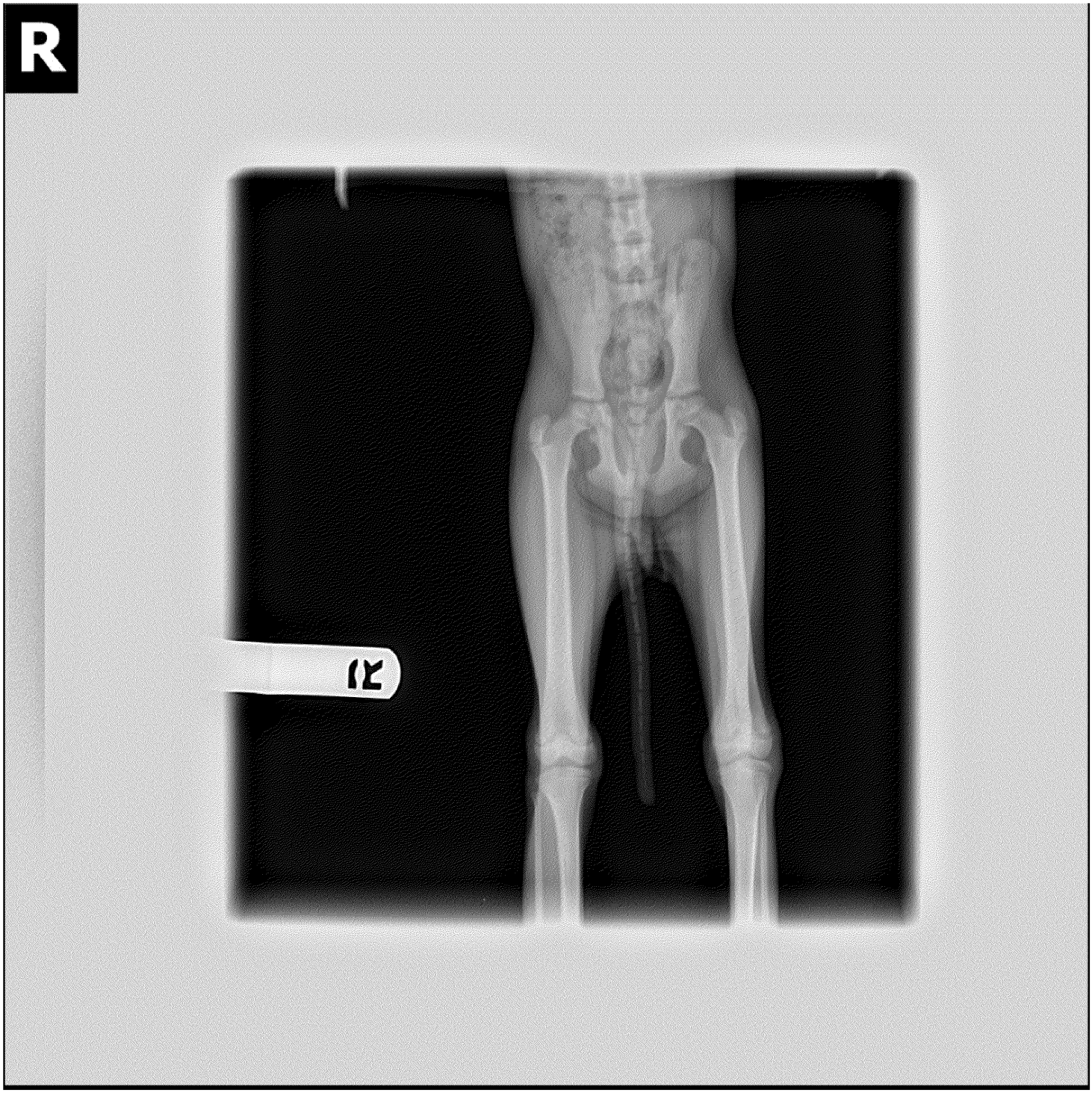
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Valley Fever Soil Collection Proposal

Problem: Valley Fever is an emerging fungal disease that is increasing in reported cases throughout the southwest. This debilitating disease affects humans as well as wild and captive animals. The organism that causes Valley Fever (*Coccidioides* spp.) lives in arid soils in the southwest but we do not understand a lot about the factors that contribute to the distribution and transmission of the fungus. There is a unique research opportunity at the Washington National Primate Research Center to study this organism. There are a number of animals that have gotten infected with Valley Fever and we can use this unique experience to gain insights into this disease that can be applied to human health.

Methods: Working with the veterinary faculty at the facility we will collect blood samples from the animals and collect soil from around the property. The veterinarians will collect the blood and we will process the samples at our lab at Northern Arizona University. No human blood or other samples will be used in this study. Soil will be collected from the soil top and from within rodent burrows on the facility property. No excavation of soil will be done and there will be minimal disturbance to the burrows. We will need approximately 100 soil samples of approximately 500 grams per sample.

What we hope to gain: We will use the blood samples to genotype the animals to determine if there are certain animals that are genetically more susceptible to getting infected by the fungus. This will help protect animals that may be at an additional risk of getting sick and possibly be applied to humans. We will use the soil samples to try and detect the fungus in the soil. This will allow us to gain more insights on how the organism is distributed in the environment and see if we can detect a source of infection to the animals in the environment.