

## Adrenal exhaustion and immunoglobulin suppression: common findings in 43 dogs with Sudden Acquired Retinal Degeneration (SARD)

Caroline D. Levin RN

Copyright © July 18, 2008. www.petcarebooks.com/research

- The author reviewed the charts of 43 SARD-affected dogs between 2005-2008. Dogs were tested/treated by their general practice veterinarian. Results were fairly consistent despite slight variations in hormone replacement therapy and lab facilities (see below). Follow-up lab results represent only a brief window in time; treatment is life-long.
- Two laboratories revised their reference ranges during this time period and those revisions are reflected below. *Note to practitioners:* reference ranges at National Veterinary Diagnostic Services are extremely narrow and slight elevations are significant, correlating closely with clinical signs of PU/PP/lethargy/confusion, etc.<sup>1</sup>
- Initial evaluation ranged from 1 week–3 years post-SARD onset (mean = 3.96 months). 42 of 43 dogs (98%) demonstrated elevations in one or more adrenal sex-hormones (progesterones, androgen, and/or estrogens). Inadequate cortisol production is a common cause of elevated sex-hormones in both dogs and humans.<sup>1-7</sup> When production of active cortisol fails during adulthood the condition is described as adrenal exhaustion.<sup>8,9</sup>
- 33 dogs had immunoglobulins assayed as well. 30 of 33 (91%) demonstrated low levels of IgM, IgG and/or IgA. However, this trend was not consistent between lab facilities. One explanation may involve sample collection or handling technique. If serum samples are permitted to warm, immunoglobulins aggregate, yielding high false-positive levels.<sup>10,11</sup> Sample age, evaporation, and reagent shelf life are also reported to erroneously affect outcomes.<sup>12</sup> Rising estrogen levels are reported to *suppress* both immunoglobulin production in humans and bone marrow activity in dogs.<sup>13-15</sup>
- 19 of the 43 dogs received low-dose cortisol and thyroid hormone replacement therapy. Duration of treatment prior to retest = 1–12 months (mean = 3.75 months). Of the dogs treated, **95% demonstrated improved sex-hormone levels** and **100% demonstrated improved immunoglobulin levels**. Three dogs (#19, 32, 34) demonstrated some degree of functional vision, confirmed by either GP veterinarian or veterinary ophthalmologist.
- Recommendations: SARD-affected dogs should be *promptly* tested—and treated for—adrenal exhaustion, as hormone replacement therapy improves sex-hormone levels and immunoglobulin production in nearly all dogs and may restore functional vision in some dogs.

1. Levin C. Sudden Acquired Retinal Degeneration, associated pattern of adrenal activity, and hormone replacement in three dogs – a retrospective study. *Proceedings of the 38<sup>th</sup> Annual Meeting of the College of Veterinary Ophthalmologists* 2007; 38: 32.
2. Guthrie GP, Wilson EA, Quillen DL, Jawad MJ. Adrenal androgen excess and defective 11-beta-hydroxylation in women with idiopathic hirsutism (abstract). *Archives of Internal Medicine* 1982; 142:729- 735.
3. Deaton M, Glorioso JE, Mclean, DB. Congenital Adrenal Hyperplasia—Not really a zebra. *American Family Physician* 1999; 59: 1190-1196.
4. Naessen S, Carlstrom K, Garoff L, Glant R, Hirschberg AL. Polycystic ovary syndrome in bulimic women—an evaluation based on new diagnostic criteria (abstract). *Gynecological Endocrinology* 2002; 22:388-394.
5. Derman RJ. Effects of sex steroids on women's health: implications for practitioners (abstract). *American Journal of Medicine* 1995; 1A: 137S-143S.
6. Plechner AJ. Cortisol abnormality as a cause of elevated estrogen and immune destabilization: Insights for human medicine from a veterinary perspective. *Medical Hypothesis* 2004; 62: 575-581.
7. Jeffries MK. *Safe Uses of Cortisol* third edition. Charles C. Thomas Publisher, Ltd, Springfield, 2004.
8. Marik PE. Adrenal-exhaustion syndrome in patients with liver disease (abstract). *Intensive Care Medicine* 2006; 32: 275-280.
9. Selye H. *The Stress of Life* revised edition. McGraw-Hill, Incorporated: New York, 1976.
10. Yoshida H, Ishikawa H, Honda S, Miura Y, Ogata M. False positive reaction of heat-inactivated sera in enzyme-linked immunosorbent assay for antibody to hepatitis C virus (abstract). *Fukushima Journal of Medical Science* 1992; 38: 35-41.
11. Luginbühl A, Nikolic M, Beck H. Complement Factor D, Albumin and Immunoglobulin G Anti-Band Protein Antibodies Mimic Serum in Promoting Rosetting of Malaria-Infected Red Blood Cells. *Infection and Immunity* 2007; 75: 1771-7.
12. Key M. *Pathology: Immunohistochemical Staining Methods fourth edition*. Dako Laboratories, Carpinteria, California, 2006.
13. Hart JE. Endocrine pathology of estrogens: species differences (abstract). *Pharmacology Therapeutics* 1990; 47: 203-218.
14. Zayed I, van Esch E, McConnell R. Systemic and histopathologic changes in beagle dogs after chronic daily oral administration of synthetic or natural estrogens with special reference to the kidney & thyroid. *Toxicologic Pathology* 1998; 26: 730-41.
15. Blum M, Zacharovich D, Pery J, Kitai E. Lowering effect of estrogen treatment on immunoglobulins in menopausal women (abstract). *Revue française de gynécologie et d'obstétrique* 1990; 4: 207-209.

## Adrenal exhaustion and immunoglobulin suppression: common findings in 43 dogs with Sudden Acquired Retinal Degeneration (SARD)

Caroline D. Levin RN

Dog	Breed, Age & Gender	Interval from SARD onset	Lab results : initial	Testing facility & normal range	Hormone replacement treatment	Lab results : post-treatment	Interval between tests
1	Beagle, 10 y/o, M/n	11 months	estradiol 23.40	<b>Cornell University</b> estradiol: males < 20 pg/ml	triamcinolone acetonide 3mg IM methylprednisilone 2mg PO SID levothyroxine 0.3mg PO BID	estradiol 6.4	2 months
2	Maltese-mix, 9.5 y/o, F/s	2 weeks	estradiol 27.22 IgA 30 IgG 1500 IgM 400	<b>Antech Diagnostics</b>  <i>estradiol:</i> spayed females and neutered males <15-20 pg/ml  <i>immunoglobulins</i> (in conjunction with Cornell) IgA: 20-150 mg/dl IgG: 1000-2000 mg/dl IgM: 70-270 mg/dl	n/a		
3	Newfoundland 6 y/o, M/n	1 month	estradiol 33.33 IgA 52 IgG >5000 IgM 400		n/a		
4	Brittany Spaniel, 9 y/o, M/n	1 week	estradiol 34.20 IgA 135 IgG 3000 IgM 150		n/a		
5	JRT, 7 y/o, F/s	1 month	androstene. 2.6/ 6.4 estradiol 45.7/ 46.4 progesterone 0.15/ 0.5 17-OH prog. 0.65/ 2.19		<b>Univ. of Tennessee CVM</b> prior to 5/2008  <i>Baseline</i> androstenedione 0.1-5.7ng/ml estradiol 30.8-69.9 pg/ml progesterone 0.01-0.49 pg/ml 17-OH prog. 0.01-0.77 pg/ml  <i>Post-ACTH</i> androstene. 2.7-39.7 ng/ml estradiol 27.9--69.2 pg/ml progesterone 0.10-1.50 pg/ml 17-OH prog. 0.40-1.62 pg/ml	triamcinolone acetonide 1.8mg IM dexamethasone sod phos 1mg IM methylprednisilone 1mg PO levothyroxine 0.15mg PO BID	androstendione 1.9/27.4 estradiol 44.1/ 36.4 progesterone 0.12/ 2.07 17-OH prog 0.09/ 1.36
6	PVGB, 12 y/o, F/s	3 months	androstene.1.5/10.1 estradiol 63.5/ 70.7 progesterone 0.28/ 0.46 17-OH prog. 0.04/ 0.26		n/a		
7	Labrador-mix, 8 y/o, M/n	2.5 months	androstene. 2.1/17.8 estradiol 49.1/ 44.4 progesterone 0.13/ 1.57 17-OH prog. 0.47/ 1.11		n/a		

<b>8</b>	Eng. Pointer, 8.5 y/o, F/s	2 months	androstene. 1.8/ 28.5 estradiol 21.4/ 26.3 progesterone 0.26/ 2.3 17-OH prog. 0.05/ 1.96	<b>Univ. of Tennessee CVM</b> prior to 5/2008	n/a		
<b>9</b>	Cairn Terrier, 9 y/o, F/s	1 year	<b>baseline only</b> androstene. 1.6 estradiol 83.3 progesterone 0.24 17-OH prog. 0.16		n/a		
<b>10</b>	Chow-mix, 8 y/o, F/s	1 month	androstene. 2.0/ 10.9 estradiol 45.8/ 59.7 progesterone 0.01/ 0.77 17-OH prog. 0.07/ 0.91		n/a		
<b>11</b>	Golden Retr-mix, 8 y/o, F/s	6 months	androstene. 2.4/ 10.1 estradiol 84.0/ 77.0 progesterone 0.45/ 2.54 17-OH prog. 0.41/ 2.68		n/a		
— Change in reference range —							
<b>12</b>	Brittany Spaniel, 6 y/o, F/s	2.5 months	androstene. 6.9/ 22.0 estradiol 55.6/ 52.9 progesterone 0.31/ 1.41 17-OH prog. 0.31/ 1.98	<b>Univ. of Tennessee CVM</b> after 5/2008	prednisone 3.33mg PO SID levothyroxine 0.4mg PO BID	androstene. 1.8/ 3.4 estradiol 49.0/ 53.7 progesterone 0.25/ 0.44 17-OH prog 0.06/ 0.57	3 months
			<i>Baseline</i> androstenedione 0.1-5.7ng/ml estradiol 30.8-69.9 pg/ml progesterone 0.25-0.49 pg/ml 17-OH prog. 0.08-0.77 pg/ml  <i>Post-ACTH</i> androstene. 2.7-39.7 ng/ml estradiol 27.9--69.2 pg/ml progesterone 0.10-1.50 pg/ml 17-OH prog. 0.40-1.62 pg/ml				

13	GSD, 9 y/o, F/s	4.5 months	total estrogen 35.19 IgA 49 IgG 989 IgM 96	<p style="text-align: center;"><b>National Veterinary Diagnostic Services</b></p> <p style="text-align: center;">prior to 8/2007</p> <p><i>total estrogen:</i> males 20.00-25.00 pg/ml females 30.00-35.00 pg/ml</p> <p><i>immunoglobulins</i> IgA: 70-170 mg/dL IgG: 1000-2000 mg/dL IgM: 100-200 mg/dL</p>	methylprednisilone 4mg PO SID levothyroxine 0.4mg PO BID	Total estrogen 35.12 IgA 56 IgG 1049 IgM 102	1 month
14	Boxer, 9 y/o, M/n	4 months	total estrogen 35.51 no immunoglobulins assayed		prednisone 5mg PO SID levothyroxine 0.4mg PO BID	total estrogen 35.31 no immunoglobulins assayed	1 month
15	Labrador- mix, 9 y/o, F/s	1 week	total estrogen 35.31 IgA 43 IgG 918 IgM 88		triamcinolone acetone 3mg IM methylprednisilone 4mg PO SID levothyroxine 0.4mg PO BID	total estrogen 35.09 IgA 58 IgG 1077 IgM 98	2 months
16	Beagle, 4 y/o, F/s	2 months	total estrogen 35.91 IgA 71 IgG 962 IgM 103		triamcinolone acetone 1.25mg IM dexamethasone sod phos 3.4mg IM methylprednisilone 4mg PO SID levothyroxine 0.4mg PO BID	total estrogen 35.16 IgA 89 IgG 1214 IgM 109	2 months
17	Springer Spaniel, 13 y/o, M/n	5.5 months	total estrogen 25.32 IgA 43 IgG 781 IgM 80		triamcinolone acetone 0.3mg IM methylprednisilone 4mg PO SID levothyroxine 0.5mg PO BID	total estrogen 25.11 IgA 63 IgG 1106 IgM 114	5 months
18	Pomeranian, 7 y/o, M/n	1 month	total estrogen 25.71 IgA 36 IgG 810 IgM 77		triamcinolone acetone 0.5mg IM dexamethasone sod phos. 0.5mg IM methylprednisilone 0.5mg PO SID levothyroxine 0.1mg PO BID	total estrogen 25.43 IgA 48 IgG 963 IgM 95	7.5 months
19	Beagle, 11 y/o, M/n	4 months	total estrogen 25.40 IgA 43 IgG 817 IgM 84		triamcinolone acetone 2.15mg IM methylprednisilone 2mg PO SID levothyroxine 0.2mg PO BID	total estrogen 24.88 IgA 78 IgG 1353 IgM 127	5.5 months
20	Australian Cattle Dog, 8 y/o, F/s	2 weeks	total estrogen 35.37 IgA 53 IgG 1462 IgM 151		n/a		
21	Cocker Spaniel, 6 y/o, M/n	1 week	total estrogen 25.08 IgA 57 IgG 989 IgM 100		n/a		

22	Dachshound 9 y/o, F/s	9 months	total estrogen 35.19 IgA 57 IgG 936 IgM 92	<p><b>National Veterinary Diagnostic Services</b></p> <p>prior to 8/2007</p> <p><i>total estrogen:</i> males 20.00-25.00 pg/ml females 30.00-35.00 pg/ml</p> <p><i>immunoglobulins</i> IgA: 70-170 mg/dL IgG: 1000-2000 mg/dL IgM: 100-200 mg/dL</p>	n/a		
23	Labrador Retriever, 8 y/o, F/s	2 months	total estrogen 35.10 IgA 49 IgG 918 IgM 89		n/a		
24	GSD-mix, 11.5 y/o, F/s	1.5 months	total estrogen 35.31 IgA 49 IgG 918 IgM 89		n/a		
25	Australian Shepherd, 10 y/o, F/s	5 months	total estrogen 35.20 IgA 52 IgG 947 IgM 96		n/a		
26	Pug, 9 y/o, F/s	5 months	total estrogen 35.36 IgA 49 IgG 968 IgM 97		n/a		
27	Akita-mix, 7 y/o, M/n	2.5 months	total estrogen 25.31 IgA 47 IgG 612 IgM 74		n/a		
28	Mini Dachshund, 11 y/o, F/s	6 months	total estrogen 35.68 IgA 53 IgG 917 IgM 93		n/a		
29	Lhasa-Apso mix, 13 y/o, F/s	2 weeks	total estrogen 35.17 IgA 57 IgG 898 IgM 86		triamcinolone acetonide 0.06mg mg IM dexamethasone sod phos 0.8g mg IM methylprednisilone 1mg PO SID levothyroxine 0.2mg PO BID	total estrogen 35.09 IgA 88 IgG 1116 IgM 95	2.5 months

— Change in reference range —

30	Husky-mix, 9 y/o, F/s	1 month	total estrogen 35.17 IgA 58 IgG 1177 IgM 96	<p style="text-align: center;"><b>National Veterinary Diagnostic Services</b></p> <p style="text-align: center;">after 8/2007</p> <p><i>total estrogen:</i> males 20.00-25.00 pg/ml females 30.00-35.00 pg/ml</p> <p><i>immunoglobulins</i> IgA: 100-200 mg/dL IgG: 1250-2000 mg/dL IgM: 100-200 mg/dL</p>	prednisone 5 mg PO SID levothyroxine 0.4mg PO BID	Total estrogen 35.11 IgA 66 IgG 1215 IgM 98	3 months
31	Brittany Spaniel, 9 y/o, M/n	3 years	total estrogen 25.15 IgA 52 IgG 927 IgM 93		triamcinolone acetonide 0.3mg IM dexamethasone sod phos 3.6mg IM methylprednisilone 2mg PO SID levothyroxine 0.2mg PO BID	total estrogen 25.03 IgA 68 IgG 1092 IgM 101	6 months
32	Springer Spaniel, 11 y/o, M/n	3 weeks	total estrogen 25.04 IgA 61 IgG 1025 IgM 99		triamcinolone acetonide 0.5mg IM dexamethasone sod phos 2.2mg IM methylprednisilone 3mg PO SID levothyroxine 0.5mg PO BID	total estrogen 24.89 IgA 74 IgG 1205 IgM 116	8 months
33	Beagle, 8 y/o, F/s	1 week	total estrogen 35.19 IgA 53 IgG 1302 IgM 105		triamcinolone acetonide 0.14mg IM dexamethasone sod phos 1.06mg IM methylprednisilone 2mg PO SID levothyroxine 0.2mg PO BID	total estrogen 35.17 IgA 58 IgG 1325 IgM 108	1 month
34	Scottish Terrier, 10 y/o, F/s	8 months	total estrogen 35.27 IgA 50 IgG 1089 IgM 81		triamcinolone acetonide 2mg IM, weekly for 4 weeks levothyroxine 3mg PO BID	total estrogen 35.22 IgA 58 IgG 1153 IgM 87	1 month
35	Mini Dachshund, 9 y/o, F/s	1 week	total estrogen 35.19 IgA 49 IgG 998 IgM 101		triamcinolone acetonide 0.4mg IM dexamethasone sod phos. 0.5mg IM methylprednisilone 1mg PO SID levothyroxine 0.05mg PO BID	total estrogen 35.11 IgA 82 IgG 1269 IgM 107	12 months
36	Shih-tzu, 8.5 y/o, M/n	2 weeks	total estrogen 25.19 IgA 47 IgG 982 IgM 93		triamcinolone acetonide 1.5mg IM, weekly for 3 weeks; then 1.1mg IM, weekly for 1 week levothyroxine 0.15mg PO BID	total estrogen 25.10 IgA 61 IgG 1059 IgM 97	1 month
37	Mini Dachshund, 7 y/o, F/s	5.5 months	total estrogen 35.14 IgA 53 IgG 1018 IgM 92		n/a		
38	GSD, 12 y/o, M/n	2.5 months	total estrogen 25.16 IgA 53 IgG 1018 IgM 94		n/a		

39	Brittany Spaniel, 8 y/o, F/s	4 months	total estrogen 35.14 IgA 91 IgG 2382 IgM 316	<p><b>National Veterinary Diagnostic Services</b></p> <p>after 8/2007</p> <p><i>total estrogen:</i> males 20.00-25.00 pg/ml females 30.00-35.00 pg/ml</p> <p><i>immunoglobulins</i> IgA: 100-200 mg/dL IgG: 1250-2000 mg/dL IgM: 100-200 mg/dL</p>	n/a
40	Pug, 7 y/o, F/s	7 months	total estrogen 35.11 IgA 58 IgG 110 IgM 94		n/a
41	Staffordshire Terrier, 14y/o, F/s	2.5 months	total estrogen 35.05 IgA 68 IgG 858 IgM 113		n/a
42	Sheltland Sheepdog, 8.5 y/o, M/n	7 weeks	total estrogen 25.13 IgA 58 IgG 1309 IgM 104		n/a
43	Chow-mix, 10.5 y/o, M/n	8 weeks	total estrogen 25.24 IgA 42 IgG 892 IgM 58		n/a