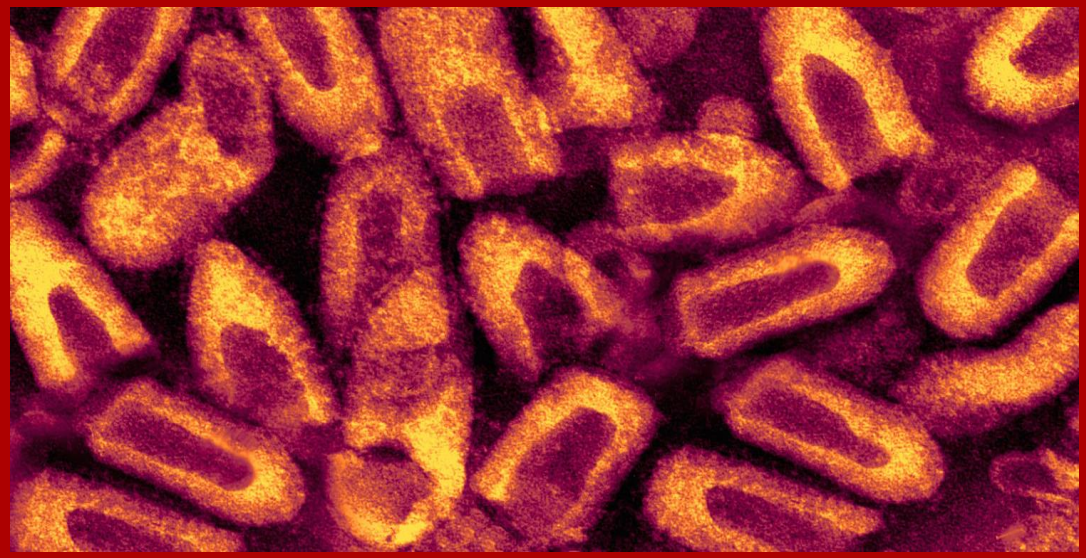

Rabies virus neutralizing antibodies in dogs

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MPH Report

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Rabies

- Viral disease responsible for ~59,000 human deaths each year in more than 150 countries and territories
- Dogs are the primary source
- Vaccination is the main preventative control measure
  - In U.S., vaccination recommendations vary
    - NASPHV, state and local, manufacturer
  - Not 100% protective
  - WHO & OIE: Minimum post-vaccination antibody level: ≥0.5 IU/mL
  - Most animals achieve titer threshold 7-14 days post-vaccination

Pet Travel

- Proof of adequate rabies antibody titer
  - Fluorescent Antibody Virus Neutralization (FAVN)
- Consequences: Turned away, quarantined, euthanized
- Possible factors influencing failure of the FAVN
  - Biological
  - Vaccination schedules
  - Period from vaccination to blood draw for testing

Field Experience

- Originally started in 2009 at KSU Rabies Laboratory
- The database included 162,739 animals samples from 2006-2010 for the purpose of exportation
- Narrowing the focus:
  - Dogs
  - Less than 1 year of age
  - Only 1 documented vaccination prior to titer test
  - n = 8,367

- Study Criteria
  - Age at vaccination
  - Size and Breed
  - Sampling interval

Criteria

Age

- Three Groups:
  - <12 Weeks
  - 12-16 Weeks
  - >16 Weeks

Size and Breed

- Purebred verse Mixed
- Toy, Small, Medium, Large, Giant

Sampling Interval

- ≤3 days
- 4 - ≤7days
- 8 - ≤15 days
- 16 - ≤35 days
- 36 - ≤77 days
- 78 - ≤154 days
- 155 - ≤224 days
- >224 days

FAVN Test

FAVN Test

- Minimum antibody level (OIE 2011, WHO 2013):

  ≥ 0.5 IU/ml = “Passing”

- FAVN results divided into three groups
  - Low Responders: 0 - <0.5 IU/ml
  - Moderate Responders: ≥ 0.5 - ≤2.6 IU/ml
  - High Responders: >2.6 IU/ml

Results

Overall

- GMT 1.49 IU/mL (STD = 1.49)
- The number of dogs failed was 1,002 which was 11.7%
- The number of dogs Passed was 7,365 which was 85.9%
- Older dogs had lower proportion of failure and higher GMT

	% Failed	GMT (IU/mL)	Standard Deviation
< 12 Weeks	16.3%	1.27	1.53
12-16 Weeks	15.4%	1.27	1.45
>16 Weeks	10.3%	1.6	1.5

Less than 12 Weeks

Overall 16.3% Failures

- Sex, Breed, and Size- No influence
- Sampling Interval
  - Highest GMT seen between 8-35 days
  - Greater proportion of High responders at 8-77 days

		LOW RESPONDERS	MODERATE RESPONDERS	HIGH RESPONDERS	CMH	Geometric Mean Titer	LN ANOVA
Age at vaccination: <12 Weeks	***TOTAL***	***49 (16.3%)***	***124 (41.1%)***	***128 (42.5%)***		***1.27***	
	Sex [a]				**0.51**		**0.93**
	Male	25 (15.9%)	77 (42.6%)	65 (41.4%)		1.26	
	Female	24 (17.2%)	56 (40.2%)	59 (42.45%)		1.25	
	Unspecified	0	1 (20%)	4 (80%)		1.72	
	Time from Vaccine Administration to Titer Check				**<0.01**		**<0.01**
	< 3 days	0	0	0		0	
	4 to < 7 days	1 (25%)	1 (25%)	[illegible]		1.32	
	8 to < 15 days	0	0	4 (100%)		3.45	
	16 to < 35 days	5 (6.1%)	29 (35.8%)	47 (58%)		1.99	
	36 to < 77 days	15(21.1%)	26 (36.6%)	30 (42.2%)		1.15	
	78 to < 154 days	19 (25%)	37 (48.6%)	[illegible]		0.77	
	155 to < 224 days	5 (15.6%)	14 (43.8%)	13 (40.6%)		1.18	
	> 225 days	4 (12.1%)	17 (51.5)	12 (36.3%)		1.49	
	Type of Dog				**0.39**		**0.95**
	Mixed Breed	10 (20.4%)	17 (34.6%)	22 (44.9%)		1.27	
	Pure Breed	32 (14.4%)	97 (44.2%)	90 (41.1%)		1.29	
	Dog Size				**0.77**		**0.46**
	Toy	4 (8%)	25 (50%)	21 (42%)		1.73	
	Small	9 (15.8%)	23 (40.4%)	25 (43.9%)		1.41	
	Medium	7 (18.4%)	15 (29.5%)	16 (42.1%)		1.18	
	Large	11 (16.9%)	30 (46.2%)	24 (36.9%)		1.10	
	Giant	1 (14.3%)	3 (42.9%)	3 (42.9%)		0.83	
	Unspecified	17 (20.2%)	28 (33.3%)	39 (46.4%)		1.13	

12-16 Weeks

Overall 15.4% Failures

- Sex and Breed- No Influence
- Size- Large breed dogs
  - Highest failure (21%) compared to 11.5-16.7%
  - Lowest GMT (1.02) compared to 1.25-1.47
- Sampling Interval
  - Highest Failure <7 days and >78 days
  - Highest Titer 8-35 days

		LOW RESPONDERS	MODERATE RESPONDERS	HIGH RESPONDERS	CMH	Geometric Mean Titer	LN ANOVA
Age at vaccination: 12-16 Weeks	***TOTAL***	***355 (15.4%)***	***1,081 (47.1%)***	***855 (37.3%)***		***1.27***	
	Sex				**0.10**		**0.25**
	Male	189 (16.7%)	530 (47%)	408 (36.2%)		1.23	
	Female	164 (14.2%)	542 (47%)	445 (38.6%)		1.30	
	Unspecified	2 (15.3%)	9 (69.2%)	2 (15.3%)		0.68	
	Time from Vaccine Administration to Titer Check				**<0.01**		**<0.01**
	≤ 3 days	7 (100%)	0	0		0.02	
	4 to < 7 days	1 (25%)	1 (25%)	2 (50%)		0.43	
	8 to < 15 days	5 (8.4%)	27 (45.7%)	27 (45. 7%)		1.52	
	16 to < 35 days	46 (5.5%)	380 (45.4%)	410 (49.0%)		1.93	
	36 to < 77 days	65 (12.9%)	248 (49.3%)	190 (37.7%)		1.85	
	78 to < 154 days	124 (23.7%)	259 (49.5%)	140 (26.7%)		0.66	
	155 to < 224 days	65 (27.9%)	113 (48.5%)	55 (23.6%)		0.65	
	> 225 days	42 (33.3%)	53 (42%)	31 (24.6%)		0.69	
	Type of Dog				**0.19**		**0.34**
	Mixed Breed	34 (13.3%)	133 (52.1%)	88 (34.5%)		1.35	
	Pure Breed	298 (16.2%)	853 (46.3%)	688 (37.4%)		1.24	
	Dog Size				**<0.01**		**<0.01**
	Toy	52 (12.2%)	199 (46.7%)	175 (41.1%)		1.47	
	Small	74 (14.6%)	236 (46.5%)	198 (39%)		1.37	
	Medium	44 (16.7%)	118 (44.9%)	101 (38.4%)		1.25	
	Large	112 (21%)	247 (46.3%)	175 (32.8%)		1.02	
	Giant	11 (11.5%)	49 (51%)	36 (37.5%)		1.44	
	Unspecified	62 (13.4%)	232 (50%)	170 (36.6%		1.25	

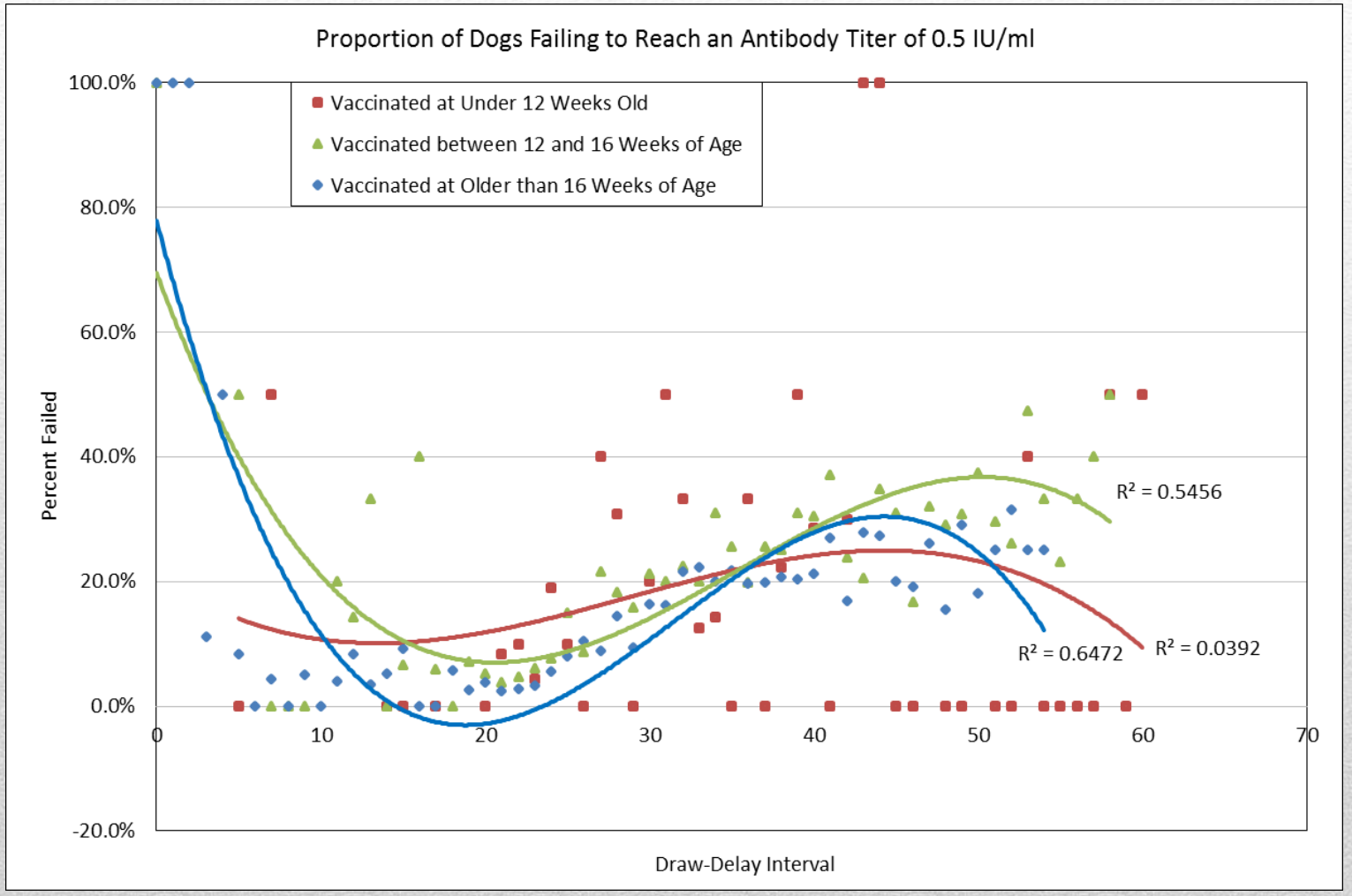
Greater than 16 Weeks

Overall 10.3% Failure

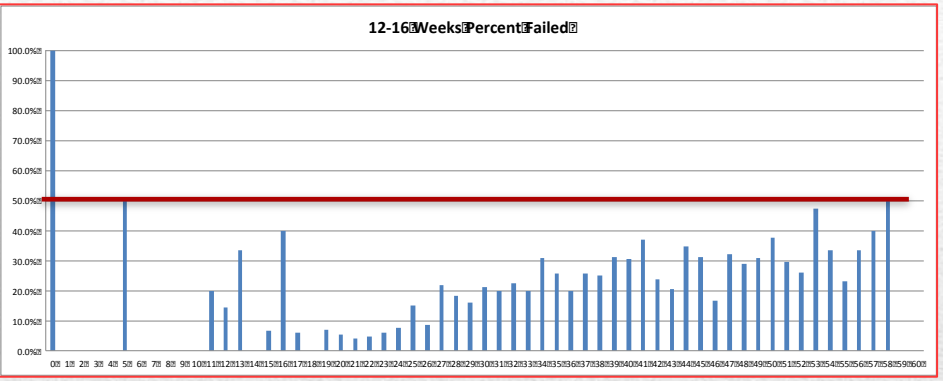
- Sex- No influence
- Breed:
  - Mix Breed Higher GMT (1.77 vs 1.57)
  - Mix Breed Lower Failure Rate (8% vs 10.8%)
- Size:
  - Toy, Small, and Medium higher GMT than Large and Giant.
- Sampling Interval
  - Highest GMT between 8-36 days
  - Highest Failure at <3 days and >78 days

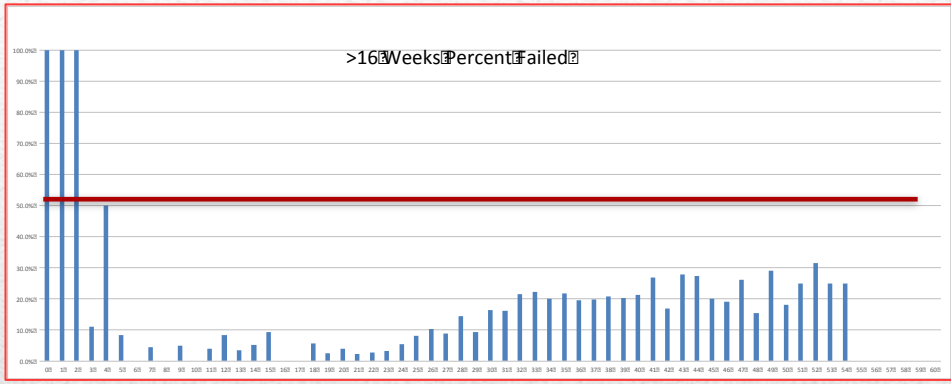
		LOW RESPONDERS	MODERATE RESPONDERS	HIGH RESPONDERS	CMH	Geometric Mean Titer	LN ANOVA
Age at vaccination: >16 Weeks	***TOTAL***	***598 (10.3%)***	***2,453 (42.4%)***	***2,724 (47.1%)***		***1.60***	
	Sex				**0.47**		**0.44**
	Male	291 (9.8%)	1263 (42.9%)	1386 (47.1%)		1.62	
	Female	301 (10.8%)	1161 (41.7%)	1316 (46.3%)		1.58	
	Unspecified	6 (8.9%)	29 (51.7%)	22 (39.2%)		1.34	
	Time from Vaccine Administration to Titer Check				**<0.01**		**<0.01**
	< 3 days	40 (100%)	0	0		0.05	
	4 to < 7 days	11 (8.5%)	35 (37.2%)	51 (54.2%)		1.65	
	8 to < 15 days	19 (5.25%)	116 (32.%)	227 (62.7%)		2.22	
	16 to < 35 days	66 (2.9%)	826 (36.8%)	1351 (60.2%)		2.30	
	36 to < 77 days	[illegible]	655 (47%)	618 (44.4%)		1.63	
	78 to < 154 days	214 (19.7%)	544 (50.2%)	324 (29.9%)		1.04	
	155 to < 224 days	113 (23.2%)	240 (49.4%)	132 (27.2%)		0.84	
	> 225 days	19 (24.6%)	37 (48%)	21 (27.2%)		0.76	
	Type of Dog				**<0.01**		**<0.01**
	Mixed Breed	66 (8%)	343 (41.8%)	410 (50%)		1.77	
	Pure Breed	498 (10.8%)	1944 (42.4%)	2138 (46.6%)		1.57	
	Dog Size				**<0.01**		**<0.01**
	Toy	124 (9.2%)	563 (41.7%)	664 (49.1%)		1.67	
	Small	142 (10.6%)	577 (43.1%)	620 (46.3%)		1.60	
	Medium	56 (10%)	241 (43.2%)	261 (46.8%)		1.71	
	Large	144 (12.9%)	480 (42.9%)	495 (44.2%)		[illegible]	
	Giant	29 (14.9%)	74 (37.9%)	92 (47.2%)		1.44	
	Unspecified	102 (8.4%)	518 (42.7%)	592 (48.8%)		1.61	

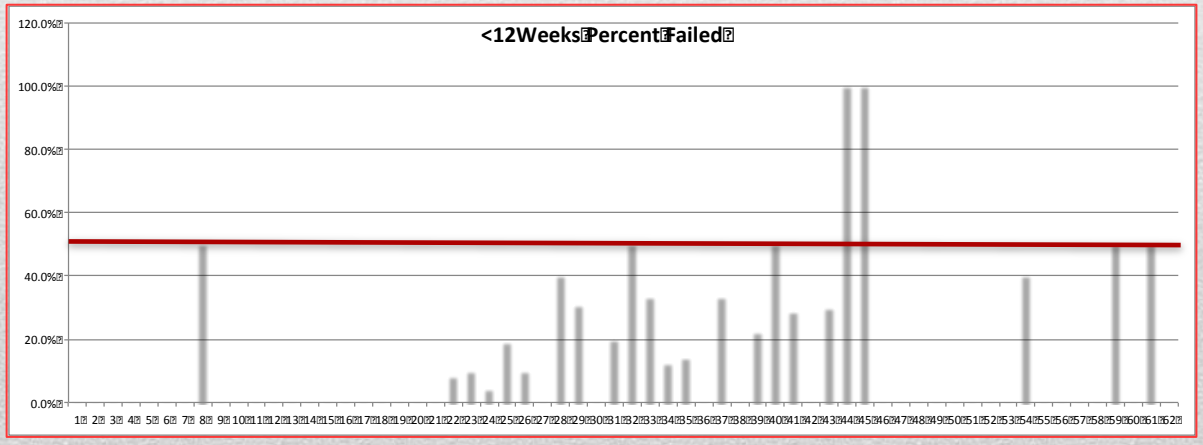
Proportion Failed



Percent Failed







Summary

Breed and/or size

- May have and influence but minimal at this time.

Age

- Dogs vaccinated later than 16 weeks of age had higher GMT
- Early vaccination not associated with higher failure or lower GMT compared to dogs vaccinated on-time.

Sampling Interval

- Too early or too late had a higher failure rate.

Implications

Pet Travel

- Veterinarians need to consider factors when preparing pets for travel to reduce test failure and complications at ports
- Optimal time for sample collection is ~ 8-36 days
  - Cliquet 2003 <60 days
  - Mansfield 2004 <21 days
  - Kennedy 2007 20-50 days
  - Jakel 2008 <120 days

  ❖ Booster vaccination may minimize risk of failure

- Further research in the effect of maternal antibodies
  - Vaccination at a young age
    - Variable response at longer intervals
    - Initial high responders