

Hypothyroidism & Reproduction: Fact based evidence for breeders

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Hypothyroidism

- Endocrine disorder in which the thyroid gland does not produce enough thyroid hormone
- Common disorder in dogs and humans
- Most common cause in dogs is autoimmune thyroiditis

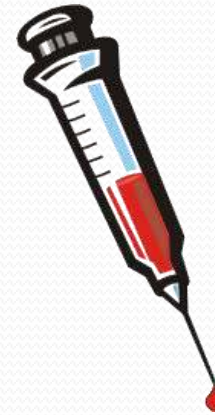


Diagnosis

- Full thyroid panel includes TT₄, TT₃, FT₄ed, FT₃, TSH, TGAA, T₄AA, T₃AA
 - Available through Michigan State University, major reference laboratories, HemoPet
- TSH stimulation test
 - Not used clinically
 - Considered “gold standard” diagnosis for research
- T₄ alone
 - Inaccurate due to many non-thyroidal factors

Thyroid testing artifacts

- Medications
 - Glucocorticoids (steroids)
 - Phenobarbitol
 - Aspirin
 - Sulfa antibiotics
 - Clomipramine (anti-anxiety)
 - Some NSAIDs
- Anesthesia
 - Do not test within 24 hours of anesthesia or surgery
- Vaccination
 - Do not test within 30-45 days after vaccination
- Non-thyroidal illness, aka euthyroid sick syndrome
 - Infection, other metabolic disease, dermatologic disease
- Breed – greyhound, Scottish deerhound, working sled dogs
 - T₄ lower than normal, full panel should still be normal



Genetics

- Mawdesley 1968 – 4500 dogs of various breeds, proposed a genetically linked autoimmune mechanism
- Musser & Graham 1968, Fritz 1970 & 1976 – 2 colonies of beagles, showed thyroiditis to be inherited
- Conaway 1985 – 4 generations of Borzoi, naturally occurring disease followed by intentional test breeding, proposed autosomal recessive inheritance



Breed predilection

Hypothyroid Dogs	General Hospital Population
Retrievers	Retrievers
Spaniels	Terriers
Terriers	Spaniels
Mixed breeds	Collies
Doberman pinschers	German shepherd dogs
Akitas	Mixed breeds
Collies	
Miniature schnauzers	
Shetland Sheepdogs	

- Diagnosed by TSH stimulation test
- 136 dogs initially suspected of hypothyroidism, 50 confirmed, 86 excluded

Breed predilection

Hypothyroid Dogs

Doberman pinscher

Great Dane

Poodle

Dachshund

Schnauzer

Irish setter

Boxer

27 other breeds comprised 50% of population

- Diagnosed by T₄ & T₃ levels
- 108 dogs examined

Breed predilection

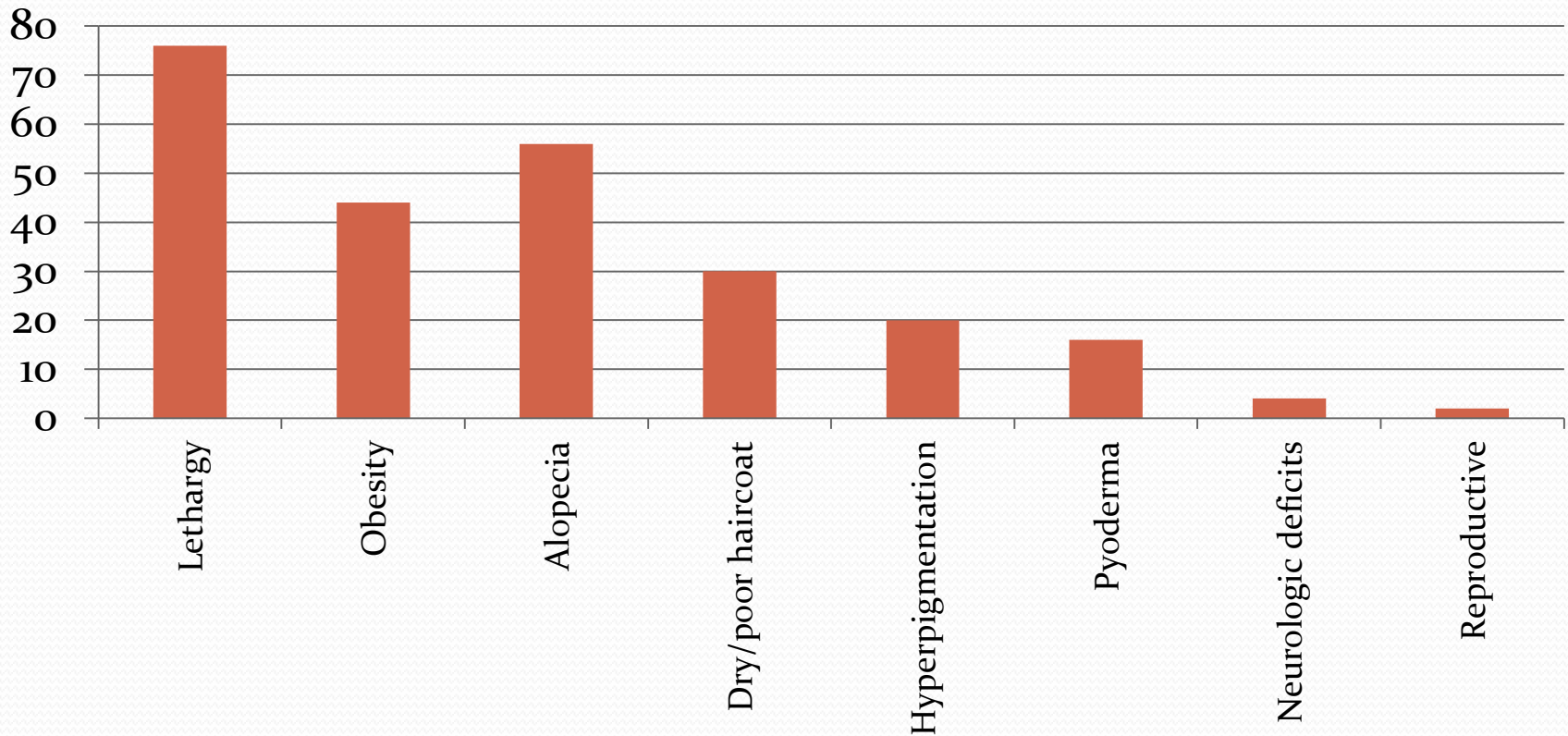
Ranking	Breed	# of evaluations
1	English setter	1096
2	Eurasier	69
3	Spanish water dog	67
4	Irish red & white setter	136
5	Dalmation	1058
6	Shetland sheepdog	1332
7	Boxer	1260
8	Kuvasz	347
9	Tibetan terrier	74
10	Welsh springer spaniel	948
...		
45	Doberman pinscher	1870

Breed predilection

# of evaluations	Breed	Ranking
4684	Rhodesian ridgeback	12
3942	Great Dane	44
3857	Poodle	81
3693	Golden retriever	34
1962	Mastiff	67
1870	Doberman pinscher	45
1450	Bouvier des Flandres	61
1332	Shetland sheepdog	6
1330	Vizsla	76
1260	Boxer	7

Clinical signs

% of hypothyroid dogs showing clinical signs



Clinical signs

- Metabolic (lethargy, obesity) – decreased cellular metabolism depresses dog's mental status & activity level, severity of signs relative to stage of disease
- Dermatologic (alopecia, hyperpigmentation, pyoderma) – change in hair growth phases, hyperkeratosis, decreased immune response in skin
- Neurologic – unknown
- Reproductive – unknown, autoimmune?

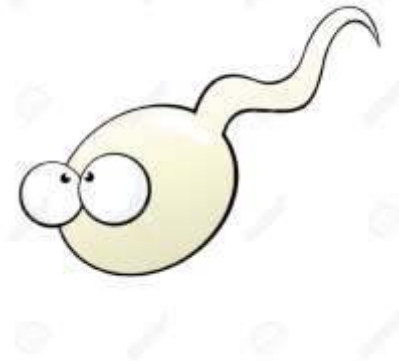
Reproductive effects

- Anecdotal reports
 - Infertility
 - Decreased libido
 - Testicular atrophy
 - Azospermia
 - Irregular estrus intervals
 - Pseudopregnancy
 - Weak or stillborn puppies



Reproductive effects in males

- Retrospective
 - Nesbitt 1980 – 55 dogs, no reproductive abnormalities
 - Beale 1992 – 25 dogs, no difference in T₄ between normal dogs & “poor reproductive performers”
- Prospective
 - Johnson 1999 – 6 dogs, 2 yr duration of study, no change in semen quality or libido



Reproductive effects in females

- Case reports
 - Peter 1989 – 1 bitch, history of missed breedings, testing “suggested a diagnosis of hypothyroidism”
 - Johnson 1989 – 1 bitch, never cycled, diagnosed with ovarian dysplasia & hypothyroidism, “unknown cause” of ovarian abnormality



Reproductive effects in females

- Retrospective
 - Nesbitt 1980 – 5/53 hypothyroid bitches showed abnormal estrus intervals, could not show causality
 - Beale 1992 – 96 bitches, “poor reproductive performers” actually had higher T₄ levels than “good performers,” no change in TSH stimulation results between groups
 - Panciera 1994 – 1/66 hypothyroid bitches, abortion
 - Dixon 1999 – 1/50 hypothyroid bitches, irregular estrus interval
- Prospective
 - Panciera et al

Reproductive effects in females

- 18 bitches (9 hypothyroid, 9 control)
- At 20 weeks after induction of hypothyroidism:
 - Normal estrus intervals, all bitches became pregnant
 - Hypothyroid bitches showed:
 - Longer whelping & weaker contractions
 - Decreased puppy birth weight
 - Increased puppy mortality
- “Results failed to support hypothyroidism as a substantial cause of infertility in the bitch.”



Reproductive effects in females

- 14 bitches (8 hypothyroid, 6 control)
- At 56 weeks after induction of hypothyroidism:
 - Normal estrus intervals & litter size
 - 4/8 hypothyroid & 6/6 control bitches pregnant
 - Not statistically significant
 - Hypothyroid bitches showed:
 - Decreased puppy birth weight
 - Increased puppy mortality
- “Inconclusive with regard to the effect of hypothyroidism on fertility”



Reproductive effects in females

- 12 bitches (6 hypothyroid, 6 control)
- After 24 weeks of thyroid supplementation:
 - Normal estrus intervals & litter size
 - 6/6 hypothyroid & 5/6 control bitches pregnant
 - No difference in puppy birth weights or puppy mortality
- Treatment of hypothyroidism “resolved the detrimental fetal effects.”



Conclusions

- No effect of hypothyroidism on male dog fertility
- Detrimental effects on birth weight and viability occur in puppies born to hypothyroid dams
- No effect of hypothyroidism on estrus interval in bitches
- Prolonged hypothyroidism may reduce pregnancy rates in bitches
 - Seen only in severely affected bitches
 - Further study needed with larger sample size

Conclusions

- Known heritable disease
 - Current studies looking for genetic marker (AKC CHF)
- Affected animals should not be bred?
- Numerous body systems affected
 - Metabolic
 - Dermatologic
 - Skeletal muscle
 - Cardiovascular
 - Neurologic
 - Behavioral?



Testing recommendations

- Full thyroid panel through approved laboratory
 - List of laboratories available at offa.org
- Test after dogs have reached sexual maturity
 - >12-18 months in males
 - At least 12 weeks after first heat cycle in females
- Re-test annually during breeding lifetime
 - Continue testing after retirement depending on age and predisposition in breed/line

Questions?

