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# Prevalence of ultrasound-determined cystic endometrial hyperplasia and the relationship with age in dogs



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#### ABSTRACT

To investigate the potential relationship between age and diagnosis of cystic endometrial hyperplasia (CEH) in the bitches, 348 ultrasound examinations from 240 bitches (Labradors, Golden Retrievers, German Shepherds, Flat Coated Retrievers, or crosses of those breeds aged between 1.6 and 7.2 years at examination) were examined. A subpopulation of 32 bitches that had completed their breeding careers at 6 years or more of age was also identified. Of all, 18.3% of the bitches were diagnosed with CEH; these cases were newly diagnosed when bitches were between 2.5 years and 7.3 years of age. The proportion of ultrasound examinations in which CEH was identified increased from 6.8% of examinations on 2-year-old breeding bitches to 60.0% of examinations on 6-year-old bitches. Logistic regression identified a positive correlation between mean age at the examination and presence of CEH ( $\chi^2=30.74$ , degrees of freedom = 1, P < 0.001). For 32 bitches that had completed their breeding career, the prevalence of CEH was 56.3%, age at the diagnosis ranged from 3.8 to 7.3 years, and the proportion of bitches affected with CEH increased from 6.3% at 3 years of age to 56.3% at 7 years of age. These data support the contention that the prevalence of CEH increases with age.

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#### 1. Introduction

Hormonal stimulation during the estrous cycle of the bitch induces changes in the endometrium including glandular proliferation and secretion [1–3]. Cystic endometrial hyperplasia (CEH) is an abnormality of uterine growth and repair arising from the endometrial glandular epithelium where there is cystic distension of the endometrial glands [4,5]. In breeding bitches, CEH seems to be an abnormal response to stimulation of the uterus by ovarian hormones; progesterone and estrogen [2,3,6–8] and can also be triggered by uterine irritants and endometrial trauma [2,3,9,10]. In CEH cases, the number and size of endometrial glands are increased, and there is disparity

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in the number and configuration of glands causing a thickened endometrium and increased secretory activity [2,11]. In bitches affected with CEH, postmating endometritis appears to impact fertility by reducing the uterine vasodilatory response to mating and impairing the clearance of uterine fluid as a result of decreased uterine contractions when compared with normal bitches [12]. A larger polymorphonuclear neutrophils influx has been observed in bitches with CEH postmating which could affect the ability of spermatozoa to attach to the uterine epithelium with related impacts on fertility [13]. Previous research has reported poor-conception rates and lower litter sizes for bitches affected with CEH without treatment [12,13]. In addition to the reduced fertility, the degenerative changes within the tissue associated with CEH can provide conditions suitable for the establishment of uterine infections, and in some cases, pyometra can develop [2,7,14,15]. The relationship between age and incidence of pyometra has been documented [16-18]. Age has been

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proposed as a risk factor for a breeding bitch being affected by CEH because of the repeated hormonal stimulation of successive estrus cycles in entire bitches as they age. Indeed, it has been suggested that older bitches are likely to have some degree of CEH [11,14,19], while Verstegen et al [15] suggest that all dogs will develop CEH with age. However, no previous work has presented data for the prevalence of CEH alone in a population of bitches by age, without associated pyometra. The seminal work by Dow [11] only included bitches with disease rather than a whole population and considered the cystic hyperplasia pyometra complex rather than two distinct diseases. In zoo canids and elephants, significant association between the development of endometrial hyperplasia and increasing age has been established and reported based on the prevalence of CEH within a population [20,21].

Therefore, this study aimed to examine a population of breeding bitches and to report on three factors; (1) the age at which cases of CEH were diagnosed; (2) the prevalence of CEH in ultrasound examinations conducted on bitches at different ages, and (3) the incidence of CEH in a population of retired breeding bitches which had been examined throughout their breeding lives.

#### 2. Materials and methods

Between September 21, 2012 and September 20, 2014, 240 bitches from a large, relatively closed, breeding population were examined as part of routine health management before breeding. Bitches were Labradors, Golden Retrievers, German Shepherds, Flat Coated Retrievers, or crosses of those breeds (Table 1), were from 68 unique sires and 126 unique dams, and were between 1.6 and 7.2 years of age at examination. One hundred and thirty-nine bitches were examined once, 94 were examined twice, and seven were examined three times within the 2-year study period.

In total, 348 detailed transabdominal ultrasound examinations were conducted using a 10-MHz transducer. In every ultrasound examination, the uterine body and distal uterine horns were studied; proximal uterine horns were examined wherever possible. Bitches were allocated to control or CEH groups as previously described [12]. Cystic endometrial hyperplasia cases were categorized as 'new case' or 'existing case' dependent on whether the bitch was diagnosed with CEH during the current examination and had not been diagnosed at any previous examination (new case) or had been diagnosed with CEH

**Table 1**The number of bitches of each breed/mixed breed examined before breeding during the 2-year study period.

Breed	N
Flat-Coated Retriever	3
Golden Retriever	30
Golden Retriever cross German Shepherd	1
Golden Retriever cross Flat-Coated Retriever	2
Golden Retriever cross Labrador Retriever	23
German Shepherd	19
Labrador Retriever	155
Labrador Retriever cross Golden Retriever	6
Labrador Retriever cross (Golden Retriever cross Labrador)	1

before the study period (existing case). Age at first diagnosis was recorded for all CEH affected bitches.

A subpopulation of 32 bitches of the 240 had retired from the breeding program after completing their breeding career at 6 years or more of age. These bitches had been examined as part of the present study but additionally had ultrasound examinations recorded prior to the study commencing. The historic data and present study data were examined to report the prevalence of CEH and to determine the proportion of CEH affected bitches at each year of age.

#### 2.1. Statistical analysis

Data were investigated using XLStat (Addinsoft, USA) and IBM SPSS Statistics 20 (USA). Age at diagnosis was described for all CEH-affected bitches. The number of ultrasound examinations conducted on bitches of each age was reported along with the proportion of examinations at each age in which CEH was observed.

To determine whether there was a relationship between age and presence of CEH, repeat examinations for individual bitches were excluded by calculating mean age at the examination. A binary logistic regression was conducted to predict presence of CEH using age as the predictor.

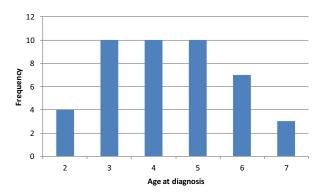
#### 3. Results

3.1. Number of bitches with CEH during the 2-year period and age at diagnosis

There were 44/240 (18.3%) bitches that were diagnosed with CEH when examined by ultrasound; 40 new cases and four existing cases. These cases were newly diagnosed when bitches were between 2.5 and 7.3 years of age (mean  $4.9 \pm 0.2$  years; Fig. 1).

3.2. The prevalence of CEH in ultrasound examinations conducted on bitches at different ages

The proportion of ultrasound examinations conducted on bitches of each year of age from 1.0 to 7.99 years where



**Fig. 1.** Age at diagnosis distribution for 44 bitches with cystic endometrial hyperplasia.

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