Gestational diabetes mellitus (GDM) is common in women with 2–12% of all pregnancies affected, but seems to be a rare disease in dogs with only 2 cases reported. Although women with GDM usually do not experience the classical clinical signs of diabetes mellitus (DM) at the time of diagnosis, the consequences may be substantial with complications such as macrosomia, dystocia, and neonatal hypoglycemia. The disease often is diagnosed by screening programs and usually resolves after parturition but increases the risk for type 2 diabetes later in life. In the 2 cases of canine GDM described recently, 1 dog remained diabetic after parturition and the other recovered fully within 2 weeks although it had been diagnosed with diabetic ketoacidosis. Both dogs were symptomatic at diagnosis.

Maternal insulin resistance is reported during pregnancy in many species, including humans and dogs, and plays an important role for the growth of the fetus. Several hormones such as progesterone, cortisol, and placental lactogen have been proposed to cause the insulin resistance seen in human pregnancies, but it is still not clear which role each of them plays, and how they interact. Glucose homeostasis in dogs may be additionally affected by progesterone-induced secretion of mammary-derived growth hormone (GH), which is generally considered diabetogenic by mechanisms of anti-insulin activity.

GDM results from an endogenous insulin supply that is inadequate to meet tissue demands. GDM has been proposed to be similar to canine diestrus DM, although insulin resistance is reported to be more severe in pregnant than nonpregnant bitches 55 days after estrus. It is not known with what frequency dogs are affected by GDM nor when in pregnancy clinical signs first occur. Insulin treatment in a pregnant diabetic dog is challenging: insulin demands may increase dramatically, and the dog is likely to experience wide fluctuations in daily blood glucose concentrations. In a colony of pregastational diabetic (ie, diabetes that preceded pregnancy) Golden Retrievers, insulin requirements started to increase during the 2nd half of pregnancy, and then decreased when labor began.

The aim of this retrospective study was to describe the clinical characteristics of GDM in dogs by a review of medical records, and to follow-up on outcome by interviewing owners and referring veterinarians.

Materials and Methods

Medical records of all female dogs diagnosed with DM from 1997 to 2007 at the University Animal Hospital, Uppsala, Sweden, and at the Referral Animal Hospital, Bagarmossen, Sweden, were reviewed to identify cases where DM was first diagnosed during pregnancy. In addition, a letter was sent to all 230 veterinary clinics in Sweden that participate in the national hip dysplasia program with a request for medical records of dogs with GDM. GDM was defined as initial diagnosis of DM during pregnancy. DM diagnosis in each dog was based on clinical signs, including polyuria and polydipsia, and persistent fasting hyperglycemia (>144 mg/dL or >8 mmol/L). Pregnancy was confirmed in all dogs by presence of fetuses or puppies at the end of pregnancy.

Case information was obtained from medical records and by phone calls to owners and veterinarians. Data collected included breed, date of birth, clinic, pregnancy number, number of days...
after mating or insemion, date of diagnosis of DM, blood and
urinalysis results, clinical signs at diagnosis, type of treatment, date of
initiating treatment, dosage of insulin if given, date of end of
pregnancy, remission from DM, date of remission if any, number of
puppies, survival of puppies until week 8 after birth, latest contact
with owner, date of death of bitch, cause of death, and any occur-
rence of DM in relatives.

Because the study population was small, it was difficult to eval-
uate normality of the variables, and thus nonparametric statistical
methods were used. The median and range were determined for
all continuous variables. The dogs were divided into 2 groups with
respect to outcome: remission from DM during the follow-up
period was classified as a successful outcome, whereas permanent
DM or death related to DM or its treatment was counted as an
unsuccessful outcome. Treatment of dogs was classified as either
treatment with insulin or immediate termination of pregnancy. The
Wilcoxon rank sum test was used to evaluate differences between
the 2 outcome groups concerning age at diagnosis, day after mating
day of pregnancy at diagnosis, and glucose concentration at diagnosis. The Wilcoxon
rank sum test was also used to evaluate age differences between the 2
treatment groups. Fisher’s exact test was used to evaluate differ-
ences in treatment between the 2 outcome groups. A 2-tailed P-
value of <.05 was considered significant.

**Results**

**Descriptive Statistics**

Thirteen dogs were diagnosed with GDM at 6 different
clinics. Six of the 13 cases came from the same
clinic. There were 9 Swedish Elkhounds, 1 Norwegian
Elkhound, 1 Alaskan Malamute, 1 Dreeser (also known
as Swedish Dachsbracke), and 1 Border Collie. One dog
(8.2-year-old Swedish Elkhound) was euthanized imme-
diately upon diagnosis of GDM. One dog (5.0-year-old
Swedish Elkhound) died within 1 day after cesarean
section and ovariolyterectomy (OHE). The other 11
dogs were followed until November 2007 or death, giving
a median follow-up time of 35 months (range, 2.5–53).
No dog was lost to follow-up.

Median age at diagnosis was 5.9 years (range, 2.1–8.2).
Diagnosis of GDM was made a median of 50 (range,
32–64) days after mating. Before diagnosis, the 13 dogs
had exhibited clinical signs consistent with DM for a
median of 3 days (range, 0–61, 2 values missing). The
dogs had a median of 3 pregnancies (range, 1–4) includ-
ing the present one. Median glucose concentration at
diagnosis was 340 mg/dL (18.9 mmol/L) (range, 203–587,
reference range, 70–100, 1 value missing). Diagnosis in
the dog with a missing glucose concentration was estab-
lished by severe glucosuria combined with consistent
clinical signs. Blood glucose in this particular dog was
measured 12 days later and found to be 432 mg/dL
(24 mmol/L).

One dog was euthanized and excluded from further
statistical evaluation, 5 dogs were treated with insulin,
and 7 dogs were treated by immediately terminating the
pregnancy. Those 7 were not given insulin and pregnancy
was terminated within a median of 0 (range, 0–4) days
after diagnosis by means of pharmaceutical abortion
with aglepristone (n = 1), OHE (n = 1), cesarean
section (n = 1), or a cesarean section combined with
OHE (n = 4). One of these dogs (5.0-year-old Swedish
Elkhound) died 12 hours postoperatively after cesarean
section and OHE owing to extensive bleeding and
hypovolemic shock. In the dogs treated with pregnancy
termination, median duration of pregnancy at diagnosis
was 62 days (range, 32–64). Five of the 12 bitches
were treated with intermediate acting porcine insulin
(n = 3) or recombinant human NPH insulin (n = 2) for a me-
dian of 18 days (range, 12–31) until whelping (n = 3) or
cesarean section (n = 2). Median duration of pregnancy
was 47 days (range, 33–50) in the dogs treated with
insulin. The dose of insulin increased with time in all
dogs and the median of the final dose of insulin at partu-
rition was 1.3 U/kg (range, 0.8–3) per day divided into 2
doses. Blood glucose concentration was measured during
the insulin treatment; the median value was 504 mg/dL
(28 mmol/L) (range, 432–684).

Eleven dogs survived >1 day after diagnosis. DM re-
solved in 7 dogs and was permanent in 4 dogs. Median
age at diagnosis was 4.8 years (range, 2.1–6.7) for the 7
dogs with transient DM and 7.0 years (range, 6.1–8.0) for
the 4 dogs with permanent DM. Six of the 7 dogs with
transient DM had been treated with immediate termina-
tion of pregnancy, and DM resolved by a median of 9
days after the end of their pregnancies (range, 7–21). All
4 dogs with permanent DM had been treated with insulin
until whelping.

Five of the cases were diagnosed between days 60 and
64 of pregnancy. Among the 10 bitches reaching full
term, 7 litters were delivered by cesarean section, 1 by
pharmaceutical induction, and 2 naturally. Nine bitches
had puppies born alive. From 8 litters with a known
number of puppies, 60 puppies, with a median of 9
puppies per litter (range, 2–12) were born and 44 (73%)
survived until 8 weeks of age. Two of the bitches had
litters diagnosed with DM. One Swedish Elkhound
puppy from a bitch included in the study was diagnosed
with juvenile DM and was euthanized at the age of 4
months.

Glucose concentration and day of pregnancy at
diagnosis did not differ between the 2 outcome groups
(P = .37 and .81, respectively). The group with successful
outcome (n = 7) had a statistically significantly lower age
at diagnosis than the group with unsuccessful outcome
(n = 5) (P = .035). There was no significant difference in
outcome between the 2 treatments (P = .072). Age at
diagnosis was compared for the 2 treatments and found
not to be significantly different (P = .023) with the insulin-
treated group being younger than the group treated by
termination of pregnancy.

**Discussion**

This retrospective study provides additional clinical
information about the rare disorder of canine GDM.
Nordic Spitz breeds were overrepresented in the case ma-
terial, indicating a possible breed predisposition for the
syndrome. There are several possible explanations why
there are fewer reports of GDM in dogs than humans.
One is that although GDM often is asymptomatic in
women, the disease usually is recognized at maternal
health checks, whereas dogs are not usually tested for DM unless they indicated clinical signs of the disease. 

The etiology of canine DM is considered multifactorial and can be broadly divided into insulin resistance and insulin deficiency. Insulin-deficient diabetes has been suggested as being caused by autoimmune destruction of insulin producing β-cells, by pancreatitis, or secondarily to chronic hyperglycemia (eg, insulin-resistant diabetes). Insulin-resistant diabetes may occur in hormonal disturbances (eg, hyperadrenocorticism, progesterone-induced acromegaly). Female dogs may develop a transient form of DM during diestrus. A nonpregnant dog has similar concentrations of androgens, estrogens and progestagens as a pregnant dog during the 2–3 months of diaestrus, suggesting that transient DM also could occur during pregnancy in dogs. In the present study, GDM was diagnosed in the 2nd half of pregnancy by a median of 50 days after mating, which is later than was earlier reported in a study of 11 bitches with diestrus diabetes in which all dogs started to indicate clinical signs of DM of 50 days after mating, which is later than was earlier reported. Both studies were, however, based on a small number of dogs. The hormones believed to be involved in the pathogenesis (eg, progesterone) reaches their highest concentrations within 15–30 days after the luteinizing hormone peak. Mammary GH is mainly progesterone-dependent and can be expected to increase together with progestosterone.

DM usually affects middle-aged and older dogs with a mean age of onset of about 9 years. The median age in the present study was lower, probably because few old dogs are bred and therefore at risk of getting GDM. In Sweden, it is recommended that dogs > 7 years are not bred without a health certificate. The earlier 2 reported cases of GDM were both 6 years old.

In Sweden, Nordic Spitz breeds are rather popular. In an insurance-based study of 182,000 dogs, about 3.6% (6,635 of the dogs) were of the breeds Norwegian Elkhound and Swedish Elkhound. The large proportion of Nordic Spitz breeds (Norwegian and Swedish Elkhounds, and Alaskan Malamute) in the present study (11/13 dogs) is, however, much higher than the frequency in the general population and suggests that there is a genetic predisposition to develop GDM in these breeds. Interestingly, the same breeds as seen in the present study (Norwegian and Swedish Elkhounds, and Border Collie), are reported to have a very high proportion females with DM compared with other breeds. One of the 2 cases earlier reported by Norman et al was a Siberian Husky, and the other was a Labrador. However, in view of the nonrandom case selection in that study and the present one, definitive conclusions concerning breed predisposition cannot be made.

In the present study, DM resolved in 7 of 13 dogs within 21 days after the end of their pregnancies despite quite high glucose concentrations at diagnosis. A majority of GDM cases are probably caused by insulin resistance and therefore reversible. DM was, however, permanent in 5 dogs, suggesting that chronic hyperglycemia had caused irreversible damage to the β-cells by means of glucotoxicity. It is also possible that another cause of DM such as autoimmune diabetes or pancreatitis may have coincided with pregnancy. One of the 2 cases described by Norman and colleagues had transient DM and the other had permanent DM.

The 5 dogs with permanent DM or death related to treatment were significantly older than the 7 dogs with transient DM. We also found that the dogs treated with insulin were significantly older than the dogs treated by termination of pregnancy, and therefore it is not possible to determine whether the association of treatment outcome with age is a causal one. The reason why the younger dogs in the present study were treated differently from the older dogs may be that the owners valued the young bitch more than the puppies, and therefore chose to terminate the pregnancy. Aging might be expected to make the development of permanent DM more likely because it is associated with decreasing insulin secretory capacity in humans. If the same is true for dogs, such a deterioration could indicate that the period for which a dog can tolerate hyperglycemia before passing into a permanent diabetic state is shorter in older dogs than in younger dogs. However, among this group of dogs, the difference in age of the treatment groups makes it impossible to determine if the difference in outcomes for each treatment was an effect of age, an effect of treatment owing to some other factor. Although no significant difference in outcome between treatments was found in this study, an effect of treatment on outcome cannot be excluded owing to the low power of the study. Six of the 7 dogs treated with immediate termination of pregnancy recovered fully and the 7th dog died postoperatively. The cause of death in this dog could have been inadequate surgical techniques unrelated to its DM. This dog was, however, included in the statistical analysis, because the fatal outcome was dependent on the treatment (surgery). The prognosis for recovery from GDM seems favorable if choosing termination of pregnancy as treatment, assuming there are no complications of surgery or medical abortion. Termination of pregnancy results in a decrease in diabetogenic gestational hormones. If there still is a viable β-cell population, the dog may recover from DM. If insulin treatment is chosen instead, good glycemic control must be achieved to avoid hyperglycemia and glucotoxicity. In the present study, only 1 of the 5 dogs treated with insulin recovered from its DM and no dog was considered to be under tight glycemic control. The insulin doses used in the 5 dogs were in 4 cases low (< 2 U/kg/d divided into 2 doses). Only 1 dog received > 2 U/kg daily. This dog was the only insulin-treated dog which DM resolved. In dogs with insulin resistance types of DM, doses > 1.5 U/kg twice daily are commonly needed. A better result for the insulin-treated group may have been achieved with higher doses of insulin.

A controlled clinical trial is preferable when comparing 2 different treatment modalities. However, in a rare disorder such as GDM, an observational study such as the present one is the only realistic option. Interpretation of our results concerning prognosis and type of treatment should therefore be made with care. 

Five of the dogs in the present study were first diagnosed with GDM when seeking medical attention...
for dystocia. Olson and colleagues analyzed the plasma cortisol concentration in healthy beagle bitches in all reproductive periods including pregnancy and labor. The cortisol concentration was not significantly increased during pregnancy but increased to very high concentrations (242 ± 35 nmol/L) during the 2nd phase of labor (birth of puppies). The increased concentrations of cortisol during labor theoretically may induce DM in a predisposed dog. In a colony of diabetic Golden Retrievers, insulin requirements did, however, decrease at the onset of labor, suggesting that DM preceded dystocia in the present study, and not vice versa. 14

The consequences of human GDM may be substantial with complications such as macrosomia, dystocia, and neonatal hypoglycemia. 3 Dystocia occurred in 8 of 10 bitches reaching full term in this study. The occurrence of macrosomia or neonatal hypoglycemia was not investigated in this study. In the present study, neonatal mortality was 27% of puppies born alive, which is somewhat higher than reported in puppies with healthy dams. 28 The increased concentrations of cortisol during labor theoretically may induce DM in a predisposed dog. In a colony of diabetic Golden Retrievers, insulin requirements did, however, decrease at the onset of labor, suggesting that DM preceded dystocia in the present study, and not vice versa. 14

This report suggests that GDM affects mainly middle-aged bitches in the 2nd half of pregnancy with a breed predisposition toward Nordic Spitz breeds. GDM may resolve within days to weeks after pregnancy has ended. Neonatal mortality seems to be mildly increased compared with offspring of healthy dams. Further research is needed to investigate optimal treatment regimens for dogs with GDM and risk factors for unsuccessful outcome.

Acknowledgments

This study was supported by grants from the Agria Insurance Foundation for Research. The authors thank the participating owners and veterinarians. The authors also acknowledge Nils Fall, Agneta Egenvall, and Jens Hägström, SLU for helpful discussions.

Footnotes

a Alizin, ChemVet DK A/S, Silkeborg, Denmark
b Caninsulin, Intervet, Danderyd, Sweden
Insulatard, Novo Nordisk, Bagsvaerd, Denmark

References


