



Helps Every Puppy Be...“PICK OF THE LITTER”

Trans Fat Free!

FOR

- Newborn & Weaned Puppies
- Pregnant & Nursing Mothers
- Joint & Soft Tissue Support

PROMOTES

- Antibodies & Resistance
- Connective Tissue Strength
- Bone Development
- Healthy, Lean Growth

NEXT BEST THING TO MOM

Puppies grow healthiest and best on mother's milk. Science has decoded the immunity and growth secrets in canine milk to reveal over 1,000 bioactive properties. PUPPY GOLD recreates canine mother's milk to promote immunity, stronger joints and lean growth.

“SWISS ARMY KNIFE” OF NUTRITION

PUPPY GOLD contains canine milk's bioactive proteins, micellar casein, colostrum, glucosamine and more to give a giant head start in life. We even include canine milk's awesome immune factors, including lactoferrin. PUPPY GOLD helps produce not just healthier puppies, but healthier, longer living adults.

FOR MOM, TOO!

The same nutrients that help puppies after birth help them grow inside mom. Feeding PUPPY GOLD to mothers helps producer healthier, more robust puppies and a stronger mom. Mothers look great during pregnancy & nursing and snap back fast afterwards .

NO MORE RUNTS

PUPPY GOLD supplies every pup the pick of the litter's share of immune, joint and growth nutrients. Because they get their fair share, even small puppies can catch up and express their true (formerly hidden) genetic potential. No more runts!

IT'S THE GOLD STANDARD OF PUPPY FORMULAS!

Questions and Answers

WHAT IS PUPPY GOLD?

PUPPY GOLD is a pure white powder mixed with food, or fed alone. PUPPY GOLD is the first formula patterned after the "gold standard" puppy formula, mother's milk. Turns out, canine milk is highly unique. PUPPY GOLD is designed to duplicate the many survival and growth advantages of mother's milk.

WHAT WILL PUPPY GOLD DO FOR MY PUPPY?

First, PUPPY GOLD helps boost immunity. Second, tissue and protein synthesis is enhanced. Finally, maybe most important, joint and connective tissue formation is promoted. The combination of immunity, growth and structural strength produces rock solid bodies and health which can last a lifetime.

IS PUPPY GOLD BETTER THAN GOAT MILK?

Goat milk is the absolute perfect formula for...goats! Goat milk and canine milk are very different, because they're very different species. Dogs are mobile, smart predators and their milk reflects it. Goats are, well, goats. It's as absurd to feed goat milk to puppies as to feed cat milk to a baby whale. Mother's milk is species specific, and PUPPY GOLD faithfully copies canine mother's milk without the use of trans fats .

HOW DOES PUPPY GOLD HELP BREEDING MOTHERS?

First, PUPPY GOLD helps develop puppies inside the mother during pregnancy, sparing mom's muscle and bone mass. Second, during lactation nutrient needs rise 400%. She extracts this enhanced need from her own body stores of muscle and bone. Instead, PUPPY GOLD supplies milk synthesizing building blocks, and spares her body's own stores. The result is a shiny, robust and healthy mother during pregnancy and nursing.

HOW CAN IT IMPROVE MY BREEDING PROGRAM?

First, there are no runts. Every puppy gets ultimate nutrition. Second, breeders get a clearer picture of what dogs to breed. Often the pup that looks the best as an adult got the most milk supply as a pup. But, that may not be the best genetic animal (genotype), but the best nourished as a baby,

and therefore, develops the most as an adult. (phenotype). PUPPY GOLD ensures every pup gets an equal share of super-rich milk. Call it the equalizer. When they grow up, you'll see which has the best genetics to breed. The true genotype value of an individual will be clearer.

<DO THEY LIKE PUPPY GOLD? >

Puppies and moms alike love PUPPY GOLD. Natural milk protein taste and smell stimulates eating in all puppies. PUPPY GOLD is ideal for neonates to mature mothers.

STUDIES RELATING TO PUPPY GOLD NUTRIENTS AND FORMULATION

Am J Clin Nutr. 2004 Nov;80(5):1322-6. Related Articles, Links

Bone mass is recovered from lactation to postweaning in adolescent mothers with low calcium intakes.

Bezerra FF, Mendonca LM, Lobato EC, O'Brien KO, Donangelo CM.

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BACKGROUND: Adolescent mothers may be at increased risk of irreversible bone loss during pregnancy and lactation, particularly when calcium intake is low. **OBJECTIVE:** Longitudinal changes in bone mass from lactation to postweaning were evaluated in 10 adolescent mothers aged 15-18 y who habitually consumed <500 mg Ca/d. **DESIGN:** Total-body bone mineral content (TBBMC), total-body bone mineral density (TBBMD), and lumbar spine bone mineral density (LSBMD) were measured at lactation (6-24 wk postpartum) and after weaning (12-30 mo postpartum). Serum hormones (intact parathyroid hormone, estradiol, and prolactin), serum calcium, and markers of bone turnover [urinary N-telopeptide cross-linking region of type I collagen (NTx) and plasma activity of bone alkaline phosphatase] were measured at lactation. **RESULTS:** TBBMC, total calcium content, TBBMD, and LSBMD increased from lactation to postweaning ($P < 0.01$). TBBMD and LSBMD were, respectively, 3.6% and 9.7% lower than predicted at lactation and 0.3% and 4.8% lower than predicted in the postweaning period. The

increase in age-matched TBBMD adequacy was correlated with the time after resumption of menses ($r = 0.86$, $P < 0.01$). Calcium accretion from lactation to postweaning correlated negatively with estradiol ($r = -0.86$) and prolactin ($r = -0.69$) and positively with intact parathyroid hormone ($r = 0.72$) and NTx ($r = 0.84$) measured at lactation ($P < 0.05$). CONCLUSIONS: It appears that adolescent mothers with habitually low calcium intakes recover from lactation-associated bone loss after weaning. The rate of bone accretion, however, may not be sufficient to attain peak bone mass at maturity. Hormones regulating bone turnover during lactation may influence bone recovery in adolescent mothers.

Br J Nutr. 2005 May;93(5):593-9.

The influence of erythrocyte folate and serum vitamin B12 status on birth weight.

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The extent to which maternal folate and vitamin B12 modulate infant birth weight is unclear. The present study investigated mothers in early gestation (mean 11.5 (sd 5.8) weeks) and neonates, at delivery. Erythrocyte (RBC) folate (mothers: n 683; neonates: n 614) and vitamin B12 (mothers: n 534; neonates: n 614) were measured. Data on smoking habits were available for 44 % of pregnancies (n 443). The relationship between vitamin levels and birth weight standardized for gender and gestational age was investigated, using linear regression and adjusting for possible confounding variables (maternal age, parity). Results are presented as standardized regression coefficients (b). Increasing maternal age was associated with elevated RBC folate (b 0.11 (95 % CI 0.08, 0.15), $P < 0.001$; n 674) and smoking was associated with a decrease in maternal RBC folate (b -1.38 (95 % CI -1.92, -0.86), $P = 0.001$; n 319). Neonatal RBC folate was predicted by maternal RBC folate (b 0.08 (95 % CI 0.04, 0.11), $P = 0.001$; n 315) and maternal vitamin B12

(b 0.08 (95 % CI 0.01, 0.16), P=0.02; n 252). Smoking influenced maternal vitamin B12 status (b -0.88 (95 % CI -1.49, -0.27), P=0.005; n 231). Using univariate regression, smoking significantly influenced infant birth weight (b -2.15 (95 % CI -3.24, -1.04), P<0.001; n 437). However, the effect of smoking on birth weight was statistically non-significant when considered in a multivariate regression model, leaving maternal RBC folate as the only significant predictor of birth weight (b 0.25 (95 % CI 0.08, 0.42), P=0.005; n 145). These findings suggest that maternal folate status is an important determinant of infant birth weight. The combined effects of smoking and reduced RBC status on birth weight require further investigation.

J Nutr. 2004 Jan;134(1):86-92. Related Articles, Links

Supplementation of sows with L-carnitine during pregnancy and lactation improves growth of the piglets during the suckling period through increased milk production.

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Recent studies showed that piglets of sows fed diets supplemented with L-carnitine grow faster during the suckling period than piglets of control sows fed diets without L-carnitine. This study was undertaken to investigate the effect of L-carnitine supplementation in sows on milk production and milk constituents. An experiment was performed in which two groups of 20 gilts each were fed diets with or without supplemental L-carnitine during pregnancy (0 vs. 125 mg L-carnitine daily/sow) and lactation (0 vs. 250 mg L-carnitine daily/sow). The experiment was continued over two reproductive cycles. L-carnitine-treated sows had larger litters (P<0.01) and higher litter weights (P<0.05) than control sows. Piglets of L-carnitine-treated sows had lower birth weights (P<0.05) but grew faster during the suckling period (P<0.01) and were heavier (P<0.05) at weaning than piglets of control sows. L-carnitine-treated sows had higher milk yields on d 11 and 18 of lactation than control sows (P<0.05). Milk of L-carnitine-treated sows had higher concentrations of total and free carnitine than milk of control sows

($P < 0.001$); concentrations of fat, protein and lactose and the amounts of gross energy in the milk did not differ between the two groups of sows. The amounts of protein ($P < 0.05$) and lactose ($P < 0.05$) were higher in L-carnitine-treated sows than in control sows; the amount of energy secreted with the milk tended to be higher in carnitine-treated sows than in control sows ($P < 0.10$). The study suggests that piglets of carnitine-treated sows grow faster during the suckling period than those of control sows because they ingest more nutrients and energy with the milk.

Antiviral Res. 2003 Nov;60(3):193-9. Related Articles, Links

Antiviral activity of lactoferrin against canine herpesvirus.

Tanaka T, Nakatani S, Xuan X, Kumura H, Igarashi I, Shimazaki K.

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Lactoferrin (LF) is an iron-binding protein that is found in milk and other mammalian secretions. We found that bovine lactoferrin (bLF) inhibited both the in vitro infection and replication of canine herpesvirus (CHV) in Madin-Darby canine kidney (MDCK) cells. Incubation of CHV with bLF prevented subsequent infection of MDCK cells. Furthermore, proteins from CHV-infected MDCK cells were resolved by SDS-PAGE, and then bLF CHV-binding proteins were identified by far Western blotting. We demonstrated that the anti-CHV activity of bLF was due to its interaction with CHV as well as with MDCK cells. Both the apo- and holo-forms of bLF inhibited virus multiplication independently of their iron-withholding properties. We also demonstrated that human LF had anti-CHV activity. Our findings suggest that LF could be effective in dogs to provide protection against CHV infection

Adv Exp Med Biol. 1994;357:71-90. Related Articles, Links

The effects of lactoferrin on gram-negative bacteria.

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Lactoferrin is an iron-binding protein found in human mucosal secretions as well as the specific granules of polymorphonuclear leukocytes. A variety of functions have been ascribed to the protein, and it appears to contribute to antimicrobial host defense. In particular, it has been shown to have direct effects on pathogenic microorganisms including bacteriostasis and the induction of microbial iron uptake systems. Still its overall physiologic role remains to be defined. It has appeared logical that antimicrobial activity of the protein arises from sequestration of environmental iron thereby causing nutritional deprivation in susceptible organisms. This argument is buttressed by the finding that selected highly virulent pathogens have evolved techniques to subvert this effect and use the protein as an iron source. However, recent observations indicate that the protein has additional properties that contribute to host defense. Work by several groups has shown that the protein synergistically interacts with immunoglobins, complement, and neutrophil cationic proteins against Gram-negative bacteria. Further, both the whole protein and a cationic N-terminus peptide fragment directly damage the outer membrane of Gram-negative bacteria suggesting a mechanism for the supplemental effects. This review will summarize these diverse observations with a consideration of how the in vitro work relates to the physiological role of the protein.

Br J Nutr. 2003 Nov;90(5):979-86. Related Articles, Links

Infant intake of fatty acids from human milk over the first year of lactation.

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Despite the importance of human milk fatty acids for infant growth and development, there are few reports describing infant intakes of individual fatty acids. We have measured volume, fat content and fatty acid composition of milk from each breast at each feed over a 24 h period to determine the mean daily amounts of each fatty acid delivered to the infant from breast milk at 1, 2, 4, 6, 9 and 12 months of lactation in five women. Daily (24 h) milk production was 336.60 (SEM 26.21) and 414.49 (SEM 28.39) ml and milk fat content was 36.06 (SEM 1.37) and 34.97 (SEM 1.50) g/l for left and right breasts respectively over the course of the first year of lactation. Fatty acid composition varied over the course of the day (mean CV 14.3 (SD 7.7) %), but did not follow a circadian rhythm. The proportions (g/100 g total fatty acids) of fatty acids differed significantly between mothers ($P<0.05$) and over the first year of lactation ($P<0.05$). However, amounts (g) of most fatty acids delivered to the infant over 24 h did not differ during the first year of lactation and only the amounts of 18:3n-3, 22:5n-3 and 22:6n-3 delivered differed between mothers ($P<0.05$). Mean amounts of 18:2n-6, 18:3n-3, 20:4n-6 and 22:6n-3 delivered to the infant per 24 h over the first year of lactation were 2.380 (SD 0.980), 0.194 (SD 0.074), 0.093 (SD 0.031) and 0.049 (SD 0.021) g respectively. These results suggest that variation in proportions of fatty acids may not translate to variation in the amount delivered and that milk production and fat content need to be considered.

Am J Clin Nutr. 2004 Jan;79(1):139-47. Related Articles, Links

Dose response of bone mass to dietary arachidonic acid in piglets fed cow milk-based formula.

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Department of Human Nutritional Sciences, University of Manitoba, Winnipeg, Canada.

BACKGROUND: The addition of arachidonic acid (AA) and docosahexaenoic acid (DHA) to infant formula was recently approved in North America. In piglets, dietary AA is linked to elevations in bone mass. **OBJECTIVE:** The objective was to investigate the effects of varied amounts of dietary AA on

bone modeling and bone mass with the use of the piglet model for infant nutrition. DESIGN: Male piglets (n = 32) were randomly assigned to receive 1 of 4 formulas supplemented with AA (0.30%, 0.45%, 0.60%, or 0.75% of fat) plus DHA (0.1% of fat) from days 5 to 20 of life. Measurements included biomarkers of bone modeling, fatty acid status, and whole-body and femur bone mineral content; bone area was measured by dual-energy X-ray absorptiometry. Differences among groups were detected with two-factor analysis of variance. Regression analyses were used to determine factors responsible for bone mineral content after dietary AA was accounted for. RESULTS: Proportions of AA in plasma, liver, and adipose were modified by the dietary treatments, but bone modeling was not affected. Liver AA was positively related to plasma insulin-like growth factor 1 and calcitriol and urinary N-telopeptide. Whole-body bone mineral content was elevated in the piglets fed 0.60% and 0.75% AA and was best predicted by dietary AA and bone resorption. CONCLUSIONS: This study confirms that dietary AA alters bone mass and clarifies the best amount of AA to add to the diet of pigs born at term. Because the amount of dietary DHA was held constant, whether other amounts of DHA are related to bone mass requires investigation.

Plasma beta-casomorphin-7 immunoreactive peptide increases after milk intake in newborn but not in adult dogs

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To determine the relation between milk intake and plasma levels of beta-casomorphins as a function of age, we studied the levels of beta-casomorphin-7 immunoreactive material (BCMI R) in 2- and 4-wk-old beagle neonates and adult dogs following milk intake. We used three kinds of milk: 1) bovine casein-based milk formula; 2) canine bitch's milk, and 3) soy protein-based (noncasein) formula. Using a new extraction technique, BCMI R was isolated from plasma and assayed by radioimmunoassay at 0, 2, 4, and 6 h after feeding. We found that BCMI R increased significantly in both 2- and 4-wk-old puppies post bovine and canine milk feeding, but not after soy protein formula. Base-line values were about 80-120 fmol/ml and increased to 100-120% 2 h after bovine casein intake in the older puppies and by 4 h in

the younger group. BCMIR levels were undetectable in adult dogs before or after bovine milk feeding. Beta-casomorphin-7 added to plasma was rapidly degraded whereas BCMIR was stable. Chromatographic profiles demonstrated that the BCMIR moiety is larger than beta-casomorphin-7. Our data suggest that the appearance of BCMIR in the plasma of neonatal dogs is a result of beta-casein degradation along a permeable gastrointestinal mucosa. We speculate that morphiceptin and beta-casomorphins can be cleaved from BCMIR and may have important physiologic effects

Am J Vet Res. 1999 Sep;60(9):1088-91. Related Articles, Links

Comparison of insulin-like growth factor-I concentration in mammary secretions and serum of small- and giant-breed dogs.

White ME, Hathaway MR, Dayton WR, Henderson T, Lepine AJ.

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OBJECTIVE: To determine insulin-like growth factor-I (IGF-I) concentrations in canine mammary secretions and serum during lactation and to compare them between small and giant breeds of dogs. **ANIMALS:** 7 gestating Beagles and 4 gestating Great Danes. **PROCEDURE:** Dogs were fed a common nutritionally complete and adequate gestation and lactation diet. Milk samples were collected at postpartum hour 12 and postpartum days 3, 7, 14, 21, and 28 after IV oxytocin administration. Two puppies/litter were identified at whelping for collection of blood samples corresponding to the days of milk sample collection plus days 35 and 42. Maternal blood samples were obtained on days 1, 7, and 42 from Beagles and days 1, 7, and 28 from Great Danes and were acid/ethanol extracted and analyzed by use of a radioimmunoassay. **RESULTS:** Maternal serum IGF-I concentration was greater in Great Danes at all sample collection times. Similarly, colostrum from Great Danes contained more IGF-I, compared with that of Beagles (70 ng/ml vs 40 ng/ml, respectively). These values decreased to approximately 10 ng/ml by day 3 in both breeds and remained between 10 and 20 ng/ml for the duration of lactation. Growth rate and serum IGF-I concentration were greater in Great Dane puppies at birth to day 42. **CONCLUSIONS AND CLINICAL RELEVANCE:** High IGF-I concentration in colostrum may be

biologically important for newborn puppies. Body mass and serum IGF-I concentration are directly correlated in growing Beagle and Great Dane puppies. Serum IGF-I concentration may be an indicator of growth potential in dogs.

Cornell Vet. 1993 Apr;83(2):107-16. Related Articles, Links

Serum chemistry and lipid profiles in neonatal beagle puppies fed homemade milk replacer formulas.

Chandler ML, Miller E, Olson PN, Ralston SL.

Department of Clinical Sciences, College of Veterinary Medicine, Fort Collins 80523.

Milk replacer formulas based on cow's milk and egg yolks are frequently recommended for use in neonatal puppies. These formulas are lower in protein, kilocalories, calcium, and phosphorus than bitch's milk. In addition, the cholesterol content is greater than bitch's milk. The effect of feeding these formulas on serum chemistry profiles, lipid profiles, and alkaline phosphatase isoenzyme profiles of 5-week-old beagle puppies was studied. Three groups of beagle puppies were fed bitch's milk (control) (n = 18), a homemade milk-egg-oil formula (Formula 1) (n = 18), or a homemade milk-egg-oil formula supplemented with additional calcium and phosphorous (Formula 2) (n = 18). Concentrations of serum urea nitrogen, albumin, and total CO₂ were lower (P < 0.05), and concentrations of serum phosphorus, globulins, sodium, chloride, and cholesterol were higher (P < 0.05) in formula-fed puppies than bitch-fed puppies. Serum potassium concentration was lower in the puppies fed Formula 1 than in the control puppies (P < 0.05), and serum potassium concentration in the puppies fed Formula 2 was not significantly different from that in puppies fed Formula 1 or the control puppies. Total triglyceride (TG) and high density lipoprotein2 cholesterol (HDL2) concentrations were similar in all three groups of puppies but the combined high density lipoprotein1 (HDL1) plus low density lipoprotein (LDL) cholesterol fraction was higher (P < 0.05) in the formula-fed puppies and accounted for the majority of the increase in cholesterol. There were no differences (P < 0.05) in total serum alkaline phosphatase (ALP) or bone-

derived ALP (BALP) concentrations among the groups, however there was a higher ($P < 0.05$) serum concentration of liver-derived ALP (LALP) in the Formula 1-fed puppies. Feeding homemade egg and cow's milk-based puppy replacement formulas is not recommended for long term use.

Probl Vet Med. 1992 Sep;4(3):545-50. Related Articles, Links

Feeding to optimize canine reproductive efficiency.

Moser E.

The relationship between nutrition and reproduction is a topic of importance to veterinarians and breeders. Nutrient deficiencies, excesses, and imbalances all are capable of altering reproductive performance. Healthy adult dogs should be fed a diet high in digestibility, low in residue, and high in nutrient bioavailability. Rarely is nutritional intervention necessary during the first half of gestation. During the last half of gestation, switching to a growth/lactation diet and increasing intake by 1.2 to 1.4 x maintenance is indicated. Depending on breed and pup numbers, at peak lactation, feed intake may need to be increased by 2 to 4 x maintenance. The feeding goals of lactation are to minimize loss of bitch body condition score and optimize milk production and pup growth. After weaning, the female who is in poor body condition should remain on a diet rich in protein, fat, and trace nutrients until she is physically/nutritionally repleted.

Am J Clin Nutr 2002 Mar;75(3):570-80

A randomized controlled trial of long-chain polyunsaturated fatty acid supplementation of formula in term infants after weaning at 6 wk of age.

Birch EE, Hoffman DR, Castaneda YS, Fawcett SL, Birch DG, Uauy RD.

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BACKGROUND: The critical period during which the dietary supply of long-chain polyunsaturated fatty acids (LCPs) may influence the maturation of cortical function in term infants is unknown. **OBJECTIVE:** The aim of the present study was to determine the relative importance for maturation of the visual cortex of the dietary supply of LCPs during the first 6 wk of life compared with that during weeks 7-52. **DESIGN:** A randomized controlled clinical trial of LCP supplementation in 65 healthy term infants who were weaned from breast-feeding at 6 wk of age was conducted to determine whether the dietary supply of LCPs after weaning influenced the maturation of visual acuity and stereoacuity. **RESULTS:** Despite a dietary supply of LCPs from breast milk during the first 6 wk of life, infants who were weaned to formula that did not provide LCPs had significantly poorer visual acuity at 17, 26, and 52 wk of age and significantly poorer stereoacuity at 17 wk of age than did infants who were weaned to LCP-supplemented formula. Better acuity and stereoacuity at 17 wk was correlated with higher concentrations of docosahexaenoic acid in plasma. Better acuity at 52 wk was correlated with higher concentrations of docosahexaenoic acid in plasma and red blood cells. No significant effects of diet on growth were found. **CONCLUSION:** The results suggest that the critical period during which the dietary supply of LCPs can influence the maturation of cortical function extends beyond 6 wk of age.

Am J Vet Res. 2001 Aug;62(8):1266-72.

Related Articles, Links

Changes in protein and nutrient composition of milk throughout lactation in dogs.

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OBJECTIVE: To evaluate changes in protein and nutrient composition of milk throughout lactation in dogs. **SAMPLE POPULATION:** Milk samples collected from 10 lactating Beagles. **PROCEDURE:** Milk samples were collected on days

1, 3, 7, 14, 21, 28, 35, and 42 after parturition and analyzed to determine concentrations of nitrogen, nonprotein nitrogen, casein, whey proteins, amino acids, lipids, lactose, citrate, minerals, and trace elements. Optimum conditions for separating casein from whey proteins and distribution of milk proteins throughout lactation were assessed by use of polyacrylamide gel electrophoresis. RESULTS: Protein concentration was high in samples collected on day 1 (143 g/L), decreased through day 21 (68.4 g/L), and increased thereafter. Concentration of nonprotein nitrogen did not change throughout lactation (5.7 to 9.9% of total nitrogen content). Casein-to-whey ratio was approximately 70:30 and remained constant throughout lactation. Lactose concentration increased from 16.6 g/L on day 1 to 34.0 to 40.2 g/L on days 7 to 42. Lipid concentration ranged from 112.5 to 1372 g/L. Citrate concentration increased from day 1 (4.8 mM) to day 7 (6.6 mM), then gradually decreased until day 42 (3.9 mM). Iron, zinc, copper, and magnesium concentrations decreased during lactation, whereas calcium and phosphorus concentrations increased. Calcium-to-phosphorus ratio remained constant throughout lactation (approx 1.6:1). Energy content of milk ranged from 1,444 to 1,831 kcal/L. CONCLUSIONS AND CLINICAL RELEVANCE: Protein and nutrient composition of milk changes throughout lactation in dogs. These data can provide valuable information for use in establishing nutrient requirements of puppies during the suckling period.

Hypertension. 2004 Jun 7 [Epub ahead of print] Related Articles, Links

Perinatal L-Arginine and Antioxidant Supplements Reduce Adult Blood Pressure in Spontaneously Hypertensive Rats.

Racasan S, Braam B, Van Der Giezen DM, Goldschmeding R, Boer P, Koomans HA, Joles JA.

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Embryo cross-transplantation and cross-fostering between spontaneously hypertensive rats (SHR) and normotensive rats (WKY) suggest that perinatal environment modulates the genetically determined phenotype. In SHR the balance between NO and reactive oxygen species (ROS) is disturbed. We hypothesized that increasing NO and diminishing ROS in perinatal life would ameliorate hypertension in adult SHR. Pregnant SHR and WKY and their

offspring received L-arginine plus antioxidants (vitamin C, vitamin E, and taurine) during the last 2 weeks of pregnancy and then until either 4 or 8 weeks after birth. Systolic blood pressure (SBP) and urinary excretion of protein, nitrates (NO_x), and thiobarbituric acid reactive substances (TBARS) were measured. At 48 weeks of age rats were euthanized for glomerular counts. Perinatal supplements reduced SBP persistently in SHR and prevented the SBP increase observed in aging WKY. Initially NO_x excretion was lower and TBARS excretion higher in SHR than WKY. There was a direct effect on NO_x excretion in supplemented pregnant SHR and their offspring, but no increase was observed after stopping the supplements. TBARS excretion was only depressed up to 14 weeks by the supplements despite persistent differences in SBP. Consistent effects on nephron number were absent. Mild proteinuria, present in control SHR at 48 weeks, was prevented in all supplemented rats. Perinatal supplementation of NO substrate and antioxidants results in persistent reduction of SBP and renal protection in SHR, although effects on NO_x and TBARS were only transient. This suggests a critical role for perinatal pro- and antioxidant balance in programming BP later in life.