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An Orthomolecular Approach To Feline Leukemia Prevention and Control

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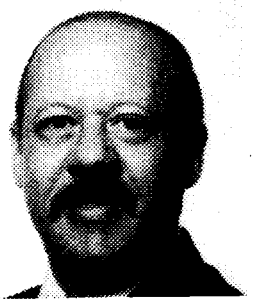

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Terminology

Orthomolecular by definition means "right molecule" and refers to a new branch of medicine developed by Dr. Linus Pauling. "Orthomolecular Medicine is the preservation of health and the treatment of disease by the provision of the optimum molecular constitution of the body, especially the optimum concentration of substances that are normally present in the body and are required for life."

INTRODUCTION

Leukemia may be defined as any malignant neoplastic proliferation of the leukocytes, their precursor, or allied cell types, when these neoplastic cells are found in the circulating blood. This disease is thought to occur in all warm blooded animals, but it is more frequent in the cat than in any other mammal commonly given veterinary care.

The causative agent, in recent years, was found to be a virus and the leukemias are classified according to the cells affected such as lymphocytic, lymphoblastic, monocytic, etc. Several cells of a series are occasionally present in essentially similar proportions, and in such cases, the leukemia is named according to the cell series, for example, myelogenous or lymphogenous. In man, studies have shown that a reasonable correlation can be made between the cell type, physical findings, and course of illness. Thus, the prefixes "chronic" and "acute" are used. Our limited experience with leukemia in animals does not permit us as yet to do this with any degree of reliability (Feline Medicine and Surgery, 1964).

FeLV Diseases

The FeLV virus can and will cause the following diseases:

1. Lymphosarcoma (LSA)
2. FeLV Non — regenerative Anemia
3. FeLV Panleukopenia-like syndrome
4. Myelogenous Leukemia
5. Thymic atrophy
6. FeLV Secondard Immunosuppressive Diseases

(Hardy, Wm. D., Jr., 1979.)

While all six of these diseases are extremely important, the two most often seen in my practice are the Thymic atrophy which affects the kittens of FeLV infected queens. The virus causes degeneration of the thymus resulting in a deficiency in the cell mediated immune response. FeLV Secondary Immunosuppressive Diseases in which the virus is an immunosuppressive agent and is indirectly responsible for several chronic secondary diseases (stomatitis, abscesses, upper respiratory infections). More cats die from these FeLV induced immunosuppresive disorders than die from LSA (Hardy, 1979).

This study was stimulated by a paper written by Dr. Francis M. Pottenger, Jr. M.D. of Monrovia, California (October 9, 1945). Dr. Pottenger performed feeding experiments with cats to determine the effect of heat-treated foods upon growth and development. This experiment stemmed from the fact that he suffered steady mortality among the cats on which adrenalectomies were performed for the purpose of standardizing adrenal cortical material. He found that feeding cooked meat scraps, together with raw milk and cod-liver oil were poor surgical risks, even though his technique was good. As his cat supply increased it was necessary to find a new source of meat. The new source came from a butcher and included muscle, bone and viscera. The raw meat was fed each day to the same group of cats. Within a very short time the cats in those pens survived the operations, the unoperated cats appeared to be in better health, and the kittens were born vigorous. The contrast in apparent health between the cats in the pens fed on raw meat scraps and those fed on the cooked meat scraps was so startling that he decided to do a feeding experiment. To summarize Dr. Pottenger's findings — those felines fed the raw meat diets were healthy and producing healthy normal progeny. Those females fed the cooked meats

were irritable and dangerous to handle. The males were more docile and unaggressive. Cats receiving the cooked meat scraps reproduced heterogeneous strain of kittens, each of the litter being different in skeletal pattern. Abortions in these queens were common, about 25 percent in the first generation and about 70 percent in the second generation. Queenings were generally difficult, many cats dying in labor. Mortality rates of the kittens were high and were often too frail to nurse. At times the queen would steadily decline in health following the birth of the kittens, dying from some obscure tissue exhaustion about three months after queening. Others experience increasing difficulty with subsequent pregnancies. Some failed to become pregnant. Osteomyelitis was common, cardiac lesions, hyperopia and myopia, thyroid disease, nephritis, hepatitis, orchitis, oophoritis, paralysis, meningitis, cystitis, arthritis and many other degenerative lesions. Vermin and intestinal parasites were abound. Skin lesions and allergies were frequent, being progressively worse from one generation to the next.

The cats receiving raw meat and raw milk reproduced in homogeneity from one generation to the next. Abortions were uncommon, litters averaged five and the mother cats nursed their young in a normal manner. The cats in these pens had good resistance to vermin, infections, and parasites. They possessed excellent equilibrium; they behaved in a predictable manner. Their organic development was complete and functioned normally.

Since this study was done in the late thirties, there was even less knowledge of feline diseases than now. It is reasonable to assume some of these cats may have had leukemia or related diseases. It was apparent to me, after reading Dr. Pottenger's paper that the raw meat contained substances that the cooked meats did not. It is generally known that most vitamins are destroyed during the cooking process.

The owners of cattery number one California Cattery enlisted my help to solve a serious leukemia problem in their cattery. Of the felines testing positive for FeLV, some females were not conceiving, some aborting, several adults dying and numerous kittens dying between the ages of 2-12 months. The situation was so bad at this cattery that the local veterinary school recommended the cattery be closed. Because of the work Dr. Pottenger had done thirty years earlier, I hypothesized the problem to be one of nutrition. There were six cats in this cattery that routinely tested positive to the IFA test. These six were divided into two groups, one with an oral multiple vitamin (RDA recommendations) and the other group with the same multiple vitamin plus 500 mg of sodium ascorbate (non-acid vitamin C). This cattery, biannually was tested for FeLV by a team of medical students as a clinical pathology exercise. Six months after the study began the three cats on the straight RDA multiple vitamins were still positive for FeLV. The three on the RDA multiple vitamins plus 500 mg of sodium ascorbate were negative. The multiple vitamin group in six months were still positive for FeLV.

The vitamin C group consisted of one male and two barren females, ages two and three respectively. Several months later both females were bred, both conceived. The two-year-old female had four healthy kittens all of which lived, the three-year-old female had three kittens all of which were alive as of the writing of this paper.

The non-vitamin C group were then placed on the vitamin C regiment and when tested six months later were all negative for FeLV. These three are now very active in the cattery's breeding program.

Cattery number two was newly formed three years ago. The breeding stock had been tested (IFA method) for FeLV. My first introduction to this cattery was testing a new adult female being introduced into the cattery for breeding purposes. Three blood smears (glass slides) were submitted to the laboratory for the IFA test — the test was positive for FeLV, and the animal was asymptomatic. Because of the positive IFA blood test, the feline was placed on an ascorbate regiment. Ten weeks later, three more blood smears were resubmitted and the test was negative for FeLV. This negative result brought a phone call from the laboratory pathologist. "This animal was positive a month and a half ago and now it's negative, what are you doing?" There were five such cases in the past three years at this cattery. We are now in the third generation of offsprings and the entire cattery is negative for FeLV.

At no time were these FeLV carriers isolated from the other members of the catteries, who were already on the ascorbate regiment. In fact, they were treated no differently than the others and permitted to socialize.

A third cattery in 1978 lost 90% of its kittens in a one-year period. Autopsies revealed no cause of the sudden infant death (SID). Each day the owner would find a kitten dead for no reason. One minute alive and apparently well, the next minute dead. These felines, like the other catteries previously mentioned were on a vitamin and mineral RDA. The queens all tested positive to the IFA leukemia test. To the RDA vitamin and mineral supplement we added 20-50 mg of sodium ascorbate to the 2-hour-old kittens and maintained this level daily, with oral dosages to weaning. Post-weaning, the vitamin C level was increased to 100-250 mg and maintained to adulthood. It was requested that the kittens be taken off the vitamin C to determine the effects,

however, the owners in the three catteries refused to cooperate for fear of losing any more animals.

Figure 1:

ORAL FELINE DOSAGES OF SODIUM ASCORBATE

KITTENS — PRE-WEANED (2 hours TO 5 wks.)	20mg.- 50mg.
KITTENS — POST-WEANED (5 wks. TO 6 mo.)	100mg-250mg.
ADULTS — MALES & FEMALES (6 months +)	500mg.-750mg.
PREGNANT QUEENS	750mg.-1.0g.

Discussion

It is apparent that the FeLV virus is immunosuppressive and raises havoc with felines, but we fell that before the entrance of the virus into the body there are other factors that permit the virus to gain a foothold in the animal. In other words, if the body defenses are up to the task, the virus would not be able to propagate and cause the problems these animals have been plagued with.

While corresponding with a Southern California organization dedicated to the eradication of feline leukemia, I was informed that, after extensive testing of FeLV animals, one of the puzzling findings was that all of the felines had high levels of lead. Upon further investigation we discovered that all felines tested for lead were being fed commercial cat foods. My inquiry to those catteries I had worked with revealed that the cats were being fed commercial cat food. An investigation of literature revealed a study by Fox, Aldrich and Boylen of M.I.T. (1976). This group did a study for lead content in 78 random samples of pet food purchased in local grocery outlets, and on 25 individual rations for laboratory animals. The lead content of 46 samples of cat food ranged from 0.1 to 7.6 micrograms per gram.

In man, as in other animals, lead exerts its toxic effect on a number of target organs, including the nervous system, the kidneys and the erythropoietic system. By inhibiting some enzyme systems, lead exerts widespread biologic effects. Some of these changes are subtle: lead has been shown to reduce the resistance of mice to bacterial infection and to reduce antibody formation and suppressed immune response to pseudorabies virus in rabbits (Fox, et al, 1976).

One interesting fact brought out by this study was that twenty-one of the tested cat foods contained more than 1.0 ppm of lead; of these, 10 had more the 2.0 ppm. If an adult, 4.5 kg cat consumed this food at a rate of 53 g/kg body weight/day, the amount of daily ingested lead would be 0.023-1.434 mg. This lead intake is 0.1-4.6 times the daily ingestion (0.3 mg/day) considered potentially toxic for children. Moreover, the feline burden of lead/kg body weight would be much higher than a child since a 2-3 year old child weighs considerably more than an adult cat (Fox, et al 1976).

Norsworthy of San Antonio (1977), made the observation that anemia is the most consistent finding of these leukemia diseases and the mechanism for its development are not completely understood. Most cases involve depression of the bone marrow. Sollmann, Torald (1948), in discussing chronic lead poisoning, indicates that there is degeneration and atrophy of the whole marrow tissue. The blood changes as a whole indicate increases destruction of the corpuscles. It is my opinion that the anemia associated with FeLV can be lead-induced, and is worthy of more investigation. Moreover, the entire predisposition of FeLV can very likely be charged to chronic lead poisioning since the M.I.T. report had brought out the possibility of reduced antibody production and suppressed immune response by the presence of lead.

Dr. Carl C. Pfeiffer's book on zinc and other micro-nutrients discusses the high concentrations of lead in pet food. He also discussed the positive effects of Vitamin C on heavy metals including lead. Dr. Pfeiffer (1978) wrote "under physiological conditions, vitamin C acts as a strong reducing agent to bring metal ions and affect their movement across biological membranes." Dr. Chattejee, et al, has reported on the dietary intake of metal ions and vitamin C metabolism. They have found that administration of any of the heavy metals — cadmium, lead or mercury — to rats, reduces the levels of vitamin C in both the liver and kidneys. Lead was administered in these experiments at a dose of 10 mg/100 g body weight raised vitamin C levels in tissues to above the control levels. Animal studies indicate that zinc and vitamin C may serve as antidotes for lead poisoning. In the *Journal of Laboratory and Clinical Medicine* (1939) vitamin C reversed lead poisoning in humans who had come in contact with lead filings.

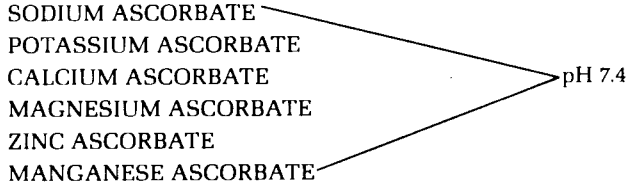
Ascorbate Regiment

Ascorbic acid, in mega doses, is not recommended because of the 3.0 pH. This vitamin C will cause gastric upset, flatulence, acidosis and diarrhea. Also, due to the tartness most felines will not consume it when mixed with food. On the other hand, the ascorbates, (Fig. 2) are neutral (pH 7.4) and do not have the negative side effects of ascorbic acid.

Figure 2:

TYPES OF ASCORBATES (VITAMIN C)

ASCORBIC ACID — pH 3.0



Affects of Ascorbate on immune components

The mechanism by which ascorbate may be involved in the control of infection is by way of the immune system. The leukocytes, in particular, contain high concentrations of ascorbate, 1.0 microgram per milligram of protein. Mononuclear phagocytes contain a higher concentration, 2.0 micrograms per milligram of protein with both peritoneal and alveolar macrophages being rich in ascorbate. It has been established the leukocyte ascorbate quality decreases following virus infection and after which returns to normal levels. Leukocytes absorb large amounts of ascorbate when they migrate into an area of infection. Ascorbate levels in leukocytes have shown to decrease in response to a variety of exogenous agents, many of which are associated with depressed immunological function. As was implied above, viral infection rapidly depletes leukocyte ascorbate (Thomas, W.R. and Holt, P.G., 1978).

Barton and Roath (1976) have surveyed leukocyte ascorbate levels in patients with a variety of abnormal leukocyte states and other hematological disorders. Levels below the normal range were found in most cases of chronic myeloid leukemia and chronic lymphatic leukemia, and in greater than 1/3 of patients with acute leukemias, lymphomas, glandular fever, myelofibrosis, polycythaemia, polymorphleukocytosis, purpura and those receiving cytotoxic drugs (Thomas and Holt, 1978).

Phagocytes

The direct involvement of ascorbate in neutrophil phagocytosis is probable since both ascorbate and dehydroascorbate are consumed in these cells during phagocytosis. Ascorbate appears to play a role in a number of neutrophil functions including increased chemotaxis, increased particulate ingestion, enhanced lysozyme meditated non-oxidative killing, protection against the toxic effects of superoxide anion radical, inhibition of the halideperoxide-myeloperoxidase system without a pronounced bactericidal effect and stimulation of the hexose monophosphate shunt (Leibovitz and Siegal, 1978). A more positive effect of exogenous ascorbate has been observed in neutrophils deficient in ascorbate. Steroid therapy depletes leukocyte ascorbate and also inhibits the phagocytic activity of human neutrophils, as judged by nitroblue tetrazolium reduction during phagocytosis of latex particles or by counting the accumulation of latex particles (Thomas, et al, 1978).

Interferon

Texas Reports on Biology and Medicine (1977) reported that in interferon, a protein produced by any nucleated cells of the body, seems to be the primary defense against viruses. Interferon production is stimulated only by the presence of viruses and is not observed when the body is not being challenged by a virus. There are two types of interferon which are linked to the chromasomes. One type attacks the virus intracellularly, surrounds it and prevents propagation. The other attacks the virus extracellularly and thought to destroy the virus by attacking the nucleic acid within the virus. In 1974, Siegal reported mice fed on an ascorbate supplemented diet displayed augmented levels of circulating interferon after stimulation with murine leukemia virus, and later (1975) demonstrated a similar phenomenon *in vetro* employing cultures of murine L cells and embryonic fibroblasts stimulated polynucleotides. Dahl and Degre (1976) had a similar finding to Siegel. Thomas and Holt (1978) observed that leukocyte interferon assayed in lung fibroblasts titrated 0.2-0.3 $\log_{12}$ units higher in the presence of 5.0 mg ascorbate than in the absence of the ascorbates.

Antibodies

The early literature on ascorbate and immunity suggests an important role for ascorbate in the humoral immune response. The addition of ascorbate to immunizing doses of antigen appeared to increase antibody production and deprivation apparently reduced the response.

At the time of this clinical study, the only test for leukemia was the IFA test. More recently the Antibody Titer Test (FeLV antibody test) is now available to aid the clinician in determining the degree of involvement of the leukemia virus. However, the standard test for FIP (Feline Infectious Peritonitis), a related viral disease, is determined by an antibody titer test. One patient was tested for FIP and had a titer of 1:400. This patient was placed on the vitamin C plus RDA vitamins and minerals and routinely retested one year later and the antibody titer was "0". The feline was retested in two days because we felt a discrepancy in the laboratory; the test once again read "0". I queried the laboratory pathologist and he informed me, "the test indicated the virus had been destroyed and, to have antibodies there must be a virus." This animal with no FIP antibodies has been exposed to other felines with FIP titers of 1:400 and developed no titer.

Antibody production is dependent on the presence of microorganisms in the body and do not appear for some six or seven days after infestation. It may be postulated that antibody production is the final line of defense for the body and antibodies may not be needed when the primary immunological defense (interferon, leukocytes, etc.) is functioning at maximum capacity.

Conclusion

In veterinary research there are no reports on the effects of exogenous ascorbate on the immune system of felines. Research is lacking because the members of our profession feel the 40 mg per kilo of

body weight (of ascorbate) produced daily in felines is adequate for all the animals' needs. This clinical study clearly shows that FeLV can be prevented and controlled with small amounts of exogenous ascorbate plus other vitamins and minerals daily in the diet. The plus in this study is the possibility of the virus being killed. In 1975, Dr. Fukumi Morishige in a paper published in Tokyo, Japan, stated that "the target attacked by 'C' is nucleic acid, and the scissions of nucleic acid strands are mainly responsible for the inactivation of the virus." Many of the now negative felines discussed in this paper for FeLV have been exposed to know FeLV carriers and they still remain free of the virus according to the test. It becomes obvious that antibody production is not necessarily the ultimate in the prevention of a virus but rather maintaining the primary immune components at maximum functioning levels with ascorbate. Antibody production appears to occur only when the ascorbate level in the primary defense components are at low levels thereby permitting some viruses to survive the primary defenses. Lead and the FeLV virus are both immunosuppressive agents adversely affecting the body defenses. Subramanian (1973), discussed the Suboptimal Compensatory Feedback. This feedback system increases the liver production of ascorbate with increased stress. This no longer occurs in felines. I would speculate this is a result of domestication. Dr. I.B. Chattejee, a renown biochemist of Calcutta, India, in a personal correspondence, informed me that he work with goats indicated that as these animals age the vitamin C production, in the liver, decreases. He further stated the reduction can be as low as ¼ of what is normally produced. Dr. Chattejee theorized that the same could be true of felines and canines. A feline producing at maximum, 40 mg per kilo of body weight of vitamin C daily (Fig. 3). This means that a 4.5 kilogram feline produces a maximum of 88 mg of vitamin C and an older feline may produce as little as 22 mg of C daily. With the intake of lead daily, considerable amounts of vitamin C will be destroyed or removed from the body. This 88 mg or less cannot carry the total burden of stress placed upon it by chronic lead poisoning and the FeLV virus. This amount of C cannot stimulate immune function to prevent FeLV; it cannot stimulate adquate cortisone to counteract stress; it is not adequate for good collagen production; and is not adequate to detoxify the impurities incorporated in commercial cat foods. It is the opinion of the author that the addition of vitamin C as previously discussed, to the RDA of vitamins and minerals stimulates the primary immune components to totally eliminate the FeLV virus from the body of felines.

Figure 3:

DAILY PRODUCTION OF ASCORBATE IN ANIMALS

ANIMAL	Ascorbate Production Milligrams/Kg Body Wgt/per day
Snake	10
Tortoise	7
Mouse	275
Rabbit	226
Goat	190
Rat	150
Dog	40
Cat	40
Monkeys, Apes, Man	0

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