# M A N A G I N G  A  R E N A L  C R I S I S

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Prevention and treatment are not the same,
and phosphorus may be more important than protein.

## *PART II: MANAGING THE RENAL FAILURE PATIENT AND FEEDING THE OLDER DOG*

In Part I of this article, we spoke in general terms about the kidney in both health and disease. This article focuses completely on kidney failure, in both advanced and early stages, focusing on two cases. The first is the most typical -- an older dog with a history of bladder infections and the onset of kidney failure due to aging as well as recurrent infections. The second is a young, pure-bred dog with a congenital destruction of her kidney. In both cases, death due to kidney failure was inevitable, despite aggressive medical management.

## *MEET NORA:*

Nora was my dog, and Table 1. lists her urea nitrogen (BUN), her creatinine (CREAT), and her phosphorus (PHOS) blood values during her decline. The accompanying Graph 1. illustrates the progressive nature of this relentless disease and her eventual euthanasia. To make the slope of the graph head downwards, the inverse of her creatinine values are plotted against time. Creatinine is always used for this demonstration, because creatinine is unaffected by any dietary changes made as illness progresses. As demonstrated, even with extensive veterinary medical care, it is difficult to actually alter the downhill slope of this graph once 75 - 80% of the kidney is destroyed. It is believed that, once the kidney is diseased, nephrons are lost at a constant rate due to the excessive work demands placed on those nephrons that remain. Restricting protein and phosphorus helps a renal failure dog feel better during the decline, but does not necessarily postpone the inevitable.

Newer studies on the use of vitamin D therapy suggest that this curve may be shifted after all. Since phosphorus (not protein) is crucial to the actual length of life an ill patient may have, then direct manipulation of this mineral by vitamin D, rather than simply restricting its intake in the diet, may actually extend the life of animals in renal failure. The clinical trials currently directed by Dr. Larry Nagode at Ohio State University will be described in detail later, but this work may provide a medical route to truly extending the length and quality of life of the renal failure patient.

***MEET SPICE:***

Spice had the ultimate change in her creatinine graph -- she got a brand new kidney and a brand new graph. She received her transplant at Canada's College of Veterinary Medicine in Guelph, Ontario within two months of the diagnosis of complete kidney failure. Since the onset and diagnosis of failure was so sudden, there are no early creatinine values available for her, and an actual graph cannot be constructed. But her death was certain had she not received a transplant; her blood values were all 5X normal prior to her surgery. Her BUN was 185 mg/dl, her CREAT was 9.4 md/dl, and her PHOS was 12.1 mg/dl.

Interestingly, analysis of her diseased kidneys showed a type of destruction most typically seen in Norwegian Elkhounds -- a progressive replacement of normal tissue with scar tissue, particularly around the glomeruli. Abnormal changes in the tubules were also evident. At less than three years of age, Spice had no functioning kidney tissue left, and her owners elected transplantation, rather than euthanasia, because of her young age and her sound health in all other respects.

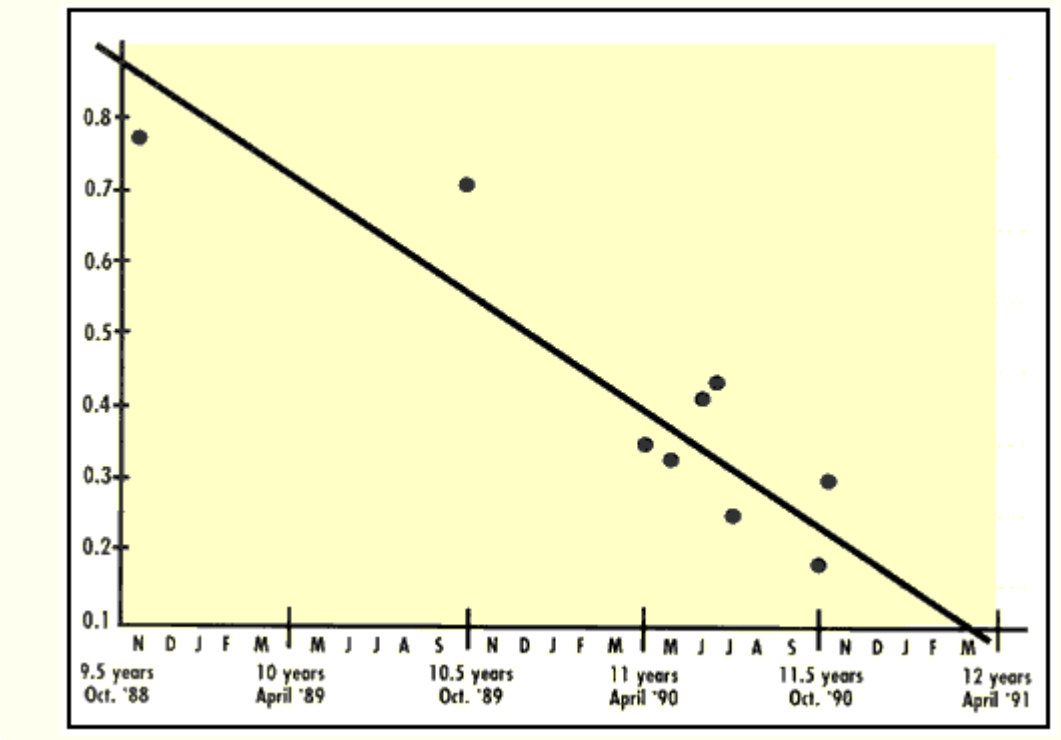
That was two years ago, and today she enjoys excellent health, but must have daily medications of prednisone, azathioprine, and cyclosporine to prevent rejection of her new kidney. Also, every month and frequently more often, she must have a physical examination, and her urine and blood must be tested. This is the only way to be sure that rejection is not occurring and that drug levels circulating in her blood are kept constant. Additionally, at least every month her urine must be cultured for bacteria. Not only does she have only one kidney, but the drugs that prevent rejection do this by markedly suppressing her immune system. She is poorly equipped to fight any infection at all, and certainly cannot afford one in her remaining kidney.

Since she is exceptionally calm, friendly, out-going, and obedient, these frequent visits cause little problems for her, but this would not be true for many other dogs. Patients who are nervous, high-strung, easily frightened, or vicious are poor candidates for kidney transplantation, so personality is just as important a factor in making such a decision as is age and general health of the patient. So is lifestyle. If a dog's greatest joy is going to Central Park twice a day to play with other dogs, then transplantation will be a sad victory for that individual. Spice enjoys her quiet country life playing with her family and best dog buddy, but she certainly cannot socialize with strangers. She cannot afford to get exposed to common viruses or bacteria from other dogs, because her immune system is suppressed. What is minor to a normal dog is potentially fatal to her, or, if not exactly fatal, then any stomach upset or loss of appetite might mean that she wouldn't get her necessary medicines for one or two days. This alone could lead to rejection of her kidney.

**Table 1. Renal Blood Values: Nora Gearhart**

| Date | BUN (Blood Urea Nitrogen) (Normal 5-20mg/dl) | CREAT (Creatinine) (Normal 0.2-1.5 mg/dl) | Inverse (of Creatinine) | PHOS (Phosphorus) (Normal 3-6 mg/dl) |
|---|---|---|---|---|
| 1988 | | 1.3 | .77 | |
| 10/09/89 | 24.7 | 1.4 | .71 | 3.7 |
| 04/12/90 | 59.7 | 2.9 | .34 | 5.7 |
| 05/14/90 | 71.6 | 3.0 | .33 | 7.4 |
| 06/11/90 | 50.8 | 2.4 | .42 | 5.1 |
| 06/25/90 | 51.5 | 2.3 | .43 | 5.3 |
| 07/26/90 | 56.0 | 4.0 | .25 | 5.9 |
| 10/01/90 | 142.0 | 5.5 | .18 | 13.4 |
| 10/12/90 | 55.5 | 3.3 | .30 | 6.2 |

**Graph 1. Inverse Creatinine**




## *MANAGING THE RENAL FAILURE PATIENT*

Historically, research has focused heavily on protein intake, because uremic renal failure dogs placed on low protein diets have a remarkably improved quality of life. They aren't vomiting; the diarrhea stops, and they no longer need to drink gallons of water to wash the urea and other waste nitrogen products from their system. Their energy levels improve, because the balance of acids, bases, and minerals in their body returns to

normal, allowing muscles to contract without quickly fatiguing. But no studies have proven that limiting protein actually stops the inexorable loss of nephrons or appreciably extends the life of a dog with kidney disease. They just feel better - the quality of their remaining life is improved.

Recent work, primarily at the Ohio State College of Veterinary Medicine, has taken a closer look at phosphorus. Many protein-restricted diets are also moderate in phosphorus, and all presecription diets are purposefully low in both because near-terminal cases of kidney failure have high phosphorus levels that must be controlled. In fact, drugs that bind phosphorus have been prescribed for years to prevent bone deposition in the kidneys and other tissues in the terminal kidney patient, because phosphorus levels get dangerously high. As an example, look at Nora's October 1, 1990 blood level for phosphorus, listed on Chart I. On that day, she was switched from a prescription, low-protein, low-phosphorus diet and phosphorus binders to a prescription ultra-low protein, ultra-low phosphorus one with additional phosphorus binders, but her decline was rapid from that point.

Is it possible that the influence of phosphorus in the very earliest stages of kidney failure has been over-looked? Have we clinicians been in error by waiting until terminal kidney failure to aggressively manage phosphorus? Several teams of researchers think so, and indeed, at least one study has taken several groups of dogs in kidney failure and fed them diets that varied in protein level and phosphorus level. The groups with severely restricted phosphorus lived longer than the groups with normal or high levels of phosphorus. The protein intake made no difference at all in longevity. This is important information, because owners are often told that high protein diets can cause premature aging of kidneys and renal failure, even in the normal dog; no experimental proof of this exists. Experiments on the longevity of renal failure patients fed different phosphorus levels is being repeated by different researchers using different models of kidney damage (surgical resection, bacterial infection, blood flow occlusion), but some clinical veterinary scientists are already looking at kidney disease from a phoshorus (rather than a protein) perspective.

It is this perspective that has led most recently to a dramatic, and controversial, new therapy for renal failure, and that is calcitriol (Vitamin D) therapy. As discussed in Part I of this article, the kidney is responsible for converting nutritional Vitamin D into its most active form, calcitriol (1,25-dihydroxycholecalciferol). When the kidney is diseased, its capacity to do this is decreased, and, without adequate amounts of calcitriol, calcium absorption from the intestines is decreased. Since calcium is essential for heart and skeletal muscle function, the parathyroid gland becomes hyper-activated to dissolve bone and thus restore calcium blood levels back to normal. Unfortunately, bone dissolution also releases phosphorus, which the failing kidney cannot excrete, so a vicious cycle is created, leading to "renal rickets," a softening of the bones due to progressive mineral loss. Additionally, mineral deposition often occurs in all body organs, especially the kidneys, hastening its failure. Restoring calcitriol to this equation helps to break the cycle, but, due to the delicate balance needed between these two minerals, Vitamin D therapy is not without risks.

Calcitriol is the only Vitamin D form suitable for this treatment, because it has a very short half-life in the body. Consequently, if it is properly dosed and if blood levels of both calcium and phosphorus are monitored very closely, calcitriol is unlikely to cause

deposition of calcium salts and mineralization in the body. Previous studies with other forms of Vitamin D, as well as earlier, higher doses of calcitriol, led to this condition and actually hastened kidney destruction through this mineralization of tissue. Creatinine graphs over time actually showed a steepening of the slope -- indicating more rapid kidney failure and the need to use lower doses of calcitriol.

Since there are risks in calcitriol therapy, many clinicians believe this drug should only be given to patients with very advanced kidney disease where phosphorus binders have not been able to decrease blood phosphorus levels. However, proponents of calcitriol (specifically Dr. L. Nagode and colleagues at the Veterinary College at Ohio State University) believe that earlier uses of low doses are beneficial and can actually extend life expectancy. They point to many other benefits and biological activities of calcitriol that are more subtle than simply maintaining a normal calcium:phosphorus ratio in the bloodstream. In graphic terms, their studies show that the steepness of that inexorable downward slope is flattened; the rate of kidney destruction is slowed, and life expectancy is extended. Presently, low dose calcitriol therapy is being evaluated in an extensive, national clinical trial coordinated by Ohio State University. Calcitriol, like protein and phosphorus, is a chemical whose roles in the processes of the failing kidney and in the therapy of the renal failure patient are hotly debated.

Another new treatment, more commonly accepted, is erythropoietin replacement therapy. By reversing the anemia, what kidney tissue is left gets a little boost by a replenished blood supply. Also, the pet simply feels better and often eats better, regaining lost weight. The hormone must be given by injection, and iron supplementation combined with frequent blood testing and careful monitoring of the patient are necessary. Since this drug is distinct from calcitriol, an intensively managed renal failure patient would be on (1) a protein-restricted and phosphorus-restricted diet, (2) phosphate binders further mixed in the food, (3) calcitriol therapy, and (4) erythropoietin therapy. Since many patients suffer from recurrent infections, long-term antibiotic therapy is likely as well. Obviously, constant monitoring of blood, urine, and general health would be just as important for a patient such as this as it is for Spice now after her kidney transplant.

## *NUTRITIONAL NEEDS*

Since urea (BUN) is a nitrogen waste product of protein digestion, dramatic reductions in BUN can be accomplished with a reduced protein diet. While increased BUN is not the only contributor to the "uremic syndrome" of severe kidney failure (weight loss, vomiting, diarrhea, excessive water consumption, fatigue, disorientation, seizures, and death), decreasing the BUN usually decreases the other chemicals and toxins that are present but not measured in the renal failure patient. BUN relates directly to protein intake, so BUN can be normal (or only mildly increased) even when creatinine is high due to kidney failure. This is the typical blood picture of the advanced renal patient. The dog is on a low-protein, low-phosphorus diet which helps to stabilize BUN and phosphorus, but nephron loss is present so creatinine remains high. You can see this picture in Nora's last data entry on October 12, 1990. Eventually, all values become elevated again, despite dietary management, and an owner must decide to maintain their

pet on treatments of intravenous fluids or dialysis (not readily available), or to receive a kidney transplant from an acceptable donor (also not readily available).

Before we can explore the nutritional needs of a dog in early, mid-, or advanced kidney disease, a brief review of nutritional requirements for the normal dog are in order. Fortunately, the American Association of Feed Company Officials (AAFCO) reviewed and published nutrient profiles for dog foods in 1992, so we have current values which are presented in Table II. More importantly, the 1992 standards also specify upper limits of many nutrients (since excess can be as dangerous as deficiency), and, finally, standards for each amino acid (the building blocks of protein) are established. This becomes particularly important for the renal failure patient. A low protein diet with a poor amino acid balance will be debilitating over time. This balance is termed "biological value," and a protein with a high biologic value contains all necessary amino acids; only eggs fit this standard and are, consequently, given a biologic value of 100. Wheat's biologic value is 60, and corn's is 54 so these ingredients must be paired with other protein sources to create a balanced diet. Not surprisingly, egg is often listed as an ingredient in prescription diets, but an egg-based diet is not mandatory. As long as a low protein diet is carefully balanced according to total amino acid composition, satisfactory results can be achieved.

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**Table II. AAFCO Dog Food Nutrient Profiles***

| Nutrient | Units DM Basis | Growth & Reproduction Minimum | Adult Maintenance Minimum | Maximum |
|---|---|---|---|---|
| Protein | % | 22.0 | 18.0 | - |
| Arginine | % | 0.62 | 0.51 | - |
| Histidine | % | 0.22 | 0.18 | - |
| Isoleucine | % | 0.45 | 0.37 | - |
| Leucine | % | 0.72 | 0.59 | - |
| Lysine | % | 0.77 | 0.63 | - |
| Methionine-cystine | % | 0.53 | 0.43 | - |
| Phenylalanine-tyrosine | % | 0.89 | 0.73 | - |
| Threonine | % | 0.58 | 0.48 | - |
| Tryptophan | % | 0.20 | 0.16 | - |
| Valine | % | 0.48 | 0.39 | - |
| Fat | % | 8.0 | 5.0 | - |
| Linoleic acid | % | 1.0 | 1.0 | - |
| **MINERALS** | | | | |
| Calcium | % | 1.0 | 0.6 | 2.5 |
| Phosphorous | % | 0.8 | 0.5 | 1.6 |
| Ca:P ratio | | 1:1 | 1:1 | 2:1 |
| Potassium | % | 0.6 | 0.6 | - |
| Sodium | % | 0.3 | 0.06 | - |

| Nutrient | Units DM Basis | Growth & Reproduction Minimum | Adult Maintenance Minimum | Maximum |
|---|---|---|---|---|
| Chloride | % | 0.45 | 0.09 | - |
| Magnesium | % | 0.04 | 0.04 | 0.3 |
| Iron | mg/kg | 80.0 | 80.0 | 3,000.0 |
| Copper | mg/kg | 7.3 | 7.3 | 250.0 |
| Manganese | mg/kg | 5.0 | 5.0 | - |
| Zinc | mg/kg | 120.0 | 120.0 | 1,000.0 |
| Iodine | mg/kg | 1.5 | 1.5 | 50.0 |
| Selenium | mg/kg | 0.11 | 0.11 | 2.0 |
| **VITAMINS** | | | | |
| Vitamin A | IU/kg | 5,000.0 | 5,000.0 | 250,000.0 |
| Vitamin D | IU/kg | 500.0 | 500.0 | 5,000.0 |
| Vitamin E | IU/kg | 50.0 | 50.0 | 1,000.0 |
| Vitamin B1 (thiamin) | mg/kg | 1.0 | 1.0 | - |
| Vitamin B2 (riboflavin) | mg/kg | 2.2 | 2.2 | - |
| Vitamin B5 (pantothenic acid) | mg/kg | 10.0 | 10.0 | - |
| Vitamin B3 (niacin) | mg/kg | 11.4 | 11.4 | - |
| Vitamin B6 (pyridoxine) | mg/kg | 1.0 | 1.0 | - |
| Folic Acid | mg/kg | 0.18 | 0.18 | - |
| Vitamin B12 (cyanocobalamin) | mg/kg | 0.022 | 0.022 | - |
| Choline | mg/kg | 1,200.0 | 1,200.0 | - |

[*] Presumes an energy density of 3.5 kcal Metabolizable Energy/gram Dry Matter, based on the "modified Atwater" values of 3.5, 8.5, and 3.5 kcal/g for protein, fat, and carbohydrate (nitrogen-free extract, NFE), respectively. Rations greater than 4.0 kcal/g should be corrected for energy density; rations less than 3.5 kcal/g should *not* be corrected for energy.

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Spice now has normal renal function. While we don't want to burden her with minerals and protein she doesn't need, we certainly do not have to limit them. Consequently, she eats an adult maintenance type of dog food. She does NOT eat a diet "suitable for all life stages as certified by AAFCO." In other words, she does not eat a diet high in calcium and phosphorus and sodium -- all of which would be necessary for the growing puppy or the lactating bitch. At some point, maybe next month, maybe not for another five years, but, at some point, her transplanted kidney will begin to fail. What will we feed her then? That answer depends entirely on the type of kidney failure that develops -- is the damage tubular or glomerular?

Nora is an example of early glomerular failure -- long before she was truly ill, she began to lose protein in her urine. One of the first signs of trouble was a loss of coat condition and a low blood value for the protein called albumin. Albumin is a small

protein that, normally, the glomerulus keeps in the capillary blood circulation, but a diseased glomerulus leaks. A dog losing protein in the urine is difficult to manage, because such a patient needs extra protein to make up for that loss and yet may not be able to tolerate protein as renal failure progresses. The solution for Nora, initially, was a ration of half and half Feline and Canine K/D mixed with extra phosphate binders. This provided for extra protein (similar to Hill's G/D) and extra potassium, but less sodium than Hill's G/D. Because of the use of phosphate binders, her phosphorus intake was similar to Hill's K/D, but her protein intake was higher. And she needed this extra protein because of loss in the urine.

This worked for nearly a year -- her coat condition was good and her activity level excellent, but when her BUN and CREAT and PHOS rose, protein restriction became necessary. At that point, her decline was rapid over the next six months as her diet was changed to Hill's K/D followed by Hill's U/D. When the point arrived that she could not be managed by diet and required intensive, continuous fluid therapy, I elected to euthanize her. Not an easy thing to do, but a clear decision to make. She loved to eat; she did not enjoy injections and fluids.

For dogs who do not love to eat, a protein-restricted diet is not always greeted with enthusiasm. Today, several products are available that may be more palatable, and these senior diets can be cut with rice according to a veterinarian's recommendations to further lower the protein content if necessary. Phosphorus binders will also be needed, as prescribed by a veterinarian, but many types can simply be mixed into the food. It is important to remember that phosphorus is more important than protein -- feeding vegetables or salt-free crackers to a dog in kidney failure will not add protein but it will add phosphorus. If your dog is well-controlled on a prescription diet for kidney failure, feed nothing else. I had a little Schnauzer patient who was well-controlled in BUN and CREAT values, yet the phosphorus remained high. The owner had continued her habit of rewarding her dog with string beans, a habit developed years before to control the dog's weight gains on biscuits. String beans seemed innocuous enough to me (mostly water), but they had to be eliminated to control phosphorus levels. Wheat products like crackers and pasta are even higher in phosphorus. Remember also that the kidney failure patient cannot tolerate sodium; any treats must be sodium-free and low in phosphorus. In rare cases, a home-made diet can be fed, but this must be done in careful and continuous consultation with the dog's attending veterinarian.

## *IMPLICATIONS FOR THE OLDER DOG*

So, should every dog over seven years of age be on a senior diet? If Nora had been on a senior diet at the age of seven, she might have been in poor condition at the age of 8 instead of the age of 9. Her kidneys were losing protein long before I knew she was sick, but a urinalysis revealed the protein loss, and, eventually, the bacterial infection that was the cause of her problems. A urinalysis should be done routinely every year on every dog over six years of age. Urine is the product of the kidneys and will reveal problems long before blood work is abnormal. Additionally, any sick dog should have a urinalysis done. We think nothing of routinely providing our own family physician with a urine sample (who frequently finds bacteria or blood, runs cultures, and then prescribes antibiotics),

but how often do we do this for our dog? Bacteria, traces of blood, watery urine, sugar -- all these are abnormalities that may need further evaluation.

Just like people, every dog ages differently, and most dogs do very well on senior diets because the protein levels are above AAFCO adult maintenance minimal requirements. But many dogs are still leading active, working lives at 11, 12, or older. Service dogs, hunting dogs, and jogging companions may need 22 % protein or higher to maintain condition. Similarly sick dogs, even ones with sick kidneys like Nora, may need extra protein for coat condition, muscle tone, and the preservation of a healthy immune system. What older dogs don't need is mineral levels as high as are necessary for growth and reproduction.

Depending on the study, renal failure is the second or the third leading cause of death in dogs, after heart disease and/or cancer. Furthermore, autopsies done on older dogs reveal abnormalities in as many as 85% of all kidneys examined in dogs over the age of five. Of course, we know that damage does not equal failure. We know that the kidney can lose 70% of it's tissue and still be functioning normally. We also that protein per se does not cause kidney failure in the normal dog. But how many of our dogs older than five are truly normal? Maybe only 15 %. Studies like these are the impetus behind urging people to feed a senior diet to their dogs.

In my opinion, senior diets are fine, but it is probably the restriction of phosphorus that is of the greatest value. Switching from an "all stages of life" diet to an "adult maintenance only" may be sufficient for many dogs; an actual "senior" diet may not be necessary. As mentioned earlier, vegetables and starches are very high in phosphorus; this is why "lite" formulae are often higher in phosphorus than are adult maintenance diets. "Lite" formulas should not be considered the equivalent of senior diets, but, regardless of the diet you choose, be sure it is a reputable, name-brand product. Generic products have no reputation to maintain and, consequently, do not always use quality, fully digestible products.

Finally, the most important thing you can do nutritionally for your dog is to be sure that your pet is free of parasites and disease. The finest diet in the world will not benefit a dog full of heartworms, hookworms, tapeworms, whipworms, roundworms, or coccidia -- the parasites get all that great nutrition. Similarly, a sick dog will lose condition even on a premium diet. Not only should your pet be examined annually and kept on a heartworm prevention program in those geographic areas where the parasite is common, but a yearly stool and urine examination is necessary as well, especially for the "senior" dog. Not only is kidney disease common, but it is easily missed on physical examination, and even on blood tests in its earliest stages. The urine, however, holds the key to revealing low-grade, chronic kidney disease. If discovered early, specific treatment and appropriate dietary management can prolong the life of an afflicted pet, or, in the case of a hidden infection, even halt the disease process if diagnosed in time.

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