Nutritional aspects of the feline urological syndrome (FUS)

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INTRODUCTION

A detailed description of the feline urological syndrome (FUS) is out of place in this talk as it has been dealt with extensively in the other lectures. It is sufficient to say that FUS is a disease of the lower urinary tract of cats and is usually characterized by one or more of the following clinical signs: haematuria, crystalluria, dysuria and partial or total obstruction of the urinary tract. The crystals most commonly associated with this syndrome are composed of struvite (magnesium ammonium phosphate hexahydrate). Many factors have been associated with FUS and at present it is accepted by most researchers that the disease can occur through several different causes; two or more causes may exist in the same cat. As to the role of diet, it is unlikely that this is the sole cause of FUS (Osborne and others, 1984) but it is certainly one of the more important factors in the disease, and there are several ways in which it can exert an influence. A brief discussion of each of these will now be presented.

DIETARY FACTORS

Moisture

It has been shown by us (Anderson, 1982) and other researchers that, if cats are fed dry food, their total water intake is decreased compared with a similar energy intake from canned (i.e. wet) food. Cats will drink more liquid when receiving dry food but the amount is insufficient to compensate for the significantly lower moisture content of this type of diet. This effect is particularly well illustrated by some work reported recently by Gaskell (1985) and summarized in Table 1. The same basal semi-purified diet was used throughout the investigation but the moisture was adjusted to various values by the addition of water. At the lower food moisture content there is a different pattern of water balance with decreased water

TABLE 1. Effect of food moisture on water balance in cats

Water content of food (%)	10	45	75
Total water intake (ml/day)	109	108	179
Urine volume (ml/day)	63	57	112
Urine specific gravity	1·053	1·053	1·034

From Gaskell (1985)

intake and urine volume and increased urine specific gravity. The theory is that an increased urine concentration will increase the ease with which struvite crystals come out of solution and thereby increase the risk of FUS. If a limited amount of salt is added to dry cat foods, this is effective at increasing water intake and urine volume. There is also some evidence from work in other animals that a high concentration of chloride in the urine (from an increased salt intake) disrupts or inhibits the formation of struvite crystals. Nevertheless this approach is not universally accepted and other researchers maintain that food moisture content is not a key factor in the disease.

Mineral content

The most important mineral in relation to FUS is undoubtedly magnesium. Many studies have shown that very high magnesium concentrations (around 0·30 per cent on dry matter or more) substantially increase the risk of FUS (Lewis and Morris, 1984). This is because of the increased formation of struvite in the urine. Nevertheless, these high magnesium concentrations are far in excess of typical levels in commercial cat foods.

Calcium and phosphorus levels are also thought to have an influence on this disease but their precise role is still not completely clear. Some researchers recommend a high calcium level to restrict phosphorus excretion, again, to inhibit struvite formation. However, we have found that a high calcium/phosphorus ratio can increase urine pH which can *increase* FUS risk (see following section). Perhaps the best course is to formulate to a dietary ratio of about 1 : 1 which is also optimum nutritionally for cats.

Urine pH

Struvite is much more soluble in slightly acid conditions—pH 6·6 or less. Thus a low pH urine is less likely to result in precipitation of crystals out of solution and this will, in turn, reduce FUS risk. This particular aspect of FUS is currently the subject of renewed attention and some researchers now believe that it is the *most* important factor in the prevention and treatment of this disease (Taton and others, 1984; Cook, 1985). There is not doubt that we shall be seeing more developments in this area in the near future.

Digestibility

We have seen earlier that the dietary concentration of magnesium has an important influence on FUS and this concentration is useful because it gives an indication of the quantity of magnesium that will be ingested. The amount of food required by the cat will depend on the digestibility of that food—the higher the digestibility the lower the intake. All other factors being equal, this means a lower intake of magnesium for the highly digestible product with a lower risk of FUS. Ideally, magnesium should be expressed in terms of digestible energy (DE) so that products can be compared on the same basis, and one which relates directly to intake.

Another factor related to digestibility is the bulk of faeces voided: a more highly digestible food will produce a lower quantity of faeces and therefore faecal moisture. For a given water intake, this will result in a higher urine volume and, in turn, would be expected to reduce FUS risk. Thus, highly digestible food seems to offer some potential benefits in reducing FUS.

Feeding Methods

After a meal is fed there is an alkalinization of the urine, usually one to two hours later, which balances the release of acid in the stomach as part of the digestive process. This effect is referred to as the 'alkaline tide'. The urine pH gradually falls during the day to the fasting value. One theory suggests that meal feeding, while producing the alkaline tide effect gives an *overall* urine pH that is lower than if cats are allowed continuous access to food and eat small quantities throughout the day: so-called 'nibbling'. The effect of nibbling may be to create a continuous alkaline tide (although less than that occurring after a full meal) and therefore a higher average urine pH. Nevertheless the mere production of the alkaline tide may increase the FUS risk during this time. So there may be little real difference in overall risk between various feeding methods. If the urine is acidified then the method of feeding may not be of great importance because the urine pH will always be sufficiently low to prevent precipitation of struvite.

THE VARIOUS THEORIES

There are, perhaps, as many views on the causes of FUS as there are research groups investigating the disease but I have tried to summarize the main theories below:

(a) Diet is not a key factor and dry foods neither induce nor exacerbate FUS (Fabricant and Lein, 1984).

(b) Diet is one of many possible factors. Susceptible cats should be treated differently from the rest of the population (comparable to an allergic reaction?) For the remainder (majority) of cats the type of food is unimportant.

(c) Diet is a key factor: urine pH is the most crucial aspect, dietary water content is of little, if any, importance.

(d) Dry foods are the key factor—water and magnesium intakes are crucial.

I tend to subscribe to the second view presented—that diet is one of many factors involved in this disease but that by no means all cats are susceptible. From surveys conducted in Europe and the U.S.A. it seems that between 0·5 to 1 per cent of the cat population are susceptible to FUS (Walker and others, 1977; Tomey and Follis, 1978). So the vast majority of cats are probably unaffected by variations in the diet (within normal commercial limits) and it is only the small percentage of sensitive cats that should be treated differently. Modification of the diet is an important aspect of this treatment but it must be remembered that it may not be the only influence on the formation and precipitation of struvite and, furthermore, there may be additional factors (completely separate from this) which are involved. It is appropriate to mention at this point that we have fed several groups of cats at the Waltham Centre our standard dry foods for long periods (in some cases many years) and have never observed any signs of FUS in these animals.

SUMMING UP

The 'ideal' diet for minimizing FUS risk may not involve a single food but would aim, by various measures, to achieve the conditions listed below:

(a) Low urine pH. This may entail the use of urinary acidifiers which must be consumed with or in the food. Some researchers say that the alkaline tide effect must be abolished for the treatment to be completely effective.

(b) Low magnesium intake. One figure quoted is a magnesium concentration of 20 mg per 100 kcal DE (about 0·08 per cent dry matter) or less. Nevertheless it appears that FUS risk is appreciably increased only when magnesium concentration reaches about 0·25 per cent dry matter.

(c) High urine volume. This entails an adequate water intake with the amount of faecal water maintained as low as possible. This in turn means highly digestible, 'low bulk' foods.

Having said this, these aspects are probably important only for the susceptible cats in the population and if all the conditions are achieved the *type* of diet fed is unlikely to be a crucial factor.

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QUESTIONS AND ANSWERS

Following our FELINFO 1 article on FIP, cat breeders and show visitors have repeatedly asked questions concerning the laboratory testing of the animals.

Question: Several cat fanciers' associations recommend to use animals for breeding only when they have FIP titres of 25 and below; if possible they should be sero-negative. How should the veterinarian react to these questions?

Answer: As mentioned repeatedly, the height of the titre has no prognostic value; it does not tell if and when a cat will become ill with FIP. A cat without coronaviral antibodies is unlikely to be a latent carrier of FIP virus. However, sero-negativity should not be overemphasized. The tests available today will not detect low antibody titres; since the lowest dilutions of serum used is 1 : 25 (eg, in Zurich) a titre of 10 will not become apparent. This means that a negative result of a sample diluted 1 : 25 is interpreted as negative although the cat may possess a titre of 10. We also know that there is hardly a cattery at the present time in which all animals are sero-negative. During our studies of more than 40 catteries in Switzerland and Germany we have not detected a single negative one; in most of them a large proportion of the animals was sero-positive and even possessed very high titres. The fact that a pedigree cat shows only low or even undetectable coronaviral antibody does not exclude the possibility that this animal may serve as a virus carrier. On the other hand healthy animals with elevated antibody titre are not necessarily FIP virus carriers. Sero-conversion could have been caused by the related enteric coronavirus. These arguments indicate that FIP serology is not useful for selection of cats for breeding—it is only the veterinarian and the laboratory that will profit from such testing.

Question: Some veterinarians were able to protect healthy animals without clinical symptoms against FIP by injecting corticosteroids until no coronaviral antibody titre was demonstrable in them. Is this procedure effective?

Answer: It has indeed been observed that corticoids applied for 4 weeks resulted in a decrease and complete disappearance of coronaviral antibody titres. It has not been proven, however, that disappearance of these antibodies also prevented FIP—pertinent experimental studies have not been done. However, treatment with corticosteroids is certainly not without possible hazards. It has been shown that it can activate a latent FeLV infection. In our opinion there is no indication whatsoever for prophylactic application of corticosteroids at the present time.

Question: During the last 6 months a veterinarian had to euthanize two cats in which the postmortem and histopathology findings resulted in the diagnosis of the intestinal form of feline leucosis. Both animals had been tested in his practice for

FeLV using an assay imported from the USA and both were negative. The practitioner wants to know whether there are tests of different qualities available. *Answer*: Concerning the tests: all assays presently available make use of the same monoclonal antibodies, which leads to comparable specificity. The sensitivity of the different tests and the stability at longer storage (shelf life) may be different. In the case mentioned, however, it is not the sensitivity of the test which is in question since not all forms of feline leucosis are caused by infection with FeLV. In one-year-old animals more than 90 per cent of the leukemia cases are FeLV positive. Animals 10 years of age and older show evidence of FeLV infection in only 20 to 30 per cent of the leucosis observed; the remainder is FeLV negative. It is especially the intestinal form which is FeLV negative in older animals. The explanation offered for the FeLV negative cases of leucosis is that the cat had experienced and survived an FeLV infection at a younger age. At that time the viral genome has been inserted into the DNA of different cells which resulted in a time bomb to explode into a tumour later in life.

Please address your questions to 'FELINFO Questions and Answers', Dr Hans Lutz, Veterinaermedizinische Klinik, Universitaet Zuerich, Winterthurer Str. 260, CH 8057 Zuerich, Switzerland; for consultation by phone call on Mondays, Wednesdays and Fridays between 8.30 and 9.30 am, Switzerland 01 3651295.

GLOSSARY

The progress in biology and medicine of the last decades has resulted in a plethora of new insights. Even for a specialist it is becoming more and more difficult to screen and evaluate the innumerable publications worldwide. How much worse is the situation for the young colleague who has just left the veterinary school and who is faced with these new data in a scientific journal or during a congress? Is it possible at all for a veterinary practitioner to absorb the essence of biotechnological progress and use some of its insights? Undoubtedly he needs this information. Developments in molecular biology, immunology and microbiology can be applied in veterinary practice to-day or will be in the near future. I am referring to eg, insulin or interferon, both produced by DNA-recombinant work. A new age has begun also for vaccines, as heralded by experimental synthetic vaccines against foot-and-mouth disease and hepatitis B in man. To answer the rhetorical question asked above: I think it is possible to be abreast with the developments: Excellent reviews are pubished in the science columns of nationwide journals; however, only exceptionally they would be of interest for the readers of FELINFO. There is another bottleneck: a new knowledge cannot be acquired due to the intricate vocabulary which is alien to the outsider and which deters him from further study of the pertinent articles. The language barrier is complete when an argot of acronyms and abbreviations is spoken or written. Consider the examples 'genetic engineering, DNA, T- and B-lymphocytes, ELISA' etc; you will find more of these.

The editorial board of FELINFO wants to help surmount this language barrier. In every issue a Glossary column will try to explain a scientific term. This will not be done in alphabetical sequence but the items will be selected at random or in a logical context.

We realize a difficulty here, namely the difference in basic knowledge of our readers. An explanation of ribonucleic acid (RNA) will appear superfluous to our younger colleagues. For those however, who finished their training in the fifties, function and importance of RNA will not be well-known. We are aware of this dilemma but we hope to offer subject for thought and perhaps criticism also for the informed reader, which brings us to the following point: proposals for improvement of this column are appreciated. Since the author is a virologist by training he apologizes that his first contribution deals with viruses, those small nomadic genes which make our lives miserable every now and then.

Virus

Viruses are the smallest infectious agents. Those causing feline panleucopenia are amongst the smallest (about 20 nanometers = nm) and poxviruses among the largest viruses (250–300 nm). The construction of viruses is very simple: a strand of nucleic acid (ribonucleic acid –RNA– or deoxyribonucleic acid –DNA–) contains the genetic information for the viral proteins, ie, the structural elements and enzymes of the agent. Genetic information means the program which causes cells infected with e.g. a poxvirus to reproduce only poxviruses—and no others. In the simplest case the nucleic acid is protected by a protein capsule called capsid. Many viruses possess an additional lipid containing envelope which is similar in its construction to the cell membrane but which carries virus-specific proteins at its surface. Lipids are fat-like substances such as cholesterol, lecithin, triglycerids etc. Distinction between naked and enveloped viruses is of practical importance since the enveloped viruses do not survive very well when having left the organism, such as feline leukaemia virus and infectious peritonitis virus. These viruses are inactivated upon short contact with household detergents. In contrast, naked viruses are very hardy, eg, the virus causing panleucopenia and the canine parvovirus. These agents can maintain their infectivity in the surrounding for months, sometimes even years. According to their morphological, physicochemical and serological relationships viruses have been assigned to families.

Due to their primitive outfit viruses depend entirely upon the metabolism of their host cells; this means that multiplication is possible only within the cells of an organism. Intracellular replication and dependence upon the host cell have as a consequence that the infection cannot be influenced by chemotherapeutics, in contrast to bacterial infections that can be blocked with sulfa drugs and antibiotics. The result of an infection is always determined by the production of interferon and (later in the infection) by the immune response of the host; treatment can be only symptomatic.

Control of virus diseases is based on prophylactic measures such as quarantine or

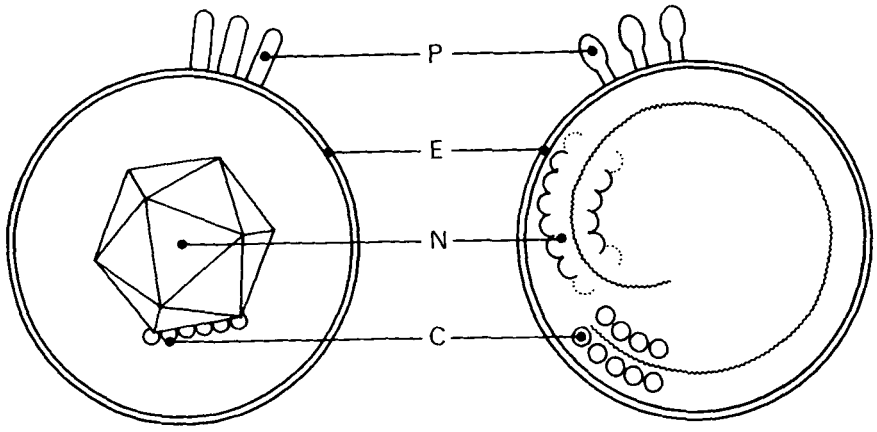

FIG. 1. Terminology of the structures of the virus particle (virion) P = peplomers, projections at the surface of the viral envelope which are used for attachment to the cell; E = envelope, a membrane which occurs in many viruses and contains lipids; N = nucleocapsid, a symmetric protein capsule which contains nucleic acid. Nucleocapsids may have the shape of an icosahedron (left) or of a helix (right) and consist of capsomeric (C) subunits.

isolation of virus carriers and shedders (feline leukosis), prophylactic vaccination (distemper, panleukopenia) and general hygienic measures. The following table gives an overview of the families of viruses encountered in small animals.

TABLE 1.

DNA viruses	RNA viruses
Adenoviruses (canine hepatitis)	Caliciviruses (feline upper respiratory disease)
Parvoviruses (feline panleukopenia)	Orthomyxoviruses (influenza)
Herpesviruses (Pseudorabies, feline upper respiratory disease)	Paramyxoviruses (canine distemper)
Poxviruses (pox)	Coronaviruses (feline infectious peritonitis)
Papovaviruses (warts)	Rhabdoviruses (rabies)
	Retroviruses (feline leukaemia)