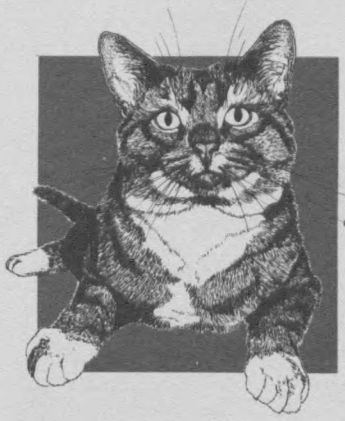

Cornell Feline Health Center
Veterinary News
Spring 1983

Autonomic Polyganglionopathy: A New Clinical Entity of Cats

Jeffrey E. Barlough, D.V.M. and Fredric W. Scott, D.V.M., Ph.D.

Since February 1982 numerous reports of an unusual, new disease entity of cats have appeared in the British veterinary literature.[1-11] The basic underlying lesion produces a functional disturbance of the autonomic nervous system, with associated clinical signs. No specific etiology has yet been demonstrated, nor has any specific treatment regimen been uniformly successful. The purpose of this brief report is to acquaint practitioners in the United States and in other countries with what has come to be known over the past year as the "Key-Gaskell Syndrome," or **autonomic polyganglionopathy (APG).**

Most cases of APG have occurred in young adult, domestic shorthair cats. Onset of signs can be variable, from a few hours to gradual development of signs over a period of weeks. In some cases, the syndrome commences as a mild upper respiratory condition, with transient fever and diarrhea. The major clinical signs which have been widely observed include:

1. **Persistent pupillary dilatation.** This sign may not be noticed initially due to bilateral elevation of the nictitating membranes. Dilatation is usually bilateral and nonresponsive to light, but sight does not appear to be impaired. In a small number of cases, dilatation has been unilateral and in at least two cases has been absent.

2. **Decreased tear production and dryness of mucous membranes.** Most affected cats have demonstrated a decrease in tear production (Schirmer test), and have developed dryness and reddening of the oral mucosa and dry crusting of the external nares. Mucopurulent ocular and nasal discharges may develop following secondary bacterial infection.

3. **Megaesophagus.** In some cases, gagging and swallowing reflex deficits have been noticed initially. These are overshadowed in many animals by chronic regurgitation which can be shown by contrast radiography to be associated with either a localized or generalized megaesophagus.

4. **Bradycardia.** The heart rate in cats with APG frequently ranges from 90 to 120 beats/minute.[3] This sign is probably reflective of sympathetic nervous system involvement.

Associated generalized signs of APG include anorexia, depression, weight loss, and constipation. In some cats there may be additional neurologic abnormalities, including fecal or urinary incontinence, bladder atony, mild hindlimb ataxia, or placing reflex deficits. In most cases hematologic examination, clinical chemistry profiles, and urinalysis are normal. Virus isolation attempts have been unsuccessful to date.

Most reports of APG have occurred as single isolated cases, although in a few instances more than one cat in a household has been affected. There is one report of APG in which 2 kittens from the same litter were affected.[10] There have been

(Continued on page 8.)

Feline Chronic Progressive Polyarthritis: A Brief Review

James W. Crissman, D.V.M.

Feline chronic progressive polyarthritis (FCPP) is an uncommon disease which has been diagnosed exclusively in castrated or intact adult, male cats. The syndrome has been recently well defined by Pedersen[1] as a specific, though dimorphic, clinical entity. Though the etiology is complex, the disease is considered to be immunologically mediated. Its two forms resemble two diseases of man: rheumatoid and Reiter's arthritises.

Pathogenesis

Pedersen found evidence of feline syncytial forming virus (FeSFV) infection in 18/18 cats, either by serology or by direct viral isolation. Sixty percent of the cats were also positive for feline leukemia virus (FeLV). Both of these values represent significant deviations from the infection rates expected in this group of cats; however several efforts to reproduce the disease were unsuccessful.

The pathogenesis of FCPP may be similar to Reiter's arthritis in its multifactorial nature. In this latter disease there is a marked preponderence of males involved, a disproportionate share of whom carry the HLA-B27 histocompatability type. While the joints are sterile, their disease is preceded by one of several infectious diseases; thus the designation of Reiter's disease as "reactive arthritis."

There are several hypotheses concerning the mechanism of interaction of these factors. First, HLA-B27 genes are linked to immune response genes, which may express an aberrant response to the infection. Second, there may be immunologic cross-reaction by antibodies directed at exogenous infectious agents with HLA-B27 gene products. Third, the HLA-B27 type may have a different distribution of tissue receptors for infectious agents.

FCPP has the same sex predilection and a strong association with FeSFV and FeLV. The pathologic similarities in the disease are also striking, tempting one to draw conclusions; however nothing is known about feline histocompatibility types. Additionally, the viral agents associated with FCPP should be contrasted with the bacterial or ureaplasmal agents associated with Reiter's disease, and it should be noted that the temporal association in FCPP between viral infection and onset of disease is unknown.

Clinical Features

Male cats generally present with painful,

Cornell Feline Health Center
Veterinary News

A publication for veterinary professionals

The ultimate purpose of the Cornell Feline Health Center is to improve the health of cats everywhere, by developing methods to prevent or cure feline diseases, and by providing continuing education to veterinarians and cat owners. All contributions are tax-deductible.

Director: **Fredric W. Scott, D.V.M., Ph.D.**
Asst. Director-Public Affairs: **Edna H. Federer**
Editor: **Joyce Tumbelston**
Secretary: **Sheryl A. Bronger**
Special Consultant: **Leo A. Wuori, D.V.M.**

symmetrical polyarthritis, with the severest lesions found in the most distal limb joints. The frequency and severity of lesions lessen in the more proximal joints of affected limbs. Lameness, soft tissue swelling and hyperesthesia of the limbs are found. Lymph nodes are generally markedly enlarged. In the initial stage of the disease, fever and malaise occur. In addition, there is intermittent anorexia and often cachexia.

Radiology

The skeletal abnormalities are usually very evident in radiographs. Periarticular erosions, coarse trabecular patterns in portions of the long bones adjacent to affected joints, and periosteal new bone formation are seen in the more common form of the disease. In the rheumatoid form, subchondral cysts may be seen, as well as the very severe erosions and the luxation of joints.

Clinical Pathology

A leukocytosis with mature neutrophilia is the common hemogram. However, this finding has been inconsistent, as several of the cats in Pedersen's study show absolute lymphocytosis or, conversely, leukocyte counts in the low normal range. The acute-phase reactant proteins, gamma-2-globulin and plasma fibrinogen, were generally elevated. In a case[2] presented to us and in most of Pedersen's cats, joint fluid was hypercellular with most of the cells being neutrophils.

Pathology

The most common form of the disease, seen in 17 of 20 of Pedersen's cases and the case we reported, resembles Reiter's arthritis. This form is characterized by periosteal reactive bone formation and osteopenia surrounding the inflamed joints. This may progress, producing moderate periarticular bone erosion, pannus formation, collapse of the joint space and, finally, fibrous amylosis of the joint. The second, or rheumatoid, form of the disease has been reported primarily in older cats and is differentiated by the very severe, marginal subchondral joint erosions, which result in joint instability and eventual deformation. This latter "rheumatoid form" is slower in onset and clinical course than the more common form. In either syndrome, lymph node hyperplasia may be so exuberant that a mistaken diagnosis of neoplasia may be made.

Treatment

Various regimens of immunosuppressive agents have been attempted with only poor to fair results. Glucocorticoids may alleviate some clinical signs and slow the progression of the disease. Temporary remissions have been gained with combination therapy using prednisolone, azathioprine and cyclophosphamide; however, severe, unwanted side effects are very common.

Summary

FCPP is a severe inflammatory disease of male cats warranting a poor long-term prognosis. It should be differentiated from degenerative joint disease and other causes of lameness in the cat including degenerative joint disease, infectious arthritis due to bacterial or mycoplasmal agents, trauma, and "transient febrile limping syndrome of kittens" caused by calicivirus, as recently reported by Pedersen et al.[3]

References

[1]Pedersen NC, Pool RR, O'Brien T: Feline chronic progressive polyarthritis. Am J Vet Res 41:522-535, 1980.

[2]Moise NS, Crissman JW: Chronic progressive polyarthritis in a cat. J Am An Hosp Assoc 18:965-969, 1982.

[3]Pedersen NC, Laliberte L, Ekman S: A Transient Febrile "Limping" Syndrome of Kittens Caused by Two Different Strains of Feline Calicivirus. Fel Prac 13:26-35, 1983.

James W. Crissman (MSU '77) is working toward a Ph.D. in Veterinary Pathology at Cornell. The subject of his research is "Arthritis in the Cat due to Mycoplasma gatae."

Recommendations for Prevention and Treatment of Kitten Mortality Complex

Cheryl A. Stoddart, B.S.

Yearly surveys conducted by the Cornell Feline Health Center in conjunction with the Research Committee of the Cat Fanciers Association (CFA) from 1975 to 1980 revealed that kitten mortality was a serious problem in many catteries throughout the United States. Over the 6-year period, a total of 9,517 kittens born in 2,309 litters from 28 breeds was surveyed, 9.3% of which were stillborn. Of the 8,630 kittens born alive, 5.8% died within 24 hours of birth, 2.8% died the second day, 13.2% had died by the first week, and 24.2% failed to reach one year of age. Stillbirths and deaths by one year of age considered together resulted in a total mortality rate of 31.1% for those kittens surveyed over the 6-year period.

During 1977 and 1978, many cat breeders and their veterinarians consulted the Cornell Feline Health Center, reporting alarming reproductive failure and high kitten mortality. These and other second-hand reports were strikingly similar. Everyone's story was the same: convincing evidence that a specific disease complex, termed kitten mortality complex (KMC), was occurring throughout the country. Kitten mortality rates in certain extensively studied catteries ranged from 40-80% during peak periods of kitten loss. It was apparently a new disease whose etiology was and still is unknown.

KMC is characterized by 3 main problems: reproductive failure, kitten mortality, and various diseases in the adult. Reproductive failures include repeat breeders, fetal resorptions between 4 and 6 weeks of gestation, abortion (usually during the last 2 weeks), stillbirths, and congenital malformations These malformations have included skull defects, open-top fontanelles, cleft palates, "open stomachs," heart defects, atresia ani, umbilical hernias, kittens with flat chests, and so-called "swimmer" kittens.

Kitten mortality is usually exhibited by the "fading kitten syndrome." The kittens either are born weak and die within a few hours or seem healthy and live for days, weeks, or even months but then become depressed and anorectic, eventually dying of starvation or secondary bacterial infections. Perhaps the most dramatic expression of kitten mortality is in acute congestive cardiomyopathy. These kittens suddenly are unable to breathe, become cyanotic, and die within a few hours. Postmortem and histologic examinations reveal hugely dilated and thin-walled hearts with acute muscle fiber degeneration, usually accompanied by fluid-filled thoracic cavities and lungs. A small percentage of kitten mortality is due to feline infectious peritonitis (FIP), usually the granulomatous (dry) form as opposed to the more typical effusive (wet) form.

In the adult cats, endometritis and pyometritis are both common and highly consistent findings in the catteries experiencing KMC. The respiratory disease is usually chronic and mild, involving the upper respiratory tract with sneezing as its most common symptom. Watery ocular and nasal discharges may also occur, but the cat seldom becomes seriously ill. Many queens (up to 40% in some catteries) have vaginal discharges; further examination usually reveals endometritis or pyometra. Other reported problems include adults and older kittens with intermittent and usually low grade fevers, acute congestive cardiomyopathy, and other cardiovascular diseases.

Although the exact causes of KMC are

not known, many feline viruses can cause reproductive failure, fetal malformations, neonatal kitten death, and various other diseases in the adult. These include feline viral rhinotracheitis (FVR), feline calicivirus (FCV), feline panleukopenia (FPL), and feline leukemia virus (FeLV). Many catteries experiencing KMC have cats which are FIP antibody-positive, and therefore FIP virus (FIPV) has been incriminated as an etiologic agent of KMC. At the present time, however, we do not completely understand the relationship between FIPV and kitten mortality and there is no conclusive evidence that FIPV is a main cause of KMC. It is important to note that the great majority of catteries have FIP antibody-positive cats, both those which are experiencing KMC and those which have had no problems whatsoever.

Since the causes of KMC are not presently known, there are no definitive methods of treatment. In many catteries, the problems have disappeared as fast as they appeared, so this may be the only consolation for cat breeders with affected catteries. For the veterinarian confronting KMC and seeking some advice, there are three main areas to explore: 1) diagnosis and treatment of infections, 2) restriction of cattery cats from exposure to infectious agents, and 3) alleviation of stress. The following items might be seriously considered in attempting to treat KMC.

Infections

1. **Proper vaccination regimen:** Kittens should be vaccinated against FVR, FCV, and FPL twice, preferably at 8 and 12-16 weeks of age to provide full protective immunity. The respiratory viruses can still be shed by a fully vaccinated asymptomatic queen, which can then infect susceptible kittens. If the queen has little antibody against these viruses, the kittens' maternal immunity will wane sooner and they may be unprotected before 8 weeks. If respiratory disease is a problem, the first vaccination should be given earlier, perhaps at 4 or 6 weeks of age. Another possibility is to vaccinate the queen before breeding to boost her immune response. Modified-live vaccines should never be given to pregnant queens. Vaccination against pneumonitis, a chlamydial infection, should also be considered for cats with respiratory problems.

2. **FeLV:** Any cattery having KMC problems should be tested for FeLV. If cats are found to be positive, a proper course of action must quickly be implemented to either isolate or eliminate those positive cats.

3. **Uterine/Vaginal Bacterial Infections.**

4. **Toxoplasmosis.**

5. **Fleas and Gastrointestinal Parasites.**

Exposure to Infectious Agents

6. **Cat Shows:** Breeders must understand the risks involved in showing their cats. Cats are particularly susceptible to infectious agents when grouped together in large numbers, especially when there is much stress involved. Infectious agents can easily be transmitted from to cat to cat via aerosols and contaminated show cages. A cat just returning to the cattery from a show is very likely to spread these agents to the rest of the cats and should be quarantined for 1 to 2 weeks, perhaps longer if feasible.

7. **Introducing New Cats:** New cats coming into the cattery either as acquisitions or for stud service are another potential source of infectious agents and should be restricted from full run of the cattery. These cats should definitely be healthy, free of respiratory disease, and tested for FeLV before admission into the cattery.

8. **Outdoor Animals:** Animals which have free run of the outdoors should not be allowed to mingle with cattery cats.

9. **Isolation of Queens:** Pregnant queens and queens with nursing kittens should be completely isolated from other cattery cats. It is also wise for the breeder to wash hands and don a clean coat or apron before coming into contact with the queen and kittens.

10. **Separation of Kittens:** The breeder may try taking kittens away from the queen shortly after nursing and hand rearing them in isolation to prevent them from contracting an infection from the queen. This is particularly helpful in the case of respiratory problems.

11. **Cattery Cleanliness:** The general cleanliness of the cattery must be kept optimal. Litter should be changed frequently and animal pens, floors, litter pans, food dishes, etc., should be regularly disinfected (Clorox diluted at 1:32 is ideal).

Stress

12. **Rest Queens Between Litters:** Queens should not give birth more than twice a year.

13. **Cat Shows:** Cats are particularly sensitive to stress and catteries in the throes of KMC should definitely avoid the stress implicit in shows.

14. **Toxic Agents:** Cats are also very sensitive to chemicals and can be adversely affected by toxic agents in their environment. Disinfectants containing phenol should not be used and cats should not be allowed to eat house plants. Although there is no evidence that they can be harmful to cats, airborne agents like cigarette smoke and formaldehyde-based blown insulation should be considered since they have been implicated in human health problems. Griseofulvin is a proven teratogen in cats.

15. **Nutrition:** Commercial cat foods formulated along NRC guidelines for growth and maintenance are far better balanced nutritionally than most home-made diets. Some foods can certainly be added to the diet, but the mainstay (80-85%) should be a good commercial product.

16. **Inbreeding:** The effects of inbreeding can be devastating to cats and must be discontinued if problems such as KMC appear in litters from very close matings. Even though the breeder is inbreeding in order to produce that certain "look" that will be successful in the show ring, they must understand the dire consequences of extensive inbreeding.

Although some of these items may be unpalatable to the breeder, impossible to implement, or simply ineffective, they should be examined and discussed. Many of the results will depend on the willingness of the breeder to confront and deal with this frustrating disease. All dead kittens should be refrigerated and autopsied as soon as possible. Tissues should be submitted for histopathology, particularly if lesions are present. Particular attention should be paid to the size and appearance of the heart since cardiomyopathy is often easily overlooked in very young kittens.

The Cornell Feline Health Center is interested in working with veterinarians and their clients who are confronting KMC and wish to have more extensive work performed. Various isolations for infectious agents can be done free of charge on an individual basis if there is sufficient interest on the part of the veterinarian and client. Please do not hesitate to contact us for more information, to give your additional suggestions, or to report on the results of these suggestions.

Cheryl Stoddart has been studying feline coronaviruses and their possible relationship to kitten mortality complex since 1979. She is currently completing her M.S. and plans to continue at Cornell for her Ph.D. in Veterinary Virology.

CATS Performance Boosts Camuti Fund

The Cornell Feline Health Center thanks every person who joined us for the special benefit performance of Broadway's "CATS" on March 5. Proceeds have been added to the fund for the Feline Consultation and Diagnostic Service in memory of Dr. Louis J. Camuti, a charter member of our Feline Advisory Council and a renowned New York City feline practitioner for 60 years. It was a fantastic show, made all the more special by the presence of Mrs. Alexandra Camuti, several of Dr. Camuti's family members and dearest friends, and a sizable contingent of veterinarians from the New York-New Jersey-Connecticut area and beyond.

The evening began with a pre-theater dinner at Gallagher's Restaurant graciously hosted by Dr. and Mrs. Lewis Berman of New York City. We are indebted to Lew and Amanda not only for their hospitality but also for the immense help they provided in planning and publicizing the entire theater event.

The show itself was a lively, out-of-this-world experience. Dancers dressed in leotards and fur, made up to look like so many different cats, leaped and roamed throughout the audience. Twice during the show, a large, orange cat came down and bestowed a big kiss on the guest of honor, Mrs. Camuti. Ruth McCarthy (wife of John B. McCarthy, the newly inducted AAHA president) appeared absolutely delighted when one of the hairy creatures led her onto the stage, whirled her around, and gallantly escorted her back to her seat.

Several CFHC staff members were especially privileged to attend a reunion of the Camuti family afterwards at Luchow's Restaurant. The genuine warmth and friendliness of those down-to-earth people made the evening even more memorable.

Several individuals gave personal assistance without which the benefit would not have been nearly as successful. In addition to the Bermans, we would like to acknowledge the valuable contribution of time and effort made by Ms. Sina Essary, who not only brought a large group of guests, but also helped with publicity and arranged for the services of the renowned photographer Claudio Edinger. Mr. and Mrs. Ellice McDonald, Jr., of Montchanin, Delaware, are to be commended for their very generous contribution, although they were not able to attend.

We are also grateful for the many veterinarians who came out, showing they stand with us in the effort to establish the Feline Consultation and Diagnostic Service. This has really boosted our determination to obtain the remaining funds needed to provide the first full-time service to benefit cats, veterinarians, and cat owners nationwide. Thanks to all of you for your support.

Feline Health Seminar in June

Our third annual feline health seminar, June 22-24, is designed for serious cat owners and shelter personnel, but will also be informative for veterinarians. Topics include feline reproductive physiology and disorders, embryology, neonatal care, genetics, neurological diseases, infectious diseases, zoonoses, FIP, newer diseases, and design of animal shelters and catteries. Faculty participants will include Drs. Fredric Scott, Robert Kirk, Alexander de Lahunta, Howard Evans, Drew Noden, Dorothy Holmes, Jeffrey Barlough, and Donald Lein, among others.

Of particular interest to veterinarians will be a section on Computerized Diagnostic Techniques in Small Animal Medicine, the trend of the future. Dr. Roy Pollock will show how computers can not only modernize your practice, but deliver perpetual continuing education as well.

Twenty hours (2 units) of continuing education credit will be awarded. The fee for the 3-day program is only $150. For more information or registration, contact Linda A. Ritzler at the Office of Continuing Education, N.Y.S. College of Veterinary Medicine, Cornell University, Ithaca, New York 14853, telephone (607) 256-5454, ext. 2200.

APG *(Continued from page 1.)*

no associated clinical signs in nonfeline contact animals or in the owners of affected cats.

The prognosis for survival is dependent upon the degree of esophageal involvement.[3] Moderate or severe impairment of esophageal motility is an unfavorable sign, and animals so affected generally do not thrive. Cats with less severe impairment can recover, although there may be residual neurologic signs, such as persistence of pupillary dilatation.

Pathologic examination of cats with APG has failed to reveal gross anatomic changes.[3,8] However, histologic abnormalities consisting of degenerative changes in the peripheral and central nervous systems have been found.[3,8] Lesions are most severe in the autonomic ganglia, and there may also be lesions in many autonomic nerves. Ultrastructural studies have demonstrated an underlying disruption of protein synthesis within affected neurons.[3]

There is currently no specific therapy for APG, and treatment is symptomatic and supportive. Persistent pupillary dilatation has responded to ophthalmic preparations such as pilocarpine[1,3,6,7,8] or physostigmine[3,10] As of this writing (February 1983) cases of this unusual disease entity appear to be confined to Great Britain.[1] However, information from practitioners in other countries regarding possible cases of APG would be greatly appreciated in order to further investigation into the etiology and pathogenesis of APG.

References

[1]Bedford PGC: A new disease in the cat. Vet Rec 111:473, 1982.

[2]Gaskell CJ, Rochlitz I: Key-Gaskell syndrome. Vet Rec 111: 564, 1982.

[3]Griffiths IR, Nash AS, Sharp NJH: The Key-Gaskell syndrome: The current situation. Vet Rec 111:532-533, 1982.

[4]Janz R: The Key-Gaskell syndrome. Vet Rec 111:401, 1982.

[5]Key TJA, Gaskell CJ: Puzzling syndrome in cats associated with pupillary dilatation. Vet Rec 110:160, 1982.

[6]Kock R: The Key-Gaskell syndrome. Vet Rec 111:469, 1982.

[7]Madeiros CA: Key-Gaskell syndrome. Vet Rec 111:540, 1982.

[8]Nash AS, Griffiths IR, Sharp NJH: The Key-Gaskell syndrome - an autonomic polyganglionopathy. Vet Rec 111:307-308, 1982.

[9]Nash AS, Griffiths IR, Sharp NJH: Key-Gaskell syndrome. Vet Rec 111:564, 1982.

[10]Power JC, Temple JD: Key-Gaskell syndrome. Vet Rec 111:540, 1982.

[11]Tutt JB: The Key-Gaskell syndrome. Vet Rec 111:353, 1982.

Jeffrey E. Barlough (Davis '79) has been with the Cornell Feline Health Center since 1980, studying the feline immune response to feline infectious peritonitis (FIP). He plans to complete his Ph.D. in Veterinary Virology next year.

Fredric W. Scott (Cornell '62; Ph.D., Cornell '68), Director of the Cornell Feline Health Center since its inception in 1974, is also a Professor of Veterinary Virology.

Cornell Feline Health Center
Cornell University
College of Veterinary Medicine
Ithaca, New York 14853