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Successful Treatment of Feline Panleukopenia: A Guideline For Rescuers and Veterinarians, Part I

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Abstract

We present a successful approach for treating feline panleukopenia, a fatal and highly contagious disease. It involves recognizing the disease early though the uses of parvo test kits or low neutrophil count; applying the drug Neupogen (filgrastim); and providing antibiotics, SC fluids and other supportive therapies. The protocol can be done in a rescue environment with subcutaneous (SC) injections and SC fluids. We have had 11 cases in which we used Neupogen and 15 cases without Neupogen, with 0.91 and 0.33 survivals respectively. Parvo test kits and prescriptions are required.

Keywords

Feline; Rescuers; Panleukopenia virus; Neupogen; rG-CSF; Filgrastim

Introduction

Over many years of feline rescue work, I have developed a successful course of treatment for feline panleukopenia virus (FPV) (also referred to as feline distemper). I have encountered about 30 cases. FPV is a highly contagious, fatal feline disease that is also stubbornly persistent in the environment. Parvoviruses are linear, non-segmented single-stranded DNA viruses, with an average genome size of 5000 nucleotides, and are among the smallest viruses at ~ 18–28 nm in diameter [1].

The FPV disease results in multiple deaths in rescue and shelter environments. It affects mostly unvaccinated kittens and younger cats. A survival rate of about 50% has been reported with supportive therapies [2]. Our rate was about 33%, before we started recognizing the disease earlier and began using Neupogen. Poor prognosis is linked to lower leucocyte count, lower serum albumin or lower potassium in the literature [3].

Much of the success in treatment provided here is due to catching the disease in earlier stages and proceeding with aggressive treatment, including Neupogen. Prevention through vaccine is by far the best way to handle the disease as outlined in ABCD guidelines [4]. However, we follow a more aggressive vaccination schedule for younger kittens and vaccinate at 4-5 weeks of age. A short review of feline panleukopenia can be viewed at Merck Manual or the on-line resource, Koret shelter medicine, UC Davis Veterinarian School.

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The information is divided into two parts. Part I provides general instructions in treating FPV. Part II outlines case histories. If you identify it before symptoms appear, you have excellent chance of survival. If you catch it late, when the WBC count has already dropped and symptoms are apparent, you have a very good chance as well with aggressive treatment. Kruse et al. [5] report there is no difference between over and under 6 months (without Neupogen) in their survival rates. They have higher numbers of cats (244) in their study. We have had good success with even young kittens in the range of 5- 6 weeks of age. We 1) identify the disease; 2) start immediate treatment with Neupogen and an antibiotic active against e-coli (gram negative); 3) address the first stage of the disease -high fever, diarrhea, and vomiting; 4) address complications in the second phase - dehydration and high liver enzymes; and 5) minimize septicemia in the third stage. Once we have identified a case of FPV and started treatment for that feline, we minimize exposure to other cats by 1) isolating the sick feline, 2) take immediate steps to vaccinate any unvaccinated or "at risk" felines with modified live vaccine (MLV), unless the cat is pregnant, and 3) disinfect all exposed areas.

Background

A few veterinary studies have reported using Neupogen in the feline. Neupogen or filgrastim is a recombinant human granulocyte colony-stimulating factor (rG-CSFs) designed to induce early release of leukocytes, the cells which fight infections. The results from these veterinary studies were mixed at first, but seem to be converging on the result that Neupogen does increase leucocyte counts in the feline with a variety of diseases, and in the healthy feline. Kraft and Kuffer [6] report the puzzling result that their feline controls (6 cats) had a higher rebound of WBC count than the G-CSF (Neupogen) treatment group (10 cats); however, they report only losing one cat in the study. Kuffer-Frank [7] in 1999 reverse their 1995 finding (two authors are the same on both papers) and report very good rise in WBC counts following Neupogen in the feline with FPV when compared to controls. Horlacher K. thesis, German, 2004, reports no improved survival with use of Neupogen in study with 876 cats. Felix [8] with 7 cats, reports good response to Neupogen in the rise of WBC counts after exposure to native FPV, and the review by Fernández-Varón and Villamayor [9] states the scarcity of the application of Neupogen in veterinary articles. Use of Neupogen in the feline with primary neutropenia (not from an infectious agent) leads to a rise in the WBC count of the feline and resolution of symptoms and treatments, which indicates the WBC count does respond to Neupogen in the feline under primary neutropenic conditions [10]. Fulton et al. [11] report increased leukocyte response to Neupogen in healthy felines. Several researchers state that in addition to increasing neutrophil counts, the administration of rG-CSF has also been shown to improve the microbicidal activity of neutrophils against bacterial and fungal infections in humans [12,13]. It's not clear if that effect would also occur in the feline. Weiss (1995) lists a number of other uses for rG-CSF in the cat, including in conjunction with cancer treatments when neutropenia is present [14]. Kraft and Kuffer [6] report a good leukocyte response for parvovirus in the dog, but Mischke et al. [15] report no improvement in parvovirus survival in the dog. A different version of the G-CSF is now available which is specifically for canine. It has been reported that the canine version, rCG-CSF, also causes

an increase in neutrophils in the healthy feline [16]. A feline version (PEGFE-CSF) has also been developed for long term use in the feline [17]. The advantage is that the feline does not produce antibodies to the product and it can be used longer term.

Our survival rates for felines with FPV using Neupogen are shown in Table 1. We see anecdotally about 33% success using supportive therapies without Neupogen to about 90% survival rate using Neupogen with supportive therapy. It becomes a curable disease. We have used the procedure described here or instructed others in doing so in about 15 cases and lost very few. We lost a young kitten to sudden death at 5-6 weeks of age, and were easily able to save the other 3 kittens in the litter. We just aided a rescuer whose 8 month old male feline had a WBC count of 0.59 10^3per µl, and he recovered from FPV with the use of procedures presented here.

Signs of the Disease: Most veterinarians do not see many cases of distemper and may not recognize it early. In addition, it is difficult to catch it early since the symptoms overlap with other conditions and the disease progresses rapidly. One important tool is early testing using a canine parvo test kit on fecal matter [18,19]. They are inexpensive, sensitive, easy to use, and will pick up cases before symptoms appear. It can be kept on hand in rescue or shelter and run when you suspect a case or have lost a cat suddenly. The second essential tool is the use of the drug Neupogen. Experienced cat rescuers will recognize signs of full blown panleukopenia, cats crouching in front of water bowl, lethargy, fever, and diarrhea with distinctive odor.

Be aggressive in treating FPV: Run a parvo snap test (Idexx) and if it's positive, that's all you need in terms of diagnostics for this treatment protocol. A negative test on parvo test kit does not eliminate FPV as the cause of illness. False negatives are relatively common. False positive parvo results are not very common, however, modified live panleukopenia vaccines can result in a positive parvo test immediately following vaccination and this positive result rarely can extend up to 2 weeks after the vaccine [20].

If you want confirmation that the symptoms are FPV (or if the parvo test is negative and you or your vet still suspects FPV), run a CBC (complete blood cell) count or a WBC (white blood cell) count at a minimum. We typically run a small blood panel (pre-op with CBC) and that will give indication of kidney, liver enzymes, and proteins, for other diagnostic purposes. If the feline is positive for parvo OR has a very low WBC count, immediately obtain the drug Neupogen though a prescription given by a veterinarian.

If the white count is suppressed considerably or the parvo test is positive, do not wait one minute, one hour, and one day. Get Neupogen and inject first dose as soon as possible. Human pharmacies dealing with cancer patients or hospital pharmacies generally have it.

Progression of the disease: Cats incur high fever, vomiting, lethargy and diarrhea, and succumb to dehydration, high liver enzymes, and later, septic shock from secondary infections, as a result of the low WBC counts. Wolfesberger et al. [2] present a detailed list of symptoms and outcomes from records of 73 cats brought to their University clinic. If you have a sudden death of kitten or adult, suspect FPV until you know otherwise. Isolate the infected feline and take measures to minimize the exposure of other cats by careful use of gloves, booties, disinfectants, vaccination, and revaccination of other animals on the premises as presented on-line at Maddie's shelter site, U of Florida.

Panleukopenia can result in the death a cat at three different stages, but if you start protecting (preparing) for the 3rd stage early in the process, you will increase survival rates considerably, and that is what Neupogen does. It also seems to have an immediate effect. It has been shown to stimulate the white blood cell production and appears to prevent losses due to secondary infections in the third phase. If you can keep the kitten or cat alive for the first 3-4 days after symptoms appear, the Neupogen will help prevent septic shock and bring you to a successful outcome.

Methods and Materials

Full treatment strategy:

Good supportive therapy: To save a distemper kitty with full symptoms and low WBC count, you must be willing to care for a debilitated feline with the idea that the cat can fully recover. Giving fluids, and stopping the vomiting must be addressed.

Neupogen(filgrastim) dose and schedule: Give Neupogen, by direct SC injection, once a day for two to three days, then a day off and then again on the fourth or fifth day. This works well most of the time. On occasion, I don't get a response by the third day and I then give those cats/ kittens four days in a row and then a day off.

- The dose recommended here is about 1/10th of a human dose for an 11 lb (5 kg) cat. This is a dose of about 6 mcg per kg. If there are multiple kittens or felines to treat you can use a lower dose of about 1/20th of the human dose (3 mcg per kg) to get more treatments per vial. If you have measured the WBC count and its low, use the higher dose. You will want to use Neupogen with 300 mcg/

Table 1: Feline survivors and non-survivors with FPV with and without use of Neupogen.

Feline age	Totals	Survivors	Non-survivors	Neupogen used
over 3 months	4	3	1 (subnormal temp when 1st seen)	yes
under 3 months	7	7	0	yes
over 3 months	3	2	1 (sudden death – no treatment)	no
under 3 months	12	3	9 (three died with no treatment)	no
Total feline	26	15	11	
Survivors w Neupogen/ total w Neupogen	10/11	0.91 [1]		yes
Survivors w/out Neupogen/ total w/out Neupogen	5/15	0.33 [2]		no

1) This ratio includes Bonnie, adult female cat who had one vaccine 5 weeks prior to the time of one of her kittens died suddenly of distemper.

2) If the four felines who received no treatment are excluded, the ratio of 5/11 is 0.45.

0.5ml or 300mcg/1 ml. The pre-loaded needle has 300 mcg in 0.5 ml. The easer-to-use packaging is a vial with 300 mcg per 1 ml, which can more easily be drawn into sterile syringes for a cat. The two packages differ in concentration by a factor of two. If you are unlucky enough to get the syringe with 0.5 ml, you can ask your vet to provide a 1 ml sterile vial for you and inject the contents and draw back out once a day using smallest volume (0.3 cc) insulin syringes.

- Plumb's veterinary drug reference guide gives the following dosages of Neupogen for feline, "1 to 5 mcg (microgram) per kg, SC once or twice a day, as long as patient has no hypersensitivity to it." Neupogen has been shown to have low toxicity.

Fluids: The amount of fluids needed is about 3 to 4.4 % of cat weight per day, if cat is not eating. You can subtract the volume you are able to feed. A 3 kg cat (6.6 lbs) will get 90 to 130 ml fluids per 24 hours. Sub-cutaneous (SC) fluids should be given slowly in sick animals. Limit yourself to 125 ml in an adult at one time and scale down for kittens. Use warm fluids (80 to 90 degrees) if body temperature is 103 degrees or below, and use room temperature (RT) fluids to bring higher temperature – above 103.5 degrees - down. Deliver the fluids slowly if they are RT. We prefer gauge 19 needles for adults and gauge 20 for kittens.

Antibiotics: Cats with low WBC counts must be given full spectrum antibiotics immediately upon diagnosis. If the temperature of the cat is low, it may require IV antibiotics. Most important is to cover e-coli pathogen, so a gram-negative antibiotic that penetrates tissues well is a good choice. My preference is injectable Baytril (5 mg/kg once a day) and an injectable penicillin drug (penicillin G procaine (20,000 units per kg 1-2 times a day). If there is a lot of vomiting, use only injectable antibiotics. We inject SC, if you are controlling the vomiting, it may be ok to use oral Clavamox with injectable Baytril. I generally find that injectable Baytril and injectable penicillin is good coverage. Never use over 5mg per kg of injectable Baytril because it can cause blindness [21,22]. If you want an extra margin of safety, inject the Baytril though IV fluid port while delivering SC fluids, to dilute it further. We give Baytril to feline at every age and have not yet had tendon damage reported in young dogs [23].

Supplements: Vitamin B12 injections (0.05 to 0.1 ml for kitten and up to 0.25 ml for adult) every day or every other day is extremely helpful and important. Vitamin B12 is more comfortable, but diluted Vitamin B-complex (which is painful on injection) can be used if you give slowly in IV fluid line port or inject into the fluid bubble under the skin of the cat after fluids are administered SC.

Temperature: The temperature should be monitored and kept under 104.0 F, but some fever may be beneficial to kill the viral infection. If it gets above 104 F, bring it down slightly with fluids or cold pack or anti-inflammatory drugs (Onsoir, Metacam, or ketaprofen). If it's lower than 103.5 F, then give fluids or cool paw pads and put on "watch". A temperature of 103.5 F or between this and normal is generally fine.

Minimal feeding: Minimal feeding of Hills diet A/D with a slight bit of karo syrup or dextrose added. We suggest just enough feeding to keep from developing hepatic lipidosis, but not so much to induce vomiting (a teaspoon to tablespoon, several times a day). Inserting a feeding tube is also an option, however the disease progresses relatively rapidly, and we have not had to apply a feeding tube. When we started the protocol, it was not available. However, don't do any treatment that interferes with the cat's will to live. There are also reports that the food is not absorbed in the damaged intestines and this may explain the voraciously hunger in cats who recover from FPV. Digestive enzymes may be of help. In many cases, the cat or kitten is too lethargic to eat anything. You can try something like Energel on the gums or just continue with SC fluids without food if you cannot get the cat to eat without vomiting. Vomiting must be kept in check with Cerenia (as directed by vet) or with injectable Zofran (ondansetron) (0.05 mg per lb or 0.1 mg per kg of 2 mg per ml). We have also used injectable Pepsid (famotidine) as a third choice, if feline is not keeping oral Cerenia down or if injectable Zofran or injectable Cerenia is not available.

Liver enzymes: The liver enzymes should be in check and what causes them to rise is excessive vomiting (and not eating), so if you control vomiting and do minimal feeding, the liver enzymes will be in function. If they are not, you can use over-the-counter milk thistle to bring down or a veterinary product with silymarin. I usually dose down a human capsule of milk thistle, to 1/20th of one capsule, and mix in A/D or water and syringe in mouth 2 times a day. (After vomiting is controlled). We rarely monitor bloods during treatment and often not at all. Run blood work only if you want to know the white blood count or have another reason to do it. It's not necessary to run blood work at all using our protocol.

Other treatments, young kittens, late stage, and bloody diarrhea cases:

If you have kittens less than 2 lbs, I recommend that you also use Tamiflu. Get a prescription from your vet and have them give you instructions on how to administer. If you have a difficult case with a bloody stool - regardless of age, it's an extra level of support for the intestines. It's especially helpful in young kittens when Neupogen may be less helpful. It has been postulated in parvo in dogs (a similar virus) the destruction of the intestinal crypt cells results in a breakdown in the normal protective intestinal barrier. Tamiflu protects the intestinal wall and is extra protection against bacteraemia. If you have a difficult case, add Tamiflu. There is an anecdotal report on line. An alternate to Tamiflu is metronidazole in older kittens and cats, but if you have severe intestinal symptoms, we recommend Tamiflu. We stagger metronidazole off times from the other broad spectrum antibiotics.

Other variations: We have had one or a few cats with very low WBC counts, but do not test positive on the parvo test. In those cases, we treat them the same as a confirmed panleukopenia case. Their low WBC count can result in death due to secondary infection no matter what virus or condition is causing the neutropenia.

Breaking through the virus: The cat will "break though" and feel better pretty suddenly and just get up, be very hungry, and want to eat and drink. Tony (our most recent survivor) started to show noticeable improvement the third day after Neupogen and 4th day after ER visit. In the first hours and days after breaking through, the feline needs a lot of nourishment in small and frequent meals of high quality foods.

However, the cat will still be infectious for about two weeks after the illness, therefore use caution in exposing other cats, particularly unvaccinated cats. Koret Shelter medicine, UC Davis states "Isolating recovered animals for an additional two weeks is the safest option to limit spread within the shelter. A negative FPV SNAP test is suggestive that significant quantities of virus are no longer being shed." It has been recommended to "bathe recovered animals prior to re-introduction to a shelter in order to remove virus persisting on the coat." To be cautious, and because we have seen lingering positive parvo tests past two weeks, we recommend three weeks of isolation after the resolution of symptoms of FPV survivor, bathing of the cat,

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and decontamination of the environment. Decontaminate what you throw out as well, unless it's going to incinerator. You will not want to expose feral or stray cats at a county dump or cats getting in trash. We also use a SNAP test on recovered kittens/cats prior to adoption, and we screen all adoptive applicants to determine if their current cats have had an FVRCP vaccine as an adult.

Do NOT move sick cats and kittens to new locations without careful considerations. The first area is contaminated if you have FPV and its better not to contaminate another space. Minimize exposure to other cats, revaccinate, and decontaminate the space you have, but don't contaminate new spaces. Leave FPV cats in the car when going to the vet and ask the vet before going in if they have a dog room or separate space where they can see the sick cat.

Discussion

Aftermath

Don't underestimate the lingering effects of panleukopenia virus. It can live on surfaces for a year or more. We recommend you do not take in any kittens into your contaminated space without a vaccine or partial vaccine. When kittens reach weaning age, we recommend you vaccinate with ½ dose (1/2 volume) of a modified live vaccine at 4-5 weeks and again 3 weeks later with full dose and give the same full dose at 12 weeks. Some reports recommend another vaccine at 16 weeks of age. It is best if you vaccinate and wait 5 to 7 days for the vaccine to build antibodies before bringing kittens into your home after having a FPV case. Remember you, your shoes, car, and clothes can be contaminated. We have found it almost impossible to insure our space is clean of panleukopenia virus in our shelter after a FPV case.

While many shelters like to use quaternary ammonium compounds for routine disinfection (Roccal, Parvosol, Triple Two, Broadside, and A33), this is not effective against FPV. The recommended way to kill the panleukopenia virus is to apply a dilute bleach solution (1-part bleach to 32 parts water) to food bowls, litter pans, cages, and other surfaces during cleaning. Whenever possible, those items should be made of stainless steel; plastic food bowls and litter pans are too difficult to disinfect after repeated use. Animal Sheltering Magazine HSUS states "Potassium peroxymonosulfate (e.g. Trifectant® or Virkon) and accelerated hydrogen peroxide (e.g. Accel/Rescue®) both have greater detergent properties and better activity in the face of organic matter compared to bleach and related products. Accel/Rescue in particular has been shown to have good activity even in the face of organic matter contamination. Either of these can be used in carpet cleaners on contaminated carpets and furniture (always check first to test for staining)." Maddie's shelter site has further details on cleaning exposure times (10 min minimum) and other details.

It is NOT recommended one vaccinate a pregnant or nursing mom with modified live panleukopenia vaccine. The kittens can develop cerebellar hypoplasia. Killed vaccine is an option if in immediate exposure conditions, but better to put unexposed nursing moms with young litters in a "clean" foster home (never had a case of FPV, EVER) and vaccinate mom (full dose) with killed or modified live after kittens have been born, and vaccinate kittens of 4-5 weeks of age with (1/2 dose) of modified live vaccine.

The literature indicates that a booster of killed panleukopenia vaccine if given at one year of age (after kitten series shots) will still be effective 7.5 years later. It may last longer, therefore, we give panleukopenia vaccine to all TNR (trap-neuter-return) cats and those cats will generally be protected [24].

Additional information

In my experience, it takes about two weeks to contract a full blown case and about a week to show slight symptoms of distemper, but a litter can contract it at different times and you may have one very sick (or sudden death) kitten and others look fine. It's very important to think ahead and treat healthy kittens who have been exposed very aggressively and give Neupogen at this time (at least one dose) and start vitamin B, fluids, and build up strength in these kittens. Keep them on careful watch and if they continue to eat and thrive, you can modify their treatment as needed. You need to be proactive and not wait for them to show symptoms. You can vaccinate kittens and cats early after exposure and with no symptoms (with negative or very light positive parvo tests) but use either intranasal (which is faster) or modified live vaccine delivered SC. Do not use the killed virus vaccine because it is too slow in building antibodies. We prefer the modified live injection, but with younger kittens, the intra nasal can be very helpful. We have at times given both, one for the first few days and ½ dose of modified live for the end of the week. Reference [4] recommends vaccinating FPV exposed cats on the normal schedule. Once you vaccinate a cat who you suspect has been exposed to FPV, you no longer can completely rely on the parvo test kit for diagnostic purposes for a few days and sometimes up to ~2 weeks. Repeating the parvo test after a day or two can give you an idea if your cat is coming down with FPV (stronger positive on testing) or dissipating from vaccine (getting weaker on testing). You have to then use blood testing diagnostics (WBC count) and symptoms such as temperature and lethargy, although, these symptoms can overlap with vaccine reactions, too.

We do not vaccinate a cat showing panleukopenia symptoms or cats with very low WBC count. We move forward with treatment outlined here.

If you suspect panleukopenia and cannot get parvo test or WBC count, you may consider giving first dose of Neupogen anyway. It is ok to do it. It is better to give one injection and then give yourself some time to put a plan in place than to wait and possibly lose the cat. It may cause an elevated WBC count, but the alternative is a cat with deadly panleukopenia.

Treatment outline

1) Identify FPV with parvo test or WBC count and symptoms. Parvo test any severely sick or deceased kitten or cat with unknown sudden cause of death. Isolate sick cats.

2) Start Neupogen, and give on days 1, 2, and 3 (optional), skip a day and resume on days 4 or 5.

3) Start two broad spectrum antibiotics, Baytril and penicillin G, typically.

4) If kitten is under about 2 lbs, start Tamiflu. (Or if a lot of bloody stool at any age); as alternative, start metronidazole if feline is over about 3 months old.

5) Start Vitamin B12 or highly diluted Vitamin B-complex.

6) Give fluids, anti-vomit meds, and feed small amounts of A/D Hills diet.

7) Keep track of temperature throughout. Keep at or below

103.5 F, but a modest elevated temperature is good.

8) Continue with supportive therapy and antibiotics for full course of treatment. (Typically 7 days, or 3 days past all symptom resolution, but at least a minimum of 5 days)

9) Cat will "break though" pretty suddenly and just get up and be very hungry and want to eat and drink, usually 3-5 days after symptoms appear.

10) Closely watch and slowly remove supportive therapies as cat is able to do for him/herself. Feed often during this time period.

11) Keep cat isolated for 2.5 to 3 weeks after recovery, bathe coat, and decontaminate environment.

Our guideline for vaccinating younger kittens:

One highly susceptible time for kittens to contract panleukopenia is when they are weaning from mother at 4-5 weeks of age. This is due to mother having some antibodies and kittens lacking enough to protect themselves when they are weaning. It is so much easier to prevent distemper than to treat, therefore, we generally vaccinate all healthy 5 week old kittens with modified live at ½ volume of a full dose (1/2 cc). Some kittens will have immunity from mother and some will not build immunity, but those that will can be protected for a few weeks until they can build better immunity. We have also used nasal vaccines; however, we have had a few cases of bad reactions to them and prefer MLV given SC at ½ volume. We then give full dose 3 weeks later (at 8 weeks) and repeat again at 12 weeks of age. Some experts suggest giving vaccines to the age of 16 weeks. Ref [2] reports a ~19% of their cats with two vaccines as kittens and stopping at 12 weeks, came down with FPV. You will then need a booster of the FVRCP at one year of age and this should be good for 3 to 7 years. Some veterinarians believe it is good for lifetime of the cat. The on-line resource, Koret shelter medicine, UC Davis, also suggests vaccinating at 4 weeks with MLV. We concur with their vaccine protocol, particularly in the shelter or rescue environment.

Epilogue

If you have a survivor, you have done very well. However, you may want to consider vaccinating the same cat with the FVRCP (panleukopenia) vaccine several weeks or months after your case, when fully recovered, because the panleukopenia vaccine has two other URI vaccines that are helpful to the feline.

If you have a survivor, and your feline had a very low WBC count (a late case), congratulations; however, be ready for the unexpected aftermath of having a possible case of fungal infection or ringworm or other opportunistic (nuisance, but not life threating) infection. It will seem like "nothing" compared to FPV.

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