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Seasonality of Heartworm Infection and Implications for Chemoprophylaxis

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The current emphasis on heartworm prevention reflects the dependable protection provided by the monthly administered macrolide endectocides. This article reviews the prerequisites for heartworm transmission and the importance of daily temperature as a limiting factor in determining the seasonality of the transmission period. The practice of some veterinarians to continuously prescribe monthly chemoprophylaxis exaggerates the actual risk of heartworm transmission in most parts of the country and unnecessarily increases the cost of protection to their clients. Guidelines are provided for making an objective, conservative estimate of the earliest and latest dates for administering monthly chemoprophylaxis; and the use of seasonal projections for other clinical applications such as timing and interpretation of heartworm testing are discussed.

Since the introduction of monthly administered heartworm chemoprophylaxis over a decade ago, there has been a major shift from treatment to prevention of this disease. This change in emphasis reflects the extraordinary safety and efficacy of the macrolide endectocides and the potentially serious consequences of infection. Dog owners need little encouragement to be convinced of the merits of prevention and very sensibly have become averse to risking a disease that can be so easily avoided. There is certainly great economy in addition to considerable peace-of-mind to be gained from this approach. There is also a tremendous financial incentive to veterinarians to promote heartworm chemoprophylaxis because they control distribution of these excellent products in a market that is already large but not yet saturated. Unfortunately, preoccupation with worse case scenarios imparted by the profession to our client's and what could be perceived as an obvious economic self interest for veterinarians to promote chemoprophylaxis has encouraged an insidious overuse of a good thing. The well-intentioned promotion of heartworm awareness and prevention may overshadow the fact that in the temperate latitudes, heartworm transmission is seasonal and chemoprophylaxis is not necessary on a continual basis.

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Prerequisites for Transmission

If a mosquito will feed on a dog, and there are many species that will, then it probably can serve in some capacity as a vector for heartworm transmission. Such mosquitoes are nearly ubiquitous and frequently plentiful. The other prerequisite that is universal is a susceptible population of domestic dogs or wild canids. Like mosquitoes, there is usually no shortage of dogs in most communities. In rural areas where dogs are widely separated, this isolation reduces transmission by providing some protection from exposure to mosquitoes infected elsewhere. Although there are physical limits to how distantly mosquitoes can be dispersed, the movement of dogs is not similarly constrained and introduction of a reservoir of infection is a constant threat made real by demographic shifts from regions where microfilaremic dogs exist. This is in fact the primary means by which heartworms continue to spread. But even if vectors, reservoirs, and a susceptible definitive host population all are in place, transmission would be impossible if the climate did not provide sufficient warmth to support incubation of microfilariae to the infective (third) larval stage within the intermediate host, the vector mosquito. Rainfall and humidity, critical variables affecting emergence of mosquitoes, and vector density are secondary factors. Although a break in any of these links is sufficient to prevent heartworm transmission, the period during which it may be possible is defined by seasonal changes in temperature.

Evidence for Seasonal Transmission

In regions where average daily temperatures remain at or below about 62°F (17°C) from late fall to early spring, insufficient heat accumulates to allow maturation of infective larvae in the intermediate host, precluding transmission of the parasite. The conjectured vector potential of overwintering adult mosquitoes and the swarms of "mosquitoes" sighted during late winter thaws, notwithstanding, there is no evidence that heartworm transmission is possible at these times. Some adult mosquitoes do overwinter but are in a diapause state during which they do not seek hosts for blood feeding. Midges and other nonhematophagous flies may emerge during transient warming cycles and can be mistaken for mosquitoes but are of no consequence because they never ingest vertebrate blood. The fact that there are too few warm days during these midseason temperature fluctuations to complete the critical mosquito-borne incubation phase is a critical limiting factor. Even if mosquitoes emerged in the warmth of indoors and were to feed, how would they become infected unless a resident dog was already infected and microfilaremic? The scenarios used to rationalize even a small chance of cold weather transmission are at odds with the biology of the vector-parasite relationship.

Although logic can be defended on principle, theories still must be tested. There have been few field studies, but the results of these are entirely consistent with models for predicting the timing of heartworm transmission. The most elaborate and discriminating investigation was performed by exposing tracer dogs to natural infection in the southeastern states of Georgia, Florida, and Louisiana.[1] Prior to this study, conventional wisdom would have predicted some transmission each month of the year at these sites located between 28°11′N and 31°56 ′N latitude. Though surprising at the time, no transmission was documented by antigen testing and necropsy confirmation between mid-December and mid-April over three consecutive years. Based on estimates of worm ages derived from measurements of body length, the earliest infections occurred about mid-July and transmission ceased about the first of October. The period of actual transmission during these 3 years ranged from approximately 8 weeks at the Florida site to 6 weeks at the Georgia and Louisiana sites.

In more northern latitudes, it is reasonable to assume the duration of heartworm transmission would become progressively shorter. This expectation is consistent with the recovery of infective larvae from the heads of mosquitoes collected in northern Indiana during the summers of 1993 and 1994.[2] Over these two summers, infective larvae were found only during a 4 to 5-week period between late June and the end of July.

Prediction Model

The relationship between constant ambient temperature and maturation rate of heartworm microfilariae to the infective third larval stage within the mosquito intermediate host is essentially linear between 65°F (18°C) and 86°F (30°C).[3] When regressed against the calculated average daily temperature in a 24-hour diurnal cycle, approximately the same rate of development occurs.[4] For development to even begin, a threshold of 57°F (14°C) must be exceeded. Larvae within the mosquito are more cold tolerant than the intermediate host itself. Consequently, when the ambient temperature is below the developmental threshold, maturation will be only temporarily suspended until warmer conditions resume. The critical denominator is the cumulative amount of heat required to complete the incubation. This heat requirement can be expressed in degree days, also referred to as heartworm development units (HDUs) in excess of the 57°F threshold temperature.[4] On average, a total of 234 HDUs on the Fahrenheit scale (130°C) are needed to support development of microfilariae to transmissible infective larvae. This cumulative threshold can be reached in as few as 8 days when the average daily temperature is 86°F but take as long as a month when it is as low as 65°F.[1] The model we have adopted assumes that an infected mosquito in the wild is unlikely to survive longer than 30 days.[4]

Our predictions of the heartworm transmission period (season) in the United States are made by calculating the 30-day moving cumulative number of HDUs derived from a climatologic database compiled for individual weather stations throughout the country.[2] Seasonal transmission is defined by the first and last calendar days on which 234 HDUs have accumulated during the preceding 29 days. To account for year-to-year variations and establish limits for the extreme earliest beginning and latest ending dates, our estimates for each site include analysis of a 30-year weather cycle. Because these transition days can vary considerably between sites within a region due to differences in terrain and elevation, identification of the first and last month in which transmission may be possible is a practical method of integrating this information. Our guidelines are established primarily for use of the monthly administered macrolide endectocides. Therefore, monthly chemoprophylaxis is recommended to begin on the first day of the month in which transmission might have been possible sometime during the preceding 30 days. Similarly, the final dose would be given on the first day of the month immediately following the expected termination of transmission. Maps depicting state and regional estimates of the duration of the heartworm transmission season and the corresponding first of the month beginning and ending dates are presented in Figs 1 and 2.

All indications are that the guidelines for monthly heartworm chemoprophylaxis based on this model are conservative and provide a wide margin of safety. When applied to the specific years during which the previously cited tracer dog[1] and mosquito collection[2] field studies were conducted, the estimated transmission periods encompassed evidence of either actual transmission or the presence of infective larvae in the vector mosquitoes.[2] In particular, transmission seems to cease at least 6 weeks in advance of the calculated end dates. Furthermore, by basing predictions on the extreme possibilities, which are truly unusual events, the redundance of the estimates in most other years makes transmission beyond these parameters an extremely remote possibility.

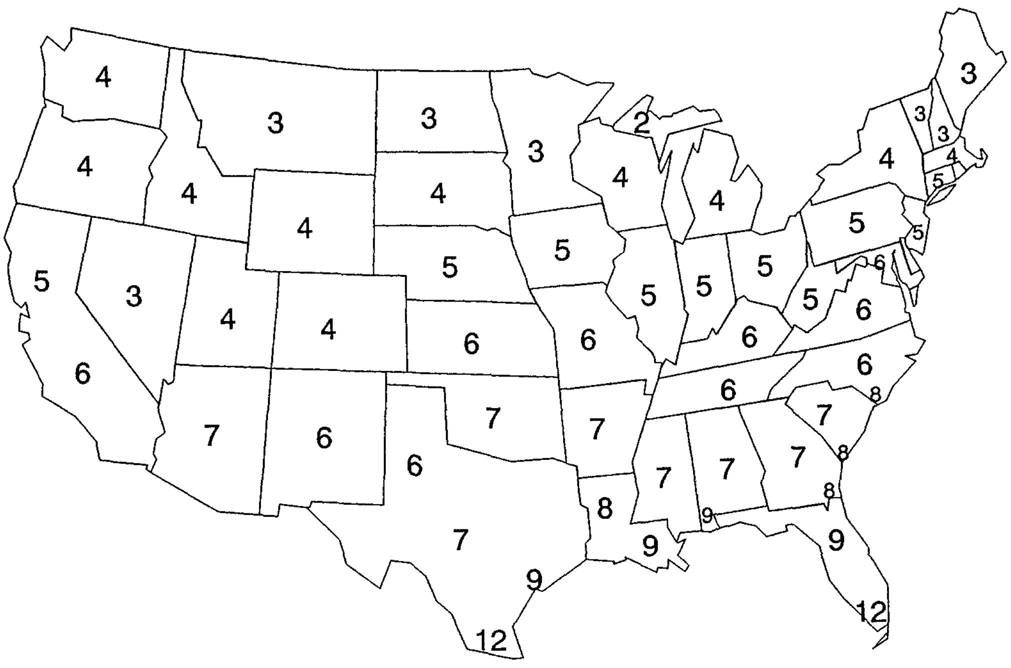

Fig 1. Numbers represent the nearest approximation of the representative duration of heartworm transmission in whole months, for each state or geographic region. These estimates are provided as guidelines only and do not reflect smaller scale regional differences.

Clinical Considerations

The data included in map format has been consolidated and is provided to illustrate the concept of seasonal transmission, not its definitive boundaries. Maps containing greater detail have already been published.[2] The number of months between inclusive first and last monthly doses of chemoprophylaxis are illustrated in Fig 1. For nearly 80% of the states, the potential for heartworm transmission is limited to 6 months or less. The primary exceptions occur in the southeastern and gulf coast states where relatively small changes in southern latitude rapidly lengthen the calculated exposure to 9 months. In the subtropical regions of Florida and Texas, conditions may support uninterrupted transmission.

Guidelines for Heartworm Chemoprophylaxis

The lengthy retroactive efficacy of the macrolide endectocides makes it unnecessary to precisely time chemoprophylaxis coincident with infection. Even if infection should precede the beginning of monthly chemoprophylaxis by 6 to 8 weeks, protection is still expected, if administration of these drugs is subsequently continued for several months.[5] There is a good chance that once pet owners start they will continue to administer the remaining doses if any commitment to heartworm prevention has been made. Although there is no value in starting monthly chemoprophylaxis before exposure to infective mosquitoes is anticipated, it is critical that administration not be discontinued prematurely before the transmission period has ended. Declining average daily temperature late in the transmission period is expected to slow maturation of infective larvae and decrease the probability that mosquitoes will survive long enough to become infective. Also, in addition to experiencing higher mortality at these times, mosquitoes seek hosts less actively. Though the temperature may still be high enough to sustain larval maturation at a slow pace, thereby theoretically extending the effective length of the transmission period, mosquito activity and viability are declining rapidly at this time of the year. This effectively reduces the

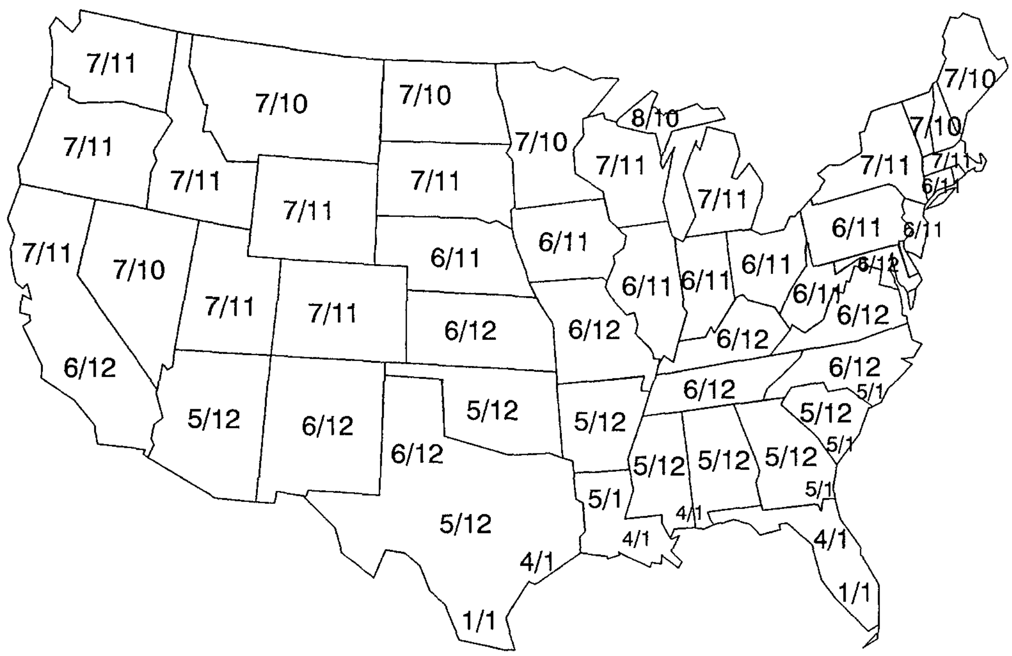

Fig 2. Each number represents the month of the year in which macrolide administration is recommended to begin and end in each state or geographic region. These estimates are provided as guidelines only and do not reflect smaller scale regional differences.

chances of infection and probably accounts for cessation of transmission weeks before the calculated date. Consequently, guidelines scheduling monthly chemoprophylaxis to start the first of the month immediately following the calculated earliest exposure and to end on the first of the month following the last likely date of exposure are both easy to keep track of and generously protective. The map in Fig 2 provides representative start and end dates for each state or region.

Based on available evidence from the field, the actual period of heartworm transmission appears to be limited to early July through late September,[1,2] with a probable gradual extension of risk at both ends of the season in the deep South. According to the model predictions, which appear to be very conservative estimates, six or fewer monthly doses are adequate in the most northern 60% of the states and very likely in the border zone to the South, as well (see Fig 2). At some length of time, seasonality as presently defined becomes less relevant as a practical concern. When there is some chance that infection is possible during more than 9 months, the expediency of maintaining continual protection may be justified at this time. It is not certain that year-round protection is ever actually necessary but the model has not been adequately tested for the possibility to be totally disregarded. Because there is no pressure from veterinarians in private practice or incentive for the pharmaceutical companies to resolve this issue, speculation will continue.

Additional Applications

It may be useful to know when heartworm transmission is likely to occur, beyond providing guidelines for the timely administration of chemoprophylaxis. Awareness of the approximate period of exposure to infective mosquitoes is a prerequisite for determining the best time to test for heartworm infection in dogs. Calculation of the latent period between infection and the appearance of microfilariae or parasite antigen (see Fig 3) requires an appreciation of when infection is possible and more to the point, when seasonal exposure is likely to end. Six and one half months is the minimum interval to ensure adequate time for detection of either microfilariae or parasite antigen, if they are going to be found at all. In this regard, it is important to realize that when routine surveillance testing is spread throughout the year, the effective testing interval may be lengthened by up to 6 months. Those who continue to emphasize the importance of annual retesting should also consider the implications of when the testing is done. The American Heartworm Society recommends retesting every second or third year, if there is a history of timely monthly chemoprophylaxis.[6]

Although routine screening for heartworm infection is not advocated for cats, other considerations aside, the latent periods for development of microfilariae and antigenemia in this species are approximately the same as in dogs.[7] However, feline antifilarial antibody may be detectable by 3 months postinfection but is frequently missed before 5 months.

Also, transmission and life-cycle timing are pertinent to analyzing other clinical issues. For example, assessing the implications of unscheduled interruptions in chemoprophylaxis, or the relationship between the onset and severity of clinical signs, in relation to when infection may have occurred, require some knowledge of the local limits of transmission. Unlike most of the major diseases we deal with, heartworm infection is controlled by recognized, tangible variables, therefore understanding of these factors can provide useful insights into the natural history of a patient's infection.

Dispensing Considerations

The macrolide endectocides are unsurpassed for preventing heartworm infection. In prophylactic doses, they are also safe, even when administered to infected dogs, if some precaution is taken at the time of the first dose in those cases with particularly high numbers of circulating microfilariae. Additionally, there is evidence that at least for ivermectin some adulticide effect is exerted.[5] With so many attributes, what harm is there in liberally dispensing these drugs? The issue that needs to be considered is whether medical justification should prevail over entrepreneurial interests in dispensing drugs intended to prevent rather than cure disease? Because veterinarians are permitted to sell the drugs they prescribe, use may not always be based strictly on medical justification. The macrolide endectocides are reasonably priced, considering their superior qualities, but incur considerable expense, particularly when more than one animal in a household needs protection. Should veterinarians be considerate of their clients' medical budget or simply let the marketplace dictate? After years of being encouraged to promote heartworm prevention with drugs guaranteed to work if only taken by the patient, some may consider it heretical to now speak of restraint. This notion and the model for predicting seasonality upon which the argument is based will take a while to gain acceptance, particularly in those areas where the climate seems to support the previously conventional wisdom. However, throughout the Northeast and midwest, as well as in the northern plains, Rocky Mountain and northwestern states, it should not be difficult to appreciate that heartworm transmission is seasonal. In these regions, the burden of proof or reasonable counterargument lies with those who persist in recommending monthly chemoprophylaxis beyond the 5-month late spring to late fall seasons.

Critique of Contrarian Rationalizations

The most commonly cited reason for encouraging uninterrupted use of monthly heartworm chemoprophylaxis in cool climates is that client habituation ensures timely administration. Although human nature suggests that this approach may work for some people, it is a policy based on misunderstanding what is required for heartworm transmission to occur. Until recently, a general lack of information on the subject has left veterinarians and their clients to act on the basis of misconception. However, given what is presently known, continued adherence to a policy of superfluous chemoprophylaxis is disquieting because financial expediency for the veterinarian conflicts with clinical objectivity, and client consent is predicated on unrealistic expectations. Clients mistakenly believe they are purchasing additional protection for their pets, but in reality they are not. If the truth were known to them, few clients would agree to unnecessarily double their expense for heartworm prevention.

Client education is every veterinarian's responsibility and is the most effective way to encourage cooperation. Even when heartworm chemoprophylaxis is obviously justified, pet owners still must elect that option and make a commitment. If exaggeration is needed to get pet owners' attention, then either their priorities are elsewhere or the message is not being delivered effectively. Our role is to make sound recommendations and guide clients toward making rational decisions. Except in matters of personal safety or humane treatment we do not have authority to dictate our personal views. Although we may consider a client to be negligent, they are ultimately responsible for their pets' welfare, and there are limits to how far we may go to ensure that our advice is followed. Distorting facts in an attempt to augment a client's resolve or coerce a course of action will ultimately undermine the client-veterinarian relationship.

If heartworm transmission under the most favorable conditions is potentially possible during only 5 to 7 months, encouraging continuation of monthly chemoprophylaxis all year diverts attention from the 3 to 4 months when the risk is probably real and definitely greatest. The summer months are the time for pet owners to be particularly conscientious about timely administration of heartworm chemoprophylaxis and renewal of prescriptions. Without an appropriate focus, treatment lapses are more likely to occur generally and, by chance alone, will sometimes happen at the most inopportune times. By placing emphasis on the seasonality of the risk, it becomes a more tangible possibility rather than a background concern that may or may not get attention. The concepts of heartworm transmission are not difficult to grasp and are more likely to register with people, if presented in a context that makes sense.

Broadening the Range of Protection

Monthly heartworm prevention has created a framework for delivering medication to control other endo- and ectoparasites. The idea has appeal and it may be useful in certain instances to combine different drugs to simultaneously target a broader range of parasites. However, in attempting to create a panacea, sight can easily be lost of the reasons for doing any of this. Whether combination products are used or not, the primary purpose of all of these is heartworm prevention. Convenience does not necessarily translate into efficiency. Ascarids and hookworms are principally problems in dogs less than 6 months and 1 year of age, respectively. In healthy, well cared for adult dogs, neither is a major cause of clinical disease and natural physiological resistence provides adequate control in all but an exceptional few. Even if monthly anthelmintic therapy is administered, the counter-adaptive tissue stages of larvae in arrested development persist and can still be activated by prolonged stress or intermittent events such as pregnancy. Whip worms are more problematic in dogs of all ages but, if necessary, can be treated appropriately with safe and inexpensive anthelmintics on an individual case basis. If heavy environmental contamination and poor husbandry put dogs at high risk of intestinal parasitism, then the background protection provided by formulated drug combinations may be worth continuing beyond the normal period for heartworm preven-

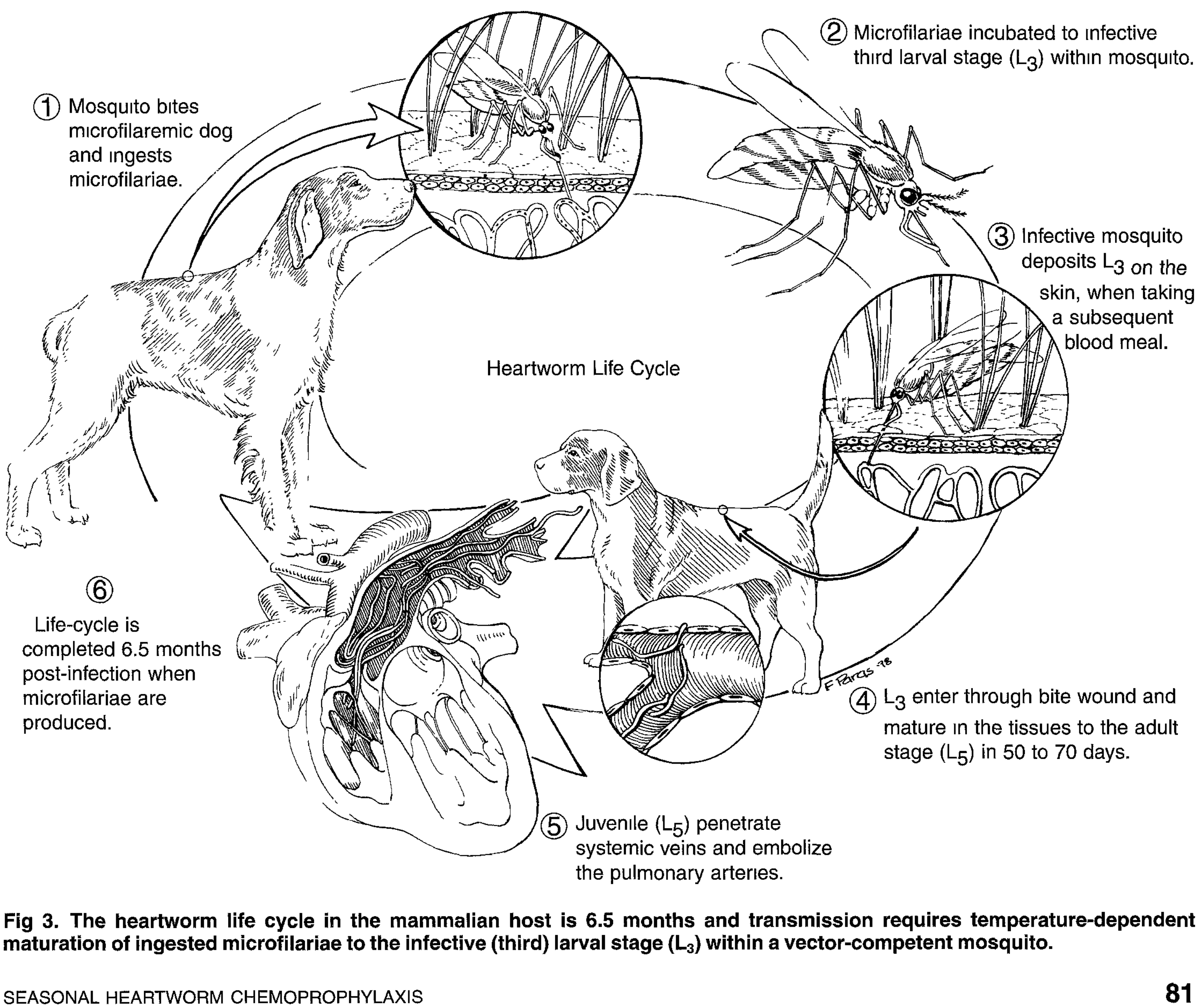

Fig 3. The heartworm life cycle in the mammalian host is 6.5 months and transmission requires temperature-dependent maturation of ingested microfilariae to the infective (third) larval stage (L_3) within a vector-competent mosquito.

tion. Similarly, if fleas are a recurring and chronic problem, they too can be dealt with on an individual basis with any of the effective options currently available, including combination heartworm chemoprophylaxis. For those patients that clearly require broad spectrum parasite control, multipurpose combination drugs address that need. However, extrapolation from this select group to the general population promotes indiscriminate treatment without regard for need and obligates pet owners to additional drug expense. The availability of these innovative treatment modalities should not be used as leverage to encourage a pattern of dispensing that habituates pet owners to administration of antiparasitic drugs whether they are needed or not.

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