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Some Considerations Relating to the Role of *Culex pipiens fatigans* Wiedemann in the Transmission of Human Filariasis*

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This paper is concerned mainly with the relationship between microfilarial periodicity and vector periodicity. The so-called " non-periodic " Pacific form of Wuchereria bancrofti *in fact shows a well-marked and relatively constant periodicity. The amplitude of this periodicity is low, which may account for the difficulty of detecting it in small clinical samples. The periodicity is well adapted to the biting cycle of* Aëdes polynesiensis, *though less so than that of the " semi-periodic "* Brugia malayi *to forest* Mansonioides. *Microfilarial periodicity is discussed in the light of recent work on circadian rhythms in other animals and it is suggested that certain possibilities have been given insufficient weight. The use of the term " migration " to describe microfilarial translocation within the host may have given rise to misunderstanding but it is in good agreement with current concepts of migration. Recent work suggests some behavioural heterogeneity in* Culex fatigans *which could render it a useful mosquito for elucidating certain important but little-understood problems.*

Despite the very extensive literature on it, *Culex fatigans* is a comparatively little-understood mosquito. The best remedy for this would be a co-ordinated series of researches on its biology, in several different parts of its range, over a period of years. This is, perhaps, too much to hope for. The best substitute would, perhaps, be a survey of the literature designed to obtain a coherent picture of the present state of our knowledge. It seems that there is some possibility of this being undertaken in the not too distant future.

The original object of the present study was to elucidate those aspects of the biology of *Culex fatigans* which seemed most relevant to the problem of filariasis. In this way it was hoped that at least some guidance might be given as to the best way of approaching the literature. As I have argued elsewhere, however, the mosquito-borne diseases are complex ecological systems in which hosts, vectors, parasites and physical environment are all equally involved (Mattingly, 1960). None of these components can be fully understood if it is studied in isolation. In the case of filariasis there are particularly strong indications of the importance of the private ecology of the parasite, within its host, in determining its relations with the vector. It has seemed best, therefore, to begin by trying to clarify the relation between microfilarial periodicity and vector periodicity in general with a view to establishing the framework within which the various periodicities governing the behaviour of *Culex fatigans* will have to be considered.

MICROFILARIAL PERIODICITY

At the present time, 24-hour rhythms in plants and animals are the subject of particularly active and stimulating research (see reviews by Harker, 1958a, 1961; Bruce & Pittendrigh, 1957; Cloudsley-Thompson, 1960, 1961. Their potential importance for our understanding of host-parasite relationships and vector-parasite relationships is very great (Mattingly, 1962b). There seems, however, to be a danger that general biologists may be misled by the picture of microfilarial periodicity which is often presented to them in textbooks of tropical medicine and the like. This is particularly true of the alleged occurrence of non-periodic forms of *Wuchereria*

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bancrofti in the Pacific area and of the various shades of meaning implied in the use of the term " migration " to describe the passage of microfilariae from the lung into the peripheral circulation. These topics will therefore be discussed from a general biological standpoint. It is hoped, however, that a brief excursion into the history of the subject may first be permitted for the sake of the light which it may throw on the important step between elucidating a 24-hour rhythm and perceiving its significance in relation to particular problems.

The demonstration by Manson (1878) of the development of *W. bancrofti* in the mosquito was the germinal event in medical entomology. Its importance in this connexion would be hard to exaggerate. Manson-Bahr (1959a, 1959b) has suggested that Manson was led to his discovery by the contemplation of nocturnal periodicity in the parasite. This, if true, would constitute a classical example of the value of this particular approach to the phenomena of life. Unfortunately, however, neither Manson's paper nor his book (Manson, 1883) gives this impression. Nor, apparently, does his diary (Manson-Bahr, 1935). All these seem to indicate that Manson did not, in fact, observe microfilarial periodicity until 1879. In view of its historical importance the issue seems worth clarifying.

DIURNAL PERIODICITY IN *WUCHERERIA BANCROFTI*

I have not seen Thorpe's paper of 1896. The earliest figures available to me are those of Bahr (1912). Since these figures played so large a part in establishing the concept of non-periodic Pacific filariasis it is interesting to find that, in fact, they justify the use of the term " non-periodic " only in a very narrow, clinical sense. When averaged (to allow for the fact that more observations were made at some times than at others) and combined, the 4-hourly figures show a periodicity which is in good agreement with that elucidated by Eyles et al. (1947) and used by them to justify the introduction of the term " diurnal periodicity ". The same applies to the only other directly comparable figures available to me, which are those of Rosen (1955). Iyengar (1955) obtained figures from New Caledonia which are only approximately comparable since his samples were taken at the odd, rather than the even, hours of the day. In spite of this the same periodicity emerges quite clearly and his figures are in good agreement with the others. In order to give a general, qualitative, picture of the periodicity I have combined all these figures for diurnal periodicity in *W. bancrofti* and averaged them in such a way as to obtain the best possible fit with all four sets of data:

2 a.m.:	13%
6 a.m.:	11%
10 a.m.:	16%
2 p.m.:	22%
6 p.m.:	22%
10 p.m.:	18%

Examination of each set of data individually reveals variations of approximately this order in the numbers of microfilariae available to the vector at these times of day in each of the four populations of infected persons. It is this aspect of the matter which is important from the epidemiological point of view and from the point of view of parasite-vector relationships, which are the main concern of the present paper. Other data which cannot be used for direct comparison, because of the irregular intervals at which samples were taken, are those of Edgar et al. (1952) from Tahiti and Symes (1960b) from Fiji. Edgar et al. considered that their data favoured the occurrence of diurnal periodicity and Symes, while unwilling to commit himself, nevertheless observed a sufficient preponderance of microfilariae in the afternoon and evening to induce him to take most of his samples at those times. Edgar et al. also quote Jachowski as having obtained evidence of microfilarial periodicity in Samoa. Some 12-hourly figures are also available, but they reveal relatively little since they were based on samples taken at 10 a.m. and 10 p.m. The figures tabulated above may suggest that it would have been more useful to take samples at 6 a.m. and 6 p.m.

The only figures I can find which might suggest a truly non-periodic form of the parasite are some small ones of Manson-Bahr & Muggleton (1952), which seem to be quite outweighed by the others. For the rest there are only general statements which seem to imply no more than that the Pacific form of *W. bancrofti* is non-periodic in the sense that it reveals no obvious periodicity in single 24-hour periods in individual hosts. To the general biologist this purely clinical use of the term is liable to be misleading. He may also form the impression that *W. bancrofti* is non-periodic over most of the Pacific but may exhibit diurnal periodicity in some areas. This, to my mind, would falsify the evidence, which is that it is non-periodic, in the clinical sense, over the whole area but periodic, in the present sense, at least in all those parts which have been properly investigated.

The most satisfactory way of confirming the existence of this rhythm would, of course, be to reverse it as has been done in the case of nocturnal periodicity. An experiment of this kind does not seem at all impossible in principle since there are a number of cases on record in which single individuals seem to have exhibited the rhythm when samples were totalled over only a very few days. It might be best to choose a patient with fairly heavy microfilaraemia since there are some indications that the rhythm may be reduced or suppressed in individuals with relatively light microfilaraemia. The evidence as to this is not conclusive but it seems worth bearing in mind in any future investigations since its epidemiological and parasitological implications could be important.

So far as indirect evidence is concerned, it may be noted that the occurrence of some form of periodicity would lend support to the theory of Hawking & Thurston (1951a, 1951b) regarding the nature of microfilarial periodicity. If, as they suggest, there is an advantage to the parasite in remaining in the general circulation only as long as is necessary to make contact with the vector, then it will clearly be better suited by a rhythm of the kind here invoked than by a non-periodic distribution, provided the rhythm matches the biting rhythm of the vector. In this case the principal vector is believed to be *Aëdes polynesiensis*, and I have taken 4-hourly readings from the charts given by Jachowski (1954) to illustrate the biting cycle of this species under a variety of conditions:

2 a.m.:	2%
6 a.m.:	18%
10 a.m.:	16%
2 p.m.:	27%
6 p.m.:	31%
10 p.m.:	5%

The average figures above represent, in each case, the total number of mosquitos taken biting during one hour and so are not directly comparable with the hourly samples of microfilariae. Nevertheless they give a general picture of the biting rhythm which is sufficiently precise for present purposes. It will be seen that there is a general correspondence between the main period of biting activity and the period of greatest microfilarial abundance. This correspondence, though far from perfect, is of such an order as materially to increase the numbers of microfilariae exposed to the vector.

The term " diurnal periodicity " is open to objection since it could lead to misunderstanding if it were taken to imply either that there is a complete reversal of the periodicity found in the nocturnal form of the parasite or that microfilaraemia is at a low level during the early part of the night. A better term should, if possible, be found. The term " diurnal " does, however, serve to emphasize the adaptiveness of this type of periodicity to the habits of a diurnal vector and, in my view, it is likely to lead to less confusion than the use of such terms as " aperiodic " and " non-periodic ", which conceal the existence of a quite patent rhythm.

NOCTURNAL PERIODICITY IN *WUCHERERIA BANCROFTI*

Lane (1948) quotes a certain Gratiano as taunting Cobbold with the question " whether the filariae carried watches ". This is a very pertinent question which is still unanswered. Before discussing it, however, something must be said of the prevailing attitude among biologists to animal clocks and 24-hour rhythms in general.

Rhythmical changes of a physiological or behavioural nature often exhibit a 24-hour (diel) or approximately 24-hour (circadian) periodicity. Such rhythms are of two kinds, those which change immediately in response to changing periodicity in the environment and those which persist for two or more 24-hour periods in an altered environment. Reversal experiments, such as those of Yorke & Blacklock (1917), Hinman (1936) and Boughton et al. (1938), are generally taken to imply the existence of a persistent rhythm in the human host, the question of the occurrence or otherwise of a rhythm in the microfilariae being ignored. Persistent rhythms have, however, been shown to occur in a great variety of animals (see the reviews quoted above) and the intuitive response of most biologists to the phenomena of microfilarial periodicity would probably be to suppose the existence of a rhythm in the microfilariae while admitting that, given time, this tends to be overridden by or brought into phase with the host rhythm. Such an assumption is in fact made by Harker (1958a) and Cloudsley-Thompson (1960, 1961), two leading authorities in this field. Harker (1958b) has herself very beautifully demonstrated the interplay between host and implant rhythm in the induction of cockroach tumours and it could well be that such phenomena play a more important part in processes of infection in general than is commonly realized.

Yorke & Blacklock found that it took 11 days to reverse the microfilarial periodicity after initiation of reversed periodicity in the human host. This compares with only 4 days required to reverse the human diel temperature rhythm (Sharp, 1961), which might suggest that extra time is needed in order to bring the microfilarial rhythm into phase with the host rhythm. On the other hand, there may be host rhythms which take longer than 4 days to reverse. The problem does not seem capable of solution without studying isolated microfilariae either *in vitro* or in a clean host. Transfusion into a clean host and maintenance thereafter of the rhythm has been shown to be possible by Knott (1935) and Kartman (1953). It might therefore be possible, in principle, to test for the presence of a persistent rhythm in the parasite by transferring it to a host with opposite rhythm. This could take the form either of a night-time transfer of microfilariae from a donor with normal rhythm to a recipient with reversed rhythm or of a daytime transfer of microfilariae from a donor with reversed rhythm to a recipient with normal rhythm. Unfortunately the existence of numerous unsuccessful night-time transfers (e.g., Knott, 1935; Hawking, 1940) suggests that other factors exist which would militate against the success of more than a small proportion of such experiments, at least with *W. bancrofti*. The only successful transfusion experiment in which persistent periodicity was observed (Knott's Case E.D.) was performed at night, when the periodicity of donor, parasite and recipient would all be optimal. It is therefore inconclusive. An experiment with some non-human filaria, involving a perfectly healthy recipient, might possibly have a better chance of success.

The lack of any current theory as to the mechanism of immobilization in the lungs renders difficult the discussion of possible *in vitro* experiments. It might, however, be pointed out that the agglutination and thigmotaxis hypothesis of Yoeli (1957b) could be extended to include diel changes in surface properties of microfilariae as well as changes in the host. Hawking (1955; and see McFadzean & Hawking, 1956) reports some work on behaviour of microfilariae in an electrophoretic cell but it is not clear that any attempt has been made to compare surface charges at different times during the diel period.

An interesting question concerns the manner in which a rhythm in the parasite may be brought into phase with the solar rhythm. This is generally achieved by exposure to some environmental change which serves as a cue. The commonest form of cue appears to be a light cue. This may be of very short duration (of the order of 1/2000 of a second in *Drosophila*) but, in general, exposure to light has to be more protracted—e.g., 5 minutes at least in *Aëdes aegypti* (Gillett et al., 1959), 2 hours in *Periplaneta americana* (Harker, 1960). In the present instance the cue could well be provided by a periodic change in the environment provided by the host. This is not, however, the only possibility. The suggestion by Harker (1958a) that the microfilarial rhythm might be imposed by the vector would account very elegantly for the difference between nocturnal and diurnal periodicity and it has the merit that it could be tested by reversing the periodicity of the vector, an easy matter (see, for instance, Haddow & Gillett, 1957). The main objection is, perhaps, that the rhythm would need to persist throughout the maturation of the larvae and then be imparted to their offspring. This would certainly be an extreme case of persistence but some such have been encountered. Thus Park & Keller (quoted by Harker, 1958a) observed an activity rhythm in the beetle *Boletotheros cornutus* which was maintained for 3 months in continuous darkness and constant humidity even though it passed during this time through the reorganization involved in developing from larva to adult. It is also possible that such a rhythm could be reinforced by a regularly timed parturition of the kind postulated by Lane (1948). It is true that experiments such as those of Culbertson et al. (1947) appear to rule out the possibility of a regular daily parturition but they do not exclude the possibility that parturition, when it does take place, does so at a constant time.

A more attractive hypothesis might be the administration of a cue by the change from vector to host environment. The fact that infective larvae are not injected direct into the host but spend a short time on the skin is interesting since it offers the possibility of a direct imposition of the solar rhythm by the external environment. An ordinary light cue of the familiar kind seems to be ruled out, however, by the fact that larvae of nocturnally periodic forms are not exposed to light at this time. It is also, perhaps, worth noting that Bray & Walton (1961) observed that *Dirofilaria uniformis* transferred to a new host by injection maintained a rhythm matching that of the mosquito vector, although in this case there was no exposure on the skin.

Although attempts have recently been made to give the word " migration " a physiological rather than a behavioural basis, it is probable that many people still think of it in terms of an active translocation on the part of the organism. It is possible that the " active " phase in the microfilariae amounts to no more than " active embarkation on some transporting vehicle " (Kennedy, 1961). This is in good agreement with observations such as those of Yorke & Blacklock (1917), which seem clearly to indicate that the effective agency in the production of microfilaraemia is a release into the general circulation rather than any particular concentration in the peripheral circulation as such. The other recent trend which is of interest here is the tendency to think of migration in terms of a physiological syndrome involving the temporary suppression of vegetative functions and the accentuation of sensorimotor ones when this becomes necessary for the continuation of the species. It will be seen that Hawking & Thurston's view of microfilaraemia as the temporary abandonment of a favoured site in the lung and the adoption of the circulating blood as a means of transport, " in order to " make contact with the vector, is in rather striking accordance with recent ideas as to the nature of migration in general.

Recent experiments designed to elucidate the nature of the physiological changes in the human host which " stimulate " the microfilariae to embark (McFadzean & Hawking, 1956; Edeson et al., 1957) are interesting, although performed under highly unbiological conditions, but they are liable to be seriously misinterpreted if attention is paid solely to the direct effect of host rhythms on the parasite when in fact these are serving mainly to cue or synchronize a rhythm in the parasite itself.

PERIODICITY IN *BRUGIA MALAYI*

Turner & Edeson (1957) distinguished two forms of *B. malayi*, from Penang and East Pahang respectively, with very distinct microfilarial periodicity. These have been characterized by Wilson (1961) as periodic and semi-periodic respectively. The term " semi-periodic " is open to objection on the grounds that, in the nature of things, phenomena are either periodic or non-periodic. It is, however, much less misleading than " non-periodic " and it is therefore retained here for the moment. The following 4-hourly figures for " semi-periodicity " of *B. malayi* have been read off from Turner & Edeson's curve and embody their own method of averaging:

B. malayi *E. Pahang form*	*W. bancrofti* *Diurnal form*
10 a.m.: 15%	2 a.m.: 13%
2 p.m.: 13%	6 a.m.: 11%
6 p.m.: 17%	10 a.m.: 16%
10 p.m.: 20%	2 p.m.: 22%
2 a.m.: 20%	6 p.m.: 22%
6 a.m.: 15%	10 p.m.: 18%

Other methods of averaging are possible but do not greatly alter the general qualitative picture. The figures for diurnal periodicity of *W. bancrofti* given earlier have been included here for comparison, the time scales being staggered in such a manner as to achieve the best correspondence. It will be seen that, while the two rhythms agree closely in amplitude, the maximum is reached during the early part of the night in the case of the semi-periodic form while, as has already been shown, it is reached during the afternoon in the diurnal form.

While this tabulation gives an adequate picture of the general nature and amplitude of the periodicity, it is quite unsuited to detailed quantitative comparisons. Haddow (1954) has emphasized the dangers inherent in the use of intervals as large as 4 hours and this is a good example. Thus a casual glance at the above tabulation might suggest that the two rhythms are out of phase to the extent of about 8 hours but this almost certainly is an exaggeration. Reference to the 2-hourly figures shows that the greatest microfilarial density, in the semi-periodic form, is recorded at 8 p.m. while in the diurnal form it is apparently reached at about 4 p.m. The difference in phase is probably, therefore, of the order of only about 4 hours. In the present instance this may not be a very important point because the amplitude of the periodicity is too small for any talk of " peaks " to have very much meaning. Thus in both cases a high level of microfilaraemia is maintained for a considerable time after the maximum is reached.

The main vectors of the semi-periodic form of *B. malayi* are thought to be *Mansonia (Mansonioides) bonneae*, *dives*, *annulata*, and *uniformis*. All these are excellent laboratory vectors and all have been found infected in nature. The first two are more widely distributed than the others (Wilson, 1961). No published data relating to the biting cycle are available but Dr Wharton has kindly allowed me to quote from a manuscript of his Ph.D. thesis (Wharton, 1960) in the possession of Dr Reid. This contains very full and excellent data including combined figures for *M. bonneae* and *M. dives* in houses and in open and shaded situations around houses, similar figures for *M. uniformis* and figures from the ground and the lower storey canopy (at about 50 feet, or 15 m) in swamp forest for *M. bonneae* and *M. dives* individually and for *M. annulata*. Outside the forest biting is largely nocturnal except in shaded situations outside houses, where about 15% of all biting takes place in the daytime in *M. bonneae* and *M. dives* and about 7% in *M. uniformis*. Biting in the forest canopy is almost exclusively nocturnal, as it is in unshaded situations outside the forest. This is to be expected since the canopy is ecologically, in many respects, to be regarded as an extension of the surrounding country rather than as part of the forest itself (Mattingly, 1960).

On the forest floor the situation is radically different. Here Wharton records 47% of all biting in *M. dives*, 40% in *M. annulata* and 34% in *M. bonneae* in the daytime. This is in striking correspondence with Turner & Edeson's figures for " semi-periodic " *B. malayi*, which show that 41%-42% of the entire sample of microfilariae were found in day blood. It cannot be doubted that this form of microfilarial periodicity is highly adaptive to transmission by forest *Mansonioides*. In contrast it is largely contra-adaptive to transmission from man to man, at least in houses, since the high daytime microfilaraemia necessarily implies an equal and balancing reduction in nocturnal filaraemia. This does not imply that *Mansonioides* spp. are not important man-to-man transmitters since there is considerable opportunity for daytime transmission out of doors in shaded situations. There is also a high level of nocturnal microfilaraemia, in fact slightly higher than in the daytime, even though this is not so high as in purely nocturnal filaria, so that intra-domiciliary transmission may well be important. It does, however, strongly suggest that man is an intruder into the situation and that the primary hosts are forest animals.

The biting cycle figures suggest that a more detailed analysis might be justified were comparable figures available for the microfilarial periodicity. Unfortunately, however, the 2-hourly samples taken by Turner & Edeson are too coarse for this purpose and their times, unlike those of Wharton, are not adjusted to take account of the time of sunset (see Haddow (1954) on the subject of " catch time").

All that can be said from these figures is that maximum microfilarial density seems to be reached between 6 p.m. and 10 p.m., though it remains at a high level at least until 2 a.m. In the forest *M. bonneae*, *dives* and *annulata* reach their biting peak during the hour after sunset (i.e., roughly between 6 p.m. and 7 p.m.) on the forest floor and in either this hour or the following one in the canopy. There is also a secondary peak shortly before daybreak in the canopy, though this is barely perceptible on the ground. In houses maximum biting is recorded for *M. uniformis* between 7 p.m. and midnight while the combined figure for *M. bonneae* and *M. dives* shows it as occurring between midnight and 2 a.m. There is thus a large area of contact between parasite and vector both in houses and in the forest. If this form of *B. malayi* were primarily a human parasite, however, it would seem reasonable to anticipate a higher level of nocturnal filaraemia.

The behaviour of the East Pahang form of *B. malayi* seems to reveal quite clearly the basic nature of the difference between nocturnal and diurnal periodicity. This is a difference in both phase and amplitude. Suppression of the massive night-time peak found in nocturnal *W. bancrofti* is a necessary corollary to the increased availability of microfilariae in the day blood. The fact that nocturnal filaraemia remains at a fairly high level rather than being completely suppressed, as would be the case were there a complete reversal of the rhythm, leads in turn to the production of relatively low peak levels with corresponding increase in sampling errors. I suspect that this is the main cause of the relatively cryptic nature of the rhythm and the difficulty of detecting it in small clinical samples. It is possible that there are also physiological factors responsible for the " instability " of the diurnal and " semi-periodic " rhythms. A proper statistical analysis would probably throw light on this.

In my view the term " semi-diurnal " would be more appropriate than " semi-periodic " for the type of rhythm found in the East Pahang form of *B. malayi*. It is, of course, fully periodic and it is clearly adaptive to vectors which do about half their biting in the daytime. The term " diurnal " similarly remains appropriate for the Pacific form of *W. bancrofti* since it indicates adaptiveness to a fully diurnal vector. It is, however, admittedly misleading in that there is no difference in amplitude from the semi-diurnal periodicity and consequently a high level of microfilaraemia is encountered at night. It is interesting, but in the present state of our knowledge probably not very profitable, to speculate as to why the Pacific form of *W. bancrofti* has not achieved a complete reversal of the rhythm found in the nocturnal form. The answer could be physiological or historical or it could be that nocturnal transmission in the Pacific area is more important than has been realized.

The principal vector of the nocturnal Penang form of *W. malayi* is not known with certainty, though it seems probable that it is *Anopheles barbirostris* (Reid—personal communication). No data are available regarding the biting cycle of this species, though some are available for African members of the group *Myzorhynchus*. Figures available for *A. obscurus* (Mattingly, 1949b) and *A. coustani* (Mattingly, 1949b; Haddow, 1954) are too small to give any idea of the biting cycle, but some which are available for *A. paludis* show a regular cycle (Mattingly, 1949b). These reveal a type of biting activity which closely resembles the periodicity found by Turner & Edeson in Penang *B. malayi*. Biting is very largely nocturnal, only about 8% occurring during the day, and there is a main peak at about midnight. A more detailed comparison is shown in the following tabulation:

Time	*B. malayi* Penang form	*Anopheles paludis* 1-hour samples	2-hour averages
11 a.m.	0	1%	1%
3 p.m.	1%	1%	1%
7 p.m.	6%	2%	8%
9 p.m.	16%	5%	11%
11 p.m.	19%	16%	18%
1 a.m.	18%	25%	23%
3 a.m.	17%	18%	16%
5 a.m.	15%	14%	13%
7 a.m.	8%	18%	10%

The figures shown for *A. paludis* in the third column are for samples collected at the same hours (by Local Standard Time) as Turner & Edeson's samples. They are not, however, directly comparable since they represent the total number of mosquitos biting during the preceding hour (see above). Averages between this hour and the hour following might make a better comparison and these are therefore shown in the last column. It will be seen that agreement is, in fact, somewhat better, but in any case it is clear that if the biting cycle of *A. paludis* is characteristic of *Myzorhynchus* and a similar biting cycle is accordingly shown by *A. barbirostris*, then in this respect the latter will be as well suited to the transmission of periodic *B. malayi* as it is in other respects. This is not true of all suspected major vectors of nocturnal filariasis, in particular *A. gambiae* (see Mattingly, 1949a; Haddow, 1954). The question of the biting cycle as a group character is an interesting one which is currently receiving attention (Haddow, 1960).

PERIODICITY IN *CULEX FATIGANS*

In a previous paper (Mattingly, 1957) I drew attention to the biological and morphological resemblances between *Culex pipiens* subsp. *fatigans* and *Culex pipiens* var. *molestus*. These are much more extensive than the resemblances between either and *C. pipiens pipiens*. Barr (1960) prefers to relate *C. p. molestus* to *C. p. pipiens* by reason of the resemblance in their terminalia, to which he attributes more significance than to any of the other characters. This appears a somewhat prejudiced stand. It is perfectly true that the male terminalia often provide excellent taxonomic characters but they possess no special intrinsic virtue. On the contrary, crossing-experiments show that the character of the male terminalia is extremely labile, a continuous range of intermediates being produced. As against this, resemblances between *C. fatigans* and *C. molestus*, all of which differentiate them from *C. pipiens*, include the following: paler colour, suppression of knee spots and of dark spots on venter (Van Someren et al., 1955) short male palps, short larval siphon, preference for foul water, frequent use of underground breeding places, facultative anthropophily, stenogamy, autogeny (recently reported in *C. fatigans* by Bhatnagar et al., (1958) with some rather odd features), absence of gonadotrophic dissociation and ability to act as natural vectors of *W. bancrofti* (Yoeli, 1957a). Differences certainly exist, as is shown by the difference in male terminalia and the difference in distribution, but there does not seem to be any experimental work on the extent to which the former can be modified by environmental circumstances. In view of their genetical compatibility and resemblances in behaviour it seems desirable to include *C. molestus* and *C. p. pallens* (probably a *pipiens-fatigans* or *molestus-fatigans* hybrid) in any review of *C. fatigans*, more especially if such a review is to be related to filariasis, since all are known vectors.

Van Someren et al. (1958) give some interesting figures for *C. fatigans* which seem to imply quite a different biting cycle in the bush from that encountered in houses and compounds. Smith (1961) also has very interesting figures relating to indoor and outdoor biting of *C. fatigans* and also to the effects of dieldrin spraying on the biting cycle. Despite his statement to the contrary, his figures seem to indicate a perceptible change in the biting cycle, the indoor biting cycle after spraying apparently conforming more to the outdoor than to the indoor cycle as observed before spraying. Such an effect could be the result of selection of an exophilic element in the population (Mattingly, 1962a) and it would be worth watching for on future occasions. In the same paper Smith gives evidence of a " dramatic change " in the biting cycle of *Mansonia uniformis* after spraying and suggests that this might imply some form of heterogeneity in the population. Suggestions of behavioural heterogeneity of this kind have previously been made in the case of the closely related *Mansonia africana* (see Mattingly, 1957). It has been suggested that the differences in biting activity might be related to differences in age or in physiological condition (with particular reference to the ovarian cycle). Subsequent work, however, seems to render this less probable (Gillett, 1957, Haddow & Gillett, 1958). A consideration requiring to be taken into account is the fact that the " biting cycle " is the expression of a variety of activities, among them general flight activity and the making of contact with the host (Mattingly, 1962a). All such factors are likely to be the subject of some degree of genetical heterogeneity in the population. If so, they must necessarily be subject to selection. This could be a very important factor in relation to current disease eradication programmes involving the use of residual insecticides, since the selection pressures which these exert may be very large. *Culex fatigans* could well be a highly suitable mosquito for studying problems of this kind, which are, at present, very little understood.

The conditions under which *C. fatigans* will bite a human host are obscure and interesting and badly in need of further study. Such studies need to be correlated with others on general flight activity and entry into houses. There is also a need for studies on long-term periodicity affecting seasonal changes in behaviour. In temperate latitudes *C. molestus* overwinters by virtue of its ability to breed in the dark. It appears that in some areas *C. fatigans* may depend on a similar faculty during unfavourable times of the year (Ansari, 1958).

The present study should be regarded as purely exploratory. It is hoped that some of what has been said may help to co-ordinate our approach to this very puzzling mosquito. Symes has publicly proclaimed it the most redoubtable mosquito of all. Waddy has replied by championing the cause of *Anopheles gambiae*. I should be inclined to press the claims of *Aëdes aegypti* were it not that all three seem to me to merit equal attention. They are the representatives *par excellence* of three very different groups of mosquitos. Each of them has something to teach us about mosquito biology which we cannot readily learn from the others. Of the three, *Culex fatigans* has received by far the least attention. This implies not only a serious gap in our knowledge of filariasis but a serious gap in our knowledge of mosquito biology as a whole.

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RÉSUMÉ

En dépit de la littérature abondante qui lui a été consacrée, *Culex fatigans* demeure relativement mal connu. Sans doute serait-il nécessaire de procéder à une étude coordonnée de sa biologie qui serait conduite en divers points géographiques et s'étendrait sur plusieurs années, afin de parvenir à une connaissance cohérente et complète de ce moustique.

Dans le présent article, l'auteur s'attache à élucider plus particulièrement les aspects biologiques de *C. fatigans* dans leurs relations avec la filariose. Il étudie notamment les relations qui existent entre la périodicité des microfilaires et celle de l'agent vecteur.

Contrairement à la notion retenue par certains traités classiques de médecine tropicale, les variétés de *Wuchereria bancrofti* rencontrées dans la zone du Pacifique accusent une périodicité bien définie et relativement constante. Toutefois, elle est de faible amplitude et, par conséquent, difficile à mettre en évidence dans des échantillons cliniques de faible importance.

Chez *Aëdes polynesiensis*, la périodicité est bien adaptée au cycle des piqûres; moins cependant que la « semi-périodicité » de *Brugia malayi* à ses principaux vecteurs, c'est-à-dire à *Mansonia (Mansonioides) bonneae*, *dives*, *annulata* et *uniformis* qui vivent dans les forêts. Alors que

la densité des microfilaires connait un maximum entre 18 et 22 h, restant élevée jusqu'à 2 h, *M. bonneae*, *dives* et *annulata* piquent au maximum entre 18 et 19 h en forêt; dans les habitations, *M. uniformis* prend ses repas de sang surtout entre 19 et 24 h, tandis que l'horaire est de 24 à 2 h pour *M. bonneae* et *dives*: la période de contact entre le parasite et le vecteur est donc très étendue, tant en forêt que dans les habitations.

L'activité de *C. fatigans* est soumise à un ensemble de facteurs qui mériteraient une étude plus approfondie; ces divers facteurs (âge, état physiologique, rythme de ponte, activité de vol, prise de contact avec l'hôte, etc.) présentent un certain degré d'hétérogénéité à l'intérieur des populations de moustiques et conditionnent leurs cycles de piqûres. Ces particularités font de *C. fatigans* un moustique particulièrement utile pour la recherche, car il serait de nature à apporter quelques éclaircissements dans certains problèmes importants et encore peu connus.

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