LABORATORY MODELS IN FILARIASIS: A REVIEW OF FILARIAL LIFE-CYCLE PATTERNS

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INTRODUCTION

While clinical, epidemiological and pathological study of filarial disease processes in man has yielded valuable results, laboratory models are pre-requisite to the detailed understanding of the basic physiological, immunological, pathological, evolutionary, chemotherapeutic and ecological considerations underlying various aspects of both "normal" and "zoonotic" filariasis. The purpose of the present paper is to discuss actual and potential laboratory models from the viewpoint of availability based on life cycle studies.

LABORATORY MODELS IN FILARIASIS

The *sine-qua-non* of the term, *laboratory model*, is knowledge of both the life cycle of the chosen agent and of its vector and the ability to duplicate these in the laboratory. The term has several additional implications: (1) in a study of host-parasite relations in the final host, the model system must mimic as closely as possible one or more features of human infection, and (2) there must be control over experimental variables related to the experimental final host, the agent and the vector. Final-host variables in filariasis-models are such things as innate susceptibility; physiological, immunological and anatomical parameters; age (including maturation rate and longevity); sex factors and nutritional status. Agent variables include species or strain, worm burden, site of inoculation and localization, age and longevity of worms and recovery rates. Vector variables include order, species and genetic strain; ease of laboratory rearing or maintenance of wild-collected species; ease of feeding, of collecting vectors from hosts and finally of recovering filarial larvae from the vector. Fig. 1 (modified after Wenk, 1967) gives an overview of human filarial parasites and their location together with some currently used and some potential laboratory models for their study. This diagram does not exhaust the potential models (see Table 1).

REVIEW OF LIFE-CYCLE PATTERNS

Spiruroid and Filarioid life cycles were reviewed in depth by Chabaud (1954a, b, c), who at that time listed 29 known filarial cycles, double the number reported earlier by Williams (1948). The number of reported life cycles was increased to 35 in the review of Lavoipierre (1958), to 39 in Hawking and Worms (1961), and to 50 by Nelson (1964). Sonin's (1966) summary included previously missed and more recent Russian studies to give a total of 59. Macdonald (1971) listed 57 cycles, including *Wuchereria lewisi*, but omitted the Diplotriaenids, which do not have hemophagous vectors. The rapid growth of knowledge and interest in this group is indicated by the recording of 93 life cycles in the present review (Table 1).

DISCUSSION

Vector - and Tissue - specificity

Reordering and analysis of known cycles (Table 1) shows several interesting patterns (or the lack thereof) that merit discussion.

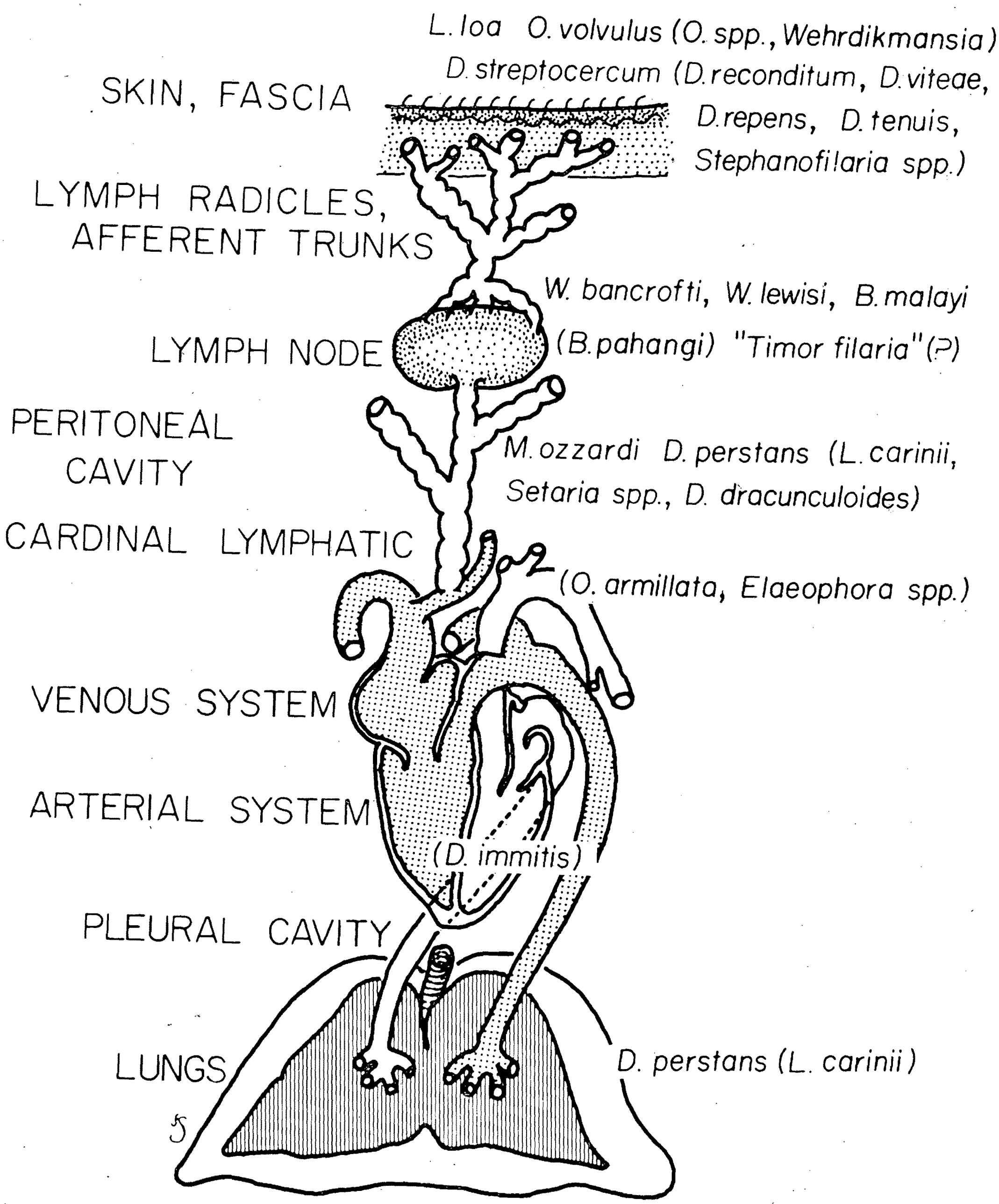

Fig. 1—Diagram to show the site of localization of the most important human filarial parasites and (in parentheses) some currently used or potential laboratory models for their study. (Modified after P. Wenk, 1967; *Z. Parasitenk*, 28: 240-263).

Table 1

Synopsis of life cycles in superfamily filarioidea.

Filaria	Definitive Host	Intermediate Host	Development Site of Larva	Reference
Desmidocercidae				
Desmidocerca spp.	Aves : Ciconiiformes	Cepepods(?)	?	Nelson, 1964; Chabaud, 1965
Diplotriaenidae				
Diplotriaenoides translucidus	Aves : Passeriformes	Grasshoppers	Hemocele	Anderson, 1957, 1962
D. isabellina	Aves : Passeriformes	Grasshoppers	Hemocele	Anderson, 1957, 1962
Serratopiculum tendo	Aves : Falconiformes	Locusts, dung-beetles	Fat body	Bain & Vassiliades, 1969
Filariidae				
Parafilaria multipapillosa	Equidae	*Haematobia atripalpis*	Fat body	Gnedina & Osipov, 1960
Setariidae				
Setaria cervi (= *labiato-papillosa)*	Bovidae	Mosquitoes	Thoracic muscles	Nelson, 1962
S. digitata	Bovidae	Mosquitoes	Thoracic muscles	Shoho, 1951; Shoho & Nair, 1960; Varma *et al.*, 1971
S. marshalii	Bovidae	Mosquitoes	Thoracic muscles	Kadenatsii, 1956
S. altaica	Cervidae	Mosquitoes	Thoracic muscles	Osipov, 1966
S. yehi	Cervidae	Mosquitoes	Thoracic muscles	Weinmann, 1972 (pers.comm.)
S. equina	Equidae	Mosquitoes	Thoracic muscles	Innes & Shoho, 1953; Nelson, 1959
S. sp. (*javensis*? *Papillosetaria* sp.?)	Tragulidae	Mosquitoes	?	Ramachandran *et al.*, 1963
Stephanofilaria stilesi	Bovidae	*Lyperosia titillans* *Haematobia irritans*	Fat body?	Ivashkin *et al.*, 1963a, b; Hibler, 1966
St. assamensis	Bovidae	*Musca conducens*	Fat body?	Srivastava & Dutt, 1963
St. kaeli	Bovidae	*Musca conducens*	?	Mullin, 1971
St. sp.	Bovidae	*Musca conducens*	?	Kono & Fukuyoshi, 1967
Onchocercidae				
Oswaldofilariinae				
Conispiculum flavescens	Reptilia: Agamidae	Mosquitoes	Fat body	Pandit *et al.*, 1929
Oswaldofilaria bacillaris	Reptilia : Alligatoridae	Mosquitoes	Fat body	Prod' hon & Bain, 1972
O. chlamydosauri	Reptilia : Agamidae	Mosquitoes	Fat body	Mackerras, 1953; Johnston & Mawson, 1943

Life cycles: filarioidea (Cont'd).

Filaria	Definitive Host	Intermediate Host	Development Site of Larva	Reference
Onchocercidae (Cont'd)				
Icosiellinae				
Icosiella neglecta	Amphibia : Anura	Ceratopogonids	Thoracic muscle	
		Psychodids	Thoracic muscle	Desportes, 1941-42
Dirofilariinae				
Loa loa	Man	*Chrysops* spp.	Fat body	Connal & Connal, 1922; Lavoipierre, 1958a
Loa papionis	Primates : Cercopithecidae	*Chrysops* spp.	Fat body	Duke, 1964
Pelecitus ceylonensis	Aves : Columbiformes, Galliformes	Mosquitoes	Fat body	Dissanaike, 1967 (in Cheong & Omar, 1970)
Foleyella brachyoptera	Amphibia : Anura	Mosquitoes	Fat body	Causey, 1939; Kotcher, 1941
F. dolichoptera	Amphibia : Anura	Mosquitoes	Fat body	Causey, 1939; Kotcher, 1941
F. ranae	Amphibia : Anura	Mosquitoes	Fat body	Causey, 1939; Kotcher, 1941
F. duboisi	Amphibia : Anura	Mosquitoes	Fat body	Witenberg & Gerichter, 1944
F. furcata	Reptilia : Chamaeleontidae	Mosquitoes	Fat body	Brygoo, 1959; Bain, 1969
F. philistinae	Reptilia : Agamidae	Mosquitoes	Fat body	Schacher & Khalil, 1968
F. candezei	Reptilia : Chamaeleontidae	Mosquitoes	Fat body	Bain, 1970
F. flexicauda	Amphibia : Anura	Mosquitoes	Fat body	Crans, 1969; Schacher & Crans, 1973; Benach & Crans (pers. comm.)
Dirofilaria immitis	Canidae, Felidae	Mosquitoes	Malph. tubules	Taylor, 1960; Orihel, 1961
D. repens	Canidae, Felidae	Mosquitoes	Malph. tubules	Fuelleborn, 1908; Webber & Hawking, 1955
D. tenuis	Procyonidae	Mosquitoes	Malph. tubules	Pistey, 1956
D. magnilarvatum	Primates : Cercopithecidae	Mosquitoes	Malph. tubules	Wharton, 1959
D. striata	Felidae	Mosquitoes	Malph. tubules	Orihel & Ash, 1964
D. subdermata (= spinosa)	Rodentia : Erethizontidae	Mosquitoes	Malph. tubules?	Highby, 1939
D. scapiceps	Lagomorpha : Leporidae	Mosquitoes	Fat body	Highby, 1943a, b
D. uniformis	Lagomorpha : Leporidae	Mosquitoes	Fat body	Bray & Walton, 1961
D. corynodes (= aethiops?)	Primates : Cercopithecidae	Mosquitoes	Fat body	Webber, 1955; Orihel, 1969
D. roemeri	Marsupialia : Macropodidae	Tabanidae	Fat body	Spratt, 1970, 1971 (pers. comm.)
Macacanema formosana	Primates : Cercopithecidae	Ceratopogonids	Thoracic muscle	Bergner & Jachowski, 1968
Onchocercinae				
Macdonaldius oschei	Reptilia : Boidae	Argasidae	Malph. tubules	Frank, 1962, 1964
M. andersoni	Reptilia : Helodermatidae	Argasidae	?	Nelson, 1964
Saurofilaria innisfailensis	Reptilia : Agamidae	Mosquitoes	Fat body	Mackerras, 1962
Cardiofilaria nilesi	Aves : Galliformes	Mosquitoes	Thoracic muscle	Dissanaike & Fernando, 1965
Aproctoides lissum	Aves : Galliformes	Mosquitoes	?	Raghavan & David, 1955
Deraiophoronema evansi (= Dipetalonema evansi)	Camelidae	Mosquitoes	Thoracic muscle	Kataitseva, 1968

Life cycles: filarioidea (Cont'd).

Filaria	Definitive Host	Intermediate Host	Development Site of Larva	Reference
Onchocercidae : Onchocercinae (Cont'd)				
Ackertia marmotae	Rodentia : Sciuridae	Ixodidae	Fat body	Ko, 1972
Dipetalonema arbuta	Rodentia : Erethezontidae	Mosquitoes	Fat body	Highby, 1943a, b
D. sp. (=mf. rosenawi)	Rodentia : Sciuridae	Argasidae	Muscle	Weinmann, 1972 (pers.comm.)
D. viteae	Rodentia : Cricetidae	Argasidae/Ixodidae	Muscle	Bain, 1967
D. setariosa	Viverridae	Ixodidae	Muscle	Nelson, 1964
D. grassii	Canidae	Ixodidae	Muscle	Grassi & Calandruccio, 1890; Noe & Grassi, 1903
D. manson-bahri	Lagomorpha : Leporidae	Fleas	Fat body	Nelson, 1961
D. reconditum	Canidae, Hyaenidae(?)	Fleas, Mallophaga	Fat body	Nelson, 1962b; Pennington & Phelps, 1969
D. dracunculoides	Canidae, Hyaenidae	*Hippobosca longipennis*	Fat body	Nelson, 1963a
D. perstans	Man	Ceratopogonids	Thoracic muscle	Sharp, 1928;Hopkins & Nicholas, 1952
D. sprenti	Rodentia : Castoridae	Mosquitoes	Fat body	Addison, 1973.
D. streptocerca	Man	Ceratopogonids	Thoracic muscle	Chardome & Peel, 1949; Duke, 1958
Mansonella ozzardi	Man	Ceratopogonids, Simuliids		Buckley, 1934; Cerqueira, 1959
Litomosoides carinii	Rodentia : Cricetidae	Mites	Fat body	Williams & Brown, 1946; Bertram, 1957, 1966
Breinlia booliati	Rodentia: Muridae	Mosquitoes	Fat body	Singh *et al.*, 1972.
B. sergenti	Primates : Lorisidae	Mosquitoes	Fat body	Ho & Kan, 1971
Elaeophora schneideri	Bovidae, Cervidae	Tabanidae	Fat body	Hibler *et al.*, 1969;
Brugia beaveri	Procyonidae	Mosquitoes	Thoracic muscle	Harbut, 1973 (pers.comm.)
B. malayi	Man; Primates: Cercopithidae; Felidae; Canidae; Rodentia : Cricetidae	Mosquitoes	Thoracic muscle	Brug, 1927; Wharton, 1957
B. pahangi	Felidae; Canidae; Rodentia: Cricetidae, Muridae *et al.*,	Mosquitoes	Thoracic muscle	Schachcr, 1962
B. patei	Canidae; Felidae; Viverridae	Mosquitoes	Thoracic muscle	Laurence & Pester, 1961
B. ceylonensis	Canidae	Mosquitoes	Thoracic muscle	Jayawardene, 1963
B. buckleyi	Lagomorpha : Leporidae	Mosquitoes	Thoracic muscle	Dissanaike, 1963 (in Nelson, 1964)
B. tupaiae	Primates : Tupaiidae	Mosquitoes	Thoracic muscle	Orihel, 1967
Wuchereria bancrofti	Man	Mosquitoes	Thoracic muscle	Manson, 1878
Onchocerca cervicalis	Equidae	Ceratopogonids	Thoracic muscle	Steward, 1933; Mellor, 1971
O. reticulata	Equidae	Ceratopogonids	Thoracic muscle	Moignoux, 1951, 1951a, 1952 (in Levine, 1968)
O. gibsoni	Bovidae	Ceratopogonids	Thoracic muscle	Buckley, 1938
O. lienalis	Bovidae	Simuliidae	Thoracic muscle	Mikhailuk, 1967
O. gutterosa	Bovidae	Simuliidae	Thoracic muscle	Steward, 1937; Supperer, 1952; Eichler, 1971; Mikhailuk, 1967
O. flexuosa	Cervidae	Simuliidae	Thoracic muscle	Frank *et al.*, 1968

Life cycles: filarioidea (Cont'd).

Filaria	Definitive Host	Intermediate Host	Development Site of Larva	Reference
Onchocercidae Onchocercinae (Cont'd)				
O. volvulus	Man	Simuliidae	Thoracic muscle	Blacklock, 1927; Bain, 1969
Wehrdikmansia cervipedis	Cervidae	Simuliidae	Thoracic muscle	Weinmann, 1972 (pers.comm.)
Splendidofilariinae				
Ornithofilaria fallisensis	Aves : Anseriformes	Simuliidae	Fat body	Anderson, 1968
Splendidofilaria californicus	Aves : Galliformes	Ceratopogonids	?	Weinmann, 1972 (pers.comm.)
S. picacardina	Aves : Passeriformes	Ceratopogonids	?	Hibler, 1963 (in Robinson, 1971)
Chandlerella quiscali	Aves : Passeriformes	Ceratopogonids	Thoracic muscle	Robinson, 1971
C. striatospicula	Aves : Passeriformes	Ceratopogonids	?	Hibler, 1963 (in Robinson, 1971)
Lemdaninae : No Life Cycle Information to Date				
Eufilariinae				
Eufilaria cypseli	Aves : Apodiformes	Mallophaga	Fat body	Nelson, 1964
E. longicaudata	Aves : Passeriformes	Ceratopogonids	?	Hibler, 1963 (in Robinson, 1971)
Saurositus agamae	Reptilia : Agamidae	Mosquitoes	Thoracic muscle	Bain, 1969
Onchocercidae *Sensu Lato*				
Filaria sp.	*Sturnus vulgaris* (Aves: Sturnidae)	Ceratopogonids	Thoracic muscle	Robinson, 1961
Filaria sp.	*Corvus frugilegus* (Aves : Corvidae)	Mosquitoes	Thoracic muscle	Schtefko, 1915
Microfilaria fijiensis	Chiroptera : Pteropodidae	Mosquitoes	Thoracic muscle	Symes & Mataika, 1959
Filaria sp.	Aves : Galliformes (exp.)	Mosquitoes	Thoracic muscle	Cheong & Omar, 1970

Of the five accepted Filarioid families-Desmidocercidae, Diplotriaenidae, Filariidae, Setariidae and Onchocercidae-the first three are oviparous, with relatively well developed first-stage larvae. Members of families Setariidae and Onchocercidae produce sheathed or unsheathed microfilariform embryos which circulate in the blood or are sequestered in cutaneous tissue fluids. Desmidocercids have thus far been completely ignored, and, if conjectured life cycles were to be borne out (Nelson, 1964; Chabaud, 1965), there would be ample added justification for moving this group to Spiruroidea (as proposed by Skrjabin, 1949). Cycles in Diplotriaenidae (Anderson, 1957, 1962; Bain and Vassiliades, 1969) are likewise remniscent of those in Spiruroidea. Only one cycle is known for family Filariidae, *Parafilaria multipapillosa*, which develops in the fat body of *Haematobia atripalpis* (Gnedina and Osipov, 1960).

Of the most medical and veterinary interest, hence the most intensively studied, have been families Setariidae and Onchocercidae. Some distinct patterns bearing both on the specificity of the filaria: vector-type relationship and on the tissue-specificity of the nematode larva within its vector are becoming clearer in these groups. These evolutionarily contrived relationships between vector and agent and their practical and theoretical importance have been touched upon in most of the earlier reviews; more information now serves to bring these ideas into sharper focus.

In family Setariidae, life cycle studies show seven species of *Setaria* to have mosquito intermediate hosts. With one possible exception (Table 1), larval development always occurs in the thoracic muscles of the vector. Likewise, in *Stephanofilaria*, the four known cycles all use muscid-fly vectors; larval development occurs in the fat body in at least two and possible in the others as well.

In family Onchocercidae, five genera have been studied sufficiently to give a reasonable resolution of patterns: *Foleyella*, *Dirofilaria*, *Dipetalonema*, *Brugia* and *Onchocerca* (Table 1). Life cycles are known for eight *Foleyella* spp.. The pattern of development is absolute whether the adults parasitize amphibians or reptiles-all use mosquito vectors with larval development in the fat body. Seven life cycles are known for *Brugia* spp.; in all cases, larvae develop in the flight muscles of mosquitoes.

Bimodal patterns are seen in *Dirofilaria* and *Onchocerca*. Ten life cycles are known in *Dirofilaria;* mosquitoes have been incriminated as vectors in nine. Of these, five or possibly six species have larval development in the Malphigian tubules; in the remainder *(D. scapiceps*, *D. uniformis* and *D. corynodes)*, larval morphogenesis occurs in the fat body. *Dirofilaria roemeri*, a parasite of Macropodids in Australia, develops in the fat body of tabanid flies (Spratt, 1972), possibly indicating that it should not be included in *Dirofilaria*.

Of the seven known cycles in *Onchocerca*, three *(O. cervicalis*, *O. reticulata* and *O. gibsoni)* have ceratopogonid vectors; the remainder use simuliids. Irrespective of the vector-type or of whether the final host is equid, bovid or human, larval development occurs in the thoracic muscles of the vector. It is of interest to note that the closely related *Wehrdikmansia cervipedis* of deer also uses simuliid vectors with larval development in the thoracic muscles (Weinmann, pers. comm., 1972).

Analysis of reported life cycles in *Dipetalonema* confirms what has long been morphologically evident: there is a complete lack of taxonomic unity in this group (Yeh, 1957). Larval development occurs variously in ticks, fleas, mallophogans, anoplurans, mosquitoes and hippoboscid and ceratopogonid flies and in any site except the Malphigian tubules. The only semblance of pattern is shown by the four species transmitted by ticks, all of which develop in the muscles (Table 1).

There are five recent instances in which a given filarial life cycle has been reported to violate the *one-filaria: one-vector-type* thesis. *Mansonella ozzardi* has been stated to develop both in *Culicoides furens* (Buckley, 1934) and in *Simulium* (Cerqueira, 1959). Nelson (1962, 1964) and Pennington and Phelps (1969) reported development of *Dipetalonema reconditum* from dogs in fleas, Mallophaga and (in the latter paper) in sucking lice. Colluzi (1964) screened a broad group of potential vectors for *Dirofilaria repens* in Italy. In addition to confirming the accepted mosquito vector, he reported development of third-stage larvae in *Haematopota variegata* (Tabanidae) 11 days post-infection. *Wuchereria bancrofti* and *Brugia malayi* (Manson, 1878; Brug, 1927) have long been known to develop in the flight muscles of mosquitoes; Burton's (1960, 1963) reports of development in *Cimex* were not confirmed either by Wharton and Omar (1962) or by Nelson (1963). Ogunba (1972) recently reported *Loa loa* to develop in *Mansonia africana*; as yet, there have been no published confirmation attempts. Similarly, in the older literature, the observations of Wellman (1907) on *Dipetalonema perstans* in *Ornithodoros moubata* and of Yao *et al.*, (1938) and Langeron (1938) on *W. bancrofti* in *Phlebotomus* require confirmation, negation or explanation. If they could be confirmed, observations such as these might point the way to the establishment of otherwise impracticeable laboratory models. Such models might be "abnormal" in the strict sense, but as soft ticks, fleas or mosquitoes are more amenable to colonization and laboratory usage than ceratopogonids, simuliids or tabanids, this approach would provide a great impetus toward the study of presently unattackable problems. The taxonomic and epidemiologic significance of reports of two vector-types for the same filaria is that it may show we are dealing with more than one parasite (Schacher and Geddawi, 1969). Judging from life-cycle patterns within the group, I would estimate the potential diagnostic error to be of at least generic magnitude.

CURRENT LABORATORY MODELS

An overview of the literature with regard to the "goodness of fit" of some currently used laboratory models (Fig. 1) shows that with the exception of *Loa papionis* and *Loa loa* in chimpanzees and baboons (Duke, 1957, 1964) and *Brugia* spp. in cats, dogs and lower primates (Schacher and Sahyoun, 1967; Schacher *et al.*, 1970, 1973; Schacher and Sulahian, 1972), none of the currently most used models mimic the corresponding conditions in man with enough precision to permit direct and general clinical and pathological extrapolation.

Cutaneous Forms

While both *Dirofilaria repens* and *Dipetalonema viteae* live in subcutaneous tissues, neither demonstrates the migratory propensities and allergenic properties of *Loa loa;* neither forms nodules or has microfilariae in the skin or eyes like *Onchocerca volvulus* or *Dipetalonema streptocercum*. *Onchocerca* spp. from horses and cattle have provided some advances and much stimulation (Nelson 1970), but other than the chimpanzee (Duke, 1962), no practical final host has been discovered or proposed for the laboratory study of onchocerciasis. The crucial point to be overcome in formuation of an onchocerciasis-model has always been the refusal of *Simulium* to mate in the laboratory; the recent reports by Wenk and Raybould (1972, 1972a) of the controlled breeding of *S. damnosum* remain to be exploited. Reports of *Onchocerca* in spider-monkeys (Caballero and Barrera, 1958) and in pigs (Ramanujachari and Alwar, 1953; Ramachandran and Eng, 1967) should be followed up; the availability of miniature swine-breeds and the similarities between porcine and human skin (Montagna, 1966; Weinstein, 1966) might here be combined to good advantage. It is entirely possible that much effort has been dissipated seeking an *Onchocerca* species *per se*, when what was really required was a filaria whose microfilariae were confined to the skin. At least two Ixodid-tick-borne forms fit this criterion: *Dipetalonema grassi* in dogs and *Ackertia marmotae* in woodchucks (Table 1). Surveys utilizing skin-snips rather than blood films might turn up other useful leads.

Lymphatic Filariae

Three *Brugia* spp. are currently available to model various aspects of the pathophysiology, immunology and chemotherapy of *W. bancrofti* and *B. malayi* infections. Introduction of the selected Liverpool strain of *Aedes aegypti* as a laboratory vector (Macdonald, 1962a, b) and the jird as a final host (Ash and Riley, 1970a, b) have expedited new avenues (particularly for chemotherapy) and reduced costs in some types of studies.

Cavity-Dwelling Forms

While *Litomosoides carinii* may in some ways mimic *D. perstans* and *Mansonella ozzardi*, our current knowledge of these forms in man is too meager to judge the correctness of fit of any laboratory model.

SPECIAL-PURPOSE MODELS

Models can be formulated which do not have the requirement that they mimic one or another of the human filariases. These models have definite value for the study of important animal-pathogens such as *D. immitis* (Bradley and Pacheco, 1972), for the clarification of immune response mechanisms and immunologic methodology (*D. immitis, L. carinii, D. viteae, Brugia* spp.), and for the study of vector (susceptibility) genetics and vector-parasite relations (*Brugia, Dirofilaria, Foleyella* spp.). Two areas where further special-purpose models could be conveniently established are for *in vitro* (Taylor and Baker, 1968) and "*in vivo*" (Yoeli *et al.*, 1958; Singh and Mammen, 1964) cultivation of filariae and in the formulation and evaluation of field epidemiological methods.

Preliminary studies clarifying *Onchocerca* field-epidemiology have made use of the model of *O. flexuosa* of red deer and *Prosimulium nigripes*/*Odagmia ornata* (Frank *et al.*, 1968). Similar studies might be established using *O. gutterosa*, *O. lienalis* or *Wehrdikmansia cervipedis* (Table 1) for other simuliid-transmitted forms. The studies of Nelson and his co-workers (Nelson, 1970) should be expanded for those *Onchocerca* spp. with ceratopogonid vectors; information gained from this model might secondarily help to devise new techniques for the field study of *D. perstans*, *D. streptocerca* and *M. ozzardi* epidemiology. While much has been learned about the epidemiology and control of *Wuchereria* and *Brugia* by the study of man and relevant vectors in endemic foci (Edeson, 1972), there have been few attempts at longitudinal studies, and none which embodied controlled experimentation were possible. Some studies on field transmission of mosquito-borne filariae have been performed using *D. immitis* in dogs (Otto, 1972). A more controllable (and cheaper) test model might be set up using *Foleyella* in frogs (Crans, 1969).

Many basic questions regarding filarial disease in man can only be approached by the use of laboratory models. The present paper only attempts to point out some of the possibilities based on review of current knowledge of life cycles and a short evaluation of models presently in use.

SUMMARY

Laboratory models in filariasis are discussed in general terms and some prerequisites to their establishment are defined.

The life cycles of 93 filarioids from man and lower vertebrates are reviewed; some follow a defined pattern with regard to the vector-type and the tissue specificity of larval stages. The taxonomic significance of biological specificity and reported exceptions to the "one-filaria: one-vector-type" thesis are pointed out, and possible uses of these exceptions (if they can be confirmed) are discussed.

Some actual and potential laboratory models for specific types of filarial disease are discussed; further possibilities are evaluated based on life-cycle review.

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