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Reprinted From
Proc. 15th Int. Congr. Entomol.,
Washington 1977

The Changing Pattern in Transmission of Bancroftian Filariasis

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ABSTRACT

In the first part, reasons are given for confining the discussion mainly to *Wuchereria*. It is also pointed out that transmission covers the whole field of epidemiology so only certain aspects more directly related to changes in transmission are discussed, namely: distribution of the disease and changing patterns created by its spread and its vectors, with emphasis on pullulation of *Culex fatigans* in undersanitated urban areas and insurgence into suburban and semirural areas. Control of the vectors and the growing opposition to the use of insecticides is mentioned plus the unexpected effect of larviciding on potential transmission. The importance of the new diagnostic techniques for revealing low density microfilaraemia and the infectability of such low densities for vectors is discussed. As always, taxonomic studies lag behind. There has been more support for such studies on the worms and these have yielded important results. It is pointed out that there is no International Reference Center for mosquitoes. The difficulties of comparing results from far and wide is largely the result of the lack of standardization, improvement is urgently required if changes in transmission are to be evaluated with any seriousness.

The filariases are considered to cover human infections with *Wuchereria, Brugia, Loa, Dipetalonema* and *Mansonella*. I propose to deal mainly with the periodic *Wuchereria* for several reasons. Firstly, it is the most important for man and our state of knowledge of the epidemiology and pathology of *Dipetalonema* and *Mansonella* is not very extensive. *Dipetalonema* is usually considered to be non-pathogenic or only mildly so over most of its distribution except Rhodesia (Clarke 1971) where it may be represented by another species. Secondly, our knowledge of the vectors of these two genera of filariae is on the whole poor. For example, what is presumably a single species of *Mansonella* occurs in vectors belonging to 2 different families of Diptera, namely, Simuliidae and Ceratopogonidae. Unless we are again dealing with two different species of parasite this seems unlikely.

Loaiasis is now better understood largely due to the work of Duke and his collaborators at the Helminthiasis Research Unit, Kumba, Cameroon. The discovery of a sibling species, *Loa papionis* Treadgold, a parasite of the lower primates and its vectors is important as it offers scope for a laboratory model so sadly lacking in *Wuchereria*. Loaiasis is, however, restricted to the African rain-forest, attacks small communities near the fringes and disappears with urbanization. The vectors are species of *Chrysops* (Tabanidae) and no dramatic changes in transmission are likely unless the parasite becomes adapted to savanna and grassland species of vectors. Dr. T.C. Orihel has shown that this is not so unlikely by the establishment of cyclical transmission in baboons and monkeys with a parasite from Africa related to *Loa loa* (Guyot) and an American vector *Chrysops atlanticus* Pechuman (WHO/MPD/75.5, p. 12, unpublished).

Apart from the work in Malaya (Edeson and Wilson 1964), the situation regarding *Brugia* is not clear. New and suspected vectors are coming along at a steady rate, new foci are being discovered, one or two old ones have disappeared and altogether it is difficult to detect any trends indicating changes in the pattern of transmission that is so obvious in periodic *Wuchereria*. The same could be said of subperiodic *Wuchereria* where it appears that each isolated group of islands has its own vector.

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The pattern of transmission of the filariases is continually being affected and changed for better or worse by a host of factors. Some of these are obvious, others not. Many of the latter are now being investigated and with the advent of renewed interest in these diseases we may expect some fruitful developments (WHO/MPD 75.5, unpublished). There will, of course, always remain some obscurities which are inherent in all biological systems but these should not interrupt progress towards control.

Transmission is not a single isolated and independent event and the vector is not a flying syringe loaded with disease. This is obvious but it bears repetition and reiteration as witness the very title of this symposium which implies that vectors bear, carry or transmit diseases. They do no such thing: they transmit pathogens. This is not merely quibbling or a question of semantics. I believe it is responsible for many mistakes in the past and even some at the present time when the whole emphasis is placed on attempts to get rid of the vectors, the so-called "carriers of disease," while the large number of factors involved in successful transmission are neglected. Some of these factors are only just coming to light as witness the recent discovery that the Fy Fy blood group genotype, found predominately in African and American blacks, is the *Plasmodium vivax* (Grassi and Feletti) resistance factor (Miller et al. 1976). How much more remains to be discovered? As Soulsby and Harvey (1972) have put it, "There has been little attempt at a multidisciplinary examination of the factors that determine the interaction between host, vector and parasite." Transmission is a dynamic system of which the vector is only a part and it covers the whole of epidemiology. To discuss this, I take it, is quite beyond the expectations of this group so I shall restrict myself to those aspects which appear to be more important and more relevant to the subject.

Events Causing or Likely to Cause Changes in Transmission

1. Distribution

This is not the place to detail the worldwide distribution of the filariases. Suffice it to know that they occur in one form or another in a wide tropical and subtropical belt between about 40° north to just under 40° south of the equator (Hawking, F. "The distribution of filariases throughout the world" Part I 1971, The Pacific Region, including New Guinea WHO/FIL/71.94: Part II, 1973, Asia: WHO/FIL/73.114, Part III 1974, Africa: WHO/FIL/74.124, unpublished). Here I will merely direct attention to those aspects which are germaine to the particular argument. The most important of these are the discovery of new foci and the spread of the disease.

Evidence from many sources indicates that some filariases are spreading both inter- and intracountry. In both situations problems may arise with respect to new vectors, changed human ecology, changed climate and new conditions caused by population movement. Many of the recently discovered foci are in fact old ones which have been missed in the past or have not been looked for. There is, however, at least one instance of intercountry spread, namely, to Burma where filariasis was undoubtedly introduced. Prior to 1941 transmission was minimal or unknown (Tin Maung Maung and Botha de Meillon 1963, unpublished report to WHO) and local Burmese were not infected though infection was common among immigrants from India. The destruction by bombing, during the last world war, of the highly efficient existing sewage system and the failure to repair it plus the massive influx of wartime refugees gave rise to a concentration of susceptible hosts and a tremendous population of *Culex fatigans* Wiedemann (=*Culex quinquefasciatus* Say) estimated at about 44 million per square mile (Lindquist et al. 1967). By 1965, 4.2% of Burmese of all ages were found to be infected by ordinary blood slide examination (WHO Filariasis Research Unit, unpublished monthly report for January, 1965).

With regard to local or spread within a country there is evidence that this is a real threat in the Oriental and Subsaharan regions. In the former it may be mentioned that in India alone the population at risk has nearly doubled to 122 million since 1960 including both rural and urban areas (World Health Organization 1974, Raghavan 1957, and Gratz 1973.)

Many workers in Africa are of the opinion that filariasis is not only increasing in prevalence but also in distribution. Evidence of this comes from: West Africa and Madagascar: (Subra 1975). Seychelles: (Lambrecht 1971). East Africa: (White 1971).

That filariasis has disappeared from some areas is also known. Parts of the Mediterranean, Australia and Reunion are now free of periodic *bancrofti* and Ceylon of *Brugia*. Over 20 years of malaria control by indoor spraying, improvement in living standards and self protection have played a major role in Reunion (Brunhes 1975).

2. *Vectors*

The situation in the Oriental and Pacific regions is far from clear, and some complications are now arising in the Subsaharan. In the First Report of the WHO Expert Committee on Filariasis 1962 the list of vectors contains 5 species not mentioned in the Third Report 1974 and the latter now mentions no less than 29 species not noted in the 1962. Needless to say the taxonomic status of some of these species is in doubt so we may expect some changes. The vectors in some localities are as yet unknown so we may therefore expect some additions to the already formidable list.

It is generally agreed that apart from the important work done in Malaya (Edeson and Wilson 1964) much remains to be done in Asia and the Pacific. Some of the problems are already being investigated as witness the work on the mosquitoes of Tonga by the Medical Entomology Project, Smithsonian Institution and the Johns Hopkins University. There is no doubt that the results of these investigations will lead to changes in the pattern of transmission.

The best and most outstanding evidence of a changing pattern – apart from Rangoon already noted – comes from Subsaharan Africa, Madagascar and islands in the sea of Zanz. Briefly, the situation, until quite recently, was that in all West Africa and most of East Africa including the coastal islands (the situation in Central Africa is largely unknown), the vectors of periodic *Wuchereria bancrofti* were rural species of *Anopheles* whose control called for indoor spraying with insecticides. This pattern, however, soon began to change with the advent of a different class of vector with a different biology and ecology, namely, *Culex fatigans.* The rise and spread of this species was well documented by Mattingly (1962). Since then numerous authors both in East and West Africa have found evidence of this phenomenon in both urban and suburban localities (Hamon et al. 1967, Lambrecht 1971, White 1971, Subra 1975). Subra (see above) has drawn attention to the fact that in East Africa and islands *fatigans* is now not only an urban species but also becoming widespread in rural areas. He maintains that throughout this area *fatigans* is already transmitting *bancrofti.* Recently large numbers of *fatigans,* as much as a hundred or more per hut, have been found in some semirural areas of the Transvaal lowveld. In the early 1930's indoor spraying with pyrethrum in the same area produced none (unpublished personal observation). The threat of the spread of filariasis to this region from an infected neighboring country is a real one. This change has come about, as elsewhere, through urbanization or semiurbanization proceeding faster than sanitation and resistance to insecticides of *fatigans.*

In West Africa, so far, *fatigans* is said still to be restricted to the urban areas where it is apparently not transmitting *bancrofti.* Experimentally, however, it has been found to be receptive to the parasite and it is probably only a matter of time before filariasis becomes an urban disease. Subra (see above) who has investigated the epidemiology in West Africa and elsewhere for many years concludes: "La colonisation du milieu rural par *C. p. fatigans* évoquée à la fin de ce travail amène l'auteur à conclure que la transmission de la filariose par ce moustique n'est plus seulement un problème des zones urbaines, mais aussi de toutes les zones occupées par l'homme."

The changed situation that has developed and continues to develop still further in the Subsaharan region is mainly the consequence of economic pressures on the population causing a drift to suburban, urban and industrial areas. This unfortunately is not often or hardly ever accompanied by adequate facilities for waste disposal. The result is the accumulation of polluted waters in pit latrines, drains and other places and so creating the very conditions which cause *fatigans* to flourish. (Gratz, N. 1974, "Urbanization and filariasis" WHO/FIL/74.119, unpublished). The situation is tragic for the developing countries who, largely because of other priorities, have not the funds to undertake the necessary action for safe waste disposal which, after all, will provide the answer to the battle against *fatigans.* Another consequence of development in W. Africa has been the creation of storage dams, reservoirs and so on. This has lead to the founding of a stable all season population of *Anopheles gambiae,* a very potent vector of *bancrofti.* Formerly this species was active largely during the rains and transmission was intermittent, now it persists throughout the year with dire clinical consequences. (Brengues, 1975).

The situation in Central and South America is largely unknown (WHO/MPD/75.5, unpublished). The vector is said to be *fatigans* and one may expect the same developments to take place here as elsewhere.

In the Orient, the situation is equally disturbing as has been recorded, among others, by Singh (1967) in Southeast Asia, by Dobrotworsky (1967) in the South Pacific and in Papua New Guinea by van den Assem and Bonne-Wepster (1964).

There is another aspect of *fatigans* biology that greatly enhances its vector potential thence the pattern of transmission especially where it is increasing in density. Here I refer to the discovery made in Rangoon (de Meillon et al. 1967) that large numbers of *fatigans* rest outdoors; that these mainly feed on man and that their *bancrofti* infective rate does not differ significantly from those caught resting indoors. This, of course, instantly changed the pattern of control which up to that time had been based on indoor insecticidal spraying (and had been singularly unsuccessful) and the pattern of transmission which was thought to take place indoors only. The same authors in Rangoon suggested that outside transmission might account for the higher infection rates in Indians, who being the poorest of the ethnic groups, were found to be among the only people who slept outdoors unprotected by house, screens, adulticides, bed nets and so on. In constrast, Europeans who head the economic list, and are best protected, have never been known to contract filariasis in Rangoon (Hairston and de Meillon 1968). The influence of human biology and ecology on transmission is, of course, well known and has been well documented in the Pacific (Jackowski and Otto 1955) and elsewhere (Dunn, F.L. 1974, "Human behavioural factors in the epidemiology and control of *Wuchereria* and *Brugia* infections." WHO/FIL/74.122, unpublished).

3. Control of the Vectors

There is ample evidence from Rangoon (Graham, J.E. et al. 1971, "Studies on the control of *Culex pipiens fatigans* Wiedemann" WHO/VBC/71.268, unpublished) and East Africa (World Health Organization 1974. 16-17) and from the Comores (Subra et al. 1973) that with larvicides the density of *fatigans* can be brought to a very low level. Unfortunately, epidemiological assessment of transmission has not kept up with the entomological achievements, a not unusual occurrence I may say in the sphere of the arbopathogen diseases. Little therefore can be said. However, there is one rather disturbing fact that has come out of the Rangoon experience and that is that larval control results in a rise in the proportion of surviving parous females after two years of larviciding and what is more, such a change in age structure of the vector population is reflected in increased transmission potential (J.E. Graham, et al. 1971, "Changes in the age structure of *Culex pipiens fatigans* Wiedemann populations in Rangoon, Burma after intensive larviciding" WHO/VBC/71.301, unpublished). If this turns out to be a common phenomenon associated with larval control then changes in transmission may be expected or at least must be looked for. The phenomenon has no ready explanation but serves once again to remind us that biological systems are complicated and that the results of interference in them by man cannot be anticipated or forecast with any accuracy.

Resistance to insecticides is a serious problem these days. Evidence for DDT resistance as far as *fatigans* is concerned comes from just about all parts of the world where tests have been made. Quite apart from resistance *per se* in *fatigans*, it appears to be accompanied by an increase in biotic potential resulting in an enormous increase in numbers of that species as reported both in India (Joseph et al. 1960) and in Africa (Smith and Bransby-Williams 1962).

Apart from resistance other objections to the use of persistent insecticides are gaining momentum resulting in increased interest in biological control. So far there are not enough data to draw any conclusions but it is quite probable that if and when applied unforeseen and unexpected consequences will result. One thing is certain and that is that the pattern of transmission will be affected.

One sure method of dealing with *fatigans* is the adequate disposal of wastes. Unfortunately the costs are high and prohibitive to most developing countries if we think in terms of modern sewage disposal in developed countries. However, much can be done to alleviate the situation among poorer rural communities where water supplies are limited. The work being done in Rhodesia is a fine example of this. A pamphlet kindly sent to me by Dr. V. de V. Clark of the Blair Research Laboratory, Salisbury, deals with 2 types, the "Watergate Unit" and the "Ventilated Dry Privy System." Both are in use and both are proving to be adequate to prevent *fatigans* breeding. ("Sanitation and Hygiene in Rural Areas" Blair Research Laboratory, Causeway, Rhodesia). Application of the principles of "bonifica integrale," so successfully applied in parts of Italy in the early 1930's, is still the safest and most effective way of dealing with many of the arbopathogen diseases. However, such a campaign has to be based on a sound knowledge of vector biology and human ecology so as to avoid the well intentioned but tragic consequences such as developed in Ceylon following the large-scale construction of pit-latrines (Abdulcader 1967).

4. Microfilaraemia and Its Periodicity

Microfilarial periodicity and subperiodicity which includes the nocturnal and diurnal forms of *W. bancrofti* are now well known. Each of these has the vector suited to its type of periodicity and this, of course, is very important because the more there is discovered about these periodicities and biting times of vectors the more will our understanding of transmission be affected.

In the first place it has recently been revealed that the old simple blood smear technique for detecting microfilariae is inadequate and that many more positives can be found by concentration techniques which had their origin in Knott's method for concentrating parasites in blood (Knott 1939). The older technique tended to miss the low densities and this has given rise to the importance of such positives and apparent negatives in transmission. The general opinion up to quite recently, and in spite of the work of Rosen (1955) and Wharton (1957), was that parasite control with diethylcarbamazine was the preferred method of control or even eradication (World Health Organization 1962:27). In some places complete or near complete success based on the old blood smear technique was claimed for parasite control. Since that time the picture has changed and the Third Report of the WHO Expert Committee on Filariasis 1974 has taken a more realistic point of view. In the light of further evidence recently produced (J. Bryan and B.A. Southgate 1973, "An investigation on the transmission potential of ultra low level *Wuchereria bancrofti* microfilaria carriers after diethylcarbamazine treatment" WHO/FIL/73.116, unpublished) it is now possible to disregard the old belief that the density of microfilariae had to reach a certain level before vectors became infected.

This relook at vector potential plus more refined methods of detecting microfilaraemia, mentioned earlier, are amongst the most important subjects likely to change our ideas of the pattern of transmission.

5. Taxonomy

Recent advances in parasite identification especially of the larval stages in the vector has thrown much light on our understanding of transmission. The outstanding example of this was revealed in Kenya where *Aedes pembaensis* Theobald was, by virtue of its high infection rate, thought to be an important vector of *W. bancrofti.* It subsequently turned out that all the larvae found in this mosquito were animal parasites belonging to no less than 6 different species (Nelson et al. 1962). Other instances of mistaken identity, no doubt, remain to be discovered. The importance of this aspect has been recognized for years and WHO has consistently supported research on identification of larvae in wild caught mosquitoes and for this purpose established the International Reference Center for Filarioidea in London.

The recent discovery of new species of filaria, namely, *Wuchereria lewisi* Schacher in Brazil and the Timor species, which as far as I know, has not yet been named, has added to the need for accurate identification of larvae in mosquitoes and this after all lies at the very base of the assessment of transmission and the incrimination of vectors. Accurate identification of vectors is equally important but there is no International Reference Centre for mosquitoes!

6. Standardization of Techniques for Collecting Data

Since the earliest days there has been a repeated cry for standardization but little has been achieved. The multidisciplinary nature of the subject involving, as it does, a whole series of biological and physical systems personed by an equally diverse group of investigators over a wide range of climate does not lend itself readily to standardization. That repeated efforts to achieve it should be made is undeniable because of the present day difficulties in interpreting results from various sources and making the necessary comparisons and evaluations. This is a long and diverse subject and it would be of no service to attempt an analysis here. It is sufficient to point out that the techniques employed and the subsequent interpretations have a strong influence on determining the pattern of transmission and the evaluation of the changes. Changes in transmission, if properly evaluated, will help tremendously in assessing failure or success in control or eradication. Even the commonest everyday words used in filarial epidemiology are variously interpreted and there is no glossary of terms as provided by WHO for Malaria Eradication. Such a glossary was prepared for the 1967 WHO Expert Committee Meeting on filariasis but it never saw the light of day.

Acknowledgments

I thank the Director, Division of Malaria and other Parasitic Diseases WHO, Geneva and many friends for information which helped me to write this paper.

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