A PRELIMINARY NOTE ON *DEMODEX FOLLICULORUM* SIMON (1842), AS A POSSIBLE VECTOR OF LEPROSY

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It is generally accepted that *Mycobacterium leprae* is the causative organism of leprosy, though the means by which this organism is transmitted remains an unsolved problem. The majority of leprologists are agreed that close and prolonged contact with an open case of leprosy is a prerequisite for the start of a new infection. DUNGAL (1960) has pointed out that though this is probably true, it does not explain how the bacilli escape from the subepidermal tissues of one individual and gain access to the subepidermal tissues of another individual. He also advanced arguments to suggest that in the great majority of infections there must be some active agent or vector, and that this vector is probably an ectoparasite or a parasite of the skin. It is not suggested that the vector is an obligatory or paratenic intermediate host for the bacilli, but that transmission is accidental with little or no physiological interrelationship. In this note Dungal's arguments are accepted.

Prior to any detailed consideration of specific animals as possible vectors it is necessary to examine the conditions that must be satisfied by an animal if it is a vector. The bacilli are found in the subepidermal tissues of man, therefore it is clear that the vector must penetrate to the subepidermal tissues at least once if it is to come into contact with the bacilli. The epidermis of a second host must also be penetrated unless it is postulated that the bacilli are passed on to a second vector. There does not appear to be any good reason to suppose that more than one vector animal is involved, though the possibility should not be ignored. The bacilli may be transmitted on the surface of the animal or within it. It is clear that the considerations applying to these two possibilities differ widely. If the bacilli are carried within the body of the vector it is unlikely that they would be found within the tissues, since this would involve mechanisms of transport into and out of the tissues and mechanisms of resistance to the tissue responses, apart from the implications of physiological interaction between bacilli and vector. It is very much more probable that the bacilli would be carried within the alimentary tract. The

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bacilli could escape from the alimentary tract of the vector in three ways, either in the faeces, in regurgitated material or by the vector being scratched into wounds inflicted by the host in response to the irritation it causes. Transmission of bacilli by these means can only occur if the bacilli are resistant to the digestive processes of the host for a length of time dependent on the habits of vector and host and their interaction. It is clear that the demonstration of acid and alcohol fast bacilli in the gut of an animal (even if the possibility of their being commensal bacteria and not *M. leprae* is excluded) is not proof that the animal is a vector, since by the time the vector penetrates a new host or causes sufficient irritation to provoke a scratching response the bacilli might have been destroyed. Knowledge of host and vector with relation to each other, and of the period of survival of the bacilli within the vector is essential if an assessment is to be made of the feasibility of such hypotheses. It is of course difficult to estimate the survival time of bacilli that cannot be cultured, though it is probable that successful staining of the bacilli indicates survival. If the bacilli are carried on the surface of the animal attention must be given to their period of survival in this situation. Finally, a vector of leprosy must occur in leprosy endemic territories, and if an important vector must be of widespread geographical distribution.

DUNGAL examined the possibility of transmission by a variety of arthropods. He did not consider the possibility of transmission by *Demodex folliculorum*. MAJOCCHI (1902) and BORREL (1909) noted the presence of the mites in the skin of leprosy patients and concluded that mites and disease were associated. The demonstration by GMEINER (1909) and others that *D. folliculorum* was common in man and not restricted to people suffering from leprosy served to discredit the ideas of MAJOCCHI and BORREL. There is now much more known of the biology of *D. folliculorum*, it therefore seems appropriate to re-examine the possibility of an association between this parasite and leprosy. It is not my purpose in this note to examine the possible effectiveness of other vectors or to assess the relative importance of the different vectors that there might be. This will be the subject of a future paper.

The details of the life cycle of *D. folliculorum* are now known; SPICKETT (1961a). The parasite is oviparous, the egg being deposited in the sebaceous gland, the newly emerged larva feeds on sebaceous material and cellular debris in the sebaceous gland. It is slowly carried to the mouth of the follicle by the flow of sebum, and undergoes two moults, firstly to protonymph and secondly to deutonymph. The deutonymph is the distributive phase, it leaves the follicle and moves over the skin surface. New infestations are started by skin to skin contact and transfer of deutonymphs. The deutonymph enters a new follicle and moults into the adult. The males

move over the skin surface entering follicles to feed. Copulation occurs in the mouth of the follicle. The ovigerous female moves further into the follicle and from there into the sebaceous gland. The entire life cycle is about fourteen days, the period between a mite leaving one sebaceous gland as a larva and entering another as an ovigerous female is about eight days. Distribution over the skin surface is accomplished in not more than 36 hours and probably is as short a period as 12 hours.

The parasite is not usually found outside the confines of the pilosebaceous apparatus except when on the skin surface. It might be thought therefore that it does not satisfy the basic requirements of a vector of leprosy, in that it should have contact with the subepidermal tissues of two hosts. However it has been noted that in infestations involving classes of individual (e.g. children) or sites (e.g. the arm) where parasitism is uncommon owing to the low level of sebaceous activity, the animals may penetrate the epithelium of the sebaceous gland; SPICKETT (1961b). *D. folliculorum* has mouthparts adapted for piercing and cutting. It has been shown that the related species *Demodex criteci* is capable of burrowing into the epidermis of the hamster; NUTTING and RAUCH (1958). Observations on *D. folliculorum* suggest that penetration of the sebaceous epithelium can occur but does so only when there is an uneconomic infestation of a follicle, that is, either when there are very many parasites in a follicle or where there are mites in follicles in which the associated sebaceous glands are relatively small or inactive as compared with those of the facial skin of adult Europeans. It may be concluded that under certain circumstances *D. folliculorum* is capable of gaining contact with the subepidermal tissues of two hosts.

D. folliculorum moults three times between leaving one sebaceous gland as a larva and entering another as an adult female. This suggests that it is unlikely that *M. leprae* could be transmitted on the outside of the parasite's body. Sections of lepromatous lesions showing mites and stained for acid fast bacilli do show bacilli on the outside of the parasite. This emphases the need for knowledge of the biology of a supposed vector in the interpretation of such observations. Bacilli have also been seen within the bodies of the parasites, but only in those sections of skin that show bacilli within the tissues. This suggests that *D. folliculorum* does not normally carry a flora of acid fast bacilli but that *D. folliculorum* does under certain circumstances ingest *M. leprae*.

It has been reported by AYRES (1930) that gross demodicidosis may produce symptoms of itching, but infestations sufficiently heavy to do this are rare in Europeans and probably so in other races. It is unlikely, but not impossible, that transmission of bacilli could be effected through self-inflicted wounds caused by scratching in response to irritation caused by the presence of the parasite.

The only external opening to the gut of *D. folliculorum* is the mouth. There is no anus. If the parasite transmits an organism from the subepidermal tissues of one host to those of another it must be through the disgorgement of the contents of the alimentary tract. Studies on the feeding mechanism of this mite have shown that there is regurgitation of part of the contents of the alimentary tract, this is probably associated with predigestion of food material. It has been found, moreover, that small particles of undigested material (plastic and resin particles were used in this experiment) may be regurgitated several days after they were first ingested; SPICKETT (unpublished). The shortest time interval between leaving one sebaceous gland and entering another is about five days in the normal life cycle. It is therefore probable that the bacilli could be transmitted by these means. Two ovigerous females have been found with acid fast bacilli in their gut. These bacilli can only have come from the sebaceous gland of another follicle since at this stage in the life cycle the sebaceous gland of the newly entered follicle has not been reached. It is probable that in these two cases the mites had come from other follicles of the same individual, however their ability to carry bacilli remains whether they come from another individual or not, and furthermore the mode of distribution of the mite is similar, whether to a follicle of the same individual or to a follicle of a different individual. It should be noted that studies on the life cycle were carried out on infestations of the facial skin of adults, it is possible that there are differences in the behaviour of the mites when follicles of low sebaceous activity are visited. Work is being done to examine this possibility.

Comparative study of infestations of *D. folliculorum* in different human races; the results of which will be reported elsewhere; show that the mite is a very common parasite. Each series of skin sections examined from many parts of the world show a frequency of infested material as great as or greater than that found in Europeans; SPICKETT (1961b, 1961c). This suggests that the parasite is ubiquitous in normal adult human beings. In all racial groups infestation has been found in children, but less frequently than in adults, also infestation has been found in sites other than the face, but less frequently than the face. It is in the less frequently infested classes that penetration of the sebaceous epithelium is most common.

It is obvious that the epidemiology of leprosy is a subject of great complexity. One of the factors that makes date of occurrence of the disease difficult to assess is the absence of any knowledge concerning the incubation period of the disease. It is widely believed that most cases originate in childhood, but as BADGER (1959) has pointed out, this view cannot be held with certainty. BADGER has shown that the pattern of occurrence with respect to age, sex and family varies widely in different communities. The variation is in all probability

attributable to differences in tradition and behaviour between communities.

There is very little knowledge concerning the variation in susceptibility between individuals and populations, it is therefore difficult to assess what the frequency of exposure must be that is correlated with frequency of occurrence.

The known facts of the epidemiology of leprosy would support the view that personal contact with an open case is a prerequisite of infection and that the greater the intimacy of contact the greater the probability of contracting the disease. It is clear that much the same consideration will apply to the transmission of a parasite, such as *D. folliculorum*, that is disseminated by skin to skin contact. If *D. folliculorum* transmits leprosy it must leave the skin of an infected person, having penetrated the sebaceous epithelium, this most commonly occurs in skin other than that of the face of adults (unless there is very heavy infestation) or from the skin of children. If sebaceous activity is relatively very low infestation is very rare, e.g. infestation sometimes occurs in the facial skin of children but very rarely in skin from other sites. It would be expected therefore that *D. folliculorum* would act as a vector to and from the skin of the neck, arms and thorax of adults and less frequently from the abdomen and upper leg, whereas in children the important sites would be at the face and scalp, and less frequently the neck. In this connection, it would be relevant to consider the site of attack of other possible vectors, particularly if comparison is made between leprosy endemic areas varying in their indigenous parasites. However, allowances would have to be made dependent upon the behaviour of the different communities particularly with respect to clothing and sleeping habits. It is proposed to examine this question in detail in a future paper.

The probability that an individual living in a leprosy endemic area will be exposed to parasite-borne infection, will vary with the frequency of any particular parasite and according to the interaction between the biology of the parasite and the behaviour of members of the community. However, even if much is known of these factors they will only become meaningful when more is known of the nature and pattern of susceptibility to leprosy in populations and individuals. There is some evidence to indicate that this might be under genetic control. Work is now being done to determine whether this is so, and if so what the nature of the relevant genetic system is.

This paper is offered in the hope that it will stimulate clinicians and others dealing directly with leprosy patients to make their own observations or to offer material for investigation, so that the possible association between *D. folliculorum* and *M. leprae* may be put beyond the realm of speculation.

Summary

1. There is evidence to show that *M. leprae* can be carried into healthy skin by arthropod ectoparasites and that such a means of transmission may be of importance in the epidemiology of leprosy.
2. Certain sets of conditions relating to the ecology of the vector, are proposed that must be satisfied before an animal may be considered to be a vector of leprosy. The presence of *M. leprae* in association with an arthropod does not justify the conclusion that an arthropod is a vector unless one of these sets of conditions is satisfied.
3. *Demodex folliculorum* does satisfy one of these sets of conditions.
4. Acid fast bacilli have been seen in the gut of *D. folliculorum* when it is in the pilosebaceous canal at a stage in its life cycle that shows that the bacilli must have been acquired from another follicle.
5. It is not possible to assess the importance of a vector unless there is detailed knowledge of the biology of the animal, the relevant behaviour of the human population and the pattern of susceptibility in that population.

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