

# HUMAN DISEASE FROM COMMON WORMS OF DOGS AND CATS\*

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Improvement in sanitation and other aspects of development have brought about a gradual decrease in the common parasites transferred directly from man to man. At a somewhat slower pace there has been a similar slackening in the transfer of some of the parasitic infections acquired through contact with animals. On the other hand, certain worm infections such as larva migrans, acquired through direct contact with dogs and cats, may possibly be increasing; in some parts of the world they are the only remaining helminthic infections of any consequence.

## *Larva migrans*

Larva migrans is best known in the cutaneous form, commonly referred to as 'creeping eruption' or 'sandworm', and long known to be caused by the penetration and migration of infective-stage larvae of dog and cat hookworms. It is not known how many different species of skin-penetrating nematode larvae may be involved in creeping eruption. Among the several known species, *Ancylostoma braziliense*, which occurs in both dogs and cats, is probably one of the chief offenders, both because of its frequency and wide distribution, and because of its tendency to persist in the skin for long periods. This was first demonstrated by American workers in the 1920s and has been confirmed by de Meillon *et al.*<sup>1</sup> and Elsdon-Dew<sup>2</sup> in South Africa and others elsewhere. The disease is too well known to need description, but brief comment on two points may be permissible.

Firstly because, of the different species which may cause the characteristic progressive, linear lesions in the skin, some may persist only for short periods, and even the most persistent ones eventually die or disappear into the deeper tissues, creeping eruption is a self-terminating infection. Failure to take this feature fully into account has resulted in hundreds of 'successful' trials of scores of different remedies, whereas actually the only known effective treatment—blistering the affected areas—is one that cannot easily be employed when, as is so frequently the case, the lesions are widespread or are located on the perineum and

genitalia. This troublesome aspect of the disease has recently been emphasized by experienced clinicians in Jacksonville, Florida,<sup>3</sup> and Durban, South Africa.<sup>4</sup>

*Loeffler's syndrome.* The other feature which needs emphasis and additional study was first observed by Wright and Gold.<sup>5,6</sup> They observed that the appearance of characteristic skin lesions was frequently followed by symptoms characteristic of Loeffler's syndrome, i.e., transient pulmonary infiltrations, with cough and peripheral eosinophilia. This suggested that at least some of the larvae penetrated to the deeper layers of the skin and reached the lungs as they would in their normal hosts. More recently<sup>7</sup> larvae in enormous numbers have been recovered from the sputum after the skin-invading stage, and the mature or immature adults of dog and cat hookworms on several occasions have been recovered from the human intestine. It is then clear that the same larvae that first produce creeping eruption of the skin may later produce pneumonitis and peripheral eosinophilia. Of great interest now is the question whether some of the larvae after leaving the skin may remain free for long periods in the tissues of the visceral organs and thus become involved in the recently recognized type of parasitism known as visceral larva migrans.

*Visceral larva migrans* was first described only a few years ago, having been recognized in a group of small children in New Orleans who, though free of recognizable types of parasitism, displayed symptoms of harbouring immature worms.<sup>8</sup> Chief among the indications of parasites in the tissues was high, persistent eosinophilia. In approximately 50 cases subsequently studied by the original authors and others, hyper-eosinophilia has in all instances been the guiding diagnostic feature. It is worth while to give this point some emphasis because, while it is a well-established fact that many other types of helminthic infections cause eosinophilia in some degree, the coexistence of unsuspected visceral larva migrans has undoubtedly caused some confusion in the interpretation of other infections that were simultaneously, subsequently or previously acquired.

Originally the term visceral larva migrans was applied to the type of infection produced by *Toxocara canis* and *T. mystax*, common ascarids of dogs and cats respectively. More recently it was re-defined to include other non-patent

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(or occult) nematodiasis, such as those due to *Capillaria hepatica*, *Gnathostoma* spp., *Dirofilaria* spp., and others. At the present time, however, larval toxocariasis is of the greatest interest.

#### Toxocariasis

*Toxocara canis* and *T. mystax* are common in dogs and cats throughout the world. Both species are found more frequently and in greater numbers in young animals than in old, the former being somewhat restricted to puppies and to male adults. *T. canis* is one of the outstanding examples of a species in which prenatal infection is a frequent, apparently natural occurrence—a high proportion of pups even in well-managed kennels being already infected when born. Except for the feature of prenatal infection, the *Toxocara* species follow much the same life-cycle pattern as the ascarids of man and pigs. Heavy-shelled, resistant eggs are produced abundantly in the faeces and become mixed with the soil, where in the course of 2 weeks or so they develop into an infective larva, which remains within the protective shell until ingested and carried to the small intestine. Here the larvae erupt from the shell and migrate through the intestinal wall to the liver and lungs and, via the trachea and oesophagus, return to the intestine and grow to maturity in 3 or 4 weeks. In mature female dogs and in both sexes of other animals, the larvae of *T. canis* tend to avoid the tracheal migration, and instead enter the systemic circulation, where they are carried to all parts of the body. However, their behaviour in different species of laboratory hosts differs somewhat, and it is not possible on this basis to describe their behaviour in the human body. It is possible to know on epidemiological evidence, however, that humans—toddler-age children in particular—frequently ingest infective *Toxocara* eggs in contaminated soil and thus acquire these in the same manner, and frequently at the same time, as *Ascaris* and *Trichuris* infections. Indeed, the examination of dooryard soil for the presence of *Ascaris* and *Trichuris* eggs often reveals the eggs of *Toxocara* and other intestinal parasites of dogs and cats. In any locality, therefore, where infected dogs and cats occur the soil becomes a potential source of infection, and, as is well known from the high incidence of *Ascaris* and *Trichuris* in many areas of the world where the use of night soil is not a contributing factor, a certain amount of soil is in one way or another ingested by children and to a lesser extent by adults. Thus the epidemiological set-up is the home or neighbourhood in which there are both children and household pets. It should, however, be noted that, for reasons not yet apparent, *Toxocara* seems to be absent in some localities.

A majority of the recognized cases of visceral larva migrans, or larval toxocariasis, have occurred in children 1-4 years of age, who presented with extreme eosinophilia—frequently above 50% of the total leucocytes—conspicuous enlargement of the liver, hyperglobulinaemia and variable symptoms including intermittent fever, cough, loss of appetite, irritability, poor weight gain, and muscle or joint pains. In a number of instances parents have complained merely that their children have been for some time 'not well'.<sup>9</sup>

#### Pathology

Biopsy of the liver and necropsy studies have demonstrated that a large percentage of the larvae in children are

located in the liver, and the enlargement of this organ is a result of multiple focal and linear eosinophilic granulomatous lesions scattered throughout that organ. They tend to be somewhat more numerous near the surface, where they are readily visible as grayish or pale areas 2-4 mm. in diameter. A narrow zone of hyperaemia may be noted at the margins. Larvae in or near similar lesions have been observed in nearly all organs of the body. At autopsy multitudes of larvae have been found in the brain, and in one instance a *Toxocara* larva was a chance finding in the brain of a child whose death was due to an apparently unrelated cause. A study of lesions in 54 eyes of children removed because of suspected retinoblastoma revealed nematode larvae in 24 of them,<sup>10</sup> and in several instances the larvae could be identified as *Toxocara*.<sup>11</sup> A similar case of *Toxocara* larva in the eye of a child was recently observed in California.

In tissue sections 3 general types of pathological picture have been described. As the result of active migration, especially in the early phases of infection, linear granulomata are produced and, as in creeping eruption of the skin, the area of tissue damage is relatively extensive in relation to the number of larvae responsible. Later, and in some tissues more than others, the predominant lesion is a fibrous capsule around one or more living larvae. The third type of reaction is a generalized hyperergia which in one recorded instance resulted in death.

The histopathological picture in the early phase consists chiefly of granulomata in various stages of progression and regression formed in the wake of moving larvae. In the immediate vicinity of the larva itself there may be little or no evidence of alteration of the tissues. In all stages up to complete encapsulation the cellular infiltration is conspicuously eosinophilic, although initially there may be a predominance of lymphocytes and neutrophils. Within the granulomata in both the migration paths and encapsulations, epithelioid and giant cells of the foreign-body type are frequently conspicuous features. There appears to be a somewhat greater reaction in the vicinity of the small blood vessels than elsewhere, and perivascular infiltration is often seen without any apparent relation to primary lesions. Associated with massive accumulations of eosinophils there are often an abundance of Charcot-Leyden crystals, especially in the early phases of capsule formation.

Apart from the number of larvae present in the tissue and the frequency of superinfection, a factor which apparently contributes importantly to the larva migrans syndrome is hypersensitivity which, in an extreme case reported by Brill *et al.*,<sup>12</sup> resulted in extensive inflammation and degeneration of the striated muscles in the diaphragm and elsewhere, although apparently very few larvae were involved.

#### Diagnosis

The diagnosis of visceral larva migrans can usually be established on clinical grounds. Physical findings and symptoms mentioned above, along with extreme and sustained eosinophilia combined with a history of contact with dogs and cats, give strong presumptive evidence of larval *Toxocara* infection. A history of pica or geophagia will oftentimes provide the most convincing evidence. In the first several cases studied, diagnosis was based on finding

the larvae in biopsies of the liver taken by laparotomy. Punch biopsy of the liver has on one occasion demonstrated the typical lesions and the causative larva. At present, however, biopsy is used only in extreme cases where there is suspicion of eosinophilic leukaemia or neoplastic lesions in the eye or central nervous system. Sero-diagnostic tests are under experiment in a number of laboratories but have not yet reached the stage of helpful routine use.

In most instances the demonstration of a nematode larva in the tissues is a difficult procedure in that it requires long, tedious and somewhat expert search of many sections mounted serially, or special involved techniques of isolating the larvae from tissues by digestion or in squash preparations. Of even greater difficulty is the specific identification of the larva after it has been found. Having in mind the possibility of encountering larvae of several of the species normally found in human tissues, Nichols<sup>13</sup> initiated comparative studies of the species of nematode larvae most likely to occur in human tissues. His work has provided criteria for distinguishing one from the other among the genera *Toxocara*, *Ascaris*, *Necator*, *Ancylostoma* and *Strongyloides*. Additional studies it is hoped may discover reliable diagnostic characters for the different species.

Larva migrans, as the term is generally used, is limited to infections involving nematodes that undergo little or no growth and development in human tissues. Infections of a similar nature but involving the juvenile or even the adult stages of species that normally complete their reproductive cycle in other animals are infrequently reported. *Capillaria hepatica*, which in nature lives in the liver of rats and other rodents, has recently been found in liver biopsies from children in America,<sup>14</sup> Hawaii<sup>15</sup> and South Africa.<sup>16</sup> As in *Toxocara*, the infective stages of *Capillaria* develop in soil and enter the human body through ingestion. There is also a large group of nematodes, the Spirurids, that occasionally invade human tissues after having been ingested in insects or lower vertebrates. In addition, some of the filarial worms, transmitted normally to wild and domesticated mammals by blood-sucking insects, occasionally undergo partial development in man and produce a larva migrans type of infection.<sup>17</sup>

These observations point to two problems, one having to do with diagnosis and interpretation of the usual parasitic diseases of man, the other dealing with prevention. As stated earlier, the visceral type of larva migrans may last in more or less symptomatic form for very long periods and, if unrecognized, may easily confuse the picture of intercurrent conditions. Trichuris infection, for example, has been described as producing high levels of peripheral eosinophilia. More recently, however, it has been found that despite a pronounced eosinophilia of the exudates in dysenteric stools, eosinophilia of the blood is characteristically of a very low order or lacking.<sup>18</sup> Another example is the striking eosinophilia that developed in individuals who were given raw liver in the diet for the treatment of pernicious anaemia. It is not yet definitely known that nematode larvae ingested with the raw liver were responsible for the eosinophilia, but it seems to be the most probable explanation in view of experimental evidence and the failure of cooked liver, liver extracts or vitamin B12 to produce this puzzling reaction.

### Prevention

The marked reduction in parasitic infections and other filth-borne diseases brought about by modern sanitary measures has amply demonstrated the soundness of the general principles on which they are based. The question may now be raised whether these or similar measures can be made to apply to the prevention of those diseases that are transmissible from animals to man. The question is especially pertinent as regards household pets whose defaecation habits are sometimes discussed and often resented but at the moment are about equally tolerated in communities of all standards. The frequency of the visceral type of larva migrans cannot be precisely determined until more suitable diagnostic methods become available. However, in localities where pediatricians are aware of it as a possible cause of illness, the frequency of established diagnosis of Toxocariasis derived from family or neighbourhood pets clearly justifies its classification as an important pediatric and public health problem, demanding the attention of public health authorities, general practitioners, pediatricians and veterinary physicians. No effective treatment for the visceral type of larva migrans has yet been found. Preventive measures must therefore be relied upon to effect whatever control is possible.

### SUMMARY

Visceral larva migrans is a disease newly added to the long list of infections transmissible from dogs and cats to man. It is related to cutaneous larva migrans (creeping eruption or sandworm infection) in that both are caused by nematode larvae that migrate for long periods in human tissues without growth or development. The two types of larva migrans are further related in that larvae causing the characteristic linear lesions of the skin tend later to invade the deeper tissues, where similar lesions are produced. Cutaneous larva migrans is caused by a variety of skin-penetrating nematode species but *Ancylostoma braziliense* appears to be one of the most frequent and most damaging among them. Even it, however, generally produces a transient condition which is self-terminating and therefore may seem to be cured by ineffectual remedies.

*Toxocara canis*, a common cosmopolitan ascarid of dogs, is probably the most important species involved in the visceral type of larva migrans. *T. mystax*, the common cat ascarid, may also be involved. Infective stages develop in contaminated soil. When ingested by humans, usually toddler-age children, the larvae hatch in the intestine, migrate to the liver, lungs, central nervous system and other organs, where they persist for many months, at first producing linear eosinophilic granulomatoses, and later becoming encapsulated. The severity of the disease depends upon the number of larvae, their location in the body, and the degree of allergic reaction to them. Many cases and a few deaths have been reported in the United States. The disease probably is common wherever children have close contact with cats or dogs.

Extreme peripheral eosinophilia, hepatomegaly, hyperglobulinaemia, intermittent low-grade fever, loss of appetite and deviations in behaviour are the usual signs, and there is often a history of dirt-eating and contact with a young dog or cat. Diagnosis, hitherto based on identification of

larvae in liver biopsies, can now usually be made on clinical grounds. Since no specific treatment is known, control depends on effective preventive measures. Less frequently, similar non-patent (or occult) visceral infections are produced by a number of nematode parasites of other animals, some acquired through eating the infective stages in insects or other lower animals, others through the bites of blood-sucking insects. A common feature of all the visceral types of larva-migrans infections is their tendency to be cryptic and therefore to be overlooked as a cause of disease. Also, their tendency to produce high, sustained eosinophilia often leads to confusion in the diagnosis and description of inter-current conditions.

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