Infection of Mammalian Hosts by Milk-borne Nematode Larvae: A Review

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STONE, W. M., AND SMITH, F. W. 1973. Infection of mammalian hosts by milk-borne nematode larvae: a review. Experimental Parasitology 34, 306-312. Milk-borne or transmammary infection has been observed to occur in several host-parasite systems. In the order of their observation, these are Uncinaria luctasi-fur seal; Strongyloides ransomi-swine; Ancylostoma caninum-dog; Toxocara canis-dog; Strongyloides westeri-horse; Neoscaris vitulorum-cow; Strongyloides papillosus-cow and -sheep; and Toxocara cati-cat. Some of these parasites are largely dependent on milk-borne infection of neonatal animals. All have a tissue migratory phase in their life cycle. Most of these parasites also utilize other modes or combinations of modes in infecting new hosts. The potential importance of milk-borne infection as a factor in human hookworm disease is pointed out as is the need for complete assessment of this avenue of infection.

INDEX DESCRIPTORS: Milk-borne; Transmammary infection; Nematode; Migration; Seal; Swine; Dog; Horse; Cow, Sheep; Cat; Neonatal infection; Ancylostomiasis; Strongyloidiasis; Ascariasis; Uncinaria luctasi; Strongyloides ransomi; Ancylostoma caninum; Toxocara canis; Strongyloides westeri; Parasitological Reviews; Neoscaris vitulorum; Strongyloides papillosus; Toxocara cati; Trichinella spiralis.

The discovery that milk-borne larvae could be the infective forms in the life cycle of a nematode was first published by Lyons and Olsen in 1962. They reported finding Uncinaria luctasi larvae in the milk of the fur seal, Callorhinus ursinus Linn., with subsequent infection of newborn pups.

Previously, transmission routes of nematode larvae to animals had been found to be only by skin penetration and by ingestion. In cases of dog hookworm, early infection had been assumed to be wholly prenatal (Adler and Clark 1922; Foster 1932; Yutuc 1949).

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Prior to Lyons and Olsen's discovery, only two other observations of nematode larvae in milk had been made. Salzer, in 1916, found larvae of Trichinella spiralis in the milk of a woman with clinical trichinosis. Kotake (1928) reported Ancylostoma caninum and Toxocara canis larvae in the milk and mammary glands of experimentally infected guinea pigs.

During the 10 years following evidence of milk-borne hookworm infection in the seal, attention has been directed toward this route of infection. The life cycle of all parasites utilizing this avenue includes tissue migration.

Instances of experimental and natural
MAMMALIAN INFECTION BY MILK-BORNE NEMATODES

Milk-borne infection with nematode larvae are reviewed here in chronological order. In each such instance, except that of *T. spiralis*, infection of the host animal has been observed to occur naturally, establishing milk-borne infection as a normal mode of transmission, operative to a greater or lesser extent in the life cycle.

**Trichinella spiralis** (Owen, 1835) Railliet, 1895. The life cycle of *T. spiralis* is considered to involve the ingestion by the definitive host of tissue which contains viable, infective, encysted larvae. Encysted larvae are freed by digestive enzymes and develop to adults which proceed to mate and produce larvae. These larvae enter the circulatory system and are distributed widely over the body. They can be found in almost any organ of the body although they encyst only in striated muscle (Denham 1966). The question of whether these somatic migratory larvae must encyst before becoming infective has still not been resolved.

Salzer (1916) demonstrated numerous larvae in the milk and excised mammary gland of a nursing woman but made no attempt to establish an infection using the larvae. Tissue migratory larvae present in milk of experimentally infected mother mice were assumed responsible for infections among five litters of infant mice (Denham 1966). Since no larvae were actually demonstrated in the milk of the mothers, only presumptive evidence of milk-borne infection was presented.

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**Uncinaria lucasi** Stiles, 1901. The life cycle of *U. lucasi*, a parasite of the fur seal, *C. ursinus* Linna., was described by Lyons and Olsen (1962) and Olsen and Lyons (1962, 1965). There are three phases in the life cycle: (1) eggs and free-living larvae in the soil; (2) tissue migrating, parasitic third-stage larvae which occur in the subcutaneous fat of seals and in the mammary glands of the mature females; and (3) adult male and female worms in the intestine of the young pups in the rookery. When free-living third stage larvae overwinter in the rookery, newborn pups are exposed to both skin penetrations by free-living invasive larvae and to milk-borne larvae. Only the larvae ingested with the colostral milk develop into mature worms in the pups. Worms become adult in 13–15 days and are lost by the time the pups are 3 mo old. Skin-invading larvae lodge in the belly blubber. Larvae were present in the milk of mother seals for only a short time postpartum; however, it was shown experimentally that pups were still susceptible at from 9 to 13 days of age to a superimposed infection. Larvae recovered from the milk of nursing dams were more advanced in development than the skin penetrating larvae found in the soil, but larvae from both sources were still third-stage. Larvae from belly blubber of non-pregnant cows, bachelor seals and bachelor sea lions did not develop into adult worms in susceptible pups. Prenatal infection was not demonstrated (Olsen and Lyons 1965).

**Strongyloides ransomi** Schwartz and Alicata, 1930. The life cycle of *S. ransomi* resembles that of other species in the genus. These nematodes are transitional between parasitic and free-living. Parthenogenetic female worms lay embryonated eggs which may develop directly into infective larvae or into free-living males and females which in turn produce infective larvae. Infection of the definitive mammalian host may occur by penetration of skin or mucosa of mouth or esophagus with migration through the lungs before establishment in the small intestine. Experimental prenatal infection has been described (Stewart, Smith, and Jones 1963) as well as naturally occurring prenatal infection (Stone 1964; Pimentel Neto et al. 1965; Zajicek 1969).

**Milk-borne infection of newborn pigs was reported by Moncol and Batte in 1966. Larval concentration 4 hr prior to parturition was approximately 1 larva per 0.06 ml of milk. By 12 hr postpartum, the number had dropped to 1 larva per 4.4 ml of milk. Pigs fed filtered milk failed to develop infections while littermate animals allowed to nurse the same mother became infected.**

In subsequent observations, Batte and
Moncol (1967) recovered larvae from inguinal, perineal and submandibular fat, following subcutaneous infection. No larvae were found in mammary parenchyma, striated muscle, omentum or perirenal fat. Some dead larvae were found in the diaphragm.

In this same study, three animals confined in strongyloid-free isolation areas after initial infection passed larvae following two pregnancies. One of the sows passed an average of 20, 3, and 1 larvae per ml of colostrum in successive farrowings. Pigs showed patent infections within 4 days in all instances. Biopsied tissue from the mammary gland before nursing showed no larvae at 30 and 10 days prepartum, but larvae were obtained at 4-6 hr prepartum and 12-18 hr postpartum.

Ancylostoma caninum (Ercolani, 1859) Hall 1913. Infection of dogs with A. caninum takes place either by penetration of the skin or through the mouth, the latter mode of entrance being considered the most usual (Levine 1968). Larvae penetrating the skin migrate to the small intestine via the lungs, bronchi, trachea, and pharynx. Ingested larvae, in contrast, do not migrate to the lungs in any numbers but enter the wall of the intestine for a few days prior to establishment in the intestinal lumen (Foster and Cross 1934).

Foster (1932) showed that prenatal infection may occur with A. caninum following both oral and percutaneous infection of the dam with a prepatent period of 10-12 days. Milk-borne infective larvae were first observed in a naturally infected bitch both prior to and just at the beginning of her first whelping (Stone and Girardeau 1966).

Enigk and Stoye (1967) found hookworm larvae in the milk of five bitches up to 18 days postpartum, following experimental infection at various times during their gestation periods. Larval recovery was greatest within 4 days postpartum and dropped rapidly thereafter. Among the five bitches from which larvae were recovered in the milk, a range of from 1 larva per 0.5 ml to 1 larva per 10.3 ml of milk was reported. A minimum of 73 to a maximum of 439 ml of milk was obtained from five animals.

Stone and Girardeau (1967) detected A. caninum larvae in the milk from three of five naturally infected dogs at parturition. A reduced number of larvae were observed in the milk of these animals 12 hr postpartum. No larvae were found in 59 pups either stillborn or examined prior to nursing, whereas hookworms were found in 27 of 34 nursed puppies at ages of 1-20 days. These data from litters produced by 25 naturally infected bitches indicate that transmammary larval transfer occurs with more frequency than prenatal infection. The largest volume of milk collected from one of these naturally infected bitches was 145 ml over an 8 day interval. Thirty-one larvae were recovered during this time. During the same period it is estimated this animal produced about 4 liters of milk containing approximately 870 larvae. These were shared among 12 pups, an average of about 72 worms each (Stone and Girardeau 1968).

A 1.15% incidence of prenatal infection among 180 pups from 20 bitches naturally infected with A. caninum has been observed (Stone, Peckham, and Smith 1970). Five prenatal infections of pups from four bitches experimentally infected (Miller 1970) were demonstrated from 10 puppies examined. In all, 17 larvae were recovered from the 10 pups examined for prenatal infection while over 800 larvae were recovered from 14 littermate animals which nursed for 15 days. Nine pups fed larvae obtained from the milk of experimentally infected bitches developed patent infections within 12-16 days (Stone and Peckham 1970). Herrick (1928) reported a prepatent period of 15-18 days for pups infected by the oral route. Apparently no difference on a prepatent period basis can be seen between milk-borne and other modes of infection.

Toxocara canis (Werner 1782) Stiles 1905. Toxocara canis is found predominantly in the dog, but has been reported from the cat, fox, wolf, and coyote. Other animals including man can act as paratenic hosts.
Dogs may become infected by eating embryonated eggs or by eating paratenic hosts containing second-stage larvae. The larvae hatching from these eggs penetrate the intestinal mucosa and follow the usual migratory path to the lungs and trachea, finally returning to the intestine when swallowed. In puppies a few larvae do not return to the intestine but are distributed throughout the body. In older dogs the greater portion of the larvae follow the latter course and may be found in various somatic sites (Webster 1958).

Sprent (1958) indicated that prenatal infection in dogs was common, and Scothorn, Koutz and Groves (1965) suggested that it is the principal mode of infection of puppies and responsible for a high percentage of stillbirths and early deaths. They considered “the presumption that all pups are prenatally infected with larvac of *T. canis* is a convenient and practical generalization.”

Borman (1957) found that the brain and the mammary glands acted as biological traps for larvae in experimentally infected mice, and that the number present in these areas increased directly with the time after infection.

Oshima (1961) observed a reduction in the recovery of somatic larvae in pregnant mice near parturition. He interpreted this as a loss of larvae by way of the feces following migration into the intestinal lumen. He observed a similar loss of somatic larvae following daily injections of certain hormones to nonpregnant, nonlactating females.

*T. canis* larvae have been recovered from the milk of a naturally infected bitch on the 9th day postpartum (Enigk and Stoye 1967), and from the 22nd to the 32nd day postpartum (Stone and Girardeau 1967).

Strongyloides westeri Ihle 1917. This strongyloid has been reported from the horse, zebra and donkey. Although *S. westeri* has been recognized as a common parasite of foals for over 50 years, no evidence of infection of adult horses has been found. Lyons, Drudge and Tolliver (1969) reported milk-borne infection in the mare, the only report of any milk-borne worm parasite of horses.

Larvae were recovered from the milk from 5 to 19 days after foaling. Larvae cultured from the feces of infected foals by these same investigators produced infections in worm-free foals either orally or percutaneously. They concluded that the probable source of initial infection in foals is milk-borne larvae with subsequent fecal contamination of the environment and buildup of percutaneous infection by infective third-stage larvae.

Neoascaris vitulorum (*Toxocara vitulorum*) (Goeze 1782). *Neoascaris vitulorum* is the only known bovine ascaridian. Mature worms of *N. vitulorum* seem to be found exclusively in calves. Prenatal infection has been reported by Herlich and Porter (1953), Cvetkovic and Nevenic (1960) and Srivastava and Mehra (1955).

Warren (1969) made the first detailed identification of *N. vitulorum* in Australia and reported larvae in the milk of several experimentally infected cows between the 2nd and 18th day postpartum. No larvae were recovered from 4.25 liters of colostrum collected from these animals prepartum. He further reported finding third-stage *N. vitulorum* larvae in the milk of two naturally infected cows at 2 and 6 days postpartum. Examination of fetal calves, unnursed neonatal calves and calves fed commercial milk from birth were all negative for *N. vitulorum* (Warren 1971).

Shooh (1970) observed larvae, presumed to be *N. vitulorum*, in the milk of a cow given a large number of *N. vitulorum* eggs prepartum. *N. vitulorum* eggs appeared in the feces of the cow’s nursing calf by the 26th day postpartum.

Strongyloides papillosus (*Wedl* 1856) *Ransom* 1911. The life cycle of *S. papillosus* of sheep and cattle is similar to that of *S. ransomi*.

Prenatal infections have been assumed in calves of cows exposed prepartum to infective larvae (Pfeiffer 1962), but no pub-
lished reference to prenatal infection of sheep has been seen by the authors.

Lyons, Drudge, and Tolliver (1970) reported *S. papillosus* larvae in milk samples of six ewes and one cow. One to 21 larvae per ewe were obtained between the 8th and 19th day after lambing. A larva was obtained from the milk of the cow on the 7th and on the 19th days postpartum. *S. papillosus* eggs were first detected in the feces of the calf on the 15th day postpartum.

Toxocara cati Zeder 1800. *Toxocara cati* occurs in the small intestine of the various members of the cat family (domestic cat, wild cat, lion, leopard, and lynx) and rarely in dogs and humans throughout the world. Swerczek et al. (1971) demonstrated milk-borne infection in a series of experiments with both experimentally and naturally infected cats. One hundred larvae were recovered from the milk of five experimentally infected queens and 7959 larvae from 12 of their infected kittens; 198 larvae were obtained from the mammary glands of six naturally infected queens. Larvae were recovered from the milk throughout the lactation period. No evidence for prenatal infection was found in 111 kittens examined at birth or taken by caesarean section. The large number of larvae recovered from the milk and mammary glands of infected queens and from their kittens points to milk-borne larvae as a primary mode of infection in the life cycle of *T. cati*.

**DISCUSSION**

At least four nematodes, *U. lucasi*, *A. caninum*, *S. ransomi*, and *T. cati*, utilize milk-transmission as a primary mode of infection of neonatal animals. It seems probable that *S. papillosus*, *N. vitulorum*, and *S. westeri* may likewise be transmitted to the offspring mostly by this means. No prenatal infection has been demonstrated for *U. lucasi*, *T. cati*, *S. papillosus*, *N. vitulorum*, and *S. westeri*. *T. canis* seems to be the only parasite among the entire group which has been shown to utilize prenatal infection of the young to any significant extent.

The high survival value inherent in possession of either the prenatal or milk-borne modes of infection would tend toward a retention of either or both systems by a particular parasite. The predominance of either of these modes when both are possible would seem to favor the selection of milk-borne infection among the host–parasite relationships observed.

Present thinking on the mechanism of migration of infective larvae from somatic sites to mammary glands and subsequent transmission to suckling young, is that hormones released during late pregnancy or just prior to parturition are responsible for such stimulation (Webster 1958; Olsen and Lyons 1965). Just which hormones are active in this regard should be investigated.

The relative frequency with which any mode or combination of modes of infection is utilized by a parasite is peculiar to that host–parasite system. The frequency represents the summation of influences of external and internal environment and the physiological and behavioral characteristics of both the host and parasite. The parasite is presumably the more adaptable of the pair. It is possible that a particular mode of infection would become more frequent under certain conditions and another under other conditions. In the seal–hookworm relationship, no prenatal infection was encountered during examination of 39 caesarean-derived pups. Larvae ensuing from eggs can complete only somatic migration. These tissue-phase larvae are the source of milk-borne larvae, the only larvae apparently capable of reaching the adult stage in the intestine (Olsen and Lyons 1965).

*T. spiralis* larvae, since they may pass in the milk (Salzer 1916), pose a threat to both human and swine populations. If larvae present in the milk of the definitive host are infective (Denham 1966), they could provide a means of transmission of *T. spiralis* through the milk to either infants or neonatal pigs without the necessity of any carrier host. Such transmission would af-
fect eradication efforts among either swine or human populations.

Few surveys for hookworm in humans have been made among infants below 1 year of age as these are considered to be relatively unexposed. However, 175 adult Necator americanus were found in a child 33 days of age (M. Hollander, Bronx, NY, personal communication 1967), and hookworm eggs were identified in the stool of children 14 days of age (Howard 1917) and 44 days of age (Costas and Torres DeVega 1968). Areas of high incidence and heavy infections are ideal for study of milk-borne hookworm infection. Intensive study may add greatly to our knowledge of the epidemiology of hookworm disease and may be of great help in devising improved methods of prevention and control. A preliminary assessment can be made in an area of known heavy incidence of hookworm by the examination of stool samples from infants from 8 to 12 wk of age. A significant number of positive samples might suggest that prenatal or transmammary infection is taking place. As a follow-up, milk samples of at least 5 ml should be obtained from mothers as soon after parturition as possible and continued for a week. Preserved or fresh samples should be examined following filtration or centrifugation.

The rapidity with which new instances of milk-borne infection have been observed since attention has been focused on this method of transmission makes it a probable part of the life cycle of any nematode with a tissue migratory phase. It is imperative that the life cycle of such nematodes be thoroughly reexamined in the light of our newly found knowledge.

References


Lyons, E. T., and Olsen, O. W. 1962. “Report on eighth summer of investigations on hookworms, Uncinaria lucasi Stiles, 1901, and hook-


STEWARD, T. B., SMITH, W. N., and JONES, D. J. 1963. Prenatal infection of pigs with the intestinal threadworm, Strongyloides ransomi. Journal of Parasitology 49 (Sec. 2), 45.


