Neglected rare human parasitic infections: Part I: Sparganosis

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ABSTRACT

Some neglected parasitic larvae and worms may cause rare human infections. They are mostly zoonotic species. Sparganosis is the infection with a plerocercoid larva of an animal diphyllolothriid cestode. The valid species incriminated in causing human sparganosis are Spirometra erinaceieuropaei, Spirometra decipiens, Spirometra mansonioides, Spirometra theileri, and the aberrant Sparganum proliferum. Other species reported to infect human in the literature are probably nonspecific. Coenurosis is the infection with a metacestode of Taenia species, mainly T. multiceps or T. serialis. Acanthocephaliasis, on the other hand, is the infection with acanthocephalan worms. Man was reported to be infected with at least nine acanthocephalan species, among them, Macracanthorhynchus hirudinaceus and Moniliformis moniliformis are the most common species. Hirudiniasis is the human attack by leeches. They are temporary parasites because they attack victims only when they are hungry and drop off when they are engorged. Among all species of leeches, only true leeches especially jawed leeches are known to attack humans. These species are either freshwater or land dwellers. This review summarizes current knowledge of the public health significance of human affections by these parasites, and the recommended methods of prevention and control.

Keywords: acanthocephaliasis, coenuriasis, hirudiniasis, neglected parasitic infections, sparganosis.

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Part I - Sparganosis

Human sparganosis is a zoonotic infection with a plerocercoid larva of an animal diphyllolothriid cestode. Thus, man acts as a second intermediate host. Unfortunately, only fragmentary and sometimes controversial information about the disease are available in the literature.

Keywords: cestoda, flatworms, plerocercoid, public health, sparganum, Spirometra.

The term sparganum (pleural spargana) is a generic name that refers to any plerocercoid larva. However, it is believed that the causative agents are species of the genus Spirometra, as well as the aberrant Sparganum proliferum. The plerocercoid larva of Spirometra spp. is a wrinkled, whitish, ribbon-shaped motile parasite, a few millimetres in width and up to several centimetres long resembling the narrow tapeworm proglottids. The anterior end of the sparganum is capable of invagination and bears preliminary signs of the sucking grooves formed on the scolex of the adult worm but has no suckers or hooklets. The most common localization of sparganum is the subcutaneous tissue. However, ocular, visceral and cerebral sparganosis have been reported. Sparganum proliferum is a branched proliferating larva characterized by a peculiar budding type of larvae that may break up into segments capable of further independent development. This type of larvae may occur almost anywhere in the human body[12]. Sparganosis may be misdiagnosed as a tumour and vice versa[13].

Human sparganosis is cosmopolitan, with the highest prevalence rates reported from South Korea, Japan, Thailand, and China[17-19].

1. Genus Spirometra (Mueller, 1937)

Synonyms: Gatesius Stiles, 1908; and Lueheella (Luheella) Baer, 1924.

The genus was established under the name Spirometra by Mueller in 1937[13]. Although this name was used by Faust et al. in 1929[13] as a subgenus, some authors synonymized the genera Spirometra and Diphyllobothrium[13]. Phylogenetic results confirmed that the genus Spirometra is clearly separate from the genus Diphyllobothrium[14]. Spirometra occurs worldwide, although most human cases were recorded from the Southeast Asian countries[15]. Some cases were diagnosed in East Africa[16-22] and the Americas[23-29], and a few others in Europe mainly from Italy[26-30].

The plerocercoids of the different species of Spirometra were described from a variety of animals such as amphibians, reptiles, birds, and mammals including man (Figure 1). Adults were found in carnivores, mainly canines and felines. These animals pass embryonated eggs containing coracidia in their faeces. To complete the life cycle, the parasite must infect two intermediate hosts. The first host is a cyclopid copepod which ingests the aquatic ciliated hexacanth coracidium. The parasite develops in the copepod tissues into the first larva which is called...
procercoid. When the infected crustacean is ingested, the second larval stage, plerocercoid, develops in the second vertebrate intermediate host, which may be an amphibian, reptile, bird, small rodent, primate, or pig\cite{37}.

Human accidentally serves as the second intermediate or paratenic host. In most cases, human acts as a dead-end host. Human sparganosis can be acquired through drinking water containing copepods harbouring the procercoid stage. An additional mean for acquiring the infection is ingestion of insufficiently cooked infected amphibians, reptiles, birds, or mammals such as pigs, which contain the plerocercoid stage. A third way of infection is application of infected frog or snake flesh as a poultice on the skin or eyes, where the larvae are activated by warmth and enter the human tissue. Using frog or snake flesh for treatment of skin ulcers and eye inflammation is common in traditional medicine of the Far East\cite{38}, and some areas of South America\cite{29}. In the human body, larvae form slow-growing migratory nodular lesions. Nodules are mainly found in the subcutaneous tissues of the anterior chest, the abdominal wall, or the inguinal region. Occasionally larvae migrate into unexpected sites of the body such as the pleural cavity\cite{39}, or the central nervous system\cite{40}, causing unusual or even fatal manifestations. Symptoms of sparganosis depend on the site of infection. Subcutaneous sparganosis presents with a cyst like, itchy, migratory nodule. It is slowly growing and may not be tender. Peripheral blood eosinophilia may be present\cite{41}. In ocular sparganosis, the eyelids are oedematous, itchy, and painful with excessive lacrimation, and a cystic nodule is present in the eyelids\cite{42-44}.

Diagnosis is made after surgical removal of nodules and identifying the characteristic larva present in an eosinophilic granulomatous reaction\cite{45}. Many species of _Spirometra_ have been described from various areas of the world as causative agents of human sparganosis. However, the species position is still very confused.

1.1. _Spirometra erinaceieuropaei_ (Rudolphi, 1819) Mueller, 1937.
_Synonyms:_ _Spirometra mansoni_ Cobbold,1882; _Spirometra erinacei_ (Rudolphi, 1819) Faust, Campbell, et Kellogg, 1929; _Spirometra houghtoni_ Faust, Campbell, et Kellogg 1929; _Spirometra ranarum_ Meggit, 1925.

In 1959, Yamaguti confirmed that _S. mansoni_ and _S. erinacei_ are synonymous and placed them under the name _S. erinaceieuropaei_\cite{46}. This species is the most common cause of human sparganosis in the world. Most cases were reported from the Far East\cite{37}. Probably this species is responsible for the human cases in Europe\cite{37}. The plerocercoids acquired orally by man do not develop in the intestine but penetrate the intestinal wall and go through various organs causing sparganosis. Therefore, the adults of _S. erinaceieuropaei_ normally do not occur in man. However, on very rare occasions, adult worms were recovered from the intestine of man\cite{47-49}. It was suggested that certain altered chemical or enzymatic environment of human gut might be responsible for the unusual adult infection\cite{37}.

1.2. _Spirometra decipiens_ Faust, Campbell, et Kellogg, 1929

In 1929, Faust and co-authors recovered specimens identified as _S. decipiens_ from a cat, a leopard, and a dog in China. They obtained the same adult worms
by feeding larvae from frogs to dogs\cite{12}. Only in 2015, human cases infected with this species were confirmed in Korea\cite{49}. The identity of the species was confirmed by using morphological and molecular data\cite{50-52}. Differentiating morphologic criteria described a spirally coiled uterus with 4.5 coils in *S. decipiens* and 5-7 coils in *S. erinaceieuropaei*, while differentiating molecular criteria based on cox1 gene sequence showed a 1:2 prevalence respectively in human patients in Korea\cite{50}. In addition comparison of the mitochondrial genome differentiated between the two species\cite{51}. In another study to differentiate spargana from snakes collected from Korea and China revealed the predominance of *S. decipiens* using a multiplex PCR assay (n=854) and phylogenetic analysis of mitochondrial cox1 sequence (n=50)\cite{52}.

1.3. *Spirometra mansonioides* (Mueller, 1935) Wardle, McLeod, et Stewart, 1947.

This species is found exclusively in the Americas. When the organism was discovered by Mueller in 1935, he did not know if *S. mansonioides* and *S. erinaceieuropaei* were two distinct species\cite{53}. In 1974, Mueller distinguished *S. mansonioides* distributed in North America from *S. erinaceieuropaei* distributed in Asian region\cite{54}. PCR-RFLP analysis of the two worms showed the two to be separate but closely related parasites\cite{55}. Experimental human infection with this species was successful\cite{53}. A second case of human infection was reported by Read in 1952 in South Texas\cite{52}. Since that time many cases were reported\cite{54,57,28}. In 1905 and till 2009, at least 16 well-documented cases of human proliferating sparganosis were reported worldwide. Cases were reported from the Far East and the Americas\cite{57,59-60}. This sparganum seems to reproduce inside the host and thus has been called *S. proliferum* or the proliferating sparganum. In humans, it could proliferate with more than one plerocercoid in one lesion and spread to other parts of the body. Thus, at autopsy many thousands of larvae may be present in the viscera as well as in the subcutaneous tissues. Most cases were fatal\cite{57,60,62,63}. Disseminated proliferating sparganum was reported as an opportunistic infection in an AIDS patient\cite{60}.

In 1968, a human case of Hodgkin disease died after repeated courses of cytotoxic chemotherapy and radiotherapy. The post-mortem examination of the man indicated that an impossible to miss parasite had multiplied and spread all through his body. The shape and structure of the parasite favoured the diagnosis as an aberrant sparganum showing uncontrolled proliferation and spread\cite{57}. Afterward, it was described as indistinguishable from *Rodentolepis nana* (*Hymenolepis nana*) in the aberrant larval form\cite{60}. More lately, the parasite was identified as a larval cestode with a previously uncharacterized 18S rDNA sequence. It was suggested that it could be a common cestode of a nonhuman, perhaps avian, host and an uncommon human disease agent\cite{60}.

### 1.4. *Spirometra theileri* (Baer, 1925) Opuni et Muller, 1974

A few cases of human sparganosis were recorded in East Africa\cite{16-22}. Most probably these cases were infected with *S. theileri*. The lifecycle of this species is summarized by the presence of the plerocercoids in wild herbivores and adults in large carnivores. The Masai are a semi-nomadic Nilotic ethnic group found in Kenya and northern Tanzania. They are among the best known African ethnic groups because of their distinctive customs and cloth, and residence near the game parks of East Africa. Like wild animals, they move across the plains of East Africa drinking from the same water holes. Sparganosis may be more common in the Masai than has been reported\cite{21}. It was identified as the only occasional chronic nodule diagnosed on excision in the Masai\cite{56}. Nelson et al\cite{56} mentioned that human may be a suitable intermediate host of the parasite because Masai's dead bodies are usually laid out to be eaten by hyaenas\cite{50}.

### 1.5. *Pseudophyllidea*

*N. decipiens* is a distinct species from *S. erinaceieuropaei* or the proliferating sparganum. In humans, it was suggested that *S. proliferum* might be a group of proliferating larvae of different species\cite{57}. Molecular data suggest that it may be a distinct species of *Spirometra*; however, the adult stage remains unknown\cite{14,58} and the biological features of the proliferating sparganum, including its taxonomic status, are still obscure. Partial sequencing of the mitochondrial cytochrome c oxidase subunit I (coI) gene from several isolates in Asian countries and evaluation of intraspecific variation of *S. erinaceieuropaei* and its phylogenetic relationship with *Diphyllobothrium*, confirmed that *S. proliferum* is a distinct species from *S. erinaceieuropaei*\cite{14}. This was proved in an earlier study also investigating the coI gene and the partial nucleotide sequences of nuclear coded succinate dehydrogenase iron-sulfur protein subunit gene (sdhB), and in addition the study confirmed that *S. proliferum* belongs to the order *Pseudophyllidea*\cite{58}. Since its first case report by Ijima in 1905 and till 2009, at least 16 well-documented cases of human proliferating sparganosis were reported worldwide. Cases were reported from the Far East and the Americas\cite{57,59-60}. *S. proliferum* seems to reproduce inside the host and thus has been called *S. proliferum* or the proliferating sparganum. In humans, it could proliferate with more than one plerocercoid in one lesion and spread to other parts of the body. Thus, at autopsy many thousands of larvae may be present in the viscera as well as in the subcutaneous tissues. Most cases were fatal\cite{57,60,62,63}. Disseminated proliferating sparganum was reported as an opportunistic infection in an AIDS patient\cite{60}.

### Sparganosis as an emerging human disease

Human sparganosis should be considered among the emerging parasitic infections of increasing concern\cite{70,71}. Such emergence may be due to intensive human travelling and migration. Sparganosis was reported in individuals who travelled to endemic regions or who migrated from endemic to non-endemic countries\cite{72}. Additionally, there is an increasing trend of human consumption of some unusual animal species, like frogs and snakes\cite{10}, which led to increased international trade and intensification of husbandry...
practice of these animal species. This emergence may be explained by the improvement of the diagnostic methods which favoured additional reporting.

Prevention and control
In endemic foci, people should be advised to avoid drinking water that has not been filtered or treated. People should, also, make sure that flesh that might contain spargana is properly cooked. The use of raw flesh of potentially infected animals in traditional poultices must be discouraged.

Surgical removal is the best treatment for human sparganosis. Nevertheless, it is possible only in case of infection with one or a few spargana. The whole body of the spargana should be removed, as any remaining scolex will result in regeneration of the body of the spargana should be removed, as any remaining scolex will result in regeneration of the body of the spargana.

The recommended dose is 120-150 mg/kg body weight, over a 2-day period. In the practice of these animal species, praziquantel is apparently effective if surgical removal does not work. In addition, α-chymotrypsin is used if surgical removal does not work. Localised treatment with 40% ethanol procaine or poultices must be discouraged.

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