Gastrodiscoidiasis, a plant-borne zoonotic disease caused by the intestinal amphistome fluke *Gastrodiscoides hominis* (Trematoda: Gastrodiscidae).

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Abstract: Gastrodiscoidiasis is an intestinal trematodiasis caused by the only common amphistome of man *Gastrodiscoides hominis* and transmitted by small freshwater snails of the species *Helicorbis coenosus*, belonging to the family Planorbidae. Human and animal contamination can take place when swallowing encysted metacercariae, by ingestion of vegetation (aquatic plants) or animal products, such as raw or undercooked crustaceans (crayfish), squid, molluscs, or amphibians (frogs, tadpoles). Pigs appear to be the main animal reservoir of any significance in most endemic areas. Its geographical distribution covers India (including Assam, Bengal, Bihar, Uttar Pradesh, Madhya Pradesh and Orissa), Pakistan, Burma, Thailand, Vietnam, Philippines, China, Kazakstan and Volga Delta in Russia, and has also been reported in African countries such as Zambia and Nigeria. The presence of *G. hominis* in Africa needs further studies, to confirm that the African amphistome in question is really that species and not a closely related African species, and to ascertain its geographical distribution in this continent. In man, this amphistome fluke causes inflammation of the mucosa of caecum and ascending colon with attendant symptoms of diarrhoea. This infection causes ill health in a large number of persons, and deaths among untreated patients, especially children. Human infection by *G. hominis* is easily recognisable by finding the characteristic eggs of this amphistome in faeces. Although comparative assays about the efficacy of different drugs against this amphistome are lacking, there is nothing impeding to suggest Praziquantel as the drug of choice for this trematodiasis. Control methods should include (i) prevention of human contamination, (ii) actions at human level to cut disease dissemination by humans, (iii) control the disease at animal reservoir level, and (iv) actions at the level of the intermediate molluscan host.

Keywords: Gastrodiscoides hominis, Gastrodiscoidiasis, review.

Resumen: La Gastrodiscoidiasis es una trematodiasis intestinal causada por el único afistómido común del hombre *Gastrodiscoides hominis* y transmitida por pequeños caracoles dulceaquícolas de la especie *Helicorbis coenosus*, perteneciente a la familia Planorbidae. La contaminación humana y animal tiene lugar por deglución de metacercarias enquistadas, al ingerir vegetación (plantas acuáticas) o productos animales, tales como crustáceos crudos o poco cocidos (cangrejos de río), calamares, moluscos, o anfibios (ranas, renacuajos). El cerdo es el principal reservorio animal, de importancia en la mayoría de áreas endémicas. Su distribución geográfica abarca la India (incluyendo Assam, Bengal, Bihar, Uttar Pradesh, Madhya Pradesh y Orissa), Pakistan, Burma, Tailandia, Vietnam, Filipinas, China, Kazakstan y el Delta del Volga en Rusia, y ha sido también citado en paises africanos como Zambia y Nigeria. La presencia de *G. hominis* en Africa precisa de estudios adicionales, con el fin de confirmar si el anfistómido africano en cuestión es en realidad la misma especie y no otra especie africana próxima, así como también para establecer su distribución geográfica en dicho continente. En el hombre, este trematodo anfistómido causa inflamación de la mucosa del ciego y colon ascendente, con síntomas de diarrea. La infección por este digénido origina enfermedad en un gran número de personas, e incluso la muerte en pacientes sin tratamiento, especialmente niños. La infestación humana por *G. hominis* es fácilmente reconocible mediante el hallazgo de los huevos característicos de este anfistómido en las heces. A pesar de que ensayos comparados sobre la eficacia de diferentes drogas contra este trematodo brillan por su ausencia, nada impide el sugerir que el Praziquantel debe ser considerado la droga de elección para esta trematodiasis. Los métodos de control deben comprender (i) prevención de la contaminación humana, (ii) acciones a nivel humano para cortar la diseminación por el hombre, (iii) controlar la enfermedad a nive

Palabras clave: Gastrodiscoides hominis, Gastrodiscoidiasis, revisión.

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1. Introduction

At present, many trematodiases are emerging in different regions (Keiser and Utzinger, 2005). Climate and global changes appear to increasingly affect the snail-borne helminthiases, which are pronouncedly

dependent from the environment. Fascioliasis is a good example of an emerging-reemerging parasitic disease in many countries as a consequence of many phenomena related to both environment change and man-made modifications (Mas-Coma, 2004a, b, 2005; Mas-Coma et al., 2003, 2005). That is why fascioliasis and other foodborne trematodiases have been very recently added to the list of important helminthiases with high impact on human development, at the occasion of the Third Global Meeting of the Partners for Parasite Control held in WHO Headquarters Geneva on November 2004 (Anonymous, 2004).

Among these trematodiases, there are diseases which affect millions of people, as fascioliasis, clonorchiasis and opisthorchiasis by liver flukes (Mas-Coma & Bargues, 1997), fasciolopsiasis by the Giant Asian intestinal fluke (Mas-Coma et al., 2005), and paragonimiasis by lung troglotrematid species belonging to only one genus (Blair et al., 1999), whereas others are considered secondary because of appearing only sporadically or affecting a lower number of persons. Among the latter, gastrodiscoidiasis is undoubtedly one of the most important owing to both the number of infected subjects, its pathogenicity and its wide geographical distribution.

Concerning gastrodiscoidiasis, studies in recent years have been less numerous and a recent, exhaustive review of the present knowledge on this disease is needed. In this paper, a review of gastrodiscoidiasis is included in the way to offer the necessary baseline for future studies.

2. The causal agent

The trematode species Gastrodiscoides hominis (Lewis et McConnell, 1876) Leiper, 1913 (Gastrodiscidae) is the only common amphistome of man. When alive, adults of G. hominis are thick, fleshy pyramidal in shape and bright pink in colour. Their size varies from 8.0 to 14.0 by 5.5 to 7.5 mm in fixed and pressed specimens (Shrivastav and Shah, 1970; Kumar, 1980). Two parts may be distinguished in its adult body: a short and conical-cylindrical anterior portion, and a large, discoidal, of up to 8.0 mm wide and ventrally excavated posterior portion. The oral sucker is provided with a small paired diverticula and the oesophagus has a posterior bulbous swelling. The unbranched caeca are slightly winding and terminate near the anterior margin of the acetabulum. The acetabulum is medium sized and ventro-terminal in position. The testes are lobed, tandem and situated in the middle third of the body. The ovary is intercaecally placed behind the posterior testis, near the centre of the discoidal portion. The uterus is intercaecal and the genital pore is located ventrally and slightly anterior to the caecal bifurcation. The vitelline glands occupy the lateral fields

of the discoidal portion (Ahluwalia, 1960; Kumar, 1980, 1999). Eggs are ovoid, measure 127-160/62-75 μ m (mean 146/66 μ m), have a pale greenish grey colour in fresh faecal specimens, and present the abopercular end generally thickened and rarely provided with a spine like elongation (Dutt and Srivastava, 1972).

The surface morphology of the tegument of the huge ventral disc has a prominent pattern of convolutions and folds, including tubercle-like protuberances well visible with scanning electron microscopy. Such a tegument characteristics extend also to the surface of the subterminal acetabulum. Along the acetabular rim there are conspicuous globular or cup-shaped, mini suckerlike protuberances known as suckerlets, which probably aid the strong anchorage of the acetabulum to the host surface of contact (Tandon and Maitra, 1983).

3. Definitive hosts and adult microhabitat

The location of this amphistome is the caecum and colon of both pig and man (Ahluwalia, 1960; Kumar, 1980, 1999). The number of flukes in pig can reach very high numbers, as up to 1886 in a pig individual and with intensity averages of 227 in pig populations (Dutt and Srivastava, 1972), which clearly indicates that the pig may be considered the normal host species of this trematode parasite.

Varma (1954) made a comparative study of the morphology of the adult fluke from man and pigs and concluded that the porcine forms differed from the human forms in their general smaller size, characters of their genital papilla/cone, and the shape and arrangements of the testes. That is why he justified *G. hominis* from pig as a separate variety, var. suis. However, this differentiation has not been generally accepted after studies involving a large number of specimens which show that those differences were not constant (Shrivastav and Shah, 1970).

Another definitive host species in which this trematode has been found is wild boar, as in the Thekaddy forest area in Kerala, India, where it was detected infected besides the domestic pig (Easwaran et al., 2003). This parasite has also been found in Napu mouse deer (Tragulus napu) from Malaya, as well as in field rat (Rattus brevicaudatus) from Java, and rhesus monkeys (Macaca mulatta) in India (Buckley, 1964; Fox and Hall, 1970). There are also records in other monkeys, as Macaca fascicularis, M. irus, M. philippinensis, and M. cynomolgus (Herman, 1967), and primates as the orangutan, Pongo pygmaeus (Pester and Keymer, 1968). In Thailand, it was found in 7.4% of rats studied (Impand et al., 1983), as well as in a spectacle monkey Presbytis molalophos from Chumphon Province (Waikagul and Radomyos, 2005).

A survey of trematode infections in introduced fur-bearing mammals in the Volga Delta, Russia, was carried out between 1993 and 1997. *G. hominis*, which locally infects wild boars, was recently been found in the introduced American muskrats (*Ondatra zibethica*) (Ivanov and Semenova, 2000).

4. Distribution

First described from an Indian patient, *G. hominis* was initially believed to have a distribution restricted to India and the southeast Asia. However, progressive studies showed that it has a larger distribution in the Palaearctic Region which covers India, including Assam, Bengal, Bihar, Uttar Pradesh, Madhya Pradesh and Orissa (Shrivastav and Shah, 1970; Murty and Reddy, 1980), Pakistan, Burma, Thailand, Vietnam, Philippines, China, Kazakstan and the Volga Delta in Russia. This amphistome has even been found in Indian inmigrants in Guyana (Ahluwalia, 1960; Buckley, 1964; Kumar, 1980; Harinasuta *et al.*, 1987; Yu and Mott, 1994; Ivanov and Semenova, 2000; Fried *et al.*, 2004).

Later, it began to appear in Africa (Goldsmid, 1975), in countries such as Zambia (Hira, 1983), and it has also been recently reported in a 7-year-old girl who was diagnosed by egg finding in stools in Nigeria (Dada-Adegbola *et al.*, 2004). The presence of *G. hominis* in Africa needs further studies, to confirm that the African amphistome in question is really that species and not a closely related African species, and to ascertain its geographical distribution in this continent.

5. Transmission and intermediate snail host

The amphistome *G. hominis* follows a diheteroxenous life cycle. Eggs when laid include an embryo in a very early stage of segmentation. The miracidium appears fully mature on day 9 at a temperature of 24-33 °C. A detailed description of the miracidium has been furnished by Zablotski (1964) and Dutt and Srivastava (1972). Hatching takes place between days 9 and 14 depending from temperature. Higher temperatures appeared to be detrimental for miracidium development. A longer maturation period of 4 weeks was required in April-May. Longer periods of up to 3 months for hatching have also been described (Dutt and Srivastava, 1972).

Only the tiny aquatic snail species *Helicorbis* coenosus (= Segmentina coenosus) (Planorbidae) has shown its capability to play the role of intermediate host. This amphistome appears to be markedly snail host specific, as experiments to infect other species (*Indoplanorbis exustus*, Gyraulus convexiusculus) failed (Dutt and Srivastava, 1966, 1972).

Gastrodiscoides hominis reports in Africa pose the question of the intermediate snail host in that

continent. A closely related amphistome trematode species, *Gastrodiscus aegypticus* (Cobbold, 1876) Looss, 1896, which mainly parasitizes equines (horse, donkey, mule) in various parts of Africa and has also been found in pig and wild boar, uses planorbid species of the *Bulinus* (*Bulinus*) forskalii group (Malek, 1971).

In *H. coenosus*, mother rediae and daughter rediae are found in the digestive gland. These are $148-747/45-140~\mu m$ in size, sausage shaped, and lack collar and locomotor organs. The rediae present a salient birthpore which is located near the level of the saccular intestine (Dutt and Srivastava, 1972).

The prepatent period ranges between 28 and 152 days, this variation apparently depending on the seasonal variations of the temperature, i.e., 51 days at a mean temperature of 24 °C (variation 20-30 °C) and 74 days at a mean temperature of 22 °C (variation 17-27 °C). This period is shortest in summer and longest in winter. The longevity of the snails varies from 10 to 147 days after the infection becomes patent, and the snails shed cercariae intermittently for 6-40 days. Positive snails stop shedding when it becomes cold.

Gastrodiscoides hominis cercariae have an ovoid to pyriform body of 403-865/192-310 μ m, with a narrower anterior end, and are provided with a pair of dark pigmented eye-spots. Their tail is slightly longer than the body, of 468-923/56-94 μ m (Dutt and Srivastava, 1966). The number of cercariae shed daily by individual snails varies from 1 to 34 (mean 6,8). The total number of cercariae shed by individual snails ranged 7-238, with an average of 74,7 (Dutt and Srivastava, 1972).

Cercarial emergence takes place in morning hours. The free swimming life of cercariae varies from 1 hour to more than 24 hours, at the end of which it encysts. Encystation generally takes place on the bottom. A few of them encyst on the shell of the snail host or any other substrate available as a stalk of *Nymphoea*. The metacercarial cyst, formed in about 2-4 minutes, is hemispherical and brownish, 201-227 µm (mean 216 um) in diameter (Dutt and Srivastava, 1972).

In infection experiments of pigs with metacercariae, all (100%) became infected and the mean percentage of metacercariae established in the definitive host was 37% (Dutt and Srivastava, 1972). Juvenile flukes, released from the excysted metacercariae in the small intestine, descend the intestinal tract to reach the caecum and colon. In these locations, the juvenile worms do not penetrate the intestinal mucosa, but mature and live as adults in the lumen by attaching to the intestinal mucosa with the aid of their acetabula (Kumar, 1999). Experimental flukes of 308 day old appear already similar than those in natural infections (Dutt and Srivastava, 1972).

6. Epidemiology

Although it is mainly a parasite of pigs, sometimes high prevalences have also been detected in humans, as is the case of the 41% prevalence detected in mainly children in Kamrup District in Assam, in northern India. Additionally, high intensities were also found in individual cases when removed by treatment. Results of the studies suggested that the infection was maintained in the human population without participation of this animal reservoir, since pigs were very scarce in Kamrup at that time (Buckley, 1939).

The prevalence in pigs is of epidemiological significance for infection in man because the pig is the main reservoir. In the water reservoirs around the pigsties where this trematode infection is known to be endemic, the molluscan species *H. coenosus* appears to abound (Kumar, 1880).

In India, many epidemiological data may be understood taking into account that *G. hominis* and the intestinal digenean species *Fasciolopsis buski* (Lankester, 1857) Odhner, 1902 (Fasciolidae) use the same molluscan intermediate host species. In Bareilly, India, 27% of a total of 233 slaughter-pigs were infected with this amphistome and in 50% of these cases the infection was concomitant with *F. buski* (Dutt and Srivastava, 1972). Similar results obtained in human surveys may be explained in the same way, i.e., prevalences of 41% by *G. hominis* and of 59.7% by *F. buski* in the same population of 221 human subjects analysed (Buckley, 1939).

Gastrodiscoides hominis showed a seasonal occurrence trend similar to that of *F. buski* in surveys of pigs in the tribal populations of Shillong (Mehhalaya), a hilly city of north-east India where rearing of pigs is a common household practice. Their prevalence rose to a peak during the months from June to September, declining thereafter to a low level during winter and early spring (November-March). The infection by *G. hominis* was not present during the first 3 months of the year, similarly as *F. buski* which was absent during January and February (Roy and Tandon, 1992).

Metacercariae of *G. hominis* are able to attach to different substrates. Therefore, it has been suggested that human contamination may occur when encysted metacercariae are swallowed with tainted vegetation (aquatic plants) or with animal products, such as raw or undercooked crustaceans (crayfish), squid, molluscs, or amphibians (frogs, tadpoles), as is the case in other species of the same family Gastrodiscidae (Yu and Mott, 1994; Fried *et al.*, 2004).

7. Pathology and symptomatology

In the infection by *G. hominis*, the pathology and symptomatology are uncertain. It is stated that in man the parasite causes inflammation of the mucosa of caecum and ascending colon with attendant symptoms of

diarrhoea. This amphistome infection causes ill health in a large number of persons, and deaths among untreated patients, especially children, have been attributed to this infection (Kumar, 1980). The specimens can be collected from the caecum, especially near to the ileocaecal valva, and at the site of its attachment as deep imprint of the fluke is seen (Yu and Mott, 1994).

The gross lesions produced by this fluke in pigs have a characteristic appearance. The acetabulum is found to drag the mucosa as a plug which stood like a papilla and occupied an eccentric position in the sharply defined circular area which developed by the continued impact of the discoidal region of the parasite on the mucosa of the caecum (Ahluwalia, 1960). Sometimes the caeca may be infected to such an extent by the parasite that any healthy tissue can hardly be seen (Shrivastav and Shah, 1970).

In human infection a picture similar to that detected in pigs might be expected. Surface desquamation, infiltration with eosinophiles, lymphocytes and plasma cells appear in sections of the lesions caused by the fixation of the parasites to the mucosa. The submucosa appears also infiltrated and displays oedema and thickening, resulting in a subacute inflammation of the caecum and mucoid diarrhoea (Ahluwalia, 1960; Yu and Mott, 1994). Marked desquamation of epithelial lining, hypersecretion of mucus and necrosis of the mucuos glands are observed in an histopathological examination. The lamina propria shows massive infiltration of eosinophiles in between the crypts of Lieberkuhn along with lymphocytes, macrophages and plasma cells. The muscularis mucosa becomes thickened, due to infiltration of eosinophils, lymphocytes, plasma cells and macrophages. The blood vessels appear hyperaemic and some show thickening of tunica intima and infiltration by eosinophils and lymphocytes (Shrivastav and Shah, 1970).

In Thailand, a 17 year-old girl was admitted to the Bhudhachinaraj Hospital in Phitsanulok Province, with the main complaint of passing urine containing faeces for 15 days and passing many worms on the day before admission. The patient had a history of weakness, anaemia and weight loss for 8 months before passing faecal urine, and having general oedema with a palpable mass in the suprapubic area. On admission the patient was emaciated and anaemic (haemoglobin = 6 g/dl), with oedema of face and legs, fever (38.8°C), leucocytosis (15,000/mm³), and no eosinophilia. The catheterized urine contained faeces, white and red cells, granular casts, and was albumin positive. No parasites were found in stools. A jejunovesical fistula was revealed by means of X-ray barium enema. The patient died after surgery to correct the fistula. The autopsy confirmed the jejuno-ileo-vesico-vaginal fistula, and additionally revealed lymphosarcoma of large intestine and mesenteric lymph nodes (Surinthrangkul et al., 1965).

8. Diagnosis

The parasitological diagnosis of gastrodiscoidiasis is by coprology. Human infection by *G. hominis* is easily recognisable by finding the characteristic eggs of this amphistome in faeces. Care should be taken to differentiate gastrodiscoidiasis from fasciolopsiasis, as both trematodiases overlap in most of the Asian endemic areas. The eggs of *G. hominis* are, however, easily distinguishable from the eggs of *F. buski*, because the eggs of the latter are oval and yellowish-brown. The adult amphistome worm is unmistakable when passed spontaneously or expelled by treatment with soap water enemas or anthelmintics (Buckley, 1964).

9. Treatment

There is no specific treatment known for *G. hominis* infection (Kumar, 1980), although it appears to respond to antihelmintics usually used against trematodiases, such as thymol, carbon tetrachloride, and tetrachloroethylene. Although comparative assays about the efficacy of different drugs against this amphistome are lacking, there is nothing impeding to suggest Praziquantel as the drug of choice for this trematodiasis. Mebendazole was also efficient in clearing a girl who was shedding thousands of *G. hominis* eggs in stools even with a single dose of 500 mg (Dada-Adegbola *et al.*, 2004).

10. Prevention and control

Theoretically, the control of gastrodiscoidiasis by blocking or interruption of the parasite life-cycle can be achieved by very simple ways. Control methods should include the following main axes: (i) prevention of human contamination; (ii) actions at human level to cut disease dissemination by humans; (iii) control the disease at animal reservoir level; and (iv) actions at the level of the intermediate molluscan host.

To prevent human contamination, the most practical method is to avoid eating raw, water-derived food. However, the reality shows how difficult it is to change century-old traditions, as appropriate measures demand fundamental changes in the eating habits and customs, as well as in the economic conditions of the people. Food preparation and eating habits are passed from one generation to the next, and water plants are a common food source in the endemic areas because they are cheap and readily available. Educational efforts should be directed primarily toward school-age children because they are less entrenched in their food and eating habits, behaviour, and customs. Unfortunately, the experience of many years show that, despite educational programmes, people still enjoy eating raw food products in many areas. However, we already know that significant results in the control of intestinal helminthiasis may be achieved by

the implementation of control programmes in schoolaged children with strong community therapy planning (WHO, 1995a, b; Mott *et al.*, 1995). Prevention of the infection might also be accomplished if the vegetables are immersed in boiling water for a few minutes. Peeling them and washing in running water to wash away the freed metacercarial cysts should also be considered as a preventive measure. In countries where eating raw plants is customary and treated water is not available, the prevention of reinfection relies on consistent educational programmes stressing the importance of thoroughly cooking all aquatic plants and boiling all water. Unfortunately, the belief that cooking food destroys the flavor and nutritional value still persists.

To cut the parasite dissemination by humans, three main initiatives should be performed: apply appropriate pharmacological treatments to infected subjects after proper diagnosis, avoid promiscuous defaecation near water bodies, and prohibite the use of unsterilized "night soil" (human excrement collected from latrines) as fertilizer.

To control the disease at animal reservoir level, measures should be adopted to restrain pigs from having access to ponds and canals. Pigs may easily acquire this disease because they are often fed with infected raw vegetables. Thus, the plants must always be checked for the presence of metacercariae. The use of aquatic green fodder for pigs shall be prohibited. Moreover, pharmacological treatment of pigs should be carried out after proper parasitological diagnosis of pig faeces. Thus, instituting modern pig farming in endemic areas should be the best initiative to control infection of this animal reservoir host

Control activities at the level of the transmitting snails may mainly include prevention of pollution of the ponds inhabited by the snails and where different aquatic plants are cultivated. Pollution of the ponds happens in different ways in the various endemic areas. Human excreta are used as fertilizer in China, promiscuous defaecation takes place in the bodies of water near the houses in Thailand, and excreta of pigs are washed into neighbouring bodies of water in many endemic areas.

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