World Health Organization

World Organisation for Animal Health

Food and Agriculture Organization

WHO/FAO/OIE Guidelines for the surveillance, prevention and control of taeniosis/ cysticercosis

Editor:
K.D. Murrell

WHO/FAO/OIE Guidelines for the surveillance, prevention and control of taeniosis/cysticercosis

Editor:
K.D. Murrell
Associate Editors:
P. Dorny
A. Flisser
S. Geerts
N.C. Kyvsgaard
D.P. McManus
T.E. Nash
Z.S. Pawlowski

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OIE (World Organisation for Animal Health), WHO (World Health Organization) and FAO (Food and
Agriculture Organization), 2005
OIE, 12, rue de Prony, 75017 Paris, France
Tel: 33-(0)l 44 15 18 88
Fax: 33-(0)l 42 67 09 87
http://www.oie.int

ISBN: 92-9044-656-0

Cover
Design: © Coup de Grace Designs, Tartu, Estonia
Conception: pbpOIE

FOREWORD

Taeniosis and cysticercosis are two parasitic diseases that in the past have not always been recognized for their importance. However, it is becoming increasingly clear that greater priority should be given to these zoonoses because of their economic impact, particularly in resource-poor countries, and their public health burden. They are also now recognized as an increasing problem in some regions, such as Africa. The now accepted linkage between epilepsy and neurocysticercosis in countries endemic for *Taenia solium* is further impetus for allocating more effort to the control of taeniosis/cysticercosis.

As is the case for all zoonoses, the control of taeniosis/cysticercosis, requires a very close collaboration between both veterinary and medical public health services at a national level. It was with the aim of assisting those responsible for taeniosis/cysticercosis control and prevention that these Guidelines were prepared and jointly published by the Food and Agriculture Organization (FAO), the World Health Organization (WHO) and the World Organisation for Animal Health (OIE). This joint publication is another example of the three organizations working together to assist their member countries in designing, implementing and standardizing control strategies against zoonoses on both national and international levels. This is the result of years of effort by FAO, WHO and OIE to educate and to organize the surveillance and control of parasitic diseases world-wide.

This FAO/WHO/OIE Guidelines for the Surveillance, Prevention and Control of Taenisosis and Cysticercosis is a compilation of the knowledge and valuable expertise of a great many internationally recognized experts on these zoonoses, accumulated over more than a hundred years of research. Without this knowledge base, effective and proven recommendations for diagnosis, treatment, prevention and control would not be possible. We would like to express our profound gratitude to these experts for their contributions and for those able to share their knowledge and advice with the authors. It is our hope that this book achieves the success it deserves.

Carlos Eddi
FAO
Food and Agriculture Organization

Francois-Xavier Meslin
WHO
World Health Organization

Bernard Vallat
OIE
World Organisation for Animal Health

AUTHORS

J.C. Allan, Pfizer Animal Health, Licensing and Business Development, Pfizer Ltd, Sandwich, United Kingdom, E-Mail: James_Allan@Sandwich.Pfizer.Com.

Guillermina **Avila,** Departamento de Microbiología y Parasitología, Facultad de Medicina, Universidad Nacional Autónoma de México, México 04510 DF, México, E-Mail: Guilleavila2000@Yahoo.Com.

J. **Brandt,** Department of Animal Health, Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerpen, Belgium, E-Mail: Jbrandt@Itg.Be.

Dolores **Correa,** Subdirección de Medicina Experimental, Instituto Nacional de Pediatría,Secretaria de Salud, México 04530 DF, México, E-Mail: mariadol@yahoo. com.

Oscar H. **Del Brutto,** Department of Neurological Sciences, Hospital-Clínica Kennedy, Guayaquil, Ecuador.

P. **Dorny,** Department of Animal Health, Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerpen, Belgium, E-Mail: Pdorny@Itg.Be.

Ana **Flisser,** Departamento de Microbiología y Parasitología, Facultad de Medicina, Universidad Nacional Autónoma de México, México 04510 DF, México and Dirección de Investigación. Hospital General 'Dr Manuel Gea González', Secretaria de Salud, México 14000 DF, México. E-Mail: Flisser@Servidor.Unam.Mx.

Hector **H. Garcia,** Cysticercosis Unit, Instituto Nacional de Ciencias Neurolo'gicas, Departments of Microbiolog)[7] and Pathology, Universidad Peruana, Cayetano Heredia, Peru.

S. **Geerts,** Department of Animal Health, Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerpen, Belgium, E-Mail: Sgeerts@Itg.Be.

A. **Ito,** Department of Parasitology, Asahikawa Medical College, Asahikawa, 078-8510, Japan. E-Mail: Akira Ito [Akiraito@Asahikawa-Med.Ac.Jp].

Niels C. **Kyvsgaard,** WHO/FAO Collaborating Center for Emerging Parasitic Zoonoses, Danish Center for Experimental Parasitology, Royal Veterinary and Agricultural University, 1870 Frederiksberg C, Denmark, E-Mail: Nck@Kvl.Dk.

Pablo **Maravilla,** Dirección de Investigación. Hospital General 'Dr Manuel Gea González', Secretaria de Salud, México 14000 DF, México-E-Mail: Maravillap@Yahoo.Com.

D**.** P. **McManus,** Molecular Parasitology Laboratory, Australian Centre for International and Tropical Health and Nutrition, The Queensland Institute of Medical Research and The University of Queensland, Brisbane, Queensland 4029, Australia, E-Mail: Donm@Qimr.Edu.Au.

H. **Meinardi,** retired Professor of epileptology Nijmegen University, The Netherlands; Past-President International Bureau for Epilepsy and International League Against Epilepsy, Netherlands, E-Mail: Meinardi@Wxs.Nl.

K.D. **Murrell,** Danish Centre for Experimental Parasitology, WHO/FAO Collaborating Centre for Emerging Parasitic Zoonoses, Institute of Veterinary Pathobiology, Royal Veterinary and Agricultural University, 1870 Frederiksberg, Denmark, E-Mail: Kdmurrell@Comcast.Net.

Theodore E. **Nash,** Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

Z.S. **Pawlowski,** Clinic of Tropical and Parasitic Diseases, University of Medical Sciences, Ul.Przybyszewskiego 49, 60-355 POZNAN, Poland, E-Mail: Zpawlows@Am.Poznan.Pl.

Vedantam **Rajshekhar,** Department of Neurological Sciences, Christian Medical College and Hospital, Vellore, India.

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INTRODUCTION

Background

The terms cysticercosis and taeniosis refer to foodborne zoonotic infections with larval and adult tapeworms, respectively. The important features of these zoonoses are that the larvae are meat-borne (generally beef or pork) and the adult stage develops only in the intestine of the human host (obligate). *Taenia saginata* ('beef tapeworm'), *Taenia saginata asiatica*[1] ('Taiwan *Taenia')* and *Taenia solium* ('pork tapeworm') are the most important causes of taeniosis in humans. Cysticercosis is a tissue infection with the larval Cysticercus or metacestode stage, and occurs most commonly in pigs and cattle; *Taenia saginata* occurs only in beef and *T. s. asiatica* in pig organs and *T. solium* primarily in pork. Humans acquire the adult stage through eating improperly cooked infected meat.

Taenia solium is unique because the larval or Cysticercus stage can also infect humans and cause cysticercosis/neurocysticercosis (man acts as an intermediate host in this case; see Chapter 1 on Biology). Infection with the cysticercus stage is responsible for almost all serious human disease caused by these taeniid tapeworms. These cestodes are cosmopolitan in distribution, and are highly endemic in Latin America, Africa and Asia where poor sanitation, and intimate contact between humans and their livestock are commonplace. Although the life cycle cannot be maintained in regions with adequate sanitation and good animal husbandry practices, these regions are still vulnerable, due to the immigration of people from highly endemic regions carrying infections of the adult stage (taeniosis). Such introduced infections account for an increased global distribution to non-endemic regions such as in the United States and Europe, where human carriers can contaminate the environment of others, leading to secondary infections.

In addition to the importance of these relatively neglected food-borne zoonoses as a cause of morbidity and mortality in many undeveloped regions, they are also being recognized as a cause of loss of income for farmers with marginal subsistence. It has been estimated that millions of persons worldwide are infected with *T. solium,* the most serious tapeworm species in human infections. For example, more attention to this zoonosis is occurring in Sub-Saharan Africa because of the growing recognition of the importance of neurocysticercosis (larval infection of the central nervous system) in epilepsy, a disease which is now the subject of a global public health campaign ('Out of the Shadows'). In this region, the rapid expansion of smallholder pig production has led to to a significant increase in cysticercosis in pigs and humans, an important problem for governments seeking to increase livestock production and rural incomes. These events are not unique to Africa, however, and are the impetus for international concern and actions, such as the recent recognition of the importance of neurocysticercosis by the 56th World Health Assembly (WHA) (2003), which issued a report on Control of Neurocysticercosis. This Report highlights important issues and actions that need to be taken to control neurocysticercosis.

Because neurocysticercosis is an important cause of epilepsy, it places particular demands on health services; likewise, its link to epilepsy will dramatically increase the burden of disease owing to the social stigmatization and discrimination surrounding this condition.

Human cysticercosis is a disease associated with poverty in areas where people eat pork and traditional pig husbandry is practiced. It is endemic in the Andean area of South America, Brazil, Central America, and Mexico; the People's Republic of China, the Indian subcontinent and South-East Asia; and sub-Saharan Africa. The spread of this disease is facilitated by poor hygiene, inadequate sanitation and the use of untreated or partially treated wastewater in agriculture. However, cysticercosis can also occur in individuals who do not raise pigs or consume pork.

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1 This parasite is considered by many to be a separate species of *Taenia.* However, there is not yet a consensus on this taxonomic issue, and for the purposes of this Guideline, it is treated as a subspecies of *T. saginata* (See Annex 4.5 for full discusssion of this issue)

The Report points out that more than a decade ago (1993) the International Task Force for Disease Eradication (ITFDE) declared *T. solium* 'a potentially eradicable parasite'. More recently, ITFDE called for a large demonstration project on effective control or elimination to be carried out; such a 'proof of concept' would probably be the greatest single stimulus to further action against this potentially eradicable disease. However, as yet no truly successful intervention programs has been completed anywhere at a national level to achieve this goal. Until then, both the WHA and the ITFDE urge medical and veterinary sectors to cooperate in establishing national prevalence and economic impact studies, and to create surveillance reporting programs. These efforts should adopt up-to-date diagnostic tools, clinical management procedures, employ anthelminthics for the treatment of humans and pigs, establish high standards of meat hygiene and veterinary control over pig husbandry and slaughter practices, and wider health education on the risks and prevention of cysticercosis, all of which are subjects discussed in these Guidelines.

In order to undertake these tasks, personnel, especially those with limited experience with taeniosis and cysticercosis must have access to the most useful and up-to-date information available. In recognition of this need, the WHO, FAO and OIE instigated the development of Guidelines summarizing the collective knowledge of experts in this field.

Objectives of the Guidelines for the Surveillance and Control of Taeniosis and Cysticercosis

This Guidelines is the successor to the earlier 1983 WHO Guidelines for Surveillance, Prevention and Control of Taeniosis/Cysticercosis (VPH/83.49). The previous Guidelines had a impact on efforts to focus attention on the problems of these zoonoses, and provided practical assistance to those charged with developing and implementing surveillance, treatment and control programs. It also stimulated research by identifying important knowledge gaps. Since that time, much has been accomplished in this field. Greater understanding of the epidemiology and effective control design of these zoonoses has been achieved, assisted greatly by the development of new and better diagnostic technologies. Clinical management and treatment approaches (especially imaging) have also greatly advanced. It is the objective of authors of this Guidelines to bring these advances together in a practical format, to help those with the responsibility for confronting these zoonoses.

The Guidelines covers the biology, systematics, epidemiology, diagnosis, prevention and control of taeniosis and cysticercosis, in humans, cattle and pigs. The Chapters include descriptions of procedures for clinical management, for conducting risk assessment studies, and for prevention and control programs. Recent technologies introduced for the detection and diagnosis of infection are described. The Guidelines provides advice and recommendations on program planning, monitoring and evaluation. Special reference is made to intersectoral coordination and collaboration, particularly between medical and veterinary services, which are crucial for effective surveillance and control efforts.

Those responsible for the production of this Guidelines are hopeful that the material provided will prove useful and effective for those personnel involved in the detection and treatment of infection, and in the development of prevention and control programs. We further hope that the information and guidance presented will enhance progress towards the objectives described above by the WHA, and promoted by the FAO and WHO.

CHAPTER 1:
BIOLOGY OF *TAENIA SOLIUM, TAENIA SAGINATA* AND *TAENIA SAGINATA ASIATICA*

A. Flisser, D. Correa, G. Avilla & P. Marvilla

1. Introduction

Infections with *Taenia saginata, Taenia saginata asiatica* and *Taenia solium* are unique among helminth zoonoses in that their life cycles are dependent upon humans as the sole definitive host. Also, the life cycles are dependent on the link between humans and cattle *(T. saginata)* and pigs (*T. solium* and *T. s. asiatica)*, so that prevention and control of taeniosis and cysticercosis should be straightforward and practical, the reality is that they have proved nearly intractable in many areas because of the highly successful dissemination and reproductive features of the parasite and because of well-entrenched cultural factors of the human hosts.

In this Chapter, a description is given of the systematics, biology and host-parasite interaction of these zoonotic cestodes ('tapeworms'). A thorough understanding of these aspects is crucial to the understanding of their epidemiology/ecology, and to the design of effective surveillance, prevention and control strategies.

1.1. Morphology

Tapeworms of the genus *Taenia* (T. *solium,* T. *saginata* and *T.saginata asiatica)* are flat, opaque white or yellowish and exceptionally long segmented parasites, measuring 1 to 12 m in their adule stage. The head or scolex is the attachment organ, and has four suckers and a rostellum that may be armed with hooks (*T. solium*), or unarmed and sunken (*T. saginata*), or with rudimentary hooklets (*Taenia saginata asiatica*) (Fig. 1.1). When hooks are present, thay are organized in two rows of 22 to 23 and range in size from 110 to 180 μm. The scolex is the size of a pin-head, and is followed by a short and undivided region, the neck, from which a long chain of proglottids or segments (termed the strobila) proliferate, thus the strobila has the appearance of a ribbon and may consist of more than a thousand proglottids. These gradually increase in size so that the posterior end of the tapeworm has the broadest, longest and oldest proglottids [23, 151, 167, 175, 177, 263, 277, 508, 534].

The neck and strobila are markedly flattened, while the scolex has a radial symmetry, therefore no clear definition of dorsal and ventral surfaces can be made. Since the testes are nearer to one surface, this is considered the dorsal surface, while female sexual organs are considered to be closer to the ventral surface; and the ganital pore or atrium is the only external marginal structure of the proglottid. Proglottids have different developmental stages: those proximal are immature, followed by mature proglottids and distal proglottids gravid with eggs. Mature segments are hermaphroditic, and contain several hundred testes, connected by fine sperm ductules that anastomose to form the sperm duct or vas deferens, which ends in the genital pore, forming the highly muscular cirrus. The female sexual system consists of one bilobulated ovary, connected to an oviduct. The vagina is a slightly sinuous tube which flows from the genital atrium to the oviduct; the vitelline glands are also connected to the oviduct. The oviduct, where fertilization takes place, transforms into the central sac or uterus, once the gonads and their ducts have attained maturity. Gravid proglottids resemble sacs full of eggs (between 54,000 and 80,000 each) and are approximately 0.5 cm wide by 1-2 cm long. The egg-containing uterus develops seven to 32 lateral branches, depending on the species. This feature allows identification if the proglottids belong to *T. solium* (seven to 11 branches) or *T. saginata* (12-32 branches) [263, 277, 508].

The scolex has a solid muscular, mesenchymatous construction and contains the central part of the nervous system and nephridial canals. The cerebral ganglia are connected via longitudinal nerve cords to

commissures found in each proglottid. Sensory and chemotactile papillae and receptors, as well as a profuse network of fibers, indicate that this system is highly developed. The protonephridial type excretory system is composed of two dorsal and two ventral longitudinal collecting ducts, connected to transverse ducts located in the posterior end of each proglottid. Tubules terminating in flame cells connect to the collecting ducts. Flame cells are located in the parenchyma; internally each cell bears a tuft of cilia or 'flame' which beats rapidly to collect excretory material [263, 277, 508, 534].

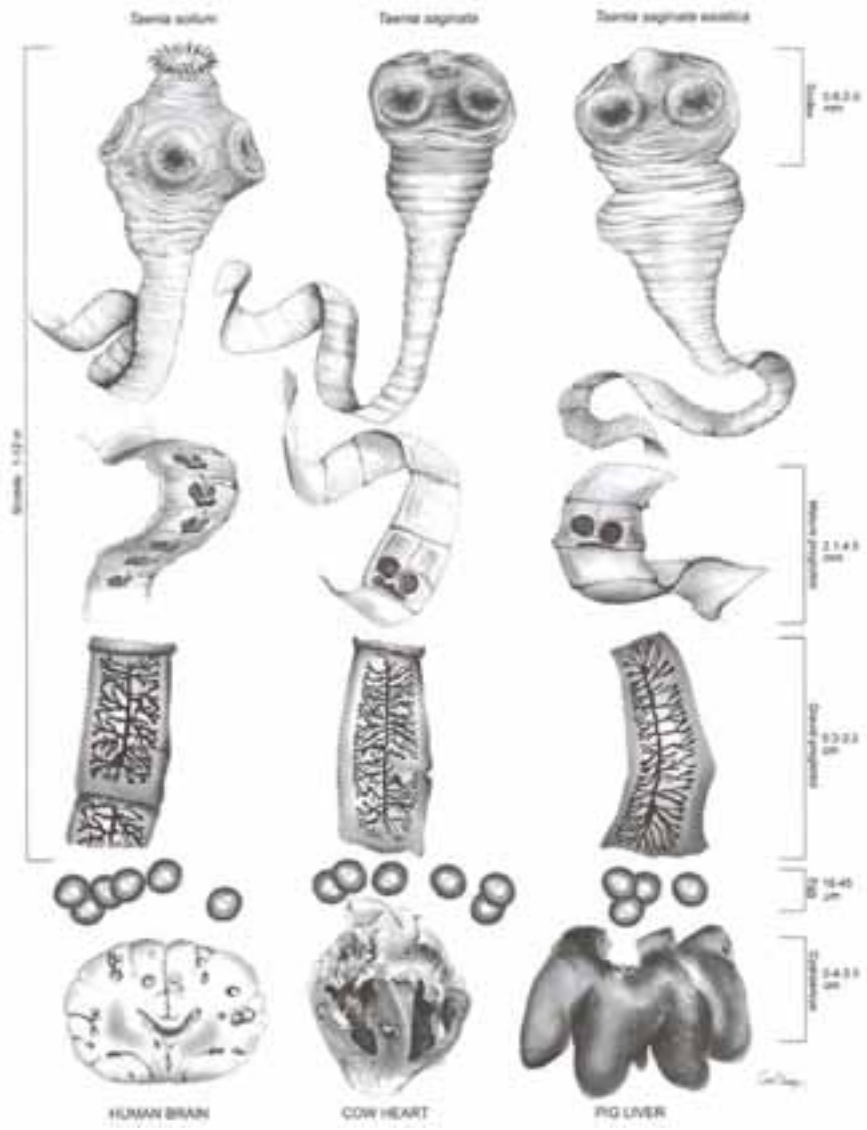

Figure 1.1. Morphology of the three zoonotic *Taenia* cestodes

(Reproduced by permission of the American Society of Parasitology)

The most conspicuous feature of tapeworms is the lack of a mouth and digestive tract. The outer cellular cover, the tegument, functions in absorption, digestion, protection, and, seemingly, traction. The tegument envelops the entire worm, the most external layer of which is a brush-border formed by microtriches that are microvilli-like structures covered by a glycocalyx (thin layer of glycoproteins and mucopolysaccharides). The internal limit of the tegument called the distal cytoplasm is anucleated and is a continuous band or syncytium that sits on a fenestrated basal membrane of connective tissue and contains various organelles. Underneath are muscle layers and the proximal cytoplasm or perikarya, connected to the distal cytoplasm by fine cell processes traversing the basal lamina. Perikarya are highly basophilic and extend well into the parenchyma. Various kinds of receptors extend to the surface mainly in the suckers and genital atria, where they provide tactile and chemical information that serves to integrate the worm's activities with its environment. The parenchyma also contains lamellate mineral concretions, the calcareous corpuscles, 10-34 µm in diameter, that have concentric rings consisting of an organic base,

made of nucleic acids, proteins, glycogen, mucopolysaccharides and alkaline phosphatase, bound to inorganic materials, such as calcium, magnesium, phosphorous and carbon dioxide [263, 277, 534].

The eggs are spherical and range in size from 20 to 50 µm. They have a radial appearance when seen under light microscopy, because the embryophore that surrounds the oncosphere is formed by blocks (constituted by a keratin-like protein) that are attached contiguously. Eggs of all taeniids are morphologically indistinguishable by light and electron microscopy. Ultrastructural studies have shown that eggs possess various layers and membranes [175, 312]. When eggs are released from the definitive host, many are fully embryonated and infective to a suitable host, but others may be at different stages of maturation. The embryophore appears as a rigid structure that protects the oncosphere while the egg is in the external environment, rendering the eggs extremely resistant and enabling them to withstand a wide range of environmental temperatures. When eggs are ingested by a suitable intermediate host, the cementing substance that joins the embryophoric blocks is susceptible to enzymatic digestion which allows the oncosphere to be released [23, 151, 167, 175, 177, 263, 277, 312, 508, 534, 573]. The main features of tapeworms and eggs are shown in Figure 1.1 and Table 1.1.

Yoshino [621, 622, 623] published histological images of the migrating *T. solium* oncospheres through the intestinal lamina propria of swine. The microscopic oncopsheres, as well as transitional forms, were observed in the intestinal mucosa from 15 to 48 hours after the eggs were ingested. After intestinal penetration, postoncospheral development leads to the formation of the Cysticercus. Macroscopic *T. solium* cysticerci were identified by Yoshino in the liver, brain and skeletal muscles of pigs six days after infection, measuring around 0.3 mm, and 60 to 70 days later they had a fully developed scolex and measured between 6 to 9 mm. The development of the scolex starts from one pole as a rudiment and ends within the receptaculum forming the neck that has a spiral or S-like shape and forms part of the spiral canal. Fully developed cysticerci measuring 8 to 15 mm may be seen between 177 and 325 days post infection. At the initial stage of the infection, young cysticerci stimulate a minimal surrounding inflammatory reaction, while older parasites, or those that have been treated with a cestocidal drug, stimulate an intense reaction that includes eosinophils, lymphocytes and macrophages [17, 183, 613, 621]. Furthermore, *in vitro* experiments showed that the presence of the inflammatory capsule that surrounds cysticerci inhibits their evagination [402]. Cysticerci or metacestodes are composed of two chambers: the inner one containing the scolex and the spiral canal is surrounded by the outer compartment that contains the vesicular fluid, usually less than 0.5 ml [447]. When a living Cysticercus is ingested by the definitive host, the first event that takes place is the widening of the pore of the bladder wall allowing the scolex and neck to evert, leaving the bladder wall and vesicular fluid to disintegrate in the host's digestive tract [447]. The tegument, nervous and excretory systems of cysticerci are similar to those described in the adult worm [17, 183, 402, 447, 613, 621, 622, 623]. Table 1.1 and Figure 1.1 present the relevant features of cysticerci from T. *solium, T. saginata* and *T. saginata asiatica.*

Only *T. solium* cysticerci may establish in humans causing cysticercosis of the central nervous system, eye, striated and heart muscle and subcutaneous tissue; there are many publications adressing this aspect (reviewed in [175, 177, 511, 537, 612]). Two morphological types develop in humans: cellulose and racemose type cysticerci. The former is a small, spherical or oval, white or yellow vesicle that measures between 0.5 and 1.5 cm (Table 1.1) and has a translucent bladder wall, through which the scolex can be seen as a small solid eccentric granule. This type of Cysticercus is generally separated from the host tissue by a thin collagenous capsule, within which it remains alive. The racemose Cysticercus appears either as a large, round or lobulated bladder circumscribed by a delicate wall, or resembles a cluster of grapes, and measures up to 10 or even 20 cm and may contain 60 ml fluid. Cellulose cysticerci may grow and transform into the racemose type if the area of localization is spacious. An important characteristic of this type of Cysticercus is that the scolex cannot be seen, and in some cases only detailed histological studies reveal its remains. An autoradiographic analysis of the germinative tissue in evaginated cysticerci identified stem cells that proliferate continuously, differentiate and migrate to the tegument, constituting the main process by which these worms develop from a Cysticercus or metacestode to the adult stage [16, 48, 155, 244, 294, 368, 448, 449, 450].

Table 1.1. Morphological differences between adult taeniids

	Taenia solium	*T. saginata*	*T. s. asiatica*
Entire body			
Lenght(m)	1-5	4-12	1-8
Width (mm)	7-10	12-14	9-12
Proglottids (number)	700-1,000	1,000-1,500	200-1,200
Scolex			
Diameter (mm)	0.6-1.0	1.5-2.0	0.2-2.0
Suckers (number)	4	4	4
Rostellum	Present	Absent	Absent or sunken
Hooks (number)	22-32	Absent	Sunken
Mature proglottid			
Testes (number)	350-600	800-1,200	300-1200
Ovary (number of lobes)	3	2	2
Vaginal sphincter	Absent	Present	Present
Length (mm)	2.1-2.5	2.1-4.5	
Width (mm)	2.8-3.5	3.1-6.7	
Gravid proglottid			
Uterus (number of branches)	7-11	14-32	12-26
Posterior protuberance	Absent	Present	Present
Length (mm)	3.1-10	10-20	4-22
Width (mm)	3.8-8.7	6.5-9.5	3-12
Cysticercus			
Size (mm)	8-15*	6-10	0.4-3.5
Fluid contents (ml)	<0.5**	NR	NR
Hooks in scolex	Present	Absent	Rudimentary
Egg			
Size (μm)	26-34	26-34	16-45
Hooks (number)	6	6	6

** In bumans racemose type cysticerci measure up to 20 cm*
***In humans racemose type cysticerci contain up to 60 ml*
NR - not reported

Taenia saginata cysticerci can be seen with the naked eye between two and four weeks post-infection as nodules in striated and cardiac muscles, measuring 2-5 mm in diameter, including the surrounding inflammatory tissue reaction. The Cysticercus, sometimes referred to as Cysticercus bovis (although this term has no taxonomic significance), is an oval bladder (7-10 mm by 4-6 mm), fluid filled and containing the invaginated scolex of the tapeworm (Table 1.1). Sporadic reports of unarmed cysticerci in llamas; pronghorn; bushbucks, gazelles; oryx, topi and other antelope; wildebeest, and giraffes have appeared [391]. *Taenia saginata asiatica* cysticerci are smaller than those of the classical *T. saginata;* both types of metacestodes have a scolex with a round rostellum surrounded by four symmetrically placed conspicuous suckers, but only the Asian *Taenia* has two rows of rudimentary hooklets, considered as a wart-like formation. *Taenia saginata asiatica* cysticerci are found in domestic pigs and wild boars [167].

The adult tapeworm inhabits the small intestine of humans who are the only definitive hosts. Experimental infections with *T. saginata* have been established in immunosuppressed golden hamsters without obtaining mature or gravid proglottids. *Taenia solium* has been established experimentally in the gibbon *(Hylobatus lar),* chacma baboon *[Papio ursinus),* golden hamster *(Mesocricetus auratus)* and recently in gerbils (Mongolian gerbils) and chinchillas *{Chinchilla laniger).* All the rodents were immunosuppressed with steroids but sexually mature tapeworms with gravid proglottids and mature eggs developed only in chinchillas and gibbons [64, 349, 581, 584, 597].

According to the literature, we consider that the most adequate terminology relating to taeniid development is the following: embryo while inside the egg, oncosphere or larvae while circulating, postoncosphere until it is transformed into the Cysticercus or metacestode in tissues, which is the post-larval or pre-adult stage, and the adult worm or tapeworm. Eggs and embryos are microscopic while cysticerci and adult worms are macroscopic and have the same scolex.

1.2. Life cycles

Taenia solium

Humans acquire taeniosis by eating undercooked or raw pork infected with cysticerci (Fig. 1.2). The scolex evaginates and attaches to the mucosa with its double row of hooks and its four suckers in the upper third section of the small intestine, which is the duodenum-jejunum. The adult worm develops and starts releasing gravid proglottids, the first expulsion taking place between eight to 12 weeks after infection. Although books state that it can survive for about 25 years in the human intestine, our unpublished experience indicates that the tapeworm remains only for short periods. The worm releases in the host's feces a few gravid proglottids daily or two to three times per week [534, 535, 621]. The domestic pig is the main intermediate host, that is, it harbors the Cysticercus; however, humans may also harbor cysticerci. A recent study showed that the prevalence of taeniosis among patients with neurocysticercosis is higher than previously reported. Therefore, the perception that tapeworms are silent guests, causing no harm to humans, is erroneous, and tapeworm carriers should be regarded as potential sources of infection to themselves and to those living in their close environment [178, 179, 230, 347, 368, 391, 449, 495, 581, 586, 595]. *Taenia solium* cysticercosis in dogs has recently been reported in countries such as Indonesia and the People's Republic of China, where, because these animals are eaten, they can be a source of human taeniosis [287, 292, 615].

The development of successful experimental models of taeniosis has allowed more in-depth investigations of the host-parasite relationship. Microscopic studies have shown that the scolex anchors in the upper third part of the duodenum; it engulfs intestinal villi into its suckers and burrows its rostellum into Lieberkuhn crypts of the subcutaneous mucosa. Histological analysis of the anchor site has shown an intense inflammatory reaction surrounding the scolex. Specific antibodies and parasite antigens have been detected in serum and feces of infected hamsters [34, 35, 349, 369].

When swine ingest eggs, bile and enzymes trigger the disaggregation of the embryophoric blocks and digest the oncospheral membrane. The activated oncosphere penetrates the intestinal wall and is then transported through the blood or lymphatics to the tissues where it develops into a Cysticercus. Cysticerci establish primarily in skeletal and cardiac muscle, as well as in the brain of pigs, a process that takes approximately eight weeks (Fig. 1.2) [17, 621, 622, 623]. They remain viable for at least one year, when pigs are usually sent to slaughter. In older pigs the inflammatory reaction surrounding cysticerci becomes evident with time. Calcified cysticerci are frequently seen only in humans [155, 448, 450, 565].

Taenia saginata

Humans acquire infection after ingesting raw or undercooked infected beef (Fig. 1.2). The development of the tapeworm is similar to that of *T. solium* and infection may remain for up to 25 years. The tapeworm becomes sexually mature after three months, producing gravid proglottids, which are mobile and either migrate from the host's anus spontaneously, usually in chains of six to nine segments, or are shed daily in the feces. Proglottids may migrate between the legs onto clothes, bedding or the ground, releasing eggs in the process. Occasionally, a large part of the strobila may be discharged and the expulsion ceases for a short period [23,176, 415, 444, 534, 561].

Gravid proglottids contain 50,000 to 80,000 eggs, with different degrees of maturation. Eggs may remain viable for several weeks or months in sewage, water or on pasture. When eggs are ingested by cattle, embryos hatch and activate under the influence of gastric and intestinal juices, and penetrate the intestinal mucosa to reach the general circulation. Oncospheres develop in skeletal and cardiac muscles and less frequently in fat and visceral organs but begin to degenerate within a few months after infection, and by

nine months a substantial proportion of them are dead and calcified. Cysticerci become infective to man in about ten weeks (Fig. 1.2) [23, 56, 229, 341, 415].

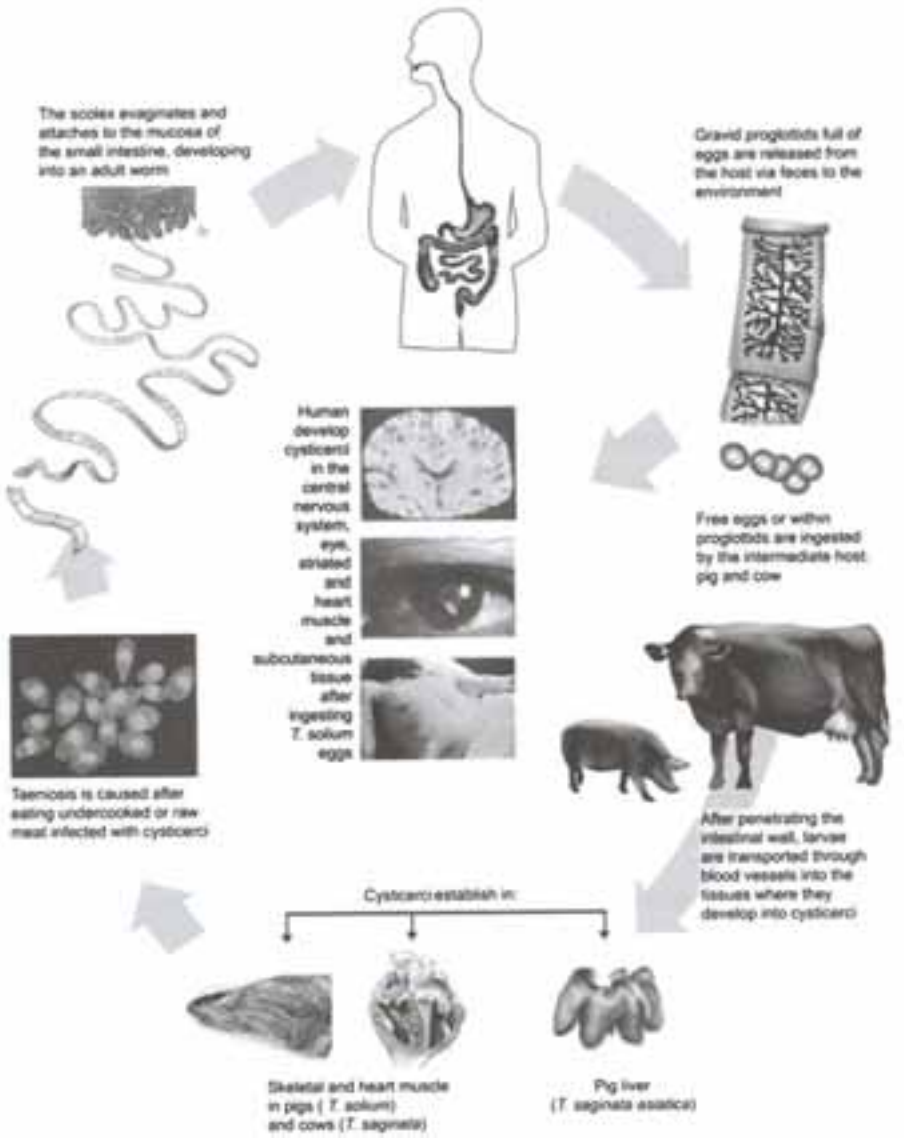

Figure 1.2. Life cycles of the three zoonotic *Taenia* cestodes

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Taenia saginata asiatica

This cestode was originally described in Taiwanese aborigines and subsequently in many other Asian countries such as Korea, Indonesia, the Philippines, and Thailand [153, 166]. This tapeworm is closely related to *T saginata,* having an unarmed scolex, a large number of uterine branches in gravid proglottids and a posterior protuberance (Table 1.1) [166]. The life cycle of this cestode differs from that of T. *saginata* in its intermediate host species as well as in organ predilection sites. Unlike *T. saginata,* which develops in skeletal muscle of cattle, cysticerci of *T. saginata asiatica* develop in visceral organs such as the liver, omentum, serosa and lungs of pigs, although cattle livers can also be lightly infected. Humans become infected by the adult stage after ingestion of raw meat or viscera. In general, the life cycle of *T. saginata asiatica* is similar to the other *Taenia* species, i.e. the adult stage develops in humans (Fig. 1.2) [153, 166].

1.3. Systematics

The main taxonomic features of tapeworms of the family Taeniidae are summarized in Table 1.2 [559]. *Taenia solium* and *T. saginata* exhibit unequivocal features which differentiate them as species, therefore they have been stable species for a long time. However, the taxonomic status of *T. saginata asiatica,* as a species or a subspecies, has been a matter of controversy since it was first identified in Taiwan ('Taiwan *Taenia')* [152, 166, 200]. Molecular differences between Taiwan *Taenia* and *T. saginata* in Southern blot analysis of ribosomal DNA fragments were found, which together with established morphological characteristics in adult and larval stages suggested that it was a new species [151, 624]. Nevertheless, the sequences of rRNA and mitochondrial cytochrome C oxidase I (COI) genes as well as the patterns obtained by the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) from COI and rDNA internal transcribed spacer 1 (ITS1) in T. *solium, T. saginata* and Asian *Taenia,* showed a close relationship between the latter two tapeworms, suggesting that the taxonomic classification for the Asian *Taenia* should be a subspecies or strain of *T. saginata* instead of a new species [60]. This information is supported by morphological characteristics of adult tapeworms and cysticerci found in several *T. saginata* and Asian *Taenia* samples therefore should be named *Taenia saginata asiatica* [167].

Table 1.2. Classification of taeniids

Phylum Platyhelminthes
Soft-bodied, flattened dorsoventrally, acoelomate, bilaterally symmetrical, triploblastic, protonephridial excretory system
Class Cestoda
Endoparasites, lack digestive system, outer body covered by a syncytial tegument with microtriches sheltered by a glycocalyx
Subclass Eucestoda
Adult with specialized anterior adhesion organ or scolex and elongated body or strobila conformed by proglottids, hermaphroditic with indirect life cycle
Order Cyclophyllidea
Scolex with four muscular suckers and a rostellum usually armed with hooks, strobila consisting of proglottids in various developmental stages, each proglottid clearly separated by external segmentation, eggs are round, non operculated and contain non-ciliated-hooked oncopsheres (one per egg)
Family Taeniidae
Adults in small intestine of carnivores and man, mammalians as intermediate hosts, genitalia unpaired in each proglottid with lateral genital pore irregularly alternating; eggs with radially striated hardened blocks (embryophore), larval stage or metacestode as a Cysticercus, coenurus, hydatid or strolbilocercus

The taxonomic review of the genus *Taenia* has been updated from a previous publication and includes seven new species and two subspecies, one of these, *T. saginata asiatica* [334, 583]. *Taenia saginata* and T. *saginata asiatica* are distantly related to T. *solium* as suggested by the results from a cladistic analysis of a numerical data matrix describing 27 characters for several species of *Taenia* [273]. An analysis of the complete nucleotide sequence of the internal transcribed spacer 2 (ITS2), as well as random amplified polymorphic DNA (RAPD) analysis of *T. solium* from the People's Republic of China, *T. saginata* from Poland and Korea and *T. saginata asiatica* from the People's Republic of China and Korea, showed that the latter has a sympatric distribution with other taeniids in mainland People's Republic of China [148].

Therefore, to date, most scientists consider *Taenia saginata asiatica* as a subspecies of *T. saginata,* in spite of the different behavior in the intermediate host and some molecular data [273, 334]. Furthermore, the three tapeworms that lodge in humans can co-exist in the same environment [148].

The use of distinct molecular techniques for clarification of the taxonomic status within cestodes has revealed new insights into the evolution, ecology, and population genetics of these parasites. The development of methods for egg detection by DNA dot-blot hybridization uncovered intra-specific DNA variability in *T. solium* isolates from India, Mexico, and Zimbabwe [364]. Sequence variation within a 366 nucleotide for COI from the three *T. solium* isolates indicated slight differences in three conservative changes in the third base position of codons of the isolate from Zimbabwe. The sequence of DNA coding for COI, ITS1, and of the diagnostic antigen Ts 14 showed low variability [262], while that of the entire COI and cytochrome b from 13 isolates of *T. solium* from various regions detected 1.7% and 2.9% variant nucleotide positions for CO1 and cytochrome b, among all isolates [385]. The phylogenies obtained show that the isolates from Asia (People's Republic of China, India, Irian Java and Thailand) form a single cluster, whereas the isolates from Latin America (Bolivia, Brazil, Ecuador, Mexico, and Peru) and those from Africa (Cameroon, Mozambique and Tanzania) form a second cluster [385]. Recently, the study of the variability in individual *T. solium* cysticerci from Mexico, Honduras and Tanzania by RAPD demonstrated 88% polymorphic loci and an average heterozygosity of 0.077 with several alleles fixed and the presence of a clonal structure, suggesting the existence of local lineages with events of genetic recombination within them [340].

1.4. Host immune responses

The immunology of human and porcine cysticercosis is particularly important because of its paradoxical relationship with disease pathogenesis. Living cysticerci may cause an asymptomatic infection through active evasion and suppression of immunity [374]. Histological studies have shown that, in humans and pigs, viable cysticerci have little or no surrounding inflammation [18, 155, 450]. Cysticerci may persist in the human host for long periods of time, often for years, without eliciting surrounding host inflammatory reaction. In contrast, the immune mediated inflammation around one or more degenerating cysts may precipitate symptomatic disease [459]. When the parasite begins to die, either naturally or following treatment with cestocidal drugs or immunization, a surrounding granulomatous inflammatory response develops in human and porcine infections [16, 18, 183]. Predominant components of this inflammatory response include plasma cells, lymphocytes, eosinophils and macrophages. The latter engulf parasite remnants, eventually leaving a gliotic scar with calcification [17, 18, 87, 155, 180, 375, 450, 478].

The humoral immune response is better understood than the cellular one. The fact that humans respond immunologically to antigens of *T. solium* cysticerci is evident from the number of immunodiagnostic assays that have been developed using different types of antigens [88, 185, 443]. Several immunoglobulin (Ig) classes are produced as specific antibodies against the parasite. The most frequent is IgG, which can be detected in serum, cerebrospinal fluid (CSF) and saliva, which suggests that infection is of long duration. It is compartmentalized, since both local synthesis of specific IgG antibodies within the brain and the presence of a given antibody class exclusively in one compartment (i.e. CSF or serum) has been demonstrated [175]. There is a correlation between the presence of antibodies and the intensity of infection, as well as the viability of the parasite; antibodies are most frequent in cases with live or dying parasites, and rarely in cases with calcified cysts [175, 185, 537]. There are also differences between benign and malignant cysticercosis, with cysticercotic encephalitis being more immunogenic. The humoral immune response in patients with neurocysticercosis is quite heterogeneous as evidenced by the number of antigens recognized; patients' antibodies may react with one to eight antigens in Immunoelectrophoresis and up to 30 antigens in western blot [88, 175, 185, 443, 510]. It has also been shown that the immune response may be transient in the households of patients with neurocysticercosis and in apparently healthy individuals in the general population [213, 371].

Precise patterns and pathways of the cellular responses in human neurocysticercosis have only recently been investigated. Studies so far have addressed molecular components in the CSF, serum and the granuloma itself. Increased levels of interleukin (IL) 1 and IL-6 have been reported in the CSF of patients with inflammatory neurocysticercosis. High levels of IL-6 in the CSF of patients with subarachnoid neurocysticercosis have also been reported, suggesting acute phase response [404]. In addition, high levels of tumor necrosis factor-alpha (TNF-alpha) have also been noted in the CSF of children with active neurocysticercosis, which is undetectable in controls and children with inactive neurocysticercosis [5].

Increased levels of eotaxin and IL-5, both eosinophil-selective mediators, have been found in the sera of patients with neurocysticercosis. These cytokines are involved in recruiting eosinophils locally as well as systemically [160J. The presence of eosinophils as the first attack cells was reported in porcine cysticercosis after cestocidal treatment and after vaccination. This suggests that eosinophils may play an important role in the degenerative phase in this parasitic infection. Another study showed that IL-2 was synthesized by the peripheral blood cells of 58% human beings with untreated, active and recently diagnosed neurocysticercosis, while interferon-gamma (IFN-gamma), IL-4 and IL-10, were only found in 11%, 10% and 14% respectively [366, 367]. Interestingly, only IFN-gamma was increased in the group of patients as compared to controls. The macroscopic disappearance of killed cysticerci takes about two months, but the immunological processes that occur within the dying granulomas are poorly understood. Very few immunohistochemical studies of the inflammatory response within Cysticercus granulomas located in the human central nervous system are available, mainly due to limited tissue specimens available. The reports suggest a mixture of Th1 and Th2 responses in human brain granulomas caused by cysticerci [463, 464, 465,475].

An immunological study of patients with neurocysticercosis treated with praziquantel (without major adverse effects) reported elevated soluble IL-2 in the CSF suggesting a Th1-type immune response to therapy, in contrast to the Th2-type immune response characteristic in animal models with viable cysticerci [99]. It was therefore hypothesized that living cysticerci facilitate immune evasion by inducing a Th2-type immune response until the death of the larval parasite allows a Th1-mediated inflammatory response to develop [180]. This model however, is not consistent with other reports and it seems likely that the regulation of immunity in *T. solium* cysticercosis is a more complex phenomenon than a simple Th1/Th2 shift.

One of the most interesting phenomena in immunoparasitology is the evasion of the host immune response by the parasite [174, 597]. Cysticerci are capable of surviving in the human host for several years before their degeneration [534]. Viable cysticerci are associated with little surrounding inflammation [182]. This allows for the maintenance of the parasite. The mechanisms underlying the survival of parasites lodged in immunologically privileged sites is undoubtedly complex and may involve masking of Cysticercus antigens by host immunoglobulins, concomitant immunity, molecular mimicry and suppression or deviation of host responses [19, 30, 313, 374, 376, 510, 554].

The immune response of the definitive host against the intestinal tapeworm has been studied only recently, since the establishment of experimental models [349]. Studies in hamsters showed that parasites survive better when the hosts are immunosuppressed with corticosteroids, and present no intestinal IgG response, even though systemic antibodies reach levels similar to those induced in untreated animals. Interestingly, in both cases coproantigens could be detected, but only in the non-suppressed animals could the antigens reach the blood [35]. Studies performed in gerbils and hamsters harboring adult T. *solium* showed interesting differences. The most evident cells are goblet cells that increase from 20 to 80 per villus in hamsters and gerbils at 13 and 18 days post-infection respectively, and mast cells that increase from two to eight per villus, at 19 days, in gerbils, but not in hamsters. Furthermore, tapeworms survive for longer periods in hamsters and become larger. These data suggest that hamsters are more permissive hosts and that mast cells are important elements in the expulsion of tapeworms [34].

CHAPTER 2:
CLINICAL CYSTICERCOSIS: DIAGNOSIS AND TREATMENT

Theodore E. Nash, Hector H. Garcia, Vedantam Rajshekhar & Oscar H. Del Brutto

2. Introduction

The clinical manifestations of cysticercosis are particularly varied and well documented in the recent literature. Therefore, this Chapter will not attempt to document all manifestations but instead will outline possible manifestations and applicable pathophysiology. There is a number of excellent recent reviews and text chapters and the reader is referred to these for additional guidance [190, 210, 216, 514, 530, 594]. Recent publications of consensus statements on diagnosis [117] and treatment [205] are available and our comments for the most part parallel those documents, although some additional information has become available since their formulation. Frequently, the diagnosis and clinical care of patients with neurocysticercosis involve the use of sophisticated and expensive radioimaging techniques such as computer assisted tomography (CT) and magnetic resonance imaging (MRI) and serological tests employing Western blots. These technologies are commonly not available in the developing world which necessitates the primary use of symptomatic care under these conditions.

The emphasis in this Chapter is on clinical cysticercosis because of its far greater disease importance relative to taeniosis (intestinal adult tapeworm). More discussion on the diagnosis and treatment of taeniosis is provided in Chapter 4, Diagnosis Section 4.1 and in Chapter 6, Control, Section 6.3.6 and Annex 6.7.5.

Burden of neurocysticercosis

Cysticercosis is a common cause of neurological disease in many areas of the developing world [50, 281, 365, 595]. Although the mature cysts may be found in almost any organ, the brain, muscles and subcutaneous tissues are the most commonly involved sites [133]. Neurocysticercosis contributes by far the most to the disease burden [133]. In Latin America, neurological symptoms most commonly signal the onset of disease [97] while in Asia subcutaneous nodules are common and rival neurological symptoms as the first clinical manifestation of infection [133]. Seizures and epilepsy are frequent in neurocysticercosis and are the cause of most of the morbidity [133]. The prevalence of seizures in excess of the expected level often suggests the presence and extent of cysticercosis in a community [106]. Headaches, varying focal neurological manifestations, hydrocephalus, chronic meningitis, lacunar infarct syndromes, neuropsychiatric manifestations, and blindness due to direct eye involvement are some of the more commonly described presentations [133, 252, 332, 356, 362, 377, 506, 512, 515, 546].

Diversity of clinical manifestations

Few neurological diseases rival cysticercosis in the variety of clinical presentations [133, 387]. This results from differences in:

- the location, number, and size of cysts and/or calcifications, and
- the presence of inflammation and edema.

Multiple lesions are common in the same individual, but these are frequently observed in different pathological states. For instance, some viable cysts are unrecognized by the host with no accompanying edema, while others demonstrate perilesional edema. Cysts may be found anywhere in the brain parenchyma, the ventricles or the subarachnoid spaces with or without accompanying inflammation. Other lesions are calcified and therefore non viable, but nonetheless may be associated with perilesional edema, seizures or other focal neurological problems. The number of lesions varies from a single cyst to hundreds of larval cysts. It is the presence of multiple lesions, commonly in various pathological states,

that *give* rise *to* the *plethora of* symptoms and signs. The radiological picture *of* these lesions presents a pattern that is highly suggestive, if not diagnostic, *of* neurocysticercosis (Figs 2.1., 2.2, 2.3.).

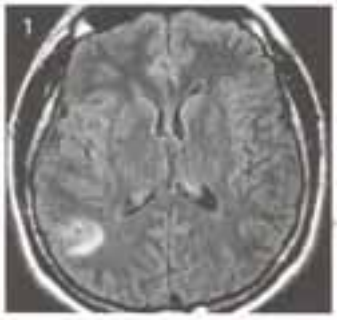

Figure 2.1.

MRI FLAIR image. Perilesional edema represented by the white signal surrounding a void or dark hole that is the appearance of calcium

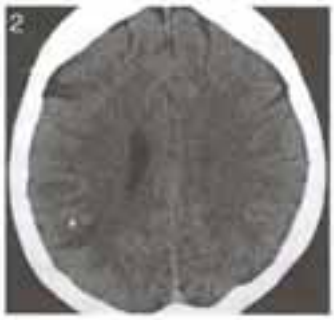

Figure 2.2.

CT scan without contrast in the same patient and area presented in Figure 2.1 showing that the void signal in the MRI is calcified. The crescent shaped region of hypodensity (dark area) near the lesion represents edema as seen in CT

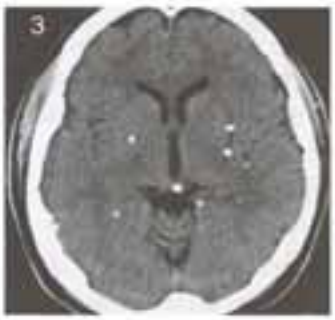

Figure 2.3.

CT scan without contrast. There are multiple round small calcifications characteristic of calcified T. solium *granulomas*

Usefulness and limitations of CT and MRI examinations

The characteristics of the MRI image and to a lesser extent the CT image are a good reflection of the pathological state of the cyst and have become essential tools in optimizing the care of patients. MRI and CT radiological studies are the most helpful methods to diagnose neurocysticercosis, gauge the need for medical or surgical treatments, and assess the effectiveness of interventions. MRI examinations are more sensitive in detecting non-calcified parenchymal, subarachnoid, or ventricular cysts and the presence of associated inflammation (bright signals on T2 and FLAIR techniques) or breakdown in the blood brain barrier as determined by leakage of injected gadolinium (enhancement) from the blood vessels [138, 336, 355, 550, 555, 565]. CT examination best detects the characteristic punctate calcifications as part of the diagnostic evaluation [45, 67, 314, 359, 478, 565] and most appropriately confirms the presence of a calcified focus associated with perilesional edema. Calcifications are easily missed using the present, commonly employed MRI techniques. Although CT studies are generally less sensitive than MRI, they are frequently available and less costly in many underdeveloped countries, and are adequate to diagnose or suggest the infection in a majority of afflicted individuals.

2.2. Natural history and disease

2.2.1. Correlation of imaging and pathology

Viable cystic lesions usually undergo characteristic changes over time [138]. Recognizing and understanding these stages or states are helpful in the management of patients because each is usually associated with characteristic disease manifestations that commonly require specific therapeutic interventions. Unfortunately, the natural history of cysts situated in the brain parenchyma is not fully documented. However, a reasonable approximation of the course of infection and pathophysiology can be deduced from autopsy studies in humans [155, 268, 566], natural or experimental swine infections [104, 105, 184, 244] and correlations between the MRI and pathological findings of surgically removed specimens in humans [307, 336, 355, 555]. After ingestion, the liberated oncospheres migrate through the blood vessels to the tissues. Under appropriate conditions, a fully developed infectious cystic larva develops after two-three months and eventually reaches 1-2 cm in diameter, although some may be considerably larger. Characteristically the cyst is hypodense on CT examination and black on MRI (TI and FLAIR techniques) (Figs 2.1., 2.2.) with an eccentrically placed roundish density in the cyst space that represents the scolex. When definitively demonstrated, this finding is practically diagnostic of cysticercosis. At this stage the cystic larva invokes little host inflammatory response and the blood brain barrier remains intact. Consequently, MRI or CT imaging reveals neither perilesional edema nor enhancement. Exactly

how long a cyst remains viable is not clear and likely depends on host factors, tissue location, and actual state of the cyst. However, information from controlled studies and from infected immigrants who reside in non-endemic countries indicates that cysts may remain viable for years. Eventually the cyst is recognized by the host, the first indication of which is the presence of enhancement. The larval cyst is still viable but there is the beginning of inflammation around the parasite that will eventually lead to its degeneration and death. Observations of patients who present with seizures within months following a brief exposure, show that some developing larvae fail to mature into typical viable cysts, perhaps due to an effective host immune response (Nash, personal observations). The initial MRI image shows nodular enhancing lesions representing degenerating larvae which are associated with varying degrees of inflammation that may at times lead to periodic seizures or other symptoms. A host-derived capsule eventually encircles the degenerating cyst. The MRI shows enhancement and the signal of the cyst using TI and FLAIR techniques changes from no signal (black) to a bright signal [555] (Figs 2.4., 2.5, 2.6). This suggests a fundamental alteration in the biochemical makeup of the cysts and indicates that the cyst is no longer viable. The cyst continues to involute and displays varying degrees of enhancement and edema. Eventually the parasite residual and host cellular response form a dense granuloma that has an unusual propensity to calcify 20% to 60% of the time. End stage granulomas may show ven' little recognizable parasitic tissue but the presence of calcareous corpuscles, microscopic roundish bodies of calcium salts present in cestodes, is highly suggestive of cysticercosis and practically pathognomonic in the correct clinical setting [73, 105].

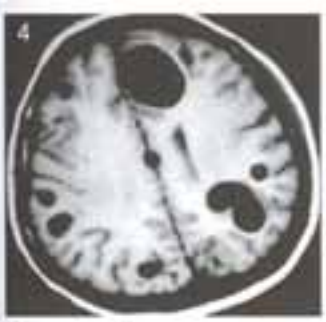

Figure 2.4.

T1 weighted MRI showing multiple viable cysticerci. A central or eccentrically placed scolex, pathognomonic of cysticercosis, is present in several. Cysts vary in size and shape but typically have a thin, non-nodular inner and outer wall

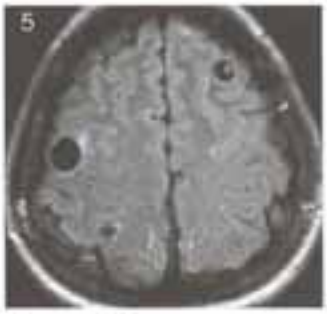

Figure 2.5.

MRI FLAIR image. Three cysts are seen. The large cyst on the left shows a region of edema represented by a small white pericystic area while a typical cysticercus containing a scolex is present on the right

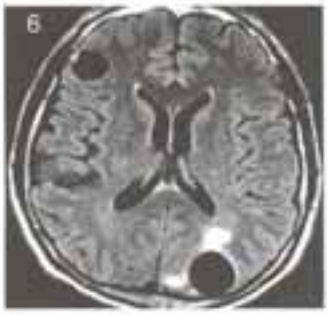

Figure 2.6.

MRI FLAIR. Two large cysts are present. Other images reveal an identifying scolex. The right occipital lesion has associated edema as noted by the white pericystic area

2.2.2. Chronic (inactive) cysticercosis associated with brain calcifications

Although many advances in our understanding of cysticercosis have revolved around diagnosis, treatments, and clinical effectiveness of treatments of viable or so called 'active' cysticercosis, there is an increasing realization that significant morbidity, e.g. seizures and epilepsy associated with cysticercosis, occurs in those with end stage disease that is recognized by the presence of brain calcifications [387]. These are usually small and round resembling buckshot but at times may be uncharacteristically large and/or take a more free-form shape. Although the radiological appearance of cerebral calcifications is non-specific in endemic populations, there is compelling evidence that most of these are due to cysticercosis. Firstly, cerebral calcifications are a frequent finding in unselected patients in endemic populations [173, 221] but uncommonly recognized in non-endemic regions. Secondly, numerous studies have prospectively followed the development of calcified lesions from typical cystic lesions [477]. Thirdly, single enhancing cystic lesions are a common cause of seizures in endemic regions and these resolve into typical calcified lesions in about 20% of cases [454]; biopsies proved these are mostly the result of cysticercal granulomas [74]. Fourthly, transient specific cysticercosis antibody responses have been documented in patients with single lesions that subsequently calcify [206] (Nash, personal observations). Lastly, histological and biochemical studies of calcified lesions have indicated parasitic remnants and specific parasitic collagen that differs from the host [249].

Calcified cysts are directly associated with seizure activity [387]. In endemic regions, the proportion of patients with calcifications is higher in people with seizures compared to those without seizures [221]. Moreover, two types of evidence directly implicate calcified lesions as foci of seizure activity. Firstly, careful EEG monitoring and focal seizure activity localized to particular calcified foci [101, 491, 531]. Secondly, patients presenting with seizures or other neurological manifestations, demonstrate perilesional edema around typical calcifications that anatomically localize to the foci [27, 110, 221, 388, 389, 520, 521]. In addition, one study implicates gliosis associated with calcifications as a risk factor in increased seizure activity in this population [440].

Early and/or preliminary studies indicate that perilesional edema around calcified lesions is relatively frequent, ranging from 23% to 35% in patients with a history of seizures and calcifications [110, 221, 389]. More exacting studies are in progress. However, given that 9%-18% [387] of highly endemic populations show one or more cerebral calcifications, the phenomenon has the potential to be the most common cause of seizures in endemic populations.

Since calcified lesions are dead, specific anti-parasitic treatment is not indicated. Other then symptomatic care, no specific treatment has been identified to prevent or treat symptomatic patients although corticosteroids have been used.

2.2.3. Patterns of presentation and type of involvement

2.2.3.1. Solitary Cysticercus granuloma

Solitary Cysticercus granuloma (SCG) is a common cause of partial and generalized epilepsy in many parts of the world, especially in India and other regions endemic for cysticercosis [75, 111, 452, 589]. It is a form of neurocysticercosis that is characterized by the presence of a single dying Cysticercus cyst in the brain parenchyma that evokes an inflammatory response around it resulting in the formation of a granuloma. Although the presentation is characteristic, it is not particularly precise but the use of diagnostic criteria allows good but not perfect differentiation from other etiologies. The response to therapy and prognosis is commonly more favorable compared to those who present with multiple lesions.

Seizures are the most common presentation. SCG can cause any type of seizures except absence seizures (petit mal epilepsy). Partial motor seizures with or without secondary generalization in a non-febrile patient is the commonest presentation but primary generalized seizures, complex partial seizures, occipital seizures are also frequently seen with a SCG. *Status epilepticus* is an uncommon form of presentation and seen in less than 10% of patients with SCG [457].

2.2.3.2. Extraparenchymal neurocysticercosis

Cysticercosis can involve other regions of the brain besides the brain parenchyma and give rise to distinctive syndromes. Cysts may localize in the ventricles where they may lead to obstruction of the ventricular system [100]. The fourth ventricle is most frequently involved [28]. Obstruction may be purely mechanical where the cyst itself blocks CSF flow or it may be a result of chronic inflammation and fibrosis that results from degenerating cysts. Cysts in the subarachnoid space and sometimes in the ventricles may grow abnormally large and lead to mass effects [112, 119, 416]. Racemous cysticercosis [22, 52] refers to a form that grows by abnormal proliferation of parasitic membranes, believed to be the result of a cyst whose scolex has degenerated. These also occur in the spaces around the brain, most commonly in the Sylvian fissure (Figs 2.7., 2.8.). When closely associated with the brain surface such as the base of the brain, it may lead to chronic meningitis and, not uncommonly, hydrocephalus. Chronic inflammation in close association with blood vessels not infrequently leads to vasculitis of the smaller penetrating vessels resulting in lacunar infarcts [42, 43, 66]. Involvement of larger vessels has also been described.

Hydrocephalus is not an infrequent complication of untreated cysticercosis [332, 333, 362, 515, 516, 517, 540, 546] and results from obstruction caused by ongoing inflammation and fibrosis or by mechanical obstruction by cysts in the ventricles. Pleocytosis occurs when degenerating cysts are in contact with the CSF and is typically moderate with a mononuclear predominance [333, 516]. An increased number of

eosinophils in the CSF, although not specific, should suggest the diagnosis [485, 545]. Hypoglycorrhachia is also relatively common [485, 545].

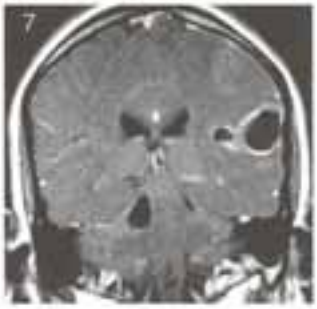

Figure 2.7.

MRI T1 weighted with contrast. There is a complex cystic mass in the region of the Sylvian fissure. The surrounding white signal represents intravascular dye that has infiltrated from the blood vessels into the brain parenchyma in the region of the cystic mass (enhancement). This likely represents a racemose cyst. These are found in and around the spaces of the brain. The mass consists of many small cystic structures usually lacking a tenkie

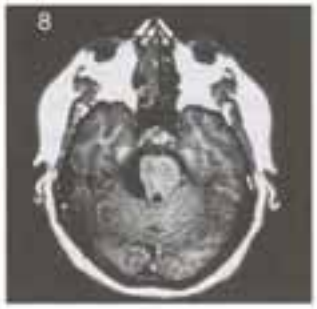

Figure 2.8.

T1 weighted MRI with contrast of the same patient as in Figure 2.7. A round cystic mass is seen in the right perimesencephalic cistern

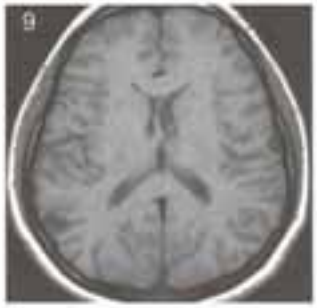

Figure 2.9.

MRI T1 weighted. Multiple viable cysticerci are evident. Two cysts (not clearly differentiated here) are seen in the left lateral ventricle

2.2.3.3. Massive infection

A massive acute infection commonly leads to cysticercal encephalitis. MRI or CT visualizes hundreds of granulomas initially with a trace of enhancement. There is massive edema and the ventricles are compressed [114]. Heavy non-encephalitic cysticercosis also occurs. Here there is massive infection with viable cystic lesions with little inflammatory response [114]. Muscular pseudohypertrophy is a presenting characteristic in some of these patients.

2.2.3.4. Involvement of other organs

Cysts have been described in almost ever)' part of the body but are particularly frequent in the muscle and subcutaneous tissue. Calcified cysts in muscle are readily recognized as sausage shaped calcified structures [133]. In patients with minimal cerebral disease, the diagnosis can sometimes be confirmed by detecting additional calcified cysts in the muscle. Subcutaneous cysts are frequent in Asia but less so in Latin America [97]. Biopsy of these may be the first indication of disease and certainly offers a direct way to suggest the presence of cysticercosis and possible brain involvement. In regions where cysticercosis is common, subcutaneous cysticercosis in the presence of a concurrent unrelated brain disease is a possibility, and some degree of clinical judgment and additional information are required to establish a definitive diagnosis (see below).

Eye involvement was frequently documented in the older literature but in recent series is not as frequent. In most series, retinal and vitreous involvement is most frequent followed by subretinal, vitreous, conjunctival and anterior segment localizations [308, 309, 445]. Orbital cysticercosis is also well described and responds effectively to medical therapy [425, 514] but cysticidal treatment of intraocular cysts is contraindicated [303]. Neuro-ophthalmologic signs occur not infrequently in patients with meningeal involvement [299].

2.3. Diagnosis

2.3.1. Overall assessment and available diagnostic tools

In general the diagnosis of neurocysticercosis is established by the recognition of a constellation of symptoms, signs, and findings. With the exception of histological identification of the parasite, a definitive

diagnosis is infrequently made, but nevertheless the constellation of findings may be so characteristic that the diagnosis is certain.

A high likelihood of exposure increases the probability of infection. Patients usually have lived or traveled extensively in endemic regions or have had close contact with someone who has a tapeworm. Uncommonly, patients are identified who have had no known exposures but these usually account for only a small proportion (a few percent) of all patients diagnosed in non-endemic countries. The presence of free-roaming pigs and the use of rudimentar)[7] methods of sewage disposal are common in highly endemic regions and allow swine access to human feces. Patients or family members may have a history of tapeworm infection or recognize that they have passed tapeworm proglottids in their feces. Family members or closely associated persons not infrequently have a history of seizures. Another sign of the presence of cysticercosis in the household is the presence of cysticercosis in family raised pigs. Local buyers frequently refuse to purchase infected pigs. This is usually a direct indication that the life cycle is established in the locality and there is a high probability of neurocysticercosis in the family and community.

Clinical presentation: The clinical presentation of patients with neurocysticercosis can be unusually varied and non-specific. Nevertheless, in the most representative series, seizures are usually the most common presenting complaint; headaches are also frequent while focal neurological symptoms are decidedly less common [133, 190, 210, 216, 252, 332, 333, 357, 362, 377, 507, 513, 516, 530, 546, 594]. Subcutaneous nodules are a common presentation [97].

Serological examinations: There are several kinds of serological examinations, the most common being detection of specific antibodies in serum. The most well documented assay is the Western blot that employs a lectin-purified fraction of cysts as antigens [443, 567, 610, 616]. In general, patients with multiple viable or dying cysts should have serum antibodies present, usually in the range of 92% or greater; the lack of specific antibodies should make the diagnosis suspect. In patients with one to two cysts or only calcifications, the test may be falsely negative, decreasing its usefulness [443, 609]. On the other hand, antibodies are not infrequently present in persons from endemic regions without obvious disease [215]. ELISA based assays are less well documented and standardized, and tend to be less specific [443]. In non-endemic areas, the background of false positive tests is low so that a positive test serves to confirm the clinical diagnosis [567]. Cysticercal antigens can be detected in the serum and/or CSF using experimental tests; these are less sensitive but very specific [89, 90].

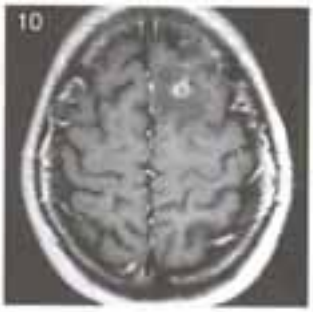

Figure 2.10.

MRI T1 with contrast. A single enhancing biopsy proven T. solium *cysticercus with edema*

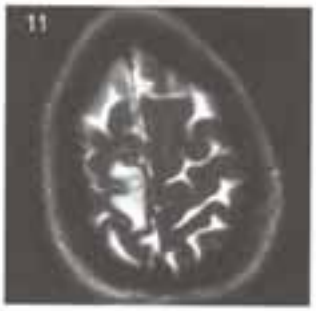

Figure 2.11.

MRI T2. A single enhancing cystic lesion with a transiently positive Western blot serology for T. solium. *The lesion subsequently calcified*

The adult tapeworm causes few if any symptoms. Taeniosis is suggested by a history of passing proglottids in feces and should be looked for in most patients with disease or potential exposure to contaminated meat. It is traditionally diagnosed by detection and direct examination of ova in the perianal region or in feces, or of tapeworm proglottids in the feces. The proglottids of *Taenia solium* have 15 or less uterine branches compared with those of *Taenia saginata* [168]. These methods of detection are insensitive and the ova of *T. solium* cannot be differentiated from *T. saginata,* the beef tapeworm, that is of little clinical significance to humans. Experimentally, the tapeworms of both species can be diagnosed with high sensitivity by detection of *Taenia*-specific antigen in the feces [7, 13]. *T. solium* can be specifically diagnosed

by detection of specific DNA by PCR of ova contained in feces [370] or the presence of serum-specific antibodies [609].

Imaging studies: As mentioned earlier, CT and MRI examinations are essential for the diagnosis and evaluation of persons with neurocysticercosis and are responsible for the major advances in our understanding of infection, disease, diagnosis, and treatment [355, 387, 628]. Since histological verification of *T. solium* infection is infrequent and the MRI and CT imaging findings are usually suggestive but not necessarily diagnostic, criteria have been developed by a panel of experts that combine clinical, radiological, serological findings and epidemiological information to yield a cumulative probability of infection [117] (Figs 2.10., 2.11.).

2.3.2. Diagnostic criteria for neurocysticercosis

2.3.2.1. Introduction

The diagnosis of neurocysticercosis is commonly uncertain despite the availability of sophisticated neuroimaging and relatively sensitive and specific serologic tests. Since an absolute pathological diagnosis of neurocysticercosis requires surgical intervention that is not often performed, other criteria are required to diagnose neurocysticercosis and prevent unnecessary surgical interventions. However, the clinical manifestations, although they may be typical and suggestive, are commonly non-specific. When these findings are considered independently, the diagnosis may be uncertain, but when combined in a rational way, both the sensitivity and specificity of the diagnosis are significantly enhanced. A panel of experts recently developed diagnostic criteria for neurocysticercosis that evaluate the clinical, radiological, immunological, and epidemiological data of patients. These are divided into absolute, major, minor, and epidemiological criteria based of their individual diagnostic strength: *absolute criteria* permit unequivocal diagnosis even if considered alone; *major criteria* strongly suggest the diagnosis but cannot be used alone to confirm or exclude the disease; *minor criteria* are frequent clinical and radiological manifestations of the disease but are relatively non-specific and therefore are unable to significantly differentiate among the diagnositic possibilitites; and *epidemiological criteria* include potential exposure that favors the diagnosis of cysticercosis. Interpretation of the criteria may result in either a definitive or probable diagnosis, according to the likelihood that the disease is present in a given patient. Although we believe these criteria accurately differentiate patients, this assessment has not been prospectively validated.

2.3.2.2. Definition of diagnostic criteria

2.3.2.2.1. Absolute criteria

Histological demonstration of the parasite from biopsy of a brain or spinal cord lesion: Visualization of the parasite or its remnants in histological sections identify the lesion as a Cysticercus [268, 436]. However, biopsy of calcified cysticerci may not confirm the diagnosis since the characteristic scolex or the membranes are no longer present.

Cystic lesions showing the scolex on CT or MRI: Only the presence of cystic lesions demonstrating the scolex should be considered pathognomonic of neurocysticercosis [138]. The scolex is visualized as a bright nodule within the cyst. This produces the so-called 'hole-with-dot' image that may be seen in vesicular cysts located in the brain parenchyma, the subarachnoid space, or the ventricular system [550].

Direct visualization of subretinal parasites by fundoscopic examination: The retina is part of the central nervous system and therefore patients with subretinal cysticerci have neurocysticercosis. Subretinal cysts are usually located over the macula and have a yellowish color with a central dark spot corresponding to the scolex. Subretinal cysticerci may rupture into the vitreous, a situation that permits the unique opportunity to visualize *in vivo* evagination and invagination movements of the parasite [337].

2.3.2.2.2. Major criteria

Lesions highly suggestive of neurocysticercosis on neuroimaging studies: These include cystic lesions without a scolex, single or multiple ring or nodular enhancing lesions, and round parenchymal

calcifications. These neuroimaging findings may also be observed in other diseases and therefore are not specific enough to establish a diagnosis [138]. Cystic lesions may be found everywhere in the nervous system [355]. Parenchymal cysts are usually 5-20 mm in diameter and rounded, and tend to lodge in the cerebral cortex or the basal ganglia. The main differential diagnosis in these cases is with low-grade astrocytomas for single lesions and cystic cerebral metastases for multiple lesions. Subarachnoid cysts may attain a size of up to 60 mm, and usually have a multilobulated appearance. These lesions must be differentiated from congenital arachnoid cysts and epidermoid tumors. Intraventricular cysts may be located in any of the cerebral ventricles and may only become evident when they cause obstructive hydrocephalus. Enhancing lesions represent a diagnostic challenge since a number of conditions may present with similar lesions on neuroimaging studies. Cysticercal enhancing lesions are usually smaller than 20 mm in diameter, are most often located supratentorially, and rarely cause displacement of midline structures. Parenchymal brain calcifications are common CT findings but are non-specific since calcifications may be found in many other conditions including metabolic disorders, vascular malformations, intracranial neoplasms, congenital anomalies, and a variety of infections [27]. However, certain patterns are considered characteristic of neurocysticercosis although other conditions may rarely result in similar patterns. Thus, only the presence of solid, dense, multiple supratentorial calcifications, 1-10 mm in diameter, in the absence of other illnesses should be considered as highly suggestive of neurocysticercosis. A common neuroimaging finding in neurocysticercosis is the presence of intracranial lesions in different stages of evolution. As the multiplicity of these findings provide further support for the diagnosis of neurocysticercosis, the presence of two different highly suggestive lesions should be considered as two major diagnostic criteria [122].

Positive serum enzyme-linked immunoelectrotransfer blot (EITB) assay for the detection of antibodies to *T. solium* glycoprotein antigens: Many serological assays to detect antibodies to *T. solium* are poorly documented and not standardized. Recent evidence suggests that only those using purified glycoprotein antigens for the detection of antibodies specific for *T. solium* are reliable for clinical diagnosis and epidemiological studies. The current assay of choice is EITB using partially purified antigenic extracts [567]. However, even the results using the EITB assay need to be critically interpreted. This assay has a documented specificity approaching 100% and a sensitivity of 92% to 98% for patients with two or more cystic or enhancing lesions [90, 609, 610]. However, this test is frequently falsely negative in patients with a single intracranial Cysticercus and in those with calcified cysticerci [90, 401, 609]. Since antibody assays reflect infection in any tissue, not only patients with neurocysticercosis, but also those with muscular or subcutaneous cysticercosis, may test positive. Paradoxically, the sensitivity and specificity of antibody detection by EITB performed with CSF are lower than those performed using serum, even in patients with evidence of central nervous system involvement [567], although this has not always been found [443].

Spontaneously resolving small single enhancing granuloma (SCG): SCG is recognized on the contrast CT or MRI as a solitary, well defined, enhancing lesion that measures less than 20 mm in its largest dimension. It is often but not always surrounded by edema that is almost always detected in patients who are imaged within a few days of a seizure. Since SCGs may resolve rapidly, they may not be visualized in scans performed several days after a seizure. Rajshekhar and Chandy have evolved a set of clinical and CT diagnostic criteria that have been validated in a prospective study. These criteria have been shown to have a high sensitivity and specificity but the presumptive diagnosis still needs to be confirmed by additional testing and careful follow-up [457, 620]. The criteria are shown in Table 2.1. A positive EITB for cysticercal antibodies in the serum of a patient suspected to have a SCG could be taken to confirm the diagnosis. However, immunological tests for cysticercal antibodies or antigens in CSF or serum of patients with SCG have a low sensitivity (40-60%) and some tests such as the ELISA suffer from cross-reactions with other diseases such as tuberculosis and brain tumors [460, 461, 529]. Therefore, immunological tests can only be complimentary to the CT or MRI studies in making a diagnosis of SCG and a negative test has no value in ruling out the diagnosis.

Spontaneous resolution of lesions visualized on CT scans in patients with an initial diagnosis of SCG managed with non-specific therapy such as anti-epileptic drugs (AEDs) is confirmatory evidence for the diagnosis of a SCG as virtually no other lesion with these CT characteristics will resolve spontaneously or result in a punctate calcification [455]. Resolution with anticysticercal drugs such as albendazole or side effects occurring during the administration of such drugs also confirms the diagnosis.

Table 2.1. Diagnostic criteria for a solitary Cysticercus granuloma

1. **Clinical** - Patient should present with seizures - There should be no evidence of persistent raised intracranial pressure (headache, vomiting, papilledema, diplopia) - There should be no evidence of progressive focal neurological deficit - There should be no evidence of a systemic disease (primary malignancy, systemic tuberculosis)
2. **Computerized tomographic** - The lesion should be solitary and enhanced following contrast injection - It should measure less than 20 mm in its largest dimension - There may be edema around the lesion but it should not be severe enough to produce a shift of the midline structures

All criteria *should be fulfilled to make an* ***initial diagnosis*** *of a SCG*

Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel: The disappearance of intracranial cystic lesions or their transformation into calcified nodules after therapy with cysticidal drugs [61, 113, 208, 538] should be considered a strong argument favoring the diagnosis of neurocysticercosis. Even for patients with enhancing lesions, some studies suggest the value of cysticidal drugs as a diagnostic tool as they accelerate the resolution of cysticerci-related enhancing lesions [39, 109].

2.3.2.2.3. Minor criteria

Lesions compatible with neurocysticercosis on neuroimaging studies: Some neuroimaging findings in patients with neurocysticercosis do not have enough diagnostic strength to be considered major diagnostic criteria. These include CT or MRI showing hydrocephalus or abnormal enhancement of the leptomeninges, and myelograms showing multiple filling defects in the column of contrast medium. Hydrocephalus is common in patients [332] with neurocysticercosis and may be related to the presence of ventricular cysts, ependymitis, or arachnoiditis causing occlusion of foramina of Luschka and Magendie [157]. Many other conditions may present with similar findings. In these cases, CSF analysis may provide useful diagnostic clues that must be interpreted in light of the clinical and radiological manifestations of the patient. Spinal subarachnoid cysts may appear as multiple filling defects during a myelogram or may be seen during MRI examinations [627]. This is also a non-specific finding that may occur in many other conditions affecting the spinal cord [316].

Clinical manifestations suggestive of neurocysticercosis: The clinical manifestations caused by neurocysticercosis are pleomorphic and include seizures, focal neurologic deficits, increased intracranial pressure, and intellectual deterioration [133, 252, 332, 333, 356, 362, 377, 507, 512, 516, 546]. More than 70% of symptomatic patients develop seizures [133], which are the primary or sole manifestation of the disease in many of the cases. Neurocysticercosis is the most common cause of adult-onset epilepsy in developing countries, and the presence of new onset seizures in an otherwise healthy middle-age individual coming from endemic areas is highly suggestive of this disease [115, 209, 366]. Fever is not a common manifestation of neurocysticercosis and its presence should suggest other diagnoses.

Positive CSF ELISA for detection of anticysticercal antibodies or cysticercal antigens: Detection of anticysticercal antibodies by serum ELISA has been associated with a large number of false positive and false negative results [131, 461, 462]. In contrast, the detection of anticysticercal antibodies by ELISA using CSF was 87% sensitive and 95% specific, and remains a useful tool for the diagnosis of neurocysticercosis in areas with limited access to the EITB assay [482]. However, this test may be falsely negative in patients with parenchymal brain cysticercosis or in those with inactive disease, and it may be falsely positive in other helminthic infections, and should only be considered a minor diagnostic criterion for neurocysticercosis. A specific antigen-detection ELISA using a monoclonal antibody may be more useful for the demonstration of excretory-secretory cysticercal antigens in CSF [90]. The test has a sensitivity ranging from 72% to 86%, with false-negative cases restricted to patients with a single intracranial Cysticercus. The specificity[7] of this assay has not been adequately assessed on samples of patients with other diseases. Several other serodiagnostic tests have been proposed for the

immunodiagnosis of cysticercosis. These assays are not sufficiently well standardized at this time for inclusion as diagnostic criteria.

Cysticercosis outside the central nervous system: The presence of soft-tissue calcifications or palpable subcutaneous cysticerci in a patient with seizures strongly suggests the diagnosis of neurocysticercosis. However, in endemic regions a patient may have systemic cysticercosis and neurologic manifestations due to an unrelated cause. Therefore, a diagnosis of cysticercosis outside the central nervous system only provides circumstantial evidence favoring the diagnosis of neurocysticercosis. Diagnosis of extraneural cysticercosis requires either histological demonstration of the parasite from biopsy of a subcutaneous nodule, the presence of multiple 'cigar-shaped' calcifications in the muscles in plain X-ray films, or direct visualization of a Cysticercus in the anterior chamber of the eye.

Epidemiological criteria: The place of birth and residence as well as the travel history, provide important information when evaluating patients with suspected neurocysticercosis. Cysticercosis is endemic in Latin America, Sub-Saharan Africa, and in some regions of Asia, including the Indian subcontinent, the People's Republic of China, Korea, and Indonesia. The disease is rare in most European countries, in North America, in Oceania, and in some Muslim countries of Asia and Africa. However, imported cases may occur even in these areas. Clinicians must be aware that cysticercosis is acquired from a human tapeworm carrier and the disease is sometimes diagnosed in persons born in non-endemic countries who have never traveled to endemic regions [25, 503, 506]. In such cases, it is of value to search for a household contact with a tapeworm infection. Definitive diagnosis of T. *solium* infection can only be established when the scolex or a gravid proglottid is available for microscopic examination or by genetic analysis. Diagnosis can be suspected in those with a history of having passed proglottids in feces as well as in those with positive fecal examinations for taeniid eggs or with a positive Coproantigen test [13].

Cestodes contain calcareous corpuscles and sometimes these are the only remaining morphological evidence that a granuloma is due to a cestode. Since other cestodes are rarely found in the human brain, the presence of calcareous corpuscles in a compatible lesion suspicious for cysticercosis is indicative of *T. solium* infection [73].

Eosinophilic meningitis is a non-specific but helpful laboratory finding suggestive of parasitic CNS infection [485, 545]. With the exception of cysticercosis, other helminthic infections of the human brain are rare and are caused by a limited number parasites that can usually be differentiated from one another. However, other conditions can also cause eosinophilic meningitis such as fungal infections and lymphomas of the CNS.

2.3.2.3. Degrees of diagnostic certainty

Definitive diagnosis: According to the chart, a definitive diagnosis of neurocysticercosis is reached in individuals who have one absolute criterion or in those who have two major criteria plus one minor and one epidemiological criterion. In such cases there is no doubt that the individual actually has cysticercosis.

Probable diagnosis: This category includes those individuals in whom the diagnosis of neurocysticercosis is likely but cannot be absolutely confirmed. A probable diagnosis requires one major plus two minor criteria, one major plus one minor and one epidemiological criterion, or three minor plus one epidemiological criteria.

2.4. Treatment of neurocysticercosis

2.4.1. Introduction

It is well proven that both albendazole and praziquantel are cysticidal and result in the resolution of T. *solium* cysts [234, 239, 538]. Although the clinical benefits of cysticidal treatment continue to be controversial, there is an increasing body of evidence pointing to the clinical benefits of treatment of some forms of neurocysticercosis. There is no standard regimen for the treatment of neurocysticercosis but the treatment varies with the type of involvement and the presence of other factors. Management of

neurocysticercosis includes the use of symptomatic medication (including anticonvulsants), anti-inflammatory drugs, anti-parasitic drugs, or surgery. This section will briefly review each of them, and discuss their specific applications in the frame of each of the more common clinical presentations.

2.4.2. Symptomatic medication

Analgesics: Headache is a common complaint in neurocysticercosis, both as an individual manifestation, as part of an intracranial hypertension syndrome, or as a post-ictal manifestation. Except for those headaches related to moderate or severe intracranial hypertension, neurocysticercosis-associated headaches usually respond well to common analgesics.

Anti-epileptic drugs (AEDs): At initial presentation most patients with seizures due to neurocysticercosis respond well to single-drug therapy with the first-line AEDs phenytoin, carbamazepine or valproic acid [120]. Indications, dosage, dose adjustments, drug addition/switch, and AED withdrawal should be followed as for any other case of secondary seizures. A summary of first-line medications and alternatives is shown in Table 2.2. AEDs can be withdrawn successfully, although patients with residual calcification are at high risk of recurrent seizures [70, 110]. Usually this approach is suggested after two years of treatment (American Academy of Neurology recommendation), although there are no data to support this. Others propose a short period of AEDs in patients with a single degenerating Cysticercus during the acute symptomatic phase but there are no studies to validate this approach either.

Table 2.2. Summary of criteria guiding clinical management

Parenchymal neurocysticercosis	
Viable (live cysts)	
One to five cysts	Anti-parasitic treatment, with corticosteroids
More than five	Anti-parasitic treatment, with corticosteroids
More than 100 cysts	Anti-parasitic treatment, with high-dose corticosteroids. Alternatively, chronic steroid management. No anti-parasitic treatment, neuroimaging follow-up
Enhancing lesions (degenerating cysts)	
Mild or moderate	No anti-parasitic treatment. Neuroimaging follow-up. Alternatively anti-parasitic treatment with corticosteroids, and as a second alternative anti-parasitic treatment. Corticosteroids only if side effects develop
Heavy (cysticercotic encephalitis)	No anti-parasitic treatment. High dose corticosteroids and osmotic diuretics
Calcified cysticerci	No anti-parasitic treatment
Any number	
Extraparenchymal neurocysticercosis	
Ventricular cysticercosis	Neuroendoscopical removal, when available. If not available, then CSF diversion followed by anti-parasitic treatment, with corticosteroids, and as a second alternative open surgery (mainly for cysts in the fourth ventricle)
Subarachnoid cysts including giant cysts or 'racemous' cysts on neuroimaging	Anti-parasitic treatment with corticosteroids. Ventricular shunt if there is hydrocephalus
Hydrocephalus with no visible cysts on neuroimaging	Ventricular shunt. No anti-parasitic treatment
Other locations	
Spinal cysticercosis, intra or extramedullary	Primarily surgical. Anecdotal reports of successful use of albendazole with corticosteroids
Ophthalmic cysticercosis	Surgical resection of cysts

Anti-inflammatory drugs: Corticosteroids are commonly used to decrease the inflammation and edema around cysts causing symptoms. 8-12 mg of dexamethasone or 40 mg of prednisone per day are reasonable starting doses that achieve good anti-inflammatory effect yet still leave room for dose increases if the inflammation continues or increases. Mannitol can be temporarily used to manage intracranial hypertension. Corticosteroid therapy is the primary management for chronic cysticercal arachnoiditis or encephalitis, where up to 32 mg per day of dexamethasone are needed to reduce brain edema and/or inflammation accompanying these conditions [120, 205].

2.4.3. Anthelminthic medications-indications and use

Anti-parasitic drugs: Praziquantel, introduced in 1979, was the first specific anti-parasitic drug for cysticercosis [156, 476]. Albendazole was later added as a cheaper and more available alternative. Praziquantel and albendazole destroy the cysts. The dose and duration of these medications depends on the clinical presentation. In the usual treatment of uncomplicated intraparencyhmal cysts, praziquantel is commonly used at 50 mg/kg/d for two weeks and albendazole is used at 15 mg/k/d for eight days [538]. At these dosages, incomplete cure rates are not infrequent and may result in the need for repeated treatments. Another strategy is to prolong the duration of treatment until cysticidal effects are noted for most or all of the lesions. Subarachnoid, racemous, ventricular cysts, cysts recalcitrant to previous therapy and meningeal cysticercosis may require both increased dosages and longer durations of therapy; this is usually determined by clinical and radiological response [205]. The use of praziquantel and corticosteroids together results in decreased serum concentrations of praziquantel but there is no evidence that this pharmacological interaction decreases its efficacy [216]. Serum levels are also decreased with the simultaneous use of phenytoin and carbamazepine [55, 293]. Albendazole has better penetration into the CSF, does not alter its concentrations when given with corticosteroids and is cheaper than praziquantel, but levels of its active metabolite are also decreased with concomitant use of phenytoin.

Following the onset of anti-parasitic therapy or after withdrawal of corticosteroids (which are simultaneously given in most cases), exacerbation of neurological symptoms resulting from perilesional inflammation and edema due to the death of the cyst, commonly occurs [544]. Administration of or an increase in the dose of corticosteroids usually suppresses this troublesome side effect. In situations where lesions are in critical locations, or a large and potentially harmful degree of inflammation and edema are initially present such as in acute encephalitis due to cysticercosis, specific cysticidal therapy may lead to uncontrollable inflammation and therefore treatment is contraindicated [120, 205]. Since calcified cysts are not viable, specific anti-parasitic therapy is not indicated.

A recently published consensus report on the treatment of neurocysticercosis [205] makes four main recommendations: (i) to individualize treatment decisions depending upon the number, location and viability of parasites; (ii) to promptly treat enlarging cysts medically with anti-parasitic drugs or surgery; (iii) to prioritize the management of intracranial hypertension when present; and (iv) to habitually incorporate symptomatic medication including adequate AEDs as part of the treatment plan. In the following section, we will discuss the use of anti-parasitic drugs in each defined type of neurocysticercosis. Situations where anti-parasitic treatment is contraindicated are specifically discussed.

Viable cysts, single or multiple: Between 60% and 85% of parenchymal brain cysticerci are killed after standard courses of treatment, with most trials demonstrating higher parasiticidal effects with the use of albendazole compared to praziquantel [112, 208, 538, 539, 553]. The consensus panel recommended antiparasitic therapy of patients with more than five cysts. After publication of the consensus report, the results of a randomized, blind, controlled treatment trial using albendazole became available that showed the clinical benefit of decreased generalized seizures after treatment of patients with one or viable cysts as well as faster resolution of viable enhancing [203]. The study confirms the prior recommendation of the consensus panel that treatment results in clinical improvement and should routinely be offered to patients who have no contraindications. There are no controlled studies evaluating the use of corticosteroids in this group but their use would be expected to control the exacerbation of symptoms that usually occurs with treatment.

Treatment of solitary Cysticercus granuloma (SCG): The management of SCG consists chiefly of AEDs. Usually monotherapy with any of the first generation AEDs such as phenytoin, phenobarbitone or

carbamazepine controls seizures in over 80% of patients. Patients should, however, be closely monitored clinically (every month if possible) to look for the development of new symptoms or signs of raised intracranial pressure or focal neurological deficits. While some patients with SCG have only one episode of seizures at the onset of the illness, others have intermittent symptomatology with recurrence of seizures and periods of remission. Recurrence of seizures should not be interpreted necessarily as an incorrect diagnosis but might indicate insufficient doses of AEDs or a requirement for a second AED. The use of cysticidal drugs such as albendazole or praziquantel at initial presentation is debated [39, 40, 116, 296, 407] and we do not generally recommend their use except for lesions that persist for several months. The dose of albendazole is 15 mg/kg per day in two divided doses administered for eight to 14 days. Use of steroids such as dexamethasone (12 to 16 mg/day in divided doses) for the first five to seven days of the course of albendazole is recommended to avoid adverse effects resulting from the destruction of the parasite. Cysticidal drugs may be helpful in the management of patients with SCG in two ways. Firstly, they may hasten the resolution of the granuloma and secondly, the occurrence of adverse effects during the administration of the drugs confirms the diagnosis of SCG. However, the occurrence of adverse effects in up to 40% of patients is a counter argument to their routine use [453]. Recent studies suggest that a short course of corticosteroids decreases the likelihood of seizures in the group [348]. The treatment trial of Garcia *et al.* [203] in which single viable cysts with enhancement were treated also suggested a benefit of anthelminthic treatment. It should be emphasized that SCG encompasses a range of types of degenerating cysts including enhancing viable cysts on one extreme to mostly degenerated non viable granulomas with associated enhancement and edema at the other. There would likely be some benefit of anthelminthic treatment in the former but none in the latter. Unfortunately, SCG has mostly been defined by its CT appearance where the differentiation between pathological types may not be clearly evident.

SCGs ultimately resolve without specific therapy but the rate of resolution is highly variable and unpredictable in an individual patient. The rate of spontaneous resolution of a SCG was studied in 210 patients and at the end of 12 months, partial resolution was seen in 87.6% and complete resolution in 62.5% of patients [454].

AEDs can be discontinued in a patient with SCG within weeks after resolution of the granuloma is demonstrated on the CT scan provided the patient has not had a seizure in the preceding three months. Patients with residual calcification might require prolongation of AED therapy.

Patients with SCG have a good seizure prognosis and, in one study, only one of 126 patients with a SCG had recurrence of seizures after withdrawal of AEDs [382]. Therefore, AEDs can safely be withdrawn in most patients with SCG.

Any patient with suspected SCG who develops new signs and symptoms and any patient whose repeat CT scan shows a lesion larger than 20 mm might require a brain biopsy and histologic diagnosis [457]. No further empiric therapy such as anti-tuberculous therapy should be offered to such patients as these patients could be harboring a secondary metastasis, glioma or other pathologies including a tuberculoma.

Multiple enhancing lesions: Treatment of patients with multiple enhancing lesions has not been specifically studied but would likely be similar to the approach taken with patients with SCG. However, these patients may differ from those with SCG since they are more likely to be serologically positive and the possible benefits of treatment could potentially increase because the small benefit gained by the treatment of one lesion is multiplied. Enhancing lesions should be differentiated on the basis of neuroimaging findings from old calcified lesions showing enhancement and peripheral edema. When many enhancing lesions are present with marked brain edema (encephalitic cysticercosis) [463] anti-parasitic drugs should not be used.

Calcifications, single or multiple: When only calcified lesions exist, there is no basis for anti-parasitic therapy since the larvae are dead.

Situations where anti-parasitic treatment is contraindicated: Patients with massive (hundreds of viable cysts) infections may develop severe life-threatening edema and inflammation as a consequence of cysticidal therapy. When many enhancing lesions are present with marked brain edema (encephalitic cysticercosis), anti-parasitic drugs should not be used [120, 205, 463].

Subarachnoid cysticercosis of the Sylvian fissure ('giant' cysts): When cysts lodge in the fissures and basal cisterns they tend to continually grow and infiltrate. Those located in the Sylvian fissure have a particular propensity to grow as cystic structures into the surrounding brain parenchyma reaching several centimeters in diameter and behaving as a tumor mass. This form is progressive and should always be treated with anti-parasitic drugs or surgery [112]. Medical treatment alone can be surprisingly effective. Thirty-three patients with this type of neurocysticercosis resolved after cysticidal treatment but most required prolonged treatment up to three months [416].

Subarachnoid cysticercosis of the basal cisterns ('racemose' cysticercosis): This type of neurocysticercosis is also progressive and carries a grim prognosis [52]. Given that surgical resection is hampered by the dispersion of the parasite, the primary therapeutic approach is anti-parasitic drugs (albendazole seems to work much better than praziquantel in these cases) for long periods of time, one month or more [233]. Corticosteroids should be given simultaneously and in high doses since there is a risk of stroke from arterial involvement by the surrounding lesions. Many of these patients become corticosteroid-dependent and suffer from its side effects. Methotrexate has been used as a corticosteroid sparing and/or replacement in a limited number of patients with some success [300].

Ventricular cysticercosis: Neuroendoscopy is considered the most recommendable approach [46, 47]. Surgical resection is a suitable alternative especially in fourth ventricle cysts. Anti-parasitic therapy can resolve ventricular cysts but there is always the risk of acute CSF blockage due to the inflammatory process.

Hydrocephalus without noticeable cysts: Hydrocephalus should be managed with a ventricle-peritoneal (V-P) shunt before considering instituting anti-parasitic treatment in these cases [120]. The possibility of intraventricular cysts or ependymitis should be considered and whenever possible ruled out by MRI.

Surgery: The contemporary role of surgery in neurocysticercosis is restricted to placement of V-P shunts in hydrocephalus, excision of well-localized, single giant cysts, and excision of well-defined seizure foci.

Obstruction of V-P shunts in neurocysticercosis is common because of the high cellularity and protein content of the CSF [38, 301]. Multiple shunt revisions are common and are associated with a poor prognosis. A number of measures may enhance shunt viability including use of an open-ended shunt, treatment with prednisolone at 50 mg three times week, and anti-parasitic treatment [301, 547]. In recent years, neuro-endoscopy has been proposed and applied as a less invasive procedure for intraventricular cysts or basal cysts [629, 632]. The use of this promising alternative is still limited by the scarcity of the equipment and trained personnel.

2.4.4. Management in field conditions

At the present time assessment of patients with possible neurocysticercosis and treatment of diagnosed patients requires a reliable medical infrastructure, knowledgeable medical personal or surrogates, a CT evaluation (and MRI if possible), and perhaps serological assays and access to medication. In many endemic countries none or part of these conditions or technologies are available. In the absence of studies that show benefit to patients treated with a possible diagnosis based on limited information, specific antiparasitic medication cannot be advocated. Medical management of symptoms is worthwhile and effective. There are specific recommendations in place for the treatment of patients with seizures of unknown cause. Phenobarbital or dilantin has been used in these studies with minimal monitoring and cost. What are the benefits, if any, in identifying patients with neurocysticercosis? And, if there are benefits, what is the best way to identify, evaluate, and possibly treat patients in regions with minimal resources? Is it better to develop resources to prevent transmission and disease rather than to treat individual patients? These are questions that require evaluation before rational treatment approaches can be recommended.

2.4.5. Screening and treatment of tapeworms

Tapeworms are present in up to 25% of patients and household members [210]. We would strongly recommend screening patients and relatives for taeniosis, despite the insensitivity of microscopy (see

Chapter 4, Section 4.1 for information on the diagnosis of taeniosis). Immunologically-based tests (Coproantigen ELISA detection) increase the sensitivity of taeniosis detection [7] but are presently not commercially available. See also Chapter 6 (Section 6.3.6 and Annex 7.7.5) for detailed discussion of treatment for adult tapeworm infections.

CHAPTER 3:
EPIDEMIOLOGY OF TAENIOSIS AND CYSTICERCOSIS

KD. Murrell

3. Introduction

The life cycles of the zoonotic *Taenia* species of tapeworms require two hosts and a free-living stage. Therefore, at any one time, the parasite population of these species consists of three distinct subpopulations: adult tapeworms in the definitive host (man), larvae (Cysticercus or metacestode) in the intermediate host (pigs or cattle), and eggs in the environment. When assessing the epidemiology of these cestodes, all three subpopulations must be taken into account and no part of the life cycle can be considered without reference to the other parts because all are interdependent.

There are several excellent reviews describing the epidemiology of the transmission of the taeniosis/cysticercosis complex [152, 178, 228, 329, 424, 506]. An understanding of the important factors in transmission, and of the stability of each parasite system to perturbation, is crucial for veterinary and medical authorities planning control tactics and strategies. This Chapter describes the geographical distribution and occurrence of these taeniid tapeworms, their important modes of transmission, their ability to survive and persist in the many ecological situations in which they occur, and the important risk factors that must guide the design of prevention and control programs.

This treatment of the epidemiology of taeniosis/cysticercosis is based on the 1983 'WHO Guidelines for the Surveillance, Prevention and Control of Taeniasis/Cysticercosis' (VPH/83.49) [601]. The discussion on epidemiology has been extensively revised and updated to incorporate significant advances in the understanding of these zoonotic tapeworm infections that have accrued over the past two decades.

3.1. Global distribution of *Taenia solium* taeniosis/cysticercosis

Taenia solium is an important zoonosis in many pork-eating countries and is usually, but not always, associated with low economic development [178, 329, 346, 419, 424, 506]. The prevalence of T. *solium* infection varies greatly according to the level of sanitation, pig husbandry practices and eating habits in a region. It is very difficult to evaluate the prevalence of *T. solium* taeniosis, because the coproscopical methods used for survey are inadequate (see Chapter 4) and usually cannot differentiate between *T. solium* and *Taenia saginata* infections [419]. Therefore, data on the prevalence of adult worm infections are generally considered very conservative. Similarly, prevalence data based on serological methods may overestimate infection rates because presence of antibody may be the result of exposure to eggs and early but non-persisting infection.

3.1.1. Africa

Taenia solium is an emerging and expanding zoonosis in Africa. Data from West and Central Africa suggest that investigations on human cysticercosis often underestimate true transmission rates, based on the prevalence observed in pig populations (Table 3.1), and there are regions of hyperendemicity (hyperendemic prevalence indicates a constant occurrence of the disease at a high transmission level) [225, 631]. The high prevalence of porcine cysticercosis should be expected to be accompanied by obvious and frequent T. *solium* tapeworm infections in humans. However, the diagnosis of taeniosis is difficult because current tests are insensitive, and because taeniosis causes little or no symptoms and, therefore, patients do not present for evaluation unless they see the proglottids in their feces and recognize their significance. The prevalence data on pigs in developing countries should also generally be considered as minimal estimates because of difficulties in diagnosis [178].

Table 3.1. Prevalence of porcine and human cysticercosis in West and Central Africa [224]

Country	% in pigs by meat inspection	% in humans by serology (ELISA)
West Africa		
Low prevalence		
- Burkina Faso	0.6	Cases reported
- Ivory Coast	2.5	Cases reported
- Senegal	1.2	Cases reported
(Hyper) endemic		
- Benin	ND	1.3*
- Ghana	11.7	Cases reported
- Nigeria	20.5	ND
-Togo	17	2.4*
Central Africa		
(Hyper) endemic		
- Burundi	2-39	2.8
- Cameroon	2-25	0.7-4.6
- Centr. Afr. Rep	ND	2.4
- Chad	26	ND
- D.R. Congo	10-30	3**
- Rwanda	20	7**

* *percent of the general population*
***: based on presence of cysticerci*
ND: no data available

A similar pattern is seen in East and Southern Africa, where prevalences in pigs are reported to be from 20 to 40% (Table 3.2) [434]. Because of the growing interest among veterinarians and agriculturists in porcine cysticercosis, the information on infection in pigs is in many instances more extensive than that for human infections (Table 3.2). The incidence data in humans are very limited due to a lack of adequate surveillance, monitoring and reporting systems, although the recognition of its status as a serious and emerging threat to public health is increasing [346].

Table 3.2. Results of prevalence studies on porcine cysticercosis conducted in Eastern and Southern African countries [434] (Survey conducted from 1985-1989)

Country	% Porcine cysticercosis prevalence	Number of pigs surveyed	Type of survey [a)]	Area surveyed
Tanzania	0.04-4.9	45,794	P	Mbulu District
	4.5-37.7	83	P	Northern highlands
	3.2-46.7	770	L	Mbulu District
	0-26.9	1,789	L	Southern highlands
Kenya	10.0-14.0	407	L	Busia and South Nyanza Districts
Uganda	33.7-44.5	600	P	Movo District
	0-33.7*	297	P	Central and Northern Districts
Zamba	20.6-56.6	1,316	S,P	Lusaka
	8.2-20.8	249	L, S	Eastern and Southern Provinces
Zimbabwe	0.03-4.3	1,000,000	P	National
	2.7-28.6	99,525	P	Western Region
Mozambique	6.5-33.3	387	S	Tete Province
South Africa	0.5-25.1	> 100,000	P	National
	0-9.1	28,242	P	National

a) P: post-mortem; L lingual examination; S: serological;
** Eight foetuses from a positive slaughtered pregnant sow were all found to be infected with cysticercosis*

Concern is growing in East and Southern Africa that the rapid expansion of pig farming and pork consumption will exacerbate the problems with T. *solium* cysticercosis because, since 1961, the pig population in Uganda, Tanzania, Kenya, Zambia, Zimbabwe, and Mozambique has increased nearly threefold (in Uganda over six-fold) [434]. The lack of adequate slaughterhouse facilities and the reliance on extensive and free-ranging rearing practices throughout the region represent serious obstacles to reducing the risk of this zoonosis (see Section 3.4.1.1).

3.1.2. Latin America

Due to very active research efforts in this region, a large amount of data has accumulated clearly demonstrating that there is a very substantial risk of infection with *T. solium* for residents of many Latin American countries, although the prevalence rates vary from country to country [3, 178, 189, 329, 419, 489] (Tables 3.3, 3.4, 3.5). The frequent finding of neurocysticercosis in autopsy cases from general hospitals (Table 3.6) [178], its notable presence (4-6%) among the patients of specialized neurological institutions [578] and the overall serological reactivity to Cysticercus antigens found in the general population (e.g. Mexico) (Tables 3.3, 3.4, 3.5), indicate an active transmission of cysticercosis in the region [178].

Table 3.3. Epidemiological studies perforimed in Mexico [189]

Community	Population sampled	% Taeniosis [a)]	% Swine cysticercosis [c)]	% Human cysticercosis [c)]
El Salado	432	1.1 [b)]	ND [d)]	12.0
Mexico City	1,000	0.5	ND	12.2
Tedzidz	475	1.5	35.0	3.7
El Sotano	134	2.4 [b)]	24.0 [e)]	6.4
Angangeo	1,552	0.3 [b)]	4.0	10.8
Xoxocotla	1,005	0.2 [b)]	6.5	4.9
Chalcatzingo	1,962	0.8	2.5 [c)]	ND
Atotonilco	2,911	1.1	1.0 [c)]	7.1

a) Coproantigen ELISA
b) Coproparasitoscopic study
c) ELISA or Western blot
d) ND, not determined
e) Tongue palpation

Table 3.4. Epidemiological studies performed in Peru [189]

Community	Population/ sampled	% Taeniosis [a)]	% Swine cysticercosis [c)]	% Human cysticercosis [c)]
Camino Real	109/38	ND	61	21
Chaupiojo	184/26	ND	41	10
Churusapa	279/48	ND	49	7
Haparquilla	371/30	ND	46	13
Macedo	421/88	1.0 [a)]	43	8
Monterredonda	1,200/41	ND	13	16
Rosaspeta	72/31	ND	33	5
Saylla	495/145	8.6/3.0 [b)]	36	24

a) Coproparasitoscopic study

b) Forty-three chicharroneros/102 general population

c) ELISA or Western blot

Table 3.5. Epidemiological studies performed in other Latin American countries [189]

Community/Country	Population sampled	% Taeniosis [a)]	% Swine cysticercosis [b)]	% Human cysticercosis[c)]
Rural/Bolivia	159	ND	38.9	22.6
San Pablo del Lago/Ecuador	118	ND	7.5	10.4
El Jocote/Guatemala	1,161	2.8	14.0	17.0
Quesada/Guatemala	1,204	1.0	4.0	10.0

a) Coproantigen ELISA
b) Tongue palpation
c) ELISA or Western blot

Table 3.6. Frequency of neurocysticercosis in autopsy cases [178]

Country	Years of study	%of neurocysticercosis
Brazil	1960-1979	2.4
Brazil	1965-1970	2.2
Brazil	1992-1997	1.5
Chile	1939-1966	0.70
Chile	1947-1979	0.09
Chile	1947-1979	0.01*
Colombia	1944-1964	0.78
Colombia	1955-1970	0.40
Costa Rica	1967	0.45
Ecuador	1947-1968	0.47
El Salvador	1961	0.40
Honduras	1951-1966	0.02
Mexico	1943-1968	0.14*
Mexico	1947-1957	2.8
Mexico	1953-1970	1.3
Mexico	1963-1973	1.5
Mexico	1963-1974	2.2
Mexico	1970-1975	0.38*
Peru	1961-1974	0.99
Peru	1961-1974	0.16*
Peru	1961-1974	5.9
Venezuela	1967	0.49

** Data from children's hospitals*

Porcine cysticercosis is also frequently found at meat inspection in the abattoirs of Latin America (Tables 3.3, 3.4, 3.5); but again, these data are thought to be conservative indicators since obviously infected pigs (often identified by simple lingual palpation) are usually not taken to the slaughterhouse, but slaughtered elsewhere (clandestine marketing) [231, 235, 434, 556, 631]. In Peru, where infection rates in pigs vary from 14%-25%, virtually no recognized infected pigs are processed at local slaughterhouses [556]. The data for human prevalence of infection are much stronger; for example, studies in Honduras, Peru, Mexico and Guatemala reveal neurological indications of infection in rural populations of between 9%-18% [178 (Table 3.6), 189, 578].

3.1.3. Europe

Table 3.7. Origin of locally acquired cases of neurocysticercosis in Europe, 1996-2000 [405]

Country	Cases
Czech Republic	1
Bosnia	1
Yugoslavia	2
Portugal	4
Spain	2
Italy	1
Total	11

Neurocysticercosis is infrequently encountered in most of Europe. However, due to increased immigration and travel, *T. solium* cysticercosis is likely to be diagnosed with increasing frequency and there is evidence that in some regions in Europe *T. solium* infection can be acquired locally [405]; a recent survey revealed that out of a total of 45 cases of neurocysticercosis diagnosed between 1996 and 2000, 11 were autochthonous cases (Table 3.7).

The Iberian Peninsula is still endemic for this zoonosis, particularly in the northern region of Portugal. These cases are considered to be examples of human to human transmission because of the comprehensive veterinary control and meat inspection typical of Europe, which has yielded rare instances of pig infection [271, 329]. In this case, human cysticercosis occurs because travelers to endemic areas acquire tapeworms and then become the source of egg infections (carriers) when they return home.

3.1.4. Asia

In Asia, this zoonosis has been known to occur for the past several hundred years, but until recently, it has not received much attention; consequently, epidemiological information for the region is not extensive [152, 329, 419, 424, 456, 459]. As shown in Table 3.8, data on taeniosis are more available than that on cysticercosis. Notably lacking are data on Mynmar, Laos and Cambodia [136].

Table 3.8. Prevalence data on *Taenia solium* taeniosis and cysticercosis in some Asian countries [459]

Country	% Human cysticercosis	% Taeniosis	% Porcine cysticercosis
People's Republic of China	3-4	0.112(0.06-19)	5.4 (0.8-40)
Indonesia	1.7-13	0.8-23	0.02-2.63
Vietnam	5-7	0.5-6	0.04-0.9
India	NA	2	9.3
Nepal	NA	10-50	32.5
Korea	3	NA	NA

Taeniosis and cysticercosis due to *Taenia solium* are common in Indonesia. Very high prevalences in the Wissel Lakes area in West Irian Jaya have been associated with an 'epidemic' of epilepsy and burns [549, 562]. The prevalence of *T. solium* infections is also high in Bali, Indonesia [459, 527]. In a 1981 serological survey, 21% of people tested in Bali were positive for cysticercosis, compared with only 3%-4% in Sumatra [84]. In a more recent survey using an immunoblot method, 13% of Balinese people tested were positive [558]. Serosurveys in Irian Jaya using immmunoblots revealed an 8%-10% prevalence rate [352]; approximately 2% of 548 examined persons had demonstrable taeniosis, half of which were diagnosed as *T. solium.* A recent review of Indonesian prevalence surveys in humans and pigs, conducted over a 23-year period, has been published (Table 3.9) [528]. Taeniosis is widespread especially in non-Muslim communities, although the *Taenia* species is not always certain; *T. saginata* is also reported frequently in Indonesia, (for example, bovine cysticercosis is reported to have prevalences of 2.2% in Riau province and 24% in Bali and Irian Jaya). Studies in Irian Jaya indicate that the majority of people with epilepsy harbor *T. solium* cysticercosis.

Cysticercosis occurs throughout all of India, particularly in the north [456]. Significantly, neurocysticercosis accounts for 8.7% to 50% of patients with recent onset of seizures. The peculiarity of the disease in India is the high incidence of patients with the solitary form of the disease; 60% to 70% of Indian patients with neurocysticercosis have SCG [455]. The prevalence of taeniosis is reported to be between 0.5% to 2%, although surveys in Uttar Pradesh found 38.7% of people in a pig rearing community had taeniosis [441]. The prevalence of porcine cysticercosis as judged from slaughterhouse data ranges overall from 7% to 12%, although the recent study in Uttar Pradesh reported a prevalence of 26% [441].

In Nepal, reliable data are difficult to obtain, chiefly due to lack of imaging equipment and epidemiological investigations. However, a recent prevalence of certain ethnic groups revealed the presence *o£ taeniid* eggs in the feces of 10%-50% of people examined [198]. Porcine cysticercosis rates are estimated to be 14%-32% [456].

Table 3.9. Human *Taenia solium* taeniosis/cysticercosis survey from 1972-1994 in Indonesia [528]

Province	Year	No. of fecal samples for *T. solium*		Serological tests for cysticercosis	
		Exam	Pos. (%)	Exam	Pos. (%)
North Sumatra (1)	1972	285	8 (2.9)	283	3(1.1)
North Sumatra (2)	1972	350	7 (2.0)	350	2 (0.6)
Irian Jaya (1)	1973	170	18 (10.5)	170	43 (25.0)
Irian Jaya (2)	1973	74	6 (8.1)	74	21 (18.4)
East Nusatenggara	1975	445	12 (2.8)	440	4 (0.9)
Bali (1)	1977	548	12 (2.2)	546	7(1.3)
Irian Jaya (3)	1979	350	7 (2.2)	350	61 (17.4)
Bali (2)	1981	351	4(1.1)	352	5 (1.4)
North Sulawesi	1981	245	0 (0.0)	245	2 (0.8)
Lampung	1981	476	5 (1.0)	473	8 (1.7)
Southeast Sulawesi	1985	243	1 (0.4)	243	0 (0.0)
Riau	1987	202	2 (0.9)	201	0 (0.0)
West Nusatenggara	1988	260	8 (3.1)	260	2 (0.8)
South Sulawesi	1989	288	14 (4.9)	283	1 (0.4)
Central Kalimantan	1990	144	4 (2.8)	144	1 (0.7)
Bah (3)	1990	515	14 (2.7)	511	9(1.8)
Irian Jaya (4)	1994	537	56 (10.4)	537	116(21.6)
Irian Jaya (5)	2000	0	0 (0.0)	70	42 (60.0)

Taenia solium infections have also been reported from Thailand [305], South Korea [152] and are sporadically reported in Taiwan [77, 78].

A recent assessment of the cysticercosis situation in the People's Republic of China revealed that human cases of taeniosis and cysticercosis occurred in 29 provinces, municipalities and autonomous regions, with five particularly endemic zones [78]. The average incidence of T. *solium* taeniosis in the regions surveyed range from 0.05% to 15.00%; while the number of people with cysticercosis was estimated at three to seven million. In the endemic areas, pig cysticercosis varied from 0.4% to 15%), and occasionally up to 40%.

3.1.5. United States of America: The impact of immigration and travel

As in Europe, most cases of *T. solium* taeniosis/cysticercosis in the United States of America (USA) are attributed to immigration and travel [505, 506]. However, it has been reported recently that among the rising number of cases being seen in the country's western states, a proportion appears to be locally acquired. A retrospective analysis of hospital records (1995-2000) in Oregon revealed 89 hospitalizations due to cysticercosis, five of which occurred in people who had not traveled or lived outside the United States [564].

In California, over a 12-year period (1989-2000) 124 cysticercosis deaths were identified, representing a death rate of 3.9 per million population; the large majority were foreignborn, predominantly in Mexico [536]. However, nearly 14% of deaths were among people born in the USA, some of whom may have been autochthonous infections, although travel-related exposure cannot be ruled out as a source of infection.

A well documented epidemic of locally acquired cysticercosis occurred among four unrelated families of an orthodox Jewish community in New York City. The households were apparently contaminated with

T. solium eggs through the employment of infected housekeepers who had immigrated from Latin America [506].

3.2. Global distribution and occurrence of taeniosis/cysticercosis due to *Taenia saginata*

3.2.1. Taeniosis

Taenia saginata is distributed globally but the infection is particularly important in Africa, Latin America, and Asia as well as in some Mediterranean countries [152, 198, 329, 424]. The prevalence of *T. saginata* in humans can be roughly classified into three groups: (i) highly endemic regions with prevalences that exceed 10%; (ii) those with moderate prevalences; and (iii) those with a prevalence below 0.1% or free from T. *saginata* taeniosis.

The highly endemic areas include the Central and Eastern African countries of Ethiopia, Kenya, and Zaire. Endemic areas occur in the Caucasian and south-central Asian republics of the former Union of Soviet Socialist Republics and in the Mediterranean (Syria, Lebanon and Yugoslavia). For example, in some parts of Serbia and Montenegro, up to 65% of children have been reported to harbor *T. saginata* [432]. Europe overall reports a moderate prevalence, as does Southeast Asia (Thailand, Vietnam, and the Philippines), India, Japan and South America [152, 329].

The prevalence of *T. saginata* (0.5%) is reportedly low in the USA, Canada, Australia, South America and some western Pacific countries, but may exceed that of Central America [424].

3.2.2. Bovine cysticercosis

The distribution of bovine cysticercosis is related, of course, to that of taeniosis in humans. The rates vary from very low, (0.03%) in North America and Europe, to very high in Africa and Latin America (10%-80%) [329, 379, 424, 535]. Eastern European cattle infection rates are generally higher than those in Western Europe [102, 271, 418]. Information on prevalences of bovine cysticercosis within African countries is limited, but rates as high as 80% (Ethiopia) occur and are reported to be increasing in Botswana and Nigeria [439]. In Asia, information is also sketchy, but reports indicate that infection rates range from 0.001% in Japan, to 0% to 100% in various parts of Korea [152, 297]. Bovine cysticercosis is described as 'very frequent' in the People's Republic of China and Thailand [305, 326]. In contrast, its prevalence is reported to be very low or rare in India [36] and the Philippines [142]. In Indonesia bovine cysticercosis is reported to have prevalences which range from 2.2% in Riau province to 24% in Bali and Irian Java) [528].

3.3. Global distribution and occurrence of *Taenia saginata asiatica* (Asian *Taenia)*

This zoonosis appears to be restricted to Asia, based on published survey data . Originally discovered in Taiwan [165], it has now been reported from the People's Republic of China, Mynmar, Malaysia, Korea, Indonesia, the Philippines, Vietnam and Thailand [152, 329]. In Korea, it has been found in 0.01% to 12% of pig livers. In Taiwan, 18% of people in mountain areas, where *T. solium and T. saginata* are considered absent, had *taeniid* eggs in their stools, presumably *Taenia saginata asiatica* [165]. The prevalence of taeniosis due to this tapeworm is not well characterized and only very limited surveys have been conducted owing to the difficulty of speciating taeniid eggs in feces.

3.4. Factors affecting transmission of taeniid cestodes

This section describes both the extrinsic and intrinsic factors that affect the transmission of taeniid eggs and larval (Cysticercus or metacestode) stages. The discussion on extrinsic factors (3.4.4) governing egg survival and dispersal emphasizes T. *saginata* because much more such research has been focused on this

species. However, the knowledge gained from that research is relevant and useful for the understanding of extrinsic factors affecting the epidemiology of both *T. solium* and Asian *Taenia.*

The discussion of the risk factors involved in transmission of the parasite between hosts is organized by taeniid species because of the unique features of their life cycles and host specificities.

3.4.1. Taenia solium

A good understanding of the epidemiology of T. *solium* transmission requires risk assessment for the acquisition of the adult worm infection and the dispersal of the tapeworm's eggs from feces to pigs and humans. Few such risk assessments have been carried out, however, but from those that have been carried out, critical points in the pig-man-pig cycle can be identified.

3.4.1.1. Transmission from pigs to humans

Consumption of uninspected pig meat is the major source of human T. *solium* taeniosis, and consequently, a major risk factor for human and pig cysticercosis [36, 136, 152, 434, 556, 631]. This makes the slaughtering and marketing systems in endemic areas critical to the risk assessment of modes of transmission of *T. solium* from pig to humans. However, because only a low percentage of pig carcasses in many developing countries are subject to veterinary inspection, it is difficult to make such assessments. In most endemic countries marketing systems vary greatly [556]. The larger producers sell their animals to slaughterhouses through intermediaries, while owners of small numbers of pigs, especially in rural areas, either kill them at home for their own consumption or sell directly to the local market or to intermediaries who may sell them clandestinely [15, 424, 434, 556]. Meat inspection is carried out in a strict manner only in the larger slaughterhouses, whereas meat is usually sold without any control in most of the small villages and hamlets.

A further complexity is government oversight of veterinary inspection, which is not always clear-cut. Meat inspection in Mexico, for example, is under the supervision of three different authorities, each having their own standards and regulations [15]: the Ministry of Health which controls about 100 slaughterhouses in large localities throughout the Republic; the Ministry of Agriculture which controls all those in which the meat is destined for export; and in villages and small towns, slaughterhouses are under the supervision of the municipality which engages a veterinarian to inspect the meat. However, lay personnel without any training can often be found stamping carcasses, frequently passing meat that is unfit for human consumption. Sick animals, or those affected by conditions that can be detected during ante-mortem inspection (such as cysticerci in the tongue), may not be offered for sale to a slaughterhouse known to carry out strict inspection but may be sold illegally to unscrupulous individuals and then offered for sale in markets or to small restaurants, thereby escaping control [15, 556]. This problem is illustrated in Table 3.10 which compares ante-mortem with post-mortem detection rates in a rural area of Mexico [15].

3.4.1.2. Transmission from humans to pigs

The transmission of T. *solium* eggs to pigs, the essential link in the pig-man-pig cycle, requires that pigs have access to human feces and that people consume improperly cooked infected intermediate host (pork) [415]. A recent risk assessment study in Tanzania revealed the very high risk associated with free-ranging pigs and the lack of household latrines [393]. Both the very high fecundity of the tapeworm and the various behavioral patterns of humans conspire to greatly facilitate egg transmission. The uterus of a mature proglottid carries up to 55,000 eggs (see Chapter 1). The mature proglottids or strobilar fragments, consisting of five-six proglottids in a chain, detach from the strobila and are usually expelled passively with the host's feces. Coprophagy is a normal activity of all free ranging and scavenging pigs. Indeed, in some parts of the world, pigs may be kept for the purpose of removing human feces and in others they may be fed feces deliberately as a cheap feed. Consequently, pigs may ingest whole proglottids along with a massive numbers of eggs [136, 225, 434, 435, 631].

Table 3.10. Frequency of cysticercosis determined by antemortem inspection compared to local slaughterhouse records in villages in the State of Mexico [15]

Village	Antemortem inspection		Slaughterhouse records
	Number of pigs inspected	% Cysticercosis	% Cysticercosis
Ixtlahuaca			1.09
Market	269	9.66	
2 farms	20	20.00	
Almoloya			1.38
7 farms	142	7.75	
Atlacomulco			0.32
3 farms	26	30.8	

With modern intensive pig husbandry practices, which involve controlled feeding of grain-based feeds, epidemic cysticercosis or 'feedlot' type infection, as seen in bovine cysticercosis (see Section 3.4.4.2), is unlikely to occur. The very high risk associated with coprophagy in the epidemiology of porcine cysticercosis is reflected in the fact that in regions where small holder pig farming predominates, restraint of pigs (to prevent free ranging and scavenging) can be very effective in interrupting the transmission of *T. solium* to pigs [575J.

3.4.1.3. Person to person transmission

Cysticercosis, whether pig or human, occurs following ingestion of eggs in human feces. The exact manner of ingestion is infrequently documented, but it is likely that person to person transmission can occur by: (i) the ingestion of eggs in contaminated food and water; or (ii) the introduction of eggs from feces into the mouth by contaminated hands [329, 424]. Outbreaks of cysticercosis among people who stringently avoid pork for religious or dietary reasons underscores the importance of person-to-person transmission [503]. Airborne infection by wind and through the ingestion of infected insects has also been suggested but this remains unproven (see Section 3.4.4). Other novel modes may sometimes occur; in some societies, for example the Bantu people, massive infection may be caused by using local medicine prepared from proglottids [601].

Auto-infection by reverse peristalsis of the intestine, once considered to be an important source of infection [601] particularly during treatment, is now largely discounted. External auto-infection, however, by eggs transmitted from anus to mouth through dirty hands or contaminated food seems to be a more probable way of contracting *T. solium* cysticercosis, than internal auto-infection [594].

3.4.2. Taenia saginata

There are three main patterns of transmission of *T. saginata* [418, 601]: (i) hyperendemic, characterized by pastoral farming in areas with a high prevalence of *T. saginata* taeniosis in man and cysticercosis in cattle; (ii) endemic, characterized, by the existence of a small number of human carriers, a wide dispersal of eggs in the environment and a moderate prevalence of bovine cysticercosis mostly of low intensity (iii) epidemic, characterized by feedlot situations in which a single human carrier, whose close contact with a herd of susceptible cattle can result in a massive outbreak of bovine cysticercosis.

3.4.2.1. Transmission from cattle to humans

The route of infection (taeniosis) of humans is via the consumption of cysticerci in improperly cooked beef. In pastoral societies raw or rare meat is part of the normal diet, however, *T. saginata* taeniosis in many developed countries is also associated with the increased consumption of raw and rare beef. The eating of raw or semi-raw beef dishes like beef tartar shaslik in Russia and Central Asian countries [1], basterma in the Near East [384], shishkebab and tikka in India [21], larb in Thailand [80], or pieces of meat simply roasted over an open fire in Central and East Africa [68] are common causes. Infection may also occur by tasting meat during mixing and cooking [329, 420]. Preference for raw or undercooked beef may run in families [418] or be associated with an occupation or profession (for example, the meat industry,

restaurant workers and food preparers). Marital status can be another risk factor (eg frequent dining out when single).

Taenia saginata has been reported in children less than one year of age as well as in adults over 80, although infection is most common in the 20-40 years age group. In an urbanized society, for example in Poland, of the 90% of carriers who admitted to eating raw meat, 44% ate it exclusively at home (mostly married women and children), 22% exclusively outside of the home (mostly single men and women), and 24% both at home and in public places (mostly married men) [417, 418]. The risk of being infected was five times greater in members of a carrier's family, 14 times greater in workers with professional contact with raw meat, and 40 times greater in raw beef eaters who had been infected previously compared with the risk of infection in the general population 1417].

3.4.2.2. Transmission from humans to cattle

Man, as the definitive host of the *T. saginata* tapeworm, is the disseminator of the eggs. The mean daily egg production exceeds 150,000 [199], but much higher egg outputs have been reported [328]. However, experimentally it has been shown that proglottid and egg output is highly variable. Humans are usually parasitized by a single T. *saginata* tapeworm and only in highly endemic areas do multiple infections exceed 40% of all tapeworm infections. Superinfection from one week to two months after ingestion of the first invasive cysticerci has been recorded [274].

Transmission to cattle can occur by the contamination of pasture, fodder or water with eggs [255, 433, 524]. The direct transmission of eggs can also occur when a human carrier with contaminated hands raises suckling calves[304, 571]. Oncospheres have been found in fingernail dirt, and water used to wash hands and underwear [416, 419, 469]. Infected farm workers and herdsmen represent major risk factors in the epidemiology of bovine cysticercosis.

In developed countries, the activities and movement of people in the form of camping and tourism provides an important opportunity for the spread of proglottids and feces to cattle raising areas [418, 432]. Uncontrolled defecation and inadequate destruction of viable *taeniid* eggs in sewage also play important roles in the spreading of T. *saginata* infection. Most conventional sewage treatment plants do not effectively remove taeniid eggs (3.4.4.2).

Hyperendemic pastoral cysticercosis

Hyperendemic pastoral cysticercosis is the common epidemiological scenario on the African continent. In one study, in the Narok district of Kenya, bovine cysticercosis was present in 53% of the cattle owned by Masai tribesmen and the overall prevalence of taeniosis among the adult Masai was 28% [198]. The Masai eat meat roasted in large pieces over an open fire, keep cattle near their huts during the day and sleep close to their stock at night. In this situation, the contamination of the manyatas (homestead enclosures) with eggs can be considerable.

Endemic urban/ rural cysticercosis

Several risk factors, particularly the movement of people and antiquated sewage treatment systems, are important in the effective spread of *T. saginata* eggs in developed as well as developing countries and in increasing the problem in some regions. Using 'trace-back' methods on almost 10,000 cattle in the Plish province of Poznan [414], it was found that there was a concentration of localities with bovine cysticercosis around urban areas (80%), recreation areas (72%), regions with developed agricultural industry (68%), as well as along rivers, main roads and railway tracks. However, in 80% of these localities with bovine cysticercosis, not a single human T. *saginata* carrier had been identified for five years [418]. It is likely that the transient visits to the area by carriers (tourists, migrant labor etc.) and poor management of sewage effluent were primary causes of such endemic foci.

Epidemic cysticercosis

Epidemic cysticercosis is usually associated with feedlots [51, 260, 261, 343, 360], and arises either from direct contamination of the feedlot with eggs or from the introduction of contaminated fodder. These types of outbreaks often result in a large number of cattle becoming infected. For example, an epizootic of cysticercosis in Texas in the USA involved approximately 6,000 feedlot cattle with infection rates among individual cattle pens varying from 0% to 4% [535, 601]. The source of infection in one feedlot was probably silage contaminated with T. *saginata* proglottids excreted by a laborer, while in another, which had a lower infection rate, a second infected worker, who was in charge of cleaning the water and feed troughs, probably infected the cattle during his work in the pens.

In Canada, an attendant with *T. saginata* taeniosis, working for less than four months in the feedlot, infected more than 500 cattle; bovine cysticercosis was diagnosed overall in 51% of the slaughtered cattle, with high larval infection densities [360]. It was found that the attendant had failed to observe required personal sanitary practices.

3.4.3. Extrinsic factors affecting taeniid egg survival and dispersal

It has been postulated that a high biotic potential (egg production) and efficient egg dispersal mechanisms are two of the most important factors contributing to stability in the host/taeniid system [228]. Together they can also cause a rapid restoration of transmission after interruption by environmental factors or by treatment procedures in control programs.

3.4.3.1. Egg output

The egg output of taeniid tapeworms was described previously in Chapter 1. The daily output may run into several hundred thousand eggs, depending on the species [328, 424, 430]. The important epidemiological feature for both species is the variety of ways in which the enormous numbers of eggs can disperse following expulsion in proglottids and feces, so that they become readily available to the intermediate hosts.

3.4.3.2. Egg dispersal agents

Infected individuals

As noted above (3.4.2.2), massive transfer of T. *saginata* eggs from humans to cattle in rural areas may occur *inter alia* by indiscriminate defecation associated with camping and tourism, especially where toilet facilities are inadequate [4]. Egg deposits may also occur along rivers, railway tracks and roads [4, 418]. As proglottids only travel a short distance, these egg deposit-sites only provide the primary deposition-site; other means (some of which are discussed below) are necessary to further disperse eggs to reach the intermediate host (other than by active coprophagia as in the case of porcine cysticercosis) [586].

Dispersal from sewage treatment facilities

Taeniid eggs voided into sewage systems can accumulate at central points such as sewage treatment plants, where their removal is very uncertain. Tapeworm eggs settle at the rate of about 0.1-0.2 m per hour [392]. Due to turbulence involving overloading and interference with natural purification processes (such as high chemical concentrations), most sewage systems permit eggs to pass relatively freely through the effluent [41, 251, 311, 368, 381, 391, 392, 525]; for example, taeniid eggs can survive anaerobic or aerobic digestion for several months [170, 392]. Dispersal in sewage effluent can be extensive. Eggs have been found 32 km below the sewage outlet into the Moscow River [574] and 250 meters out into the Caspian Sea at Baku [20].

There are several ways in which the eggs of *T. saginata* can become available to cattle through sewage. In systems which use primary settling tanks, grit tanks, sedimentation tanks or aeration tanks, eggs in the effluent will pass through these systems into rivers or farms using sewage. Flooding of the rivers will ensure that the eggs are dispersed onto livestock pastures. If the outlet falls directly into the sea from a raw

sewage collection plant, segments will be present and the eggs can then be disseminated onto pastures by birds (see below). Epizootics attributed to faulty sewage systems have been described in the USA, in Germany and in the United Kingdom [123, 373, 473, 523, 524].

By deliberate irrigation of pastures and crops with sewage plant effluent

A second method of dispersal is through the deliberate use of raw sewage or sewage effluent to fertilize cattle pastures or pastures which are used for growing cattle fodder [251, 344, 379, 381, 386, 424, 525, 535]. A similar egg dispersal will result from the emptying of septic tanks and toilet pails on to pastures [525]. Using 'tracer' calves, it has been found that eggs dispersed on pasture by deliberate irrigation with effluent, remained available and infective for at least 4.5 months [63] and in silage for up to 4 months or longer at 32°C. However, eggs lose their infectivity when pressed and dried in pellets because the temperature exceeds 50°-60°C during the pelleting process [63]. Prolonged settling is necessary before effluent can be used for irrigation of cattle pastures [32, 418, 419]; this is discussed in detail in Chapter 5.

Sewage sludge has also been linked to cysticercosis 'storms' on pasture in Denmark [386].

Dispersal of eggs from the site of fecal deposition

There is, potentially, a number of ways for eggs to disperse from fecal deposits. Newly shed proglottids are capable of moving several meters from the fecal mass [162, 329, 469]. However, more frequently the eggs are expelled from the proglottids into the feces before the latter are voided, and because the distances traveled by proglottids certainly do not approach those reported for eggs, there must be other agents for egg dispersal [563]. Numerous candidates have been suggested, including the wind, birds, insects (particularly flies and beetles), oribatid mites, and annelids [318]. Although the wind has widely been assumed to be responsible for a significant dispersal of taeniid eggs, there is little experimental evidence supporting this assumption.

Role of Birds

Seagulls, starlings, rooks, sparrows, and other scavenging birds have been implicated in the transfer of eggs of T. *saginata* from sewage works to pasture [94, 95, 254, 525], but there is little information on the behavior of birds other than seagulls with respect to interaction with feces. If birds are in regular contact with fecal material they could represent an important mechanism for egg dispersal, particularly in long distance dispersion. This aspect requires further study.

Role of arthropods

Many arthropods have been implicated in egg dispersal, including flies, beetles, mosquito larvae, moths, ants, fleas, cockroaches, oribatid and gamasid mites [54, 232, 317, 318, 342]. Of these, blowflies and dung beetles seem to be the most likely candidates for this role due to their close ecological association with fecal material. The total number and proportion of each species are influenced to a great extent by the weather and the freshness of the feces. Many workers have observed helminth eggs, including those of T. *saginata,* attached to the outer surface of flies both in the laboratory and in field studies [37, 256, 383]. There have also been many reports of flies carrying eggs internally in both experimental and field studies [256, 484, 552].

It is likely that other insects in contact with fecal material may also play subsidiary roles. Many beetles feed on proglottids and pick up eggs externally including those of T. *saginata,* but more commonly they ingest them with the fecal material [53]. The few studies on the dispersal behaviour of beetles indicate that they do not travel great distances. Nevertheless, it is possible that they may contribute to the short-range dispersal of taeniid eggs. If arthropods are important egg-carriers, and account for short and middle distance dispersal, the spread may well be seasonal in temperate zones.

Role of earthworms

Earthworms have been shown to contain taeniid eggs in areas endemic for *T. saginata* [29, 335]. Thus, they may play a role in egg dispersal, particularly as earthworms are a common food for some birds.

Rapid dispersal in feedlot facilities

Epidemic outbreaks, characteristic of large feedlot situations, have special features regarding egg dispersal. These include the natural spread of eggs from deposited segments, promiscuous defecation, faulty sanitation systems, and the contamination of fodder and drinking water [261, 381, 535]. This can result in the contamination of feedstuffs intended for thousands of cattle.

Dispersal of T. solium *eggs*

As discussed above, the studies on dispersal mechanisms for eggs of T. *solium* are few in comparison to those for other taeniid species, although presumably the eggs are subject to similar mechanisms (sewage, birds, insects, etc.). Field experiments have shown that taeniid eggs can be dispersed rapidly within 100 meters around a fecal deposition site or a sewage effluent or sludge deposition site for irrigation or fertilization of vegetables or pastures [228]. This may pose a significant risk for pigs in certain rearing systems, as well as for people consuming such vegetables or water.

3.4.3.3. Factors affecting egg viability and survival

Duration of egg survival in the environment

The survival of taeniid eggs is very dependent upon temperature and moisture (Table 3.11). Under laboratory conditions, the viability of isolated eggs of *T. saginata* is much higher than those inside a proglottid; the shorter life of oncospheres contained in proglottids is probably due to putrefaction processes [551]. With regard to humidity, the eggs of T. *saginata* do not survive *in vitro* in the absence of surface moisture [523]. With the relative air humidity varying from 44 to 96%, eggs contained in proglottids remain viable for a period from 12-13 hours to one to two days at a temperature of +19°C to +37°C, 35 to 37 days at -4°C and from 24 to 26 days at -30°C. In a damp temperate climate, the eggs of T. *saginata* can survive in the environment for about ten months and remain viable for 130 days in water [519].

Table 3.11. Summary of observed survival times of *Taenia saginata* eggs stored under various conditions in the laboratory and in the field

Environment	Viability or infectivity assay used	Storage conditions	Maximum reported survival (days)	References
Laboratory	*in vivo* infectivity	2°C-5°C	95	[430]
Laboratory	*in vivo*	In silage, 10°C	60-80	[147]
Field	*in vivo*	On pasture	101	[430]
Field	*in vivo*	On pasture, Kenya	413	[140]
Field	*in vivo*	On pasture, winter	159	[162]
		Summer	58	
Field	*in vivo*	In stored hay	21	[338]
Field	*in vivo*	On pasture, Denmark	164-194	[386]

However, in summer, the eggs are destroyed on the soil surface within two days; under the protection of plant cover they can survive for up to 40 days. In a warm climate, eggs (in proglottids) can survive on the soil surface in winter and spring for as long as five months, four months in summer and up to eight to nine months in summer and autumn [486].

In the microclimate of a cattle barn, the longevity of eggs has been estimated to be about 18 months [519]. Eggs in hay or grass silage lose their infectivity in about 70-90 days [147] or at about 168 days at 4° to 5°C. Eggs have survived at least 16 days at 18°C in liquid manure, for 71 days in an underground cistern and up to 150 days on grass [290]. They may survive for six months on pasture in Denmark [283] and a year in the highland of Kenya [147] (Table 3.11). Clearly, low to moderate temperatures with adequate humidity are important for long-term survival [140].

Heterogeneity of infectivity within egg populations

Studies have shown that *in vitro* embryo activity varies from as low as 5% to 80% or higher in eggs from different 'ripe' proglottids of the same or different *T. saginata* [522, 523]. These include immature, infective and senescent organisms, with ratios varying from proglottid to proglottid. Based on these *in vitro* studies, it has been suggested that in the natural environment some immature embryos can continue their development and become infective. This heterogeneity may be one of the variables determining the infective pattern in intermediate hosts, as well as accounting for the 'sterile' immunity which appears to occur in some animals in endemic regions [227].

3.4.4. Intrinsic factors affecting transmission

In the preceding sections, research on the extrinsic factors that determine the infection pressure were reviewed. It was found that a high biotic potential, effective egg dispersal mechanisms, and the ability of the eggs to survive under a wide range of climate conditions lead to a high infection pressure. If these were the only regulatory mechanisms, infections with larval cestodes (metacestodes) would be cumulative and could lead to overloading in highly endemic zones, possibly entailing the death of the host population and cessation of transmission. However, the survival of the parasite population is also dependent upon the intrinsic regulatory mechanisms of the intermediate host population [228].

3.4.4.1. Immunological mechanisms

Host immunity

Some of the earliest experiments demonstrating the importance of acquired immunity to helminth parasites were carried out with T. *saginata* in cattle [194, 197, 201, 571, 577]. It was found that in highly endemic zones, calves became naturally infected almost from birth and gradually acquired resistance. This also demonstrated the difficulty of experimental research in areas with a high infection pressure. However, it is now generally agreed that acquired immunity plays an important role in determining transmission patterns.

Although there has been a considerable amount of work carried out on *Taenia saginata* attempting to characterize the host's immune response and its role in the epidemiology of this zoonosis, less has been done for *T. solium* (and even less for Asian *Taenia).* Therefore, most of the discussion below on the importance of the immune response as an intrinsic factor regulating transmission involves T. *saginata.* It is clear from the broader work on taeniid immunity with a variety of taeniid species, that the larval stages (oncosphere, metacestode) of this group of cestodes are quite immunogenic and usually induce strong protective immunity in their hosts (see Chapter 1 and [87, 159, 327, 580]). Thus characteristically pronounced responses, particularly the production of antibodies, have enabled the development of excellent serodiagnostic tools that are increasingly being employed in epidemiological studies [2] (see also Chapter 4). It can be assumed, therefore, that the pig's immune response to *T. solium* and Asian *Taenia* plays a role in transmission similar to that in cattle infected with *T. saginata.*

Prenatal infections

To date, there is no unequivocal evidence that prenatal infection occurs in either T. *saginata, T. s. asiatica,* or T. *solium* infections in cattle or pigs. The role, if any, played by prenatal infections in specific acquired immunity and the epidemiology of transmission remains to be determined.

Neonatal infections and survival of T. saginata *larvae in their host*

In highly endemic zones, animals may become infected with metacestodes early in neonatal life [194, 195, 196, 571], and such neonatal infections may be associated with the prolonged survival of metacestodes in the host, perhaps for the life of the bovine in the case of T. *saginata* [543]. The extended survival of neonatally acquired metacestodes may be associated with an inability of the neonate to respond immunologically to the infection [543]. Indeed, calves may not be fully competent to recognize all the functional antigens of the appropriate bovine metacestodes until several weeks of age [466]. In addition, while neonatal infections do not interfere with the development of protective immunity to reinfection at a later age, the immune response induced by such reinfection may not affect parasites established during the early neonatal period [467].

Maternal transfer of immunity

A variable degree of immunity to taeniid cestodes such as T. *saginata, T. hydatigena,* and T. *ovis* is transferred maternally via the colostrum [196, 329, 331, 467]. Most of the studies demonstrating this included active immunization of the mother. There have been several failures to transfer immunity to *T. saginata* where the mothers were naturally immune but not experimentally immunized [196]. There may be host and parasite variability in this respect, but from an epidemiological point of view, colostrum-transferred immunity appears to wane in the absence of consistent egg exposure. The role of colostrum in the regulation of larval tapeworm infections in hyperendemic regions is not fully understood.

Influence of age on acquisition of immune status

One of the important factors that determines the infective pattern is the time interval that immunologically competent animals remain susceptible to superinfection after the ingestion of the first eggs. It has been found that in cattle strong immunity was acquired to *T. saginata* within two weeks after the ingestion of eggs [202, 342, 608]. The practical reality of this in endemic zones is that there is only a very short period in their lifetime (about two weeks) during which animals can acquire cysticercosis. This important information has not yet been confirmed for porcine cysticercosis. The number of eggs required to induce resistance to reinfection or superinfection to cysticercosis in cattle and pigs also has not been precisely determined.

The survival of T. solium *larvae in immunologically competent animals*

The survival of T. *saginata* cysticerci in cattle has been variously described as from a few months to several years [127, 201, 202, 306, 361, 424, 429, 571, 577]. The persistence of *T. solium* in pigs as a factor in the epidemiology of porcine cysticercosis is problematical, however, since most pigs are slaughtered in the six to 12 month period after birth. Older animals such as sows and boars could, if larvae survive for long periods in the host, represent important risks for humans. Unfortunately, there have been very few studies directed at this question. From some studies it is apparent that the Cysticercus can survive for long periods, somehow avoiding the hosts immune response, and several 'immunological sequestration or avoidance' mechanisms have been suggested [87, 159]. It should be noted, however, that there is some evidence that the established Cysticercus is not completely protected from an immunological attack, and that repeated large antigenic challenges (reinfection) can induce an inflammatory attack against the established Cysticercus [87, 159, 541, 542].

Role of immunity in cattle under field conditions

In pastoral bovine cysticercosis, where human defecation habits and the irrigation of pastures with sewage may lead to massive, one-time exposure to egg contamination of a prescribed area, it may be expected that almost all animals within that area will become infected and acquire immunity to superinfection as early as two weeks after initial infection. This immunity will last for at least six to 12 months until the eggs in the environment have lost their infectivity or have become unavailable to the animals. The introduction of immunologically naive animals onto risky pastures is, therefore, contraindicated for up to 12 months from the time of the deposition of the eggs.

Immunity acquired against the adult intestinal stage in humans

While there is evidence in experimental animal models that the definitive host may reject a tapeworm or cause it to destrobilate and that antibody may be present, virtually nothing is known of the importance of acquired immunity in regulating adult T. *saginata* and *T. solium* intestinal populations, as evidenced by the superinfections that occur in *T. saginata* infections [87, 328].

3.4.5. The role of livestock management in transmission

The term 'infection pressure' describes the proportion of animals in a population that become infected during a given time. Infection pressure results from egg output, egg dispersal and egg survival, and these form the total of the extrinsic factors already described in this Chapter. Feeding behaviour and livestock management practices are major influences on infection pressure [323, 586]. For example, the pig is a natural scavenger of feces and there are many reported cases in which pigs are actively encouraged to act as 'sanitary policemen' [15, 393, 586]. This may lead to massive infections during the time interval between the ingestion of the first eggs and the onset of immunity. Similarly, irrigation of pastures with poor quality sewage effluent often leads to cysticercosis 'blooms' because of heavy egg contamination.

These important risk factors and others are summarized below (Section 3.5) to highlight those livestock husbandry practices that should be emphasized in education efforts, especially in developing profitable, sustainable and safe livestock production systems [323].

3.5. Summary of risk factors for taeniosis and cysticercosis

3.5.1. Taenia solium

Transmission from humans to pigs

The major risk factors related to transmission of eggs from humans to pigs can be summarized as follows:

- extensive or free-range pig rearing in households lacking latrines and outdoor human defecation near or in pig rearing areas
- allowing pigs to scavenge and eat human feces ('sanitary policemen')
- deliberate use of human feces as pig feed
- connecting pig pens to human latrines ('pig sty privies')
- use of sewage effluent, sludge or 'night soil' to irrigate and/or fertilize pig pastures and food crops
- human carriers involved in pig rearing and care.

In a risk assessment study in Cameroon [631] it was demonstrated that confined pigs not fed human feces have a significantly lower prevalence rate than roaming pigs allowed such access. In this same study, other risk factors identified were lack of household latrines, low level of personal sanitation and pig age. Similar findings have been reported in Peru [236] and Mexico [575]. The incentive to feed feces to housed pigs, however, is strong in resource poor communities because it is a relatively nutrition-rich, cheap feed [506], in spite of the fact that it represents a major risk factor in porcine cysticercosis. Recently, new strategies have been proposed to substitute locally-produced safe feeds which are cheap, along with inexpensive pig housing designs, both of which could help to lower the risk of infection [323].

Transmission from pigs to humans

The risk factors important to the transmission of cysticerci to humans are:

- lack of comprehensive and satisfactory meat-inspection at pig slaughter
- clandestine marketing of pigs to avoid inspection
- cultural preferences for eating raw or improperly cooked pork.

These aspects have been discussed in Section 3.4.1.1. Studies that have shown that the problems of illegal slaughter and marketing are widespread and their solution will require substantial efforts in veterinary control [136, 225, 346, 424, 434]. The habit of eating raw or improperly cooked pork is also a very strong cultural trait, but, hopefully, this can change through education [78, 152, 346].

Human-to-human transmission

The most important risk factors involved in human-to-human transmission are:

- low economic status, low level of household sanitation and low personal hygiene standards
- history of passing proglottids by a member of a household or a member of the community in frequent contact with such a household. Household or community foodhandlers and childcare givers present very high risk factors
- preparation of both raw and cooked meat on the same chopping block. The contamination of household utensils, such as chopping blocks is often overlooked, but needs to be a part of any education program [423, 505, 506]
- frequent pork consumption.
- use of 'night soil' in vegetable production
- large population of flies on the premises.

3.5.2.Taenia saginata

The major risk factors in *T. saginata* taeniosis/cysticercosis are similar to those for *T. solium* infections.

Transmission from humans to cattle:

- outdoor defecation in or near cattle rearing facilities or pastures
- lack of effective fly and bird control around cattle facilities
- use of sewage effluent, sludge or untreated human feces to irrigate or fertilize feed crops and pastures
- human carriers involved in the rearing and care of cattle
- indiscriminate deposition of feces on campgrounds, along highways, and along rail tracks.
- *Transmission from cattle to humans:*
- the major factor is the consumption of raw or inadequately cooked beef
- lack of satisfactory meat inspection (veterinary control).

3.5.3. Taenia saginata asiatica

The epidemiology of this recently recognized zoonotic tapeworm is not well characterized, but information at hand indicates that it shares features similar to both *T. saginata* and *T. solium.* The risk factors associated with transmission of eggs from humans to pigs is similar to that discussed above for *T. solium:* close association with humans, exposure of pigs to human feces, coprophagy, etc. [152, 329].

Infection of humans from pigs appears to be dependent on the eating of undercooked pig viscera, particularly liver; however, unlike the situation with *T. solium,* transmission of cysts via undercooked muscle (pork) does not appear to be important [152]. Although pigs are the major source of infection, *T. s. asiatica* has been established experimentally (as metacestode or Cysticercus) in monkeys, wild boars, cattle and goats, although with difficulty [152]. There is no evidence that this *Taenia* species causes cysticercosis in humans.

CHAPTER 4:
DETECTION AND DIAGNOSIS

P. Dorny, J. Brandt & S. Geerts

4. Introduction

In this Chapter, the diagnosis of taeniosis and cysticercosis in humans, and cysticercosis in pigs and cattle is reviewed. *Taenia solium, Taenia saginata* and Asian *Taenia saginata asiatica* are adressed. Classical coprological, morphological and meat inspection diagnostic methods, as well as immunodiagnostic and molecular methods, are critically reviewed.

4.1. Diagnosis of taeniosis

Several techniques are available for the diagnosis of taeniosis (adult worm intestinal infection): questioning, feces microscopy, the peri-anal adhesive tape test, the ELISA for Coproantigen or circulating antibodies, the differentiation of somata based on morphology or isoenzyme patterns and molecular tests such as the polymerase chain reaction (PCR). All have advantages and disadvantages, which are discussed in detail in this Chapter.

4.1.1. Diagnosis based on morphological criteria

The eggs of T. *solium, T. saginata* and *T. s. asiatica* cannot be distinguished morphologically. Up to now the only reliable technique to distinguish them is by PCR (see Annex 4.5). Although it is theoretically possible to distinguish the three adult taeniids on the basis of morphological characteristics of the scolex or the mature proglottids (see Table 4.1), the former is rarely available after treatment with modern anthelmintics, whereas the latter need to be fixed and stained in order to examine the ovarian lobes and the vaginal sphincter, a laborious procedure. The staining procedure is described *inter alia* by Morgan and Hawkins [378]. In order to improve the recovery of the scolex and the quality of the expelled proglottids, a purge with electrolyte-polyethyleneglycol salt (EPS), (a product which is commonly used to prepare patients undergoing colonoscopy), two hours before and two hours after niclosamide treatment can be applied [291]. However, even using this EPS regimen, the scolex is recovered in only about one third of patients. Since morphological abnormalities are not uncommon in taeniids, the presence or absence of hooks on the scolex does not automatically indicate that it is *T. solium or T. saginata/T. s. asiatica* [480].

In most cases, gravid proglottids of *T. saginata* and *T. solium* can be distinguished on the basis of the number of unilateral uterine branches (Table 4.1). However, some overlapping might occur [582]. Therefore, if the number of uterine branches falls between 11 and 16, it is advised to confirm the identity of the tapeworm using molecular tools or enzyme electrophoresis. Proglottids of *T. saginata* and *T. s. asiatica* can only be distinguished using molecular tools (see Annex 4.5). Counting of the uterine branches can be done by squashing a gravid proglottid (after putting it on filter paper to remove excessive fluid) between two glass slides or between the underside and the cover of a Petri dish. In order to facilitate the counting, dyes such as carmine or Chinese ink can be injected using a fine needle. Longitudinal histological sections stained with haematoxylin-eosin allow a more accurate counting of the branches [358].

4.1.2. Differentiation based on enzyme electrophoresis

Le Riche and Sewell [319, 320] described a simple technique to differentiate taeniid somata, based on glucose phosphate isomerase (E.C.5.3.1.9.) zymogrammes. The technique is faster and less labour intensive than staining tapeworm material. It can be applied on a routine basis when direct morphological

observations remain indecisive; however, it requires preferably fresh or frozen material. Typical preservative solutions for segments such as alcohol or formalin will destroy enzyme activity.

Table 4.1. Morphological differences between *Taenia solium, Taenia saginata* and *Taenia saginata asiatica* (adapted from [167, 339, 424])

	T. solium	*T. saginata*	*T. s. asiatica*
Scolex			
– rostellum	Present	Absent	Present
– hooks	22-32	Absent	Absent
Mature proglottids			
– number of testes	375-575	800-1200	324-1216
– ovary	3 lobes	2 lobes	2 lobes
– vaginal sphincter	Absent	Present	Present
Gravid proglottids			
– number of unilateral uterine branches	7-16	14-32	11-32
– branching pattern	Dendritic	Dichotomous	Dichotomous
– expulsion from host	Passively* (in groups)	Actively** (single)	Actively** (single)

*: *usually with feces*
**: *outside defecation*

4.1.3. Differentiation based on molecular techniques

In order to overcome limitations in the identification of *Taenia* species based on morphology or enzyme electrophoresis, various molecular approaches have been developed, including the use of DNA probes [118, 264, 471, 472], PCR, or PCR coupled to restriction fragment length polymorphism (RLFP) [245, 247, 284, 357, 479] and multiplex-PCR [620]. The use of DNA probes is time consuming and relatively insensitive; however, PCR with oligonucleotide primers derived from such species-specific probes provides a rapid and sensitive method [245]. PCR-RFLP and multiplex-PCR permit differential diagnosis of T. *saginata, T. s. asiatica* and *T. solium,* even when examination by morphology cannot be performed, because these methods do not rely on the availability of intact gravid proglottids. Molecular techniques can be applied on fresh, frozen or ethanol-preserved parasitic material. More details about these diagnostic techniques can be found in Annex 4.5.

4.1.4. Questioning of tapeworm carriers

Spontaneous expulsion of proglottids (independent of defecation) generally occurs with *T. saginata* and *T. s. asiatica,* and exceptionally this has been observed for T. *solium* [480]. Therefore, T. *saginata/T. s. asiatica* carriers are often aware of the presence of a worm, which is not necessarily the case for *T. solium* carriers, where the expulsion of proglottids is passive (together with feces). Furthermore, it has been observed that patients cannot always distinguish tapeworm proglottids from nematodes like *Enterobius vermicularis* leaving the body or the spontaneous expulsion of the large roundworm *Ascaris lumbricoides,* resulting in false positive answers. Therefore, questioning can be used as an auxiliary method for the diagnosis of T. *saginata /T. s. asiatica,* but is certainly not reliable in the case of *T. solium.*

4.1.5. Coprological examinations

4.1.5.1. Conventional fecal examinations

Coprology for taeniosis should include both macroscopic and microscopic examinations. In the case of T. *saginata* loose gravid proglottids may be found in the underwear or in bed. Both T. *solium* and T. *saginata/T. s. asiatica* proglottids can be found in the feces, but expulsion does not necessarily occur daily. Therefore, repeated macroscopic examinations are advised. Similarly the efficacy of microscopic examinations for the presence of *Taenia* spp. eggs increases when repeated [259]. Various concentration techniques (e.g. sedimentation and formalin-ether concentration methods) can be used, but it is generally

agreed that they lack sensitivity [417]. Anthelmintic treatment has been shown to detect many more tapeworm carriers than either coprological techniques or questioning [13, 108, 259]. Cleansing the intestine with a purge immediately before and again after treatment improves the recovery of parasite material, including the scolex, which facilitates species identification [211].

4.1.5.2. Peri-anal swabs

Taenia spp. eggs sticking to the skin in the peri-anal region can be detected by using adhesive tape ('Scotch' tape), also known as the method of Graham. For the detection of T. *saginata* eggs the peri-anal swab is considered to be more sensitive than a single coprological examination [417]. Although less data are available for T. *solium,* the eggs of this parasite are also frequently found using the 'Scotch' tape technique [108,504].

4.1.5.3. Coproantigen detection

Taenia coproantigens are parasite specific products in the feces of the host that can be detected by a polyclonal antibody-based sandwich ELISA (see also Chapter 6 on Control). These antibodies are obtained from hyperimmune rabbit sera raised against T. *solium* adult worm somatic antigens [7]. The use of this test increases the detection of parasitologically proven intestinal *T. solium* cases by a factor of at least 2.6 times in comparison to microscopy [10]. Coproantigens are stable for weeks in unfixed fecal samples kept at room temperature and for years in frozen samples or in chemically-fixed samples (e.g. formalin) kept at room temperature. Coproantigens can be detected prior to patency and they are no longer detectable within a week of treatment. A major disadvantage of this test is that it is only genus specific, making it impossible to differentiate *T. solium* and *T. saginata* infections. However, the test shows no cross-reactions with other intestinal helminth infections including *Ascaris, Trichuris* and *Hymenolepis* spp. [13]. Coproantigen testing for *Taenia* has also been carried out using a dipstick ELISA format [10]. This field test proved faster, but less sensitive, than the micro-plate assay.

4.1.5.4. Copro-PCR

Methods have been developed to extract DNA of *Taenia* spp. from human feces, which can be used in a PCR for diagnosis of taeniosis [397, 617]. The high sensitivity and species-specific detection of the immature stages are definite advantages of this test. However, current DNA extraction methods are too expensive for use as a routine test.

4.1.6. Serological tests

The possibility of diagnosing T. *solium* taeniosis by the detection of species-specific circulating antibodies has been demonstrated [609]. This test uses excretory-secretory antigens derived from *T. solium* tapeworms in an EITB. Molecules ranging from 32.7 to 42.1 kDa are highly specific for *T. solium* taeniosis infections. No cross-reactions have been demonstrated in this test with sera obtained from individuals with other intestinal infections, including *T. saginata, Echinococcus* spp. and *H. nana,* and in patients infected with the metacestode stage of T. *solium.* The major advantages of this test are that it allows species specific diagnosis and avoids the handling of feces contaminated with *T solium* eggs [14]. A drawback may be that antibodies persist after removal of the intestinal tapeworm.

4.2. Diagnosis of *Taenia solium* cysticercosis in humans

4.2.1. Parasitological diagnosis

The diagnosis of *T. solium* cysticercosis (extraintestinal metacestode stage) is made parasitologically by demonstrating the scolex with the hooks or fragments of the bladder wall in biopsy or autopsy material. In some parts of Asia, especially, where subcutaneous cysticercosis is rather frequent [459], it is easy to obtain biopsy material for further histopathological confirmation. With less invasive techniques such as fine needle cytology, the diagnosis of cysticercosis can often be made [31, 298].

4.2.2. Imaging

Various imaging techniques, such as radiography, CT-scanning, magnetic resonance imaging, etc., are available for the diagnosis of human cysticercosis and are described in Chapter 2.

4.2.3. Serological diagnosis

Immunological methods for the diagnosis of human cysticercosis can be used for the detection of individual cases or for epidemiological surveys. In the former, sensitivity is more important than specificity, since the diagnosis is usually made on an individual who has symptomatology suggestive for cysticercosis. For epidemiological purposes, the specificity of the test is an important factor.

Immunodiagnostic techniques include detection methods for specific antibodies and for circulating parasite antigen in serum or CSF.

4.2.3.1. Antibody detection methods

Infection with T. *solium* results in a specific antibody response, mainly of the IgG class [69]. Different techniques have been described to detect antibodies to *T. solium,* such as the complement fixation test, haemagglutination, radioimmunoassay, ELISA, dipstick-ELISA, latex agglutination and immunoblot techniques [134]. Antigens used in these tests are either cyst fluid or crude homogenates of *T. solium* cysticerci or crude preparations of the related parasite *T. crassiceps,* which can be maintained in laboratory rodents [410]. These unpurified antigens have moderate sensitivities and relatively poor specificities [171, 172,504].

Research on the antigenic properties of cyst fluid and surface-associated glycoproteins, and improved protein purification techniques have resulted in much more reliable serological tools [248, 286, 410, 567]. The most specific test developed is the EITB, an immunoblot of seven Cysticercus glycoproteins, purified by lentil lectin-purified chromatography, which gives close to 100% specificity and a sensitivity varying from around 70% to 90% [567]. However, a sensitivity of only 28% has been found in cases with single, enhancing parenchymal cysts in the brain [616]. In developing countries, ELISA is preferred because of its better availability, its simplicity and its lower cost compared to immunoblot [483]. Purification of glycoproteins from cyst fluid by single step preparative isoelectric focusing was shown to produce very specific antigens, which are applicable both in immunoblot and ELISA [286]. The specificity and sensitivity of this ELISA were reported to match those of the immunoblot [288].

Since the preparation of purified antigens relies on the availability of parasite material and may be subject to the quality of this material, attempts were made to produce recombinant antigens and synthetic peptides. Different authors synthesised 10, 7-10 and 14 kDa recombinant polypeptides that can be used in immunoblot and ELISA [81, 487]. While the specificity of these antigens is reported to be high, the sensitivity is generally lower than with the native antigens. The use of synthetic peptides in ELISA is another promising option [171].

4.2.3.2. Antigen detection methods

Several assays have been developed to detect parasite antigens, but only the monoclonal antibody-based ELISA directed at defined parasite antigens may ensure reproducibility and specificity [62, 134, 265]. Antigen detection may be done on serum as well as on CSF [79, 214, 217]. Because of the localisation of the cysts in the brain, antigen detection in CSF may be more appropriate for diagnosis than in serum; however, sampling of CSF is more cumbersome than blood sampling.

Ag-ELISA's detect only cases of active cysticercosis, i.e. the presence of living cysticerci [154, 205, 211, 395]. The sensitivity of the Ag-ELISA is very high, even in light infections. In one study, in patients with a single viable cyst or only enhancing lesions, the sensitivity was only 65% [217]. The Ag-ELISA is very specific, and no cross-reactions have been observed in sera from patients with confirmed infections with *Schistosoma,* hydatid cysts, *Ascaris, Trichuris,* filaria, *Entamoeba, Plasmodium* and *Trypanosoma* [154].

4.2.3.3. Immunodiagnosis in epidemiological studies

In humans, no clinical features are specific for cysticercosis, even asymptomatic brain lesions are not uncommon, and imaging methods are not appropriate for epidemiological studies. Therefore, definition of cases is often based solely on immunodiagnostic methods [178]. In surveys on cysticercosis, immunodiagnosis is useful in estimating the prevalence and identifying the risk factors associated with transmission of *T. solium;* a high seroprevalence in a community indicates a 'hot spot' where preventive and control measures should be applied [220, 548]. Immunodiagnostic tools also offer the possibility of surveillance of the infection during and after control programs [217, 495, 575].

Antibody detection tends to overestimate the prevalence of cysticercosis because a transient antibody reaction may occur following exposure to *T. solium* eggs, without establishment of cysticerci, or with self-cure [213]. Antigen detection assays in epidemiological studies, however, measure active cysticercosis, not merely exposure [134].

4.2.3.4. Immunodiagnosis of neurocysticercosis

Serological tests may also be used for the diagnosis of neurocysticercosis. They can be applied both on serum and on CSF [89, 401, 630].

Serological tests can be very useful for confirmation of imaging techniques, for differential diagnosis of other 'cyst forming conditions', including echinococcosis, brain tumours and tuberculosis [76, 122]. The general opinion is that consistent diagnostic criteria of neurocysticercosis should be based on combined neuro-imaging studies, serological tests, clinical presentation and exposure history.

Antibody detection is particularly useful for the identification of neurocysticercosis as the etiological agent of epilepsy since dead cysts are more often responsible for epileptic seizures than living cysts [394]. Ag-ELISA only detects active cysticercosis, which may be an advantage when a decision has to be taken on whether or not anti-parasitic treatment should be started, according to the consensus guidelines proposed by Garcia *et al.* [205]. Patients with only calcified cysts, who don't need anthelmintic treatment, are consistently negative in the Ag-ELISA [205].

Antigen detection has also proven to be an efficient tool for the follow-up of neurocysticercosis patients after treatment since circulating antigen disappears within one to three months from the serum of cured patients, which is not the case if the patients are not cured [205, 394].

4.2.3.5. Limitations of immunodiagnosis

Immunodiagnosis contributes to a better understanding of the prevalence and the epidemiology of the infection, and to the diagnosis of neurocysticercosis and the follow-up of treatment. However, because of the polymorphic clinical manifestations of neurocysticercosis, immunodiagnosis cannot replace neuro-imaging for the clinical management of neurocysticercosis. Anthelmintic treatment of epileptic patients that have a positive antibody or antigen serology, without a CT-scan or MRI examination, is considered to be very hazardous.

Finally, efforts should be made to make cheap, reliable and standardised immunodiagnostic tools more widely available.

4.3. Diagnosis of porcine cysticercosis

4.3.1. Porcine cysticercosis due to *Taenia solium*

4.3.1.1. Tongue inspection

In many endemic countries tongue inspection is carried out by the local population in order to identify pigs infected with *T. solium* cysticercosis. If carried out correctly (both palpation and visual inspection

throughout the base) by experienced people, it is generally agreed that the specificity of this technique is 100% [135, 238]. The sensitivity of the technique, however, depends very much on the degree of infection of the animals. Although in heavily infected animals tongue inspection might detect up to 70% of the cysticercotic pigs, in lightly infected animals the sensitivity is much lower. Several studies have shown that in experimentally or naturally infected pigs harbouring less than 100 cysts, none of the animals could be detected by tongue inspection [135, 395]. In moderately to heavily infected animals (>100 cysts) the sensitivity is lower than 50% [434, 438]. In Zambia, using Bayesian analysis the overall sensitivity of tongue inspection was estimated at 21% (CI: 14-26%) [135].

4.3.1.2. Meat inspection

The procedures for the detection of T. *solium* cysticercosis during conventional meat inspection vary widely from one country to another (see also Chapter 5). In some countries, visual inspection only is carried out on one or several so-called predilection sites, such as the heart, diaphragm, masseter muscles, tongue, neck, shoulder and intercostal and abdominal muscles. In other countries, regulations also require incisions in some of these muscles. It is obvious that the efficacy of meat inspection will depend not only on the thoroughness of the inspection methods, but also on the degree of infection of the pigs. Given the fact that, in rural areas of Africa and South America, lightly infected animals have been shown to occur more frequently than previously believed [135, 511, 512], meat inspection in these areas will seriously underestimate the real prevalence of porcine cysticercosis. Using a Bayesian approach, the overall sensitivity of meat inspection in Zambia (only visual examination of masseter muscles, triceps brachii, tongue and heart) was estimated at 22.1% (CI: 15-27%) [135].

4.3.1.3. Serological techniques

Immunodiagnosis in pigs is used in prevalence surveys, community-based surveys and in intervention studies. In endemic areas, pigs can also be used as sentinels to measure the environmental contamination of T. *solium* eggs.

Most of the techniques developed for the diagnosis of cysticercosis in humans have been adapted for analysing pig sera, including the EITB [569], Ab-ELISA using isoelectric focusing-purified glycoproteins [286, 499], and Ag-ELISA [135].

The benefits of immunodiagnosis in pigs are: (i) tests offer diagnosis on live animals; (ii) blood sampling followed by serological testing is more sensitive than the tongue examination; and (iii) the tests are relatively inexpensive and easy to perform on large numbers of serum samples [134].

However, there are some problems related to sero-diagnosis in pigs: (i) it has been reported that the sensitivity of the available techniques is low in pigs with low levels of cyst burdens [512], although other authors [394] were able to detect pigs harbouring one single cyst using an Ag-ELISA; (ii) when measuring antibodies, antigen exposure is measured rather than actual infection; as in humans, the problem of transient antibodies may have to be considered to also apply to pigs, (i.e. a transient antibody response to a *T. solium* infection, without the establishment of a patent infection); (iii) interpretation of sero-positive results in young pigs may be complicated by maternal antibodies, transferred by colostrum from a seropositive sow to its piglet, which may persist for up to seven months; this has to be considered in pig prevalence studies [243]; and (iv) cross-reactions with *Cysticercus tenuicollis* are the rule rather than the exception in most antibody and antigen detection tests [134]. *C. tenuicollis* infection in pigs is uncommon in Africa and most regions of Latin America, but very common in the People's Republic of China and Vietnam. Ab-ELISA using isoelectric focusing-purified glycoproteins was claimed not to cross react with *C. tenuicollis* antigens [499].

Using Bayesian analysis on Zambian village pigs, the overall sensitivity and specificity of Ag-ELISA were estimated at 87% (CI: 62-98%) and 95% (CI: 90-99%), respectively [135]. For Ab-ELISA (using crude somatic *Taenia crassiceps* antigen) the sensitivity was only 36% (CI: 26-41%) and the specificity 92% (CI: 85-99%).

4.3.2. Porcine cysticercosis due to *Taenia saginata asiatica*

4.3.2.1. Parasitological diagnosis

Pigs are also the most important intermediate hosts of *T. s. asiatica* [164]. Contrary to the cysticerci of *T. solium,* which are mainly found in the muscles and only rarely in the organs, the predilection site of the cysts of *T. s. asiatica* is the liver (at the surface and/or in the parenchyma). Besides the liver, cysts are sometimes found in the lungs or attached to the omentum or the serosa of the colon [83, 153]. The cysticerci of T. *s. asiatica* are much smaller than those of T. *solium* and possess a rostellum and rudimentary hooklets. Just like the cysticerci of *T. saginata* the bladder surface of *T. s. asiatica* shows wartlike processes. The cysts surrounded by host tissue capsules have a diameter of about 2 mm when they are living or somewhat larger when they are degenerating [150]. In naturally infected animals, the cysts of *T. s. asiatica* are often degenerated and have to be distinguished from the liver lesions caused by *Ascaris suum* larvae (the so called white spots).

4.3.2.2. Serological diagnosis

Similarly to immunodiagnosis in *T. solium* infections, both antibody and antigen detecting assays may be used for the diagnosis of *T. s. asiatica.* Excretory/ secretory products of *T. s. asiatica* metacestodes and crude somatic antigen of *T. crassiceps* have been used as coating antigens in Ab-ELISA; and monoclonal antibodies raised against excretory/ secretory products of *T. saginata* have been used in a sandwich-ELISA to detect circulating parasite antigen [163, 225]. While antibodies can be detected from three weeks postinfection onwards and may persist for at least nine weeks post-infection, circulating antigens may be detected as early as one week post-infection but disappear soon after the cysticerci degenerate [163, 225]. Infection with as few as five *T. s. asiatica* viable cysticerci can be detected by Ag-ELISA [163].

4.4. Diagnosis of *Taenia saginata* cysticercosis in cattle

4.4.1. Meat inspection

In many countries the 'knife and eye' method is used whereby the so-called predilection sites (heart, tongue, masseter muscles, oesophagus and diaphragm) are visually examined and/or incised to detect cysticercosis (see also Chapter 5). However, several studies have shown that, except for the heart, none of the other muscles should be considered as real predilection sites [310, 345]. Detailed dissection of carcasses of lightly infected animals has proven that, in 51% to 56% of them, cysticerci are not present in these presumed predilection sites [361, 590]. Therefore, it is not surprising that routine meat inspection (if carried out properly) detects only the more heavily infected animals and underestimates the real prevalence of bovine cysticercosis by at least a factor of three to ten [158]. Another disadvantage of current meat inspection techniques is the fact that they are labour intensive and very subjective. It depends very much on the skills and motivation of the meat inspector as to whether or not cysticerci will be detected [158]. Living cysticerci, which are usually present in small numbers, are especially difficult to detect. Once the cysticerci die and become caseous or calcified, they have to be differentiated from other lesions. Immunohistological staining of sections of these lesions using monoclonal antibodies allows confirmation of the parasitic nature of degenerated lesions [398]. PCR can also be used to demonstrate parasitic DNA, which might still be present in this kind of lesions (Geysen *et al.,* unpublished results).

Note: cysticerci in the liver of cattle can be either *T. saginata* or *T. s. asiatica;* the latter are much smaller [153, 164]. Data on the prevalence of T. *s. asiatica* cysticercosis in cattle in Asia are lacking.

4.4.2. Serological techniques

Immunodiagnosis of bovine cysticercosis has been utilized in epidemiological studies and for individual and herd diagnosis. Both antibody and antigen detecting tests have been developed, the former to measure exposure to the parasite, the latter to detect active infections. The majority of techniques in general use for the detection of immune responses have been employed, with ELISA being the most popular test. Various antigens have been used in Ab-ELISA, from crude somatic extracts, excretory/secretory products, to

recombinant antigens [466] and synthetic peptides [169]. For Ag-ELISA, monoclonal antibodies produced against cyst fluid or excretory/secretory products of the metacestode are used [62, 265]. In slaughterhouse cattle, antigen detection is three to 10 times as sensitive as meat inspection [137, 400] and is therefore an interesting tool for estimating prevalence and studying risk factors for infection at the farm level. However, there is generally little agreement between cattle found positive at meat inspection and those found positive by antigen detection ELISA [137, 400]. One possible reason is that Ag-ELISA detects only live cysts, while lesions left by dead cysts are more noticeable at meat inspection. Another problem in immunodiagnosis in cattle is that of low sensitivity in light infections [62, 533, 572, 592], which are the rule rather than the exception, not only in industrialized countries but also in the tropics. The sensitivity of Ag-ELISA is near 100% when 50 or more viable cysticerci are present in the carcass, but is less than 50% in lighter infections [572]. Therefore, greatest value of immunodiagnosis lies in its application as a screening test in a cattle herd, rather than as a diagnostic test at the individual animal level.

Annex 4.5: Application of molecular techniques for identification of human *taenia* spp.

D. P. McManus and A. Ito

4.5.1. Methods for identification

The most accurate methods for identifying the *Taenia* species infecting humans are based on molecular and immunological diagnostic approaches combined with comparative morphology [284]. This review covers the use of deoxyribonucleic acid (DNA)-based techniques. Immunological and morphological approaches are described in Chapter 2.

4.5.1.1. Molecular identification of specimens collected from patients or domestic animals

Parasite samples should be freshly obtained, rinsed several times in physiological saline solution and frozen or fixed in ethanol without delay. DNA analysis on formalin-fixed samples is difficult and thus formalin fixation/storage is not recommended. Fixing samples in 75% ethanol is the method of choice due to the convenience for transportation and the ease of storage.

Adult proglottids expelled from human carriers, whole worms expelled after chemotherapy and eggs are all amenable to molecular identification. Fecal samples collected in endemic areas are useful for DNA detection of worm carriers; fecal samples frozen or fixed in ethanol are suitable for the copro-DNA test [397, 617]. It is best that frozen fecal samples be examined as soon as possible after collection and within ten years as a maximum [617]. Metacestodes, collected from domestic animals after necropsy, should be washed in saline and then fixed in ethanol for DNA analysis.

DNA from samples is prepared by proteinase K digestion, phenol/chloroform extraction and ethanol precipitation. Alternatively, a range of commercial kits, such as the DNeasy Tissue Kit (Qiagen, Hilden, Germany) is available for isolation of DNA.

4.5.1.2. Principles of methods

A number of techniques has been employed for DNA identification of *Taenia* species [60, 364, 284].

4.5.1.3. Restriction fragment length polymorphism

Restriction fragment length polymorphism (RFLP) of nuclear ribosomal DNA (rDNA) or other genomic regions, including mitochondrial DNA, can be used to detect differences between taxa. The DNA is digested by restriction enzymes, the resulting fragments are electrophoretically separated on an agarose gel, transferred to a nitrocellulose or nylon filter and hybridized with a specific DNA probe that has been radioactively or otherwise labelled in a Southern blot approach (RFLP-SB) [60, 471, 625].

The rDNA RFLP technique has been linked with the RFLP-PCR or PCR-linked RFLP to provide a greatly simplified and less time-consuming procedure, without loss of resolution or accuracy [60, 626].

During the PCR, a fragment of DNA, defined by oligonucleotide primers at either end, is amplified several million fold using a thermostable Taq polymerase.

Ribosomal RNA genes are organised into rDNA units with the very highly conserved coding regions separated by relatively poorly conserved non-coding spacer regions. Internal transcribed spacer 1 (ITS1) has been used successfully as one target sequence for PCR amplification [60]. Primers were designed based on highly conserved regions at the 3' end of the 18S rRNA gene (forward primer BD1) and within the 5.8S rRNA gene (reverse primer 4S). The PCR product, which spans ITS1 of the rDNA repeat unit and includes most of the 5.8S gene, can be amplified from various *Taenia* species and digested with one of a number of 4-base cutting restriction enzymes. Characteristic RFLP patterns are produced when samples of the various species are analyzed by agarose gel electrophoresis. Other markers including mitochondrial (mt) cytochrome c oxidase subunit 1 *(cox 1)* [60, 557], mt 12S rDNA [480] and other target DNA sequences [246] have also been used with success in PCR-RFLP analysis.

4.5.1.4. Comparison of PCR-amplified DNA sequences

The nucleotide sequences of fragments of targeted genes are determined using pairs of conserved PCR primers. The variable segment between the primers is PCR-amplified for a particular *Taenia* sample and then directly sequenced [60]. The sequences obtained can then be directly compared with sequences already published for *T. solium, T. saginata* and the Asian ('Taiwan') *Taenia, T. s. asiatica* and the identity of a particular sample thus determined. The mt *cox1,* NADH dehydrogenase subunit 1 *(nad1),* cytochrome b *(cob)* and 12S rDNA genes, and nuclear 28S rDNA and ITS1/ITS2 rDNA genes have proven valuable markers amenable to this approach [60,149, 222, 246, 284, 285, 322, 399, 588, 591].

4.5.1.5. Random amplified polymorphic DNA-PCR (RAPD-PCR)

This is a technique by which genomic DNA is amplified by PCR using a single oligonucleotide primer of arbitrary' nucleotide sequence [149, 351, 576]. This technique is relatively simple, requiring only small amounts of DNA (approximately 25 ng) and it is rapid. However, reliable results are only obtained under carefully controlled conditions, especially with regard to the quantity and quality of template DNA. Therefore, it is recommended that RAPD-PCR should be used simultaneously with one or other of the DNA techniques available.

4.5.1.6. Single-strand conformation polymorphism (SSCP)

This is a mutation scanning method with the potential to discriminate DNA sequences differing by a single nucleotide. The method is based on the principle that the electrophoretic mobility of a single-stranded DNA molecule in a non-denaturing gel is dependent on its size and structure. A mutation or base change at a particular site in the primary sequence can modify the conformation of the molecule that alters its electrophoretic mobility. SSCP has been used for the direct visual display of sequence variation in PCR-amplified fragments of the mt *cox1* and *nad1* genes of different *Taenia* species [222]. Although, the technique has to be very carefully controlled, it has the advantage that there is no need for DNA sequencing or restriction analysis, and large numbers of samples can be analyzed in a short period.

4.5.1.7. Multiplex-PCR

Multiplex-PCR uses primers of interspecies-conserved and species-specific sequences for the simultaneous differential diagnosis of *Taenia* taxa. This is an easy and time saving technique that does not require DNA sequencing. The approach uses a combination of different primer pairs in the same amplification reaction with the aim of producing different specific PCR products that can be distinguished after electrophoresis on an agarose gel [246, 617, 618]; for example, a multiplex-PCR based on mt *cox1* as target gene has been developed. Using mixed species- or genotype-specific primer sets, diagnostic 827 bp and 269 bp-products are amplified from *T. saginata* and T. s. *asiatica,* respectively. In *T. solium,* 720- and 984 bp-products are amplified from the American/African genotype and Asian genotype, respectively.

4.5.2. Comments on the taxonomy and population structure of the human *Taenia* spp.

Phytogenies derived from sequence comparisons of complete PCR-amplified *cox1* and *cob* genes obtained from a number of geographically distributed samples of *T. solium* provide molecular evidence for two genotypes; one is restricted to Asia and the other occurs in both Africa and America [385]. Whether the two genetic forms of *T. solium* differ in important characteristics such as infectivity or the pathology they cause remains to be determined. Minor sequence differences for the mt *cob* gene have recently been reported between isolates of *T. saginata* [322]. Minor sequence variation in the mt *cob* and nuclear rDNA ITS2 genes have also been shown between isolates of Asian *Taenia* [321].

There has been considerable discussion over a number of years regarding the taxonomic position of Asian *Taenia* and whether it should be regarded as a genotype, strain, sub-species or sister species of *T. saginata* [364]. Early DNA-based studies by Zarlenga and his group [624, 626] showed that Asian (Taiwan) *Taenia* is genetically, and hence phylogenetically, more similar to *T. saginata* than to T. *solium.* Bowles and McManus (60) compared mt *cox1* (~366 base pairs) and nuclear 28S rDNA DI region (~300 base pairs) sequences for *T. saginata, T. solium,* Asian *Taenia* and a number of other recognized species within the genus *Taenia.* The sequence comparisons indicated that the Asian *Taenia* is much more closely related to T. *saginata* than the recognized taeniid species are to each other. The 28S rDNA sequences were identical and there were only nine nucleotide differences in the *cox1* sequences. Importantly, the sequence information clearly showed also that both T. *saginata* and Asian *Taenia* are distantly related to T. *solium.* These molecular genetic studies supported those of Zarlenga and his team [624, 625, 626] and provided evidence that classification of Asian *Taenia* as a subspecies or strain of *T. saginata* was more appropriate than its designation as a separate species. Wang and Bao (591) came to the same conclusions after DNA diagnosis of *Taenia* samples from four areas of Yunnan and Guizhou provinces, the People's Republic of China. Using *cox1* as a marker, they identified the *Taenia* prevalent in Lanping, Dali and Duyun as T. *saginata asiatica,* while that isolated in Congjiang was the typical T. *saginata.*

Molecular phylogenetic analysis [273, 447] using previously published mt *cox1* and nuclear 28S rDNA DI region sequence information, not surprisingly, showed that *T. saginata* and Asian *Taenia* are very closely related. Eom *et al,* (149) undertook phylogenetic analysis based on nuclear rDNA ITS2 sequence obtained for *T. saginata,* Asian *Taenia* and T. *solium.* The comparison showed distinct features for Asian *Taenia* and T. *saginata* with many insertion/deletion (indel) regions which they suggested argued against subspecies status for the two taxa. It is noteworthy, however, that some of the indels were not present in all three Asian *Taenia* isolates examined, whereas others were present in T. *saginata* and also in some of the Asian *Taenia* isolates. More sequence information for the ITS2 region from additional T. *saginata* and Asian *Taenia* isolates may help to further clarify the phylogenetic position of Asian *Taenia.* It is noteworthy, however, that multiple rDNA repeats or rDNA genes are present in T. *saginata* [626]. If a similar situation, as seems likely, occurs in the other *Taenia* taxa, this will complicate future phylogenetic analysis that targets the rDNA repeat unit.

Hoberg *et al,* (272) and Ito *et al,* (285) have advocated that Asian *Taenia* and *T. saginata* should be considered as sister species, distantly related to T. *solium.* It is noteworthy that the morphological phytogenies produced by Hoberg *et al,* (272, 273) again show a very close relationship between Asian *Taenia* and T. *saginata.* No hybrids between Asian *Taenia* and T. *saginata* have yet been identified in sympatric zones such as the People's Republic of China where both taxa occur [149, 617]. Though this argues against subspecies status and supports independent species status for the two forms, the number of isolates that have been examined from sympatric endemic areas is limited, and definitive cross-breeding experiments have not yet been done [285]. The available molecular genetic data do not support independent species status for Asian *Taenia* and T. *saginata.* What is in agreement is that both taxa are closely related to each other but distantly related to T. *solium.* This is important in public health terms as it predicts that cysticercosis in humans attributable to Asian *Taenia* does not occur, because cysticercosis is unknown in T. *saginata.*

4.5.3. Selected laboratories experienced in using DNA techniques for identification of *Taenia* taxa

- Dr Minoru Nakao, Department of Parasitology, Asahikawa Medical College, Japan
- Dr Hiroshi Yamasaki, Department of Parasitology, Asahikawa Medical College, Japan
- Dr Munehiro Okamoto, Department of Laboratory Animal Science, School of Veterinary Medicine, Tottori University, Japan
- Dr Keeseon S. Eom, Department of Parasitology and Medical Research Institute, Chungbuk National University College of Medicine, Chongju, Chungbuk, South Korea
- Professor D.P. McManus, Molecular Parasitology Laboratory, Queensland Institute of Medical Research, Brisbane, Australia
- Dr Robin Gasser, Department of Veterinary Science, University of Melbourne, Victoria, Australia
- Dr.Kathy Hancock, CDC, Atlanta, United States of America
- Professor Ana Flisser, Direccion de Investigacion, Hospital General Dr Manuel Gea Gonzalez, SSA, 11400 Mexico, DF, Mexico
- Dr Thanh Hoa Le, Department of Immunology, Institute of Bio-technology of Vietnam, Hanoi, Vietnam.
- Dr C.M. Nunes, Department of Animal Health and Production, Universidade Estadual Paulista Julio de Mesquita Filho, Curso de Medicina Veterinaria, UNESP, campus Aracatuba, Rua Clovis Pestana, Jd. D. Amelia, Aracatuba, Brazil
- Dr R. Rodriguez-Hidalgo, Laboratorio de Immunodiagnostico e Investigacion, Facultad de Medicina Veterinaria y Zootecnia, Universidad Central del Ecuador, Quito, Ecuador
- Dr L.M. Gonzalez, Ministerio de Sanidaday Consumo, Instituto de Salud Carlos III, Centro Nacional de Microbiologia, Madrid, Spain.

CHAPTER 5:
PREVENTION OF TAENIOSIS AND CYSTICERCOSIS

Niels C. Kyvsgaard & K.D. Murrell

5. Introduction

The overall prevalence of taeniosis and cysticercosis can be greatly reduced even with presently available technology. Experts consider *Taenia solium* taeniosis/cysticercosis as 'potentially eradicable' [72]. The disappearance of *T. solium* from most of Western Europe during the 20th Century demonstrates that this is possible; the prevalence of *Taenia saginata* infections has also declined considerably in these countries. However, these zoonoses persist. This Chapter describes the potential for prevention of taeniosis/cysticercosis with emphasis on existing tools and measures, and discusses the challenges for the implementation of these measures.

5.1 Prevention of taeniosis in humans

There is a consensus that, from the standpoint of disease transmission to humans and maintenance of the parasite's life cycle, the adult tapeworm is of premary importance ([189, 231]. Although taeniosis *per se,* due to *T. saginata* and *T. solium,* is not considered of great public health concern, carriers of the latter species of tapeworm are an important public health target because the eggs they shed may infect humans, resulting in the more serious larval infection (cysticercosis). The prevention of infection of humans and subsequent environmental contamination with *taeniid* eggs (Fig. 5.1) is of paramount importance in both prevention and control schemes. The development of improved sanitation and hygiene practices have had a major impact on the occurrence of cysticercoosis in developed countries, and also among urban dwellers in developing countries, becuase of their effect on the transmission of *taeniid* eggs [231]. As discussed in Chapter 3, the transmission of *Taenia* in rural areas is greatly facilitated where exposure of pigs and cattle to human feces is high. The installation of adequate sanitation and the adoption of safe animal husbandry practices, however, are very problematical in these resource poor areas, and therefore, prevention strategies must rely on multiple approaches, tailoring each to the special features of the particular endemic area (Fig. 5.1).

Figure 5.1. Potential intervention points for preventing transmission of *Taenia*

In general, these strategies are:

1. mear inspection to prevent human infection
2. improved farm management to ensure that pigs and cattle are protected from ingesting feed or water contaminated with human feces to prevent cysticercosis in animals,

3. screening of farm workers for taeniosis, and treatment if warranted,
4. proper treatment of sewage effluent and sludge to kill *taeniid* eggs, and regulation of the use of effluent and sludge for agricultural purposes,
5. control of pig and cattle marketing systems, including the provision of incentives to ensure owner compliance,
6. health education of both farmer and consumer, especially on cooking of meat [231, 415].

The following sections discuss these strategies in detail.

5.1.1. Marketing of pigs and cattle for slaughter

The clandestine marketing problem

The clandestine marketing and slaughter of livestock are serious problems in endemic areas [231]. High rates of infection are supported by the bypassing of regulated marketing and inspection channels. In Peru, for example, it is estimated that 55% of all pigs are illegally slaughtered [556]. For many other developing countries, only a fraction of the animals slaughtered pass through certified meat inspection facilities. Furthermore, in the case of *T. solium,* ante-mortem diagnosis through the detection of tongue lesions may encourage clandestine slaughter [231]. Similarly, cattle owners in many endemic areas avoid the slaughter of animals in places where meat inspection exists, fearing condemnation. Thus, they revert to 'bush killing' and increase the risk of infection, especially to the poorer consumers [354].

Among the reasons for this behavior are government policies that yield disincentives for the farmer and slaughterhouse, primarily in the form of carcass condemnation without compensation [231]. Without some form of compensation, owners are encouraged to avoid veterinary control and to seek out small, unregulated slaughterhouses or practise home slaughter. Alternative approaches have been proposed for situations like these [231]. These include:

a) purchase of infected meat at market prices by government and the processing of it in a safe manner (see Section 5.1.1), so that it can be sold,

b) provision of a subsidy in the form of a premium payment to farmers who produce a clean animal for slaughter (certified meat) which could stimulate a higher demand and price from consumers, and

c) greater emphasis on alternatives to the rearing of pigs in free-range scavenging systems (see Section 5.2.5).

Until this critical issue of improvements in safe slaughter and meat inspection is addressed by governments in the endemic regions, it will be difficult to achieve interruption of the parasite's transmission cycle and removal of cysticerci from the food chain.

Prevention of illegal slaughtering and illicit sale of meat

If control is to be established over slaughtering and the sale of infected meat in rural endemic areas, butchers at licensed village abattoirs must notify the health authorities of the days and times when slaughter will take place (see also 5.1.1). Meat or health inspectors must be allowed to oversee meat hygiene procedures and ensure that all infected carcasses are treated appropriately. Inspected carcasses should be stamped to overcome problems of illegal slaughter and sale.

Periodic inspections of butcher shops and restaurants may also be necessary to enforce compliance.

5.1.2. Development of safe slaughtering facilities in village communities and undeveloped rural areas

This section should be read in conjunction with the *Guidelines On Small Slaughterhouses and Meat Hygiene for Developing Countries* [600]. They deal with the construction of slaughter facilities, slaughter processes,

handling of meat and by-products, meat hygiene, environmental sanitation, local energy sources suitable for small slaughterhouses and prevention of meat-borne diseases [354, 600].

The site and requirements for village animal slaughter facilities

In many endemic areas where there are no public slaughterhouse facilities, butchers slaughter animals wherever they choose, such as in an empty room in a dwelling-house, a backyard in a densely-populated area, the branch of a tree or a thicket in a banana grove [600]. This uninspected meat is then used for feasts or perhaps sold on the spot or marketed in towns. These unhygienic practices can be resolved by the creation and licensing of slaughter slabs and slaughterhouses. However, to be effective they must be equipped with facilities for trained meat inspectors to work under good conditions.

In remote and sparsely populated areas, where the consumption of meat is small and only occasional slaughtering is undertaken, the local administrators should erect a slaughter slab. The basic difference between a slaughter slab and the smallest slaughterhouse is that the latter consists of several slaughter slabs under a roof, while the slab has neither roof nor walls. Both require basic facilities for humane slaughter and for the maintenance of a good standard of hygiene and meat inspection.

Design and equipment

The slaughter place should:

1. not be part of a dwelling-house;
2. not be on a road leading to a dwelling-house;
3. be at a reasonable distance from human habitation so that it does not become a nuisance to the neighborhood;
4. be away from public latrines;
5. be screened from view;
6. have a hard, smooth, impervious flooring, sloping towards a drain and grooved to give better footing to beasts and staff;
7. be provided with a wooden or iron frame, not less than 3.60 m above floor level, with hoisting facilities; a basic factor in hygienic slaughtering and producing meat of good keeping quality, is the lifting of the carcass. The most primitive form of hoist is required to lift the carcass by means of ropes thrown over a horizontal beam 3.60 m high. Owing to the effort involved, this method is justifiable only when the occasional beast is slaughtered. No matter how small a slaughter slab or house may be, it must be equipped with proper lifting facilities which can be operated by one or two men.
8. be provided with one or more floor rings to secure the animals;
9. be provided with a water point on the slaughter slab, or a hose-pipe of sufficient length to connect to the nearest water point if this is not more than 7.5 m away;
10. have adequate facilities for the disposal of effluent, condemned meat and blood (pits);
11. be provided with meat and offal hanging rails;
12. have a scalding vat for pigs;
13. have electric or pressure lamps to give adequate light to both butcher and inspector if slaughtering takes place at night; and
14. be properly fenced to prevent access of other animals, or unauthorized persons.

Licensing of slaughterhouses

All slaughterhouses must be licensed before activities commence. Legislation should be enacted making it an offence to use premises for slaughtering purposes unless the butcher holds a valid license to operate on these premises. Licenses should be granted for a period of not more than one year. A veterinarian's or health officer's written report to the effect that both premises and equipment were inspected and found to

be in good working order and that sanitary conditions have not deteriorated since the previous inspection, should be conditional to the renewal of a license.

5.1.3. Meat inspection, meat treatment and development of safe slaughtering facilities

Introduction

In large national and exporting slaughter establishments meat inspection is of a high standard. Nevertheless, with both *T. saginata* and *T. solium* cysticercosis, there are serious limitations to the detection of infected carcasses, particularly those with light infections. The Codex Alimentarius Commission, which operates under the aegis of the Joint FAO/WHO Food Standards Programme, has prepared codes of practice which include those for inspecting and treating infected meat. As well, EEC Directive No 72/462 of 1972 stipulates that meat originating from animals carrying one or more live or dead cysticerci cannot be imported into EEC countries.

Until meat inspection as well as rural and village slaughterhouse facilities reach a similar high standard, and clandestine slaughtering is eliminated, both *T. saginata* and *T. solium* are likely to remain focal and hyperendemic in epidemiological pattern in much of the developing world.

Distribution of cysticerci in carcasses

Inspection methods for the presence of cysticercii in animal carcasses are not foolproof, but their sensitivity can be improved with a good knowledge of techniques for finding them. It should be kept in mind that the present meat inspection procedures are more efficient in detecting the heavily infected carcasses than light infections [135, 310].

Meat inspection regulations [250] generally prescribe the following procedures relevant to the control of *Taenia saginata:*

- incisions of the internal and external masseters parallel to the mandible,
- incision into both ventricles of the heart followed by inspection of the surfaces and myocardium,
- inspection of the surface of the liver, and
- inspection of the carcass surfaces including the surface of the diaphragm.

Pigs are inspected by examination of the muscular surfaces revealed by slaughter with special attention to the thigh muscles, the pillars of the diaphragm, the intercostal muscles, the heart, the tongue and possibly the psoas muscles. National rules may prescribe additional procedures such as incisions into thigh and shoulder muscles.

Taenia saginata

Many workers have attempted to determine whether or not there are specific sites of predilection in *T. saginata* cysticercosis [128, 143, 360, 590], The evidence is against there being any favored site or sites, which if found uninfected, would guarantee freedom of the carcass from cysticerci.

However, there is agreement between the studies that certain muscles and organs have a higher density of cysts compared with the rest of the carcass. The higher density is most commonly seen in the heart [310, 345], whereas there is more diversity for the other muscles (Table 5.1). The muscles and organs receiving most attention during meat inspection (heart, masseters, diaphragm, and tongue) are those with the highest cyst density. In some cases, the triceps brachii muscle has also been shown to have a cyst density above that of the whole carcass [345].

If the animal is heavily infected, there is a high probability that at least one of the cysts will be located at the inspected surfaces. This probability is reduced in animals with a low number of cysts [223, 310].

Table 5.1. Distribution of cysticerci of *Taenia saginata* in different parts of the carcass found by slicing [270]

Part	Number of animals with cysts	Percentage of animals with cysts*	Cysts per kg of muscle
Hind legs	46	76.7	1.03
Fore legs	42	70.0	1.25
Back and ribs	28	46.7	0.64
Neck	24	40.0	1.26
Lumbar region	15	25.0	0.96
Heart	15	25.0	2.14
Liver	15	25.0	0.61
Abdominal muscles	14	23.3	0.47
Tongue	13	21.7	1.33
Head muscles	8	13.3	--
Lung	6	10.0	0.25
Diaphragm	5	8.3	--
Oesophagus	3	5.0	--
Kidneys	0	0	0
Spleen	0	0	0

*: *Percentage based on 60 infected at limais*

--: *Not available.*

Taenia solium

Diagnosis of porcine cysticercosis is also based on the identification of the parasite in carcasses, although in heavy infections, positive identification can often be made ante-mortem by an examination of the tongue. Heavy infections are readily detected after slaughter [269].

In studies on the distribution of cysticerci in swine musculature it is apparent that, in general in endemic areas, cysts are distributed throughout the carcass, including the brain. Similar problems in the detection of light infections occur in pigs as in cattle [135, 269]. In countries where it is usual to make a limited incision in the musculature (to avoid decreasing the commercial value of the carcass) infection may be missed. For example, in 1,000 pigs in which cysticercosis was not detected by a routine incision of the anconeus muscle, further examination showed 1.1% to be infected with cysticerci in the masseters or tongue.

Improvements in meat inspection

Various studies have shown that improvement in the effectiveness of inspection staff depends upon such factors as training, rewards, motivation, psychological disposition, adequate lighting and improving methods of processing carcasses. These are important, but they do not overcome the problem that there is no specific site for examination that can be relied upon to detect all infected carcasses.

Failures in the detection of cysticercosis during post-mortem inspection may be reduced if meat inspection is practised by experienced and conscientious inspectors under optimal conditions which should include adequate rest periods, good lighting, a low noise level and a system of inspection integrated with slaughtering procedures. Meat inspection manuals should be explicit in their directions for the examination of carcasses and organs for cysticerci. Meat inspection should be well planned, organized and managed at every slaughterhouse. It has been observed that the efficiency of meat inspection diminishes after two hours of routine work in a given position.

Regulations vary in different countries depending on the number of cysticerci found at inspection. Where few (e.g. up to five or ten *per* carcass) cysticerci of *T. saginata* or *T. solium* are identified, the carcass is retained for treatment. Where more (e.g. six to 20) cysticerci are found, the meat may be used only for

processing (see below). Where heavy infections (e.g. more than 20) are involved the carcass must be destroyed.

Treatment of infected carcasses

When heavy infections are detected, the carcass is condemned, buried, rendered or incinerated [266, 354]. Lightly infected carcasses, however, can be decontaminated by freezing, boiling or pickling in common salt. Several recommendations have been made on the freezing times and temperatures required to kill *T. saginata* and T. *solium.* Freezing of beef carcasses at -20°C for 10 days is effective [258]. In a carefully controlled study, it has been shown that 12 and 16 week-old *T. saginata* cysticerci are much more susceptible to the lethal effects of freezing than 24 week-old cysticerci (Table 5.2) [270]. The time and temperature combinations required to ensure the death of all cysticerci irrespective of age were 360 h at -5°C, 216 h at 10°C and 144 h at -15°C or lower. With respect to boiling of meat for sterilization, beef can be rendered safe by boiling 2 kg pieces in an open boiler for 3 h at a steam pressure of 0.5 atmospheres. Pork infected with cysticerci can also be rendered safe provided meat internal temperature reaches 80°C. For effective salting, beef or pork should be cut into 2.5 kg pieces and covered with ordinary salt and pickled for 20 days. With respect to all treatments, the size of the meat joint determines the time required for adequate sterilization.

Consumption of raw or undercooked meat is common in many parts of the world. This can be due to local preferences, such at *boeuf tartare* or may be due to unintended insufficiency of the cooking method. Barbecued meat may be prepared over charcoal on the street and sold directly, but the procedure requires good regulation of the heat to ensure thorough cooking. The local health authorities may assist in awareness creation about proper cooking.

5.1.4. Pre-slaughter drug treatment of pigs

Chemotherapy of infected pigs has been proposed as an effective strategy to interrupt the transmission of T. *solium* cysticerci, thereby reducing the adult tapeworm infection in humans [237]. This method could also be used to 'clean-up' an infected pig prior to slaughter. Currently, this approach is being seriously evaluated as part of a combined intervention strategy involving mass treatment of humans and pigs [189, 235, 237, 493]. The projected cost for such a combined intervention may be relatively inexpensive. In Peru, for example, where approximately 40% of the population is at risk, treatment would be applied to 9 million humans and 900,000 pigs. At a cost of $1.00 per dose for pigs (oxfendazole) and $0.25 per dose (praziquantel) for humans (1999 figures), the total cost for such a mass treatment campaign would be about $5 million for drugs, not including cost of transportation, gasoline and staffing [231].

Table 5.2. Time and temperature required to kill 24 week-old cysticerci of *Taenia saginata* in beef. Results expressed in percentage of dead cysticerci [270]

Temp.	Time (mn)												
(°C)	72	84	96	120	132	144	168	192	216	240	264	288	360
-5	–	–	–	75	0	50	63	–	100	–	86	–	100
-10	–	–	20	82	88	100	84	–	100	–	100	–	100
-15	20	63	90	80	–	100	–	100	–	100	–	100	–
-20	25	100	89	100	–	100	–	100	–	100	–	100	–
-25	60	100	0	100	–	100	–	100	–	100	–	100	–
-30	50	63	72	68	–	100	–	100	–	100	–	100	–

Similar detailed studies for T. solium *cysticerci are not available.*

Oxfendazole appears to be the drug of choice for pigs. In controlled and field experiments it was demonstrated that the drug is nearly 100% effective in killing pig cysticerci with a single dose of 30 mg/kg; all cysticerci were eliminated by eight to 12 weeks post-treatment [237]. It was also demonstrated that oxfendazole-treated infected pigs were immune to reinfection for at least three months after treatment [236].

This approach has several potential obstacles that must be anticipated. Although the drug is relatively cheap, in a mass intervention campaign governments may still have to subsidize the cost of the drug because many pig owners will be too poor to pay for it themselves [493]. There will be an additional cost to pig owners, because of restrictions on selling or eating meat for at least three months after treatment (e.g. oxfendazole); this will also incur monitoring and veterinary control oversight costs [493]. An educational campaign prior to drug treatment may be needed to persuade the community that this approach, despite its additional costs, will have greater benefits than current prevention measures such as boiling or freezing pork [493].

5.2. Prevention of cysticercosis in animals and humans

The potential risks associated with infection (cysticercosis) of food animals from human activities such as animal husbandry, sanitation and waste disposal have been discussed in detail in Chapter 3. The following describes practical measures for mitigating the risk of transmission of *taeniid* eggs from infected humans (taeniosis) to livestock.

5.2.1. Basic sanitation

Provision of basic sanitary facilities is a first step in the prevention of a number of fecally transmitted diseases. Water and sanitation programs have therefore attracted donor focus, and a number of affordable models of latrines have been developed. Such projects have had a varying degree of success, however (see below). Where the projects in the 1980s were basically donor-driven, employing a blueprint approach, more recently there has been a move towards community participation. However, latrines have not always been high on people's priorities, and some projects have been abandoned. A key factor seems to be that projects should address *felt* needs and latrines should therefore be introduced later in a process after health education and the solving of some of the more immediate priorities [598]. An integrated approach to water and sanitation is also needed, one that provides for latrines and improved water supply and health education.

Several designs for low-cost sanitation are available. However, the introduction of latrines is not a guarantee that they will actually be used. There may be several reasons for not using them, such as foul odors, flies, cockroaches, flooding etc. Provision of latrines also does not necessarily prevent all risks of transmission. The quantity and distance to the water seems to be more important than the quality of the water [103, 598]. If access to water and sanitation is to reduce disease transmission, a component of health education on better hygienic practices will be required as well [33, 103].

Sanitation is very much needed for farm workers, as negligence in this respect may lead to cysticercosis outbreaks (Chapter 3).

Latrine waste and septic tank contents must be disposed of correctly. For latrines a longer resting period is recommended before the emptying. Septic tank contents should also be considered a source of infected material and not spread on pasture or fields used for the cultivation of feed crops. There are numerous examples of cysticercosis outbreaks (even cysticercosis storms) in cattle due to accidental or deliberate spreading of septic tank contents on pastures. One of the possible hazards occurs when septic tank contents are accidentally mixed with animal manure in the same equipment and subsequently spread on pastures [280, 386].

5.2.2. Urban sanitation, waste treatment and disposal

Increasing urban populations have placed heavy demands on water resources and have stimulated the need for more complete treatment of waste water and re-use of the treated effluent. For example, 187,000 tonnes of dry solids, or 15% of the 1.25 million tonnes produced by the United Kingdom waste water industry, are deposited onto grazing land each year [275]. However, irrigation of pasture with sludge and effluent is a common method of water re-use, but this provides the opportunity for the contamination of agricultural lands with taeniid eggs [279, 311].

The sewage treatment systems that must be of concern in regard to efficiency of removal of taeniid eggs include grit tanks and screens, primary sedimentation tanks, cold sludge digestion, mesophilic sludge digestion for the production of methane, sand filtration, outdoor sludge drying beds, sewage farms, gravity drainage into holding tanks with final discharge of the effluent into rivers, sea or sewage farms. Most urban sewage systems also capture rain water from the streets, but are designed to receive only a certain volume. They may therefore have to shunt the waste-water directly into the recipient streams or the sea in case of heavy rainfall.

At the village and rural levels, septic tanks, out-houses and pails are used. These latter are of particular importance in the spread of *T. solium* cysticercosis, when they are emptied onto horticultural land.

5.2.2.1. Biological and physical sewage treatment methods

Effuent treatment

After primary sedimentation, sewage effluent can be treated in various ways to decompose suspended solids and organic material with the aid of microbes. At the end of these processes this activated sludge is separated from the effluent in secondary sedimentation tanks.

Trickding filtration

The efficiency of this process in removing helminth eggs ranges from 0 to 30%. Even under laboratory conditions, it does not exceed 70%, therefore this filter cannot be regarded as an effective method of removing eggs from the effluent [392].

Oxidation ditch

Even after a three-month detention time, helminth eggs, except those of *Fasciola,* are not destroyed. This is also the case for *taeniid* eggs, therefore the effluent from oxidation ditches poses a hazard if it is used for agriculture or is fed into rivers [146].

Sand filtration

This process seems to be the only efficient method of removing *taeniid* eggs from the effluent of secondary sedimentation tanks. To be effective, the sand filter should have a depth of at least 0.6 m with a sand of 0.5 mm effective size and 2.2 uniformity coefficient [392]. This method of sand filtration is used increasingly as a tertiary sewage treatment at sewage works. It appears that this method can compensate for the failure of other purification steps to remove the eggs of T. *saginata* from sewage.

In conclusion, at present primary and secondary purification processes in sewage treatment plants cannot be relied upon to produce effluent free of viable *taeniid eggs.*

Sludge Treatment

Activated sludge process

Observations in practice and in laboratory experiments indicate that the activated sludge process has no apparent deleterious effect upon *taeniid* eggs. In laboratory scale experiments eggs have survived for five months in this process.

Anaerobic digestion of sludge

Sludge is the product of primary, secondary and, in some of the more modern sewage works, tertiary sedimentation processes in settling tanks. While the retention time in settling tanks is in many cases not sufficient for the natural sedimentation of *taeniid* eggs, it seems likely that in tanks with depths of several metres, eggs trapped by sewage particles will be given additional downward velocity. Thus they

should end up in the sludge, which consists of pathogens not only from the helminth group but also bacteria and viruses, and can be subjected to various degradation processes.

In many sewage treatment plants the sludge is subjected to anaerobic, mesophilic, alkaline digestion at temperatures in the range of 28°C to 34°C. However, even under these conditions *taeniid* eggs can survive the digestion process. If a detention time of 56 days could be achieved *taeniid* eggs will be inactivated although this may be unrealistic in practical terms.

Drying of sludge

Drying beds for dewatering sludge have no effect on many helminth eggs. The same is true for dewatering sludge with belt presses, chamber-filter presses or centrifuges. These mechanical processes, even if combined with flocculation by addition of chemicals as conditioners, have limited effect. Drying sludge with high temperatures, usually between 100°C and 200°C will, however, destroy taeniid eggs. This method is very energy' intensive, however, and only likely to be used in large sewage works.

5.2.2.2. Egg-dispersal from sewage works

The removal of taeniid eggs during the treatment of sewage has proved to be more difficult than expected. It should be kept in mind that most sewage treatment plants operate under mesophilic conditions and a rapid elimination of taeniid eggs requires either a low rate of humidity [318] or a temperature above 40°C [226].

Epidemics attributed to faulty sewage systems have been described in the United States [509], in Germany [532] and in the United Kingdom [96]. Almost all types of sewage systems in common use have been studied for their ability to retain animal parasite eggs and cysts and there is good evidence that sewage discharges overflowing onto pastures or directly into rivers and their estuaries, disperse animal parasites including taeniid eggs [251, 266, 392, 525, 526]. For example, although tapeworm eggs settle at the rate of about 0.1-0.2 m per hour [392] suggesting that settling out of effluent should be practical, turbulence involving overloading and interference with natural purification processes due to high chemical concentrations [251, 306, 525] in most sewage systems permit eggs to pass relatively freely through the effluent. Taeniid eggs can also survive anaerobic or aerobic digestion for several months [392].

There are several ways in which the eggs of T. *saginata* can become available to cattle through sewage. In systems which use primary settling tanks, grit tanks, sedimentation tanks or aeration tanks, eggs in the effluent will pass through these systems into rivers or to farms that use sewage effluent. Flooding of the rivers will also ensure that the eggs are dispersed onto pastures. If the effluent outlet falls directly into the sea from a raw sewage collection plant, segments will be present and the eggs may also be disseminated onto pastures by gulls and possibly starlings [95].

The second important method of dispersal is through the deliberate use of raw sewage to fertilize pastures or pastures which are used for growing livestock fodder [251, 525]. A similar dispersal will result from the emptying of septic tanks and pails on to pastures [279]. Using 'tracer' calves, it has been found that T. *saginata* eggs dispersed on pasture by deliberate irrigation with effluent, remained available and infective for at least 4.5 months and in silage for up to four months or more at 32°C, although eggs failed to infect when the silage was pressed and dried into pellets because the temperature exceeded 50°C-60°C during the pelleting process [63].

5.2.3. Guidelines for agricultural utilization of sewage and sludge contaminated with *taeniid* eggs

The current consensus is that conventional sewage treatment is inadequate to eliminate tapeworm eggs from sewage or sewage sludge. However, utilization of sludge for agricultural purposes is possible under certain conditions.

Effluent

Access of livestock to surface waters which receive effluent from sewage treatment plants must be prevented to avoid the ingestion of taeniid eggs. If sewage is used for the irrigation of fields and crops, it should not be applied to pasture or land for green forage and crops for raw consumption. If this is unavoidable for local reasons, livestock should not be allowed to graze directly and green fodder should not be harvested from such area; instead grass and green forage crops should be used only as well cured hay or silage or pelleted [162].

Sludge

Livestock should not be allowed to graze pasture treated with undigested sludge for at least six months after application. This precaution is particularly necessary because of the longevity of taeniid eggs on pasture; the viability of the eggs is greatly reduced after six months [280]. However, the possibility that cattle may still become infected cannot be ruled out, especially if the pasture resting period takes place in the winter months when lower temperatures increase egg survival. It is, therefore, inadvisable to use undigested sludge on grazing land if the risk of infecting cattle with taeniid eggs is to be avoided.

Livestock should not be allowed to graze pasture treated with digested sludge for at least 30 days or until there is at least 100 mm growth of herbage, whichever requires the longer period. Digested sludge is defined as sludge produced either by storage of untreated sludge for two or more years or by controlled anaerobic mesophilic digestion. This advice applies only where the sludge is not mixed with any undigested sludge prior to land application. The resting period is designed to reduce bacterial infection and may be inadequate to prevent infection of cattle with any tapeworm eggs that have survived the digestion period. A resting period for at least six months is necessary to reduce the risk of such infections to an absolute minimum.

If these guidelines on the disposal of sewage and sludge are not strictly adhered to no control over cysticercosis in cattle can be expected.

5.2.4. Other sanitation measures to prevent cysticercosis

In some areas, human defecation in the feeding range of livestock plays an important role in transmission. Most notable is the use of pigs as 'sanitary policemen' in free-range systems, or the positioning of household latrines directly over pig pens. Another risk factor that also occurs in developed countries, is due to sanitation practices associated with intensified tourist traffic, and the growing number of highway picnic areas and camping accommodation. Indiscriminate defecation in these areas may result in contamination of nearby farmlands. These risks can only be overcome by establishing adequate sanitary installations.

On farms which are not connected to public sewers, the effluent of the occupants should be collected separately from those of the livestock. Generally, the contents of cesspits or household waste should not be distributed onto pastures, meadows or forage growing areas. Preferably, they should be transported to a nearby sewage treatment plant. Where this is not possible, they should be spread on to arable land before the beginning of the crop growing season and immediately plowed into the soil.

5.2.5. Improved animal husbandry practices

As described in Chapter 3, there is a number of critical factors related to the rearing of food animals that must be monitored to ensure prevention of infection. As discussed above, farmers should be informed of the risks associated with: allowing animals, especially pigs, access to human feces; using human sewage for fertilization and/or irrigation of pastures; and inadequate toilet facilities for their own and workers' families. Farm workers are of particular concern because they move from farm to farm, and if infected with tapeworms they may contaminate several environments.

General guidance

Livetock owners should be advised to: (i) prevent their animals from having contact with human feces or materials directly or indirectly contaminated by feces (confinement); (ii) have their animals inspected at slaughter and if this is not possible, to learn how to detect cysticerci in the meat; (iii) use the infected meat only if properly treated by cooking or freezing; (iv) clean all tools used to cut the meat, in order to prevent the transfer of cysticerci; and (v) report and have treated all cases of taeniosis occurring in themselves or within their families.

Confinement or restraint of pigs and cattle

The behavior of animals with regard to the ingestion of feces of their own and other species will almost certainly influence the acquisition of *Taenia.* Cattle normally avoid grazing the ground around fecal material, but under some ecological circumstances such as adverse climatic conditions, drought, and high stock densities, they may even ingest feces, including those of man.

The pig is a natural scavenger of feces and there are many reported cases in which pigs are actively encouraged to act as 'sanitary policemen.' This may lead to massive infections during the time interval between the ingestion of the first eggs and the onset of immunity. The free-range pig rearing system has many advantages for small farm situations in resource poor regions, however, it is also clear that restraint of pigs greatly reduces porcine cysticercosis [58, 162, 189, 496, 501]. For these reasons, cost to the community in health terms may outweigh the value of allowing pigs free-range and scavenging.

The reasons for smallholder farmers keeping their pigs on free-range should be investigated and addressed before they can be convinced to efficiently enclose their pigs. Some of the issues are:

- Efficient confinement means construction costs. In a community study in Tanzania it was observed that even though the larger pigs were kept confined, the piglets were able to escape [58].
- The pig may find an essential part of its diet by grazing and scavenging, which mean a substantial reduction of feed costs for small-holder farmers. It may be otherwise difficult to provide a well-balanced feed with locally available maize, cassava or sorghum, and free-range may help in this respect by providing minerals and essential amino-acids [323]. Solving these concerns through research on low-cost feed formulation would improve the acceptance of any effort to make farmers keep their pigs enclosed.

Feedlot situations

Explosive outbreaks of bovine cysticercosis may occur in intensive production systems. These may occur in two ways: firstly, by direct contamination of the environment with eggs by unhygienic toilet habits, and secondly by the feeding of cattle on food from egg-contaminated pastures.

In the first situation this can be prevented by routine tests of all staff for tapeworms at regular intervals as part of a health care program for agricultural workers. Visitors should be strictly supervised. Another precautionary measure is the installation of sufficient toilets with effective drainage for the disposal of eggs, even though many of the eggs will be dispersed due to the escape of the proglottids. Human and cattle effluent systems must be separated and fresh water supplies provided.

In the second situation, cattle forage should not be obtained from pastures that have been fertilized in the previous 12 months with human sewage. Alternatively, high temperature processing of grass or pelleting may be applied.

5.2.6. Vaccination of pigs and cattle

An alternative approach to interrupting the transmission cycle of T. *solium* cysticercosis is the vaccination of pigs [181, 186, 231, 494]. Several research groups are actively pursuing a vaccine, using different approaches or antigens [65, 181, 276, 327, 437, 580]. Although none of these candidate vaccines has yet

reached the commercial stage, their promise is such that some are likely to enter large-scale field trials in the not too distant future [327].

If and when a vaccine appears, its impact on the prevention of cysticercosis in pigs will be very dependent upon its cost. For instance, the most important clientele for a vaccine are rural communities, which will have difficulty in allocating restricted resources for a vaccine strategy.

Other issues include the age at which pigs should be immunized; pigs are often infected very early in life and vaccination of already infected pigs is not effective [161, 231]. Compounding this issue is the fact that the presence of maternal antibody in young pigs may inhibit an effective response to a vaccine [236]. While these questions are not unanswerable the research needed to provide the optimal strategy for using a vaccine needs to be encouraged now.

5.3. Health education

Health education can be regarded as the key factor in obtaining the commitment for, development of, and continuing involvement in a prevention and control program. Health education campaigns targeted to *T. solium* cysticercosis have demonstrated their value [488, 493]. In Mexico, as an example, a long-term reduction in the swine cysticercosis rate was achieved through a multidisciplinary community education effort that focused on changing attitudes and practices [494].

Proper health education should be principally oriented towards:

a) diminishing the number of tapeworm carriers, thus lowering environmental egg contamination

b) reducing pig and cattle cysticercosis

c) changing attitudes, traditions, socio-cultural and behavioral factors that favor a high infection pressure in the community, and

d) educating people on the risks of human and animal cysticercosis and on their mitigation.

In developing countries there are special educational problems to be solved. By and large, experience suggests that any initial health education effort should be closely integrated with the development of primary health care and directed not exclusively towards taeniosis and cysticercosis, but rather towards the development or improvement of:

a) effective fresh water supplies,

b) safe toilets,

c) composting of human excreta, and

d) training in elementary hygiene, to ensure that once these necessities have been supplied, they are used.

It follows that the elementary principles of sanitation must be developed and that changes be accepted or, better still, requested by the community.

Education interventions, however, are often not economically feasible for many at-risk communities unless the local, national and international political will commands the funds needed for a multidisciplinary prevention and control program [488, 493]. Education programs should be implemented at the beginning of a prevention and control program because of their relevance and support to other intervention actions, thus offering a chance to widen support for prevention.

Prior to designing and implementing health education programs tailored to the specific features of the target communities, a diverse cast of individuals must be prepared for their roles in the effort [488]. These include community leaders, researchers, health care professionals and students; to play their roles they must be well informed and able to deliver clear messages [470].

This section summarizes the different elements involved in health education against cysticercosis: (i) identification of target groups, (ii) design of information packages and methodologies, and (iii) evaluation of the impact of health education upon the taeniosis/cysticercosis prevention programs.

5.3.1. Target groups

The general public, especially communities in endemic areas, have to be made aware of the dangers of taeniosis/cysticercosis to health as well as its economic impact. To do this, full use should be made of the mass media. All available means of informing each community should be used, but the most effective methods include discussions within small groups. In such discussions, the health worker (educator) suggests concrete action, for example, persuading tapeworm carriers to have treatment. Meetings of this kind have also proved extremely useful in the initial phases of several echinococcosis control programs (readers should consult the 2003 *WHO/FAO/OIE Guidelines on Echinococcosis/Hydatidosis Surveillance, Prevention and Control,* VPH/81.28, as many of the issues in health education are similar for both zoonoses).

In securing community support and participation, it is very important to enlist the aid of: (i) opinion leaders who are identifiable in all communities, (ii) parents, especially mothers of children at risk; (iii) persons who have undergone treatment for taeniosis/cysticercosis or still suffer from this disease; and (iv) persons who suffer direct economic loss because of condemned beef and pork.

Another important group to be consulted in the early stages is national policy makers. Community support and involvement in the program can often help to achieve a political commitment with appropriate funding. Cost-benefit studies are probably crucial in convincing political leaders of the benefits of preventing these zoonoses.

In the operational phases of the program, special attention should be paid to the target groups described below.

5.3.2. Training of professionals - 'training of trainers'

Any health education effort has to be planned and conducted through a net of professionals who are working in the field or who have contact with the public. Among them are:

Meat inspectors

Meat inspection in larger slaughter houses is in most countries under the veterinary authority of the agricultural ministry. The authority and obligation to carry out meat inspection in the smaller towns and communities may vary between countries, belonging either to local municipal government, the agricultural ministry or to the ministry of health. Local police may even be involved when meat is condemned. The meat inspectors may have other duties and will often have ven[7] different educational backgrounds. Proper training is therefore crucial.

The role of health workers

The primary health worker plays a central role both in the identification of human carriers and in the promotion of better hygienic practises in the community.

Training of health workers and school teachers

As far as possible, health educators should be drawn from the community in which they will be working. Everyone involved directly or indirectly in preventing taeniosis/cysticercosis must participate in carrying out public health education. It is, therefore, essential that this subject should have an important place in staff training. Such training should be planned and preferably imparted by a speciahst, who should also advise on the selection of appropriate educational methods and preparation of educational material suited to local conditions and to the various phases of the program. The general training that health workers may have received in schools of public health also needs to be supplemented with briefings on the various aspects of the local situation. It is useful to prepare and distribute a poster, booklet or manual dealing with

the technical, administrative and educational aspects of the program. This can then be used by all persons involved in the project, including lay members of committees or other groups set up to obtain public cooperation and support. A manual helps to avoid confusion caused by different answers to the same questions given by different people.

The role of schools

Taeniosis/cysticercosis is an appropriate subject to be introduced into schools along with discussions on food hygiene, food habits, environmental sanitation, man/animal relationships, life cycles of the organisms and their zoonotic importance. In many endemic areas this is an important opportunity for education to reach isolated farms. The preparation of teachers to become active health educators should be encouraged.

The role of pharmacists

Pharmacists play an important role locally, as they sell taeniacides, often without medical prescription and/or are asked to diagnose taeniosis. They can be actively involved in health education particularly in the supply of educational materials. The training curricula of pharmacists should include a course of lectures on diagnosis, treatment, prevention and control of taeniosis/cysticercosis.

5.3.3. Training of the public

Farmers

Farmers should be informed of the risks associated with: allowing cattle and pigs to have access to human feces and the use of human sewage for fertilization and/or irrigation of pasture, and they should be instructed on the benefits of providing effective toilet facilities for their own and workers' families. Farm workers share the same responsibilities as farmers because in moving from farm to farm, they may contaminate several environments. Therefore, they should be convinced of the importance of: (i) having all cases of taeniosis reported and properly treated; and (ii) using effective toilets when available or, if not available, avoiding defecation in places either directly accessible to susceptible animals or with potential for contaminating their feed.

Cattle and pig owners should be informed of the life cycle and the health risks to their families and to the consumers of the meat they produce. They should also be informed of the economic implications (possible sanctions or restrictions by the health authorities and the loss of income). Sometimes the best way to involve these animal owners is through their children, who can be taught at school the life cycle of these parasites and the means to prevent infection.

These animal owners should be advised to: (i) prevent their animals from having contact with human feces; (ii) have their animals inspected at slaughter, but if this is not possible, to learn how to detect cysticerci in the meat; (iii) use the infected meat only if properly treated by cooking or freezing; (iv) clean all tools used to cut the meat, in order to prevent the transfer of cysticerci; (v) report and have treated all cases of taeniosis occurring in themselves or within their families.

Butchers

Butchers should be required to: (i) cooperate in veterinary inspections to detect cysticerci; (ii) in the absence of veterinary inspections, be trained to detect cysticerci, and properly treat the infected meat; and (iii) avoid tasting, eating or selling suspect, untreated raw meat.

Food handlers and consumers

Food handlers should be educated to: (i) look for cysticerci and use infected meat only if it has been previously treated by freezing or cooking; (ii) use suspect (uninspected) meat only if it has been previously treated by freezing or cooking; (iii) thoroughly clean hands, and all kitchen tools (e.g. knives, chopping-boards, etc.) which have been used in preparation of meat; and (iv) avoid tasting raw or insufficiently cooked, infected or suspect meat.

Persons involved in home slaughtering

Some people raise cattle or pigs for home slaughter and distribute meat to their families or to local consumers. This is one of the activities where education is most needed in the village situation, as it is probable that the carcasses are not inspected.

Community education or prevention

All members of the community should be informed of the life cycles and of the public health and economic impacts of these parasites. They should be encouraged to: (i) report and have treated all cases of taeniosis; (ii) insist that proper public and private toilets with effective sewage disposal are made available and are used; (iii) keep pigs in pens or behind fences; and (iv) insist on adequate meat inspection services.

Campers and tourists

These groups are often exposed to taeniosis if they eat raw or improperly cooked meat. Because they frequently defecate in the fields, campgrounds or by the roadside, they should be informed about the life cycle of taeniosis and advised to: (i) refrain from eating unsafe, raw beef or pork in countries where cysticercosis is endemic, (ii) inspect their feces for tapeworm proglottids and report for treatment, and (iii) use toilets when available and if these are not available, avoid defecating in places accessible to cattle and pigs, or bury their feces.

Hunters

Hunters have responsibilities similar to campers and tourists in general, particularly in the use of uninspected meat as food for their families or for local consumers. Hunters should be advised to: (i) have wild pig meat properly inspected, and if it is found to be infected, to have this meat properly treated by cooking or freezing; (ii) learn how to detect cysticerci if inspection is not feasible, and (iii) cook the meat thoroughly and avoid tasting before it is cooked.

5.3.4. Exploiting media for local education programs

The educational material used should take into full consideration the beliefs, perceptions, behavior, expectations and needs of the people (felt and unfelt). This highlights the need to carry out preliminary sociocultural and socioeconomic studies to ensure that the information imparted will be accepted by each target group. There is a need to measure the impact of each educational program to ensure that it does meet the needs and cooperation capabilities of the target group.

A potentially powerful use of the electronic media for prevention and control education efforts is in the training of educators in the project with interactive media presentations or tutorials [488]. Recently, an example of an interactive media presentation was presented at an international workshop on *T. solium* cysticercosis [488], and is highlighted here to increase awareness of the opportunities this technology offers. The intensive tutorial (CD-ROM) on *T. solium* is bilingual, increasing its usefulness *to* multinational users, its message is presented with characters and cultural traits appropriate to the target communities, and it contains hyperlinks to additional information. The presentation includes original illustrations and photos to show parasites, and clinical and diagnostic tools; original music and audio enhance the messages' impact. The approximately one hour long presentation is designed to be shown in schools and universities, and to decision-makers in government. It is also intended to be used for specific training of project personnel in future control programs [488]. The use of such new technologies can greatly extend and enhance educational materials traditionally employed in health education programs.

A recent project on porcine cysticercosis in Tanzania expanded the use of electronic media options by introducing an educational video to inform the rural communities of the health risks and prevention of *T. solium* infections [469]. The product of this research was a video that could be taken to even very remote locations and presented to community members as either a VHS videotape (with TV screen) or with a DVD player (installed in a laptop PC) and an LCD projector. Power for the portable presentation equipment was provided with either a portable generator, or a 12 volt car battery; the battery is recharged

while driving to and from the location [470]. Details of the potentially useful means of delivering a prevention education program with an attractive, well-designed and produced video film are presented in reference 470.

5.4 Conclusions

The measures to control taeniosis/cysticercosis can be considered as either specific or non-specific. The **specific** control measures include measures designed to prevent or control the infection with the particular parasite:

- human mass treatment with cestodicidal drugs,
- rapid detection and treatment of *Taenia* carriers,
- vaccination of pig or cattle, and
- treatment of cysticercosis-positive animals.

There are a number of **non-specific** measures which are implemented to prevent a range of infectious diseases, such as diarrhea and intestinal parasites which are also very applicable in preventing taeniosis and cysticercosis.

- basic sanitation and hygiene,
- enclosure of pigs,
- meat inspection, and
- proper cooking of meat.

The future may hold more specific control measures such as vaccination, but in the meantime the control of taeniosis and cysticercosis should be based on of improved hygiene and meat inspection, where cysticercosis prevalence may be a good indicator of any change in practice, and hence, the effectiveness of preventive and control programs.

CHAPTER 6:
CONTROL MEASURES FOR TAENIOSIS AND CYSTICERCOSIS

Z.S. Pawowski, J.C Allan & H. Meinardi

6. Introduction

This Chapter on control measures discusses active interventions as potential packages, with primary focus on the reduction of mortality and morbidity caused by *Taenia solium* infection. Control, in its wider aspect, includes also some preventive activities, and these are presented in detail in Chapter 5.

6.1. Evolution of control measures

6.1.1. History of control measures

The oldest prevention and control measure against *T. solium* infections was abstention from consuming pork, suggested by ancient Egyptians as well as the Jewish and Muslim religions [253]. The effect of these cultural rules can be seen today as determinants of the global distribution of *T. solium* taeniosis/cysticercosis (see Chapter 3, Epidemiology).

After elucidation of the transmission of *T. solium* between humans and pigs in 1853, public instructions and warnings were issued to be careful with pork; the simplest preventive measure suggested then was the proper cooking of all pork to kill parasites. At about the same time, the East German population, which was fond of eating raw meat or semi-raw meat products, was afflicted by several severe epidemics of trichinellosis, which provoked even a stronger fear of consuming pork than neurocysticercosis was able to achieve [253]. It is worth mentioning that in the 1860s, the prevalence of cysticercosis in humans in Berlin was about 2% according to post-mortem examination data [324]. In 1886 the prevalence of cysticercosis in pigs in Berlin was nearly 6% and in the next 20 years it declined to less than 0.3% [402], due mainly to the adoption of meat hygiene practices.

Introduction of meat inspection in Germany by the end of the 19th Century was the first official preventive measure introduced in Europe. The role of rigorous meat inspection in Germany as an effective control measure is often overestimated, however. Other equally important measures were improvements in general sanitation, higher education levels, as well as more hygienic pig husbandry. At that time the available taeniacide drugs (Filix mas, kamala, Kosso flowers) were not widely used for control purposes because of their moderate efficacy and high risk of adverse side effects. For example, amongst 121 cases of intoxication with Filix mas there were 47 cases of permanent blindness and 17 deaths [257, 587].

It took several decades in Europe to control *T. solium* infections to where it is now, not even a minor public health problem in most of the continent. Occasional breakdowns occurred, for instance during World War II, when clandestine meat consumption became popular. Considerable increases in *T. solium* cysticercosis in humans and pigs occurred in some occupied territories i.e. in Poland and in Serbia in the 1940s. In the 1990s, there were still sporadic indigenous cases of transmission of *T. solium* in some European countries, including Germany [405] (see also Chapter 3, Epidemiology).

6.1.2. The growing scientific interest in control measures

The first large international conference on *T. solium* infections in developing countries, dealing mainly with laboratory and clinical aspects of the disease, was organised in San Miguel de Allende, Mexico in 1981. Although research oriented, the need for undertaking applied research on the control of cysticercosis in small endemic communities was formulated [315]. This was confirmed at a WHO Technical Consultation

in Geneva in 1983, which summarized the existing knowledge on *T. solium* prevention and control measures [601]. Following the suggestions raised at these meetings, several field research studies and interventions were undertaken, mainly in Mexico and Ecuador [98, 189]. In 1984 the WHO carried out a large operational intervention in Ecuadorean Andean endemic areas, which documented a focal distribution of *T. solium* infection in humans and pigs and also raised questions about the practicability of mass treatment of human *T. solium* carriers [98].

In 1988 a symposium on neurocysticercosis 'C-now' was organised in Rotterdam to discuss mainly progress in chemotherapy of neurocysticercosis; one of the conclusions was that baseline data on control of taeniosis/cysticercosis were still scarce [191]. Focal oriented chemotherapy of human taeniosis, as a control measure, was first suggested at the 33rd Southeast Asian Ministers of Education Organization (SEAMEO) Seminar in Chiang Mai, Thailand in 1990 and the definition of the focus of taeniosis/cysticercosis was formulated there [422]. Attention also was directed towards an 'economic cycle' of *T. solium* transmission in some endemic areas, which involves 'subsistance' pig farming, pig handlers, and meat suppliers [422].

At the 1990 Pan American Health Organization (PAHO) Informal Consultations in Porto Allegre Brazil, an urgent need for short-term control measures in endemic areas was accepted [408]. Immediate action was felt necessary to reduce the existing mortality and morbidity due to neurocysticercosis in humans in developing countries. This was supported by subsequent PAHO/WHO consultations held in 1995 [409].

6.1.3. International Task Force for Disease Eradication statement

The growing interest of the research and public health sectors in control of taeniosis/cysticercosis was increased in 1993 by an opinion of the International Task Force for Disease Eradication, that T. *solium* infection was potentially eradicable, even though greater experience in evaluating the efficacy and feasibility of control measures was required [71, 501]. This statement was based on the following reasons:

1. Tapeworm infection in humans is the only source of infection for man and pigs.
2. The reservoir of infection in pigs is restricted by the life span of these animals (rarely exceeding one year).
3. There is no significant reservoir of infection in wildlife.
4. Effective, inexpensive, easily deployed drugs are available for the treatment of human infections.
5. T. *solium* infections already have disappeared from most of Europe and the feasibility of significant reduction of *T. solium* transmission by population-oriented chemotherapy has already been demonstrated.

The statement of the International Task Force for Disease Eradication was a turning point in designing control measures against T. *solium* infections. For more than a century, the preventive and control measures were the responsibility and domain of veterinary services, but now the main responsibility for eradication of T. *solium* infections had shifted to medical services, which should be involved in the treatment of human taeniosis because it is the only source of cysticercosis in humans and in pigs.

It has to be emphasised that medical services were not fully prepared for an immediate change in approach to control measures because of:

- difficulties in the diagnosis of human taeniosis,
- a lack of availability of effective taeniacides, wherever needed,
- weaknesses in health infrastructures in rural endemic areas,
- inadequate co-operation between the medical and veterinary services,
- insufficient general professional understanding and political will to accept neurocysticercosis as an important public health problem in endemic areas, and finally,
- low levels of sanitation and health education in endemic areas.

6.1.4. Towards more active approaches in control measures

As a result of the International Task Force for Disease Eradication statement on potential eradicability, the importance of chemotherapy of human carriers has been generally accepted, along with chemotherapy in pigs, vaccination of pigs, improvements in sanitation and promoting education. The development of new diagnostic tools was promoted and several community-oriented control projects were undertaken. Operational knowledge and expertise concerning the efficacy of various interventions in endemic areas have since accumulated [189]. Recent advances in research and control measures were discussed at the North Atlantic Treaty Organization (NATO) Seminar on Emergent Zoonoses, held in Poznan, Poland in 2000 [92], at the International Action Planning Workshop on T. *solium* cysticercosis/taeniosis in Arusha Tanzania in 2002 [59] and at the SEAMEO Seminar in Bangkok Thailand in 2003.

In 2002 the problem of T. *solium* taeniosis/cysticercosis was presented at the World Health Assembly for the first time to attract attention of the Member States [605]. An operational project on the control T. *solium* in Peru has been financially supported by the Bill and Melinda Gates Foundation (Annex 6.7.4.). At the same time, the opportunity has been provided to include the control of human taeniosis into the Global Action on Epilepsy (see 6.2.).

There are also a few examples of governments of endemic countries with significant involvement in control measures e.g. in the People's Republic of China, Indonesia, Mexico, Poland, the Union of Soviet Socialist Republics and Vietnam [178, 193, 418, 419, 611].

6.1.5. Conclusions

By the first part of 20th Century, T. *solium* infections had been almost eradicated in Europe. This process took several decades and it was possible not only due to the enforcement of rigorous meat inspection but also to improvements in general sanitation and pig husbandry, and to improved economic and educational conditions in European societies. The epidemiological situation in some developing countries is now similar to that in Germany at the end of 19th Century.

For more than a century, control programs focused on the prevention of pig cysticercosis as a responsibility of veterinary services. In the 1990s control strategies were revised, placing more attention and responsibility on medical services with a focus on human taeniosis. This change in approach was possible due to the development of new diagnostic and chemotherapeutic tools useful for controlling human taeniosis. The concept of short-term control projects, based on chemotherapy of human T. *solium* tapeworm carriers and preventive measures such as sanitation and education, was developed. The chemotherapy and vaccination of pigs are more recent tools which may provide further options (see Chapter 5). Some diverse small control projects in various countries have been carried out on the initiative of individuals or groups of people, mainly academicians. The international community, especially the WHO, has supported many of these projects.

6.2. Justification for control of taeniosis/cysticercosis

6.2.1. Medical and economic justification

The control of taeniosis/cysticercosis is justified for medical and economic reasons. Intestinal tapeworm infections, such as *Taenia saginata,* T. *solium* or *Taenia saginata asiatica* taenioses, usually have a moderate impact on human health. Exceptionally, they may cause fatal complications or deep psychological stress [587]. However, the presence of a large worm in the intestinal tract is by itself frequently responsible for interference with digestive processes, and abdominal and psychological discomfort [302, 417, 425]. The major medical justification for T. *solium* taeniosis/cysticercosis control, however, is the mortality, morbidity and disability due to neurocysticercosis in humans.

In addition to causing health problems and complications, human neurocysticercosis is an expensive and socially important disease. The cost of the necessary laboratory and imaging diagnosis, and surgical or chemotherapeutic treatment of brain or ocular infection by T. *solium* metacestodes in individual patients

may reach hundreds of US dollars. The degree of disability due to epilepsy, mental retardation, psychological problems or vision impairment, caused by neurocysticercosis, is considerable. The global disability-adjusted life years (DALY) for epilepsy in developing countries is difficult to calculate mainly because of insufficient data being available. An individual's ability to cope with basic functions may vary widely from 0.1 to 0.8 points in DALY classification. Probably the quality-adjusted life years (QALY) approach would be more appropriate, when measuring the global burden of epilepsy due to neurocysticercosis.

Cysticercosis in animals, caused by *T. solium, T. saginata* and/or T. *saginata asiatica* is responsible for substantial losses including the cost of meat inspection, the reduced quality of meat, carcass condemnation, and obligator)' freezing or irradiation before consumption. These costs are carried by governmental agencies, feed lots and individual farmers [474].

Thus, in addition to a reduction in clinical problems and economic losses, control of taeniosis/cysticercosis can have a considerable positive social and political impact. This is trueof any attempt to improve human health and wellbeing, especially involving diseases which are visible and lead to social stigmatization, such as occurs in epilepsy.

6.2.2. Epilepsy is common and prevention is the most effective intervention

Epilepsy is a major scourge in the developing world. Ninety percent of the world's 40 million people with epilepsy live in developing countries. The available community-based prevalence data on epilepsy are relatively complete for industrialised countries but largely unavailable for the developing world. Examples of the prevalence rates in communities of various countries: England 3.3/1,000, USA 6.6/1,000, People's Republic of China 4.6/1,000, Ecuador 17/1,000, Liberia 26-40/1,000, Tanzania 20/1,000, and Uganda (some regions) 57/1,000.

The vast majority of epileptics in the developing world are currently not receiving regular treatment. Prevalence studies indicate that, for example, in Africa the prevalence of epilepsy is on average threefold greater than that in Europe or North America and in certain populations even tenfold. Furthermore, incorrect perceptions about epilepsy are often the reason why people with epilepsy are stigmatized and this can be an incentive to hide the presence of epilepsy. Further, symptoms from which certain persons suffer may not be recognized as a sign of epilepsy. Both these factors are a source of underestimation when assessing the prevalence of epilepsy.

The International League Against Epilepsy, International Bureau for Epilepsy, World Health Organization (ILAE/IBE/WHO) Global Campaign Against Epilepsy was established specifically to address a variety of issues, amongst which were that epilepsy is a non-communicable disorder with a substantial lack of public awareness and which requires a long duration of treatment and for which, even at the primary health care level, there is a general lack of understanding [278]. Although palliative treatment for seizures is possible, it has to be continued for many years and requires a considerable health infrastructure and drug supply. Considering its health impairment as well as social and economic losses, the prevention of epilepsy will be the most cost-effective long-term intervention.

6.2.3. Epilepsy and neurocysticercosis

There are many risk factors in epilepsy [282, 490]: genetic disorders, pre-, peri- and post-natal events, head injuries, bacterial and viral infections, and parasitic infections.

Infections are probably the most common preventable cause of epilepsy worldwide [282]. Among the parasitic invasions, neurocysticercosis is the most important as it may account for two-thirds of late-onset epilepsy i.e. starting above age 20. The relevance of neurocysticercosis in the etiology of epilepsy has become increasingly clear in the past 25 years. In particular, the availability of computerised tomographic scanning has been helpful in revealing that neurocysticercosis is an important factor contributing to the high prevalence of epilepsy in developing countries.

The relationship of epilepsy with neurocysticercosis in Africa has been extensively reviewed recently [132, 434, 442]. The prevalence of human cysticercosis in the general population, according to publications published between 1989 and 1994, ranged from 1.5% to 3.8% with the exception of some data from Madagascar reporting a prevalence of 18% [372]. However, the prevalence of cysticercosis in humans with epilepsy according to publications in the years 1987-1995 ranged from 10.8% to 50.9%. Among epileptic patients, there was a progressive increase of cysticercosis with age: prevalence rose from 13.5% for those in their twenties to 66.6% for those over 50 years of age [139].

A recent review of cysticercosis in Asia notes that neurocysticercosis is diagnosed in up to 50% of Indian patients presenting with partial seizures [459].

In Latin America a diagnosis of cysticercosis in epileptic patients increased to 29% after the advent of CT-scanners [107], while it has been reported that, in Mexico, 50% of people who showed an onset of epilepsy after age 25 were found to have neurocysticercosis [366].

Apart from epilepsy and repeated symptomatic seizures, neurocysticercosis can present other symptoms such as intracranial hypertension (ICH) or psychiatric symptoms. In a report from South Africa, ICH was found as a presenting symptom in 24% of 61 children with neurocysticercosis [560]. In India after the advent of CT-scanners, there was great interest in distinguishing between tuberculoma and neurocysticercosis, in particular with respect to single small CT lesions [452].

Cysticercosis is typically a disease of less developed countries, where good sanitary conditions are only available to the more affluent section of society. Epilepsy typically reduces the socio-economic status of families and therefore the high association of epilepsy and neurocysticercosis may be enhanced by the fact that families which already have a member with epilepsy often live under conditions that facilitate neurocysticercosis infections.

6.2.4. Anthelminthic treatment may reduce epilepsy

Anthelminthic treatment of human taeniosis reduces the incidence of cysticercosis both in humans and in pigs, and thus lowers the potential risk for epilepsy. The use of anti-parasitic drugs in neurocysticercosis has been the subject of controversy for more than 20 years. However, in a recent controlled study including only patients with 20 or fewer parenchymal cysts, a significant reduction in the rate of seizures with generalization and a non-significant decrease in the rate of partial seizures were observed in the treatment group (albendazole and dexamethasone) [218]. (See Chapter 2 on Clinical aspects for a fuller discussion on treatment).

6.2.5. Conclusions

There is no doubt that neurocysticercosis contributes to a higher prevalence of epilepsy in developing countries. Therefore, prevention of T. *solium* taeniosis will reduce the incidence of epilepsy. On the other hand, epilepsy can be considered an important marker of the presence *T. solium* infection, including neurocysticercosis.

The ILAE/IBE/WHO have initiated a global campaign against epilepsy intended to prove that identifying people with epilepsy and offering them an affordable therapy, combined with increasing public awareness about epilepsy, its causes and its consequences, will greatly reduce the burden of epilepsy in the developing world. In this respect collaboration with a control program to reduce cysticercosis should be mutually beneficial.

6.3. New tools for control of taeniosis

There are two key issues in controlling human taeniosis by chemotherapy i.e. the identification of human carriers and the availability of effective and safe taeniacides to eliminate the egg-producing adult worms. This section details the application of methods to improve the detection of human infections (taeniosis) by new antigen-detection methods which can greatly improve the chances for success in control programs

(see also Chapter 4 on Diagnosis for other methods). This section also discusses currently used drugs against taeniosis.

6.3.1. Diagnosis of taeniosis in humans

Classical parasitological techniques for the diagnosis of intestinal *Taenia* infections have limitations in both their sensitivity and specificity (see also Chapter 4 Diagnosis). The periodic absence of eggs or proglottids from infected host feces means than none of the classical approaches will always diagnose infection [417]. For example, diagnosis of *T. saginata* by microscopic detection of eggs in feces following the application of a concentration method was demonstrated to have a sensitivity of approximately 68% [259] whilst the application of a similar method for *T. solium* was shown to detect only 38% of cases [12]. Furthermore, since the eggs of T. *solium* and *T saginata* appear identical under the light microscope, speciation is not possible by this method. The questioning of patients regarding the expulsion of *Taenia* segments or parts of the strabilia may be of some diagnostic value but also has limitations [189, 417].

It is for these reasons that the previous WHO guidelines [601] promoted research to improve detection of the carriers of adult T. *solium* and T. *saginata.* In the intervening years a number of immunological or molecular approaches have either been developed or further refined in an attempt to achieve this goal [289, 352, 579]. One of these approaches, based on the detection of taeniid antigens in infected host feces, has been applied on a reasonably large scale in both epidemiological and control studies (Table 6.1).

6.3.2. Taeniid Coproantigen detection

The principal behind Coproantigen detection is the identification of parasite-specific antigens in the feces of infected hosts using antibodies raised against parasite material. By detecting parasite antigens the technique should be capable of diagnosing current infections. If these antigens are produced independently of the parasite's reproductive status, a diagnosis should be possible during the prepatent period and during other periods when parasite eggs are absent from feces. An alternative immunodiagnostic approach, based on the detection of specific antibodies in sera, exhibits low sensitivity and may remain positive for relatively long periods after the end of the intestinal infection [14].

All tests reported to date have been based on antigen capture type ELISAs. The antibodies used in these tests have been raised by the hyperimmunization of rabbits. The following material has been used as the basis of the antigen used for immunizing the rabbits:

a) homogenized adult T. *saginata* [7] or T. *solium* proglottids [7]

b) *T. solium* [6] or *T. saginata* [124] excretory-secretory antigens

c) surface fraction of adult T. *solium* [338] or *T. saginata* tapeworms [340].

These tests and work carried out in animal models for human taeniid infections [8, 125] have all shown remarkably consistent results including:

- Genus level specificity has been achieved: *T. saginata* and *T. solium* are both positive in the tests but no cross reactions occur with feces from people infected with other gastrointestinal parasites including *Hymenolepis* spp.
- Diagnosis is possible prior to patency (several weeks prior in animal models) with Coproantigen levels independent of the presence or number of eggs in the feces. There are also data from animal models that indicate that Coproantigen levels may vary somewhat on a day-to-day basis.
- Coproantigen levels drop to background within approximately one week of successful treatment of the infection.
- *Taeniid* coproantigens are stable for days in unfixed fecal samples held at room temperature and for months or years either in frozen samples or in samples fixed in formalin and kept at room temperature.
- Assay sensitivity is dependent on the quality' of the antisera used (high titre antibodies are recommended) and on the assay format (both microplate and dipstick formats have been used to date) but has generally been good.

Table 6.1. Performance of the *Taenia* Coproantigen test in field trials

Analysis of diagnostic data collected in epidemiological studies using the Coproantigen test based on antibodies to *Taenia solium* in either the microtitre format [7] or dipstick format [10]

Test Type/location	Total samples	Total parasitologicall y confirmed *Taenia* cases *	*Taenia* cases diagnosed by Coproantigen (% of all cases cor	*Taenia* cases diagnosed by microscopy rectly diagnosed)	Coproantig en false positives (%)
Microtitre Guatemala (5)	414	2	2 (100%)	2 (100%)	0 (0%)
Microtitre Guatemala (6)	1,582	56	55 (98%)	21 (38%)	12 (0.8%)
Microtitre Mexico (87)	475	7	7 (100%)	0 (0%)	3 (0.6%)
Microtitre Indonesia; Bali (83)	415	3	3 (100%)	3 (100%)	0 (0%)
Microtitre Indonesia; Papua (63)	58	5	5 (100%)	1 (20%)	0 (0%)
Microtitre multistudy results**	2,944	73***	72 (99%)	27 (37%)	15 (0.5%)
Dipstick Guatemala (5)	1,710	33	25 (76%)	18 (55%)	3 (0.2%)
Dipstick Mexico (5)	2,018	8	6 (75%)	5 (63%)	1 (0.05%)
Dipstick multistudy results**	3,728	41****	31 (76%)	24 (59%)	4 (0.1%)
Microtitre peru***** (39)	1,620	21	45?	20?	ND

* *Parasitological confirmation was made on the basis of detecting eggs in feces and/ or recovery of tapeworm material post treatment*

** *The two multistudy analyses are carried out where the study designs were largely similar; all fecal samples mere collected pre-treatment and treatment of all Coproantigen and/ or microscopy-positive individuals was made with niclosamide to confirm infection. Microscopic techniques varied somewhat from study to study but in most cases involved an egg concentration method*

*** *48* T. solium, 3 T. saginata *and 22* Taenia *spp.*

**** *29* T. solium, / T. saginata *and 11* Taenia *spp.*

***** *The Peruvian study methodology differed from that of the other studies as follows diagnostic fecal samples were collected immediately follwing mass treatment of the population with praziquantel and definitive parasitological confirmation of all Coproantigen positive results was not pursued. Some of the 45 Coproantigen positive results may therefore represent false positives. The Coproantigen test correctly diagnosed 17 of 21 parasitologically confirmed Taenia infections (81%).* Taenia *species identification nas not carried out*

6.3.3. Field study using Coproantigen test

To date one test, based on antibodies raised against adult *T. solium* tapeworms recovered from immunosuppressed hamsters [7], has been used in field studies and has been reviewed recently [14].

Most studies have been carried out using a microtitre-based ELISA format where testing has been carried out in a laboratory but a dipstick type format has also been used where testing has been carried out in rural villages [10]. The latter test was less sensitive than the microtitre-based format but performed well under field conditions and was nonetheless more sensitive than microscopy [10]. Some sensitivity was lost in the dipstick test in order to ensure a high level of specificity and because it was not practicable to add fetal calf serum to the fecal samples during testing which led to approximately 10% of tests being uninterpretable due to the effects of the fecal material on the test strips [8].

One useful feature of the test when it comes to its field application is the ability to test fecal samples that have been stored in 5% formalin solution [8, 12]. It is recommended that, if this approach is taken that

samples are collected and stored in 5% formalin solution diluted in phosphate buffered saline pH 7.2 containing 0.3% Tween 20 [12]. Stored in this way, samples are stable for months.

Results of a number of field studies involving these tests are given in Table 6.1. It should be noted that the data obtained in these field studies relates mainly to *T. solium* and, to date, the test's field performance against T. *saginata* remains largely uninvestigated. However, it has been shown, that a similar ELISA had a high specificity and sensitivity in detecting patients with intestinal *T. saginata* infection [124].

The studies, carried out in largely *T. solium* endemic areas, have demonstrated that microscopy diagnoses only approximately one third of intestinal *T. solium* cases, while the Coproantigen test based on the microtitre format typically produces a positive result in between 81% and 100% of all parasitologically confirmed cases i.e. between two and three times as many cases as are detected by microscopy. The differential diagnostic advantage of the Coproantigen test over microscopy in the diagnosis of the more fecund T. *saginata* parasite may be lower. It was shown, that 85% of the infected patients were identified by Coproantigen ELISA and 62% by egg detection [124].

The test is not completely specific and it does produce some false positives, though specificity has consistently been greater than 99% in all studies. It is recommended that, despite the high specificity of the tests, worm recovery through treatment should be used as a technique to confirm infection at least randomly [12].

6.3.4. Practical issues of coproantigen testing

The improved sensitivity and high specificity of Coproantigen tests for intestinal *Taenia* have allowed the practical application of the tests in both epidemiological and intervention studies on *T. solium.* However, the performance of these tests in field studies on *T. saginata* remains largely unknown (see also Chapter 4 Diagnosis).

The test is still not widely available, being produced only by certain research laboratories. Currently no commercially available test is on the market. Most existing commercial ELISAs based on a similar antigen capture format, for example for *Giardia,* are relatively expensive and this has limited their wide scale application in many developing countries. The technology itself is, however, not complicated and it may thus be useful to establish a system of reference laboratories, which could provide tests. The provision of cheap standardized tests for use in epidemiological or control studies on intestinal *Taenias* in the developing world would improve the quality of data available in many parts of the world. Sera from a single rabbit can be used to develop tests for in excess of 40,000 individuals (Allan, personal observation) thus a relatively small number of reference laboratories could generate relatively large amounts of reagents without much difficulty.

The application of microtitre format tests requires a reasonable level of laboratory equipment (including centrifuges, refrigerators, ELISA plate readers, pipettes etc.). Nonetheless it has proved possible for a single trained operator to test in excess of 100 samples in three to four hours. This compares favourably with microscopy.

Further work is ongoing to characterize the nature of taeniid coproantigens with a view to improving test performance. The coproantigens are predominately of large molecular weight (approximately 150 kDa to 600 kDa) and heavily glycosylated [144, 192]. With a better understanding of the nature of the molecules involved, it may be possible to further refine the test format to make it simpler to apply under conditions of minimal laboratory infrastructure.

6.3.5. Drugs for treating human carriers: older taeniacide drugs

For a long time, treatment of human taeniosis was both toxic and not fully effective. Among several traditional drugs, only pumpkin seeds *(Cucurbita pepo, C. maxima)* were non-toxic but the efficacy of a single dose of 250 g was only around 65% [85, 412, 417]. Areca nuts are widely used in Asia as a national remedy against parasites and/or commonly chewed in rural areas. However, Areca nuts are implicated as a frequent cause of oral cancer and their use is discouraged [619]. Kosso flowers, still widely used in

Ethiopia, containing koso-toxin, closely related to filicic acid, are responsible for some cases of hepatic carcinoma and blindness [126, 481, 570]. An extractum of male fern, *Dryopteris filix-mass,* containing filicic acid, was widely used in Europe in the early 20th Century and was banned in the 1950s because of several cases of toxicity. Out of 121 reported cases of intoxication, there were 47 cases of permanent blindness and 17 deaths [257]. Older synthetic drugs such as thymol and some newer ones such as tetrachlorethylene, carbon tetrachloride, dichlorophen, bithionol and hexylresorcinol were neither well tolerated nor very effective [253]. Atabrine, introduced in the 1940s was effective, especially when given in a solution by a duodenal tube; it was also withdrawn from the market in the 1960s because of considerable side-effects and potential carcinogenicity. Tin compounds, consisting of metallic tin and tin oxide, used in the 1950s, were very effective but their use was reduced after niclosamide was introduced [413].

6.3.6. Currently used drugs for treating taeniosis in human carriers (see also Chapter 2)

6.3.6.1. Niclosamide

Niclosamide was introduced in 1959 as the first effective, synthetic and non-toxic taeniacide [427, 428, 601]. Niclosamide is a halogenated salicylanilide, and as very little is absorbed from the gastrointestinal tract, it is well tolerated and safe. It works specifically against intestinal cestodes (T. *solium, T. saginata, Diphyllobothrium* spp. and *Hymenolepis nana)* by blocking glucose uptake. The efficacy of niclosamide for taeniosis is about 85%; generic drugs and long series of treatment may be less effective due to time-dependent polymerization of the active particles. There are no known contraindications to niclosamide, except concomitant use of alcohol and an age of less than two years. Niclosamide can be used in pregnant women infected by *T. solium* tapeworm.

Niclosamide is produced in 500 mg tablets, which should be chewed thoroughly before swallowing and washed down with some water. A saline purgative is not necessary except in chronically constipated patients, who should be appropriatelytreated the evening before the therapy. Niclosamide is given in a single dose of 2 g for adults, 1 g for patients below 35 kg and 0.5 g in children below 10 kg of body weight. Side effects are rare and negligible, frequently related to the disintegrating tapeworm. Following treatment, it might be difficult to find the expelled scolex as it may become detached from the strobila. Therefore, the therapy is accepted as successful, if a patient remains free of infection two and one-half months after treatment (absence of expelled proglottids, negative Coproantigen test, absence of *taeniid* eggs in coproscopical examination or on anal swabs).

Since 1977 niclosamide has been on the WHO Essential Drugs list [604, 607]. The cost of the cure is usually higher than that of praziquantel. Mainly for economic reasons, niclosamide has been rarely used in *T. solium* mass treatment interventions [11].

6.3.6.2. Praziquantel

In 1972 praziquantel was introduced as a safe and very effective drug against a wide spectrum of cestodes and flukes [24]. Praziquantel is an acylated isoquinoline-pyrazine, well absorbed from the intestine and therefore active against tissue parasites such as cysticerci, certain species of liver fluke and schistosomes. The mechanism of action is not fully understood; the drug increases calcium permeability and causes blisters on the integument. The use of praziquantel is contraindicated in patients with ocular cysticercosis, as it may provoke an intensive inflammatory reaction around the damaged cysticerci. This mechanism may also be responsible for some neurological symptoms provoked sporadically during praziquantel treatment of asymptomatic cases of neurocysticercosis [187]. However, this adverse effect is not a reason to cease using praziquantel in mass treatment interventions because sooner or later some asymptomatic cases of neurocysticercosis may become symptomatic due to the natural course of infection; treatment with praziquantel may accelerate this process on sporadic occasions. The use of low but still effective doses of praziquantel decreases the risk of such complications [98, 421]. A warning was given that, during mass treatment of schistosomiasis with high doses of praziquantel (40 mg/kg) in areas endemic for cysticercosis, a brisk localised oedematous reaction may occur. No evidence is on record that this has ever resulted in serious sequelae [604]. Safety in children under four years of age has not been established. There are no formal contraindications for the use of praziquantel in pregnancy. Adverse reactions are rare, mainly in the form of abdominal discomfort, pyrexia and urticaria [604].

Praziquantel is produced in two tablets sizes: 150 mg against intestinal tapeworms and 600 mg against the other helminthoses, including *T. solium* cysticerci. The therapy against intestinal tapeworms consists of a single day treatment, while in cysticercosis the treatment may be continued for a few days. Also, the size of the dose differs from 5-10 mg/kg b.w. in intestinal *Taenia* invasions, to 15-25 mg/kg in hymenolepiosis and diphyllobothriosis and up to 40-60 mg/kg in schistosomoses [604]. It was confirmed that even a dose as small as 3 mg/kg may be effective against *T. saginata* taeniosis [98, 420]. The calculation of the exact dose per kg of body weight is difficult. The drug can be very bitter and has to be swallowed quickly and washed down with water. In *T. solium* and T. *saginata* infections, half a tablet (75 mg) should be given to individuals weighing 8-15 kg (dose range 5-10 mg/kg); one tablet (150 mg) should be given to individuals weighing 15-30 kg (dose range 5-10 mg/kg), two tablets (300 mg) should be given to individuals weighing 30-60 kg (dose range 5-10mg/kg) and three tablets (450 mg) or one tablet 600 mg should be given to people over 60 kg of body weight (dose range 10 mg/kg or less).

Praziquantel is relatively well tolerated. The efficacy of the therapy in human taenioses is around 95%. The cure can usually be accepted as effective after two and a half months using similar criteria as for niclosamide treatment.

Since 1985 praziquantel has been listed on the WHO Essential Drugs list [604, 607]. A single treatment with praziquantel is cheap and costs about ten US cents per case; discount prices are given by buying larger quantities through the WHO.

6.3.6.3. Albendazole

Albendazole, widely used against nematode invasions such as ascariosis, trichuriosis and hookworm infections, showed some efficacy against tapeworms when given in much larger doses over a few days [82]. Albendazol should not be used in pregnant women. In practise, albendazole is now used against T. *solium* cysticerci only.

6.3.6.4. Nitazoxanide

Nitazoxanide, a nitrothiazolyl-salicylamide, having a structure close to niclosamide, has been introduced recently as a broad spectrum antiparasite agent [596], It is effective mainly against intestinal protozoan infections such as cryptosporidiosis and giardiosis but it works also against some soil-transmitted helminthoses and taenioses. Its feasibility in *T. solium* control interventions has to be confirmed.

6.3.7. Conclusions

The presence of *Taenia* spp. tapeworms in humans may be suspected by questioning and analysis of a patient's medical history (late epilepsy cases). Confirmation of the infection by classical parasitological methods has several limitations. Coproantigen tests are now possible and have a high sensitivity. However, they are still not widely used in *T. solium* endemic areas. Species-specific diagnosis, differentiating T. *solium* and T. *saginata,* can be made by examination of the scolex and proglottids of the parasite and also by some molecular and immunological techniques, Coproantigen tests included. Wider availability of Coproantigen tests in endemic areas would be beneficial for effective surveillance and control of T. *solium* infections.

Presently there are two well-known synthetic, safe and highly effective drugs against tapeworms in humans, i.e. niclosamide and praziquantel. In developing countries, the non-toxic natural remedies, such as pumpkin seeds, can be accepted for individual treatment but the use of other natural remedies, such as Areca nuts and Kosso flowers has to be discouraged because of their high toxicity and/or carcinogenicity. The choice of drug for individual treatment and mass intervention depends mainly on availability and cost, although sporadic contraindications have to be respected as well. There is still room for the development of new formulations of natural remedies, such as pumpkin seeds, for the confirmation of the practicability of new products such as nitazoxanide, or for reconsidering the use of tin compounds.

6.4. Implementation of control measures

6.4.1. Focus of control measures

Taenia solium infection has a definite priority for the control of human infections with the Taeniidae, because of the impact of neurocysticercosis, its clinical sequelae and its considerable public health, social and economic significance. *T. saginata* infections, whilst common in several developed and developing countries, usually causes only moderate medical problems of little public health importance, although it may cause some economic losses [415, 474, 602]. There is not yet enough data on T. *saginata asiatica,* which is not likely to be responsible for human neurocysticercosis, to evaluate its public health importance and to plan its control [285]. In practice, however, all taeniid infections, including T. *saginata* taeniosis/cysticercosis, will benefit from *T solium* control programs because control measures cover all taenioses:

- different species of *Taenia* frequently co-exist in the same regions,
- differential diagnosis between the Taeniidae is difficult and sometimes uncertain without considerable parasitological experience, and availability of expensive immunological and molecular techniques, and,
- drugs for treatment of human taeniosis act against all three *Taenia* species involved.

In many situations in which the exact species diagnosis is not available, the most pragmatic control approach is to treat all diagnosed or suspected case of taeniosis in humans, without spending money and time in differentiating the species. This approach does not, however, exclude the need for the differentiation of *taeniid* species parasitizing humans for research and surveillance purposes [285, 396, 505]. Some basic information about the approximate occurrence and prevalence of *T. solium* and *T. saginata* infections in a region could also come from local meat inspection data.

6.4.2. Objectives of control measures

The International Task Force for Disease Eradication has described the important factors, that make T. *solium* eradicable [71, 501]. However, in contrast to some other parasitic infections (e.g. dracunculosis and ascariosis), the effective eradication of *T. solium* infection, although theoretically simple, is in reality veny difficult in practise and currently cannot be foreseen in the immediate future [145]. The effective control of *T. solium* infections in most of Europe took several decades and required many changes in economic, educational and sanitary standards, and improvements in the effectiveness of medical and veterinary services, especially meat inspection. These are not likely to be duplicated soon in many parts of the developing world.

The risk factors responsible for T. *solium* transmission in endemic areas in developing countries are (see also Chapters 3 and 5 for more detailed discussion):

- a low level of general sanitation and education in endemic areas,
- the low cost of 'subsistence' raising pigs in unsanitary conditions,
- unregulated animal traders and meat sellers, selling infected pigs or meat,
- other local health priorities,
- inadequate local health service infrastructure,
- insufficient local cooperation between medical and veterinary services,
- difficulties in identifying human *T. solium* carriers,
- the lack of taeniacides where they are needed, and
- risky local customs [346].

Major factors such as lack of sanitation, low level of education, inadequate economic motivation and deficient legislation are unlikely to change within a few years. Therefore, the realistic aim of control is to reduce the incidence and prevalence of *T. solium* infections in humans and pigs to the level that human neurocysticercosis does not constitute a major public health and economic problem in a given endemic area.

6.4.3. Strategies for *Taenia solium* infection control

Potential strategies for the control of *T. solium* infections have been up-dated recently [9] (Table 6.2.). Of the six proposed approaches, three (based on medical and veterinary interventions) have the potential to meet short-term control goals. These are:

- treatment of human carriers,
- treatment of cysticercotic pigs, and
- vaccination of pigs.

The other three are are more appropriate as components of long-term programs or have a supportive value in short-term control projects:

- improved sanitation,
- changes in pig husbandry, and
- higher levels of general education.

The treatment *of* human tapeworm carriers is now accepted as a key factor in the strategy for controlling *T. solium* infections [179, 211, 212, 422, 494]. Treatment breaks the transmission chain immediately and protects other human beings and pigs against infection. There are several examples from field studies indicating that treatment of T. *solium* carriers has a beneficial effect on the prevalence of cysticercosis in pigs a year after intervention [71, 98, 189]. Mass therapy of the entire population in endemic areas, however, as shown in the early WHO operational studies in Ecuador [98], may not be effective or justified because of the focal distribution of *T. solium* infections. Mathematical modelling of the efficacy of the mass treatment of T. *solium* infections suggests that eradication can be achieved after 11-15 rounds of anthelminthic therapy [242], Therefore, it is sensible to replace mass treatment by focus-oriented treatment wherever possible.

Definition of control focus

The focus in endemic rural pig breeding areas is defined [408, 421, 422] as:

- a locality with a high percentage of cysticercotic pigs, or
- a farm supplying cysticercotic pigs.

In rural and urbanised areas outside the cysticercosis endemic areas, the focus might be:

- a patient with late epilepsy (also other family members),
- any case of detected or suspected taeniosis, irrespective of *Taenia* species being involved.

Because the identification of human *Taenia* spp. carriers in a population at large might be difficult, encouraging and educating the community in self-detection of taeniosis and offering diagnostic and treatment services (possibly free) are of value. In Poland the diagnosis and treatment of T. *saginata* taeniosis has been free of charge since the 1970s; infections were officially reported and administrative pressure was exerted by health authorities on those who were not willing to be treated or re-treated. The results of such a policy led to a substantial reduction of *T. saginata* infection in the population from 35/100,000 in the 1970s to 3.2/100,000 in 1997 [418, 422],

The potential impact of chemotherapy or vaccination of pigs, a potential source of infection to humans, is presented in Chapter 5 on Prevention. Treatment of the pigs and vaccination are, however, auxiliary approaches, and do not have an immediate effect on the existing pool of human carriers who, if left untreated, will continue to produce eggs for at least some years.

Promotion of safe meat production and consumption requires legal support and the education of consumers (see Chapter 5).

Table 6.2. Synopsis of intervention strategies available for *Taenia solium* taeniosis / cysticercosis [9]

Intervention strategy	Advantages	Disadvantages
Elimination of infected pig carcasses (meat inspection)	• Known contribution to elimination of parasite from several developed countries • Relatively easy to integrate with meat inspection for several other important diseases	• Pigs in many endemic countries do not go to formal slaughter • Infected pigs can be diagnosed *ante-mortem* (tongue inspection) and slaughtered outside regulated system to avoid condemnation of carcasses
Improved sanitation, hygiene and pig husbandry	• Known contribution to elimination of parasite from several developed countries • Provides benefits beyond control of *T. solium*	• Economically difficult in many existing endemic areas
Health education	• Provides benefits beyond control of *T. solium* • New media now widely available	• Improved knowledge does not always result in change of practises • Inefficient as sole strategy
Treatment of intestinal taeniosis	• Highly efficacious drugs now available (some generically produced niclosamide may have low efficacy) • Demonstrated short-term benefits • Removes known significant transmission risk	• Would require repeated interventions for long-term control • Requires specific infrastructure; not self-sustainable • Praziquantel should be used with caution in cases of cysticercosis
Vaccination of swine	• Long-term protection • Possible to integrate with existing veterinary and/or pig husbandry practices • Provides economic benefit to end user (avoidance of carcass condemnation) • Compliance monitoring possible (serological testing)	• Many existing producers in endemic areas do not currently vaccinate against other diseases with high economic impact on swine production • Vaccines not available now (other than at experimental level)
Chemotherapy of infected swine	• Drugs available now • Highly effective • Producers have economic motivation (avoidance of carcass condemnation) • Other production benefits: can affect other economically important parasites of swine	• Producers often do not treat for other economically important parasites despite economic benefits • Existing systems of avoiding meat inspection reduce economic advantages

6.4.4. The categories and timing of various control programs

The actual plans for *T. solium* control programs vary by the scale of intervention, timing, organizational complexity and cost (see Table 6.3). There are three major categories of T. *solium* control programs:

- specific long-term, usually nation-wide,
- specific short-term, usually concentrated on local endemic areas, and
- alternative programs, nation-wide and based on existing medical and veterinary services.

Table 6.3. Basic characteristics of various *Taenia solium* control programs

	Long-term program	Short-term program	Alternative program
Aim			
Eradication	X		
Lowering mortality & morbidity		X	X
Strategies			
A package of preventive measures	X		
Focus oriented chemotherapy		X	
Taeniosis chemotherapy at large			X
Range			
Nation-wide	X		X
Endemic areas		X	
Timing			
Decades	X		
Years		X	X
Priority			
National	X		X
Local		X	
Organizational Framework			
Special committees	X		
District coordinator		X	
Existing services plus academic institutions			X
Cost			
Considerable	X		
Moderate or low		X	X
Intersectorial cooperation			
Multifarious	X		
Medical and Veterinary. Services		X	
Teaching and training			X
Evaluation			
Indirect	X		X
Direct in foci		X	

6.4.4.1. Long-term programs

Long-term programs, designed to be carried out over decades, are aimed at ultimate eradication of T. *solium* infections in a country or region. These programs involve appropriate legislation, health education, modernization of swine husbandry practises, and more efficient and all-inclusive coverage of meat inspection. Political and economic realities in many endemic areas provide little hope that all these measures can be implemented in the near future [505, 506].

There are two detailed plans for long-term control programs for *T. solium* control in Latin America [408] and South-east Africa [59]. Both were elaborated on a regional scale and are to be managed by special committees under a governmental umbrella (see Annexes 6.7.1 and 6.7.2). The PAHO document addresses both long-term and short-term programs, with an emphasis on the treatment of human carriers [408]; the long-term program is characterized by high organizational complexity and considerable costs but it has had some implementation difficulties in Latin American countries. The Cysticercosis Working Group in Eastern and Southern Africa (CWGESA) program is a long-term program based mainly on prevention of cysticercosis in pigs; only some elements of the short-term program, such as chemotherapy of human carriers, have been included [59].

6.4.4.2. Short term programs

A short-term program approach has been proposed for Latin America by PAHO [408] (see Annex 6.7.3). The objectives are an immediate reduction in the number of human *T. solium* carriers by targeted interventions e.g. focus oriented therapy. Although the required effective and safe taeniacides are available, major obstacles to carrying out the plan have been the difficulty in identification of tapeworm carriers, insufficient taeniacide supply, ineffective local cooperation of medical and veterinary services, insufficient health education and competing local priorities [91].

Short-term control programs do not require a large administrative apparatus, only a responsible country or district coordinator with the capability and power to integrate the local activities of existing services (mainly medical and veterinary). Existing knowledge can to be applied and no additional research is required although some operational research may be needed to evaluate and improve implementation of the program.

6.4.4.3. Alternative programs

An alternative program for consideration is based on the maximal use of existing medical and veterinary services to control specific foci of *T. solium* infections. The implementation of an alternative program, however, requires adequate health service infrastructures [493]. This alternative program, potentially long lasting, is primarily based on:

1. the education and training of medical and veterinary staff,
2. ensuring mutual cooperation of the above, and
3. an adequate supply of effective and safe taeniacides to treat diagnosed or suspected cases of human taeniosis.

(NOTE: Until the specific diagnosis of T. *solium* taeniosis in humans is both widely available and cheap in endemic areas, the clinical severity of human neurocysticercosis justifies specific treatment not only in diagnosed cases but also in cases suspected on clinical or epidemiological grounds).

Firstly, standardized protocols on how to define potential foci of *T. solium* infection (a case, a family, a locality) and on how to treat (praziquantel, niclosamide) human tapeworm carriers in a foci have to be developed and communicated to all levels of medical services, especially those in endemic areas that deal with peripheral health units assigned to primary health care.

Secondly, the terms of cooperation between local medical and veterinary services in defining *T. solium* foci and the exchange of available information must be developed and promoted.

Thirdly, a supply of effective, possibly free or inexpensive, taeniacides must be assured.

Finally, a system of supervision to ensure that the program is implemented and managed correctly has to be established, and any identified obstacles removed (see Annex 6.7.4.); this must include a sound plan for evaluation of the program.

6.4.5. Scope of a control program

The scope of a control program and its measures must be considered for any given area and for any given group of people that are to be covered by the program.

Taenia solium

A *T. solium* control program can be region-wide or nation-wide, or area specific. Any long-term intervention would have to be organized on a national or region-wide scale. However, the prevalence distribution of *T. solium* taeniosis/cysticercosis is not always uniform; frequently, only some areas are affected. These are usually parts of the country or communities with abundant small private pig farms.

Thus, short-term control programs, especially in cases where only limited resources are available, can be applied in an area-specific manner. The task is to first identify such areas and next to concentrate all control interventions in those areas. The eradication of taeniosis/cysticercosis in several endemic areas would certainly have an impact on the prevalence of taeniosis in humans in other parts of the country as well.

There are two major groups of people to be considered for control by chemotherapy of human taeniosis. One is a rural local community, where transmission occurs between infected people and susceptible pigs living in close proximity and from where infected meat is widely distributed, putting at risk the local population and individuals living outside the endemic area. Most of the control projects undertaken to date have been aimed towards such groups of rural people [93, 129, 130, 189, 220, 395, 496].

The other, somewhat invisible group, is a widely dispersed subpopulation of human T. *solium* carriers, responsible for spreading human cysticercosis (through human to human infection) at national or international levels. One can find these carriers anywhere e.g. in urbanized or peripheral regions and amongst travellers or immigrants to other countries [506]. The control of such a dispersed body of tapeworm carriers is difficult and is frequently overlooked in *T. solium* control programs. However, they constitute a large reservoir of T. *solium* tapeworms, producing potentially enormous quantities of T. *solium* eggs over a period of several years that can be transmitted as a fecal-borne infection, directly to individuals close to the carrier and indirectly through contamination of the environment. The size of this group of dispersed T. *solium* carriers is difficult to estimate but is probably considerable, judging from individual patient histories or sporadic epidemic observations in non-endemic countries [488, 502, 503, 506].

6.4.6. Optimal choice of a control strategy

As discussed above, control strategies vary widely in scale (region, nation, area), timing (decades, years), priority (high, low), organizational framework (committees, supervisors) and responsibility (considerable, moderate or low), and their intended or actual effect (eradication, lowering mortality and morbidity) (Table 6.3).

Available data suggest that choosing a single approach to T. *solium* control may not be sufficient. Better results would probably be achieved by certain combined approaches e.g. chemotherapy of *T. solium* carriers and education [493], chemotherapy of human carriers and pigs [240, 241], and/or the promotion of hygiene and restraint of pigs [575]. The choice of a strategy for a control program has to be based on the collection of objective hard data to answer the following questions: Why? Where? Is it a priority? Whose responsibility? For how much? And with what support?

For the question **'why?'** subchapter 6.2. on Justification suggests an answer.

The answer to the question **'where?'** could come from surveillance data, reports from veterinary services or hospitals, and locally performed studies (see 6.4.4.1). A detailed and complete picture of the epidemiological situation in a country may not be achieved easily but hyperendemic areas can be identified without too much effort e.g. by an analysis of meat inspection data (regardless of how deficient these data may be).

Depending on the epidemiological situation, the national priority for the control of T. *solium* might be low in comparison with the other national health problems, such as AIDS, tuberculosis, malaria, but the local priority may be high. The involvement of local communities and its leaders is essential to start local control programs.

The organizational responsibility may be delegated to special committees or specific coordinators and supervisors (see Table 6.3).

In programs based on the chemotherapy of human *T. solium* carriers, an unavoidable cost is that associated with the supply of the drug and its delivery. The other costs, such as program coordination, supervision and evaluation can be covered by the general health budget.

A *T. solium* control program has many unique approaches and facets, and it might be difficult to combine such a program with other health or developmental projects. However, a *T. solium* control program does have some strong links with water and sanitation projects, primary health care initiatives, food safety campaigns (see also Chapter 5) [605, 606, 607], health education initiatives and soil-transmitted helminthoses control [500]. Any *T. solium* control program should also have some coordination with the Global Epilepsy project with strong working relations with its activities [278]; see also Section 6.2.2).

6.4.7. Evaluation of the control program

Several indicators of the efficacy of control programs exist and a selection can be made from these. One of the most useful is observations on the prevalence of cysticercosis in local pigs, detected by meat inspection; this will demonstrate changes in the dynamics of T. *solium* transmission in a reasonably short time frame, i.e., within a year (the survival time of most of the pigs). Pigs raised in an area covered by the program can serve as a control group of sentinel animals, and cost relatively little [98, 241]. The rate of clinical cysticercosis detected in hospitals and/or the rate of notified cases of cysticercosis or taeniosis in a given population can be analyzed only over several years, due to the long duration of infection by both the intestinal and tissue stages of the parasite. One of the rarely used indicators of T. *solium* taeniosis prevalence is the examination by specific Coproantigen tests of a selected uniform group within the population e.g. military recruits, students, food chain workers, hospitalized patients, and pregnant women under constant medical care. There are some good examples of such a surveillance in street vendors and military recruits [204, 219].

6.4.8. Conclusions

Taenia solium infection has a definite priority for control within the range of human taeniid infections. Difficulties in diagnosing human tapeworm carriers in an endemic area or in a focus of *T. solium* infection suggest that any diagnosed or suspected case of taeniosis in humans should be treated, without spending efforts on differentiating the species. This approach results in all taeniid infections in humans and animals coming under the same control measures and benefiting from the *T. solium* control program. The eradication of T. *solium* infections, although theoretically simple and feasible, is very difficult in practise and cannot be easily realised within a defined time frame.

Thus, the realistic aim of control is to reduce the incidence and prevalence of *T. solium* infections in humans and pigs to the level where human neurocysticercosis does not constitute a major public health and economic problem in a given area. Experience with the population-based treatment of human carriers of *T. solium* tapeworms suggests that wherever possible mass treatments should be replaced by focus-oriented treatments. There are three major categories of control programs: specific long-term nation-wide programs; specific, local short-term programs; and certain alternative programs. These programs differ in their scale, timing, organizational complexity, costs and expected results. Most of the studies undertaken to date have been conducted in rural endemic areas. However, there exists a widely dispersed population of human *T. solium* carriers outside the endemic rural areas. There is evidence that free-of-charge, specific diagnostic and treatment services offered to the population at large have lowered the prevalence of T. *saginata* taeniosis on a national basis. Indicators for the evaluation of the control measures are necessary and practicable (e.g. by the use of locally raised pigs as sentinels or indicators of human infections). The choice of the optimal control strategy, on whatever scale, has to be done on a national or regional level. This is urgent because neurocysticercosis is a growing serious public health problem in many developing countries, especially in Africa; and delay will only make the situation far worse [434, 435].

Descriptions of actual national or regional control program models or protocols are described in Annexes 6.7.1 to 6.74. These are accompanied by comments on their features and implementation issues, and will assist readers in formulating their own protocols.

Standards and the management of human taeniosis control measures are summarised in Annex 6.7.5.

6.5. A summary of research and logistic needs[2]

A successful implementation of sustainable and cost-effective control programs, however simple, requires some preparatory specific activities in research and logistics. The following briefly describes some of these research needs:

6.5.1. Basic research needs

- Simplification of the specific antigen-based diagnostic tests for human tapeworm carriers, possibly using saliva instead of fecal material. A test for population studies should be technically simple and have acceptable sensitivity and specificity. The test must be relatively inexpensive in order to permit its use in mass diagnosis of humans and animals.
- Further development of effective, safe and cheap taeniacides for use in treating human tapeworm carriers and pigs suspected of cysticercosis; for example, studies on active substances in pumpkin seeds *(Cucurbita pepo),* and reconsideration of tin compounds as taeniacides.
- Further development of a vaccine, which can be widely applied in pigs.

6.5.2. Operational research

- Conduct of local pilot research projects using various control and preventive strategies (chemotherapy, vaccination, sanitation and education), in order to select the most successful and cost-effective approaches in a given endemic area acceptable to national authorities.
- Development of simple but objective indicators for risk assessment in the local epidemiological situation as well as for the evaluation of preventive and control activities.
- Objective evaluation of the efficacy of the focus-oriented short-term control interventions. This should include a traceback system from infected pigs to tapeworm carriers and the identification of tapeworm carriers in/or around epileptics, as well as searching for solid arguments for the introduction of free-of-charge diagnosis and treatment of taeniosis in humans, both in endemic rural areas and in the population at large.
- Evaluation of the feasibility of and opportunity for conducting a control program in cooperation with other locally on-going programs such as the Global Campaign against Epilepsy, the Partnership for Parasite Control program, and programs on food safety, water and sanitation improvement, Health Education Promotion and the primary health care system.
- Collection and wide distribution of data on the health burden and impact of *T. solium* cysticercosis on humans, the risk of spreading T. *solium* infection through the migration of human carriers, and the export of infected animals or meat, as well as the economic losses due to cysticercosis in humans and animals (T. *saginata* included).

6.5.3. General logistics and management of control programs

- Establishment of a committee or nomination of a single person to be responsible for the implementation of preventive and control measures at various organizational levels (regional, national, district or community). International agencies such as the WHO and FAO, and also the Centers for Disease Control and Prevention (CDC), should designate an officer responsible for the coordination of various control approaches and activities.
- Creation of a reporting system, as simple as possible, at all levels of existing medical (taeniosis, cysticercosis) and veterinary (cysticercosis) services. A protocol for active surveillance activities in endemic areas, commensurate with the local human and technical resources should be produced and distributed. The incoming data should be regularly analyzed and used for further decision making at the national and/or local levels.

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[2] This section was developed with the contributions of Prof. J. Eckert (Zurich), Drs D. Engles and F.-X. Meslin (WHO), and P. Schantz (CDC), all of whom have considerable experience in this field

- Training of medical, public health and veterinary services in the implementation of the preventive and control measures relevant to the local human and financial resources, as well as to the local cultural, environmental and economic conditions. Special effort should be made to include prevention and control measures in the academic teaching/learning curriculum and post-diploma refresher courses; these measures should include modern communication and health education technologies to reach the population at large (internet network, mass media).
- Attempts to increase the availability of inexpensive taeniacides and the local production of Coproantigen tests.
- Creation of, at the national or local levels, groups of people involved in the development and implementation of prevention and control programs in highly endemic areas. Support of those groups with the scientific, logistic and financial assistance required to carry out the plan.
- Revision of legislation related to the prevention or control of taeniosis/cysticercosis, including that relating to animal production and meat distribution as well as sanitation, diagnosis and treatment of human tapeworm carriers.
- Promotion and justification of control programs at district, national and international levels using valid estimates of the health and economic burden of human taeniosis/cysticercosis.

6.6. Support for the implementation of *Taenia solium* control measures

6.6.1. World Health Organization (WHO)

Department of Communicable Diseases Control, Prevention and Eradication
World Health Organisation, Ch-1211 Geneva, Switzerland
D. Engels and F.X. Meslin
E-Mail: mailto:engelsd@who.int
mailto:meslinf@who.int

Support from the WHO has been offered recently [145]. For years the WHO has given increasing attention to the problem of taeniosis/cysticercosis. Several guidelines have been produced and distributed [408, 409, 599, 601, 603]. In 2003 the issue was brought to the attention of the 55th World Health Assembly [605]. The WHO's mandate is to assist Member States in assessing the disease burden, and establishing simple evidence-based cost-effective and sustainable control strategies [145]. The WHO also facilitates the exchange of experiences and information on the subject, coordinates initiatives and approaches the donor community. Three WHO programs play an essential role in promoting activities in taeniosis/cysticercosis: those dealing with parasite control, zoonoses monitoring, prevention and control, and supporting the Epilepsy Global Campaign. Other WHO departments dealing with health macroeconomics, food safety, essential drugs, water and sanitation, primary health care promotion, and health personnel training, may contribute to the goal of taeniosis/cysticercosis prevention and control. The WHO's Collaborating Centres on parasitic infections (WHO Collaborating Centre for the Molecular Epidemiology of Parasitic Infections in Perth, Australia) and parasitic zoonoses (WHO Collaborating Centre for Training and Research on Emerging and Other Parasitic Zoonoses, in Copenhagen, Denmark) constitute a valuable source of expertise and information on taeniosis/cysticercosis control problems.

6.6.2. Food and Agriculture Organization (FAO)

Animal Production and Health Division, FAO,
Viale delle Terme di Caracolla, 00100 Rome, Italy
C. Eddi
E-Mail: carlos.eddi@fao.org

The potential involvement of the FAO in the prevention and control of T. *solium* infections world wide has been described recently [141]. It consists of supporting initiatives in improving animal production and distribution of safe meat, and in organizing internationally specific seminars and workshops on prevention and control of infections with Taeniidae important for human health and animal production economy. There are plans to create four regional veterinary public health networks for Latin America, Eastern and Central Europe, Asia and Africa. The networks will provide a basic framework to spread information related to diagnosis, prevention and control of major zoonotic diseases through electronic conferences,

discussions, newsletters and a directory to establish contact with people involved in veterinary public health.

A Technical Co-operation Programme (TCP) has been developed as a technical tool to help Member States to create the basic environment to control emerging zoosanitary problems such as zoonotic diseases. Requests for a technical assistance may be submitted also by non-governmental institutions.

6.6.3. Centers for Diseases Control and Prevention (CDC)

Division Of Parasitic Diseases
CDC
Atlanta GA, United States of America
P. Schantz
E-Mail: mailto:Pschantz@Gdc.Gov.

The activities of CDC in control and prevention of taeniosis/cysticercosis have been discussed recently [505]. CDC is known for its international outbreak assistance, global approach to disease surveillance, promotion of applied research on diseases of global importance, application of proven public health tools, global initiatives for disease control, and public health training and capacity building. In the last mentioned area, the Field Epidemiology Training Programmes and International Emerging Infectious Diseases Laboratory Fellowship are very[7] active. CDC has been for years interested in taeniosis/cysticercosis surveillance, prevention and control with a special emphasis on USA imported cases of neurocysticercosis, cooperation with field projects in Poland, Mexico, Peru and in the People's Republic of China, as well as in developing immunological tools for detection of neurocysticercosis.

6.6.4. Donor agencies

Several donor agencies have long been involved in the promotion of research activities related to the prevention and control of taeniosis/cysticercosis. Among those recently involved in elaborating optimal control measures in Peru is the Bill and Melinda Gates Foundation. (Annex 6.7.4).

6.6.5. Non-governmental agencies

It would be difficult make a complete list of all the academic and pharmaceutical industry institutions that have made research contributions on the Taeniidae and the prevention and control of taeniosis/cysticercosis. However, a special acknowledgement is due to the Task Force for Disease Eradication based in Altanta, Georgia (USA) which has promoted the eradication of T. *solium* infections [71, 500]. Considerable help is also expected from the rapidly expanding activities of the International Campaign for Epilepsy [278].

6.6.6. Local communities

Local communities, especially in Ecuador, Mexico and Peru, have been actively involved in the realisation of early field projects on the control of T. *solium* infections [98, 189, 207]. Gaining the support from local leaders and communities for an effective implementation of a local control program is very important. However, it must be accepted in active surveillance activities that an intervention — be it chemotherapy, education or sanitation or all combined — must be invoked when any focus of T. *solium* infection in the field is detected. Therefore, before any local surveillance is planned, appropriate prevention or control interventions should be prepared, and then implemented at the end of the project. Otherwise, the local population and local authorities may become frustrated and non-cooperative in future activities.

Annex 6.7. Current control programs and agencies involved

Annex 6.7.1. The Pan American Health Organization (PAHO) long-term control protocol

The PAHO organized in 1990 in Porto Alegre Brazil a conference on epidemiology and control of taeniosis/cysticercosis in Latin America. The proceedings of that meeting were published in Spanish in 1993 [408]. After considering the basic epidemiological and biological data, clinical expression of neurocysticercosis, available diagnostic techniques and accessible taeniacides, the participants of that conference agreed that the control of taeniosis/cysticercosis in Latin America should be a health priority in several countries.

It was agreed that epidemiological surveillance should be carried out at four levels: national, departmental, municipal or district, and local. This is indispensable to the initiation of control activities. The responsibilities at each level were defined i.e. a wider use of available information, introduction of a notification system for human and pig cases, the active collection of the data from local studies, and the supervision and quality evaluation of the work of the veterinary and medical services involved. This should lead to the identification of the foci of infection in individuals, families, communities and/or regions and to the definition of the responsible risk factors facilitating transmission.

The major objectives of any long-term control program are a considerable reduction of the mortality, morbidity and disability caused by neurocysticercosis, and the reduction of economic losses due to pig cysticercosis.

The control strategies to be adopted should be determined by the local epidemiological situation. There should be specific strategies such as defining endemic areas and foci of infection, treatment of human carriers in the foci, both diagnosed and suspected, as well as the identification and treatment of human cases of neurocysticercosis. The complementary strategies would be: improvement of water supply and sanitation, elimination of mechanical vectors, better meat inspection, and promotion of community participation as well as intersectorial cooperation.

The following steps in implementation were defined:

- promotion of a political will,
- selection of endemic areas,
- collection of basic data on the local situation,
- identification of the foci,
- planning of feasible activities and methods of evaluation,
- identification of resources,
- organization of social support (school teachers, pig breeders and handlers, religious groups),
- reorganization of the responsible central agencies (parasitological, diagnostic and serological laboratories, veterinary inspection, health inspection),
- defining the responsibilities of medical services, veterinary services, health services and services responsible for education.

Although there is no information on whether PAHO's long-term program design has been implemented in any Latin American country, several small local projects have been carried in in the region. The model developed appears sound and should be reviewed by any group planning a control program.

Annex 6.7.2. Cysticercosis Working Group in Eastern and Southern Africa (CWGESA) long-term control program

At the International Workshop on *Taenia solium* cysticercosis/taeniosis, held in Arusha, Tanzania in 2002, CWGESA was convened and a regional control plan was developed and announced [57]. The components of the control and surveillance project are:

- document the burden and impact of *T. solium* infections,
- increase awareness on the part of relevant stakeholders,
- establish regional and national multidisciplinary working groups for the promotion of scientific exchange and cooperation, as well as coordination of research and control activities,
- establish a regional reference centre and secure medication and diagnostic and other needed equipment to ensure the necessary infrastructure for research, training, surveillance and control activities,
- educate and train health, veterinary, and other relevant professionals about cysticercosis/taeniosis,
- ensure the transfer of technology necessary for surveillance and control,
- encourage basic and applied research on cysticercosis/taeniosis, socioeconomics and potential interventions,
- formulate guidelines for the management of cysticercosis/taeniosis,
- promote integration with traditional health and livestock systems,
- review and revise as needed national pork inspection and control regulations,
- establish a regional program aimed at improving smallholder pig production and health, and
- encourage regional and international cooperation.

A more detailed long-term action plan for combating *T. solium* cysticercosis/ taeniosis in Eastern and Southern Africa has also been elaborated [59]. It deals with the following items:

1. **Organization:** A national task force consisting of ministries of health, agriculture, environment and education plus relevant personnel from research and academic institutions, non-governmental development organizations and other partners should be established in each country. The regional working groups should meet on a regular basis (annually) and should receive guidance and support from the regional/subregional offices of the WHO, FAO and other relevant United Nations agencies. A small multidisciplinary, intersectorial Technical Advisory Group of specialists with expertise in cysticercosis science and program management should be formed. The Technical Advisory Group in conjunction with the Regional Working Group will have responsibility for:
   a) identifying priority research needs
   b) reviewing country/regional plans
   c) monitoring progress of control programs and
   d) providing technical oversight of support activities.
2. **Surveillance:** Survellance should be accomplished through regional centres using both passive and active surveillance methods, a simple reporting system, and rapid epidemiological assessment aiming at evaluation of the burden of cysticercosis in humans and animals.
3. **Prevention and control** is based mainly on identification and implementation of cost-effective, sustainable, integrated methods. Regional reference laboratories should be established using available diagnostic technology. Prevention may require some changes in legislation. A program for improving smallholder pig production and health should be developed.
4. **Research:** Existing information should be reviewed and gaps in existing knowledge identified.

5. **Training:** A regional centre for training and building capacity to control cysticercosis/taeniosis should be established. An emphasis should be given to incorporation of cysticercosis/taeniosis control measures into national primary health care package.
6. **Networking:** Internet sites, meetings, availability of documents, and international consultation should all be encouraged and supported.

This is a long-term plan, putting most of the attention on prevention and control of cysticercosis, both in humans and in animals, and little emphasis on control of taeniosis although some elements of a short-term or medium-term program such as action through primary health care workers is included. It is also a large, complex infrastructure (centre, working groups, etc.) which may require considerable financial, managerial and scientific support. This may compete with other health and agricultural priorities such as HIV infections, malaria, livestock viruses, tuberculosis, malnutrition, and integrated programs for child health.

The chairperson of the CWWGESA is Dr Mathias Boa, from the Faculty of Veterinary Medicine, Sokoine University of Agriculture, Morogoro, Tanzania; e-mail: workinggroup_2000@yahoo.com.

Annex 6.7.3. PAHO short-term control project

In addition to the long-term programs, requiring decades, immediate short-term interventions have also been suggested by the PAHO (Porto Allerge conference in 1990) [408].

The following phases of implementation were suggested:

- selection of an area,
- identification of the T. *solium* foci,
- formulation of a action plan,
- identification of human resources,
- definition of control responsibilities,
- provision of diagnostic and therapeutic tools,
- registration and information,
- chemotherapy interventions,
- operational surveillance, and
- evaluation.

Several research projects in Latin America have adoped this protocol, but only a few followed it exactly. The results of these projects have not been published.

Annex 6.7.4. The new Peruvian control project

The CDC recently announced (press release November 2003) that the Bill and Melinda Gates Foundation had awarded a grant of $14.2 million in direct costs ($15.5 million total costs) over a seven year period to eliminate cysticercosis from a major disease-endemic area of Peru, in order to establish a model by which the disease can be eradicated throughout the world.

The project leadership is comprised of researchers from the Peruvian Ministry of Health (Dr Fernando Llanos, current Head of the Peru NIH), Universidad Peruana Cayetano Heredia (Dr Hector Garcia), the Universidad Nacional Mayor de San Marcos (Dr Armando Gonzalez), the Centers for Disease Control and Prevention (Dr Victor Tsang) in Atlanta, USA, and the Johns Hopkins University Bloomberg School of Public Health (Dr Robert Gilman) in Baltimore, USA.

Diverse control strategies will be applied, monitored, and their efficacy measured. Data obtained will serve to plan a strategy to be applied in the last four years of the project in close collaboration with the Ministry of Health in the area. Concomitant efforts will be made to optimize a vaccine for pigs, and to develop easy and economical diagnostic tests that can be used in the villages to detect infected humans and pigs.

The possibility of eradicating human cysticercosis worldwide now exists thanks to extensive knowledge of the disease, the development of accurate diagnostic methods, and the availability of effective treatments. The proposed program is an essential first step. It also represents a highly productive international and multidisciplinary collaboration between Peruvian and US institutions.

Annex 6.7.5. Standards and management of human taeniosis control measures

Z.S. Pawowski

Treatment of human tapeworm carriers is the most important taeniosis/cysticercosis control activity to be applied in addition to the veterinary and health preventive measures and educational efforts. Unfortunately, the frequency of treatments for taeniosis in humans remains low despite good evidence that it is effective, safe and cost-effective. It is also the most direct way to remove the source of cysticercosis in humans. In an area endemic for *T. solium* infection, neurocysticercosis is the major cause of epilepsy in the adult population and a frequent cause of severe neurological complications.

The standard management of human taeniosis is expected to facilitate teaching and training activities in the control of taeniosis/cysticercosis. These activities should be prepared in the simplest possible way in order to serve the needs of anyone involved in control measures i.e. health policy makers, public health officers, medical specialists and family doctors, veterinari,' services, educational personnel as well as primary health workers.

A. Definitions:

1. Confirmed case of taeniosis with species indentification e.g. *T. solium* or *T saginata* or *T. saginata asiatica* infections:
   - Molecular techniques (PCR) or
   - Parasitological examination of expelled scoleces or proglottids *
2. Confirmed case of taeniosis without species identification e.g. *Taenia* spp. infection, only:
   - Finding *Taenia* spp. eggs in feces * or
   - Finding specific *Taenia* coproantigens in feces *
3. Probable case of taeniosis:
   - Self-diagnosis by finding tapeworm proglottids or
   - Positive questioning about proglottids being expelled
4. Suspected case of taeniosis:
   - Living in a *Taenia* spp. endemic area and
   - Eating raw meat and/or
   - Having symptoms suggesting taeniosis (early morning abdominal pain, nausea, vomiting, excreting 'worms')
5. Focus of T. *solium,* where most likely T. *solium* carrier(s) exists:
   - A farm supplying cysticercotic pigs
   - A locality with a high rate (>5%) of cysticercosis in pigs
   - A family with a neurocysticercosis case (especially with a late epilepsy)
   - An epileptic individual (frequently also a tapeworm carrier).

*Re-occurrence of gravid *Taenia* proglottids after unsuccessful treatment or a spontaneous expulsion of part of strobilla may be confirmed by:

- Re-appearance of specific coproantigens after two to three weeks or
- Re-expulsion of tapeworm gravid proglottids within two to three months.

B. Standard diagnosis of taeniosis (see definitions above) by:

- Questioning for expulsion of tapeworm proglottids (positive in about 50% cases of the *T solium* taeniosis and above 90% in *T. saginata* infections)
- Finding tapeworm proglottids in feces (30%-50%)
- Finding *taeniid* eggs in feces or on anal swabs (30%-50%)
- Finding specific *Taenia* coproantigens (90%-100%)

Warning: *Taenia* proglottids or fecal material from a suspected person should be handled with caution because of a risk of cysticercosis. Attempting to find *Taenia* scolices in feces after treatment also carries some risk.

C. Standard treatment:

Because of some difficulties in the identification of *Taenia* species and a risk of neurocysticercosis caused by tapeworm carriers expelling *taeniid* eggs, treatment of any case of tapeworm infection is justified, irrespective of whether it is a confirmed, probable or suspected case (see definitions). After using modern taeniacide drugs, it is difficult to find expelled scolices; in this case, the efficacy of the treatment can be confirmed when gravid proglottids or *taeniid* eggs do not re-appear in feces within three months after therapy, or specific coproantigens cannot be identified within some weeks after treatment.

The following taeniacide drugs (see the WHO Essential Drugs list) are proposed:

- Praziquantel

  One single dose 5-10 mg/kg b.w. i.e. adults (60 kg or more) — one 600 mg tablet or three to four 150 mg tablets; patients 30-60 kg — two 150 mg tablets or half of a 600 mg tablet; children below 30 kg, one 150 mg tablet; the tablets are to be swallowed on an empty stomach and washed down with some water. There are no contraindications except in the case of ocular cysticercosis. Treatment is well tolerated and can be used in pregnancy.

- Niclosamide

  One single dose of four 500 mg tablets (2 g) for adults, 2 500 mg tablets (1 g) in children below 35 kg b.w. and one 500 mg tablet in children below 10 kg b.w. Tablets, given on an empty stomach, should be chewed thoroughly before swallowing and washed down with some water. There are no known contraindications but alcohol should not be consumed during niclosamide therapy. Treatment is well tolerated and can be used in pregnancy.

D. Implementation of control measures:

The existence of *T. solium* taeniosis/cysticercosis in developing countries is deeply rooted in their economic and educational status and especially in inadequate health services delivery, mainly due to the lack of initiative and organisation, insufficient personnel and financial resources, and inadequate education and training. Implementation of effective control measures depends therefore on taking some initiatives and decisions as well as a close cooperation among various medical and non-medical services as listed below:

1. Health policy makers:
   - Collect all possible information of medical and economic importance on taeniosis/cysticercosis in a country and consider the need, priority and feasibility of undertaking control measures.
   - Create a positive atmosphere for all interested bodies, including mass media, about the necessity of implementing control measures against *T. solium* taeniosis and cysticercosis.
   - Select optimal ways of implementing control measures in a country and designating person(s) responsible for coordination and implementation

- Regularly evaluate progress in control activities.

2. Public health officers:
   - Collect hard data on taeniosis/cysticercosis from medical, veterinary and research institutions and create or strengthen existing continuous information system.
   - Define endemic areas or foci of taeniosis/cysticercosis as well as local resources (personnel and funds) necessary for successful control.
   - Strengthen the laboratory diagnostic base for identifying *Taenia* proglottids and/or finding specific coproantigens or *taeniid* eggs.
   - Ensure the availability of effective and cheap taeniacides listed in the essential drugs list and decide what to do if the drugs are not available when needed.
   - Train medical, laboratory and veterinary services in the implementation of control measures.
   - Promote cooperation among medical, veterinary and non-medical institutions in the implementation of control measures.
   - Establish person(s) responsible for the implementation of control measures and the mechanisms for the periodical evaluation of control activities.
3. Medical personnel:
   - Include training in diagnosis, treatment, prevention and control of *T. solium* infections in academic curricula and postgraduate teaching as well as organize special courses related to control measures.
   - Keep medical personnel informed about the basic principles of control measures:
     - try to organise, in cooperation with veterinary services, an active search for human carriers in *Taenia solium* foci and endemic areas
     - ensure taeniacide availability and constant supply
     - treat suspected and confirmed cases of taeniosis
     - evaluate, in cooperation with veterinary services, progress in local implementation of control measures.
   - Take part in educational activities addressed to populations in endemic areas.
   - Inform health authorities when needed taeniacide drugs are not available.
   - Analyze the amount of taeniacides being used in an area as one of the indicators of implementation of control measures.
4. Veterinary services:
   - Promote meat inspection and analyze the infection rate in pigs and the origin of cysticercotic pigs diagnosed locally.
   - Try to organize the examination of pigs for cysticerci before slaughter and instruct farmers and rural people on how to avoid infection in humans and pigs.
   - Identify local foci of taeniosis/cysticercosis and ask medical services to treat diagnosed or suspect tapeworm carriers.
   - Inform veterinary authorities about the local epidemiological situation and control measures being undertaken.
5. Educational personnel:
   - Collect educational materials (basic information on taeniosis/cysticercosis and epilepsy) as well as data on the occurrence of *T. solium* taeniosis/cysticercosis and the frequency of epilepsy.
   - Distribute and use available educational materials and invite mass media and school teachers to include taeniosis/cysticercosis prevention and control measures in their health education activities.

- Ensure that anyone involved in health education knows how to obtain educational materials and support.

6. Primary health workers:
   - Collect information on cysticercosis in humans and pigs, and cases of epilepsy in the local area and pass the information to appropriate health authorities
   - Identify, in cooperation with veterinary services, the local foci of *T. solium* infection (see definitions)
   - Educate farmers on how to prevent cysticercosis in humans and pigs, emphazing the risk of epilepsy and economic loss
   - Try to get support from local community leaders for the implementation of taeniosis / cysticercosis control measures
   - Treat with praziquantel or niclosamid any confirmed, probable or suspected case of taeniosis in humans.

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