

Echinococcus granulosus: Is eradication an option for Nepal?

Abstract

Echinococcus granulosus is a zoonotic cestode that causes hydatid disease in man and animals. The parasite is world wide in distribution, but endemic in central Asia, Europe, South America, and some countries of Africa. The range of intermediate host varies widely according to the strain of the parasite as well as the geographical location. The biology of *E. granulosus* is reviewed with reference to the developmental stages and host parasite relationship in the light of latest information available. The distribution of various strains in different parts of the world and their zoonotic significance is outlined.

With the development of precise imaging techniques, the disease is better understood in humans and animals. The surveillance programs have now provided more reliable data on the epidemiology of this disease. A brief description of the epidemiology of echinococcosis in humans and animals in different parts of the world, diagnostic methods used and common treatments practiced, is presented. A few countries of the world, mostly the island ones, have been able to control this parasite. Recent development of vaccines for immunization in the intermediate hosts has opened new opportunities for control in the continental countries too. The phases of control programs and preventive measures to be taken and new control options e.g. vaccination, are discussed in detail.

In Nepal, hydatid disease is of considerable economic and public health significance, yet there has been little work undertaken on the epidemiology of the parasite. There have been no control attempts for this disease till now. A brief outline of the geographical location of Nepal, epidemiology, and transmission patterns is presented. With regards to the availability of new control options, the feasibility of hydatosis control in Nepal is discussed.

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1 Introduction

Echinococcus granulosus, the causative agent of hydatid disease, is a cosmopolitan parasite of man and animals. The parasite has at least nine host adapted strains, most of which are occurring throughout the world (Thompson, 1995). Dogs are the usual definitive hosts, while a wide range of mammals including man can be intermediate hosts. The parasite has three developmental stages; adult, egg and larva. The usual size of the adult worm is 3-6mm long, possesses anteriorly a specialised organ for attachment called scolex with two rows of hooks on the rostellum and four muscular suckers. The body or strobila is segmented and consists usually of 3 to 4 (rarely more than six) reproductive units called proglottids. Eggs are similar to other Taeniid parasites; spherical to ellipsoidal in shape with an oncosphere. The adult parasites are found in the small intestine of the definitive hosts, while the larval stages occur as a cyst in the visceral organs (mainly on liver and lungs) of the intermediate host, causing hydatosis. The parasite is of zoonotic and economic significance in the intermediate and the aberrant host where the larval parasite develops into a hydatid cyst.

This paper reviews the past as well as latest information on biology of the parasite, epidemiology, zoonotic potential, control measures, and treatments methods. Implementation of control program in the resource poor countries like Nepal, in the light of development of vaccines for intermediate host, has also been discussed.

2 Life cycle and biological parameters

The parasite differs from other Taeniid in having a relatively low specificity in the larval stage while having a great reproductive potential (Thompson, 1979). The **definitive host** of *E. granulosus* are almost invariably canid carnivores like dogs,

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wolves and jackals. Interestingly, Thompson (1995) has mentioned a lion strain in which lion is the definitive host, but little information is given to support this claim.

As these carnivores eat the carcass containing hydatid cysts with viable protoscolices, they become infected. The evaginated protoscolices then attach to the definitive host intestinal mucosa, where growth and development takes place, and sexual maturity is reached in about 28 to 35 days post-infection (McManus *et al.*, 2003). Now the host starts shedding eggs or gravid proglottids in the faeces, which serves as a source of infection for **intermediate hosts**, which includes a wide range of herbivores and man.

Following ingestion of egg by a suitable intermediate host, oncosphere larva comes out, which then penetrates into the lamina propria of the intestine and is transported passively through blood or lymph lacteals (Heath, cited in Soulsby, 1982) to visceral organs where the oncosphere larva develops into hydatid cyst (Metacestode larva).

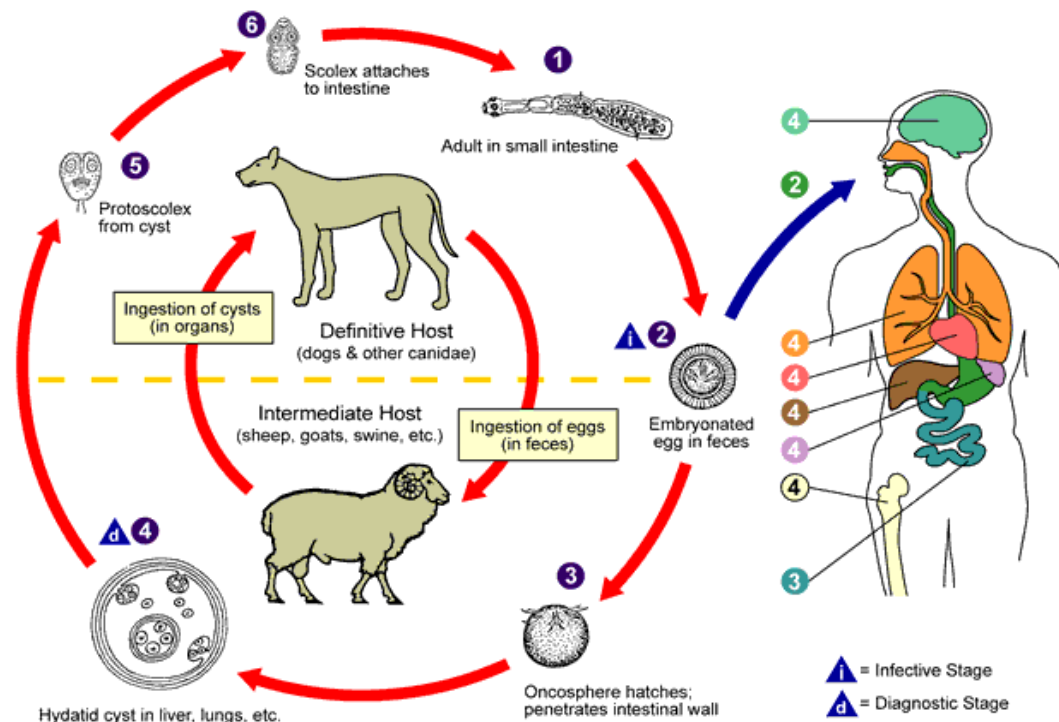


Figure 1. Life cycle of *Echinococcus granulosus*.

(Source: http://www.dpd.cdc.gov/dpdx/HTML/Echinococcosis.asp?body=Frames/A-F/Echinococcosis/body_Echinococcosis_page1.htm)

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The spectrum of intermediate hosts is determined by the factors like infecting strain of the parasite (Table 1), and occurrence of various intermediate hosts in that region (Rausch, 1995).

Table 1 Strains of *E. granulosus* (Thompson, 1995; Torgerson and Budke, 2003)

Strain	Definitive hosts	Intermediate hosts	Approximate geographical location	Zoonotic significance
Sheep strain (G1)	Dog, fox, dingo, jackal, hyena	Sheep, cattle, pigs, camels, goats, macropods, Man	Worldwide	Cystic Echinococcosis
Tasmanian Sheep strain(G1)	Dog, fox	Sheep, cattle, man	Tasmania, Argentina	Cystic Echinococcosis
Buffalo strain (?)	Dog, fox?	Buffalo, cattle? man	Asia	?
Cattle strain (G5)	Dog	Cattle, man	Europe, India	Cystic Echinococcosis
Cervid strain (G8)	Dog, wolf	Cervids, man	Europe, Russia, South America	Cystic Echinococcosis
Lion strain	Lion	Wild African ungulates	Eurasia, North America Africa	?
Camel strain (G6)	Dog	Camels, goats, cattle? man?	Middle east, Africa, China, Argentina	Cystic Echinococcosis
Pig strain (G7/G9?)	Dog	Pigs, man	Europe, Russia, South America	Cystic Echinococcosis
Horse strain (G4)	Dog	Horse and other equines	Europe, Middle east, Asia	None

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As the life cycle depends on carnivores feeding on the flesh of infected herbivores, accidental occurrence in human beings disrupts the cycle (McManus *et al.*, 2003). However, this doesn't always happen. In the Turkana district of Kenya (Africa), the humans sometimes act as intermediate hosts. This is because these pastoral tribes don't bury their dead properly and dogs and other wild carnivores are able to scavenge on these corpses (Macpherson, cited in Rausch, 1995).

The parasite has three developmental stages, namely; adult, egg and larva (Metacestode) that interact in different ways with their respective hosts.

2.1 Metacestode to Adult

Adult parasites are harboured in the small intestine of the definitive host, which is always a canid carnivore. However, in the felids initial development of the parasite may occur, but soon terminates. This may be due to the specific physiochemical and immunological requirement of the parasite (Thompson, 1995).

Definitive hosts pick infection by eating hydatid cysts containing viable protoscolices. Protoscolices are then released from the cyst by the masticatory activities of the host. Enzymatic actions of the stomach also facilitate this excystment (Smyth, cited in Thompson, 1979). The protoscolex remains invaginated until before excystment of the brood capsule in an attempt to protect its scolex and to remain infective (Thompson, 1995). As evagination occurs, the protoscolices become very active at the beginning which is a basic requirement for establishment in the small intestine of the final host (Thompson, 1995). The evaginated protoscolices are then found in between the villi or within the crypts of Lieberkuhn of the final host (Thompson, 1977). This is necessary for the young parasites to be prevented from being removed out of the small intestine (Thompson, 1986). At this time, suckers and hooks help the parasite to become attached to the mucosal epithelium. The developing adults move

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between the adjacent villi (Thompson, 1995) but as they attain maturity, become localised to the proximal third of the small intestine (Derbala and El-Massry, 1999).

After about 35 days post infection, the parasites are found in their typical position (proximal third of small intestine) with suckers and hooks holding the mucosa, and the rostellum being embedded into the crypts of Lieberkuhn (Thompson, 1995). However, the parasites could be found at this location as early as 3 to 10 days post infection and their scolices might remain embedded at periods of 13 to 23 days post infection (Derbala and El-Massry, 1999). Histological examination shows distension of the Lieberkuhn crypts and thinning of the intestinal wall (Derbala and El-Massry, 1999) however, there is no pathological changes in the tissues involved (Thompson, 1995).

Development of adult parasite from larva comprises of a series of independent events like proglottization, maturation, growth and segmentation and involves germinal and somatic differentiation (Figure 2). Thompson (1995) has mentioned these events as following. Ingestion and evagination is followed by elongation till the 10th day. By 11th to 14th day, lateral excretory canals and genital rudiment appears which is the first indication of proglottization. There will be division of genital rudiment into two, which then occurs unilaterally on the fully formed first segment by about 14th to 17th day. By 17th to 20th day, testes appear in the rudimentary form for the first time in the first segment and formation of second proglottid begins. Two segments appear with developed male genitalia and still developing female genitalia by about 20th to 28th day. This is followed by fully matured male and female genitalia in the third segment, and the penultimate segment with developing genitalia by about 28th to 33rd day. Strobila becomes 3 or 4 segmented and ovulation and fertilization occurs in the terminal segment by about 33rd to 37th day and fully mature worm develops by about

45 days. Derbala and El-Massry (1999) have reported this period to be 56 days for the camel strain. When full maturation occurs, the terminal segment accounts for more than half of the worm length (Soulsby, 1982).

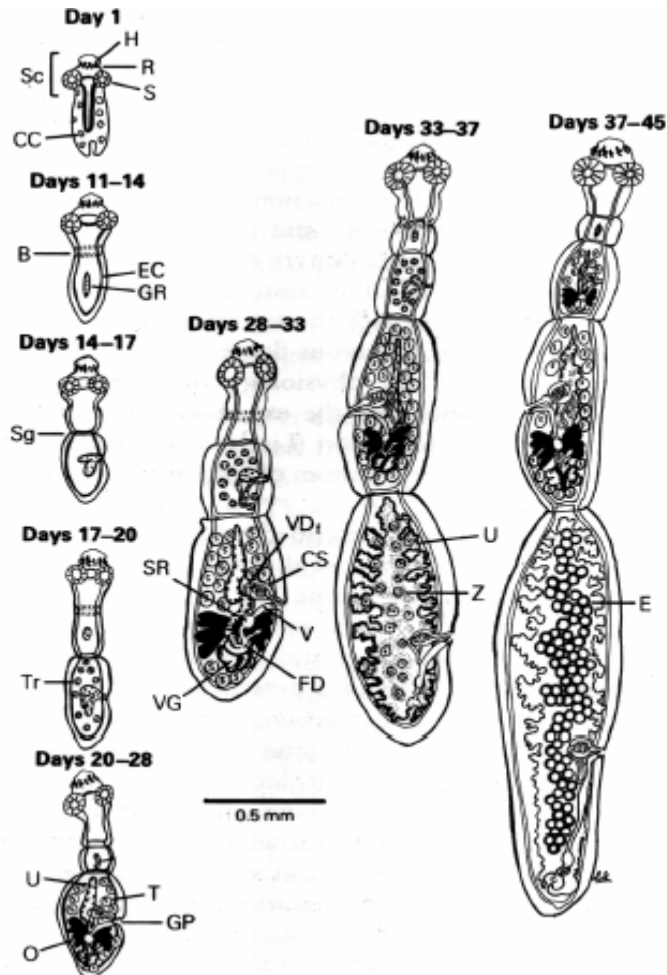


Figure 2. Stages of development of adult *E. granulosus* in the definitive host.

(From Thompson, 1986)

The mature worms are hermaphrodite and have ability of self-fertilization (Soulsby, 1982). There is no clear evidence whether cross-fertilization between parasites occurs or not, in spite of some studies suggesting the occurrence of both self and cross-insemination in the parasites found in the domestic hosts (Thompson, 1995).

The initial onset of egg production in *E. granulosus* ranges from 38 to 58 days (Thompson and Eckert, cited in Thompson 1986). Little information is available on the events that follow. There is wide variation on number of eggs produced per

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proglottid as it may range from 100 to 1500 (Thompson, 1995). The intervals between shedding of proglottid are also quite variable, averaging two weeks (Schantz, 1982). The eggs are liberated either as within the gravid proglottid or as free eggs since the gravid proglottid may disintegrate before exiting the definitive host (Soulsby, 1982).

2.2 Egg to Metacestode

After the eggs are passed out from the final host, they are fully embryonated and capable of infecting an appropriate intermediate host. The eggs are extremely resistant and can withstand a wide variation of environmental temperatures.

The eggs represent the characteristic feature of Taeniid eggs and are ellipsoid to spherical in shape, usually measuring 32 to 36 μm by 25 to 30 μm in diameter (Soulsby, 1982). Ultrastructural examination shows four membranes and layers covering the embryo or oncosphere, which are the vitelline membrane, embryophore, germinal layer, and oncospherical membrane (Figure 3).

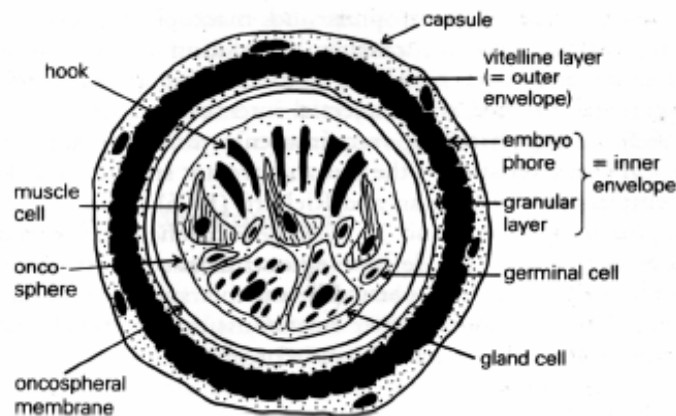


Figure 3. Egg of *E. granulosus*. (From Thompson, 1986)

The diameter of the oncosphere is about 0.018 mm, and it contains the hexacanth hooks, muscle fibres and gland cells which help in penetration and movement within the intermediate host (Schantz, 1982). Following ingestion of egg by an appropriate intermediate host, they are hatched and become activated. Hatching comprises of

disintegration of the egg envelopes and membranes and release of oncosphere which may require the action of proteolytic enzymes in the stomach and/ or intestine (Thompson, 1979). Although hatching and activation is promoted by the gastrointestinal factors, it may occur extra-intestinally (Thompson, 1995).

The penetration of hatched and activated oncosphere into the mucosa and the circulatory system is facilitated by the hooks and the penetration glands (Heath, cited in Thompson, 1979). Penetration occurs at the tips of the villi in the proximal ileum and jejunum of the small intestine (Heath, cited in Thompson, 1995).

The factors that influence the final localization of the larva may be anatomical and physiological features of the host, in addition to the strain of the parasite (Thompson, 1995). The reason that ruminants have cysts commonly located in lungs is due to their large villus diameter in contrast to the non-ruminants, in which cysts are common in liver (Heath, cited in Thompson, 1995). Additionally, the holding of the cysts in liver or lungs is facilitated by the microvilli present on the surface of the early metacestodes (Harris *et al.*, 1989). As soon as the predilection site has been attained by the oncosphere, postoncospherical development begins resulting into the formation of metacestodes larva (Thompson, 1995).

2.3 The metacestode

The completely developed metacestode is spherical in shape and is characteristically unilocular (Schantz, 1982) which is fluid filled. However, the cysts occurring in the lungs of the sheep are usually multilocular (Soulsby, 1982). This fluid filled cavity is surrounded by a germinal layer internally and a tough elastic acellular laminated layer externally (Figure 4). The latter is supported by fibrous capsule of host origin. Increase in size of this single chambered cyst occurs by concentric enlargement (Thompson, 1995). Capsule is produced by the asexual multiplication of the cyst

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germinal layer. These brood capsules in turn produce multiple protoscolices by polyembryony (Schantz, 1982).

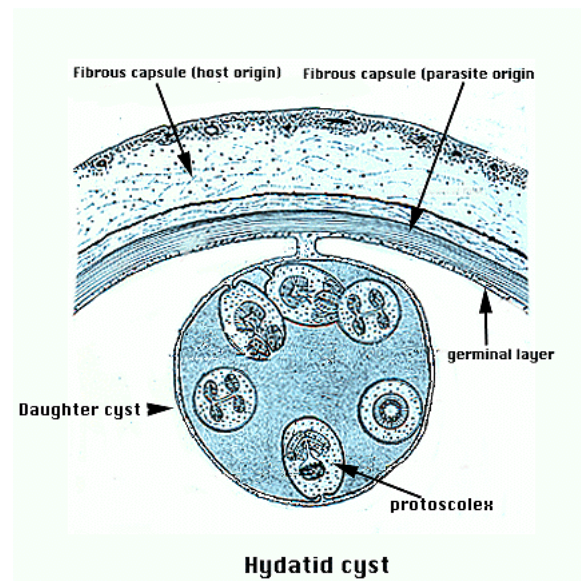


Figure 4. Schematic illustration of a hydatid cyst (Metacestode).

(Source: <http://www.soton.ac.uk/~ceb/Diagnosis/Vol8.htm>)

Sometimes, several cysts may come closer to each other and fuse to form group or cluster of small cysts of different size (Thompson, 1995). Formation of daughter cysts is common in some hosts like man, where the size of the cyst is usually large (Soulsby, 1982), containing large volume of fluid and protoscolices (Schantz, 1982). Secondary hydatid cyst may be produced from the protoscolices if the cyst within the intermediate host bursts (Thompson, 1979).

Not all hydatid cysts are fertile enough to produce brood capsules and protoscolices, and this depends upon host species and site of development (Thompson, 1979; Soulsby, 1982). The initial rate of development is fast as oncosphere recognition and formation of laminated layers occurs within first 14 days of infection (Thompson, 1995). The developmental events that follow are slow and are thought to be affected by the strain of the parasite, species and strain of the host and the intensity of infection (Thompson, 1986). The rate of growth of the cyst is variable, but generally

increase in diameter occurs by about 1 to 5 cm per year, depending on factors yet unresolved, and protoscolex formation may require more than one year (Schantz, 1982).

3 Zoonotic significance

3.1 Epidemiology

E. granulosus has worldwide distribution (Figure 5). It is found on all continents, with highest prevalence in parts of Europe, Asia, north and east Africa, Australia and South America (Eckert *et al.*, 2000). Nevertheless, the parasite has been eradicated from a few countries like Iceland, New Zealand, Tasmania (Australia) and the Falkland Islands. In Europe, the disease is highly endemic in the eastern parts and in the Mediterranean areas (Torgerson and Budke, 2003). In Asia, China is the most endemic country, where the number of existing cases in 2000 was estimated to be 600,000 to 1.3 million, and the population at risk was believed to be 60 million (Ito *et al.*, 2003). The occurrence of this parasite is also higher in the Indian sub-continent and the Middle East. In Africa, hydatosis is common in both northern and southern countries, especially among the pastoral tribes of Turkana, Kenya (Torgerson and Budke, 2003).

The sheep-dog-sheep cycle is seen to be occurring most abundantly throughout the world, however, in the countries like Nepal (Joshi *et al.*, 1997a) and Poland (Pawjowski and Stefaniak, 2003), the parasite cycles between pig and dog. Moreover, life cycle patterns involving other ungulates and domestic dogs are also important. Wild animals are involved in sylvatic cycles in different parts of the world although, their zoonotic importance is generally small as compared to the domestic cycles. There is also overlapping of both domestic and sylvatic cycles. In the mainland of Australia, besides the domestic cycle, there is sylvatic cycle between wild canids

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(wild dogs; dingoes and feral dogs) and macropod marsupials (kangaroo and wallabies) and sheep becomes sometimes involved in this cycle (Grainger and Jenkins, 1996). Another sylvatic cycle occurs towards the northernmost parts of North America and Eurasia between wolves or sled dogs and cervids like moose and reindeer (McManus *et al.*, 2002). In African countries, sylvatic cycle involves lions, hunting dogs, jackals and hyenas as final host and buffalos, zebras, and wildebeest and warthogs as intermediate hosts (Schantz *et al.*, cited in Thompson, 1995).

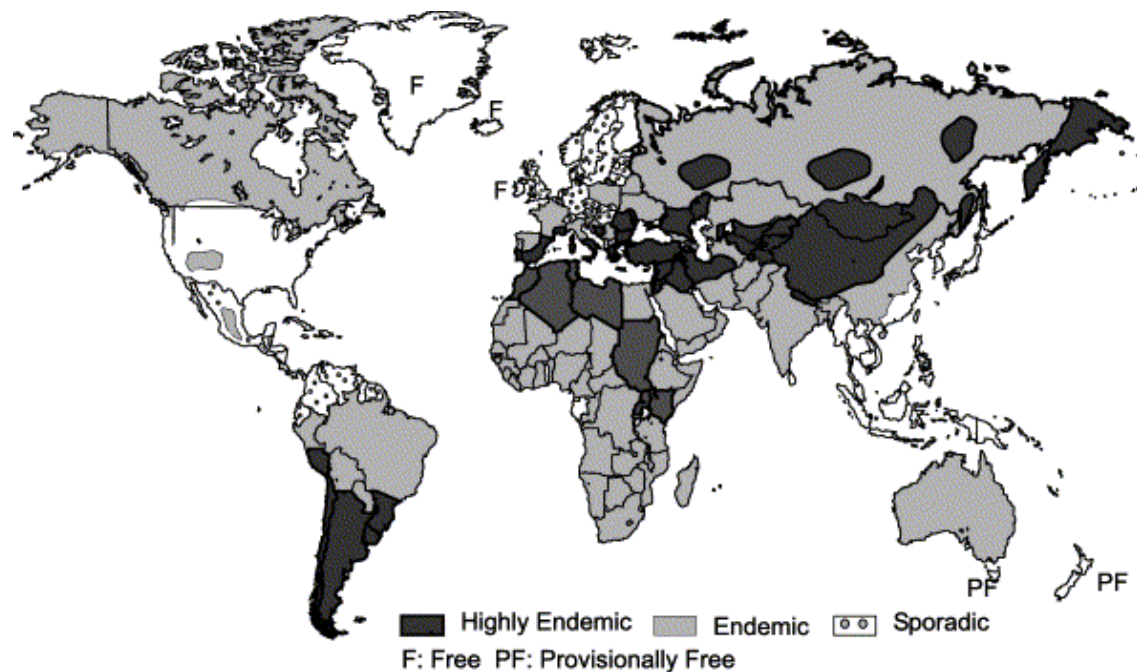


Figure 5. Approximate geographical distributions of the zoonotic strains of *E. granulosus*. (Adapted from Eckert *et al.*, 2000)¹

3.2 Echinococcosis in Animals

The adult parasite is considered to be rather harmless to the definitive host, except when it occurs in large numbers and may cause severe enteritis (Soulsby, 1982). The number of worm occurring in the intestine of definitive host varies widely among

¹ (New Zealand is declared free of Echinococcosis since 2002)

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individuals. The mature worm penetrates deeply between the villi into the crypts of Lieberkhunn of the small intestine. There are few pathological lesions in rare occasions in spite of this host parasite relationship (Torgerson and Budke, 2003). Derbala and El-Massry (1999) found no significant pathological lesions in experimentally infected dogs 50 days post infection.

The parasite however produces considerable ill effects in the intermediate host. Torgerson and Budke (2003) have reviewed these clinical aspects. Wide range of mammals harbour hydatid cysts, which are of slow growing nature, sometimes even taking years to develop. The most commonly affected organs where cyst formation takes place are liver and lungs and less frequently occur in other visceral organs including the central nervous system. The morphology of the cyst is variable and large numbers of them may occur in a single organ. This morphology and location is influenced by the host factors as well as the strain of the parasite involved. Commonly, no symptoms are seen in the intermediate host animals throughout their lifespan (Schantz, 1982). By contrast, in case of humans, symptoms can be severe and in low proportion of infected animals, some clinical symptoms like anaphylaxis may be seen (Torgerson and Budke, 2003).

There is slight variation among species regarding the location of cysts. In ovines and caprines, multiple and pleomorphic cysts are found in liver and lungs. In bovines also, the cysts are multiple and the most common organs are liver and lungs, but the cysts are unilocular and when cattle strain infects them, lungs is the predominant site (Torgerson and Budke, 2003). However, in equines and pigs, liver is the most frequent site for cyst growth (Torgerson and Budke, 2003). In case of wild animals like the moose and the wallabies, lungs are the most common organ for cyst formation.

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It seems that economic impact resulting from the disease is significant in animals rather than the disease itself. The economic losses are mainly due to the carcass condemnation in meat animals (Schantz, 1982), as well as decreased production (Torgerson and Budke, 2003). Examples of reduced production due to Echinococcosis are like reduced feed conservation ratio, decreased meat production, impaired reproductive efficiency and downgrading of wool and hide from them (Polydorou; Ramazanov, cited in Torgerson and Budke, 2003).

3.3 Zoonotic potential

The domestic cycle of transmission occurs more frequently than the sylvatic one, thus is more important regarding the impact on public health. Occurrences of new cases of human infection are often found to be high in the areas where intimate relationship exists between man, dogs and livestock, e.g. among the sheep farming communities. In these communities, dogs commonly get infected by feeding on the infected sheep viscera, which often contains sheep strain larva. As these dogs build up high level of infection, they serve as a highly potential infection source to humans. The sheep strain is thought to be responsible for most cases of human cystic Echinococcosis, whereas, the horse strain is now considered as a separate strain (*E. equinus*) and is found not to be infective for humans (Torgerson and Budke, 2003).

Socioeconomic conditions of a community often determine the occurrence of hydatid disease. Macpherson and Craig (2000) have mentioned a number of socioeconomic factors like; lack of knowledge about the parasite, lack of veterinary and medical services, practice of home slaughter of and lack of policies regarding the control of the disease, which increases the potential of domestic transmission of *E. granulosus* in poor countries. In such worst situations, it is not surprising for the infection level to reach between 20% to 50% in dogs and more than 50% in sheep (Torgerson and

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Budke, 2003). Political instability and deteriorating economic conditions in developing countries is also responsible for increase in incidence of human infections. Study done in Bulgaria (Todorov and Boeva, 1999) is a good example of such situations where control programs implemented in 1960 reduced the incidence substantially from 6.2 to 2.0 per 100000 people, but by 1982 the incidence again rose to 3.3 per 100000, following administrative irregularities and economic changes, and became endemic or even hyper-endemic in some regions. Similar situations resulted in the central Asian countries that became independent from the former USSR. Cystic Echinococcosis, which was sporadic in these countries before the break of the USSR, has emerged as an epidemic (Torgerson and Budke, 2003). This was due to privatization of the farms, collapse of veterinary service due to lack of funding and transformation of farming to subsistence type (Shaikenov *et al.*, 2003).

3.4 Echinococcosis in humans

When eggs that have been shed in the faeces of the definitive host are ingested, humans become infected. In the beginning phases of infection, there are virtually no clinical symptoms. When produced, after a highly variable incubation period, symptoms are diverse with varying degrees of severity that are never suggestive of Echinococcosis (Schantz, 1982). Symptoms may become apparent if the cyst ruptures or exerts a mass effect (McManus *et al.*, 2003). The symptoms are determined by organ of localization, size of the cyst and their condition (Schantz, 1982). The organ most commonly involved is the liver (50-70%), followed by lungs (20-30%) and other organs (like the spleen, kidney, heart, bones, central nervous system etc.) in less than 10% of the cases (Schantz, 1982; Torgerson and Budke, 2003). Infection is mostly acquired during the childhood in patients in which the disease is diagnosed between 10 to 50 years of age (Schantz, 1982). In some parts of the world, prevalence rate is

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relatively higher in children and women as they are in frequent contact with dogs (Macpherson and Craig, 2000), however, overall prevalence is similar in both sexes (McManus *et al.*, 2003). Mortality and case fatality rate has been recorded to be around 0.2 per 100000 population and 2.2% respectively (McManus *et al.*, 2003).

3.5 Diagnosis in man

As mentioned earlier, symptoms are non pathognomonic. Asymptomatic hepatic Cystic Echinococcosis is common in endemic regions and up to 75% of the infected people may remain symptom free for more than 10 years (Frider *et al.*, 1999). The confirmatory diagnosis of most case of Cystic Echinococcosis can be done by various physical imaging techniques like x-ray examination, ultrasonography, computer tomography (CT) scanning and magnetic resonance imaging (MRI) (Ammann and Eckert, 1995; McManus *et al.*, 2003). Besides, highly specific and sensitive serological tests like antigen B-immunoblot, antigen B-ELISA and EgCF-ELISA has been developed that uses cyst fluid for diagnosis of Echinococcosis (Ito *et al.*, 2003).

3.6 Diagnosis in animals

In the definitive host, post-mortem examination of the intestine is the most reliable and accurate method of diagnosis and recording worm burdens (Schantz, 1982; Macpherson and Craig, 2000). However, diagnosis in live animal is more relevant as those are required in the surveillance programs. Examination of faecal sample doesn't differentiate the *Echinococcus* egg from other Taeniid eggs (Soulsby, 1982), so is not suitable for this purpose. Arecoline purgation of the definitive host and microscopic examination of the purged material for the presence of adult worms is the most widely used method till now in spite of its drawbacks. Although the method is highly specific, it is still not ideal as it fails to induce purgation in about 20% of the dogs (Gemmell, cited in Schantz, 1982) and is also undesirable due to time

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consuming and being hazardous to the operator and as well the dog (Macpherson and Craig, 2000) and unable to detect recent infection (Lightowlers and Gottstein, 1995). Immunological and molecular tests have been developed to overcome these imperfections. Coproantigen ELISA test involves the detection of parasite specific antigens in faecal samples. This test is highly specific (up to 99%) and sensitive (up to 93%), but may not be useful when the worm burden is very low of less than 20 parasites (Torgerson and Budke, 2003). PCR based tests are needed in such low infection levels and one for *E. multilocularis* has been developed, but that for *E. granulosus* is yet to be developed (Torgerson and Budke, 2003).

In the intermediate host, the only realistic method is necropsy examination of visceral organs for the presence of hydatid cysts (Schantz, 1982), and is very suitable of prevalence studies, however, there are chances of biasness in slaughterhouse samples (Torgerson and Budke, 2003). Ultrasound has low specificity (about 54%), nevertheless, serum antibody tests reflect the infection at the herd level, and may also be useful in surveillance programs when the cyst are small to be detected at post-mortem examination (Torgerson and Budke, 2003).

3.7 Treatment in humans

Treatment is generally restricted to the patients with cysts producing symptoms or those affecting the vital organs of the body. Surgery is the most effective treatment option and other two are PAIR and chemotherapy, generally regarded as supplementary or alternative options in certain cases (Ammann and Eckert, 1995).

Surgery is the treatment of choice for the cysts those are large in size or located superficially and likely to rupture or that are infected or those are occurring in vital anatomical structures or are exerting a considerable mass effect (McManus *et al.*, 2003). The objective of surgical intervention is to completely remove the cyst

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without allowing the spillage of cyst contents, so is not suitable for patients with multiple cysts in various organs or in areas lacking technical expertise and infrastructure (McManus *et al.*, 2003). Recurrence occurs in up to 25% of the surgically treated cases (Romig, cited in Ammann and Eckert, 1995), which may be either due to inadequate removal of the cyst or earlier unidentified cysts (McManus *et al.*, 2003).

The Puncture, Aspiration, Injection, Reaspiration (PAIR) technique involves puncture of the cyst under ultrasound guidance, aspiration of the cyst fluid as much as possible, introduction of a protoscolicide agent inside the cyst and reaspiration of the cyst contents after 15-20 minutes later (Anon, 2001a). PAIR is suitable for patients with multiple hepatic cysts of 5 cm or greater diameter and also for recurring cyst after surgery, however, contraindicated for superficial, inaccessible, calcified and communicating cyst (McManus *et al.*, 2003). PAIR combined with chemotherapy produces effective form of management for hepatic cysts (Ammann and Eckert, 1995). Chemotherapy is of value in patients with inoperable conditions, widely disseminated cysts and high surgical risk. Two benzimidazole compounds, namely; albendazole and mebendazole have been widely used as chemotherapeutic agents for the treatment of Cystic Echinococcosis. Horton (1997) found that treatment with albendazole @ 800 mg daily resulted in the disappearance of about 48 % (n= 664) cysts and improvement was seen in further 24% , and mebendazole (@ 40-50 mg/kg/day in three divided doses) has lower efficacy than albendazole. Combination of albendazole with praziquantel has greater efficacy than albendazole alone for the treatment of Cystic Echinococcosis in Man (Momahed *et al.*, cited in McManus *et al.*, 2003).

3.8 Treatment in animals

Praziquantel is the most effective anthelmintic drug for treatment in dogs and single oral dose of 5 mg/ kg body weight produces satisfactory results (Macpherson and Craig, 2000). Arecoline hydrobromide was widely used until the late 1960s for surveillance as well as, as anthelmintic despite of its ineffectiveness (Schantz, 1982). In case of intermediate hosts, no practical and effective treatment is available; however, vaccination is a burgeoning concept with these hosts. Details about vaccination are given on the control section.

4 Control/ Eradication

Control and eradication are two distinct concepts. Economides *et al.* (1998) have defined these terms as follows: Control is the “active implementation of a program by a recognised authority on an instruction from the legislature to limit prevalence of a specific disease”, where as eradication means the “purposeful reduction of a specific disease prevalence to the point of continued absence of transmission within a specific area by means of a time limited campaign”.

A typical Echinococcosis eradication program has the following four phases (Economides *et al.*, 1998; Meslin *et al.*, 2000).

Preparatory or planning phase: This phase is concerned with estimating the losses due to Echinococcosis to the community, methods to be used and the resultant benefit from control.

Attack phase: This second phase involves controlling of stray dogs and registration and dosing of the owned dogs. This is the most costly among the four phases.

Consolidation phase: During this phase, surveillance of food animals’ infection is done at meat inspection and subsequent quarantine is imposed to the infected farms.

Maintenance of eradication phase: When no infected animals are detected at meat inspection, maintenance of eradication phase is entered. Meat inspection and quarantine of animals are the only measures taken at and after this phase.

However, it is very difficult to ascertain the time point when eradication has been attained, even though mathematical model has been developed to predict the results of control programs (Torgerson, 2003a).

Successful control and/or eradication have been achieved in a few countries like Iceland (1869-1979), New Zealand (1959-2002), Tasmania (1964-1997), the Falkland Islands (1965-1997). The control programs are underway in some other countries like Cyprus (First introduced-1971, reintroduced-1994), some provinces of Argentina, Chile, China, Uruguay, and a pilot program in Turkana; Kenya (Meslin *et al.*, 2000).

The fundamental preventive measures that are being undertaken while implementing the control programs include; health education, proper disposal of infected offal, reduction of dog population, periodic diagnostic testing and deworming of dogs, legislation, and immunization of the intermediate host animal. Immunization of animals has been undertaken only in the recent control programs because of its unavailability until the recent past and it seems to be the key measure to implement control programs in continental countries.

4.1 Health education

More or less all successful control programs were greatly dependent on health education to initiate and maintain control. Experiences from the countries like Iceland and New Zealand from where the disease is eradicated suggests that health education is necessary to aware the people about the disease and bring about change in their behaviour. Education measures are also important to permit the introduction and acceptance of control programs (Schantz, 1982). In Iceland, a booklet about

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Echinococcosis written in local language had a significant role in eradication of the disease there (Meslin *et al.*, 2000), where the infection level was about 25% (Economides *et al.*, 1998) at the time of introduction of control program. In New Zealand, educational measures were mainly focused towards the dog owners through the use of various media like posters, booklets, leaflets, articles, newspaper advertisements, radio talks and advertisements, films etc. (MacLean, 1963?)

4.2 Control of slaughtering

Slaughtering of food animals on farm or household premises should be avoided. This is the main control measure undertaken in Cyprus (Schantz, 1982). Slaughtering should be done only under the veterinary inspection, preferably in centralised abattoirs having proper offal disposal system. If done on farm, there should be provision of dog proof killing facilities and appropriate offal disposal system.

4.3 Diagnostic testing and dog control

As discussed earlier, the most reliable and practical diagnoses available till now are ELISA Coproantigen test and to some extent arecoline purgation and examination of the purge. Registration of the owned dogs and elimination of the stray dogs is important. The control program of Cyprus involved euthanasia of all positive dogs, spaying of the bitches and charging of high registration fee for the unspayed ones (Meslin *et al.*, 2000).

4.4 Dog treatment

As the approximate prepatent period of *E. granulosus* is 6 weeks, this has been taken as the treatment interval (Torgerson and Budke, 2003). The drug of choice is oral praziquantel since the 1970s, as mentioned earlier. Recently, subcutaneous implants of praziquantel have been developed in China, to overcome the inconvenience of frequent dosing (Ito *et al.*, 2003). In spite of its high efficacy, the six weekly

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anthelmintic treatment intervals seem unsuitable for poor countries because of its high cost. Torgerson (2003b) has shown that the treatment interval can be lengthened to at least 3 months and still reduce the prevalence rates in dogs and live stock to less than 1% within 10-15 years. This is due to the fact that mean time required for reinfection in the dogs is usually sufficiently longer than six weeks (Torgerson and Budke, 2003).

4.5 Legislation

Experience from New Zealand suggests that imposition of legislation e.g. making it illegal to feed raw offal to dogs, right from the beginning of a control program may not be helpful to reduce the incidence of this disease (Gemmell, 1959). However, it is very important in the later phases of a control program and all such programs must incorporate legislations (Schantz, 1982). Attempts should be made to encourage the full participation of public during initial stages, so that they can be convinced about the importance of the control program.

4.6 Immunization

One of the latest developments in control attempts is the formulation of vaccines for intermediate hosts. A recombinant antigen vaccine designated as EG95 has been developed (Lightowers, 1996). Trials carried out in sheep in Australian and Argentina has shown that the vaccine confers high degree of (96-100%) protection against different isolates of *E. granulosus* (Lightowers *et al.*, 1999). The vaccine is also protective to other species like goat and cattle (Lightowers *et al.*, 2003). However, the vaccine has no effect on cysts and many of the older livestock already infected will remain a source of infection for dogs, and the dogs will continue to infect humans (Lightowers *et al.*, 2003). As the vaccine doesn't eliminate cysts from the intermediate host, rather prevent new infections only, numbers of years will be required to eliminate the infected animals from the herd. In this context, vaccination

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combined with deworming (of dogs) and public health education would be more effective (Torgerson and Budke, 2003). An ideal control program seems to be one which combines 6 monthly deworming of dogs and vaccination of the intermediate host animals (Heath *et al.*, 2003). The vaccine is found to be safe and effective when used in lambs, and two vaccinations are recommended at 1 month interval. For example, primary vaccination can be done at 4 weeks of age and secondary at 8 weeks, and the vaccine remains protective for at least 12 months after immunisation and subsequent boosting at 12 months interval is usually necessary for maintenance of high level of immunity (Lightowers *et al.*, 2003). For use in control programs, the vaccine is in large scale trials in China and that is shortly being manufactured in Beijing (Lightowers *et al.*, 2003).

The controls that have been achieved till now, almost all in the island countries, were thorough the use of anthelmintics and life style changes. The problem in continental countries is the presence of extensive and unprotected borders with the neighbouring ones; in which hydatosis is prevalent that provides a continuous source of new infection. This problem may be solved by using of vaccines to prevent reinfection in the intermediate host. Thus the most effective control measure would be one using combination of health education, legislation on animal slaughter, control measures in dogs, and vaccination of the intermediate host.

5 Echinococcosis in Nepal

5.1 Country background

Nepal is a small, landlocked country situated between China and India, at 80° 04' E to 88° 12' E longitude and 26° 22' N to 30° 27' N latitudes. It has a total area of about 14.7 million hectares and a rectangular shape extending from east to west. The human population is about 23 millions (Anon, 2001b). There are approximately 7.0

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million cattle, 3.6 million buffaloes, 6.5 million goats, 0.9 million pigs, and 0.8 million sheep in Nepal (Anon, 2002). Although, Yaks constitutes significant proportion of livestock in the northern region, no information is available on the actual numbers. The number of registered veterinarians working currently in Nepal is about 347, most of them on governmental services (Anon, 2003). Nepal is the only Hindu kingdom in the world and slaughtering of cattle is prohibited by law. Until recently, there was no official meat inspection regulation in the country, however in 1999; His majesty's the government of Nepal legislated as a yet-to-be implemented "Animal slaughtering and meat inspection act", which obligates the slaughter of animals only at abattoirs under veterinary inspection and animal quarantine.



Figure 6. Map of Nepal -sharing borders with India and China.

Most of the animals for slaughter are imported from neighbouring countries; e.g. goats and sheep from Tibet of China and buffalo and goat from northern India. Buffalo is the predominant meat animal in Nepal that contributes to about 64% of the

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meat consumed followed by goat meat 20%, pork 7%, poultry 6%, and mutton 2% (Joshi *et al.*, 2003).

5.2 Epidemiology

Little information is available about the epidemiology of this parasite in Nepal which may be due to the absence of disease surveillance and reporting throughout the country.

Whatever work has been done covers some urban areas of the capital city; Kathmandu. According to Joshi *et al.* (1997a), in contrast to most parts of the world, the parasite here cycles most commonly between dog and pig, in addition to sheep, goat and buffalo cycles. This may be due to the studies centered only on urban areas where a considerable number of pigs are raised, and lack of information from the sheep farming areas. In Nepal, three strains of *E. granulosus*, namely; sheep strain, cattle strain and camel strain have been found to occur in buffalo, sheep and human hosts (Zang *et al.*, cited in Thompson and McManus, 2002).

Most of the information available about Echinococcosis in Nepal is from a three year (1993-1995) study of Joshi *et al.* (1997a), in which prevalence is figured out in humans, dogs and animals brought for slaughter in Kathmandu. ELISA of human serum samples collected randomly from residents of butchering area (n=347), red cross blood bank (n=227) and hospitals (n=230) revealed the overall prevalence to be 14.1% (n=804), with highest prevalence of 25% (n=192) among residents of one of the butchering areas. Similarly, ELISA testing of serum samples of patients admitted to different hospitals of Kathmandu valley showed that the disease had slightly higher prevalence among the males (53%, n=17), and considerably higher among the people of 35 or older age group (76%, n=17). The higher prevalence among males may be due to their greater contact with dogs while butchering. As seen usually, the

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predominant organ for cyst formation was liver (55%) followed by lungs (43%), kidney (2%) and other organs (1%).

Coproantigen ELISA test of dog faeces also suggested high prevalence among dogs of the butchering areas. Out of 88 dogs examined from livestock slaughtering areas, 5.7% were found to be positive, in contrast to 1.8% (n=173) positive dogs in non-slaughtering areas (Baronet *et al.*, 1994). Post-mortem examination of the dogs killed by the municipality revealed that the worm burden to be 1-5 worms per dog (Joshi *et al.*, 1997a). The examination of carcass of food animals in 17 slaughter houses of Kathmandu valley found hydatid cysts to be occurring in 5% buffalos (n=3065), 3% goats (n=1783), 8% sheep (n=150) and 7% pigs (n=143) (Joshi *et al.*, 1997a). Although the yaks are not brought for slaughter, an epidemiological study on them from 55 farms of different parts of the country by Joshi *et al.*, (1997b) found 31% of the animals infected with echinococcosis. Rangarao *et al.* (1994) has also mentioned hydatid cyst in Yaks of Sikkim region of India, a neighbouring province to Nepal. As almost all the animals are brought to Kathmandu valley from various parts of the country (as well the neighbouring countries), the prevalence is presumed to be the representative of the country as a whole.

5.3 Transmission pattern

Butchering in Nepal is generally done by the people of lower cast, who are usually less educated. It is common practice to slaughter animals in open air, mainly near water sources like the bank of a river, streams, ponds and public taps where meat and viscera can be washed conveniently. Sometimes, household yards and near by streets are used as slaughter and selling site. The discarded offals and slaughter by products are then usually left as such in the slaughter site or disposed near by. In the countryside, animals are usually slaughtered and sold during periodic local markets,

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or during religious ceremonies. Once the animal is slaughtered, all the meat is usually consumed immediately as there is no access of ordinary people to refrigeration. The situation is somewhat different in the cities, but there is virtually no infrastructure to accommodate the slaughter and sale of meat.

A large number of stray dogs occur in Nepal, mainly in the cities, besides owned dogs by individuals or the community. The unowned dogs survive on garbage and remain wandering in search of food, mainly around the slaughter site. Butchers often throw inedible meat pieces, viscera or bones to these dogs or the dogs have easy access to the slaughter wastes, which if contains cyst of *Echinococcus* infects them. As the dogs are freely roaming, they defecate wherever they wish, commonly on the river bank or any other free space which is often used as playground or foraging ground, and thus re-infect man and animals. This is assumed to be the most common mode of transmission throughout Nepal.

5.4 Past control attempts

There has been no formal control attempt of Echinococcosis in Nepal until now, however some attempts were made to prevent meat borne infections. In the 1970s and the 1980s, the Danish foreign aid agency built the first self contained abattoir outside Kathmandu valley, and the German government build garbage disposal systems in Kathmandu valley. Campaigns for controlling stray and unowned dog population by using poisoning bait are being carried out periodically by municipalities in most of the urban areas.

However, these attempts seemed unfruitful. The Danish built abattoir stood empty because the cast and religious minded butchers didn't want to move in an animal killing factory outside their community. This was partly also because of the liking of meat from freshly killed animals by the consumers. The streets again filled up with

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garbage and animal wastes and the street dogs were again fed by the butchers around their slaughter site.

However, the scenario is not the same at present, as the government has passed the meat inspection act in 1999 and implemented it in some urban areas. Private sector is being attracted towards investing in the meat industry and to build modern abattoirs. Due the better veterinary services and public health education, people are quite conscious about echinococcosis, and regularly deworm their dogs, at least in the city areas. The number of municipalities is increased to cover new urban areas and they are controlling stray dog population using different means like spaying of bitches, however the efficacies of such campaigns are questionable.

5.5 Feasibility of eradication

To address this question honestly, the geographical and socio-economic features of Nepal have to be analysed and compared with the countries in which the disease is controlled or even eradicated. Nepal is a small landlocked country wedged in between two big countries India and China, both endemic for echinococcosis. Most of the Livestock consumed in Nepal are imported from bordering provinces of these countries. The northern part of India, from where most of the buffaloes are imported to Nepal, has a prevalence rate of about 48% in this species (Singh and Dhar, 1988). Countries like New Zealand, Iceland, Tasmania (Australia), Cyprus etc. from where the disease is eradicated or nearly eradicated, are islands by nature, industrialised ones, heavily dependant on sale of livestock for their income, at times in their development when government had sufficient funds to subsidise such programs. Nepal doesn't have this combination of characteristics where large population of dog is unowned, regulations and slaughtering facilities are almost absent, livestock for consumption are imported and government is very poor, do not fit to this category.

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However, as development of vaccines has opened new opportunity to devise effective control in continental countries, Nepal can expect to get rid of this parasite. It is clear that control and eradication programs have worked best in those countries which are highly educated. The ways in which people are exposed to these parasites is an integral part of economic and cultural activities having to do with human-dog relationships, slaughtering and eating practice and general hygiene. So it is difficult to determine what recommendation on control and eradication in Nepal might be effective without accounting for their full complexity. Changing butchering practices seems to be an essential part of any strategy, which involves major cultural and economic changes. Following recommendations seem valuable to achieve control of echinococcosis in Nepal:

- Study the feasibility of vaccination,
- Inspecting and controlling infected imported animals,
- Meat inspection,
- Registration of owned dogs,
- Regular deworming of owned dogs,
- Control of stray dog population,
- Public health education.

The economic, cultural and family bases of human-dog relations and butchering practices can't simply be altered by legislation. Butchering and food hygiene practices depend not only on knowledge, but also on availability butchering facilities and consumers demand. When the consumers are not aware about meat borne infections or there is even shortage of clean water to wash offals, it seems control is impossible to achieve in Nepal. Even if the dogs are treated with oral praziquantel, it is clear that communities involved would still be left with serious public health

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problems, some of which are more pressing than this particular parasite. So eradication of this parasite from Nepal seems to be irrelevant, as long as the living standards of people are not made better. Eventhough the prospects of control by vaccination seem promising, for Nepal, where most of the food animals are imported, one can't be very optimistic unless controls are implemented simultaneously with the neighbouring countries.

6 Conclusion

In spite of the eradication of *E. granulosus* from several countries, this parasite still has a very wide geographical distribution and continues to possess a serious economic and public health problem. It is re-emerging in those areas where it was thought controlled or occurring at low levels (Eckert *et al.*, 2000; Ito *et al.*, 2003). Since control and eradication program requires long-term projects and good deal of money, the developing countries are not in the position to get rid of this parasite as easily the rich counties got till now. The geographical location of a country also seems to be an important factor for eradication, as all the eradication programs has been successful in Island countries. Nepal, a landlocked developing country, does not meet these requirements. As the new control measures like vaccines are being developed, one can be optimistic about Nepal, also since the neighbouring countries exporting livestock to Nepal like China is instigating control programs (Ito *et al.*, 2003). Moreover, the government of Nepal is implementing the meat inspection act and animal quarantine; there is now availability of efficient veterinary service and public health education. So it seems that eradication of *E. granulosus* is not impossible from Nepal, provided resources and uniquely planned control program.

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