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CONTROL OF FOODBORNE TREMATODE INFECTIONS

Report of a
WHO Study Group



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Manila, 18–26 October 1993

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1. **Introduction**

A WHO Study Group on the Control of Foodborne Trematode Infections met at the WHO Regional Office for the Western Pacific in Manila from 18 to 26 October 1993. Dr Liu Xirong, Director, Programme Management in Manila, opened the meeting on behalf of the Regional Director and the Director-General.

Foodborne trematode infections affect more than 40 million people throughout the world, and are particularly prevalent in WHO's South-East Asia and Western Pacific Regions. The epidemiology of the infections is determined by food-related, ecological, and environmental factors, and is strongly influenced by poverty, pollution, and population growth. The parasites' mode of transmission is closely linked to human behavioural patterns, and specifically to methods of food production and preparation in the endemic countries.

For all the parasites of greatest public health significance – *Opisthorchis*, *Clonorchis*, *Paragonimus* and *Fasciola* species and certain intestinal flukes – aquatic or semi-terrestrial snails act as the first intermediate host, through which the parasite passes to reservoir hosts that include certain fish, crustaceans, water plants, and mammals. Human infection then results from ingestion of raw or inadequately processed foods, in particular fish, shellfish, and aquatic plants, that harbour the trematode metacercariae. The type and severity of the clinical manifestations of infection are variable, but disease can be severe and even fatal.

The public health and economic impact of foodborne trematode infections is considerable in terms of morbidity, loss of productivity and absenteeism, health care costs and agricultural losses. Intervention to minimize this impact requires the development of effective control strategies. The objectives of the Study Group convened by WHO were therefore:

1. To review recent advances in the study of foodborne trematode infections and to identify gaps in knowledge and ways of improving control.
2. To assess the epidemiological status of foodborne trematode infections, with emphasis on clonorchiasis, fascioliasis, opisthorchiasis, and paragonimiasis.
3. To define control strategies that will be appropriate to the epidemiological situation, the potential for intersectoral collaboration, and the available human and financial resources in endemic countries.

2. **The basis of the strategy for control of foodborne trematode infections**

The strategy for control of foodborne trematode infections clearly requires collaboration between the sectors of public health, agriculture, fisheries and aquaculture, food industry, food safety, and education, as

well as the marketing, consumer, and political sectors. The necessity for broad cooperation may be viewed as an opportunity to focus on the fundamental need for safe food.

2.1 **Pattern of distribution**

Foodborne trematode infections, one or more of which have been reported from every country of the world, cause a complex of different diseases. In the past these diseases were limited to the populations of well defined watershed boundaries. Now both the geographical limits and the populations at risk are expanding and changing in association with environmental degradation and as improved routes of transportation permit the extension of markets and facilitate population movements (Fig. 1). These infections are now recognized increasingly in urban areas and all social classes are at risk.

2.2 **Recognition of the problem**

The emergence of human foodborne trematode infections as a severe public health problem has made action imperative. In 1991 the Southeast Asian Ministers of Education Organization – Tropical Medicine and Public Health Project (SEAMEO-TROPMED) held a seminar on foodborne parasitic zoonosis (*I*). The report of this meeting includes comprehensive documentation on the health significance of foodborne trematode infections and calls for collaboration and a global plan of action.

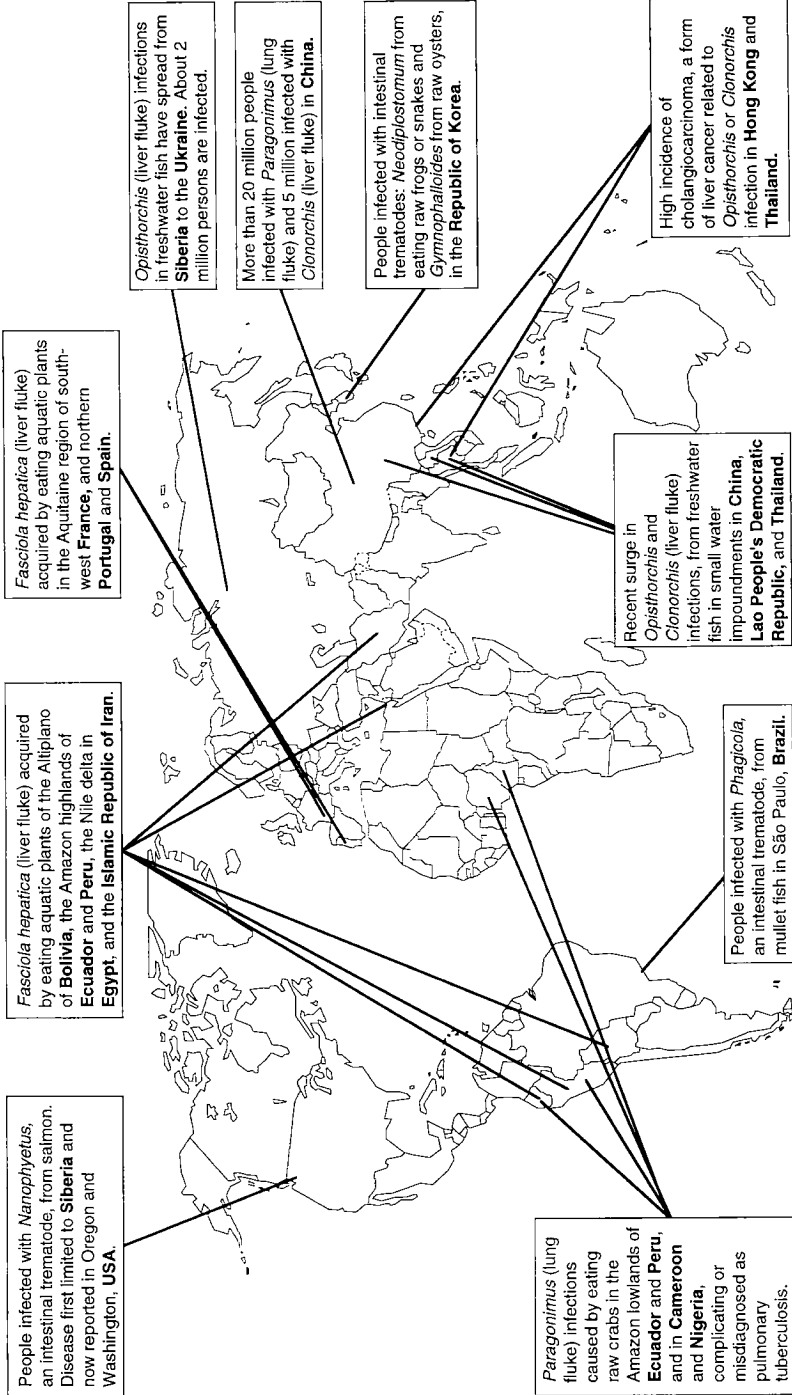
In WHO's Western Pacific Region, foodborne trematode infections are recognized as a public health problem closely linked to the development process. Increased production of freshwater fish has been making an important contribution to improved nutrition in the Region. But if proper precautions are not taken, fishborne trematode infections such as opisthorchiasis and clonorchiasis can spread dramatically. A new awareness of the importance of opisthorchiasis as a public health problem has resulted from a large-scale programme on the control of schistosomiasis undertaken in the Lao People's Democratic Republic and supported by WHO's Regional Office for the Western Pacific since 1988.

The severity of opisthorchiasis as a long-standing problem in Eastern Europe has been brought to public attention for the first time following the recent dramatic changes there. The extent to which opisthorchiasis causes suffering due to hepatic disease in the former USSR was previously unknown. Millions of people are infected, including all members of certain minority ethnic groups in Siberia. Moreover, cholangiocarcinoma linked to opisthorchiasis is one of the most frequently diagnosed types of cancer in the region.

In Thailand about 7 million people are estimated to be infected with opisthorchiasis. In recognition of the extent of the problem, the

Figure 1

Foodborne trematode infections: the global distribution is changing with the environment and human behaviour



WHO 82719E

The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

government has sought and received bilateral support through the German Agency for Technical Cooperation (GTZ) for control activities throughout the endemic area.

The public health significance of other foodborne trematode infections is also increasingly being recognized. Paragonimiasis, for example, is frequently misdiagnosed as pulmonary tuberculosis in both endemic and non-endemic areas. Human fascioliasis is a public health problem in the Altiplano of Bolivia, the highlands of Ecuador and Peru, the Nile delta in Egypt and the Caspian area of northern Islamic Republic of Iran, where an outbreak between 1989 and 1991 affected more than 10 000 people.

2.3 Links with the food-chain

The transmission of these parasites via food is the common denominator for understanding their health importance and for future strategies of control. The increased awareness of public health authorities and practitioners of clinical medicine about the seriousness of foodborne trematode infections is partly due to improved diagnostic methods and better surveillance, but a real increase in incidence coupled with changing epidemiological patterns has also been documented. Some of the factors (mostly food-related) that may be responsible for this increase are listed below.

- Raw, insufficiently cooked, or inadequately processed aquatic foods are the cause of many foodborne trematode infections. Unsafe preparation techniques practised according to different cultural and social traditions or even modern nutritional food fads are a challenge for change and improvement.
- Production of freshwater fish is rapidly increasing (2). In Asia the increase in foodborne trematode infections is attributable mainly to natural water bodies and traditional fish-ponds being contaminated by untreated human excreta and being open to fouling by animal reservoirs of trematodes. The snail intermediate hosts are often present.
- Food plants, such as watercress and water caltrop, may be cultivated in unhygienic locations where infected snails are present.
- International trade in fisheries products, some of which originate from endemic areas, is increasing.
- The increase in travel and tourism within and between countries exposes visitors to unsuspected risks of infection.

2.4 Links to poverty, pollution, and population growth

Poverty, pollution, and population growth make up the triad of underlying determinants that directly influence the rate and magnitude of change in the epidemiology of foodborne trematode infections. The United Nations Conference on Environment and Development in Rio de Janeiro in June 1992 focused global attention on the need for immediate

action to thwart irreversible environmental change and its Agenda 21 emphasized the health consequences. In the Altiplano of Bolivia, for example, reduced availability of green vegetables and inadequate protein intake coupled with poverty and poor sanitation have created the right conditions for trematode transmission. A similar situation has occurred in Siberia as a result of poor sanitation, rampant environmental pollution and population growth. In both regions, transmission of foodborne trematodes has been sustained by poverty and continuing environmental degradation.

In some areas shortage of fuel in poor homes may permit only partial cooking of fish. Children in endemic areas often look for and consume raw plant food (e.g. water caltrop) growing in local ponds. Increasing population pressure in the endemic areas leads to deterioration of the environment and increased pollution of surface waters with sewage, night-soil, and animal excreta. Moreover, irrigation dams – many of which have been built in the last four or five decades – create water reservoirs highly suitable for snails as well as fish, which are the intermediate hosts of trematodes.

2.5 Tools for control

Current understanding of the epidemiology of foodborne trematode infections is sufficient to implement a strategy for control in the areas of high risk. There are many gaps in knowledge of the fundamental biology of the parasites and their intermediate hosts. But the available information does not suggest that resistance to treatment, reinfection, and the appearance of alternative routes of infection are current problems.

The overall control strategy can be effectively built upon a combination of approaches. Community-based education and mass communication are essential foundations for control programmes. Diagnostic techniques are adequate to identify infected individuals and for surveys to determine the proportion of infected people in an endemic area. A range of options for community-based treatment approaches – from mass treatment in areas of high prevalence to selective treatment of infected individuals – can be used according to the capacity of the health care delivery system. Throughout the endemic areas, construction and use of toilets would form part of the overall development programme.

Food safety authorities should incorporate measures for the control of foodborne trematodes into the regular programmes of food inspection services, including use of the Hazard Analysis and Critical Control Point (HACCP) approach (3). If this approach is properly applied, no other system or method can provide such a high degree of food safety. Its great advantage is that it is a systematic, multi-disciplinary system that is both adaptable and cost-effective. It provides for comprehensive coverage of the food-chain, from the origin of the food (farm, river, lake, fish-pond) to consumption, and requires food producers and traders to accept greater

responsibility for food safety through their integration into a national plan of action.

Most importantly, models for controlling foodborne trematode infections, particularly those transmitted by freshwater fish, have been tested and proved effective in the long term. Japan and the Republic of Korea have undertaken systematic case detection and treatment for more than 40 years, in conjunction with health education, sanitation, and legislation on food safety and management of human excreta. A programme to control opisthorchiasis was set up in 1988 in Thailand. In the large pilot project, the control measures included extensive annual large-scale treatment with praziquantel, including mass treatment in communities in which the prevalence of infections was high. Selective treatment was used where the prevalence of infection was lower and both treatment programmes were combined with intensive community-based education and participation, with partial cost recovery through payment for diagnosis and drugs. These measures have successfully reduced opisthorchiasis to low levels of prevalence.

2.6 **Coordination between sectors**

Coordination between sectors is necessary to achieve sustainable control of foodborne trematode infections, and involvement of the community is also important. Cultural differences mean that control will require culturally specific control approaches.

Control of foodborne trematodes should be based on a national plan of action, integrating the responsibilities and actions of each sector. Health promotion and food safety are relevant to all control strategies. A comprehensive approach, which includes health education, would define the role of each sector. The likelihood of failure of inappropriate or poorly planned public health education programmes is well recognized. The change to safer food habits and adoption of safe techniques for food preparation are long-term objectives for health promotion.

To achieve intersectoral collaboration in endemic countries, it is desirable to establish an interministerial committee with executive powers to support intersectoral actions and establish the regulations necessary to maintain trematode-free foods. Such bodies may already exist in many countries as food authorities or commissions representing food producers and consumers.

3. **Public health impact**

The acute phase of foodborne trematode infections can cause great pain and discomfort, while chronic infections can lead to severe disabling disease, which greatly reduces human productivity and the quality of life.

The diseases that most concern the health services in the endemic areas are: cholangiocarcinoma in *Opisthorchis* infections; cholangiocarcinoma and gallstones in *Clonorchis* infections; and severe clinical liver disease in *Fasciola* infection. Moreover the misdiagnosis of tuberculosis in people with paragonimiasis is a concern in both endemic and non-endemic areas.

It is noteworthy that the epidemics in developing countries have caught health authorities unprepared and in each instance there has been a long interval of up to one year before the cause of the outbreak has been determined. For example, fascioliasis epidemics in Cuba in 1983 and in the Islamic Republic of Iran in 1989 were first diagnosed as visceral larva migrans due to *Toxocara canis*.

Intestinal trematode infections have generally been considered to cause low morbidity, but in the Philippines, the Republic of Korea, and Thailand these infections have increasingly been associated with chronic diarrhoea.

Reducing the public health and economic impact of foodborne trematode infections will be a challenge for the public health sector as well as many other sectors of development.

Strategy of control

4. Epidemiological determinants

The distribution of foodborne trematode infections is determined by human food-related behaviour. The distribution of the trematodes and their intermediate hosts in the environment is far greater than that of human infection. Ultimately the triad of poverty, pollution, and population growth contributes to the changing epidemiological patterns.

To understand the distribution of infection it is necessary to utilize all the epidemiological information available, such as the relationship between the host, the parasite, and the environment. In some countries, ethnic or traditional food habits are well described, but this information has seldom been used to orient epidemiological surveys. Epidemiological investigations could begin in the areas of high-risk food behaviour.

The spatial distribution of infection is aggregated or clustered at all levels: family, village, district, province, and country. Thus, the distribution of foodborne trematode infections should be assessed by the prevalence of the infection in the smallest administrative unit. Moreover, the distribution of heavy or severe infections is also overdispersed, i.e. only a few people, a few villages, or a few districts have clinically detectable disease. Morbidity rates tend to parallel the prevalence and intensity of infection.

The incidence of foodborne trematode infections is difficult to measure. The early stages of infection are sometimes not apparent or not specific and, from their clinical features, can be confused with other causes of disease. The later chronic stages of infection are difficult to identify except by detailed clinical examination or on occurrence of a specific clinical manifestation such as obstructive jaundice, biliary stones, or cholangiocarcinoma.

The underlying cause of epidemics of foodborne trematode infections, particularly fascioliasis, is the use of animal manure in agriculture. Animal infections are cumulative – the parasite does not multiply in the host. When there is a coincidence of high prevalence and intensity of infection in animals and optimal climatic and environmental conditions, the risk of human infection markedly increases. However, the level of risk may depend on the species of parasite, the habitat of the intermediate host, and the closeness of contact between people and animals. When infection does occur, the onset may be remarkably sudden and, depending on the extent of exposure, large numbers of people may be infected before any clinical manifestations attract the attention of health authorities.

4.1 Food-related determinants

Human foodborne trematode infections result from the ingestion of raw and inadequately processed fish, shellfish, and water plants or from drinking water contaminated with metacercariae. Food habits are therefore the basis of risk of human foodborne trematode infections. Several sociocultural, economic, and behavioural factors promote the infection of aquatic food or favour transmission of infection to humans.

Perceptions of food are related to beliefs, culture, taboos, and traditions and are increasingly influenced by mass communication. Food habits are formed under particular social and economic conditions. When adapted by individuals or groups to other settings, they may be unsuitable or can even be harmful to health. For example, rural or indigenous peoples moving to urban areas or migrant workers, tourists, or refugees living in foreign communities often maintain their food habits although the conditions for food production, preparation, or processing may be inappropriate or inadequate.

The sensory properties of a food, the anticipated consequences of ingestion and knowledge of the nature or origin of the food all interact to influence food choice, but the hedonistic response – like or dislike – is the major determinant.

Understanding the food-related determinants of foodborne trematode infections is the crux of any control strategy and is important for assessing the suitability of any alternative food sources or preparation methods proposed. Ultimately these determinants will affect the extent to which changes in methods of food preparation and processing will be accepted and implemented.

4.1.1 **Social and cultural determinants**

The mode of transmission of foodborne trematode infections is closely related to behavioural patterns determined by the socioeconomic and cultural conditions in the endemic countries (4).

Consumption of raw or undercooked fish and shellfish is widely prevalent around the world, particularly in areas near lakes, streams, and ponds, where fresh fish is readily available. In the Republic of Korea, raw fish is usually served at male social gatherings as an accompaniment to rice wine; this can result in infection with *Clonorchis* spp. and many species of intestinal fluke. In southern China slices of raw fish are dipped in boiling soup for a moment and eaten with or without spices or sauce; another popular dish in China is raw fish in hot rice congee.

Crab soaked in soy sauce (*ke-jang*) is the main source of *Paragonimus* infection in the Republic of Korea, and pickled or wine-soaked (“drunken”) crabs are considered a delicacy by the Chinese living in endemic areas of paragonimiasis. *Kinilow* (raw crab or fish) and *sinigang* (which includes crab) are favourite dishes in endemic areas of paragonimiasis in the Philippines, as is *pla-poo* (raw crab) in Thailand.

Opisthorchis infection is acquired by eating raw or inadequately cooked, frozen, salted, or smoked fish, for example in the form of *koi-pla* (raw fish) in Thailand. Similar local dishes are available in many other endemic countries.

In northern Luzon, in the Philippines, a 69% prevalence of *Echinostoma malayanum* infection in one area was associated with the long-standing tradition of eating raw *Lymnaea* snails.

Among plant carriers of trematode infections, some species of watercress (e.g. *Nasturtium officinale*) are most commonly, though not always, responsible for human fascioliasis when eaten raw in green salads. Watercress is frequently consumed in southern Europe and outside Europe in countries to which south Europeans have migrated. In Algeria, during the French occupation, outbreaks of fascioliasis occurred among Europeans living there, whereas no cases were recorded among native Algerians who did not eat watercress. A favourite snack, especially for rural children, is water caltrop (*Trapa natans*), the most important plant vector for fasciolopsiasis in east Asia. Changes in dietary habits towards “organically” grown or wild leaf vegetables are increasingly associated with human fascioliasis in Europe and Latin America among members of the upper social classes.

Traditional eating habits are part of the deeply rooted culture of a community and are therefore resistant to change. The reluctance to change food habits is sometimes linked to the belief that raw animal food increases vigour and improves potency and health. For instance, people in the Republic of Korea have become infected with *Fibricola seoulensis* by eating the raw viscera and muscle of certain snakes which are

paratenic hosts of the fluke. The inhabitants of this area hold the traditional belief that snakes have a special nutritional and medicinal effect on health.

Crayfish are usually not eaten raw in the Republic of Korea. However, the traditional practice of using the raw juice of crushed crayfish as home treatment for measles has been a significant source of infection, and may cause devastating neurological sequelae from cerebral paragonimiasis in children. In certain Cameroonian (Bakosi) and Nigerian (Calabar) tribes, raw crabs are believed to increase women's fertility. In Ecuador, parents grind up crabs (*Hypolobocera* spp.) and give the supernatant to their sick children as a medication.

Sometimes economic, environmental, and social factors impose the consumption of raw or insufficiently cooked aquatic food on the community or on individuals. Some poor people are unable to cook food properly because of the prohibitive cost of fuel, and people living or working on fishing boats may not have adequate cooking facilities. Wars may also impose changes in food preparation habits. Following the civil war in Nigeria (1967-1970), an increase in clinical cases of pulmonary paragonimiasis was observed in eastern Nigeria and was attributable to the consumption of inadequately cooked crabs during and after the war. A similar situation occurred in China, Japan, and the Republic of Korea when people were obliged to resort to eating raw crustaceans because of the shortage of food during the Second World War.

In east Asian countries, the practice of using human excreta as fertilizer and the habit of indiscriminate defecation contribute to the contamination of the water bodies where snail hosts of the parasites breed. In areas of China in which clonorchiasis is highly endemic and in areas of Asia with ethnic Chinese communities, toilets have been built on ponds as a source of fish food. This practice is decreasing with modernization.

4.1.2 **Food cultivation**

Traditional methods of cultivation may tend to promote foodborne trematode infections. In addition, natural disasters, economic constraints and environmental considerations can force changes in cultivation patterns or techniques that may promote the spread of infection (for example a greater use of animal manure rather than chemical fertilizers).

Watercress (*Nasturtium officinale*) is the main source of *Fasciola hepatica* infection. However, a wide range of other plants may support the metacercariae. While safe cultivation techniques are important in reducing the risk of infection in plants, the ultimate goal is to reduce the infection of animals through the use of anthelmintics and grazing management. In many areas of the world watercress is traditionally grown using animal manure as the primary fertilizer. In other areas, the effluent from livestock pens or slaughterhouses has been used to fertilize the watercress plots. Many outbreaks of human fascioliasis have also

been associated with wild watercress. In many countries it is fashionable to collect and eat wild watercress, which is touted as a healthy natural food.

Conditions for transmission of *Fasciolopsis buski* are present in areas of cultivation of water caltrop (*Trapa natans*), water chestnut (*Eliocharis tuberosa*), water hyacinth (*Eichhornia crassipes*), water bamboo (*Zizania aquatica*), *Salvinia natans*, and duckweed (*Lemna polyrrhiza*), which in China are physically linked to the drainage systems of pig farms. The farms provide manure which is used as a fertilizer for the cultivated plants.

In Thailand, nearly all aquatic macrophytes in endemic areas of fasciolopsiasis can support the metacercariae, but only five species are frequently consumed by people, livestock, or both. These are: water caltrop (*Trapa bicornis*), water hyacinth (*Eichhornia crassipes*), lotus (*Nymphaea lotus*), water mimosa (*Neptunia oleracea*), and water spinach (*Ipomoea aquatica*).

Fish cultivation (aquaculture) continues to grow in economic importance worldwide. In most of the world, particularly in Asia, cyprinids (carp) are the most commonly cultured fish. These are the principal host species of *Clonorchis sinensis*, *Opisthorchis felineus*, and *O. viverrini*. The consumption of inadequately prepared or preserved aquaculture products is therefore not without risk since the fish-ponds may offer excellent habitats for intermediate snail hosts and may be contaminated by untreated human or reservoir-animal excreta. Through appropriate aquaculture practices, contamination of the cultured fish and the risk of these infections can effectively be reduced or eliminated.

4.1.3 **Food preparation and preservation**

Fish is a perishable food and it deteriorates quickly at the high temperatures that prevail in the tropics and subtropics. In the absence of chilling facilities, traditional techniques for fish processing have been developed on the basis of rapid sun-drying and air-drying, assisted by salting and occasionally smoking. Although marine fish are most often used in making traditional food products, freshwater fish are also used, especially by people who live near inland lakes, rivers, and brackish waters. Freshwater fish are more commonly processed in the home and in cottage industries than in industrial processing plants.

Fermentation is a traditional preparation procedure for freshwater fish, especially in Cambodia, the Lao People's Democratic Republic and Thailand, but new trends in the marketing and consumption of semi-fermented fish shortly after its preparation are increasing the risk of human infections. In southern Asia, in general, fermented fish pastes and sauces are of greater importance than fish preserved by salting and drying, whereas in west Africa, hot smoking is used frequently, and is also practised in other tropical countries.

Some traditional preparations of freshwater fish are safe. In Myanmar, fish paste, locally called *ngapi*, is traditionally prepared by fermentation of raw freshwater fish in brine for up to several months. Before use the paste is brought to the boil with a small amount of water and then served with boiled or green vegetables. Another type of *ngapi* is commonly prepared by roasting fish on an open fire and it is eaten after thorough heating with oil or chilli according to taste. Since all the methods of preparation of fish paste require heating, fishborne trematodes are not a public health problem in Myanmar, in contrast to neighbouring countries. However, paragonimiasis does occur among the ethnic groups at the Myanmar border with India where crabs are traditionally eaten raw.

Cooking is the most widespread technique for preparing fish for consumption, but if cooking is inadequate because it has been too rapid or the fish is too large, the risk of transmission of viable parasites is increased. In some societies, ritual food preparations require that the plant or the fish remain raw and untreated. Furthermore, the recipient, who may be a religious leader, has no right to refuse whatever food is offered.

Watercress and other aquatic plants are eaten raw as salad or added as a seasoning with spices to other foods. Apart from extensive washing, no specific preparation procedure can reduce the risk from contaminated plants. Preliminary studies do indicate, however, that 4% potassium permanganate tends to reduce the viability of metacercariae.

The known effects of various techniques of food preparation and processing on the infectivity and viability of metacercariae are summarized in section 12. Most of the physical variables (temperature, pH, etc.) of the processing techniques commonly used for fish, shellfish, and aquatic and semi-aquatic vegetables have been studied only inadequately, and additional research is urgently needed.

4.2 **Ecological and environmental determinants**

Control strategies will be shaped by the ecological and environmental determinants of the epidemiology of foodborne trematode infections. Ecological factors determine the distribution of the intermediate snail host, and of the amphibian or aquatic and mammalian hosts. Environmental degradation has contrasting effects: it can create conditions for transmission in one region while decreasing the incidence of infection in another.

4.2.1 **Water resources development**

The effects of water resources development on the transmission of human foodborne trematode infections have been documented in several parts of the world. These infections become evident later than other parasitic diseases commonly associated with development of water resources –

lymphatic filariasis, malaria, and schistosomiasis (5) – because of their complex life cycles and low morbidity in the early stages.

In the area of the Nam Pong Resources Development Project in Thailand, irrigation has promoted the creation of snail habitats and increased freshwater fish populations, which, linked to poor hygiene habits and lack of sanitation, have led to intense transmission. The prevalence of opisthorchiasis due to *O. viverrini* is higher among the residents in the project area than in the surrounding non-irrigated areas. Furthermore, fish from the area are sold over a wide region, so that infection has spread to populations at some distance from the project.

The E. I. Martsinovsky Institute, Moscow, Russian Federation, in collaboration with the Ministry of Health, maintains an ecological and health surveillance programme for 20 large reservoirs in the Dnepr, Volga, Kama, Don Daugava, Yenisey, Ob, Seym, and Amudar'ya river basins. Among the people living near these reservoirs, diphyllbothriasis and opisthorchiasis are important public health problems.

In the Irgiz-Turgay region of the former USSR, opisthorchiasis due to *O. felineus* is highly endemic. However, the construction of the Irtysh-Karaganda-Dzhezkazgan canal, which incorporates several reservoirs, has reduced the prevalence of the disease. This amelioration is due to:

- changes in fish populations which have reduced the numbers of fish intermediate hosts of the parasite;
- salination;
- drainage of part of the watershed;
- reduction of rodent reservoir hosts;
- decreased contamination by sewage effluents.

In addition to water resources developed specifically for aquaculture, small water impoundments can also provide opportunities for the production of freshwater fish, molluscs, and crustacea. However, public health considerations must be taken into account. Small unregulated impoundments can become sites of intense transmission of fishborne trematode infections and other tropical diseases. Where national registration is not obligatory, the numbers and locations of these small dams are unknown to administrative and planning authorities. Small dams may be sponsored on behalf of a village by the local authority with government support, or may be constructed by nongovernmental organizations, missionary societies, chiefs, and local community groups. Road contractors with heavy equipment who are working in the vicinity on road building may be privately hired to construct the dams. Dams that are not financed by the government are particularly prone to problems of inadequate maintenance, seepage, and poor discipline in water usage, all of which favour the extension of vector habitats. Such dams compound the problem of disease transmission regardless of whether or not they improve the agronomic situation. The formation of local, nongovernmental voluntary organizations, including traditional village groups, should be

promoted to assist in planning and management of these small reservoirs. Such organizations could help to prevent foodborne trematode infections and other parasitic and infectious diseases.

4.2.2 ***Aquaculture and fisheries***

The increasing global importance of aquaculture is directly related to the quantifiable contribution it is making to narrowing the growing gap between supply and demand for fish and fishery products. Aquaculture is also a source of foreign exchange revenue in many developing countries from the export of high-value products. It also creates employment, particularly in economically depressed coastal regions and other remote areas and contributes to the household economy of farmers.

Since aquaculture was first practised in China about 4000 years ago, eastern Asia has become the most important aquaculture region in the world. Several countries, such as Japan, the Philippines, and Viet Nam, have long traditions of aquaculture dating back some 300–400 years.

Although aquaculture is increasing in most Asian countries (Table 1), particularly in Cambodia, China, the Philippines, the Republic of Korea, Thailand, and Viet Nam, it still accounts for only a small proportion of total freshwater fish production in some countries. For example, in 1990 the percentage of cultured freshwater fish was 4.9% in Myanmar, 9.3% in Cambodia, 12.5% in the Lao People's Democratic Republic, 13.9% in the Philippines, 46.2% in Thailand, 47.9% in the Republic of Korea and 80.3% in China. Thus (with the exception of China) most freshwater fish still comes from the natural water bodies in the endemic countries, despite the rapid development of cultured fish production in the region.

For the peoples of Africa and Asia, fish is a staple food, together with grain, and is the main source of animal protein. Further development of aquaculture is assured since it is a rapidly growing entrepreneurial activity, rather than a subsistence activity.

Aquaculture extension services and personnel should be actively involved in national control programmes to prevent and reduce foodborne trematode diseases, in view of their close participation in community activities. Aquaculture extension services exist in one form or another in most countries, but the number of extension workers correlates closely with the wealth of the country, or with its interests in fish production. A well developed network exists throughout much of eastern Asia, though it has insufficient workers in the poorer areas of the Lao People's Democratic Republic and Viet Nam. Extension services are also insufficient in most of sub-Saharan Africa, Latin America and the Caribbean. A major problem for areas where there are few extension workers has been their lack of mobility, though this is now being rectified in many countries.

Table 1
Production of cultured freshwater fish (in tonnes) in selected countries

| Country | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Cambodia | 1 149 | 3 140 | 2 340 | 2 640 | 4 741 | 6 282 | 6 080 | 6 090 |
| China | 1 811 100 | 2 379 300 | 2 931 500 | 3 484 100 | 3 897 500 | 3 915 169 | 4 199 195 | 4 289 592 |
| Democratic People's Republic of Korea | 5 000 | 5 500 | 5 500 | 6 000 | 8 000 | 10 000 | 11 000 | 11 000 |
| Lao People's Democratic Republic | 2 500 | 2 500 | 2 600 | 2 800 | 3 000 | 3 200 | 3 400 | 3 600 |
| Myanmar | 3 944 | 5 044 | 5 797 | 5 487 | 5 668 | 6 940 | 7 083 | 4 237 |
| Philippines | 32 417 | 50 238 | 61 825 | 83 737 | 81 232 | 89 223 | 81 077 | 81 567 |
| Republic of Korea | 692 | 1 182 | 3 439 | 5 119 | 7 381 | 8 788 | 12 603 | 10 109 |
| Thailand | 49 145 | 73 334 | 84 728 | 78 157 | 90 702 | 83 218 | 89 588 | 98 811 |
| Viet Nam | 100 000 | 110 000 | 110 000 | 115 000 | 115 000 | 115 000 | 115 000 | 130 000 |
| Grand total | 2 005 947 | 2 630 238 | 3 207 729 | 3 783 040 | 4 213 224 | 4 237 820 | 4 525 026 | 4 635 006 |

Source: Csavas I. FAO Regional Office for Asia and the Pacific (1993).

4.2.3 **Urbanization**

The world's urban population has almost tripled in the past 30 years, mostly in developing countries. High growth rates and population density in urban areas have exceeded the capacity of these areas to provide adequate resources (housing, employment, and other services). This has resulted in the exposure of increasing numbers of peripheral urban dwellers to the hazards of poverty, unemployment, inadequate housing, poor sanitation, pollution, disease vectors, poor transport, and psychological and social stress.

The risk of transmission of foodborne trematode infection due to urbanization has not been documented. In Asia aquaculture is becoming increasingly periurban in order to be close to urban markets and to reduce transport costs. In addition, gardens provide an efficient and economic means of vegetable production in the periurban areas. If these activities are poorly managed and untreated human or animal excreta are used as a fertilizer, the potential for transmission should be monitored. Clonorchiasis is reported only occasionally in Singapore, while in Hong Kong and Macao it is the most common parasitic infection reported by public health laboratories. In the Republic of Korea, the pollution of the urban and periurban waterways has reduced the quality, and hence consumption, of natural fish, which were formerly a source of infection.

4.2.4 **Refugees**

The Office of the United Nations High Commissioner for Refugees has estimated that there were more than 18 million refugees in 1992 and another 20 million displaced persons within national boundaries: one out of every 134 members of the global population of 5.2 billion people has been forced to leave home. More than 1 million refugees are in south-eastern Asia and the western Pacific region, mainly in areas where foodborne trematodes are endemic. Many of the refugees have had prolonged stays in camps where health problems are common because of severe overcrowding, limited supplies, and lack of sanitation facilities.

Foodborne trematode infections are one of the health problems of refugees. In refugees from Asia, the prevalence of *Opisthorchis* infections has been put at between 5% and 20% in different studies (e.g. 6). Cholangiocarcinoma associated with liver fluke infections is also observed in Asian immigrants to Europe and the United States.

Fascioliasis has been observed both in Ethiopian migrants to Israel and among Mozambican refugees, and heavy infections have been reported to be a cause of death in Mozambican refugee children.

In refugees from south-east Asia, pulmonary paragonimiasis has been diagnosed frequently in France and the United States of America. The diagnosis is often a challenge to clinicians and radiologists in the non-endemic regions since paragonimiasis mimics, and may coexist with, tuberculosis.

Favourable conditions for transmission of trematode infections may be found in refugee camps where poor sanitation practice, limited availability of food, unsafe eating habits, and a favourable biological environment (susceptible intermediate hosts) exist. The large quantities of food required in refugee camps have necessitated the promotion of aquaculture to meet the minimum protein requirements. Untreated human faeces have been inappropriately recommended as a food source for the fish in certain camps in Cambodia and the Lao People's Democratic Republic. A high prevalence of opisthorchiasis has been observed in both Cambodians and Laos in refugee camps.

Labour migration contributes significantly to the potential for spread and introduction of foodborne trematode infections. In the Russian Federation, extensive migration of workers to and from the oil fields of Siberia has contributed to the spread of the diseases. In Kuwait and Taiwan, China, immigrant Thai workers were found to have *O. viverrini* infections, but so far no evidence of transmission to the local population has been established.

4.3 Situation analysis

The distribution of foodborne trematode infections has not previously been analysed with strategic objectives. The cumulative data have been based mainly on index cases and follow-up surveys in the locality of origin. The risks of foodborne trematode infections have not been mapped according to the distribution of the populations with high-risk food habits, although such studies can provide valuable information on the epidemiological determinants of infection. For example, epidemiological surveys for paragonimiasis could be targeted to areas in Ecuador where the distribution of certain groups who eat raw crabs has been determined.

The global distribution and estimates presented in this report are based on a systematic review of the scientific literature, supplemented with questionnaire surveys of WHO Member States administered by the WHO regional offices, and personal communications with scientists throughout the world. The total population data are derived from United Nations sources, while data referring to smaller administrative units are derived from national sources to establish a more disaggregated estimate of risk. The estimates of prevalence and morbidity are based on actual surveys or on extrapolation from available epidemiological studies. Certain data sets have been partially integrated into a geographical information system (GIS) for analysis. The data presented in this report should be interpreted with caution since in many countries the surveys are limited and the laboratory confirmation of diagnosis is lacking. Improved accuracy of future epidemiological data will require surveillance and monitoring with collaboration between anthropologists, social scientists, and specialists in agriculture and aquaculture.

4.3.1 **Global distribution**

Throughout the world over 40 million people have foodborne trematode infections out of a total of 750 million people at risk (see Annex 1).

Since 1950, human fascioliasis has been reported from 61 countries and areas. In the 8 countries from which infections are currently being reported, over 180 million people are at risk of infection and 2.4 million of these are estimated to be infected with either *F. hepatica* or *F. gigantica*.

Of the fishborne trematode infections, clonorchiasis has been reported since 1970 from 9 countries and areas: the Russian Federation and 8 countries and areas in the Western Pacific Region. About 290 million people are at risk, of whom over 7 million are infected. Opisthorchiasis due to both *O. viverrini* and *O. felineus* has been found in 4 countries and areas of the European, South-East Asia, and Western Pacific Regions. About 64 million people are at risk and 10.3 million of these are infected.

Paragonimiasis is global in its distribution in freshwater crabs. Human infections have been reported from 39 countries and areas, although the major endemic areas are in Asia. About 195 million persons are at risk, of whom 20.7 million are infected.

Some 30 countries and areas have reported infections due to over 70 species of intestinal trematode (see Annex 2). Because these infections are focally distributed, it has not been possible to determine reliably either the population at risk or the number of infected people; however, a minimum of 1 million people infected is an informed estimate.

High prevalences of clonorchiasis and the clinical sequelae of biliary tract gallstones and cholangiocarcinoma have been reported among Chinese communities in Canada and the United States. Among Lao immigrants in France and the United States, opisthorchiasis has frequently been reported. Raw food clandestinely imported from endemic areas for consumption by particular ethnic populations often bypasses import inspection and can be a source of infections in non-endemic countries.

Fascioliasis

Animal fascioliasis results from infections with *Fasciola hepatica* or *F. gigantica*, and is a cause of serious economic loss in the animal husbandry industry. It is a common disease of ruminants, especially sheep, goats, and cattle, although many other domestic and wild animals may also be infected. The distribution of the parasite is cosmopolitan. In comparison with animal infections, human infections are uncommon. However, clinical cases of fascioliasis have been reported from 61 countries and areas in Africa, the Americas, Asia, Europe, and the western Pacific. The largest numbers of infected people have been reported from Bolivia, Ecuador, Egypt, France, the Islamic Republic of Iran, Peru, and Portugal.

Fasciola hepatica is considered to be more adapted to the human host than *F. gigantica*. Human disease due to the latter has been reported in comparatively few geographical areas.

High rates of fascioliasis in domestic animals and the frequency of human infection show no consistent quantitative relationship, but are linked temporally and spatially in all reported outbreaks. In some areas, fascioliasis is a sylvatic zoonosis and its importance in maintaining the parasite in the environment is recognized. The following situation analysis reviews fascioliasis in selected countries. The status of human fascioliasis in Bolivia, Ecuador, Egypt, the Islamic Republic of Iran, and Peru is reviewed on pages 99–102.

Animal fascioliasis is endemic throughout the Americas including Canada and the United States, but human infections are rare in most of these countries (see Table 2).

On the Caribbean island of Cuba, which has approximately 6 months of rain and 6 months of drought per year, human infection due to *F. hepatica* was first reported in 1923. The intermediate snail host is *Fossaria cubensis* and animal fascioliasis is widespread on the island. Watercress (*Nasturtium officinale*), locally known as *berro*, is the major source of infection. Epidemics were reported in 1944 and 1947–1948, each associated with an unusually long rainy season. More than 1000 human infections occurred in an epidemic in 1983; the highest rates were observed in the municipalities of Santo Domingo (121.5 per 100 000 population) and Quemado de Güines (213.9 per 100 000 population) in Villa Clara Province. Data on the present distribution of animal fascioliasis and the exact frequency of human infection (which is currently low) are not available.

In north Africa and south-east Asia, animal fascioliasis is widespread in Algeria, Bangladesh, Indonesia, the Libyan Arab Jamahiriya, Malaysia, Morocco, Thailand, and Tunisia, but few confirmed human infections have been reported although the potential for human fascioliasis exists. Animal fascioliasis is also widespread and highly prevalent in all the 30 provinces of China, but only 41 isolated human infections were reported before 1988. However, at least 161 human infections have been detected in the past five years.

Animal fascioliasis is a major veterinary problem in Europe, but data on the current frequency of human infection are not available from most European countries.

Since the first description of *F. hepatica* in animals and its association with marsh fields by Jean de Brie in 1379, France has had recurrent epidemics of fascioliasis and in certain areas the disease is still endemic in animals. Between 1956 and 1982, about 10 000 human infections were documented in France. Two peaks of frequency occurred in 1956–1958, with outbreaks in the Lyon region, and in the Pyrénées-Atlantiques and Lot-et-Garonne departments, and in 1965–1967 in the Lyon region and

Table 2

Geographical distribution of foodborne trematode infections^a

| Country or area | <i>Fasciola</i> | <i>Clonorchis</i> | <i>Opisthorchis</i> | <i>Paragonimus</i> |
|-------------------------------|-----------------|-------------------|---------------------|--------------------|
| African Region | | | | |
| Algeria | C | – | – | – |
| Burkina Faso | – | – | – | C |
| Cameroon | – | – | – | B |
| Central African Republic | – | – | – | C |
| Côte d'Ivoire | C | – | – | C |
| Equatorial Guinea | – | – | – | C |
| Ethiopia | B | – | – | – |
| Gabon | – | – | – | C |
| Guinea | – | – | – | C |
| Liberia | – | – | – | C |
| Madagascar | C | – | – | – |
| Mali | C | – | – | – |
| Mozambique | C | – | – | – |
| Nigeria | – | – | – | B |
| Sierra Leone | – | – | – | C |
| Zaire | – | – | – | C |
| Zambia | – | – | – | C |
| Zimbabwe | C | – | – | – |
| Region of the Americas | | | | |
| Argentina | C | – | – | – |
| Bolivia | A | – | – | – |
| Brazil | C | – | – | – |
| Canada | – | D | D | C |
| Chile | C | – | – | – |
| Colombia | C | – | – | C |
| Costa Rica | C | – | – | C |
| Cuba | B | – | – | C |
| Dominican Republic | C | – | – | – |
| Ecuador | C | – | – | A |
| El Salvador | C | – | – | C |
| Guatemala | – | – | – | C |
| Honduras | – | – | – | C |
| Mexico | C | – | – | C |

Table 2 (continued)

Geographical distribution of foodborne trematode infections^a

| Country or area | <i>Fasciola</i> | <i>Clonorchis</i> | <i>Opisthorchis</i> | <i>Paragonimus</i> |
|---|-----------------|-------------------|---------------------|--------------------|
| Nicaragua | – | – | – | C |
| Panama | – | – | – | C |
| Peru | B | – | – | A |
| Puerto Rico | C | – | – | – |
| United States | C | D | D | C |
| Uruguay | C | – | – | – |
| Venezuela | – | – | – | C |
| Eastern Mediterranean Region | | | | |
| Egypt | A | – | – | – |
| Iran (Islamic Republic of) | A | – | – | – |
| Iraq | C | – | – | – |
| Kuwait | – | – | D | – |
| Lebanon | C | – | – | – |
| Morocco | C | – | – | – |
| Saudi Arabia | C | – | – | – |
| Syrian Arab Republic | C | – | – | – |
| Tunisia | C | – | – | – |
| Yemen | C | – | – | – |
| European Region | | | | |
| Austria | C | – | – | – |
| Belgium | C | – | – | – |
| Bulgaria | C | – | – | – |
| Commonwealth of Independent States ^b | B | B | A | C |
| France | A | – | – | – |
| Germany | C | – | – | – |
| Greece | C | – | – | – |
| Hungary | C | – | – | – |
| Ireland | C | – | – | – |
| Israel | C | – | – | – |
| Italy | C | – | – | – |
| Norway | – | – | D | – |
| Poland | C | – | – | – |
| Portugal | A | – | – | – |

Table 2 (continued)

Geographical distribution of foodborne trematode infections^a

| Country or area | <i>Fasciola</i> | <i>Clonorchis</i> | <i>Opisthorchis</i> | <i>Paragonimus</i> |
|-------------------------------------|-----------------|-------------------|---------------------|--------------------|
| Slovakia | C | – | – | – |
| Spain | B | – | – | – |
| Sweden | C | – | – | – |
| Switzerland | C | – | – | – |
| Turkey | C | – | – | – |
| United Kingdom | C | – | – | – |
| Yugoslavia | C | – | – | – |
| South-East Asia Region | | | | |
| India | C | – | – | C |
| Indonesia | – | – | – | C |
| Myanmar | – | – | – | C |
| Nepal | C | – | – | C |
| Thailand | C | – | A | B |
| Western Pacific Region | | | | |
| Australia | C | – | – | – |
| Cambodia | C | – | C | C |
| China | B | A | – | A |
| Hong Kong | – | B ^c | – | – |
| Japan | C | C | – | A |
| Lao People's Democratic Republic | – | – | A | B |
| Macao | – | B ^c | – | – |
| Malaysia | – | C ^c | – | – |
| Philippines | C | – | – | B |
| Republic of Korea | C | A | – | A |
| Singapore | – | C ^c | – | – |
| Viet Nam | C | A | – | C |
| Total ^d | 61 | 9 | 4 | 39 |

^a For *Fasciola* and *Paragonimus* infections, estimates are based on the numbers of cases reported since 1950 in the scientific literature and by ministries of health: A, more than 1000 cases documented; B, 100–1000 cases documented; C, less than 100 cases documented.

For *Clonorchis* and *Opisthorchis* infections, estimates are based on the best available information, mostly in the form of informal reports made since 1970: A, estimated number of cases around or more than one million; B, high infection rate reported in some communities or endemic foci; C, low prevalence; D, imported cases.

Data were not available for countries omitted from the table or, in individual countries, for infections for which letter codes are not given.

^b These are: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, Uzbekistan.

^c Infection due to consumption of imported fish or in residents originating from endemic areas.

^d The Commonwealth of Independent States has been counted as a single entity. The totals exclude countries and areas in which only imported cases have been reported.

the Maine-et-Loire department. The areas in which the highest frequency of human infection occurred corresponded with a high prevalence in animals. The outbreaks in France have been associated with temperatures 0.5–1.0°C above the normal seasonal levels in the period from June to August and with an annual rainfall 100 mm greater than the previous 15-year average.

On the island of Corsica, *F. hepatica* is a zoonosis involving cattle, sheep, horses, and rats (*Rattus rattus*). Between 1952 and 1982 a total of 24 human infections were confirmed by demonstration of the eggs on faecal examination or of the parasite during surgery.

Although animal fascioliasis is widespread in Portugal, most human infections have been reported from the northern part of the country, mainly in the districts of Braga, Porto, and Viana do Castelo. Outbreaks of human infection were identified in three foci in the districts of Braga and Viseu North in 1970, 1974, and 1983; the most recent outbreak was in the Santarem district in 1990. About 1300 human infections due to *F. hepatica* have been reported by Portuguese public health laboratories during the past two decades.

The public health surveillance system in Spain does not require reporting of human fascioliasis. However, between 1970 and 1990, about 275 cases were reported from 12 autonomous regions, the majority from the Basque Country, in particular from Vizcaya where the infection rate was 5 per 100 000 population. Half of the infected persons aged 40–50 years gave a history of eating watercress.

Clonorchiasis

The epidemiology of clonorchiasis in China, Japan, and the Republic of Korea is reviewed on pages 97–99.

In Viet Nam, clonorchiasis is mainly endemic in the north in areas such as the Red River delta. It has been estimated that 28.4% of the residents in this area are infected. The infection rate is more than 40% in adults and 8% in children; men are more often infected than women. The highest infection rate (73%) has been reported from two endemic foci within the Red River delta (Haiphong and Hanoi). The only people found to have clonorchiasis in south Viet Nam are migrants from the north.

Clonorchis sinensis infection is endemic in the Amur River valleys to the far east of the Russian Federation. The prevalence of infection in the

native Nanai population is 24% in the most affected villages. The total population at risk is 341 000 people and the estimated number of infected people is 3000.

Clonorchiasis is an important health problem in Chinese communities living outside China. Among the Chinese people autopsied in Hong Kong in 1973, 23% were shown to have clonorchiasis. Of the Hong Kong residents of Chinese origin applying for emigration to Canada during 1979-1981, 13.4% had *C. sinensis* infections. Clonorchiasis is also the cause of most cases of pancreatitis initially diagnosed as being of unknown etiology among Chinese immigrants. Most of the *C. sinensis* infections reported in Malaysia and Singapore are probably acquired either while travelling in neighbouring endemic countries or from eating inadequately cooked fish imported from an endemic region.

Opisthorchiasis

Opisthorchiasis due to *Opisthorchis viverrini* is endemic along the Mekong River basin. Detailed epidemiological data on the Lao People's Democratic Republic and Thailand are given on pages 89-92. The Ministry of Health of Cambodia has recognized that opisthorchiasis due to *O. viverrini* is a major public health problem in the Mekong River basin north of Phnom Penh, especially in Phnom Penh Municipality, and in Takao and Kompong Cham Provinces.

Opisthorchiasis due to *O. felinus* is the most prevalent and widely distributed human trematode infection in the Russian Federation; it is also a public health problem in Kazakhstan and Ukraine. Information on its distribution and public health importance in these countries is given on pages 92-93. Limited endemic foci of opisthorchiasis in some areas of the Baltic States, eastern Germany, and Poland were described before the Second World War. No recent information on the distribution of human infection in Europe is available.

Other opisthorchid trematodes may infect humans. For example, human infection with *Amphimerus pseudofelineus* has been reported in Ecuador. In Canada, an outbreak of human infection due to *Metorchis conjunctus* occurred recently after ingestion of raw white sucker (*Catostomus commersonii*), a freshwater fish, prepared as sashimi. Other cases of this human infection have occasionally been reported in Canada and Greenland.

Paragonimiasis

Paragonimiasis is known as lung fluke disease, pulmonary distomiasis, endemic haemoptysis, or parasitic haemoptysis. Some countries in which paragonimiasis is endemic (Cameroon, China, Ecuador, Japan, Peru, and the Republic of Korea) are reviewed on pages 94-97.

A specific diagnosis is based on finding parasite eggs in a specimen of sputum or faeces, or eggs or worms in cutaneous lesions. However, it is

often difficult to make a parasitological diagnosis, particularly in the infection caused by *Paragonimus skrjabini* for which humans are not the most susceptible final host. The intradermal test is therefore used for epidemiological investigation in many areas, although a positive reaction is not necessarily an indicator of active paragonimiasis.

There are at least six species of *Paragonimus* in Thailand; of these, only *P. westermani* and *P. heterotremus* infect humans. The disease is prevalent in the central, northern, and north-eastern parts of the country. Two endemic areas have been identified in the central region in Sara Buri and Nakhon Nayok Provinces. In the north, endemic foci have been reported in Chiang Rai and Phitsanulok Provinces; however, sporadic cases have been found in mountain villages throughout the north.

In the Lao People's Democratic Republic, a low frequency of paragonimiasis (0.5%) has been found among patients suspected of having pulmonary tuberculosis; only 151 egg-positive sputum samples were found among those examined in the laboratories of five medical institutions between 1968 and 1972. Out of 1531 intradermal tests with *P. westermani* antigen in the general population in Pakse, Suvanaket, Vientiane, Ban Xon, Sanakha, Huang Prabang, and Huay Sai, 151 (9.8%) were positive; 22 active infections were found among those with intradermal reactivity. *P. heterotremus*, which can also cause human paragonimiasis, has been reported in stool specimens from patients treated in Vientiane hospitals.

Endemic foci and/or sporadic cases have been reported from Cambodia, the Manipur district of India, Indonesia, Myanmar, Nepal, the Philippines, Primorskiy territory in the far east of the Russian Federation, and Viet Nam.

Paragonimus uterobilateralis is the dominant species in Nigeria. Human infections occur in a large endemic focus in the Imo and Cross River basins in eastern Nigeria. In the 1970s up to 10% of schoolchildren were intradermally reactive to *P. westermani* antigen. Most infected people were under 20 years old, and the peak prevalence was in 10-14-year-olds.

Human infections have also been reported from Burkina Faso, Central African Republic, Congo, Côte d'Ivoire, Equatorial Guinea, Gabon, Guinea, Liberia, Sierra Leone, Zaire and Zambia. In some countries, transmission is suspected to occur occasionally in young children who eat raw crabs or are given traditional medicine based on raw crab juice. More surveys are necessary to evaluate the level of infection and the geographical distribution of paragonimiasis in Africa.

Several species of *Paragonimus* have been found in the Americas. Among them, *P. mexicanus* (= *P. peruvianus* or *P. ecuadoriensis*) is known to infect humans. The country in which paragonimiasis occurs most often is Ecuador, where thousands of cases have been recorded; the disease is also endemic in Peru. Limited endemic foci or sporadic cases occur in Canada, Colombia, Costa Rica, Cuba, El Salvador, Guatemala, Honduras,

Mexico, Nicaragua, Panama, the United States, and Venezuela. Four cases have been reported in Brazil, all in Japanese immigrants.

Autochthonous human infection has been confirmed in the Cajigal District, Sucre State in the Coastal Cordillera of north-east Venezuela, where *Didelphis marsupialis* (opossum) and the predominant freshwater crab, *Eudaniela garmani* (= *Pseudothelphusa garmani*), are naturally infected. The intermediate snail host has not yet been confirmed. In this area about one-third of the population is estimated to eat raw crabs and the intradermal positivity rate in one survey was 13%. It is noteworthy that the index case was diagnosed as cavitory pulmonary tuberculosis, and that the frequency of the diagnosis of pulmonary tuberculosis in the area is high, perhaps because it is confused with pulmonary paragonimiasis.

Intestinal fluke infections

Intestinal flukes are regarded as being a less important public health problem than liver or lung flukes. However, about 70 species of intestinal trematode have been reported to infect humans; many of them cause severe disease and some are widely distributed.

Annex 2 shows the geographical distribution of human intestinal trematode infections. Out of the countries and areas from which human infections have been reported, Bangladesh, Cambodia, China, Egypt, India, Indonesia, the Islamic Republic of Iran, Lao People's Democratic Republic, Philippines, the Republic of Korea, Thailand, and Viet Nam have the highest prevalences.

The geographical distribution of *Nanophyetus salmincola* is restricted to the north-western coast of the continental United States (the states of Washington and Oregon, and northern California) and to a region of the Amur River north-east of the Chinese border and Sakhalin Island in the far east region of the Russian Federation. The distribution of the trematode is determined by the presence of the snail, *Ugia* spp. Over 20 cases have been confirmed in Oregon, USA, and up to 80% of the indigenous minorities in some villages along the Amur River in the Russian far east have been found to be infected.

4.3.2 **Global monitoring and databases**

Monitoring of foodborne trematode infections is a challenge for modern technology and collaboration between sectors. The increasing feasibility of using electronic messaging networks, including electronic mail, fax, and linked databases, for global monitoring is now being demonstrated.

An adequate database for foodborne trematode infections should incorporate data from several sectors:

- agricultural data on climatic and soil conditions, and the distribution of fascioliasis in animals;

- aquacultural data on freshwater locations and types of fish or shellfish cultured;
- anthropological, social science, and behavioural data on food habits;
- ecological data on the distribution of intermediate snail hosts, aquatic fauna, and plant and mammalian reservoirs;
- information on the distribution of health care, food inspection, and agriculture and aquaculture services;
- data obtained from research and training institutions;
- epidemiological data on the distribution of human disease.

As a step in database development, WHO is attempting to determine the smallest administrative units that can be considered endemic for foodborne trematodes. The collection of data on the distribution of disease in large cities and metropolitan areas is problematic. In these population centres, the distribution of disease is determined by the distribution of food that has been transported from elsewhere, often over great distances. Transmission may not be occurring in the urban area itself and the data must be interpreted with caution.

Foodborne trematode infections are not identified separately in national reporting systems, but are included in summary statistics as parasitic infections. Data on foodborne trematode infections therefore generally have to be derived from epidemiological surveys and hospital record surveillance.

4.3.3 ***Geographical information systems***

Geographical information systems (GIS) technology provides a powerful new tool for epidemiological studies on vector-borne diseases with strong environmental determinants. By use of statistical and image analysis methods, GIS allow computer-based analysis of multiple layers of mapped data in digital form, including earth-observation satellite data, agroclimatic databases, and maps of host populations, vector distribution, and disease prevalence. All GIS data layers are registered so that their scale and geographical projection are identical to those of a reference base map. This allows analysis of all information by location, including descriptive data sets that are “attached” to specific locations or areas. The computer systems needed to run GIS, including image analysis and GIS capabilities, are now available at the microcomputer level at a reasonable cost.

Once created, GIS provide dynamic, easily updated mapping systems that can be used by health management officers to plan and monitor disease control programmes. By virtue of their potential to “match” the relative suitability of various environments to the life cycle and transmission dynamics of host-parasite systems, GIS provide a new way to address Pavlovskii’s classic concepts of “landscape epidemiology” and the essential focal nature of disease (7). Recent applications include

schistosomiasis, fascioliasis, Rift Valley fever, African trypanosomiasis, and East Coast fever.

The GIS applications for development, planning, and management of inland fisheries and aquaculture have been evaluated by FAO since 1986 (8). The orientation of this approach has been to optimize land use and site selection.

The unique biology and life cycle of *Fasciola hepatica* make it amenable to effective use of GIS control models. Its climatic sensitivity, fluctuations in the intermediate snail host populations, livestock population dynamics, and the potential for integration of geographical, mathematical, and cost-benefit analysis models offer unexplored opportunities for use of this new technology.

Exciting new developments are occurring in the form of networks of collaboration in GIS, such as that operating between the *Observatoire du Sahara et du Sahel*, the United Nations Institute for Training and Research, and the United Nations Sudano-Sahelian Office to integrate GIS programmes on the African continent to monitor environmental change. Health data can be integrated into these systems.

5. **Justification for national control programmes**

The control of foodborne trematodes will relieve the suffering of the millions of people affected, particularly women and children, and reduce the economic cost to endemic countries in terms of lost productivity and absenteeism.

5.1 **Public health importance of foodborne trematode infections**

National disease control programmes generally have sufficient data convincingly to demonstrate the public health importance of foodborne trematode infections, and to justify government priority for intervention. Specific data can be collected and analysed from national cancer registries and hospital records, from epidemiological surveys, and from the scientific literature, including that not indexed at international level.

Control of animal fascioliasis has not generally been given priority by ministries of agriculture, even in areas of high prevalence of human *Fasciola* infection such as the Altiplano of Bolivia, the highlands of Ecuador and Peru, the Nile delta of Egypt, and the Caspian area of the Islamic Republic of Iran (Fig. 1). A high prevalence of animal fascioliasis increases the risk of human infection, which can be fatal, especially in children.

The high rates of cholangiocarcinoma in certain areas of China, the Lao People's Democratic Republic, northern and north-east Thailand, the former USSR and Viet Nam are largely preventable by control of opisthorchiasis and clonorchiasis.

Lung disease caused by *Paragonimus* spp. is a public health problem in certain countries, and is frequently confounded with pulmonary tuberculosis in both endemic and non-endemic areas. Moreover, the frequency of epilepsy caused by central nervous system paragonimiasis is significant in some endemic areas.

Epidemics of these diseases, particularly fascioliasis, have caused extensive suffering and economic losses. Effective integrated control programmes could alleviate these problems. Veterinary public health services should also have a role in control of these diseases.

5.2 **Economic impact of foodborne trematode infections**

The cost of disease can be estimated in terms of absenteeism, hospitalization, disability, losses in the agricultural sector due to effects on animal health, and potential losses in fish export markets (see section 6.8.4, pages 46-47). Information on the economic impact of foodborne trematode infections, as with other parasitic infections, is generally lacking and is a research priority for the future.

5.2.1 **Costs due to loss of productivity and absenteeism**

The impact of foodborne trematode diseases on the productivity and absenteeism of farm labourers is difficult to assess. However, there have been some attempts to obtain this kind of information to provide economic justification for control activities. For example, in Thailand, the wages lost owing to the high frequency of opisthorchiasis in 15-60-year-olds are estimated to be US\$ 65 million per annum. The estimated direct cost of medical care is up to US\$ 19.4 million per annum. The total direct cost of opisthorchiasis infection in the workforce is estimated to be at least US\$ 84 million per annum. In areas of water resources development in Thailand where opisthorchiasis is endemic and the prevalence is above 50%, the residents suffer from two or three clinical episodes annually, which may require symptomatic medical treatment.

5.2.2 **Direct costs to the health care system**

The direct costs of foodborne trematode infections to the health care services of developing countries are enormous. Both inpatient and outpatient services are subject to demands for treatment. However, no systematic studies on the health care costs of foodborne trematode infections have been done.

Clonorchiasis

Clonorchiasis causes biliary tract infections, lithiasis, and cholangiocarcinoma; the direct costs of this disease to health services are considerable, even in non-endemic countries. For example, hospitals in North America serving the immigrant Chinese communities have reported that a significant proportion of biliary surgery is related to clonorchiasis.

Opisthorchiasis

In Cambodia and the Lao People's Democratic Republic concomitant opisthorchiasis and schistosomiasis due to *Schistosoma mekongi* cause severe liver disease requiring treatment in hospital. The incidence of cholangiocarcinoma secondary to opisthorchiasis is high in all endemic areas and places a heavy burden on health services.

Paragonimiasis

The cumulative individual case reports of children and adults with paragonimiasis suggest that invasive diagnostic or surgical procedures to determine the cause of unknown pulmonary disease are a major cost to health services.

The involvement of the central nervous system in paragonimiasis is costly in terms of control of epileptic seizure by medical management and, possibly, neurosurgery. In Ecuador up to 13% of people in some tuberculosis treatment centres have actually been found to have paragonimiasis, the treatment for which is 100 times less costly than that for tuberculosis.

Fascioliasis

Acute fascioliasis can be confounded with a number of other diseases and its diagnosis is usually delayed. The cost of investigation or prolonged observation to await definitive clinical symptoms is high. Diagnosis is also difficult in the chronic stages. Ultimately, a person with fascioliasis may be submitted to unnecessary exploratory surgery to establish the cause of disease.

Although the number of human cases of fascioliasis has increased in recent decades, an estimate of the cost to the health services has not been attempted. Human infections are closely associated with the distribution of domestic animal infections, but they are not related in a predictable way nor is human infection proportional to the prevalence among animals. In many developing countries, where fascioliasis is highly endemic, the resources for conducting the required epidemiological studies are not available. Such analyses are needed to allow public health authorities to establish health priorities.

Fasciolopsiasis and other intestinal trematode infections

The acute and chronic recurrent diarrhoea caused by these infections does not respond to the treatment recommended for diarrhoea caused

by bacteria and viruses. Misdiagnosis can result in costly repeated treatments.

5.2.3 ***Economic losses in the agricultural and aquacultural sectors***

Acute fascioliasis is an important cause of morbidity in cattle and sheep, mostly in young animals. The parasites actively feed on parenchymal cells and blood, and their effects on animal growth and productivity can be serious. These effects are related to the number of parasites present. In cattle, approximately 200 flukes per animal cause subacute or chronic clinical disease and significant production losses may occur in herds with infection prevalences greater than 25%. In experimental trials, calves with 40 or more adult *F. hepatica* worms gained 8% to 28% less weight than uninfected calves. Infection in adult cows adversely affects both milk production and milk quality. Additionally, in heifers, infections of 300 or more flukes may cause delays of up to 30 days in onset of first estrus, and reduce milk yield on calving. Infection in sheep may have a significant impact on wool production. In Peru, the total cost of loss due to fascioliasis in animals amounts to US\$ 11 million annually. Unfortunately, there have been few large-scale, well controlled studies on economic loss due to fascioliasis in livestock. However, the studies done so far are consistent in demonstrating that the disease is very destructive and warrant the conclusion that it deserves serious attention throughout the world from agencies with responsibilities for animal and public health.

The increased production of cultured fish and shellfish has opened new domestic and international markets. The potential losses that would result from banning the export of fish products from endemic areas need to be taken into account in economic planning and in deciding what priority should be given to the control of foodborne trematode infections.

5.3 **Feasibility and costs of control**

The Study Group supported an innovative concept of control, integrating the activities of the health, food and fish safety, aquaculture, agriculture, education and other sectors in a coordinated approach. The tools are available in each sector to ensure the effectiveness of their specific interventions.

Up to now, the cost of control of foodborne trematode infections has mainly reflected the cost to health services of providing diagnosis and treatment. The cost of an integrated approach involving food safety and other sectors has not been calculated but is not expected to be considerable.

In north-eastern Thailand, the control of opisthorchiasis among 3 million people living in seven provinces began in 1988. The initial programme (described in more detail on pages 90-92) was supported by national

resources and operated from 1988 to 1993. The Ministry of Health assumed responsibility for drug purchases and for support of the mobile teams, including community members, that performed stool examinations at village level. Residents paid a small fee for the stool examination and for drug treatment. The total cost of the project was about US\$ 8.3 million: about US\$ 2 million were provided by the Thai Government for drugs, and US\$ 3.3 million for training, education materials, and community participation came from the German Government, which collaborated in planning and organizing the control programme. Another US\$ 3 million were contributed by the villagers in the seven provinces for stool examinations and drugs for treatment of opisthorchiasis. The total cost of control in the project, if calculated as a cost per person, may be considered high; however, the actual cost to the Thai Government and the donor agency was reduced by the direct contribution from the target population in the endemic area.

In the Republic of Korea, the private sector, through the Korea Association of Health, provides low-cost health examinations and treatment. Mobile teams are supported by cost recovery from fees charged to individuals for laboratory examinations and by the government. The Association receives in the range of US\$ 2.5 million to perform about 15 million examinations per year.

The cost of lack of control of foodborne trematode infections is cumulative. Complacency about the problem and the institution of half-hearted measures for prevention and for monitoring and surveillance will only delay the reduction of prevalence and morbidity and will not control the diseases. For example, if aquacultural production costs are cut by economizing on surveillance and supervision of the use of human excreta (either by direct application or in the form of sewage), the risk of diseases such as hepatitis, polio, and bacterial infections as well as foodborne trematode infections may increase.

5.4 **Models for control programmes**

Models for controlling foodborne trematode infections have been tested and proved effective in the long term. No model for control is complete or applicable to all situations. Thus, critical analysis and adaptation of existing programmes to national situations will be necessary. National plans of action should include detailed descriptions of each of the approaches to be used in the programme. The experience of Thailand may be cited as an example. This country has an agriculturally based economy and a high prevalence of foodborne trematode infections. A similar situation exists in other south-east Asian countries. Opisthorchiasis has been recognized as an important public health problem in Thailand due to the high prevalence in the north and north-east of the country, especially in the economically productive age groups and in the areas targeted for development.

In 1981, a small pilot control programme was initiated in Khon Kaen Province, using a combination of annual single-dose chemotherapy (40 mg/kg of praziquantel), intensive health education directed at improving food habits, and promotion of latrine construction and use (9). After two years, opisthorchiasis was brought under control: the initial prevalence of 56% was reduced to less than 10% and the incidence of new infections and mean faecal egg output were also reduced.

In 1988, this model was adopted by the Ministry of Health and a large project covering 3 million people in seven provinces in north-eastern Thailand was initiated (see pages 31–32 and 90–92). This programme has shown that the control of foodborne trematode infections can be achieved through community participation and the cost of control can be shared by the people themselves.

In Japan and the Republic of Korea, another “model” has been used that integrates control of foodborne trematodes into broad-based national programmes for the control of parasitic infections, immigration, and family planning. The creation of nongovernmental organizations for management and planning has been a hallmark of these programmes: the Japan Association of Parasite Control and the Korea Association of Health make annual diagnosis, treatment, and intensive health education available to the entire population. Partial cost recovery contributes to the maintenance of the programmes. The near absence of clonorchiasis in Japan and its reduction in the Republic of Korea, as well as the reduction of paragonimiasis to low levels in both countries, attest to their achievements.

6. **National strategies for control**

The national strategy for control should have four components:

- development of a national plan of action and identification of resources;
- establishment of mechanisms of coordination between different national and international sectors:
- training;
- monitoring and surveillance.

For the development of a national plan of action, the following points should be taken into account.

National coordinating body

In developing countries where foodborne trematode infections are endemic, the human and financial resources of the individual sectors involved in a coordinated intersectoral control activity may not be adequate to set up and support a “vertical” control programme for foodborne trematode infections alone. Thus a “horizontal” programme is

desirable. An advisory and planning body with executive power should be established to prepare a plan of action, secure financial resources, and ensure that an adequate workforce is available. The head of this body should be appointed by the government and associated with the leading ministry in the programme. All government agencies concerned as well as the food industry, consumers, and nongovernmental organizations should be represented. In some countries, interministerial bodies for the environment or other government programmes are already functional and a programme for the control of foodborne trematodes can be integrated into their activities without the need to create a new bureaucracy.

Planning and management

The planning process and management are unique for each country. There are several important features. Overall economic planning should include input from the private sector as well as from all the government ministries whose responsibilities will have an effect on foodborne trematode infections, including the ministry of health. At central level (i.e. the ministry of health), the priority, financing, and lines of responsibility for control of foodborne trematode infections and coordination between different parts of the health sector should be defined.

Experience in endemic countries has shown that operational planning is best done at the provincial or district level, taking account of operational and disease control objectives and procedures to be used for programme monitoring. Operational planning at peripheral rather than central level allows precise analysis and harmonization of different objectives with the help of local data.

In the broadest sense, planning and management will contribute to the success or failure of efforts at control. The financial resources allocated to health and food-safety control activities are limited in many endemic countries. The negative effects of the widespread structural adjustment policies of the international lending agencies on the social sector, including health, have now been recognized. Efficient financial management in ministries of health should ensure that limited resources are used effectively.

Training

Implementation of a plan of action will require trained staff with the skills needed to accomplish their tasks (pages 47-48). Among the control approaches, two phases, implementation and maintenance, can be identified, for which appropriate training will be required.

In the *implementation* phase, control operations should be coordinated between the food safety, agriculture, aquaculture, and health sectors. In areas of high prevalence, mass treatment may be considered; otherwise selective treatment of infected persons after individual examination is appropriate in areas of both high and low prevalence. During this period,

intensive training of food and fish inspectors, aquaculture and agriculture extension staff, and peripheral health workers should begin. Wherever possible, staff from different sectors should be trained together. A public awareness campaign should be organized, with the involvement of non-governmental organizations, women's groups, and community leaders. Management of control activities will require integration of, and coordination between, the existing health care and food control systems in the relevant government, private, and community organizations. Effective coordination will ensure that the staff of each organization involved understand the rationale of the integrated approach. The mechanisms for mobilization of resources may require the identification of sources of funds from the different sectors involved. The certainty of a commitment to financial support for a specified length of time is an important factor for effective planning.

The *maintenance* phase will begin once the prevalence has decreased to a predetermined low level; diagnosis and treatment will then be available at all levels of the health care system. A national epidemiological surveillance system should be set up to include reporting of all foodborne trematode infections. The food and fish inspection services, aquaculture sector, agriculture sector, and nongovernmental agencies should support the running of periodic training and information exercises.

Integration and coordination

The integration of control activities within peripheral health services should include the use of community groups or organizations to promote compliance with treatment or behavioural change. Target groups for training include agricultural and aquacultural extension workers, members of local health committees and teachers, all of whom can support health workers in the diagnosis and treatment of infections and the promotion of appropriate food safety measures.

6.1 Health education

The first step in the organization of a health education programme is to characterize fully the risk posed by the food habits of the people of the endemic areas. The social science sector (psychologists, anthropologists, and social scientists) should be involved in the intersectoral programme for control of foodborne trematodes.

Foodborne trematode infections are acquired mainly by eating infected fish or other freshwater food that is raw or improperly prepared and, to a much lesser extent, as a result of cross-contamination during food handling. An essential measure to prevent and control these infections is, therefore, to educate communities in ways to avoid unhygienic eating habits and to prepare and process food safely. The aim should be to inform every person in the endemic areas about the life cycle and the mode of transmission of the parasite and the most practical approaches to prevent the disease, and to make people aware that their actions will

affect not only their own health but the health of others in the community. Educational efforts should be directed primarily towards schoolchildren because it is during the early years that people are most likely to become infected. Furthermore, children can influence the food-related behaviour of their parents.

The change away from food habits that favour infection is of vital importance, but it is often difficult to change people's behaviour, particularly when the behaviour is related to cultural traditions. Hitherto, efforts to induce people to give up raw or insufficiently heated food by health education (sometimes backed by legislation) have been largely unsuccessful. However, experience in some countries where opisthorchiasis or paragonimiasis is endemic indicates that control can be more successful when health education has been introduced into the project. A field study in paragonimiasis-endemic villages in the Jiangxi and Anhui Provinces of China indicated that after 3 years a programme of health education had reduced the percentage of villagers who ate raw crabs from 48.3% to 0% in Jiangxi Province and from 50.3% to 0.3% in Anhui Province. At a recent conference on foodborne parasitic zoonoses held in Thailand (1), control of opisthorchiasis through single-dose drug treatment and health education aimed at altering food habits was reported to have been successful in Thailand, although this approach had limited success in several other countries.

In spite of the possibility of failure, health education with the aim of changing hazardous food habits is the priority approach to the control of foodborne trematodes under subsistence conditions. Simply to provide information about the dangers of eating raw food is not enough to change risky habits. A WHO Consultation on Health Education in Food Safety (10) recommended that, before educational activities are initiated, a systematic awareness campaign should be undertaken. First, government authorities should be made aware and convinced of the importance of the problem and of the necessity for health education. Then health staff should be trained and equipped to carry out their part. Nongovernmental organizations and local groups, including women's groups, should be formally invited to participate in the educational and intervention programmes. The educational messages should be based on sound epidemiological information and on the results of sociocultural and anthropological studies; the food preparation and food processing techniques recommended should be effective and have been well reviewed and tested by experts. Communication of such messages to all levels of society in an endemic country will promote long-term success in control of foodborne trematode infections. The mass media should be integrated into the plan of action where appropriate, but sensationalism and exaggeration of the problem rather than the solution can be counterproductive. Periodic evaluations should be carried out and the programme modified as and when necessary. Two basic requirements for eventual success in achieving change have been identified by a Joint

FAO/WHO Expert Committee on Food Safety (11): perception of the advantage of change by the community; and acceptability of both the economic and the social costs of the change.

6.2 Public information and communication

All public means of communication can be used for messages to increase awareness of the problem of foodborne trematodes, progressively improve food safety, and improve sanitation. Professional advice should be sought about public advertising campaigns. The target audience must include all levels of society, especially the rural poor. Food producers, processors, suppliers, and vendors need to understand the risk of foodborne trematode infections and their own role in providing safe food to the consumer.

Schools in endemic countries should be supplied with textbooks that include descriptions of foodborne parasites as health problems, basic parasite/host biology, and environmental hazards that influence the risk of infection. Teachers should be trained to communicate appropriate information about foodborne trematodes.

There is a lack of general knowledge among the public about the simple means that can be used to avoid foodborne trematode infections. WHO's Golden Rules for Safe Food Preparation (Annex 3) emphasize the importance of safe food preparation and, after adaptation to the control of foodborne trematodes, could be used as a tool for raising public awareness. Simple, inexpensive, and culturally acceptable communication techniques are likely to have the greatest impact, particularly if they are at a technical level that can be understood and taught by members of the community. Public information can be disseminated by posters, films, the mass media (especially radio and television), community meetings, traditional storytellers, and religious and community leaders, or through individual counselling by health workers. Television is being increasingly used as an instrument for communicating brief health messages.

Coordinated community-based plans will be required for health education and public communication involving different sectors (e.g. health, agriculture, and aquaculture). In schools, the increasing educational emphasis on the environment and healthy food habits offers new opportunities to improve understanding about food safety and parasitic diseases in both teachers and students. In countries where the agriculture and aquaculture extension programmes are well developed, health issues can be included in environmental management programmes. Health education targeted at, or channelled through, women's groups is likely to result in the rapid spread of knowledge about these diseases and their prevention within the community.

Community participation is essential in any strategy to control foodborne trematodes and reduce health risks. An opportunity for such participation

is afforded in the many areas where the construction and maintenance of aquaculture systems are community-based activities, but success requires the provision of adequate information and sustained supervision.

Local authorities and government administrators should understand the importance of foodborne trematode infections as preventable diseases linked to development. There is a general lack of awareness of the problem among staff working for health, food safety, and agricultural authorities. Instruction on foodborne trematodes should be included in the curricula of medical and veterinary trainees. The specific curriculum should be based on the national situation and experience.

6.3 Food control

As far as food is concerned, the strategy for controlling foodborne trematode infections involves:

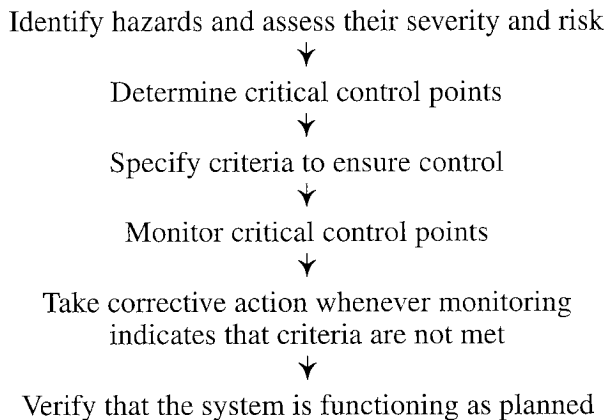
- prevention of consumption of food containing infective metacercariae;
- prevention of contamination of food with infective stages (metacercariae);
- rendering the metacercariae that are present on or in food non-infective.

Food control measures are particularly important for aquatic plants and for fish and shellfish products that are to be eaten raw or undercooked (e.g. watercress, *ceviche* (a marinated raw fish paste), sashimi and sushi-type products, lightly salted or fermented fish, marinated fish, and cold smoked fish).

The prevention of infection of fish or shellfish and contamination of vegetation depends on environmental control of surface waters where fish are caught, hygienic aquaculture, and the control or elimination of the first intermediate hosts (snails). In addition, the treatment of the definitive host (animal and human reservoir) is an important control measure. There are many potential difficulties in the implementation of these measures. For example, monitoring and control of large bodies of surface water (rivers, lakes) may be impracticable in developing countries. The improvement of aquaculture practices to exclude foodborne trematodes (12) may be possible with the cooperation and participation of the people involved. Fish-ponds should be protected from pollution with sewage and other wastes, and untreated human and animal excreta should not be used as fertilizer or as fish food. Waste material from fish and shellfish processing and market-places should be adequately treated. Similar measures should be adopted to avoid contamination of ponds where food plants are cultivated that may serve as vehicles for the transmission of fascioliasis.

Control measures to reduce the public health problem related to the presence of parasites should include legislation and surveillance action.

Control should be based on the principles of the Hazard Analysis and Critical Control Point (HACCP) system, which offers a systematic and sequential approach to the control of food hazards, including foodborne trematodes, and avoids the many weaknesses inherent in the traditional inspection approach (3). The system is based on the recognition that hazards to health exist at various points of a food chain, from catching or harvesting to the consumer, but that measures can be taken to control these hazards. Once the system is established, the main control efforts are directed towards the critical control points, and away from endless testing of the final product. Schematically, the HACCP system comprises the following sequential steps:



In the case of fish, the application of the HACCP approach to the control of foodborne trematodes would start with assessment of the risk that certain species of fish (e.g. carp) caught or harvested in endemic areas are infected. The risk of disease would also be determined; this will depend on the specific parasite and whether the possibility of acquiring the trematode infection through eating fish is eliminated by cooking or another preparation process before consumption. A risk will exist if fish from endemic areas are consumed raw or inadequately processed. The HACCP approach is unique for every product and for every production unit: in each case a detailed study of the food producing/processing/marketing/preparation flow is necessary to identify hazards and the critical control points.

When the HACCP analysis is complete and the programme is ready for implementation, training must take place. All the people involved in the programme, from fish farmers, traders, and processors to food-sellers, restaurant managers, etc., must understand the principles, and have a clear idea of their own role in the system. For the HACCP approach to be fully operational and generally applied, increased communication to promote understanding and collaboration between the scientific community, the general public, and the food regulatory agencies will be required.

6.4 Sanitation, wastewater, and excreta use

National programmes for the improvement of sanitation can effectively contribute to reducing environmental contamination by human excreta. A programme for the promotion of latrine construction and use integrated into community development can result in a long-term decrease in the risk of foodborne trematode infections. Community-based initiatives in latrine construction should be encouraged.

The use of wastewater in agriculture and aquaculture is increasing. Its proper management is one of the keys to the elimination of health risks related to foodborne trematode infections. Proper disposal of excreta is fundamental to decreasing the contamination of snail habitats; in some countries cultural traditions may need to be changed, for example in China, where human faeces are used for fertilizer. In the past night-soil was widely used in the Republic of Korea, but its use is now prohibited by law.

Although the hazards of use of untreated wastewater and untreated human excreta in agriculture and particularly in aquaculture should not be overlooked, there is no real evidence that *hygienic* disposal of treated excreta, sewage, and sludge by use in well managed fish-ponds is more hazardous, from the public health point of view, than other methods of disposal feasible in the rural areas of developing countries.

There is a progressive tendency towards integrated livestock–fish production systems (13). The potential for transmission of foodborne trematodes within these systems should be recognized and monitored.

6.5 Diagnosis and treatment

The diagnostic techniques and treatment currently available for foodborne trematode infections can be adapted to all control strategies. All foodborne trematode infections can be treated with praziquantel, with the exception of human fascioliasis, whose current treatment is unsatisfactory. It is expected that triclabendazole will become the treatment of choice for fascioliasis, but its registration is pending completion of the clinical trials.

Diagnosis and treatment should be available at all levels of the health care system. However, availability is not the only requirement; staff must be trained and quality control should be assured. The technical details of diagnosis and treatment are given on pages 83–88. In some endemic countries, for example Japan and the Republic of Korea, nongovernmental organizations have been instrumental in providing diagnosis and treatment (page 33).

6.5.1 Hospitals

Many people with foodborne trematode infections may be hospitalized without preliminary diagnosis, especially in the acute phase of infection.

Hospitals can provide the range of diagnostic tests and the facilities to manage acute disease or intercurrent complications and thus facilitate proper diagnosis and treatment.

6.5.2 **Health centres and dispensaries**

Health workers should be aware of the risk of foodborne trematode infections in their catchment areas since they are usually the first point of contact with the patient. The ability of health workers at the periphery to distinguish between different causes of clinical manifestations is usually determined by their personal experience, degree of supervision and training, and understanding of the epidemiology of foodborne trematodes in their catchment area.

6.5.3 **Peripheral laboratories**

Peripheral laboratories are essential components of a good health care service and facilities for microscopic diagnosis of foodborne trematode and other parasitic infections are particularly important. Trained personnel and provision of adequate supplies and equipment to the laboratories should be made a priority by the agencies that support peripheral health services.

6.6 **Primary health care**

The village health worker has a specific role at the community level as an agent for communication of ways in which basic hygiene and food safety can be achieved. The role of the health worker in control of foodborne trematode infections may include activities integrated with the aquaculture and agriculture sectors. A well trained health worker, preferably from the same community as the patients, makes an important contribution towards change in health-related behaviours.

6.7 **Monitoring and surveillance**

A range of epidemiological indicators can be used to monitor progress in control of foodborne trematode infections, and for surveillance of changes in the epidemiological patterns. Parasitological indices such as prevalence, incidence, and intensity of infection, with accurate population denominators, or in well defined population samples, should be determined at appropriate intervals.

The seasonal and geographical variability in the intermediate snail host populations limits the reliability and the feasibility of monitoring surveys. Nevertheless, if specialized services or research institutions have an interest in snail monitoring, they can be encouraged to collaborate with national control programmes.

There is no standard method for monitoring infection of the second intermediate hosts – fish, crustaceans, or plants. Practical sampling procedures for monitoring have not been established. The sample size necessary to detect parasitism in fish will depend on the population dynamics of the host species, the size of the fish, the probability of contamination, and other variables. For foods that are marketed or traded, data may be obtained by fish and shellfish inspection services from the point of production, marketing, or importation. Animal health services can provide useful information on the geographical distribution of animals at risk of infection. If these data are collected in a standardized manner, they can provide useful information on changes in prevalence or incidence.

Assessment of changing food habits provides data on the effectiveness and coverage of the health education and public information activities of the control programme. However, the use of a survey technique designed to determine food habits by recall of the amount of raw food eaten usually gives an underestimate of actual consumption. A comprehensive survey to determine total food intake rather than intake of potentially infected foods alone should provide more reliable data on the foods related to transmission of foodborne trematodes.

Morbidity due to foodborne trematode infections can be assessed by certain clinical manifestations. In areas where opisthorchiasis and clonorchiasis are endemic, changes in the incidence of disorders such as cholangitis, cholecystitis, bile calculi, hepatomegaly, and cholangio-carcinoma are useful indicators. Generally, these clinical manifestations are not reported in national epidemiological surveillance reports, but data can often be obtained from hospital records.

In the Republic of Korea the impact of control is evaluated every five years by a standardized survey of a random sample of households determined independently by the Statistical Office. This population sample of approximately 0.1% of the residents of the endemic areas is examined by the Korea Association of Health using the Kato-Katz (faecal thick-smear) technique. Large-scale voluntary surveys are done annually in Japan by the Japan Association of Parasite Control. The compliance rate in these surveys is over 90%, which means that reliable estimates can be made.

An innovative surveillance method to enable clinical services to detect human fascioliasis infections was tested between 1984 and 1988 in Corsica and could be applied in endemic countries. Research investigators and 227 of the 235 physicians on the island participated in the prospective screening. All patients with an eosinophilia of greater than 10% were classified as suspected of having fascioliasis. Serological examination of 218 such patients led to the diagnosis of fascioliasis in 14. In 1989 two out of eight people with eosinophilia had fascioliasis, and in 1990 two more cases were identified. During the period 1984-1990, a total of 18 cases were detected (about 1 case per 100 000 population). The

sensitivity of this method has not been tested, i.e. the frequency of seroreactivity or egg-positivity in people living in endemic areas who do not have eosinophilia.

The Study Group was not aware of the existence of any mathematical models to predict the epidemiology and geographical distribution of human foodborne trematode infections. However, human infections are known to be related to fascioliasis in animals. For instance, the peak of animal liver condemnations in England in 1970-1972 corresponded to the period of outbreaks of human infection in the same areas. Several predictive models for the incidence of animal fascioliasis have been developed. The earliest empirical deterministic model used by agricultural services in Great Britain, and adapted for use in France, was based on two key meteorological variables: temperature (the development of the parasite being favoured above 10 °C); and the presence of free water in the environment.

More recently in Northern Ireland the data on liver condemnation since 1969 have been integrated with a concurrent meteorological database to develop a multivariate model which, within 95% confidence limits, accurately predicts the prevalence of animal fascioliasis for the following year.

6.8 Policy and legislation issues

The development of policy and legislation for the mitigation and prevention of foodborne trematode infections involves many sectors.

6.8.1 *Health and development*

Many, if not most, of the epidemiological determinants of foodborne trematode infections are strongly associated with social and economic developmental processes, which are important in determining quality of life and environmental and economic sustainability. An agenda of work (Agenda 21), which aims to meet the need for sustainable development, was adopted by the 1992 United Nations Conference on Environment and Development.

Agenda 21 addresses all major sectors of development with the aim of integrating environmental and development concerns, leading to the fulfilment of basic needs, improved living standards for all, better protected and managed ecosystems, and a safer, more prosperous future. The following programme areas of Agenda 21 have a connection with food safety and are therefore of relevance to the objectives of the Study Group:

- combating poverty
- changing consumption patterns
- human health
- human settlements

- protection of the atmosphere
- agricultural and rural development
- biotechnology
- fresh water protection.

The links between these areas of development and food safety are complex and not easily described or quantified. Nevertheless, general observations can be made. For example, many food processing methods consume energy and pollute the environment, indirectly affecting human health (the outbreak of fascioliasis in the Islamic Republic of Iran in 1989 was partly linked to slaughterhouse effluent). As energy and water costs mount, those responsible for storage and processing of food will be under pressure to cut costs, which could lead to increased food contamination and damage. Increased prices will limit the choice of food available to the poor and may lead to the consumption of foods of lower quality that carry a higher health risk.

The response to such issues and relationships should be to strengthen intersectoral collaboration. Agenda 21 clearly calls for collaboration to address a large number of issues that concern humanity. Food safety in general and foodborne trematode infections in particular will gain attention in such a wide-ranging agenda only if the links with the wider issues detailed in Agenda 21 are clarified and shown to be important.

In the context of intersectoral collaboration in development, the World Food Programme tries to coordinate the assessment of planned food-related projects with WHO, so that health risks are evaluated. As a result, recommendations have been made to mitigate and prevent the foodborne trematode infections and other diseases whose spread might be promoted by the many water resources development, agricultural, and aquaculture projects supported by the World Food Programme, particularly in Africa and Asia.

6.8.2 ***Disposal and use of excreta, wastewater, and sewage sludge***

Legislation covering the use of human excreta, wastewater, and sewage sludge varies from country to country. The health-related components of agricultural and aquacultural legislation and policies, and their implications for foodborne trematode infections, are discussed in a publication of the International Reference Centre for Waste Disposal, a WHO Collaborating Centre (14).

In *Chile*, where human fascioliasis occurs sporadically, various government authorities are involved either directly or indirectly in the management of water and wastewater, and the promotion of public health. In general, enforcement of the regulations governing water safety appears to be difficult and has had limited success. Landowners' associations and market and socioeconomic forces are probably the main factors preventing effective control and enforcement.

In *Indonesia*, large areas are given over to aquaculture and irrigation-based agriculture. The Study Group noted that human fishborne trematode infections are not endemic in Indonesia. Although there is extensive use of rivers and streams for defecation, alternative methods of, and installations for, disposal of excreta have been introduced in recent years. Prior to the construction of the new water supply and sanitation facilities, overhung latrines (most of which have now been removed) were in common use, water piped from nearby paddy fields was used for washing and bathing, and drinking-water was fetched from wells.

Fish are produced in nearly all the ponds in Indonesia, while water vegetables (e.g. *kangkung* and *genjer*) are grown only in some. A number of pond owners allow water hyacinths to grow for use as fish food. Formerly, ponds were fertilized with excreta discharged from the overhung latrines and by the addition of rice bran which farmers purchased from nearby rice mills. Since the overhung latrines were abandoned, increased quantities of rice bran have been used to replace the excreta. Fish production has improved with the increased quantity of bran, which is applied more regularly than before.

The Government of Indonesia has recently adopted the strategy of decentralizing government services and responsibilities. Thus, many functions that previously were mainly (though not exclusively) carried out by the central ministries will be gradually shifted to the local governments and administrations. The local authorities will be responsible for improvements in infrastructure, including projects relating to the disposal and use of excreta and wastewater, while the central authorities will mainly formulate policies, fulfil monitoring and control functions, provide technical assistance, and channel central government funds to the local government authorities.

In *Peru*, the wastewater quality and treatment standards, as well as wastewater use regulations, are specified in the *Ley General de Aguas* (general water law) passed in 1970 and amended in 1983. The law stipulates, among other items, that crops growing close to the ground and root crops that may be eaten raw may not be irrigated with raw sewage or untreated wastewater.

In the *Republic of Korea*, the institutional and regulatory framework has played a significant role in the control of foodborne trematode infections, besides bringing about dramatic reductions in other water-related and excreta-related diseases. The fundamental legislation is the Waste Cleaning Law and the complementary enforcement ordinances and regulations, promulgated in 1961-1962. These have been progressively amended and form the current legal basis for collection, treatment, and disposal of non-hazardous wastes, including night-soil and domestic sewage.

6.8.3 **Food control and inspection**

The practice of eating raw or undercooked food can be discouraged by health education in situations where wild fish is caught or vegetables are gathered for direct domestic use. However, control measures to reduce the public health problem caused by foodborne trematodes can, and should, also include legislation and surveillance. To this end, existing legislation related to food control and inspection should be reviewed to allow the inclusion of measures to control foodborne trematodes if necessary.

In principle, the problem of fish- and shellfish-borne trematode diseases can be addressed by food-control agencies through the implementation of appropriate preventive measures. However, not all of the following suggested measures will be applicable in every country, and there is a lack of scientific information on the efficacy of some of them.

1. Avoid capture, culture, harvest, or selling of fish or shellfish host species (e.g. Cyprinidae), or at least:
 - (a) avoid capture, culture, harvest, or selling of fish or shellfish host species from areas known to be endemic for foodborne trematodes;
 - (b) when applicable, control the size or age at which fish and shellfish host species may be harvested or sold;
 - (c) allow only the skinless fillets of fish host species to be sold for eating, if infective stages are found only in the skin or the scales;
 - (d) when applicable, inspect, sort, and reject foodborne trematode-infected fish or shellfish or remove foodborne trematodes from fish and shellfish before sale.
2. Require fish and shellfish to be subjected to processing techniques to kill foodborne trematodes (e.g. cooking, freezing, salting, or irradiation).
3. Require food labelling to inform the consumer of the need for proper preparation.

Generally, measures 1c, 1d, 2, and 3 would apply only to fish products sold commercially.

The application of HACCP principles is the preferred approach for use by food-control and inspection authorities involved in the control of foodborne trematode infections (3). These principles can readily be incorporated into national food (fish or shellfish) control regulations, and would promote voluntary cooperation with the private sector (e.g. farmers, industry, trade, and consumers), community participation, and compliance by consumers through health education.

6.8.4 **International trade**

More than 45% of the fish and fishery products currently traded on the international market comes from developing countries, including some

areas in which foodborne trematodes are endemic. A number of reports, particularly from south-east Asia (e.g. Hong Kong, Malaysia and Singapore), have pointed to imported fish from areas where foodborne trematodes are endemic (e.g. China and Viet Nam) as the source of infection. As mentioned in section 4.3.1, raw food clandestinely imported from endemic areas for consumption by particular ethnic groups often bypasses import inspection and can also be a source of infection in non-endemic areas.

International commerce in food has attracted the attention of the General Agreement of Tariffs and Trade (GATT), and will in the future be regulated, as regards sanitary and phytosanitary requirements, by agreements embodied in the final act of the Uruguay Round of multilateral trade negotiations. New sanitary requirements for the production and marketing of fish and fishery products were issued by the European Economic Community (EEC) in its Directive 91/493/EEC of 21 July 1991, and other major fish-importing countries, such as Australia, Canada, Japan and the USA, have similar requirements. These measures have implications for the safety standards of fish and fishery products exported from other countries, in particular developing countries; control legislation and inspection services in these countries must be able to ensure that fish and shellfish and their products are free of foodborne trematodes if required by an importing country. The Recommended International Codes of Practice for Fish and Fishery Products elaborated by the Codex Alimentarius Commission (Annex 4) should, after revision to include concerns relating to foodborne trematodes, be used for guidance in meeting these requirements, particular attention being given to the draft Code of Hygienic Practice for the Products of Aquaculture.

6.9 Health services infrastructure

In most countries it is feasible to control foodborne trematode infections without creation of a costly “vertical” or specialized programme. Control can be integrated with the other activities of the different government sectors, including the various branches of the health sector (which includes food safety services). However, it is important that specific responsibilities and tasks are set at each level of the health care system.

6.9.1 *Training*

The effectiveness of the health services infrastructure in the control of foodborne trematode infections will depend largely on the coordination of training programmes by the health, agriculture, and aquaculture sectors (see also pages 34–35).

In addition to funding, control programmes require a sufficient number of appropriately trained personnel. Well organized staff development using fully proven training methods is necessary to ensure proper use of

available funds, but training, while essential, will not remedy problems such as high staff turnover or lack of motivation due to poor conditions of service. Low salaries, lack of career development policies, and poor supervision contribute to difficulties in developing and managing disease control programmes in many endemic countries.

The integration of control activities within peripheral health services should make use of community groups or organizations to promote compliance with treatment or behavioural change. Target groups for training may include agricultural and aquacultural extension workers, teachers who support health workers in community diagnosis and in the treatment of schoolchildren, and members of local health and agricultural development groups.

6.9.2 *Planning the control strategy*

Once it has been decided that intervention is necessary, the information required for planning a suitable strategy for control of foodborne trematodes should be collected from pilot, short-term, or long-term feasibility studies. The operational plan of action should involve the ministry of health and other relevant sectors at both the central and peripheral levels – in particular the education, water resources development, agriculture, finance, and planning sectors; nongovernmental organizations should also take part, including relevant consumer groups, as should the pharmaceutical, chemical, and food industries.

The central level of the health service may be responsible for purchasing supplies and for organizing the training of personnel for implementing the control programme, but the current trend is to decentralize planning as much as possible. The peripheral health services must be involved in the development of any national plan of action, although a central specialized team, which may also be responsible for the control of other diseases, can have a useful role in both planning and supervising field operations.

6.9.3 *Participation in control activities*

At both central and peripheral levels the major challenge for health services in control of foodborne trematode infections will be coordination of, and communication between, the various branches of the health sector (food safety, curative and preventive services) and other sectors such as education, tourism, industry, trade, agriculture, and aquaculture.

The activities and responsibilities of each level of health services should include:

- coordination with the other sectors
- development of public education messages

- diagnosis and treatment
- preventive measures.

Primary health care is most important in the implementation of the control programme. Primary health care units should be responsible for active and passive case-finding and for a reliable delivery system for treatment; this is particularly important during the maintenance phase of the control programme. The primary health care system should also be responsible for health education in the community. In the planning phase of the programme, training should focus on the means by which health education messages may be communicated, on household visits, and on techniques of community motivation, especially for improving sanitation. The help of a professional health educator is essential in mobilizing community support for the control programme.

Health workers should also be trained in technical tasks, such as the collection of demographic data, individual and population-based community diagnosis and treatment, survey techniques for snail habitats and transmission sites, and snail control, where appropriate.

Supervision and quality control are essential for effective control operations and evaluation. Senior workers should therefore be responsible for supervising the work done by their staff and ensuring its quality. Detailed job descriptions should define each worker's areas of responsibility for the various tasks required.

6.9.4 *Maintenance of control*

Surveillance and monitoring of foodborne trematode infections should be the main activities of health services during the maintenance phase. The health sector should provide surveillance reports to the agricultural and aquacultural sectors to ensure that they are aware of the importance of disease.

6.9.5 *Fish and shellfish control and inspection services* (see also section 6.3)

In countries where aquatic food forms a substantial part of the diet, the food safety services should have special sections for dealing with aquatic food. Professional and other staff should be trained in this aspect of food safety. Some useful suggestions on the organization of fish inspection services and training of staff are made in a number of publications by FAO and WHO (see, for example, reference (12)).

The Committee on Fish and Fishery Products of the FAO/WHO Codex Alimentarius Commission is currently elaborating a Code of Hygienic Practice for the Products of Aquaculture, intended to assist those engaged in aquaculture to produce high-quality fish that is safe for human consumption (Annex 4). The proposed code deals with key hygienic practices from selection of a site for aquaculture to the final phase of live fish production, i.e. harvesting, inspection, and loading for delivery.

6.9.6 **Coordination with control of other diseases**

Integration of the control of foodborne trematode infections into general health services is possible and desirable at all levels, but there may be particular opportunities for integration with other disease control programmes. The coordination of different disease control activities is determined partly by the epidemiological situation and partly by the shared requirements for similar tools, e.g. microscopes. Financial constraints may also force services to pool resources such as transport. However, there has so far been only limited systematic experience of cooperation between different disease control activities.

Expert teams established at central level with responsibility for parasitic diseases in general, rather than only for a single disease, can promote balanced strategy development and the coordination of control and evaluation efforts at the peripheral level. This multi-disease approach also allows for flexible answers to acute epidemiological problems, and for a cost-efficient use of staff and logistic organization of the central epidemiological services. Nevertheless, even in such a close association, it is difficult to merge control objectives, methods, and strategies in a consistent way.

6.9.7 **Data management**

The available epidemiological data on foodborne trematode infections are not systematic and, in some countries, lack the reliability required for programme planning and management. Data management for a national programme should be integrated with the data management system of the ministry of health.

Since foodborne trematode infections are not notifiable diseases in any of the endemic countries, a first step in the development of national programmes is to clarify how data on these infections are to be reported. Responsibilities should also be assigned for data analysis and its use in planning and management of the control programme. The mechanisms for communication of data between the different sectors should be established to ensure forewarning of changes in the epidemiological distribution of disease; for example, if metacercariae of foodborne trematodes are detected in fish in an aquaculture system, the health authorities should be alerted to the possibility of eventual human infection.

Monitoring through general health services statistics

Within the health care system, provision should be made for reporting and analysis of data from, and feedback of results to, all outpatient facilities (including the most peripheral health unit) and hospitals.

Data from control programmes

If foodborne trematode infections are endemic or of high priority in only a small area in a country, then intensive surveys with mobile teams can accurately define the distribution of the diseases. Adequate resources will

be required for the analysis of such data and to ensure its usefulness for planning future control strategies.

Evaluation

The control programme should be evaluated periodically by a group of scientists, each specializing in one of the following disciplines: clinical parasitology, epidemiology, food safety, animal health, fisheries, and health education. Evaluators should examine data concerning changes in the prevalence of foodborne trematode disease in humans, infection in intermediate hosts, the presence of metacercariae on plants, the occurrence of fascioliasis in domestic ruminants, and food habits, together with related information. The methodology of health systems research should be used when appropriate. Any changes of policy, strategy, and plan of work indicated by the evaluation should be made promptly by the management of the control programme.

7. Integration with other sectors

Collaboration between sectors is the key to a successful control strategy. As responsibilities for health and food safety are becoming more decentralized in many countries, intersectoral integration should take place not only centrally, but also at the local level. The responsibility for providing safe food should be shared between governments, consumers, and the food industry, from farmers and fish producers, to processing, retailing, and food services establishments. Providing people with the means to determine priorities for, and to maintain, safe food production is a new challenge for all sectors.

7.1 Agriculture

The agricultural sector has a clear role in communicating with farmers regarding appropriate irrigation and production practices to avoid transmission of foodborne trematode infections. The training curriculum for staff of agricultural extension services should include information on preventive agricultural practices.

The agricultural authorities and the food-control and inspection authorities should be made aware that transportation of aquatic vegetables to which snail eggs or adult snails are attached has been implicated in the spread of intermediate snail hosts. In the market place as well as in the home, contaminated water containing metacercariae may be used to freshen vegetables, particularly leafy vegetables.

7.2 Animal health

Human fascioliasis occurs only in areas of animal fascioliasis caused by *F. hepatica* or *F. gigantica*, which is a major animal-health problem

throughout the world. Human fasciolopsiasis due to *Fasciolopsis buski* is generally linked to a high prevalence in pigs. High levels of animal fascioliasis and fasciolopsiasis are found both in endemic areas of human infection and at the sites where outbreaks of human infection most frequently occur.

An FAO Expert Consultation on Helminth Infections of Livestock in Developing Countries (15) and a recent FAO review (16) have highlighted the importance of *Fasciola* infections. In terms of pathogenicity and impact on livestock production, these trematodes are generally less well documented than the nematodes. The FAO Expert Consultation recommended further research to assess the relative economic importance of the various trematode parasites, especially losses related to liver condemnations, and also urged that the importance of liver fluke infections and animal schistosomiasis as zoonotic diseases be emphasized to public health authorities.

The objective of control of trematode infections in animals is to reduce economic losses and contamination of the environment with parasite eggs. The use of anthelmintics should be kept at the lowest cost-effective level. The indiscriminate use of molluscicides in control approaches is never justified. It is preferable to focus efforts on good animal and pasture management practices.

The range of anthelmintics available to treat trematodes in livestock is considerable, encompassing both broad-spectrum and narrow-spectrum drugs. However, the recommended drugs need to be active against both liver and gastrointestinal flukes. It is also highly desirable that the anthelmintic is active against both larval and adult parasitic stages (15). Ideally, it should also be an ovicidal agent.

The control of animal fascioliasis should be based on sound epidemiological principles. Thus in any area of high prevalence of animal infections, it is important to coordinate human and animal epidemiological data to ensure a cost-effective approach to control.

7.3 Fisheries and aquaculture

Aquaculturists in the endemic areas may not be aware of the public health problems caused by clonorchiasis and opisthorchiasis. Collaboration between health authorities, food safety services, fishery officials, and aquaculturists would raise the awareness of disease risks. There is a great need for information in written and other forms to explain the problem and the solution to various sectors of society, including the general public. Manuals for rural farmers have been developed which include a specific preventive health message regarding the use of human excreta and the necessity for location of latrines at a proper distance from aquaculture ponds (17).

Individual and entrepreneurial aquaculture is not controlled by national regulations, but governmental fisheries and aquacultural agencies as well

as nongovernmental agencies do usually provide technical advice on the construction and maintenance of aquaculture ponds. This provides an opportunity to communicate information on health risks and preventive measures for avoiding foodborne trematodes.

There are many opportunities for dissemination of information and training by nongovernmental organizations that are involved in research and promotion of aquaculture in the developing countries, for example the International Centre for Living Aquatic Resources. Many bilateral donors, including the Danish International Development Agency, the Swedish International Development Authority, and the United States Agency for International Development, support aquaculture and fish inspection services in developing countries.

At the international level, FAO has an extensive training and advisory programme for those involved in fisheries, aquaculture, fish utilization, and marketing, as well as fish inspection. Several important interregional and regional development projects are now being carried out. For example, Aquaculture for Local Community Development (ALCOM) is an FAO interregional programme involving countries of the Southern Africa Development Commercial Community (SADCC); in West Africa, Integrated Development of Artisanal Fisheries (IDAF) supports small-scale fisheries development; and the Bay of Bengal Programme (BOBP), a regional programme that includes Bangladesh, India, Indonesia, Malaysia, Maldives, Sri Lanka, and Thailand, is renowned for its success at the grass roots level. The FAO Network of Marketing and Technical Advisory Services for Fishery Products (INFO Services) includes former FAO regional projects that are now intergovernmental organizations – INFOFISH (Asia and South Pacific), INFOPESCA (Latin America and Caribbean), INFOPECHE (West African countries), and INFOSAMAK (Arab countries). It publishes information on fisheries, aquaculture, fish utilization, and marketing, including a quarterly newsletter, *The fish inspector*, which is the voice of an international cooperative effort in fish inspection and quality assurance.

7.4 **Food industry**

Food industries have a key role in the prevention of foodborne diseases, including foodborne trematode infections, but their influence will depend on the extent to which market forces favour the sale of food products that have been processed according to Codex Alimentarius standards and codes of practice. Commercial freshwater fish products will become increasingly available through aquaculture and may supplement if not replace, traditional and domestically prepared dishes. The food industry's responsibilities will also include commercially available aquatic or semiaquatic plants such as water chestnuts, watercress, and lotus, which should not pose significant health risks if produced and handled hygienically.

7.5 **Tourism**

The number of international tourist arrivals reported by the World Tourism Organization reached 476 million in 1992 and is expected to rise to 660 million by the year 2000. East Asia and the Pacific are expected to experience the fastest growth, from 58 million in 1992 to 101 million in 2000. Revenue in 1992 from international tourism reached US\$ 278 billion.

Tourist movements provide an added global dimension to the monitoring and surveillance of foodborne trematode infections. The expansion of tourism means that more people are consuming the traditional foods of host countries, and the increase in travel to remote and less-frequented areas is associated with an increased risk of exposure to high-risk foods, both for tourists and for visitors from elsewhere in an endemic country. Foodborne trematode infections are among the diseases that have been reported in tourists.

The diagnosis of clonorchiasis in a tourist from a non-endemic country can be explained either by consumption of freshwater fish that has been transported from an endemic area to a non-endemic country, or by infection from fish eaten by the tourist while travelling through an endemic area.

If the income from tourism in an endemic country is significant, the country has a valid additional reason to develop a national strategy for control of foodborne disease. The tourism sector may contribute to these efforts, both to protect health and to improve food safety.

The World Tourism Organization has collaborated with WHO to promote safe food practices in the tourism sector and safe food habits among tourists themselves (18). Enforcement of food safety standards in tourist areas has both short-term and long-term benefits for the host country. Recognition that foodborne trematodes can be transmitted in foods that are attractive to tourists, and the application of adequate controls, will reduce, and could even eliminate, the risk of infection among tourists and at the same time benefit the population of the host country. National tourism agencies and hotel and restaurant associations should promote food safety.

7.6 **Education**

Ministries of education should be partners in an intersectoral effort to control foodborne trematode infections. In recent years, the United Nations Educational, Scientific and Cultural Organization has been instrumental in increasing the awareness of the international community of the needs of school-age children who make up a significant proportion of the national population in many developing countries. The unfavourable influence of undernutrition and ill-health on children's educational experiences has been emphasized; the physical conditions of the school environment itself are often deleterious to health and well-

being. In endemic areas, schoolchildren may be exposed to the risk of infection by foodborne trematodes either at home or at school. School health programmes and hygiene instruction have an important role in the promotion of a safe environment. Instruction should cover hygienic excreta disposal, use of latrines, and the relationship between agricultural and aquaculture practices and the life cycle of the parasites. Teachers can also explain how to apply food safety measures to the preparation of traditional foods through their teaching in various subject areas, e.g. science and home economics. School food vendors and those responsible for school meal programmes must be supplied with appropriate information on safe food preparation and there should be periodic supervision of food preparation as well as food inspection. In Thailand, school health education programmes have been effective in promoting the objectives of the national opisthorchiasis control programme by means of poster contests and school drama productions.

Recently, the United Nations Children's Fund, Educational, Scientific and Cultural Organization, and Population Fund and WHO have collaborated in the preparation of a new edition of *Facts for life* (19), which contains the most basic information required to promote health. National editions are being prepared and inclusion of information about foodborne trematodes is an attractive option to be considered in endemic countries.

7.7 Nongovernmental organizations

Many nongovernmental organizations are involved in community development projects, e.g. livestock raising, aquaculture, and vegetable production, which can contribute to the spread of foodborne trematode infections. They are therefore in a good position to collaborate in the prevention and control of these infections.

Nongovernmental organizations are particularly active in refugee camps, where they promote agricultural and aquaculture development. The necessity for adequate food sources may lead to aquaculture being encouraged without either adequate safeguards against the contamination of fish-ponds by human excreta or an appropriate means of reducing the intermediate snail population. Nongovernmental organizations working with refugees could therefore play an important role in prevention and control of foodborne trematode infections, as could those caring for migrant workers.

Consumer organizations can help to increase public awareness and demand for high-quality food products, and women's groups whose aim is to improve maternal and family nutrition can help to distribute and communicate information and provide education on the selection, preparation, and processing of food. Mass media organizations should be informed of the importance of foodborne trematode infections so that they can disseminate accurate information on their control.

Technical issues in control

8. **Morbidity and mortality due to foodborne trematodes**

Most trematodes have mammalian hosts other than humans. A few foodborne trematodes can cause severe, even fatal disease in humans. *Fasciola* spp., for example, are markedly pathogenic in humans while domestic animals can support enormous worm burdens without developing severe disease (20). The pathogenic effects of foodborne trematodes, unlike those of schistosomes, which are also trematodes, are due mainly to the adult worms rather than the eggs. In humans and in animals, no consistent correlations between the degree of morbidity and intensity of infections have been observed in either clinical or population-based epidemiological studies.

8.1 **Clinical assessment**

Acute human foodborne trematode infections except those due to *Fasciola* spp. are rarely diagnosed clinically. The many clinical manifestations of the initial phase of trematode infections vary in both quality and intensity; some infections are asymptomatic, with or without eosinophilia, while others cause acute severe generalized symptoms. The frequency of acute infections reported by health services represents only a small proportion of the actual number of infections. The absence of pathognomonic clinical manifestations, the low incidence of infection, and the confounding of diagnosis with other prevalent diseases all lead to under-reporting.

Physical examination and laboratory investigations are the standard methods for clinical assessment. Ultrasound has proved its value in the differential diagnosis of fascioliasis. Portable ultrasonography equipment can be used in epidemiological surveys – in villages, if required – to improve diagnostic accuracy and sensitivity.

The clinical manifestations of each of the foodborne trematode infections fall into specific groups, which require laboratory confirmation for differential diagnosis. In many developing countries, diagnosis can be confirmed only in tertiary or teaching hospitals. Examples of potential errors and difficulties include: the recognition of human paragonimiasis after misdiagnosis of tuberculosis, the presumption of visceral larva migrans or toxoplasmosis in a patient with fascioliasis who presents with an intermittent febrile syndrome and high eosinophilia; and chronic diarrhoea resistant to conventional treatment that is finally recognized as echinostomiasis.

8.1.1 **Opisthorchiasis**

In *Opisthorchis felineus* infection, the incubation period between ingestion of metacercariae and the appearance of the first symptoms

usually varies from two to four weeks, and rarely is as short as one week. The acute clinical manifestations are fever, abdominal pain, dizziness, and urticaria. Acute infections due to *O. felineus* have rarely been observed among aboriginal ethnic groups and indigenous Russians in areas such as Tyumen, Russian Federation, where the prevalence of chronic infection is high – in epidemiological surveys, children as young as one year of age and nearly 100% of children up to 10 years of age have been found to be infected. Acute opisthorchiasis has, however, been reported among new arrivals from other territories and occasionally among indigenous Russians who have probably been reinfected after treatment. In areas of low prevalence, such as the Ukraine, acute infections are rarely diagnosed.

No relationship has been found between the presence of acute clinical manifestations and the number of *O. felineus* eggs in faeces. Few *O. felineus* eggs are found in the faeces of patients with acute clinical manifestations.

Maturation of the larval worms in the distal bile ducts initiates inflammatory and proliferative changes of the biliary epithelium. These changes are accompanied by fibrosis of the distal biliary branches. In heavy infections, the pathological changes may extend to the proximal bile ducts and gall-bladder or be associated with mild periportal fibrosis.

The signs and symptoms of chronic opisthorchiasis include diarrhoea, flatulence, fatty-food intolerance, epigastric and right upper quadrant pain, jaundice, fever, hepatomegaly, lassitude, anorexia, and, in some cases, emaciation and oedema. Although local damage may be considerable in the distal biliary tree where the worms are lodged, there is usually no measurable effect on liver function. Most individuals with light to moderate infection show no significant signs or symptoms of disease when compared with uninfected matched control groups. Pathological studies have revealed no gross changes in the liver in light or early infections. Epidemiological studies of *O. viverrini* and *O. felineus* have consistently shown that liver enlargement, whether assessed by physical or ultrasound examination, is not directly related to intensity of infection. An enlarged non-functional gall-bladder correlates closely with heavy infections. In highly endemic areas, manifestations of chronic infection include cholecystitis, cholangitis, liver abscess, and gallstones. Cholangiocarcinoma is associated with *O. viverrini* infection; limited data support the same association with *O. felineus* infection.¹

¹ Note added in proof: for an evaluation of the carcinogenic risk to humans posed by infection with liver flukes, see *Schistosomes, liver flukes and Helicobacter pylori*. Lyon, International Agency for Research on Cancer, 1994 (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 61).

8.1.2 *Clonorchiasis*

After ingestion of *Clonorchis* metacercariae, eggs appear in the stool after four weeks. Acute infections due to *Clonorchis sinensis* are usually asymptomatic and rarely reported, so their frequency is unknown (21). In chronic infections, the major pathological findings are in the liver. The mechanical injury caused by the suckers of the parasites, and chemical stimulation by their metabolic products, may contribute to the changes in the epithelium of the bile ducts. The eggs can serve as nuclei for the formation of stones in the biliary tract and gall-bladder. Hyperplasia and desquamation of epithelial cells, adenomatous tissue formation, and marked proliferation of the periductal connective tissue with fibrosis of the bile duct wall are the main morphological changes. In chronic infections, the adenomatous tissue is gradually replaced by fibrous tissue that causes thickening of the bile duct wall, but hepatic cell function and liver structure are unaffected.

About one-third of chronic infections are asymptomatic. In patients who do have symptoms, gradual onset of discomfort in the right upper quadrant, anorexia, indigestion, abdominal pain or distension, and irregular bowel movements are the usual complaints. In heavily infected patients the symptoms include weakness, weight loss, epigastric discomfort, abdominal fullness, diarrhoea, anaemia, and oedema. In the late stage, jaundice, portal hypertension, ascites, and upper gastrointestinal bleeding may occur. Repeated or heavy infection during childhood has been reported to cause dwarfism with retardation of sexual development. The liver is usually enlarged with predominance of left lobe enlargement. The spleen can be palpated only in a small proportion of infected cases.

Recurrent pyogenic cholangitis is the most important complication of clonorchiasis. The bile contains a high proportion of mucus as a result of goblet-cell metaplasia in the bile duct epithelium. The mucinous bile combined with the parasite and its ova in the bile duct causes cholestasis and provides a favourable environment for secondary bacterial infection, most frequently by *Escherichia coli*. The ova and bacteria serve as *nidi* for the formation of biliary stones; bilirubin stones are the most common in this situation, in contrast to the cholesterol stones that are associated with gall-bladder disease in patients without clonorchiasis.

The pancreas may be involved in *C. sinensis* infection, especially in patients with heavy infections. The flukes are usually found in the main and branch ducts of the pancreatic tail, and the ducts may be dilated and packed with worms. The pathology of pancreatic clonorchiasis is similar to that of the hepatic lesion, namely, adenomatous hyperplasia of ductal epithelium. When acute pancreatitis occurs, features of acute inflammation are present.

Cholangiocarcinoma is associated with clonorchiasis; it is more frequently observed in areas where clonorchiasis is endemic than in non-endemic areas.¹

¹ See footnote page 57.

8.1.3 *Paragonimiasis*

Following ingestion in infected crustaceans, the metacercariae of *Paragonimus* spp. excyst in the duodenum of the host and the larvae penetrate the intestinal wall and migrate beneath the peritoneum, where they remain for five to seven days. Rats, wild boar, pigs, and chickens are paratenic hosts of *P. westermani*. The early stages of human infection are usually asymptomatic; however, heavily infected people may experience fever, fatigue, generalized myalgia, and abdominal pain with eosinophilia.

Over a period of about two to three weeks after infection, the immature worms penetrate the diaphragm, enter the pleural cavity, and then move into the lung parenchyma, where they mature. At this stage eggs may be present in the sputum, without the host showing any symptoms. In the initial stage of lung infection, the adult worms migrate in the tissue and cause focal haemorrhagic pneumonia. After 12 weeks, the worms in the lung parenchyma typically provoke a granulomatous reaction that gradually proceeds to development of fibrotic encapsulation. Extrapulmonary lesions are caused by worms that reach, and develop in, ectopic foci.

Pleuropulmonary paragonimiasis

Light infections are asymptomatic, although eosinophilia may be detected in peripheral blood and incidental lung lesions observed on routine chest X-ray films. When infections are heavier, dyspnoea and chest pain are frequent symptoms of early paragonimiasis, due to pneumothorax, pleural effusion, or hydropneumothorax. The most common clinical presentation is cough and production of rusty sputum with a foul fish odour. Over 50% of paragonimiasis infections in the Republic of Korea are associated with pleural lesions. Pulmonary involvement is frequently associated with systemic symptoms of fatigue, fever, myalgia, chest pain, and dyspnoea. When only chronic cough is present, patients may be misdiagnosed as having chronic bronchitis, bronchial asthma, or bronchiectasis. Gross haemoptysis is rare. Chest X-rays taken at this stage are characterized by hazy infiltration, cystic lesions, and conglomerated cysts or nodules. Peripheral blood eosinophilia and leukocytosis are moderately high and serum IgG and IgE levels are usually elevated.

Pleuropulmonary paragonimiasis is frequently confused with tuberculosis. When a patient is unresponsive to antituberculosis therapy or peripheral eosinophilia is belatedly recognized, confirmation of a diagnosis of paragonimiasis should be considered by egg detection in the sputum and/or a serological test.

Ectopic paragonimiasis

The mechanisms of the extrapulmonary localization of *Paragonimus* spp. are not known, but most patients with extrapulmonary lesions have an associated lung lesion or a history of lung disease, especially in the case of *P. westermani* infection. Cerebral involvement is the most serious

complication of human paragonimiasis. Migration of the worm through the brain can cause cerebral haemorrhage, oedema, or meningitis. Severe headache, mental confusion, seizure, hemiparesis, hypaesthesia, blurred vision, diplopia, homonymous hemianopsia, and meningismus may occur. The case-fatality rate is highest among patients with intracranial hypertension. In a population-based study in the Republic of Korea, cerebral involvement was estimated to occur in 0.8% of all cases of paragonimiasis. In one study in China, 25% of all people seeking medical treatment for paragonimiasis had cerebral involvement.

Abdominal masses and associated abdominal pain, tenderness, diarrhoea, nausea, and vomiting may be observed in patients with paragonimiasis. Granulomas are sometimes present in the intestinal wall, mesentery, omentum, liver, and spleen. Liver involvement is more frequently seen in children; in one study reported from China up to 51% of infected children exhibited involvement of the liver.

Abdominal or subcutaneous extrapulmonary manifestations occur occasionally in infections with *P. westermani* and frequently in infections with *P. skrjabini*, *P. heterotremus*, and *P. mexicanus*, for which humans are not the most suitable hosts. Migratory subcutaneous nodules are commonly seen on the chest, abdominal wall, and extremities.

8.1.4 **Fascioliasis**

The clinical incubation period between the ingestion of metacercariae of *Fasciola* spp. and the appearance of first symptoms is usually between four and six weeks, but varies considerably depending on the number of metacercariae ingested and the host's response (20). The initial manifestations are fever, sweating, abdominal pain, dizziness, cough, bronchial asthma, and urticaria. The parasitic prepatent period between the ingestion of metacercariae and passage of ova is usually about 4 months, but ranges between 3 and 18 months.

In children the acute infection is accompanied by severe clinical manifestations, including right upper quadrant or generalized abdominal pain, fever, and anaemia, and can be fatal.

The major pathological changes are seen during the migration of the immature flukes through the liver parenchyma for four to six weeks, or longer, before they enter the biliary tree. The flukes digest hepatic tissue and cause extensive traumatic and necrotic lesions in the liver parenchyma, including linear necrotic lesions heavily infiltrated with eosinophils. The immature flukes are sometimes trapped in the organ and die leaving cavities filled with necrotic debris. When these heal, considerable areas of the liver may be replaced by scar tissue. After arrival in the bile ducts, the larvae develop into adults, provoking inflammatory and adenomatous changes of the biliary epithelium, with enveloping fibrosis of the ducts. Pressure atrophy of the liver parenchyma and extensive periductal fibrosis may ensue if the pathological process in

the biliary tract continues and the number of worms is considerable. Moreover, the gall-bladder frequently undergoes the same pathological changes as the bile ducts and may also be invaded. In heavy infections the epithelium is eroded and the worms may migrate into the liver parenchyma to form abscesses. Extensive fibrotic changes in the bile ducts seem to be mostly related to the large amounts of proline produced by the adult worms.

Chronic fascioliasis has been reported to be generally asymptomatic, though the proportion of asymptomatic cases is unknown. The clinical manifestations, when they are reported at this stage, are similar to but milder than those observed during the acute stage, except in heavy infections, when anaemia is one of the most characteristic symptoms. Blood loss into the bile (haemobilia) is one factor that contributes to severe anaemia. Abdominal colic, obstructive jaundice, and cholelithiasis have occasionally been reported. If the juvenile flukes deviate during their normal migration to the liver they may cause ectopic fascioliasis in the intestines, pancreas, lungs, heart, brain, skin, and other organs.

8.1.5 *Fasciolopsiasis*

Most infections with *Fasciolopsis buski* are light and asymptomatic. In heavier infections the first symptoms are diarrhoea with epigastric pains, which simulate a peptic ulcer. The generalized toxic and allergic symptoms appear in the form of oedema, particularly of the face, abdominal wall, and lower limbs. The appetite is usually not affected, but nausea and vomiting are pronounced in some patients. Slight macrocytic anaemia and moderate leukocytosis with eosinophilia are observed.

Mortality has been reported due to profound intoxication in children with heavy infections in China, India, and Thailand. A study in Thailand concluded that the usual level of infection was not associated with clinical disease or malabsorption.

8.1.6 *Other foodborne trematode infections*

Echinostomiasis and infection due to Echinochasmus spp.

The pathology of echinostomiasis has not been well studied. The flukes attach themselves to the mucosa of the small intestine and inflammatory lesions may develop at the site of attachment, together with a generalized toxic response. Heavy infections may produce necrosis and increased cellular infiltration in the intestinal mucosa. Experiments have shown that adult *Echinostoma hortense* dwell in the lumen of the upper small intestine of the rat, and pathological changes are chiefly confined to the mucosa, with marked destruction of villi and loss of mucosal integrity. There has been no well documented study on the clinical aspects of the infection, but it is known to cause only very mild disease. In heavy infections there are vague abdominal manifestations such as flatulence, intestinal colic, and loose bowel movements. In children, diarrhoea, abdominal pain, anaemia, and oedema have been reported.

A self-infection by ingestion of 113 metacercariae of *Echinochasmus japonicus* resulted in abdominal discomfort and pain, intestinal gurgling, and diarrhoea about 10 days later, followed by recovery (22).

Heterophyiasis, metagonimiasis and other heterophyid infections

In the usual infection with *Heterophyes* spp., there is mild inflammatory reaction at the sites where the minute worms become attached to the intestinal mucosa or burrow into it. Shallow ulcers and mild irritation or superficial necrosis of the mucosa can occur. Following the ingestion of metacercariae and the prepatent period, which averages nine days, mild, intermittent and mucous diarrhoea, dyspepsia, and colicky pain are sometimes noted with eosinophilia. Myocarditis has also been observed, and surgical intervention in patients with neurological manifestations has demonstrated adult *H. heterophyes* or eggs encapsulated in the brain tissue.

Metagonimus yokogawai infection in humans shows similar pathological features to heterophyiasis. In a study from the Republic of Korea, worms were detected within the crypts of Lieberkühn in the middle part of the small intestine at early stages of infection and between the villi at later stages. The pathological changes were characterized by villous atrophy and crypt hyperplasia, with a variable degree of inflammatory cell infiltration. The invasion of worms was confined to the lower mucosal level and the worms were never found in the submucosa in immunocompetent hosts.

The most frequent symptoms of patients infected with *M. yokogawai* are abdominal pain, diarrhoea, and lethargy. The severity of the symptoms depends on the number of worms present, the depth of their penetration into the wall of the intestine, and the individual susceptibility or resistance of the patient. Heavy infections are not always associated with clinical symptoms; in one person, for example, an infection with over 60 000 adult worms was associated only with such complaints as mild indigestion and epigastric pain.

In a study in the Philippines, intestinal lesions similar to those due to *H. heterophyes*, *M. yokogawai*, and other small heterophyids were described in patients who had died of cardiac failure; eggs of three *Haplorchis* species (*H. yokogawai*, *H. pumilio*, and *H. taichui*) and *Diorchitrema pseudocirratum* were detected in the cardiac lesions of these patients and, in one case, an adult heterophyid was found in the epicardium (23). Eggs, tentatively identified as those of *Haplorchis pumilio*, were also found in sections of the spinal cord at the levels of lesions responsible for loss of motor and sensory function.

Nanophyetiasis

It was previously thought that humans were refractory to infections by *Nanophyetus salmincola*, but recent studies show that the presence of symptoms is dose-dependent. Infections of 100 or more worms elicit

symptoms reminiscent of influenza with general involvement of the gastrointestinal tract including diarrhoea. Without treatment, symptoms can continue for eight months or more, although it is generally believed that if there is no reinfection, the trematodes rarely survive in the human host for more than a year.

Diagnosis is generally made by the presence of eggs in stool specimens. However, misdiagnosis is possible since the eggs resemble those of tapeworms of the genus *Diphyllobothrium*. Misdiagnosis does not normally cause problems with treatment since the drugs used are equally effective against both *Nanophyetus* and *Diphyllobothrium* spp.

8.2 Nutrition and foodborne trematode infections

The joint FAO/WHO International Conference on Nutrition, in its Declaration (24), confirmed that access to sufficient amounts of nutritious and safe food is a basic human right. This statement is based on the recognition that unsafe food and certain dietary habits may cause, or may be a contributory cause of, disease and/or undernutrition. In the case of foodborne trematode infections, the vehicle is usually a nutritious food which contains the infectious stage of a trematode and is thus unsafe. The objective of intervention is either to render the food safe through appropriate processing (e.g. cooking, freezing, or irradiation) or to change dietary habits so that certain unprocessed foods are no longer eaten.

There have been few published studies on the nutritional impact of foodborne trematode infections. Other parasitic and infectious diseases are usually highly endemic in the same areas and can hence interact synergistically with foodborne trematode infections. Clonorchiasis in China has in the past been associated with dwarfism and with retarded growth and development (21). In the south of the Lao People's Democratic Republic, where opisthorchiasis is more widely prevalent than any other parasitic disease including malaria and schistosomiasis due to *S. mekongi*, 69% of children weigh less than 80% of the normal weight for their age, 56% are at least two standard deviations below the normal height for their age, and 32% weigh less than 90% of the median weight for their height. Multivariate analysis has shown that opisthorchiasis is a major determinant of this malnourished state (A. Sleight et al., personal communication 1993). Chronic diarrhoea caused by intestinal foodborne trematodes has been reported in clinical studies, but its nutritional impact on individuals or communities is not known.

8.3 Carcinoma and foodborne trematode infections

Numerous studies have shown that liver flukes are associated with cholangiocarcinoma far more frequently than can be explained by chance, but the exact pathogenesis of cholangiocarcinoma is still unclear.

Liver cancer is one of the most common malignancies that occurs in south-east Asia; Khon Kaen, Thailand, has the highest well documented incidence. The high incidence of cholangiocarcinoma, or bile duct cancer, which elsewhere accounts for only a minority of liver cancers (most of which are hepatocellular) is particularly striking. In 1988 in Khon Kaen, 89% of liver cancers were cholangiocarcinomas. The age-standardized incidence rates for 1988 were 89.2 per 100 000 males and 35.5 per 100 000 females. A cancer registry established in the northern province of Chiang Mai, where the infection is rare, reported rates of 5 and 3 per 100 000 males and females respectively. An independent retrospective study of hospital records in Khon Kaen yielded an estimated annual age-standardized incidence rate of 135.4 and 43.0 per 100 000 males and females respectively. Since cholangiocarcinoma and *Opisthorchis viverrini* are both prevalent in north-east Thailand, the geographical relationship has been recognized for many decades. In recent cross-sectional studies using ultrasound and endoscopy for diagnosis of asymptomatic cholangiocarcinoma in people drawn randomly from endemic communities, those found to have cholangiocarcinoma were much more likely to have heavy *O. viverrini* infections than no eggs in the stool.

A correlation between *O. felineus* infections and cholangiocarcinoma has been reported in the former USSR. Between 1968 and 1973, in the south of Tyumen, Russian Federation, where 0.5% of the population was infected with *O. felineus*, the average prevalence of cholangiocarcinoma was reported to be 4.4 per 100 000 population. In the central part of Tyumen region, where the prevalence of *O. felineus* infection was 45%, the rate of cholangiocarcinoma was 49.8 per 100 000 population (10 times higher than in the south). In the high-prevalence area of Tyumen, autopsies of 146 patients with opisthorchiasis revealed the frequency of cholangiocarcinoma to be 81.5%, while in the same consecutive series, 125 autopsies carried out on patients without the infection showed that 34.8% had cholangiocarcinoma.

The rates of cholangiocarcinoma in countries where *Clonorchis sinensis* infection is endemic are not available.

Cholangiocarcinoma is one of the major histological types of primary cancer of the liver. Strictly speaking, only tumours of the intrahepatic bile ducts are cholangiocarcinomas, although it is often difficult to distinguish clinically between intrahepatic and extrahepatic cancers of the hilar region. Although cholangiocarcinoma is regarded as a specific morphological entity for classification purposes (with a specific morphology code in the tenth revision of the International Classification of Diseases), it is histologically identical to adenocarcinoma, and diagnoses such as duct carcinoma and adenocarcinoma are considered to be synonymous.

The mechanisms of carcinogenesis in opisthorchiasis and clonorchiasis have been the subject of considerable research; it seems that the presence

of parasites induces DNA damage and mutations as a consequence of the formation of carcinogens or free radicals and of cellular proliferation of the intrahepatic bile duct epithelium. As in other situations where cancer is a sequel of long-term infectious processes, nitrosation and nitrosamine production consequent upon fluke infestation probably contribute to the etiology of cholangiocarcinoma.

It has been postulated that immunological reactions are involved in pathogenesis of cholangiocarcinoma, on the basis of a correlation between *Opisthorchis*-specific IgG antibody and changes in the biliary tract diagnosed by ultrasound in patients in an endemic area. It seems equally likely that this association is indirect and that the antibody levels simply reflect, for example, the duration or intensity of opisthorchiasis. There is currently a great interest in the relationship between specific mutation spectra in proto-oncogenes (such as *ras*) and tumour-suppressor genes.

Studies on experimental *O. viverrini* and *C. sinensis* infections in Syrian golden hamsters have demonstrated that liver fluke infestation alone rarely induces cholangiocarcinoma, but if infected hamsters are treated with hepatocarcinogens such as *N*-nitrosodimethylamine and *N*-nitrosodiisopropanolamine, they can develop bile duct tumours resembling those seen in humans. The development of cholangiocarcinoma in both clonorchiasis and opisthorchiasis has been suggested to be a multifactorial process in which the parasite plays the role of a promoter.

No association between *Fasciola hepatica* infection and carcinoma has been reported. However, aflatoxin B₁ has been shown experimentally to have greater mutagenic activity in *F. hepatica*-infected mice than in uninfected controls.

8.4 Other infectious diseases and foodborne trematode infections

Paragonimiasis has both masked and confused the diagnosis of tuberculosis for more than 100 years. Haemoptysis is the most frequent clinical sign of paragonimiasis and the cardinal sign of tuberculosis: health workers without laboratory support will generally assume that patients with haemoptysis have tuberculosis. When disease is more advanced, i.e. when there is cavitation or fistula formation, and the sputum is negative both for acid-fast bacilli and in culture, only staff with clinical acumen based on epidemiological knowledge would be likely to suspect paragonimiasis as the true cause. In areas where paragonimiasis is endemic, and tuberculosis is suspected, sputum examination should be used as a means of excluding paragonimiasis.

In Manipur, India, paragonimiasis was not recognized until 1982. During a subsequent 18-month period, it was reported that 60% of consecutive patients with paragonimiasis had previously been diagnosed as having tuberculosis and 40% had been classified as suffering from chronic respiratory disease.

No association between hepatitis and foodborne trematode infections of the liver has been reported. Further clinical research on a possible link is recommended. In Egypt, *F. hepatica* occurs in areas endemic for *Schistosoma mansoni* and *S. haematobium*, and in Cambodia and the Lao People's Democratic Republic *O. viverrini* occurs in the same areas as *S. mekongi*. No clinical studies on the interaction between these infections have yet been reported.

8.5 Human immune responses

No protective immunity associated with foodborne trematode infections has been demonstrated. The infections invoke specific antibodies, but reinfection easily occurs following treatment and cure. The mechanisms of cell-mediated and antibody-mediated immune responses to fluke infections vary from host to host and in the same host according to the phase of infection.

Serum levels of IgG, IgM, and IgE are usually elevated in *F. hepatica* infections. Specific IgE antibodies are detected in about half of those infected. Moreover, total and specific IgE levels have been shown to be positively correlated with the egg burden, age, clinical features, and degree of eosinophilia. IgA levels are usually normal.

The antibody response to infection with *Opisthorchis* spp. and *C. sinensis* is characterized by an early rise in serum levels of IgM followed by elevations of IgA and IgG. In chronic infections, serum IgA is normal, whereas IgG and IgM levels are elevated. Serum IgE in clonorchiasis patients has been reported to be several times higher than normal, and a high level of *C. sinensis*-specific IgE has been detected in patients with chronic infection. A close correlation has been found between the serum IgE level and *C. sinensis*-specific IgE in infected individuals, and a weak correlation has been reported between both serum and specific IgE and eggs per gram of faeces.

8.6 Mortality

The mortality rates of foodborne trematode infections are rarely reported although death directly attributable to the infection does occur. Death from fascioliasis, particularly in heavily infected children, is due to massive bleeding into the bile ducts or the abdominal cavity. Migration of adult and juvenile trematodes into the central nervous system may cause severe intracranial hypertension, especially in the early invasive stage, although death has rarely been reported. The mortality due to cholangiocarcinoma associated with opisthorchiasis and clonorchiasis is discussed on pages 63–65.

9. The parasites

The Study Group focused on four major foodborne parasites that infect humans (*Opisthorchis* spp., *Clonorchis sinensis*, *Paragonimus* spp., and *Fasciola* spp.) and some intestinal trematodes (see Annex 2 for a list of intestinal flukes). The foodborne trematodes are digenetic parasites, that is they pass through two or more hosts; they are hermaphroditic and reproduce by self-fertilization. The parasites may live for up to 45 years in a human host, producing 1000–2500 eggs per day (*Clonorchis sinensis*).

9.1 Genetics

Fasciola spp.

Fasciola spp. are the most comprehensively studied of all the trematodes. *F. gigantica* is generally diploid (20 chromosomes) and *F. hepatica* is triploid (30 chromosomes). The molecular genetics of the genome of *F. hepatica* have been extensively studied.

Many complementary DNA (cDNA) libraries of *F. hepatica* have been prepared. An *F. hepatica* cDNA clone of 2 kilobases, which is highly repetitive, has been expressed in *E. coli*, and the antigen produced may be useful in immunodiagnostic tests. The DNA sequences in *F. hepatica* encoding glutathione *S*-transferases have been characterized. These enzymes show potential for use in vaccine development.

Paragonimus spp.

C-banding techniques have been extensively used to study *Paragonimus* spp. Both diploid and triploid forms of *P. westermani* have been described. The distribution of restriction enzyme sites in the repetitive DNA sequences is similar in both genotypes. Polymorphism of isoenzyme patterns has limited the usefulness of this technique as a tool for answering questions on taxonomy, although all *Paragonimus* species endemic in Japan show similar isoenzyme patterns. A tetraploid *Paragonimus* species has been described in China.

Opisthorchis viverrini

The phylogenetic classification *O. viverrini*, as determined by comparison of ribosomal gene sequences (rRNA), is compatible with the conventional taxonomic classification. *O. viverrini* has neither CpG nor A methylations, and highly repetitive elements have been demonstrated in its genomic DNA.

9.2 Taxonomy

All the species dealt with by the Study Group belong to different families of the subclass Digenea. The debate on the taxonomy of lung flukes of the genus *Paragonimus*, family Troglotrematidae, has continued for decades. Forty-eight species/subspecies of *Paragonimus* have been

reported, some of which may not be valid. It is generally agreed that the following species are responsible for human paragonimiasis:

- *P. westermani*: causes typical lung disease in many Asian countries;
- *P. skrjabini*: endemic in mountainous areas of China; migrating subcutaneous nodules and marked eosinophilia are the most striking clinical features of infection;
- *P. miyazakii*: causes pleural paragonimiasis in Japan;
- *P. philippinensis*: occurs in the Philippines;
- *P. heterotremus*: occurs in south China, the Lao People's Democratic Republic, and Thailand;
- *P. kellicotti*: causes pulmonary infection in North America;
- *P. africanus*: causes pulmonary infection in Nigeria;
- *P. uterobilateralis*: causes pulmonary infection in the west and south of Africa;
- *P. mexicanus* (*P. peruvianus*, *P. ecuadoriensis*): causes pulmonary infection in Central and South America.

In the family Opisthorchiidae, the most important species that infect humans include *Clonorchis sinensis*, *Opisthorchis felineus*, and *Opisthorchis viverrini*, which are endemic in Asia. There are also a few endemic foci of *O. felineus* in eastern Europe.

Two other species of liver fluke, *Fasciola hepatica* and *Fasciola gigantica*, and the intestinal fluke *Fasciolopsis buski* belong to the family Fasciolidae.

About 70 species of intestinal fluke have been reported in humans. Nearly 30 species are members of the family Heterophyidae; the important representatives are *Heterophyes heterophyes* and *Metagonimus yokogawai*. Other families include: Echinostomatidae (representatives in humans: *Echinostoma ilocanum* and *Echinochasmus perfoliatus*), Diplostomidae (*Alaria americana*, *Neodiplostomum seoulensis*), Gastrodiscidae (*Gastrodiscoides hominis*), Gymnophallidae (*Gymnophalloides seoi*), Lecithodendriidae (*Phaneropsolus bonnei*), Microphallidae (*Spelotrema brevicaeca*), Nanophyetidae (*Nanophyetus salmincola*), Paramphistomatidae (*Watsonius watsoni*), Plagiorchiidae (*Plagiorchis philippinensis*), and Strigeidae (*Cotylurus japonicus*). For a few species of intestinal trematodes, the synonymy or validity of the taxonomic names remains controversial. For instance, it is not yet certain whether *Nanophyetus salmincola* belongs to the Nanophyetidae, the Troglotrematidae, or the subfamily Nanophyetinae.

9.3 Snail-parasite relationships

The snail intermediate hosts of the most important foodborne trematodes are listed in Annex 5.

The eggs of *Clonorchis* spp. and *Opisthorchis* spp. are mature at excretion and are capable of immediate infection of the appropriate

freshwater snail. The embryonated egg is ingested by the snail, and other stages of the asexual life cycle are completed in the snail. The eggs of *Fasciola* spp., however, require at least a week outside faecal material to mature and *Paragonimus* spp. may require up to several weeks before the parasite in the egg (the miracidium) is fully mature and capable of penetrating the appropriate snail within 24–48 hours after hatching. Each parasite develops only in a specific type of freshwater aquatic snail. After a series of complex asexual cycles, hundreds of cercariae emerge from the snail.

The compatibility between populations/species of snail and different species of *Fasciola* varies. For example, *Lymnaea tomentosa* is a more efficient intermediate host than either the Australian or the New Zealand strains of *L. columella*. In a comparison of the compatibility of *F. gigantica* from sheep and buffalo with *L. auricularia* in Iraq, the sheep isolate exhibited a lower rate of infection and slower larval development and produced fewer cercariae. Many subspecies of *L. auricularia*, such as *L. a. swinhoei*, *L. a. rufescens*, *L. a. rubiginosa*, and *L. a. gedrosiana*, serve as intermediate hosts for *F. gigantica* in Asia, but they are less susceptible to *F. hepatica*. A comparison of the compatibility of *L. viatrix* and *L. columella* with *F. hepatica* demonstrated that *L. viatrix* was more compatible, as measured by the number of snails that became infected.

In a study in Morocco, peak densities of *L. truncatula* were found during the spring, and this coincided with peak transmission of *F. hepatica* in sheep. In northern Nigeria, the snail population also showed seasonal variations, with the lowest number of *L. natalensis* snails at the very end of the dry season. Many juvenile snails developed at the end of the wet season and the beginning of the dry season and the population density peaked in the middle of the dry season. *Fasciola* spp. infections in the snails occurred throughout the year, but the majority appeared to be acquired at the end of the wet season, which resulted in a high infection rate (up to 25%) at the beginning of the dry season.

Only limited information is available on the population dynamics of the snail intermediate hosts of other foodborne trematodes.

9.4 Intermediate hosts of foodborne trematodes

The second intermediate hosts of the foodborne trematodes harbour metacercariae infective to definitive hosts, including humans, and have an important role as sources of transmission. They include fish, crustaceans, edible water plants, and molluscs (Annex 5).

9.4.1 Fish

Freshwater fish are the most important intermediate reservoir hosts of foodborne trematodes. They also represent a plausible point of approach for control.

Fish belonging to the family Cyprinidae (carp) are the major intermediate hosts of *Clonorchis sinensis* and *Opisthorchis* spp. However, there is strong evidence that the composition of trematode parasite communities in freshwater fish is largely stochastic and that interactions between fish and trematode species play only a limited role in structuring the communities. This implies that more than one fish species in any aquatic environment can become infected. Thus, the absence of trematode infection in a fish species at any one time, or – for a newly introduced species – the absence of previously documented infection in other areas where transmission is known to occur, is no basis for assuming that the species cannot harbour a trematode capable of infecting humans.

More than 100 species of freshwater fish have been shown to be naturally infected with *Clonorchis sinensis* and more than 35 with *Opisthorchis* spp. The reason for the lack of specificity is not known. In some areas there is a lack of baseline survey information. In others, the interaction between human and non-human trematode infections of fish has not been adequately studied.

Of around 113 species of freshwater fish belonging to about 13 families that have been recorded to be hosts of *Clonorchis sinensis* in China, Japan, the Republic of Korea, and the former USSR, 95 are members of the family Cyprinidae. Of these species, the most notable are: *Pseudorasbora parva*, which occurs in all four countries; *Ctenopharyngodon idellus*, *Mylopharyngodon aethiops*, *Abbottina* spp., *Rhodeus* spp., and *Hemiculter* spp. in China; *Sarcocheilichthys sinensis*, *Hemibarbus labeo*, *Acanthorhodeus gracilis*, *A. taenianalis*, *Puntungia herzi*, *Pseudogobio esocinus*, and *Gnathopodon* spp. in the Republic of Korea; and *Gnathopodon elongatus*, *Sarcocheilichthys variegatus*, and *Acheilognathus lanceolata* in Japan. However, the only fish eaten raw in Japan are *Cyprinus carpio* and *Carassius* spp.

Fifteen species of fish from 7 genera have been reported to be intermediate hosts of *Opisthorchis viverrini* in Thailand; of these, *Cyclocheilichthys apagon*, *C. armatus*, *C. repasson*, *Puntius leiacanthus*, and *Hampala dispa* are believed to be the most important. In the former USSR, 22 species of 17 genera of the family Cyprinidae have been found to be infected by *Opisthorchis felineus*. *Abramis bramae*, *A. sapa*, *Aspius aspius*, *Leuciscus idus*, *Rutilus rutilus*, *Tinca tinca*, and *Phoxinus* spp. are among the most important vectors.

Numerous species of at least 45 genera of fish can serve as the second intermediate hosts of intestinal flukes, including all 30 species of heterophyids, about half of the echinostome species and 2 species of *Nanophyetus*. Among the frequently described fish species are *Mugil* spp. for *Heterophyes*, *Haplorchis*, *Metagonimus*, *Echinochasmus*, *Phagiocola*, *Procerovum*, and *Stellantchasmus* spp.; *Salmo* spp. for *Nanophyetus* and *Metagonimus* spp.; *Cyprinus* spp. for *Centrocestus*, *Haplorchis*, and *Metagonimus* spp.; *Oncorhynchus* spp. for *Nanophyetus* spp.; *Acheilognathus* spp. for *Echinostoma* spp.; and *Acanthogobius* and

Carassius spp. for *Heterophyes* and *Metagonimus* spp. Loach can also serve as a second intermediate host of trematodes; for example, *Misgurnus anguillicaudatus* is a host for *Centrocestus armatus* in Japan. There have been few epidemiological studies of this group of flukes since only rare human infections have been reported and the listing of fish hosts is incomplete (Annex 5).

9.4.2 **Crustaceans**

Paragonimiasis is contracted by humans and other mammalian definitive hosts following the ingestion of infectious metacercariae of *Paragonimus* spp. in raw or undercooked crab or crayfish tissue. Fifty-three species from 21 genera of freshwater crab and crayfish have been reported to be second intermediate hosts of *Paragonimus* spp. throughout the world. The main species responsible for transmission of human paragonimiasis are: *Eriocheir japonicus* for *P. westermani*, and *Potamon dehaani* for *P. westermani* and *P. miyazakii* in Japan; *Sinopotamon denticulatum* for *P. westermani* and *P. skrjabini*, *Sinopotamon yaanense* for *P. skrjabini*, and *Cambaroides daurucus* for *P. westermani* in China; *Eriocheir sinensis* and *Cambaroides similis* for *P. westermani* in the Republic of Korea; *Parathelphusa dugasti* and *Ranguna smithiana* for *P. heterotremus* in Thailand; *Libernautes l. latidactylus* for *P. uterobilateralis*, *Sudanaonates africanus*, *S. aubryi*, *S. pelli*, and *Potamonemus asylos* for *P. uterobilateralis* and *P. africanus* in west African countries; *Pseudothelphusa* spp., *Ptychophallus* spp., *Potamocarcinum* spp., and *Hypolobocera* spp. for *P. mexicanus* in Central and South American countries.

It has been reported in China that three species of freshwater shrimp, *Caridinia nilotica gracilipes*, *Macrobrachium superbum*, and *Palaemonetes sinensis*, can serve as second intermediate hosts of *Clonorchis sinensis*, and metacercariae of *Paragonimus westermani* have been found in the shrimp *Macrobrachium nipponensis* in the Republic of Korea. There is, however, no epidemiological evidence of an association between eating raw shrimps and human infection.

9.4.3 **Plants**

Watercress, *Nasturtium officinale*, commonly supports the metacercariae of *Fasciola* spp. However, from the outbreaks of fascioliasis in Cuba and the Islamic Republic of Iran and in the endemic areas of Bolivia, there is evidence that a variety of plants may be sources of infection.

Fascioliasis is a worldwide problem in ruminants, and human infection has been recorded in 55 countries. However, fascioliasis has largely been overlooked as a public health problem. As a result, the plants that are contaminated with encysted metacercariae have not been well investigated. In an area of the Islamic Republic of Iran where a large outbreak of human fascioliasis occurred, metacercariae were recovered

from the most commonly used vegetables such as wild mint (*Mentha pipesota* L.), *Eryngium coerulesce*, watercress (*Nasturtium officinale*), and aquatic mint (*Mentha aquatica*). An experimental study in Egypt indicated that cercariae of *Fasciola* spp. prefer to encyst on dark green leaves with a hairy epidermis (such as those of mint), followed by leaves with a serrated and mamillated epidermis, such as garden rocket (*Eruca sativa*), lettuce (*Lactuca sativa*), parsley (*Petroselinum sativum*), and the clover *Trifolium alexandrium*. Plants with a smooth chitinized epidermal surface carried the fewest metacercariae. In countries in Asia where fasciolopsiasis is endemic, the cercariae of *Fasciolopsis buski* encyst on the seed pods of the water caltrop (*Trapa natans*, *T. bicornis*), the bulb of the water chestnut (*Eliocharis tuberosa*), the roots of lotus, water bamboo, and other aquatic vegetation including *Valisneria* spp., *Salvinia natans*, and *Lemna polyrhiza*.

Water plants are also believed to serve as hosts for encystment of metacercariae of certain intestinal flukes (*Watsonius watsoni*, *Fischoederius elongatus*, and *Gastrodiscoides hominis*).

9.4.4 Other intermediate hosts

Molluscs

Various kinds of mollusc (snails and bivalves) serve as second intermediate hosts of many species of intestinal trematodes. Important examples are: *Cipangopaludina japonica*, *Corbicula lindoensis*, *Gyraulus convexiusculus*, *Indoplanorbis exustus*, *Parafossarulus manchouricus*, *Pila conica*, *Radix japonicus*, and *Viviparus javanicus* for *Echinostoma* spp.; *Crassostrea gigas* (oyster) for *Gymnophalloides seoi*; *Lymnaea* spp. for *Plagiorchis muris*; and *Mya* spp. and *Mytilus* spp. for *Himasthla muelhensi*.

Amphibians and snakes

Amphibians can also be parasitized and act as a source of human infections. The frog *Rana nigromaculata* is the second intermediate host of *Neodiplostomum seoulensis* in the Republic of Korea. As paratenic hosts, terrestrial snakes (*Rhabdophis tigrina* and four other species) play an important role in transmission of *Neodiplostomum seoulensis* in humans.

Insects

The aquatic insects *Chironomus* spp. serve as second intermediate hosts of *Plagiorchis muris* in Japan. The Ilocanoan inhabitants of the Philippines are believed to have acquired infection with *Plagiorchis philippinensis* by eating the grubs of certain insects. In Thailand, the odonate insects dragonflies and damselflies have been found to be the second intermediate hosts of *Phaneropsolus bonnei* and *Prosthodendrium molenkampi*. People can also be infected by consumption of raw metacercariae-encysted naiads (water nymphs of dragonflies).

9.5 Mammalian reservoir hosts

The definitive natural hosts of *Clonorchis sinensis*, other than humans, include: pigs, dogs, cats (*Felis domesticus*, *F. bengalensis*), civets (*Viverricula indica*), hares (*Lepus cuniculus*), and rodents (e.g. *Rattus rattus*). Cats, dogs, pigs, and rats are the most important reservoir hosts because of their wide distribution and large populations: their importance in the epidemiology of clonorchiasis is confirmed by their high infection rates in the endemic areas. However, the intensity of human infections is usually heavier than the infection of reservoir animals. Therefore, it is the infected humans rather than the reservoir hosts who play the major role in the dynamics of transmission of the disease; reservoir animals may serve primarily to maintain the presence of transmission.

Twenty-eight species of mammals are involved in the transmission of *O. felineus* in the former USSR. Of these cats, foxes, muskrats, corsac foxes, and dogs are the most important reservoir hosts.

Opisthorchis viverrini is common in cats and dogs in Thailand and the Lao People's Democratic Republic and these animals play a role in maintaining transmission.

Unlike *Clonorchis sinensis* and *Opisthorchis* spp., *Fasciola hepatica* and *F. gigantica* are mainly parasites of ruminants, and humans are incidental hosts. The major natural reservoirs are cattle, sheep, goats, and buffaloes; camels, llamas, deer, pigs, horses, rabbits, and certain other wild mammals can also serve as reservoir hosts. In heavily endemic areas of fascioliasis with a prevalence of 30-50% in cattle or sheep, it is not uncommon to find a prevalence of over 90% in other domestic or wild ruminants.

The natural definitive hosts of *Paragonimus* spp. other than humans include the pig, beaver, tiger, cat, wild cat, leopard, fox, wolf, dog, and other carnivores such as *Nyctereutes procyonoides*, *Viverra zibetha ashtoni*, *Viverricula indica pallida* and mongoose (*Herpestes urva*, *H. javanicus rubrifons*). *Melogale moschata* and the masked palm civet (*Paguma larvata*) play an important role in transmission of *P. skrjabini*. Immature worms of *P. westermani* in the muscle tissue of wild boar are infective, and human infection acquired by eating raw flesh from boars has been reported in Japan. In Africa, the black mongoose (*Crossarchus obscurus*), civet cat (*Viverra civetta*), and drill (*Mandrillus leucophaeus*) are the best known reservoir hosts of *Paragonimus* spp.

The commonest reservoir hosts of the intestinal trematodes are the dog, cat, rat, and duck. Birds, pigs, foxes, and various species of wild mammal can also serve as definitive hosts of certain species of flukes.

10. Intermediate snail hosts

All the parasites described in this report have freshwater snails as their first intermediate hosts. In order to understand the epidemiology of the diseases caused by these flukes and initiate disease control, a comprehensive knowledge of the taxonomy and ecology of the snail hosts is important.

10.1 Taxonomy of intermediate snail hosts

With some exceptions, the taxonomy of the intermediate snail hosts is well established. *Clonorchis sinensis* is transmitted by a wide range of operculate snails. *Parafossarulus manchouricus* is the main molluscan host, but *Alocinma longicornis* and *Bithynia fuchsiana* also play an important role in the life cycle of this parasite.

Opisthorchis spp. are transmitted by aquatic snails of the family Bithyniidae, mainly of the genus *Bithynia* in all endemic areas. In the former USSR, the major snail hosts for *Opisthorchis felinus* are *Codiella (Bithynia) inflata*, *C. troscheli*, and *C. leachi*; in Thailand the main hosts for *Opisthorchis viverrini* are *Bithynia siamensis gonimphalus*, *B. s. funiculata*, and *B. s. laevis*.

According to most authors, the intermediate snail hosts of *Fasciola* spp. all belong to the genus *Lymnaea* (synonyms: *Galba* and *Radix*) of the family Lymnaeidae, which has a worldwide distribution. However, snails belonging to other genera of the family Lymnaeidae may also serve as intermediate hosts in certain areas.

In Europe and north-west Africa, *Lymnaea truncatula* is the main snail host for *F. hepatica*; *L. auricularia* is the intermediate host for *F. gigantica*, and *L. columella* can act as an intermediate host for both parasites. In the eastern Mediterranean region, *L. truncatula*, and *L. columella* act as the hosts for *F. hepatica*, while the hosts for *F. gigantica* are *L. auricularia* complex, *L. natalensis*, and *L. palustris*; *L. cailliaudi* is the most important snail host for both species of *Fasciola* in Egypt. Snails of the genera *Fossaria*, *Lymnaea*, and *Pseudosuccinea* are believed to be the intermediate hosts of *F. hepatica* in the Americas: *Fossaria cubensis* in the Caribbean and the Gulf of Mexico areas; *Fossaria viatrix* and *L. diaphana* in South American countries; and *P. columella* in North America, the Caribbean, and some Central and South American countries. *Lymnaea* spp. serve as snail hosts of *Fasciola* spp. in China and Japan.

About 40 species of large aquatic snails in 14 genera and 4 families (Pleuroceridae, Thiariidae, Pomatiopsidae and Assimineidae) have been reported to be responsible for the transmission of paragonimiasis in Asia. Although some taxonomic questions may need to be clarified, the important snail hosts for *Paragonimus* spp. are well described. *Semisulcospira libertina* is the most important snail host of *P. westermani* in China, Japan, and the Republic of Korea. *Brotia* spp. are the main hosts

in south-east Asia. In China and Japan, *Tricula* spp. and *Erhaia* (*Bythinella*) spp. act as snail hosts for *P. skrjabini*, and the host for *P. miyazakii* is *Bythinella nipponica akiyoshiensis*. In Thailand, the first intermediate snail hosts of *P. westermanni* and *P. heterotremus* have not been identified.

In west Africa, subject to confirmation, the first intermediate hosts of *P. uterobilateralis* are probably *Afropomus balanoides* and *Potadoma sanctipauli*; *Potadoma freethii* is thought to be the snail host of *Paragonimus africanus*.

Small aquatic or semi-terrestrial snails of the genera *Aroapyrgus*, *Littoridina*, and *Pomatiopsis*, family Hydrobiidae, are the intermediate snail hosts of *Paragonimus* spp. in the Americas.

The intermediate snail hosts of *Fasciolopsis buski* are *Gyraulus chinensis*, *Hippeutis cantori*, and *Polypylis hemisphaerula*. For other intestinal flukes, examples of snail hosts are: *Austropeplea ollula*, *Gyraulus convexiusculus*, *Hippeutis umbilicalis*, *Indoplanorbis exustus*, *Parafossarulus manchouricus*, and *Lymnaea japonicus* for echinostomes; and *Cerithideopsisilla cingulata*, *Pirenella conica*, and *Semisulcospira libertina* for heterophyids. Knowledge of the life cycle, including the intermediate hosts, of many species of small intestinal flukes is limited, and further studies are clearly warranted.

10.2 Control of intermediate snail hosts

Snail control is one way of interrupting the life cycle of the parasite and thus preventing human infection. However, control of foodborne trematode infections by use of molluscicides or other snail-control methods has not been attempted except in the case of animal fascioliasis. Before introducing chemical snail-control measures, the environmental impact should be considered, as should the potential of these chemicals to leave residues in the edible parts of fish and shellfish.

Appropriate snail-control approaches should be based on an adequate understanding of snail ecology and the environment. Most of the intermediate hosts of *Fasciola hepatica* live in marshy ground and water is essential for snail reproduction and for transmission of the parasite; it is therefore possible to reduce snail populations by physical means, such as the installation of drainage channels. The habitats of the intermediate snail hosts of *Clonorchis sinensis* and *Opisthorchis* spp. are generally ponds, swamps, and rice fields with a high content of organic matter, rather than flowing water.

Niclosamide is currently the only safe and acceptable molluscicide according to the WHO Pesticide Evaluation Scheme. Neither the introduction of new snail species nor any other method of biological control of snail intermediate hosts is currently recommended. Land reclamation and drainage systems are effective in reducing populations of snails, in particular *L. truncatula*.

10.3 Spread of snails

The spread of intermediate snail hosts through importation of tropical fish and aquatic plants etc. is now well documented. If regulations permitted only fish eggs to be imported for the establishment of aquaculture systems using non-native fish species, the incidental importation of snails or snail eggs that can act as intermediate hosts of foodborne trematodes would be decreased and possibly eliminated.

An important means of dispersal for snails is flowing water, in the form of either flood water or streams and rivers, which carry the snails across territories and national boundaries. Another natural mechanism of dispersal involves the attachment of snails or their egg-masses to the legs and feathers of waterfowl and other migratory birds. This latter method permits the spread of snails between geographically discrete bodies of water.

Lymnaea columella, which acts as an intermediate host for both *F. hepatica* and *F. gigantica* in Africa (except the north west), was extremely rare in South Africa before 1944, but by 1967 it was considered to be the most successful among invader freshwater snail species to enter the country. A later investigation confirmed that this species had succeeded in markedly extending the boundaries of its geographical distribution in South Africa because of its high reproduction rate and short generation time, its ability to utilize a large variety of niches, and its successful dispersal. The prevalence of fascioliasis in South Africa has increased since the arrival of this invader snail species from the Americas. The reasons may be that *L. columella*, as a potential intermediate host of *F. hepatica*, is more widely distributed geographically than the traditional host *L. truncatula*, and that it causes more effective transmission of *F. gigantica* than the traditional host, *L. natalensis*. *L. columella* is now spreading up through the African continent from the south, partly because of the development of irrigation schemes. The same species has been introduced to many other areas of the world, including Europe and the eastern Mediterranean region.

11. **Water quality, sanitation, and wastewater usage**

Poor sanitation and inappropriate use of wastewater are closely linked to the risk of foodborne trematode infections. Thus, specific technical guidelines and measures to reduce risk from these sources should be developed with the responsible sectors in each country.

11.1 **Water quality**

A great variety of helminth eggs and larvae have been detected in drinking-water. However, drinking-water contaminated with metacercariae of *Fasciola* spp. has rarely been a source of infection, and the

metacercariae of other foodborne trematodes are not released from their intermediate hosts in water. WHO's *Guidelines for drinking-water quality* (25) do not set guideline levels for trematodes.

11.2 Sanitation

Usual sanitary practices for the disposal of human and animal wastes can interrupt the life cycle of foodborne trematodes, whereas poor sanitation and personal hygiene can introduce and spread foodborne trematode infections and maintain transmission in the community. The availability and utilization of latrines are therefore key issues in the control of foodborne trematode infections. Latrine use will be influenced by the traditions, occupation, and economic status of the inhabitants of the endemic areas; farmers, for example, may be accustomed to defecating in the fields while at work. The construction of latrines and toilets is nevertheless rapidly increasing in the endemic areas. Promotion of latrine use should be part of the health education programme for control of foodborne trematodes. In areas where human excreta and night-soil are used as fertilizer, changes may be required in the use of standard pit latrines.

11.3 Wastewater and excreta usage

Wastewater is not the only form in which animal and human excreta are used in agriculture and aquaculture (26, 27). Night-soil, or stored human excreta, has been used for centuries in Asia as a fertilizer. This locally developed technology, which originated in China, has spread throughout the region, primarily to Cambodia, Indonesia, and Viet Nam, but its use is now progressively decreasing.

Wastewater usage for agriculture will continue to increase and its use in aquaculture is becoming more widespread in developing countries. However, raw or minimally treated wastewater or excreta are used for crop and fish production in many countries, contrary to legislation and against the recommendations of health authorities. If mandated to enforce legislation, ministries of health may lack the necessary resources, personnel, or administrative mechanisms for surveillance and investigation.

The removal of all the pathogens from wastewater is generally expensive, technically complex, and largely unnecessary; improvement of wastewater use practices is preferable. However, the treatment of wastewater in stabilization ponds is an effective and low-cost method of pathogen removal. Fish species (e.g. catfish) that are not susceptible or only minimally susceptible to foodborne trematodes may be grown in aquaculture systems using wastewater.

All foodborne trematodes require one or two aquatic intermediate hosts; thus wastewater and excreta *per se* do not cause transmission of the parasites. The risk of fascioliasis, for example, can be increased by use of

raw wastewater from livestock production facilities, but the intermediate snail host must also be present in the system using the wastewater for transmission to occur. The elimination of snail hosts is an important and neglected aspect of control. The factors that determine survival of trematode eggs in different wastewater systems are not fully understood. The maturation stages of the eggs vary between the different species of foodborne trematodes (see section 9.3). Thus, the type of intervention will vary according to the species of parasite present in a particular area.

A WHO Scientific Group on Health Guidelines for the Use of Wastewater in Agriculture and Aquaculture (28) emphasized that in many developing countries the main risks of wastewater usage were associated with helminth diseases and that the safe use of wastewater would require a high degree of helminth removal. The Scientific Group recommended that only ≤ 1 helminth egg per litre remain in wastewater used for crop irrigation (28). However, the appropriate helminth quality guideline for all aquacultural use of wastewater is the absence of viable trematode eggs. This is unlikely to be achieved in practice, especially in the small subsistence ponds common in Asia; nevertheless the only feasible means of control is to try to remove all viable trematode eggs from the wastewater before it enters the ponds. Furthermore, stabilization ponds must be devoid of the snail intermediate hosts if the risk of infection is to be reduced.

While there is little evidence that fish grown in ponds at the currently recommended coliform concentrations of less than 1000 per 100 ml (28) will accumulate enteric organisms, there is no correlation between this indicator and the level of trematode infections in fish.

Conventional wastewater treatment systems are not generally effective in removing helminth eggs and have little effect on chemical contaminants in wastewater. Rapid sand filtration has been shown to be effective against eggs of *Schistosoma* spp., but its effectiveness at removing other trematode eggs is not known. The general guidelines for treatment of sludge from wastewater treatment specify heating at more than 55 °C; however, the effectiveness of such heating has not been specifically tested against trematode eggs.

12. **Food processing technologies and foodborne trematode infections**

A large range of technologies are currently applied in food processing. Processing conditions under which inhibition of infectivity of foodborne trematode metacercariae has been observed are listed in Table 3. However, there are important gaps in the data available. Further studies are therefore urgently needed on the precise physical and chemical parameters at which various species of metacercariae are affected by food processing methods (Table 4).

Table 3

Processing conditions under which inhibition of infectivity of foodborne trematode metacercariae has been observed

| Process or variable | Parasite | Processing parameters | | References |
|-----------------------------|--|-----------------------|-----------|--------------------|
| Heating | <i>O. viverrini</i> free metacercariae | Temperature | Time | 29 |
| | | 50 °C | 5 hours | |
| | | 70 °C | 30 min | |
| | | 80 °C | 5 min | |
| Acidity ^a | <i>O. viverrini</i> free metacercariae | Concentration | Time | 29 |
| | | 4% | 1 hour | |
| | | 4% | 1.5 hours | |
| | | 4% | 1.5 hours | |
| | | 4% | 1 hour | |
| Salting (NaCl) ^b | <i>O. viverrini</i> free metacercariae | Concentration | Time | 29 |
| | | 0.9% | 10 days | |
| | | 10% | 3.6 hours | |
| | | 20% | 12 hours | |
| | | 30% | 1 hour | |
| | <i>Opisthorchis</i> metacercariae in fish | 13.6% ^c | 24 hours | 30 |
| Irradiation | <i>O. viverrini</i> metacercariae in fish <i>C. sinensis</i> metacercariae in fish <i>P. westermani</i> metacercariae in crabs | Absorbed dose | | 31 32, 33 34 |
| | | 0.1 kGy | - | |
| | | 0.15 kGy | - | |
| | | 0.25 kGy | - | |

Table 3 (continued)
Processing conditions under which inhibition of infectivity of foodborne trematode metacercariae has been observed

| Process or variable | Parasite | Processing parameters | | References |
|---------------------|--|-----------------------|--------------|---|
| Freezing | <i>Clonorchis</i> and <i>Opisthorchis</i> metacercariae in fish <i>F. gigantica</i> <i>F. hepatica</i> <i>O. felineus</i> metacercariae in fish | Temperature | Time | 35 |
| | | - 10°C | 5 days | |
| | | - 20°C | not stated } | 36 |
| | | - 20°C | not stated } | |
| | | - 28°C | 32 hours } | Recommendation of Ministry of Health, USSR, to the fish pro- cessing industry, Moscow 1990 |
| - 35°C | 14 hours } | | | |
| - 40°C | 7 hours } | | | |
| Drying | <i>F. buski</i> | Temperature | Time | 37 |
| | | 27°C | 19 hours | |

^a pH not measured.

^b a_w (water activity) not measured.

^c Percentage salinity in fermented fish.

Table 4

Suggestions for further study on the influence of certain parameters on the survival and/or infectivity of metacercariae^a

| Process ^b | Parameters whose influence needs to be investigated | Parameters to be kept constant during the process | Types of foods that could be studied |
|---------------------------|---|---|--------------------------------------|
| Heating | Temperature-time | None | Fish, crustacea, snails, vegetables |
| Acidification | pH, exposure time, nature and concentration of agent | Temperature, water activity | Fish, crustacea, snails, vegetables |
| Salting | Water activity, exposure time, nature and concentration of agent | Temperature, pH | Fish, crustacea |
| Drying (dry-storage) | Water activity, dry-storage time | Temperature | Fish, vegetables |
| Freezing (frozen-storage) | Temperature, freeze-storage time | None | Fish, crustacea, snails, vegetables |
| Smoking | Temperature, exposure time, nature and concentration of smoking agent | None | Fish |
| Disinfection | Exposure time, nature and concentration of agent | Temperature | Vegetables |
| Irradiation | Absorbed dose | Temperature | Fish, crustacea, snails, vegetables |
| Pressure treatment | Pressure-time | Temperature | Fish, crustacea, snails, vegetables |

^a As it cannot be assumed that metacercariae of different trematodes respond identically to the various parameters, all species would need to be studied.

^b As a first step, each process should be investigated alone. Depending on the effects of each process on the survival and/or infectivity of metacercariae, the influence of a combination of two or more processes could be investigated. For example, the combined effect of salting and acidification could be studied; the parameters to be considered in this case would be pH, water activity, concentration and nature of additives (salt and acidifying agents), and time of exposure.

A common method of food processing is heat treatment, i.e. cooking, roasting, grilling, baking, or frying. Heat treatment is considered effective in killing metacercariae in fish if the flesh is heated until it assumes a firm texture and a white or pale colour throughout. However, the Study Group was informed of studies in Thailand (29) which indicated that metacercariae of *Opisthorchis viverrini* needed at least 30 minutes' heating at 70 °C for inactivation; in this context, it should be recalled that bacterial and viral pathogens such as *Vibrio cholerae*, hepatitis A virus, and salmonellae are inactivated when the temperature of food is raised to 70 °C (no additional time requirement) (see Annex 3).

Freezing is another commonly used method of fish processing. Freezing at temperatures of -28 °C for 32 hours has been found to be effective in killing metacercariae of *Opisthorchis felineus*. This and similar methods were recommended by the Ministry of Health of the USSR to the fish processing industry in 1990 (see Table 3).

Canning, according to the appropriate Codex standards, ensures a product safe from foodborne trematodes, but this method is not always feasible, particularly in developing countries which include many of the areas where foodborne trematodes are endemic.

Methods of food processing such as salting, drying, smoking, fermenting, and marinading, or combinations of these methods, e.g. salt-drying, are used extensively worldwide, particularly in developing countries. However, in many areas where foodborne trematodes are endemic, particularly in south-east Asia, these traditional processing methods cannot always be relied upon to eliminate foodborne trematodes.

Irradiation of fish and shellfish has recently proved to be a very effective method of eliminating metacercariae, and other parasites and pathogenic microorganisms (32, 33, 38). Low-dose irradiation (0.10–0.25 kGy) is sufficient to inactivate metacercariae of *Clonorchis sinensis*, *Opisthorchis viverrini*, and *Paragonimus westermani* in fish and crabs without affecting the flavour, taste, and texture of the food, which can then be safely eaten raw (39). This method is suitable for application to fish that is handled in bulk. Standards for ensuring the safety and efficacy of food irradiation facilities have been issued (40).

The susceptibility of metacercariae to microwave cooking needs further investigation. Rather than the application of heat, the process of cooking using microwaves involves the production of heat through the excitation of water molecules within the food. Any guidelines developed for microwave cooking as a means of killing metacercariae must consider the variables inherent in microwave ovens, including the wattage of the individual oven, the presence of “hot” and “cold” spots within the oven during cooking, and the use of a turntable.

International codes of practice for various techniques of fish processing have been recommended by the Codex Alimentarius Commission (see list in Annex 4). However, they have been developed on the basis of

experience in Europe and North America and do not take into consideration foodborne trematode infections in fish and shellfish. There is an urgent need to develop similar codes for application in the tropics and subtropics.

13. **Diagnostic techniques**

The confirmed diagnosis of a particular foodborne trematode infection rests on the demonstration of parasite eggs, or less frequently of the adult parasite or one of its earlier stages, in humans. Parasitological examination using a microscope to observe the eggs of foodborne trematodes is the only reliable technique to demonstrate active infection (see reference 41). Occasionally the adult parasite is expelled by coughing (*Paragonimus* spp.), detected during surgery of the biliary tract (*Fasciola* spp.), or expelled in the faeces (all others).

Laboratory staff adequately trained in parasitology are essential for public health programmes and clinical services. National quality control programmes have been established in certain countries (for example in France, Japan, the Republic of Korea, and the USA) over the past 20 years and have raised the level of accuracy and reliability of the results of parasitological diagnosis. It has been noted that the lowest rates of correct identification of parasite eggs and the highest rates of “missed” diagnosis have occurred with the large operculate eggs of *Echinostoma* spp. *Fasciola* spp., and *Paragonimus* spp. There is often confusion between abnormal *Clonorchis sinensis* eggs (without typical shouldering) and mature eggs of *Metagonimus* spp. Differentiation between the eggs of *Opisthorchis* spp. and other minute intestinal trematode eggs is problematic.

Immunodiagnostic tests, such as the complement-fixation and precipitin tests and enzyme-linked immunosorbent assay (ELISA), are useful in the diagnosis of extraintestinal and tissue-dwelling trematode infections. Newer methods such as DNA detection and the polymerase chain reaction are being evaluated for diagnosis of several of the trematode infections.

13.1 **Diagnosis for public health programmes**

The sensitivity of parasitological techniques used for large-scale mass surveys is adequate for the identification of infected people for treatment programmes and epidemiological studies. Stool surveys can be made using standard faecal examination techniques such as the sedimentation or the modified cellophane faecal thick-smear technique (Kato-Katz technique); these are simple and reproducible methods for the detection of foodborne trematode eggs. The Kato technique also permits storage of slides for later re-examination for quality control.

In large-scale programmes for the control of paragonimiasis, intradermal screening has been successful. When an antigen derived from the adult worm is used, the sensitivity is almost 100% and the specificity is estimated to be 97%. The intradermal reactivity persists for up to 20 years after treatment.

In areas where *C. sinensis* is under control and now has a low prevalence, the population's willingness to submit stool specimens is decreasing. In the Republic of Korea, screening is done by serological examination using a crude *C. sinensis* antigen in an ELISA. Stool examinations are then performed only in seroreactive people and treatment is given only to those who are egg-positive.

13.2 **Diagnosis for patients**

All diagnostic tests (stool and serological) used in public health programmes are also employed in clinical diagnosis. In hospitals, immunodiagnostic tests are in frequent use. Non-invasive imaging techniques such as ultrasonography and computerized tomography are used by clinical services, but their sensitivity and specificity have not been tested. Methods for detecting excretory-secretory antigens of foodborne trematodes in blood, urine, faeces, and other body fluids by counterimmunoelectrophoresis, ELISA, and DNA techniques have been reported.

A possible method for early immunodiagnosis of fascioliasis using specific antigen E2 in a passive haemagglutination test has been demonstrated in animals and could be applied to human disease. Other immunoreactive materials should be sought, for example by analysis of trematode ecdysteroids.

13.3 **Diagnostic techniques for food inspection**

The Study Group noted that fish inspection services have not so far used specific techniques to detect foodborne trematodes, although several different techniques are available for inspecting fish, crabs, and crayfish for the presence of these parasites (Annex 6). The selection of a particular technique is determined by the available resources, the type of product to be analysed, the organism suspected to be present, the training and experience of the inspector, and the degree of certainty required by the inspection (e.g. presence of parasite versus intensity of infection).

14. **Chemotherapy**

Community-based treatment is an essential part of the strategy for control of foodborne trematode infections. Praziquantel is effective against all human foodborne trematode infections except fascioliasis.

Although current treatment of fascioliasis is not satisfactory, encouraging results have been obtained in Phase IIB dose-finding clinical trials of triclabendazole against *F. hepatica*, coordinated by WHO and the manufacturer. This drug is also effective against paragonimiasis. A wide range of veterinary drugs are available for the control of foodborne trematode infections in animals.

14.1 Current drugs

14.1.1 Praziquantel¹

Praziquantel, which is structurally unrelated to other anthelmintics, is highly active against most foodborne trematodes, although its mode of action in the adult worm is not known. It is rapidly absorbed by the patient when taken orally; it undergoes first-pass metabolism, and 80% of the dose is excreted as metabolites in the urine within 24 hours. Trematode worms, in contrast, absorb but do not metabolize praziquantel. After exposure, there is an instantaneous tetanic contraction of the parasite musculature and a rapid vacuolization of the syncytial tegument; the worms then gradually disintegrate. A 10-fold higher concentration of praziquantel is required to paralyse *Clonorchis sinensis* completely than to paralyse *Schistosoma mansoni*.

Surface alterations occur very rapidly after *in vitro* exposure to praziquantel and reach a maximum after 5 minutes in *Clonorchis sinensis*, *Opisthorchis viverrini* and *Metagonimus yokogawai*. The effect on *Paragonimus westermani*, which has an exceptionally thick and condensed tegumental structure, is less noticeable. There are no surface alterations in *Fasciola hepatica*, whose tegument has an even higher content of fortifying fibrils. Vacuolization is most pronounced on the ventral surface in the region of the suckers of *O. viverrini* and *C. sinensis*.

Clinical information

Praziquantel is highly effective in the treatment of intestinal, liver, and lung fluke infections, in particular those caused by *C. sinensis*, *Fasciolopsis buski*, *Heterophyes heterophyes*, *M. yokogawai*, *O. felineus*, *O. viverrini*, and *Paragonimus* spp. No treatment failures due to drug resistance of the parasites have been reported.

Praziquantel is suitable for the treatment of adults and children over four years of age. A single dose of 25 mg/kg is recommended for intestinal fluke infections due to *F. buski*, *Heterophyes* spp., *M. yokogawai*, and all others listed in Annex 2. A single dose of 40 mg/kg is effective against liver fluke infections due to *C. sinensis*, *O. felineus*, and *O. viverrini*. In outpatient clinics and hospitals it is accepted practice to use a dose of 25 mg/kg three times a day for up to two consecutive days: this produces

¹ Much of the information presented in this section is taken from reference 42.

cure rates of virtually 100% in the majority of liver and lung fluke infections. In the case of ectopic paragonimiasis higher doses are required.

Contraindications and precautions

Patients with ectopic paragonimiasis should always be treated in hospital, especially if there is involvement of the central nervous system. When a population group is treated for pulmonary infection, mass treatment under the supervision of a physician is common in endemic areas. If praziquantel is used in areas endemic for cysticercosis, there is a possibility that its parasitocidal effect on cysts in the central nervous system may provoke a brisk, localized oedematous reaction.

Praziquantel is not recommended for use in pregnancy although it has not been shown to be mutagenic, teratogenic, or embryotoxic. It is preferable to defer treatment until after delivery unless immediate intervention is considered essential. Restriction of physical and occupation-related activity is recommended for at least two hours after medication.

Praziquantel is exceptionally well tolerated. However, it occasionally causes abdominal discomfort, nausea, headache, and dizziness, and rarely, pyrexia and urticaria. Drowsiness and tachycardia have also been reported. Praziquantel tablets should be kept in well closed containers, protected from light.

14.1.2 **Other drugs**

The currently recommended treatment for human fascioliasis is bithionol, in dosages of 30 mg/kg of body weight per day for five days. However, it is anticipated that triclabendazole, a benzimidazole anthelmintic active against *Fasciola hepatica* and *F. gigantica*, will become the treatment of choice. It is given in a dose of 5 mg/kg of body weight twice postprandially on the same day with a 6–8 hour interval between doses (total dose 10 mg/kg). Triclabendazole is effective not only against the adult parasites present in the bile ducts, but also against the immature flukes which migrate through the liver parenchyma. In domestic animals, a dose of 5 mg/kg of body weight kills almost 100% of adult flukes and around 85% of the immature stages. A dose of 10–12 mg/kg is nearly 100% effective against even the immature parasites. Triclabendazole has also been shown to have activity against *Paragonimus* spp. Its mode of action has not yet been elucidated.

Triclabendazole has a low toxicity in experimental animals; it is not mutagenic and, in contrast to many benzimidazole-2-carbamates, it is not teratogenic. It has not yet been registered by national drug regulatory agencies for human use in any country except in the Islamic Republic of Iran, where it was granted exceptional emergency approval.

During the fascioliasis epidemic in the Islamic Republic of Iran in 1989, when a wide range of treatments and treatment schedules were

monitored, albendazole, levamisole, mebendazole, and praziquantel were all shown to be ineffective against *Fasciola* spp. Dehydroemetine was shown to be partially effective when given under strict medical supervision.

14.2 Re-treatment schedules

The use of chemotherapy in the control of foodborne trematode infections should be based on sound epidemiological data about the target population. It may be feasible to examine a high-risk group, such as school-age children, as an indicator of the prevalence in an entire population. This approach must be based on adequate epidemiological studies. Community-based treatment without epidemiological data for monitoring its effect is not recommended. In most control programmes, annual treatment is provided for the target population for up to three years. After this initial phase, reduced prevalence can be maintained by treatment through local health services.

Several approaches to community-based treatment can be used. They include:

- Mass treatment: treatment of entire populations without regard to individual infection status.
- Selective population treatment: treatment of infected people identified by a diagnostic survey of the whole population.
- Selective group treatment: treatment of all members or of infected members of a high-risk age or occupational group.
- Phased treatment: use of the above strategies in a sequence of progressively greater selectivity.

Epidemiological data indicating a high prevalence of infection at the beginning of a control programme may justify the treatment of entire populations without further individual diagnosis. If the response is satisfactory, according to predefined goals for coverage of the population and reduction of infection levels, selective approaches are then recommended. Unnecessary treatment is unacceptable; after mass treatment, various minor, transitory side-effects are likely to be seen in the treated population.

Longitudinal studies on the re-treatment of opisthorchiasis have now been completed in endemic areas in the Lao People's Democratic Republic and Thailand. In Thailand, 90% of the people treated (all of whom had initial egg counts of less than 10 000 eggs per gram of faeces), remained egg-negative two years after a single treatment. Among the 10% who remained egg-positive, the new infections were light and no unusual clinical symptoms were noted. In general, re-treatment for opisthorchiasis should be carried out at yearly intervals for up to three years, after which the need for it should be determined by epidemiological surveillance.

14.3 Effects of chemotherapy

Chemotherapy reduces the prevalence and intensity of infection in the target population as measured by faecal egg counts. Moreover, treatment reduces morbidity, although the effects are greater in the initial stages of disease than when the disease process is advanced. After chemotherapy, reinfection occurs repeatedly in endemic areas, but faecal egg counts in reinfected individuals are much lower than before treatment.

In Thailand, ultrasound examinations showed increased gall-bladder emptying and decreased gall-bladder size after treatment of opisthorchiasis. In the Republic of Korea, post-treatment ultrasound findings in *C. sinensis* infection were similar, and also included a reduction in the diameter of the biliary tract.

14.4 Resistance to treatment

There have as yet been no confirmed reports of parasite resistance to a therapeutic dose of praziquantel. However, in one instance, refugees from the Lao People's Democratic Republic with paragonimiasis showed resistance to bithionol and had to be re-treated with praziquantel.

14.5 Treatment of acute foodborne trematode infections

Clinical management and supportive therapy are required for patients with acute trematode infections during the initial phase of migration of the parasite to the liver or lungs. The severe morbidity is due to tissue damage by the parasite. Hospitalization may be necessary to manage severe clinical manifestations.

14.6 Concurrent infections and drug combinations

In most endemic countries, foodborne trematode infections may coexist with intestinal and other parasitic infections. When a patient has concurrent infections, parasites that may be stimulated to migrate should be treated first, followed by the foodborne trematodes. *Ascaris* spp., for example, are known to migrate when exposed to an ineffective drug.

Praziquantel has a wide spectrum of activity against foodborne trematodes and attempts are being made to expand its range by combination with other drugs. Drug combinations require further study before being considered for large-scale use.