Little *in vitro* screening of potential chemotherapeutic drugs has been carried out. Clunies-Ross [b] in 1917 undertook one of the earliest of such studies, using survival time of protoscolices in the presence of drug as the criterion of activity. This test was time-consuming and difficult to interpret. An *in vitro* manometric technique for drug-screening was more recently introduced by Schwabe et al.,[c] in which the inhibition of respiration of protoscolices by drugs was used as an index of drug activity. The advantage of this test was that drug effects were detectable within 5 minutes of the contact between the drug and protoscolices being established in the reaction chamber. *In vitro* activity was demonstrated in this manner for gentian violet, tartar emetic, emetine and acriflavine. Stibophen, diethylcarbamazine, tetracycline and oxytetracycline were inactive. One disadvantage of the manometric method for routine *in vitro* drug-screening was the partial insolubility of a number of potentially useful drugs under the pH and buffer conditions of the test. Sakamoto et al.,[d] using a refinement of the approach of Clunies-Ross, have observed the *in vitro* effects of a number of drugs upon protoscolex viability. Promising results have been obtained with gentian violet, niclosamide, bithionol and dichlorophen.

Until recently the only experimental animals available for *in vivo* drug-screening were sheep and other expensive domestic animal hosts of the parasite. The cost of drug-screening in these animals was prohibitive. Alternative drug-screening models were available in *Taenia crassiceps*, *Taenia taeniaeformis* and other cystic taeniid infections in rodents,[e] but dissimilarities between these parasites and *Echinococcus* lessened their value for that purpose. With the finding that both *E. multilocularis* [f, g, h] and *E. granulosus* [i] can be serially passaged in rodents, a useful experimental model has been created which is favourable to the *in vivo* screening of drugs against both of these parasites.

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[c] Schwabe, C. W., Hadidian, K. & Koussa, M. (1963) *Amer. J. trop. Med. Hyg.*, **12**, 338-345.

[d] Sakamoto, T., Yamashita, J., Ohbayashi, M. & Orihara, M. (1965) *Jap. J. vet. Res.*, **13**, 127-136.

[e] Hinz, E. (1964) *Z. Tropenmed. Parasit.*, **15**, 332.

[f] Lubinsky, G. (1960) *Canad. J. Zool.*, **38**, 149-151.

[g] Lubinsky, G. (1960) *Canad. J. Zool.*, **38**, 1115-1125.

[h] Norman, L. & Kagan, I. G. (1961) *J. Parasit.*, **47**, 870-874.

[i] Schwabe, C. W., Luttermoser, G. W., Koussa, M. & Ali, S. R. (1964) *J. Parasit.*, **50**, 260.

Epidemiology of Echinococcosis

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Echinococcosis or hydatid disease is a cyclozoonotic infection of world-wide importance, caused by the closely related cestode parasites, *Echinococcus granulosus* and *E. multilocularis*. The adaptability of these parasites to an unusually wide variety of host species has made possible the broad geographical distribution of the infection from north of the Arctic Circle to as far south as Tierra del Fuego and Stewart Island of New Zealand. Today hydatid disease is a medical and, to a lesser extent, an economic problem on all of the inhabited continents.

Epidemiological studies of hydatid disease usually have as their object the elucidation of facts about the disease which are essential to its control in a particular country or region. A multiplicity of host factors, environmental factors and agent factors account for differences in the observable patterns of distribution of the hydatid parasite and its transmission in different areas. As is the case with other infections, knowledge of these factors is necessary in order to identify vulnerable points for practical attacks on the infection and to provide the baseline data essential to an evaluation of the control effort as it proceeds.

Host factors

Prevalence of infection in man. In considering the local necessity for hydatid disease control, it is essential to determine, first of all, whether or not a public health problem exists. Compared with some other infections, the prevalence of symptomatic hydatid infection in man is not very high in most parts of the world. In fact, present evidence would suggest that man is relatively resistant to infection. However, it is not its prevalence alone that makes hydatid disease a public health problem anywhere, but its prevalence in relation to the prognosis. The present absence of chemotherapy and the seriousness and expense of surgical treatment heighten the importance of echinococcosis as a disease.

Statistics even approximating the true prevalence of hydatid infection in man are not available for any country. Statistics published by governments are usually based upon the incidence of surgical cases only, and frequently only those for government hospitals. Second or subsequent operations are often included with new cases. In addition, not all cases originate within the country reporting. Some of the 5–10 deaths per year from hydatid disease in the USA, for example, represent infections acquired elsewhere, usually in the Mediterranean countries.

Such qualifications aside, incidence rates for surgical cases are of considerable value on a comparative basis in the evaluation of control efforts, if they have been properly compiled. That is, new surgical cases must be differentiated from second operations, all hospitals which perform major surgery must be included, and the proper data must be collected. Information must include, for each patient, name, age, sex, occupation, a detailed residence history, an operative history and, in some areas, religion or ethnic group, and history of dog ownership or other close contact with dogs. Where control measures are intended, echinococcosis should be made a reportable disease.

Comparisons of name and residence may disclose familial outbreaks. In Tasmania, for example, it was found that 4 members of one family of 6 persons had been operated on for the disease. The father had had lung cysts removed in 1959 and 1961; in 1963 the mother was operated on for a subcutaneous cyst and the 10-year-old son for a cyst of the liver. Finally in 1965, the 22-year-old daughter had had two liver cysts removed. This unfortunate family owned 3 dogs, one of which was kept as a pet in the house.

Although it is a commonly held belief that human hydatid infection is usually acquired in childhood, there is as yet no direct evidence that this is so. Some indirect support for this contention is found, however, in the fact that approximately 64% of operations for hydatid cysts of the brain are on children 15 years of age or less. The incubation period for hydatid disease of the brain is, presumably, of relatively short duration. It is likely, too, that the habits of children are such as to expose them more readily to the risk of infection. In addition, it is known that mice below the age of sexual maturity are appreciably more susceptible to intraperitoneal hydatid infection than are mature mice.

Because of this generally variable and often prolonged asymptomatic period in *Echinococcus* infections, " age at operation " statistics are of limited value. Attention to the younger age-groups, however, suggests more clearly than any other measurable rate the risk of infection in a population in the comparatively recent past. For example, the following age-specific surgical incidence rates (per 100 000 population) from New Zealand indicate a progressive decrease in human infections there:

Period	*Under 10 years old*	*10-19 years old*
1946-49	3.6	4.8
1958-61	2.0	3.0
1961-63*	1.0	2.1

* Provisional figures.

Occupational associations may be of particular importance in planning control efforts. An unexpectedly high level of infection in shoemakers in Lebanon, for example, led to a disclosure of the formerly common practice of bateing hides in a mixture of dog faeces and water, a method of preparing leather which was once in use in many parts of the world, and has not disappeared altogether even today.

Residential history is of considerable value except in instances of extremely mobile populations (i.e., because of the variable but often prolonged incubation period in the disease). Even so it may be used to determine autochthonous infections. In some situations it is possible to correlate geographical areas of high risk in man with areas of similarly high infection rates in dogs and possibly also with significant factors in the environment.

Awareness of particular religious or ethnic group associations with infection, where they exist, may lead to useful approaches to control. In New Zealand, for example, a higher rate of infection among Maoris than " Europeans " is associated with the generally less satisfactory conditions for maintaining and feeding sheep-dogs in most Maori areas and less satisfactory standards of general sanitation. On the other hand, a significantly higher rate of infection in Lebanese Christians as compared with Lebanese Moslems is probably related directly to Moslem beliefs about the uncleanliness of the dog, beliefs that could be expected to aid in control efforts. Thus cultural practices of different segments of a population may be of considerable significance.

History of dog ownership or other close contact with dogs is particularly useful for educational purposes. A study of former hydatid disease patients in Beirut has shown, for example, that persons in that city who own or have owned dogs are at 21 times greater risk of acquiring hydatid disease than are non-dog-owners.

While mass miniature chest radiography is a potentially useful tool for disclosing cases additional to those revealed by hospital records, its value is limited by the fact that only approximately one-third of hydatid cysts in man occur in the lungs. Even so, extrapolations of prevalence figures can be obtained in this way. Mass radiological examination of a large segment of the population of one department of Uruguay, for example, suggests a total infection rate there of about 125 per 100 000.

The skin test of Casoni is at present of limited value for epidemiological surveys. Although its sensitivity may be as high as 90%, the crude antigens commonly employed and variations in the technique yield many false positive results. However, recent work suggests that these difficulties may be overcome, at least in part, by the use of partially purified antigens and by rigid attention to technique and to the recording and interpretation of test results. The indirect haemagglutination test is approximately as sensitive as the skin test (except for cysts of the lungs) and, in man, it is more specific. However, no epidemiological use has yet been made of the blood-drop modification of this test, nor have dried filter-paper methods or other newer sero-epidemiological techniques been evaluated in hydatid disease field studies.

Species of hosts involved. If control is justified by the extent of human infection, it is next essential to know for any given area what hosts other than man are found infected in nature and, for each, whether they represent incidental infections only, and are therefore of little epidemiological significance, or whether they represent the active reservoirs of infection upon which the parasite locally depends for its survival. Unilocular echinococcosis, as it exists in many parts of the world, involves principally a dog–sheep cycle. Other domestic species, such as cattle, swine and horses, can also serve as intermediate hosts and may or may not play an important role in maintaining the cycle depending upon local circumstances of livestock husbandry and animal slaughter. The local significance of infections in populations of wild ungulates, such as in Canada, Alaska, Siberia and parts of Africa, depends upon the densities of these populations, the prevalence of infection among them, the extent of intercourse between domestic animal and wild animal populations and the alternative domestic animal pathways available for perpetuation of the cycle.

In addition to a variety of possible intermediate hosts, other carnivores than the domestic dog are known to harbour the adult stage of the parasite in some areas of the world. Thus, in parts of Australia a dingo–wallaby cycle occurs; in Africa the hyena, jackal and Cape hunting dog (*Lycaon pictus*) all serve as definitive hosts; and in much of the northern hemisphere the alveolar form of the disease is maintained chiefly by foxes and microtine rodents.

One important step in contemplating control, therefore, is a local faunal survey involving representative sampling of each possible host species.

Prevalence of infection in the dog. For most parts of the world the prevalence of echinococcal infection in dogs is the most readily obtainable index of the extent of infection in a local area and of the relative degree of risk of infection to man. Such prevalence rates may be obtained either by examining all available dogs or by taking samples of dogs for examination. Preferably, both procedures should be carried out, but for quite different reasons. It should be mentioned that, because of the identical morpho' logy of most taeniid ova, the finding of ova in dogs-stools is of no value in determining the prevalence of echinococcosis.

Representative samples of dogs from cities, towns and farms within a control area should be available for autopsy examination. This is the only certain way to make a diagnosis. The dogs should, if possible, be held for several days on a low-residue diet and starved for 24 hours before examination. Adult, and particularly immature, *Echinococcus* are difficult to detect; therefore, this examination must be undertaken by a competent individual.

If serious control efforts are contemplated, a complete survey of all dogs will also be required. This will be dependent upon effective dog registration. The only diagnostic procedure available at present for use on a living dog is the administration of arecoline hydrobromide, restraint of the dog until it purges, and careful examination of the complete purged specimen for mature and immature *Echinococcus*. Bones and bulky foods should be withheld from the dog for several days before this examination is carried out. Because some dogs will not purge, a repeat examination may be necessary. Even so, the relative inefficiency of arecoline in removing *Echinococcus* is such that many infections, particularly light ones, will be overlooked. An estimate of the efficiency of detection should usually be possible by comparison of the arecoline rates for local populations of dogs with the autopsy rates obtained from properly selected samples of these same populations. Because of this uncertainty, arecoline-testing should be viewed as a " premises screening procedure ", that is, an indicator of premises (farms, homesteads, etc.) on which conditions for infection of dogs exist. A continuous recording of infected premises by repeated arecoline-testing of all dogs enables control authorities to pin-point problem areas and, ultimately, problem dog-owners.

Prevalence of cystic infections in domestic animals. Measurement of the prevalence of cystic infections in older market sheep (or, occasionally, in cattle or swine) is the most reliable indicator of the extent of environmental contamination with *Echinococcus* eggs in a given geographical area. Infections in old animals, however, give little indication of recent conditions. In addition, at least two difficulties arise in the proper collection of such statistics. The first concerns diagnosis. The proper examination of sheep requires a thorough post-mortem inspection of at least the livers and lungs. This cannot be done as part of routine meat inspection because of the thoroughness of examination which is required to detect all cysts and because of the difficulties in differentiating young liver cysts of *E. granulosus* from those of *Taenia hydatigena.* A second difficulty is related to the marketing and slaughtering routines themselves. The killing-lines in large slaughtering establishments move so rapidly that, even with several examiners present, only every fifth or tenth animal can be selected for proper inspection. It is necessary, too, that the livers and lungs examined be related to the carcasses from which they came and the carcasses identified as to their sources. In some establishments this is difficult or even impossible under the routines followed. In many countries, too, market lambs and sheep pass through several hands between the farm and the slaughterhouse and it is nearly impossible to trace infected animals back to their sources.

For these reasons, available statistics on livestock infection rates for different countries may be of greater or lesser usefulness depending upon the thoroughness and the reliability of the procedures by which they were obtained. For example, in Lebanon most of the sheep slaughtered in the larger abattoirs have been imported alive from a number of neighbouring countries. The sources of any one group of animals usually cannot be determined on the killing floor. Even though infection statistics have been carefully determined for such animals in Lebanon on several occasions and recorded in the literature, they give no indication of the extent of exposure within the country itself. In Lebanon, swine are the only slaughter animals produced solely within the country and therefore the only possible indicator of the local extent of livestock infection.

Environmental factors

Factors such as topography, climate, soils, vegetation, systems of agriculture and animal husbandry and the like may influence both the host and the *Echinococcus* parasite in epidemiologically significant ways. For example, topography may determine the degree of isolation of infected and non-infected premises, hence the practicability of local quarantines. Climate and soils will influence not only the system of agriculture and husbandry followed but the ability of *Echinococcus* eggs to survive during their free-living existence. The type and extent of vegetation will determine the importance of animal husbandry as an industry, the types of animals maintained, the livestock-carrying capacity of the land and, hence, the relative concentrations of animals, the closeness of contact of grazing animals with contaminated soil and the extent to which soil is contaminated by working-dogs.

Very little is known about the survival and availability of *E. granulosus* ova under different environmental conditions. Recent work has shown that eggs of the related parasite, *Taenia ovis*, are resistant to 30 hours' exposure to ultraviolet radiation if they are maintained in a moist state. The resistance to dryness of the eggs of different species of taeniid tapeworms varies considerably. Those of *T. hydatigena*, for example, survive 0% humidity for 7 days while those of *T. pisiformis* are killed in 15 minutes. Present evidence suggests that the resistance to drying of *E. granulosus* eggs resembles that of *T. pisiformis* more than that of *T. hydatigena*, that is, they are quite susceptible to drying. Within the range of non-lethal temperatures, longevity will almost certainly always be greater at lower temperatures, at least in the temperature range above freezing. Even in the low-temperature range, however, eggs of *E. multilocularis* have survived 54 days at −26°C.

One field study has shown that, at the end of the 4-month winter period in a quasi-continental climatic region of New Zealand, some eggs of *E. granulosus* seeded on a pasture were still available and infective to grazing sheep. These eggs were on a pasture composed of 10%–20% bare ground and were exposed to conditions of dryness (3 inches (76 mm) of rain) and repeated freezing and thawing. After the following hot, dry summer, however, although recovered eggs were still infective when fed to sheep, they no longer were available to grazing animals on the experimental pasture. It is likely that high winds typical of this region carried off many of the eggs under these field conditions.

In another region of oceanic climate in New Zealand, a 27-inch (686 mm) rainfall on a dense pasture sward spread over 4 months was not enough to prevent infection of grazing sheep, but 120 inches (3048 mm) of rain over a period of a year carried the eggs sufficiently far into the soil with the gravitational water that they were not available to grazing animals. These results suggested that in excessively wet areas with rapid grass growth rotational grazing as an auxiliary tool in the control of *E. granulosus* would be impracticable. In dry areas, however, where grass growth is only a few inches a year and the carrying capacity is low, rotational grazing periods of about a year might be of some use. These observations in New Zealand suggest a fairly broad zone of tolerance for *E. granulosus* eggs, but they give little indication of the factors which cause the eggs to die.

In any control effort it would be worth while to seed fenced, uncontaminated pasture plots with known densities of viable *E. granulosus* eggs and to determine the periods of their survival and availability to grazing sheep under the range of local climatic conditions.

While it is at present impossible to differentiate morphologically between the eggs of *Echinococcus* and other taeniid tapeworms, studies on the extent of natural faecal contamination of soil and vegetables by taeniid ova are nevertheless valuable. Educational use can be made of such statistics in that they indicate the degree of faecal contamination by dogs (or by man in areas in which *T. solium* or *T. saginata* also occur). In some sections of Beirut, Lebanon, for example, systematic examinations of street dirt have revealed taeniid ova in up to 36% of samples. Up to 34% of the samples of salad greens bought at local markets were similarly contaminated.

Agent factors

In addition to determining the host range for *Echinococcus* in any given control region, it is necessary to determine, too, whether or not strain differences exist in the parasite itself which limit its infectivity to certain species of hosts. It is now known that *E. multilocularis*, the parasite responsible for alveolar hydatid disease, can be distinguished morphologically from *E. granulosus* in the adult stage, as well as in the larval stage. Its definitive hosts are the fox and dog and its normal intermediate hosts are various species of microtine rodents. Somewhat less clear than this is the existence of strains (or subspecies) within the species responsible for unilocular infections. The most clear-cut example concerns *E. granulosus* of horses in the United Kingdom and possibly elsewhere. This parasite matures in foxes as well as in dogs and infects sheep with some difficulty. On the other hand, *E. granulosus* from sheep will not mature in foxes and, at least in New Zealand, will not infect horses. Similar differences in infectivity to hosts may possibly be evidenced by the strain of *E. granulosus* responsible for the wolf–moose cycle in North America or for mature infections in the hyena, jackal, and Cape hunting dog (*Lycaon pictus*) in Africa. Differences between parasite strains may also occur in South America and Asia. In consequence, in areas where silvatic cycles exist, some or all species of domestic animals may be resistant to infection and the susceptibility of man may also vary to different strains of the parasite. Such information, of vital importance to the proper direction of control efforts, can be obtained only by experimental cross-infections carried out with material from different local host species and subsequent morphological studies of any parasite variants which are disclosed.

Transliteration from Cyrillic characters

The "International System for the Transliteration of Cyrillic Characters", set out in Recommendation ISO/R9-1954 (E) of the International Organization for Standardization, is normally used in the *Bulletin of the World Health Organization* for personal names, titles of publications, etc. However, papers accepted for publication may contain names transliterated differently, and if the original Cyrillic spelling is not recognizable inconsistencies may occur.

For convenience the transliteration from Russian according to ISO/R9 is given below:

Translittération des Caractères cyrilliques

Le « Système international pour la translittération des caractères cyrilliques » présenté dans la Recommandation ISO/R9-1954 (F) de l'Organisation internationale de Normalisation est généralement utilisé dans le *Bulletin de l'Organisation mondiale de la Santé* pour les noms de personnes, les titres de publications, etc. Cependant des articles acceptés pour publication peuvent contenir des noms translittérés différemment et si l'orthographe cyrillique originale n'est pas reconnaissable un manque d'uniformité peut s'ensuivre.

A toutes fins utiles, la translittération du russe selon la recommandation ISO/R9 est indiquée ci-après:

Cyrillic character / Caractère cyrillique	Transliteration from Russian / Translittération du russe	Examples and remarks / Exemples et observations
А, а	a	Адрес = Adres
Б, б	b	Баба = Baba
В, в	v	Вы = Vy
Г, г	g	Глава = Glava Голова = Golova
Д, д	d	Да = Da
Е, е (ё) [1]	e (ë)	Ещё = Eščë
Ж, ж	ž	Журнал = Žurnal
З, з	z	Звезда = Zvezda
И, и	i	Или = Ili
Й, й	j	-ый, -ий, -ой = -yj, -ij, -oj
К, к	k	Как = Kak
Л, л	l	Любить = Ljubit'
М, м	m	Муж = Muž
Н, н	n	Нижний = Nižnij
О, о	o	Общество = Obščestvo
П, п	p	Первый = Pervyj
Р, р	r	Рыба = Ryba
С, с	s	Сестра = Sestra
Т, т	t	Товарищ = Tovarišč

Cyrillic character / Caractère cyrillique	Transliteration from Russian / Translittération du russe	Examples and remarks / Exemples et observations
У, у	u	Утро = Utro
Ф, ф	f	Физика = Fizika
Х, х	h	Химический = Himičeskij
Ц, ц	c	Центральный = Central'nyj
Ч, ч	č	Часы = Časy
Ш, ш	š	Школа = Škola
Щ, щ	šč	Щека = Ščeka
(medial, médial) Ъ, ъ	″or″ ″ou″	In modern Russian, where ′ sometimes replaces medial ъ, transliteration is still ″. En russe moderne, où le ′ remplace quelquefois le ъ médial, la translittération reste ″.
(final)	(Not transliterated. Non translittéré.)	
Ы, ы	y	Был = Byl
Ь, ь	′or′ ′ou′	Маленький = Malen'kij
Э, э	e̊	Это = E̊to
Ю, ю	ju	Южный = Južnyj
Я, я	ja	Яйцо = Jajco

[1] Cyrillic ё to be transliterated by ë only when the diacritical appears in the original. Le ё cyrillique ne doit être translittéré par ë que lorsque la diacritique apparaît dans l'original.