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HYDATID DISEASE:
THE PROBLEM, CURRENT RESEARCH AND PROSPECTS
FOR CONTROL IN LATIN AMERICA

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Hydatid Disease: The Problem, Current Research and Prospects for
Control in Latin America*

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INTRODUCTION

Hydatid disease or echinococcosis is a cycle-zoonotic infection caused by the cystic larval stages of cestode parasites of the genus Echinococcus Rudolphi, 1801. The life cycles of Echinococcus spp. require two mammalian hosts having an essentially obligatory predator-prey relationship. The final definitive host is a carnivore, and the larval form occurs in one or more species of herbivorous animals upon which the final host is dependent.

Of more than a dozen "species" of Echinococcus described in the literature only three can be regarded as valid (Pausch, 1968). These are Echinococcus granulosus (Batsch, 1786), E. oligarthrus (Diesing, 1863) and E. multilocularis (Leuckart, 1863). The distributions of these three species in the Americas and elsewhere has recently been described by Williams, Lopez Adaros et al. (1971). The former two species are found in Latin America while E. multilocularis, the agent of alveolar hydatid disease in humans, is restricted to northern Eurasia and North America occurring in foxes and small rodents. The southernmost extension of this latter species known geographic range in the Americas is Iowa (Leiby, et al., 1970). A fourth specie, E. patagonicus has been reported from Argentina in foxes captured in the pre-Andean cordillera (Szidat, 1960). Because it was

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described only in the strobilar stage from an area where E. granulosus infection is highly prevalent in dogs its status as a distinct species remains unclear.

The life cycle of E. oligarthrus is thus far confined to sylvatic animals involving at least 3 species of wild felids as definitive hosts and the Agouti, the spiny rat and possibly other rodents as intermediate hosts (Sousa, 1970). It appears that this parasite is endemic to the tropical lowland areas of Northern South America as well as parts of Central America. Only recently has this species been implicated in human infection. In Panama it was found responsible for "multilocular" of polycystic hydatids in both animals and man (Thatcher and Sousa, 1966). Since "multilocular" cysts in man are also reported from Colombia and Ecuador (Thatcher, 1970) it is possible that this parasite will assume greater public health importance as further investigation is carried out.

Of the known species of hydatid parasites it is E. granulosus which is by far the most important. This parasite causes classical hydatid disease in man in which the cyst, typically spherical and unilocular, usually localizes in the liver or lungs and much less frequently in other organs or tissues. Although, this parasite evolved and still exists in some regions in sylvatic animals (Rausch, 1967) it became adapted to domestic animals in cycles involving dogs and a wide variety of domesticated ungulates (sheep, cattle, goats, pigs, horses, camelids and others). It is these domestic cycles which permit the present broad geographical distribution of unilocular hydatid disease. The disease presently exists as a public health and economic problem on every continent extending from north of the Arctic Circle to as far south as Tierra del Fuego and Stewart Island of New Zealand (Fig. 1). The areas of highest prevalence, however, are regions where the raising of livestock is a major industry (Schantz and Schwabe, 1969). It is in these regions where the simultaneous

presence of large number of suitable hosts combine with the ignorance or irresponsibility of man to produce conditions in which the cyclic transmission of E. granulosus is possible. Because transmission is maintained by allowing domestic dogs, through man's intention or neglect, to feed upon the viscera of infected livestock, unilocular hydatid disease is essentially a "man made" disease.

Man acquires the disease by ingesting eggs passed in the feces of an infected dog or other carnivore. The public health importance of this disease is heightened by the absence of medical treatment. Surgical extirpation of the cyst, a serious and expensive procedure, is the only present treatment of human hydatidosis.

THE PROBLEM IN LATIN AMERICA

Considering the global distribution of the parasite, Latin America has long been recognized to be one of the areas where infection by E. granulosus reaches its greatest prevalence in both man and lower animals (Gemmell, 1960; Schantz and Schwabe, 1969).

Williams, Trejos, et al. (1971) recently reviewed the current global distribution and prevalence of hydatidosis with special reference to the Americas and pointed out the relative medical and economic significance of the disease between countries.

The infection exists at varying intensity throughout Latin America. Occasional autochthonous cases in man from Mexico are reported and low level infection in sheep, cattle and pigs are known to occur in that country (Mazzotti, 1959). Nevertheless, a complete evaluation of the problem has not yet been performed. A similar situation of sporadic, low level occurrence exists throughout Central America and northern South America. Within the tropical lowland areas of South America, E. granulosus is replaced by E. oligarthrus the importance of which was discussed above.

It is in the southern countries of South America where infection by E. granulosus reaches its greatest significance. In terms of both human and animal prevalence, the greatest problems exist in Argentina, Southern Brazil, Chile, Peru and Uruguay. As was mentioned above the quantitative importance of the disease throughout the world is associated with the presence of large numbers of suitable intermediate hosts. The disease in the Americas is clearly associated with concentrations of the ovine populations. Fig. 2 (Williams, Trejos, et al., 1971) shows the distribution of sheep population densities within the American continent. Approximately 50 percent of the entire ovine population of the continent is concentrated in the South temperate zone, in an area representing 10 percent of the land mass (especially Argentina, southern Brazil, Chile and Uruguay). Within the tropical zone the population density is very much reduced except in the Peruvian Sierra where climatic and geographic conditions permit sheep husbandry on a scale similar to that south of the tropic of capricorn, and hydatidosis in Peru is essentially confined to this zone (Otarola Salcedo, G., 1966).

In Latin America, as elsewhere, prevalence data for infection by E. granulosus in man are far from complete. The disease is not a legally reportable disease in most countries and everywhere there is considerable under-reporting, particularly in rural areas where infection is most frequent. Nevertheless, the annual incidence of surgical cases is the most frequently used parameter of the quantitative importance of the disease and, when properly collected, permits comparisons between geographical regions. Table 1 shows the annual incidence of surgical cases of hydatid disease reported from those countries of Latin America where the disease is most important. Morbidity figures at the national level, however, fail to indicate the true importance of the disease because all populations

are not at equal risk. Even in Uruguay, where the average annual surgical incidence rate of 20 per 100 thousand inhabitants is the highest national figure ever reported, almost half of the population lives in Montevideo where they are exposed to a much reduced infection risk. In some of the interior departments the surgical incidence exceeds 80 per year.

In Argentina, the 1970 census showed that more than 70 percent of the population lives in urban localities. Although the national surgical incidence of hydatidosis is only 2.0 per 100,000, in some southern provinces the figure is greater than 50 per 100,000 and in one predominantly rural population studied in southern Argentina this figure for 1969 was 143 (Schantz, Williams, et al., 1971).

Similarly, the intensive sheep rearing state of Rio Grande do Sul in southern Brazil has an annual surgical incidence of only 0.1 per 100,000 inhabitants (Machado, 1964) though Leal de Moraes (1961) reported that in parts of the southern half of the state the rate was as high as 6.5 per 100,000.

Even in Bolivia for which there is no information available in the published literature, the problem may be severe. A recent limited field study in the altiplano showed a high rate of skin test reactivity to hydatid antigens among abattoir employees and revision of hospital records revealed 75 pulmonary hydatid cyst operations among 1500 thoracic operations performed during the last 10 years (Schantz, unpublished observations, 1970). The real importance of the disease in Bolivia, surrounded by countries of high hydatid endemicity, remains to be determined.

Economic losses due to human hydatidosis are difficult to estimate accurately. Losses arise from the prolonged hospitalization required by most patients (generally about 7 weeks). Since about 70 percent of all hydatid cases are diagnosed in individuals between 20 to 60

years of age (Neghme and Silva, 1970) the reduction in the communities effective labor force is considerable. In Argentina public health authorities estimate current hospitalization costs at \$ 150,000 (U.S.) and Neghme and Silva (1970) give a figure of \$ 300 to \$ 500 thousand (U.S.) per annum for Chile. Neither figure takes into account welfare payments or loss of manhours.

In Uruguay, Purriel et al. (1965) estimated that during 1962 to 1964 the costs of surgical attention to the cases of hydatidosis admitted to five major hospitals amounted to \$ 200,000 (U.S.). Losses to the diseased individual are even greater, however, because they do not cease upon his release from the hospital. A followup survey of 357 surgical cases in Uruguay revealed that approximately 60% were unable to return to work or normal household routine before 4 months following hospital release and 40% were incapacitated 6 months or longer (Purriel and Schantz, 1971).

Directly measurable economic losses to the livestock industry result from the condemnation of infected viscera. These losses as calculated in all the endemic countries are considerable.

RESEARCH IN LATIN AMERICA

Research on hydatidosis in Latin America has not been commensurate with the magnitude of the problem and there is, perhaps, no other place in the world where the need to increase research in this infection is more pressing. With few exceptions experimental research is scarce and not of high quality and it has only been recently that epidemiological studies have begun to quantify the prevalence of the disease in man and lower animals.

The Pan American Zoonoses Center (PAHO/WHO) located in Argentina has developed to become the major center for hydatidosis research in Latin America. At present the

Center's program of research includes studies of the immunology and immunodiagnosis of this infection, its epidemiology, ecology, the chemotherapy of canine infection, and a variety of other aspects of the host-parasite relationship in both the definitive and intermediate hosts. A major goal of the Center's program is to stimulate further research throughout Latin America by providing training in laboratory and epidemiological methods and offering diagnostic assistance and standardized antigens. The Center is presently collaborating with national authorities from several countries in carrying out local epidemiological studies.

In this section a brief review is made of current research on E. granulosus infection in Latin America. Not to be reviewed here, but deserving of special mention are the outstanding studies by Dr. Moisés Agosin on the biochemistry and physiology of the parasite carried out at the University of Chile between 1955 to 1968. This investigation earned him international recognition as a leader in this field (for review of this work see Agosin, 1968, and Kagan and Agosin, 1968).

Although only work carried out in Latin America is reviewed, reference is also made to work carried out elsewhere when necessary to provide a perspective for evaluating the significance of the research under review.

Epidemiological Studies:

Extensive surveys by Purriel and collaborators have demonstrated the importance of the disease throughout rural Uruguay (Purriel et al., 1965; Purriel et al., 1970; Purriel and Schantz, 1971). In this country of less than 3 million inhabitants between 500 and 600 hydatid cases are operated on each year with a case-fatality ratio averaging 6%. The annual surgical incidence for this country, which averages 20 per 100,000 inhabitants, gives Uruguay the dubious honor of being number one in the world. But these surgical

cases are but the "tip of iceberg" because thoracic radiograph surveys carried out since 1948 have detected a prevalence of 375 cysts per 100,000 persons in the intrathoracic localization alone. Autopsy studies of persons dead for causes not related to hydatid disease reveal an even higher prevalence. With the exception of the urban Department of Montevideo, cystic infection in humans and livestock occur at a high level throughout the country. Between 1963 and 1965, of more than 50 thousand slaughtered cattle examined at the "Frigorifico Nacional", 60 percent were infected with cysts and this rate in older sheep approaches 100 percent (Purriel et al., 1965) imposing considerable loss to the agricultural economy due to rejection of the infected viscera. These extremely high prevalence figures distributed uniformly throughout the rural interior of the country suggest a virtual "saturation" of the susceptible population. That hydatidosis is now the number one rural health problem in Uruguay is demonstrated by the figures presented in Table 2. The number of new cases of pulmonary tuberculosis detected by mass chest radiography in the Department of Flores has progressively decreased from a high of 11.2 per 1,000 persons examined in 1949 to 0.7 per 1,000 in 1969. Rates for intrathoracic hydatid cysts in the same study group have actually shown a slight increase from 0.9 per 1,000 to 1.2 per 1,000 (Purriel and Schantz, 1971).

A survey of the national importance of hydatid disease has also been carried out in Chile by Neghme and Silva (1970). Between 1945 and 1967 there occurred from 600 to 800 surgical cases per year with average case-fatality ratio of 6 per cent. Hydatidosis in Chile ranks number 10 in morbidity among transmissible diseases. The economic losses occasioned by this disease in Chile have been mentioned above.

A national survey carried out in Peru (Otarola Salcedo, G., 1966) indicated that the disease is highly endemic throughout the Peruvian Sierra. The poor living conditions

and sanitary standards of the majority of the indigenous population appears to contribute significantly to the high level of transmission in this region.

Studies have recently been initiated in several countries to link socio-economic, cultural and livestock husbandry factors with patterns of transmission. One population in a hyperendemic area of southern Argentina was studied in depth utilizing immunodiagnostic screening to detect asymptomatic or undiagnosed cases of hydatid disease (Schantz, Williams et al., 1971). The study group showed a variety of factors intrinsic to their "way of life" which facilitated the parasites transmission. More than half of the adult males had occupational contact with livestock and 63 percent of the families practiced home slaughter of sheep or goats. Eighty percent of the families owned dogs and 70% of the dog owners admitted to feeding them raw viscera. Less than 5 percent of this population had received schooling past the primary level and their knowledge of hydatid disease was understandably poor. Although most persons recognized hydatid cysts in their animals at slaughter (which they refer to as "water bags") less than 10 percent understood what they were or how they were transmitted. Virtually no one practiced preventive measures and many were actually observed to selectively feed dogs infected viscera while retaining cyst-free viscera for their own consumption. There is little wonder that the annual surgical incidence rate in this area was 143 cases per 100,000 inhabitants in 1969 and that more sensitive case-finding techniques such as mass chest radiography and immunodiagnostic screening suggest prevalence rates approaching 2 percent (Schantz, Williams, et al., 1971). Similar human practices predisposing to hydatid transmission are seen in other endemic areas of Argentina such as southern Mendoza Province (Minoprio et al., 1965).

The practice of feeding dogs the raw viscera of home slaughtered animals is also of major importance in the epidemiology of the infection in Uruguay. Initial diagnostic testing of dogs in a pilot control project in the Department of Flores revealed at least one infected dog in 51 percent of farms in which the residents admitted feeding dogs raw viscera whereas a "farm-infection rate" of only 12 percent was found where the residents denied feeding raw viscera (Purriel and Schantz, 1971). The large canine population, averaging 3 per farm, is another important factor contributing to the spread of the disease.

Although it is apparent from the above review that hydatidosis in Latin America reaches its greatest importance in rural areas, at least in some areas there is considerable urban transmission. Studies by Dr. Félix Nájaira and his colleagues at the Universidad Nacional de San Agustín in Arequipa, Peru, have disclosed an annual surgical incidence of approximately 10 per 100,000 inhabitants counting only cases autochthonous to that city. (Nájaira et al., 1970, and Nájaira, 1971, personal communication). Direct questioning of these individuals revealed that they had never left the immediate surroundings of Arequipa, a city of 350,000 persons located in the southern Sierra. Retrospective followup of these cases has associated the majority of them with the deplorable sanitary conditions existing in the city's ^{few} eleven slaughterhouses /of which have veterinary inspection. It was discovered that dogs enter the slaughterhouse at will and infected viscera are carried from the slaughterhouses for a variety of purposes including sale as dog food. In this way focal canine infection occurs scattered throughout the city. Cases autochthonous to other cities are reported also from many other Latin American cities although the circumstances relating to their transmission have not yet been disclosed.

Studies on Sylvatic Echinococcosis:

The role of wild animals in the perpetuation and dissemination of E. granulosus infection has never been clarified in Latin America although such information is fundamental to the rational design of control programs. Large fox populations exist in most sheep raising areas of South America and high rates of infection have been demonstrated in several different localities in Argentina. Blood and Lelijveld (1969) demonstrated 3.6 percent and 15.5 percent infection rates in the Pampas Gray Fox (Dusicyon gymnocercus) and the Patagonian Gray Fox (D. griseus) respectively. Szidat (1963) reported 12 percent infection in the South American Red Fox (D. culpaeus) captured in the pre-Andean cordillera. Because the parasite isolated from D. culpaeus showed morphological characteristics which differed from E. granulosus the author believed it to be a new species which had previously named E. patagonicus (Szidat, 1960). It has never been determined if the parasite isolated from foxes is infective for sheep.

Cystic infection in sylvatic animals has never been associated with the infection in foxes although extensive surveys in potential intermediate hosts have been performed in Argentina (Blood and Lelijveld, 1966) and in Chile (Alvarez, 1961).

The preliminary results of an investigation recently initiated (April, 1971) in the Argentine pre-Andean cordillera have demonstrated infection in 4 of 16 red foxes (D. culpaeus) (Schantz, Lord, et al., 1971). Search for cystic infection in small mammals preyed upon by this fox revealed Echinococcus cysts in 4 of 71 european hares (Lepus europaeus). This is the first finding of Echinococcus spp. in this host and the first association in South America of larval infection in sylvatic animals with infection in foxes. The species identification of this parasite remains to be determined. Cyst material from

hares has been fed to dogs and if the infection "takes" transmission studies in a wide variety of potential intermediate hosts including sheep will be carried out. Field investigations are continuing to determine seasonal changes in the prevalence in foxes and to determine if other sylvatic animals may be involved in this cycle.

Studies on immunodiagnosis:

Pre-operative diagnosis of hydatid cysts is often difficult due to the varied clinical manifestations and the frequent localization of cysts in organs not readily demonstrable by even the most modern clinical diagnostic techniques. It is frequently necessary, therefore, to resort to immunodiagnostic tests. Reviews on the evaluation of diagnostic tests and on the antigenic components of E. granulosus have been published by Kagan (1968) and Kagan and Agosin (1968). Since that time, however, considerable advances have been made and a variety of new serological procedures and antigenic preparations have been evaluated. The principal tests currently in use include latex agglutination, indirect hemagglutination, bentonite flocculation, immunoelectrophoresis, indirect immunofluorescence and intradermal tests for hypersensitivity. Although each of these procedures has certain limitations, most of them when correctly carried out and interpreted, show a high level of sensitivity. The exact degree of sensitivity in any given evaluation depends upon, among other things, the localization of the cysts among the study group (Kagan, 1968; Williams, Oriol, et al.: 1970; Apt & Knierim, 1970) and the condition of the cyst (Kagan, 1968; Purriel, Capron, et al.: 1970). Immunodiagnostic efficiency is always enhanced by performing a combination of two or more tests on each serum.

The fluid within the larval (i.e. hydatid) stage is the most commonly used source of diagnostic antigens. Although this liquid is rich in parasite antigens it also contains

a large number of antigens which are host specific (Chordi and Kagan, 1965). Furthermore Echinococcus has been shown to share antigens with a variety of other helminths (Biguet et al.: 1962). The complexity of this antigenic mixture has impeded the standardization and lowered the specificity of immunodiagnostic techniques.

Recently a purified fraction of sheep hydatid fluid has been prepared and evaluated in diagnostic tests. The fraction prepared by a simple, two-step fractionation procedure, consists of two major lipoprotein components and was shown to contain less than 2% of contaminating host serum protein (Oriol et al.: 1971). This fraction was compared with whole sheep hydatid fluid as antigen in hemagglutination, immunoelectrophoresis and skin hypersensitivity tests for the diagnosis of 91 cases of confirmed human hydatidosis (Williams, Oriol, et al.: 1971). Although the majority of serological reactors could be detected with this fraction, a significant proportion reacted with other components of sheep hydatid fluid which had been eliminated during the fractionation procedure. Used in the skin test the antigen was highly reactive and showed little evidence of non-specific reactivity. It is clear that multiple antigen-antibody systems are involved in diagnostic reactions for hydatid disease because some patients gave negative results with the purified antigens but were positive with the whole sheep hydatid fluid. Further research in this area might result in the characterization and isolation of all important antigens which pooled together might provide optimum sensitivity in diagnosis.

A major effort of the Pan American Zoonoses Center has been aimed at the improvement and simplification of diagnostic tests and towards the establishment of standards for their performance and interpretation. If such uniformity were achieved it would greatly facilitate the comparative analysis of results in different laboratories and in different countries.

The performance and interpretation of the slide latex agglutination test described by Szyfres and Kagan (1963) has been made even more convenient and practical by its adaptation to the Boerner slide (Williams and Prezioso, 1970).

Advances have been made in the widely used indirect hemagglutination test (IHA). the preservation of sensitized cells using glutaraldehyde and formaldehyde (Williams and Prezioso, 1971) permits prolonged storage of frozen or lyophilized cells without significantly altering the sensitivity of the test. Distribution of these stabilized cells from a single reference laboratory might serve as one method of standardization of this serological procedure.

The highly sensitive indirect immunofluorescence test has been evaluated using soluble antigens adsorbed to micropore filters (Williams and Fife, 1971). This system offers the advantage of objectivity in reading and overcomes the problem of non-specific fluorescence which often complicates the interpretation of tests performed with scolex antigens. A recent comparison of this test with the IHA method for the diagnosis of 52 patients with hydatid disease showed 69 percent positive in the soluble antigen fluorescent antibody (SAFA) test, whereas 79 percent were positive by IHA (Williams and Fife, 1971). The slightly lower sensitivity of the SAFA test compared with IHA is counterbalanced by the convenience and rapidity of the method, which could readily find application in the large scale screening of serum samples.

Workers in France (Capron et al.; 1970) and in Uruguay (Yarzabal, 1970) obtained excellent results with the immunoelectrophoresis test. These authors claim a sensitivity approaching 90% for pre-operative diagnosis and an absolute specificity. Their criterion for positivity depends upon the visual identification of one specific band in the electropositive position among the many which appear using sera from patients with hydatidosis and other

diseases. The results of other workers found this method to have a lesser sensitivity than those described above (Sorice and Castagnari, 1969; Williams et al., 1971) and it is suspected there may be more than one electropositive band in hydatid fluid which are of diagnostic value.

The intradermal test for immediate hypersensitivity has been widely used since its introduction by Casoni in 1911. The non-specificity resulting from the use of crude antigens has limited the value of the reaction particularly in Latin America where little attention has been paid in the past to standardization in terms of its performance, interpretation or the antigen used. An important contribution towards overcoming non-specificity was made by Kagan et al., (1966) who were able to demonstrate an association between the nitrogen content of the antigen and the degree of non-specific reactivity in non-hydatid persons. Recently an antigenic preparation has been prepared from boiled sheep hydatid fluid which is markedly reactive in the Casoni test (Williams, 1970). This preparation, virtually free of host components, contains one parasite antigen detectable in gel-diffusion and immunoelectrophoretic tests. Adjustment of this antigen to low N concentration and considering only differences of 1.1 cm^2 between antigen and control wheals as positive reactions eliminated non-specific reactions in patients with non-parasitic infections and gave a degree of sensitivity comparable to that observed by other authors using crude antigens.

This antigen is presently being produced and distributed by the Pan American Zoonoses Center to research workers in various countries of Latin America in an attempt to standardize the performance of this technique.

Immunodiagnostic techniques show great potential for epidemiological screening of rural populations. The use of these techniques would be of great value for comparing prevalence in humans in different areas of Latin America since the rates are not subject

to the administrative and legal factors which limit the value of surgical incidence rates. A recent comprehensive epidemiological study in southern Argentina evaluated the Casoni test for mass screening of nearly 1,700 persons of all ages. In one geographical locality 700 persons were studied in detail. A battery of serological procedures (latex agglutination, indirect hemagglutination and immunoelectrophoresis) were performed on the sera of each skin test positive person and an age and sex-matched control and thoracic radiographs were performed on the entire population. Among the 49 skin test positive reactors the sera of 11 persons gave positive serological results. Hydatid cysts have been detected in 5 of these individuals and the rest are being investigated further by radiological and other clinical diagnostic techniques. Among the skin test negative group no hydatid cysts have been detected and the serum from only one person gave a positive reaction in one of the three serological tests employed.

The results described above demonstrate the usefulness of standardized immunodiagnostic tests for screening populations for hydatid disease in rural areas of southern Argentina. The use of identical techniques in Bolivia and Peru, however, has not yet shown proven value. Skin testing of groups of slaughterhouse employees and shepherders resulted in high rates of skin reactivity but the number of serological positives was markedly lower than expected (Schantz, unpublished observations 1970 and 1971). The possibility exists that other helminth infections which exist in these countries, such as cysticercosis and fascioliasis, are producing cross reactions with the hydatid antigen utilized in the skin test. Investigation of this possibility, which could be a major impediment to the use of these tests for screening similar populations, is presently underway.

The use of immunodiagnostic tests in animal intermediate hosts has thus far given dissappointing results. Although in some regions sheep develop detectable serological and skin sensitivity responses, poor correlation exists between these responses and the presence of cysts (Blundell-Hasell, 1969 and Schantz, 1971). One author evaluating the intradermal test and the IHA and bentonite flocculation test in naturally and experimentally infected sheep concluded that due to the relatively weak immune response of this species and to frequent infection by Taenia hydatigena which produces cross reactions to Echinococcus antigens it is impossible at present to suggest reliable criteria for interpretation of immunodiagnostic tests in sheep (Schantz, 1971). Due to the potential value of effective immunodiagnostic tests for epidemiological and control purposes, these investigations are being pursued further.

Studies of the effects of chemical and physical agents upon the survival of E. granulosus eggs:

Research workers performing studies utilizing E. granulosus eggs are continually faced with the danger of self contamination or contamination of others with this highly infectious material. Studies recently reviewed by Gemmell (1968) have failed to reveal a practical ovacidal agent. Although boiling water and dessication are reported to render eggs harmless it is often difficult to insure that all infectious material within the working environment is properly treated by these physical methods. Since theoretically hydatid cyst infection may result from ingestion of only one egg, there is an urgent need for the development of effective procedures for sterilization of infectious material or laboratory equipment.

A research project was initiated at the Pan American Zoonoses Center to evaluate the effects of chemical and physical agents upon the survival of taeniid eggs. The initial step was the development of a reliable but practical method for determining the infective ability

of the eggs. The method of in vitro activation of embryos (Silverman, 1954) which has been widely used for this purpose is fraught with difficulties both in performance and interpretation and it has been shown that in vitro observations on the proportion of oncospheres becoming activated were of little value as a guide to the infectivity of the parasites. (Williams and Colli, 1970). Instead a system was developed based upon the infectivity of eggs in vivo. It was found that primary cystic infections could be produced in white mice and jirds (Meriones unguiculatus) by intraperitoneal inoculation of eggs or oncospheres of both E. granulosus and T. hydatigena (Williams and Colli, 1970). The percentage of inoculated eggs which developed into cysts was similar to that which occurs in sheep following oral infection. It was felt that the evaluation of egg infectivity by this method, although less expedient and rapid than the in vitro system, might lead to more significant and reliable conclusions of practical value. More recently it was found that excellent infection results were obtained in the same laboratory animal species by the oral administration of eggs although the percentage of eggs administered which developed into cysts was much reduced (Williams, J. F., 1971, personal communication). This latter finding is expected to have particular application as an indicator of survival and infectivity of eggs under different climatic conditions and will also provide a laboratory model of larval E. granulosus infection experimentally infected by the natural route.

Using the method of intraperitoneal inoculation of eggs in laboratory animals for assessment of egg survival, studies have proceeded to evaluate the effects of extremes of temperature (Colli and Williams, 1971) and ionizing radiation (Williams and Colli, 1971) on E. granulosus eggs.

It was found that the eggs are remarkably resistant to sub-freezing temperatures. Eggs treated at -10°C , -20°C and -30°C for 24 hours were equally as infective as the control eggs. Infectivity was markedly reduced after exposure to -50°C and no infections developed in animals inoculated with eggs subjected to -70°C . The effect of heat was also studied. All animals inoculated with eggs treated for 5 minutes at 45°C became infected, and the proportion of cysts developing was similar to that in the controls. With increasing temperature significantly fewer animals in each group became infected and with fewer cysts. It was concluded that the survival limit for an exposure of 5 minutes to moist heat probably lies between 55°C and 60°C (Colli and Williams, 1971).

Studies of the effects of ionizing radiation on E. granulosus eggs showed a remarkable resistance to X irradiation. Although dose levels higher than 10 Kr produced progressively greater reduction on the number of cysts developing in individual animals as compared with controls, some cysts developed from eggs subjected to doses as high as 30 Kr. It was noted that eggs stored for 60 days were less susceptible to X irradiation than those stored for 15 days prior to exposure. Ultraviolet irradiation for 24 hours was seen to have a detrimental effect upon the eggs. A significant reduction occurred in the number of cysts developing per animal at all egg dose levels and at the lower dose levels none of the animals inoculated with irradiated eggs became infected (Williams and Colli, 1971).

The studies are continuing to determine the minimum lethal dose of X irradiation and the effects of storage time on the susceptibility of eggs to ionizing irradiation as well as the effects of other physical and chemical agents.

Studies on chemotherapy of canine infection:

In Latin America, reliance for hydatidosis control has often been placed on the use of anthelmintics for treatment of canine infection. The Pan American Zoonoses Center has

carried out laboratory and field trials to evaluate the efficiency of various compounds for this purpose (Blood et al., 1968).

At present, the drug most commonly used in hydatid control programs is arecoline hydrobromide. This drug has a purgative effect and often eliminates the majority, but rarely all of the tapeworms in an infected dog. Multiple treatment are required to effect complete clearance. This compound, therefore, has only limited value in canine treatment but has a major function in epidemiological studies and control programs as a diagnostic agent. The presence of the parasites in the purged stool can easily be detected by appropriate examination by experienced technicians. Periodic dosing of all dogs within a control program allows authorities to assess the compliance of dog owners with provisions against the feeding of raw viscera to their dogs. Recent investigations at the Pan American Zoonoses Center have been aimed at the assessment the efficiency of this drug (Trejos et al., 1970) and the influence of different modes of administration (Williams and Trejos, 1970).

Another drug presently utilized against E. granulosus is bunamidine hydrochloride. This drug is taeniacidal and its efficiency in worm removal was evaluated in controlled trials in New Zealand and Argentina by Gemmell and Shearer (1968) and Blood et al. (1968) respectively. Although the drug shows up to 90% efficiency against mature infections, its effectiveness against immature infections is no greater than that of arecoline hydrobromide (Trejos et al., 1970). This drug has not yet been properly evaluated in the field for mass treatment of dogs and is presently being used in control programs in New Zealand and Tasmania for individual treatment of dogs found infected by arecoline dosing.

Recently it was shown that bunamidine hydrochloride had a marked detrimental effect on E. granulosus eggs using the in vivo model described above for assessing egg survival (Williams, J. F., 1971, personal communication). Although the mechanism of this ovacidal

activity is not yet known, should it prove possible to demonstrate a similar effect on eggs in adult parasites following bunamidine treatment of infected dogs a reassessment of the value of the drug in the treatment of canine echinococcosis will be required.

PROSPECTS FOR CONTROL IN LATIN AMERICA

Hydatidosis in Latin America shows no signs of diminishing in importance. In some areas where other rural health problems are being reduced the problem of hydatidosis is made more apparent and where efforts are being made to expand and upgrade livestock populations the high prevalence of hydatid infection becomes increasingly intolerable. More and more interest in the implementation of control programs is being shown in all countries where the disease is endemic.

Effective control of hydatid disease has been rarely achieved even though, theoretically, control of this parasitic disease is a simple matter. If the infected viscera from sheep and other intermediate hosts were not fed raw to dogs the infection would eventually disappear from lower animals and man where the main source of infection is the domesticated dog. In practice, however, a variety of social, economic and technical factors have prevented the implementation of effective control measures. This has been the case with many campaigns conducted in the past in Latin America, apparently without substantially modifying the situation.

It has been said that hydatid control is not a technical problem but rather a problem of people. The point made was that continued transmission of E. granulosus primarily depends upon the unfortunate practices of man who permit dogs to feed on the infected viscera of domestic animals. Effective control is largely a question of convincing people to change these practices. In effect, the local population must be educated to the dangers of the disease and motivated to do something about it. This latter point is especially important

because it has been observed that education is sometimes achieved without a resultant change in human behaviour. The aim of education in hydatid disease control is to achieve active participation by the local population in the control effort.

That control of hydatidosis can be achieved has been demonstrated by successful programs in Iceland, New Zealand and the Australian state of Tasmania. In these countries a combination of educational, technical and legislative measures have resulted in a considerable reduction in the prevalence of the disease and even, in the case of Iceland, apparent eradication (Schantz and Schwabe, 1969).

These areas share certain characteristics which are recognized as having contributed to their success. These characteristics include the highly developed nature of their pastoral economies and the nearly 100 percent literacy rates. Furthermore, all of them are relatively small islands.

Most of Latin America where the disease is highly prevalent is characterized by quite different conditions. Factors such as low socio-economic levels of the rural population, large and uncontrolled canine populations, vast continental geographic conditions and the occurrence of large sylvatic animal populations which are potential hosts for E. granulosus create special problems for control. It has been questioned whether "conventional" control measures applied in these areas can be expected to achieve the same results as in Iceland, New Zealand and Tasmania. Rather, in these zones, it may be necessary to evolve different approaches.

These questions can best be resolved by studying control methods in carefully designed pilot projects in different areas. Experience obtained in these programs will suggest changes or modifications of "conventional" control measures appropriate to local conditions and can be expected to avoid considerable waste of time and money that might

occur if a program were initiated on a nation-wide scale from the beginning. Of fundamental importance to any control program is an initial epidemiological assessment of prevalence in man and lower animals to provide baseline data against which future progress can be measured.

In 1970, two pilot hydatid control projects were initiated in Latin America, one in the Argentine Province of Neuquen and the other in the Department of Flores in Uruguay. The Government of Peru is presently considering the initiation of a third pilot project within its Agrarian Reform Program in the Central Sierra. Both of these former projects involve the collaboration of public health and agricultural agencies and have developed with the assistance of the Pan American Zoonoses Center and other consultants to the Pan American Health Organization. It is still premature to attempt an evaluation of either of these efforts, however, both projects have been designed on the principles described above and experience in these programs may be determining factors in the possibilities for control of hydatid disease in Latin America at least in the immediate future.

SUMMARY

Hydatidosis (Echinococcosis) is a cyclo-zoonotic infection caused by the cystic larval stages of a cestode parasites of the genus Echinococcus. E. granulosus and E. oligarthrus, two of the three accepted species in this genus occur in Latin America. E. granulosus, whose life cycle mainly involved dogs and a variety of domesticated ungulates (sheep, cattle, goats, pigs and auchenids) is by far the most widely distributed and prevalent. Infection by this parasite is mainly associated with concentrations of the ovine population and reaches its greatest prevalence in Uruguay, Argentina, Chile, southern Brazil and the Sierra of Peru. The medical importance of this parasite is emphasized by the present absence of medical treatment. The rejection of infected viscera in livestock occasions considerable economic losses in all countries where the disease is endemic.

Research on hydatidosis in Latin America has not been commensurate with the magnitude of the problem. Recently, however, studies in several countries have begun to quantify the prevalence of the disease in human and lower animal populations and to relate differences in prevalence and distribution to local cultural, socio-economic and agricultural conditions.

Current research being carried out at the Pan American Zoonoses Center and elsewhere is reviewed. It is pointed out that, perhaps, nowhere else in the world is there a more pressing need for increasing research in hydatidosis than in Latin America.

Public health and agricultural authorities in all endemic countries are showing increasing interest in the implementation of programs for the control of this disease. It is not known whether the control measures employed with success in other countries can achieve similar results in Latin America where cultural, socio-economic and agricultural conditions are very different. It is expected that experiences gained in recently initiated pilot control projects in Argentina and Uruguay will help in determining those changes or modifications in "conventional" control measures appropriate to local conditions.

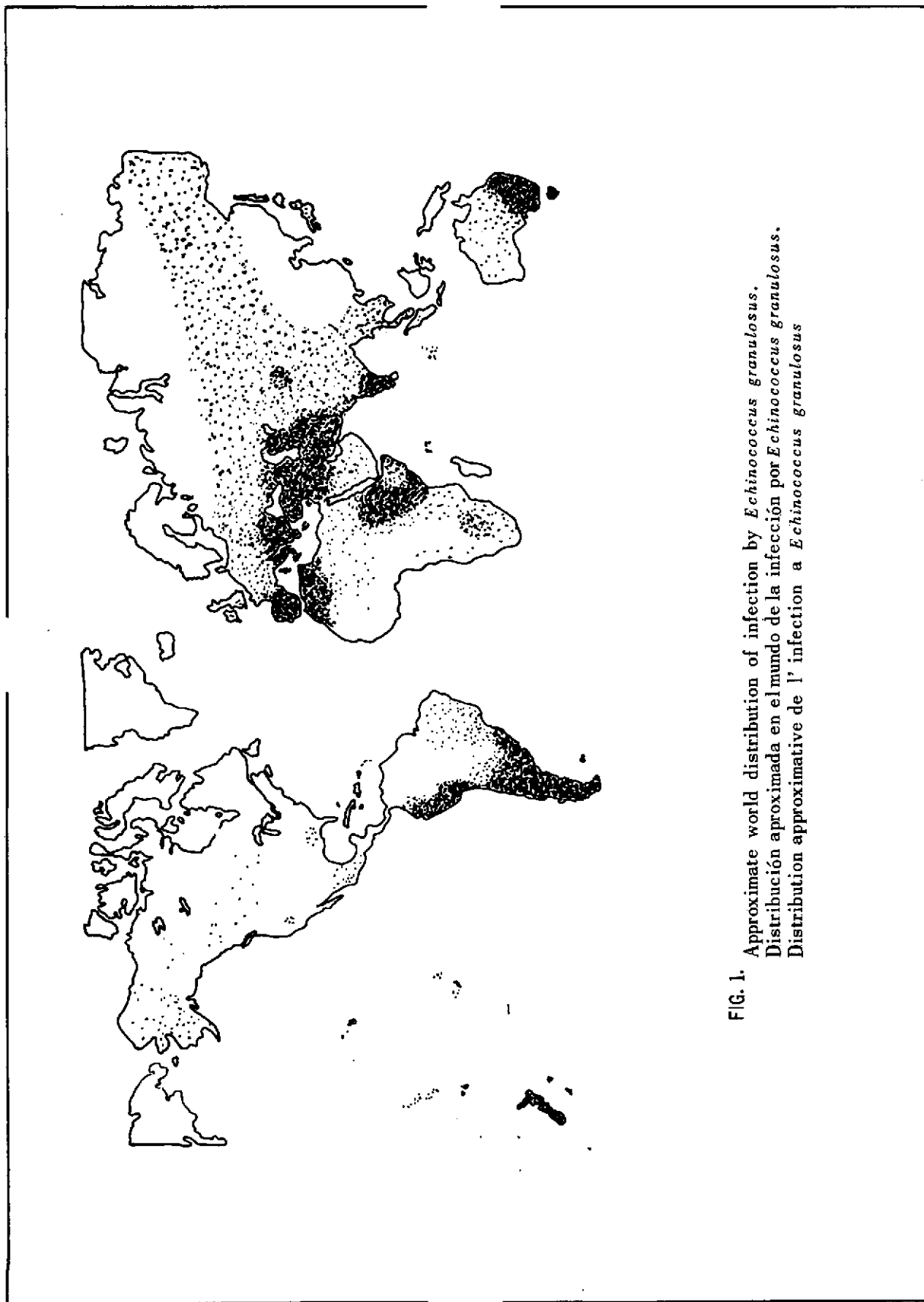
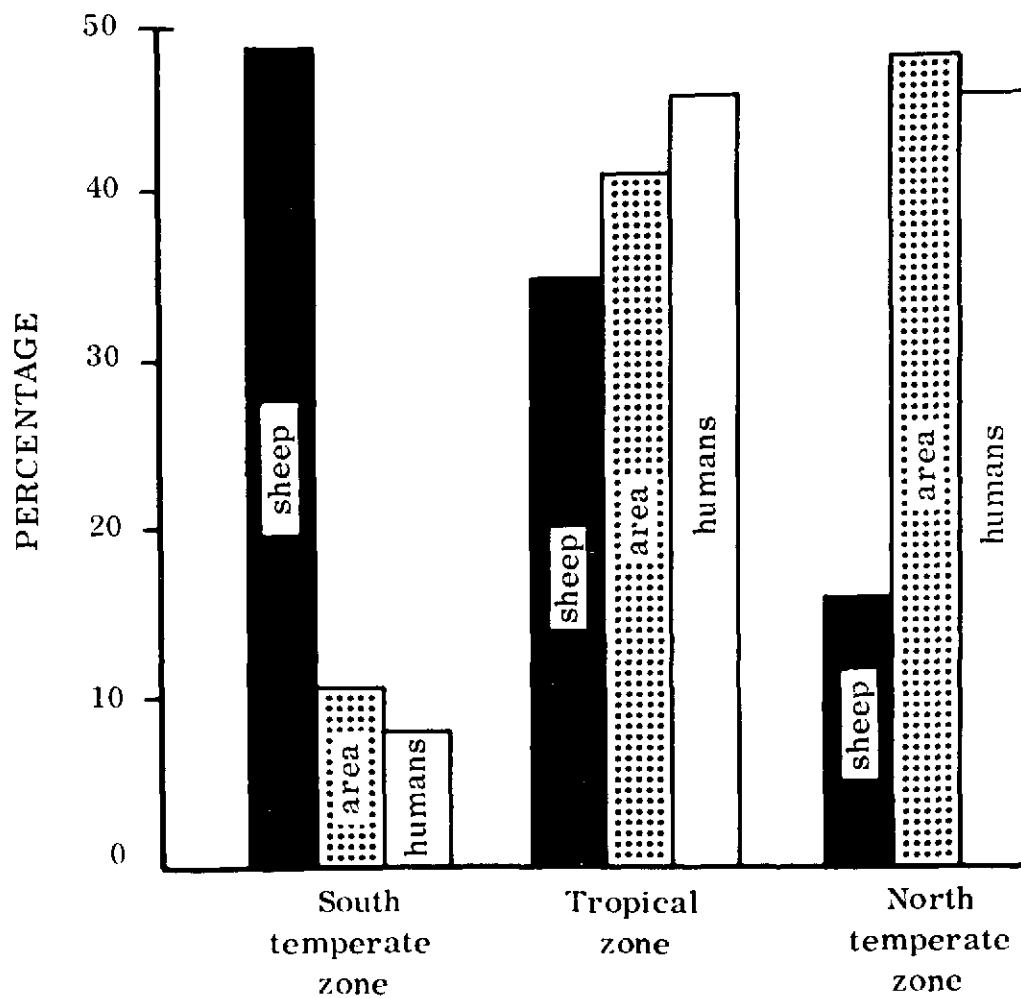


FIG. 1. Approximate world distribution of infection by *Echinococcus granulosus*.
Distribución aproximada en el mundo de la infección por *Echinococcus granulosus*.
Distribution approximative de l' infection a *Echinococcus granulosus*

FIG. 2

DISTRIBUTION OF SHEEP AND HUMAN POPULATIONS AND LAND AREAS
IN THE THREE CLIMATIC ZONES OF THE AMERICAN CONTINENT (1967)



From: Williams, J.F. *et al.*, 1971

Table 1. Annual Incidence of Surgical Cases of Human Hydatid Disease in Several Countries of South America

Country	Year(s)	Incidence of surgical cases/100,000 population per year	Reference
Argentina	1966	2.0	Sec. Estado Salud Pública, 1967
Chile	1960-1967	6.8-8.6	Neghme and Silva, 1970
Peru	1966	1.0	Min. Salud Pública y Asist. Social, 1967
Uruguay	1962-1968	17.9-23.8	Purriel <u>et al.</u> , 1970

Table 2. Prevalence of Pulmonary Tuberculosis and Hydatid Cysts as Determined by
Mass Chest Radiography, Department of Flores, Uruguay, 1949-1969*

Date	No. Persons Radiographed	New Cases Detected			
		Tuberculosis		Hydatid Cysts	
		Number	Rate per 1000 Radiographs	Number	Rate per 1000 Radiographs
1949	11,874	133	11.2	11	0.9
1951	10,255	59	5.7	9	0.9
1954	11,718	38	3.2	12	1.0
1962	15,514	56	3.6	18	1.2
1969	15,810	12	0.7	19	1.2

* From Purriel and Schantz, 1971

ERRATUM

- p.3, paragraph 4 - Williams, Trejos et al., 1971, should be Williams, Lopez Adaros et al. 1971.
- p.4, paragraph 1 - Williams, Trejos et al., 1971, should be Williams, Lopez Adaros et al. 1971.

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