WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

BIBLIOTHÈQUE OMS
19 DEC
WHO LIBRARY

WHO/PDP/84.5
WHO/CDD/PAR/84.2

ORIGINAL: ENGLISH

PARASITIC DISEASES PROGRAMME
DIARRHOEAL DISEASES CONTROL PROGRAMME

WHODOC 84.1

Amoebiasis - D & C - Cancer

Informal Meeting on Strategies for Control of Amoebiasis

(Geneva, 6-8 February 1984)

The issue of this document does not constitute formal publication. It should not be reviewed, abstracted or quoted without the agreement of the World Health Organization. Authors alone are responsible for views expressed in signed articles.

Ce document ne constitue pas une publication. Il ne doit faire l'objet d'aucun compte rendu ou résumé ni d'aucune citation sans l'autorisation de l'Organisation mondiale de la Santé. Les opinions exprimées dans les articles signés n'engagent que leurs auteurs.

CONTENTS

LIST OF PARTICIPANTS

Professor H.M. Gilles, Liverpool School of Tropical Medicine, Liverpool, United Kingdom (Rapporteur)

Dr K.N. Jalan, Kothari Centre of Gastroenterology, The Calcutta Medical Research Institute, Calcutta, India

Professor A. Martinez-Palomo, Patología Experimental, Centro de Investigación y de Estudios Avanzados del IPN, México, D.F., Mexico

Professor E. Meerovitch, Institute of Parasitology and National Reference Centre for Parasitology, McGill University, Macdonald College, Ste-Anne-de-Bellevue, PQ, Canada (Chairman)

WHO Secretariat

Dr D. Barua, Diarrhoeal Diseases Control Programme (Consultant)

Dr A. Davis, Director, Parasitic Diseases Programme

Dr M. Merson, Director, Diarrhoeal Diseases Control Programme

Dr Z. Pawlowski, Senior Medical Officer, Parasitic Diseases Programme (Secretary)

Mr K. Schultzberg, Sanitary Engineer, Environmental Health Technology, Division of Environmental Health

ACKNOWLEDGEMENTS

The Group expresses its gratitude to Dr J.A. Cook, Director, Programme in Tropical Disease Research, The Edna McConnell Clark Foundation, New York, N.Y., USA, and Professor R.L. Guerrant, Head, Division of Geographic Medicine, University of Virginia, Charlottesville, VA, USA, for their written contributions which served as a valuable basis for discussions.

1. INTRODUCTION

Amoebiasis, an infection of humans with the protozoan Entamoeba histolytica, has a world-wide distribution[1]. Its pathogenic effects and clinical expression depend on many host and parasite factors and their dynamic interplay, which makes it difficult to draw a clear-cut distinction between infection and disease.

Amoebiasis as a disease can be caused only by potentially pathogenic E. histolytica strains, the characteristics of which are:

- a higher rate of erythrophagocytosis;
- a greater propensity to agglutinate with the lectin concavalin A, reflecting a higher number of exposed glucose- and mannose- containing receptors, and a characteristic N-acetyl-D-galactosamine (GALNAc) inhibitable binding to target cells via a soluble lectin[2].
- a lack of overall surface charge, which may facilitate interaction with the negatively charged mammalian cells;
- a more potent cytopathic effect in vitro;
- an ability to grow in semisolid media;
- the production of lesions in experimental animals[3]; and
- a typical isoenzyme pattern .

Isoenzyme electrophoretic mobility analyses performed on amoebae isolated from stool samples from four continents have so far identified seven potentially pathogenic and 11 non-pathogenic zymodemes[4].

Major host factors contributing to the unpredictability of amoebic infections in man are:

(i) The degree of immunological resistance: Specific antiamoebic antibodies are produced when tissue invasion occurs. Immune serum produces rapid lysis of E. histolytica trophozoites in vitro. Accumulated experimental evidence strongly suggests that cellular immunity plays an important part in controlling the recurrence of invasive amoebiasis[5].

(ii) The physico-chemical environment in the gut.

An understanding of both parasite and host factors, and of the conditions that modulate them, should facilitate more accurate prediction of the outcome of infection, and also the implementation of appropriate control measures.

The term "invasive amoebiasis" reflects both parasite and host factors which result in pathological lesions. Invasive intestinal amoebiasis is characterized by the following markers:

- symptoms and signs of amoebiasis;
- presence of haematophagous trophozoites in the stool or rectal scrapings;
- characteristic changes in the intestinal mucosa at endoscopic examination;
- positive serological tests for specific antibodies.

"Non-invasive" intestinal amoebiasis reflects the opposite condition and is characterized by:

- an asymptomatic course;
- the absence of haematophagous trophozoites;
- lack of endoscopic changes; and
- negative serological tests for specific antibodies.

In invasive amoebiasis many gradations of pathological change and clinical expression occur.

The existence of chronic intestinal amoebiasis as a clinical entity, characterized by a prolonged course, non-specific bowel or general symptoms with a tendency to recur, and cellular infiltration of the intestinal mucosa, still requires confirmation.

2. REVIEW OF CURRENT INFORMATION

2.1 Magnitude of the problem

The distribution of lumenal infection with the parasite, as measured by the presence of cysts in stools, is world-wide. These infections are asymptomatic and may affect from less than 5% to over 50% of any given population. A recent overall estimation indicated that, in 1981, 480 million people carried E. histolytica in their intestinal tract[6].

Only a small percentage of those having intestinal infection will develop invasive amoebiasis, the main forms being dysentery and liver abscess. Serological surveys for antibodies, which are used to measure the proportion of the population with past or current invasive disease, suggest that approximately one-tenth of the total number of infected people – i.e., some 48 million people annually[6], have intestinal mucosa or liver invasion; amoebic dysentery occurs five to 50 times more frequently than liver abscess.

In Mexico City, up to 15% of cases of acute diarrhoea in children requiring hospitalization were found to be associated with E. histolytica[7,8], while in Caracas, Venezuela, 11% of children with diarrhoea were infected with this parasite[9].

Amoebiasis causes death mainly when it manifests itself as liver abscess or fulminating colitis. Two to 10% of persons with liver abscess may die whereas the mortality among those with fulminating colitis is almost 70%. It is probable that invasive amoebiasis accounts annually for 40 000 to 110 000 deaths in the world. Thus, after malaria, amoebiasis takes the second place on the list of parasitic causes of death on a global scale.

Amoebiasis is more closely related to sanitation and socioeconomic status than to climate. It is known to be a major health problem in China, Mexico, the eastern portion of South America, West and South-east Africa, and the whole of South-east Asia including the Indian subcontinent, but reliable information is available from only a few countries.

In addition to being a potentially lethal disease, invasive amoebiasis has important social and economic consequences. Temporarily incapacitating infections are frequent in adult males during the wage-earning years, requiring several weeks of hospitalization and from two to three months for full recovery. Amoebiasis may cause clinical problems in persons with immunodeficiency, homosexuals, immigrants from certain tropical countries, and travellers.

In view of the substantial morbidity and mortality caused by E. histolytica, more research into better methods of diagnosis, treatment, and prevention is clearly necessary and an improvement of control strategies essential.

It is to be hoped that the impact of the International Drinking-Water Supply and Sanitation Decade (1981-90) will reduce the magnitude of the problem, but adverse factors such as population growth, uncontrolled urbanization, and economic crises may militate against success in control.

2.2 Clinico-pathological forms of amoebiasis

In countries where amoebiasis is an important health problem, the majority, approximately 90%, of individuals with colonic E. histolytica infections are carriers, while the remainder have invasive intestinal amoebiasis[10].

The latter condition is characterized clinically by either acute amoebic dysentery with bloody, mucous stools, colicky pain, and rectal tenesmus, or by intermittent diarrhoea, frequently with blood-stained faeces. In general, there is no fever or other systemic manifestation and symptoms disappear after a few days of treatment or even spontaneously.

There are three forms of clinically severe intestinal amoebiasis that are more common in adults than in children: fulminating amoebic colitis, amoeboma of the colon, and amoebic appendicitis.

Fulminating amoebic colitis is characterized by the passage of numerous bloody stools, generalized abdominal discomfort, colicky pains preceding evacuation, and rectal tenesmus which tends to be constant and intense. General manifestations include fever, dehydration, and rapidly progressive prostration. Advanced lesions frequently produce intestinal haemorrhages, or perforation followed by peritonitis[3]. Specific antiamoebic treatment may be ineffective and surgery may be required.

Amoebomas are pseudotumoral lesions that occur predominantly in the vertical regions of the colon, the caecum, and the rectum and are associated with vague abdominal symptoms, occasional bloody diarrhoea, and a palpable mass. They respond well to specific treatment.

The clinical manifestations of amoebic appendicitis are similar to those of bacterial appendicitis. Diarrhoea with blood-stained stools is a frequent accompaniment and a distinguishing feature.

The most common extraintestinal form of invasive amoebiasis is amoebic liver abscess. Amoebic abscesses are 10 times more common in adults than in children, with a higher frequency in males (3:1). Only about 9% of patients may have an associated amoebic recto-colitis. The clinical features of liver abscess, which may be of abrupt onset, are pain and tenderness in the region of the liver, wasting, and fever associated with chills and profuse night sweats.

2.3 Diagnostic methodologies

2.3.1 Clinical and laboratory diagnosis. In the great majority of cases of invasive colonic amoebiasis, rectosigmoidoscopy and immediate microscopic examination of rectal smears and/or fresh stool samples for the presence of motile haematophagous trophozoites of E. histolytica are the most reliable diagnostic procedures. In these cases, differentiation of amoebae by charactistics of nuclear structure is rarely necessary. The presence or absence of pus cells in the stool may be very significant (Table 1). Because of the amoebic cytolethal effect, pyknotic or disrupted leukocytes are characteristically seen in the stool[11]. A good quality microscope is needed, as is adequate training of the laboratory personnel. Merthiolate-iodine-formaldehyde (MIF), polyvinyl alcohol (PVA), and sodium acetate formalin (SAF) can be used for the fixation and transportation of stools, whenever confirmation of the diagnosis in a reference centre is required. The serological test for antiamoebic antibodies is positive in approximately 75% of cases of colonic invasive amoebiasis. X-ray examination is particularly helpful in fulminating colitis, amoeboma, or peritonitis.

Table 1: PRACTICAL DIFFERENTIAL DIAGNOSIS OF PATIENTS WITH BLOOD AND MUCUS IN THE STOOL

Condition	Macroscopic Examination		Microscopic Examination	
	Blood	Mucus	Trophozoites with red blood cells	Pus cells
Acute amoebic dysentery	+	+	+	+ –
Shigellosis	+	+	–	+++

In the majority of cases of amoebic liver abscess, in addition to the clinical presentation, a polymorphonuclear leucocytosis is present. Antiamoebic antibodies can be detected in the serum of 95% of infected patients. X-ray examination shows elevation and hypomotility of the right hemidiaphragm. Scintillography, ultrasonography, and computerized axial tomography have greatly facilitated determination of the location and number of amoebic liver abscesses and evaluation of treatment.

2.3.2 Serological diagnosis. Many serological tests for specific antibodies have been introduced as adjuncts to the diagnosis of amoebiasis. The various tests employed include indirect haemagglutination (IHA), enzyme-linked immunosorbent assay (ELISA), indirect immunofluorescence (IIF), counter current-immunoelectrophoresis (CCE), and agar gel diffusion (AGD).

These serological tests are particularly useful in the detection of extraintestinal amoebiasis such as amoebic liver abscess, since stool examination is often negative for E. histolytica in such cases. All patients thought to have inflammatory gut disease should have a serological test for amoebiasis because of the potentially fatal consequences of giving steroids to patients with amoebic colitis and the uncertain quality of the parasitological stool examination in many laboratories. The tests are also useful as an epidemiological tool for the detection of invasive amoebiasis in a population. However, since positive titres may persist for months or years after successful treatment, it is difficult to differentiate active and past infections[3].

Tests for the detection of circulating specific antibodies:

Various workers have shown the usefulness of the IHA test in the diagnosis of invasive amoebiasis - i.e., liver abscess and acute amoebic dysentery - and have also used it to classify individuals as asymptomatic carriers, or symptomatic patients, requiring treatment. Furthermore, certain cut-off titres have been suggested for the establishment of a diagnosis of amoebic liver abscess and intestinal amoebiasis. However, in highly endemic areas this test is of very limited diagnostic importance, since a large number of persons may have a very high titre due to a past infection without the presence of any active amoebic disease. In an endemic area all tests for the detection of antiamoebic antibody - e.g., AGD, CCE, immunofluorescent antibody (IFA), latex agglutination, and ELISA - suffer from the same limitation as the IHA test, and for that reason tests based on antigen detection need to be developed and improved.

Tests for the detection of circulating amoebic antigen:

An immune complex dissociation radio-immunoassay (RIA), as well as an ELISA, have been developed for circulating E. histolytica proteins. The technique is an improvement on the previously described Sandwich assay for the detection of E. histolytica antigen[12]. For such RIA procedures it is essential to use an extensively purified antibody, raised against washed E. histolytica trophozoites. The critical feature is the need to deplete those antibodies against culture-medium-derived-bovine-serum- proteins, which cross-react with human proteins. Essentially, the RIA approach (as followed in India at the Khotari Centre, Calcutta) involves the precipitation of immune complex from serum by polyethylene glycol (PEG), followed by dissociation with glycine urea buffer, and absorption on paper discs; the E. histolytica antigen is finally detected with a highly purified radio-labelled antibody. In the case of the ELISA, instead of radio-labelling, peroxidase conjugated rabbit anti-E. histolytica antibody has been used.

It is now possible to use this test system in clinical studies since it does not have the disadvantage (detection of antibodies) of the IHA and other serological tests which fail to distinguish between present and past infection. The RIA could thus be of particular value: (i) for confirming a clinical diagnosis of invasive amoebiasis; (ii) for studying the sequelae of E. histolytica infections in man, as well as (iii) as a marker of disease activity; and (iv) as a tool for molecular biologists studying these parasites, particularly to screen for the expression of E. histolytica proteins in recombinant bacterial clones.

If, in further studies in different endemic countries, the test is indeed found to be a reliable marker of disease activity and invasiveness, it could be used for epidemiological studies by selected workers or centres.

Tests for the detection of amoebic antigen in faeces:

An ELISA for the detection of E. histolytica antigen in stools has now been developed. The applicability of this test at different levels of health services requires assessment and evaluation. If successful, this test may eventually replace microscopy for survey purposes.

2.4 Treatment

The drug of choice for the treatment of invasive amoebic disease is metronidazole, but the treatment is relatively expensive. Emetine, or its synethetic derivative dehydroemetine, despite their toxicity, are still indicated for patients who are either unable to take oral medication or are critically ill. Closed drainage of a liver abscess may be necessary if the abscess cavity is large and there is no substantial improvement within 48 hours of starting chemotherapy. The variation in the pathology and clinical expression of amoebiasis in different parts of the world requires that the preferred treatment regime should be based on local experience (see also Section 3.3).

Diloxanide furoate, diiodohydroxyquinoline, or paromomycin are used as intralumenal amoebicidal drugs. However, there is no single-dose treatment available that can be advocated.

Although in some countries the total consumption of antiamoebic drugs is high, their use by the poorer segments of the population, where amoebiasis is most common, is limited because of their relatively high price.

2.5 Prevention and control measures

The basic means of preventing amoebic infection is the improvement of living conditions and education in countries where invasive amoebiasis is prevalent. Specifically, methods of attack are aimed at assuring:

(i) environmental sanitation including water supply and food safety;

(ii) early detection and treatment of infections and/or disease, and

(iii) health education[13].

E. histolytica cysts are remarkably resistent to chemical disinfectants, including chlorination, and can survive a wide range of pH values and osmotic pressures. They die rapidly if dried, heated (to about 55°C), or frozen[14]. Direct faecal-oral transmission via hands or food is very common. Therefore, sanitation and personal hygiene have priority in the prevention and control of amoebiasis. The availability of sufficient water for washing hands and food may be more important than the quality of the water alone.

As there is usually no direct time and place relation between exposure and onset of disease, and epidemic situations are rare, health education on amoebiasis should form part of the general education programme on the control of infections transmitted by the faecal-oral route addressed to mothers, school-children, and persons with influence in the community.

3. POSSIBLE CONTROL STRATEGIES

Control of amoebiasis will be achieved through national and international programmes for the improvement of sanitation, water supply, and food safety. Until such improvements become a reality in regions endemic for amoebiasis, some specific modifications or extensions of already existing programmes will need to be devised and implemented.

3.1 Improved excreta disposal, water supply, and food safety

The most effective preventive measures for amoebiasis are the safe disposal of human faeces coupled with the elementary sanitary practice of washing hands after defaecation and before eating.

The protection of water supplies against faecal contamination is also important because the cysts of E. histolytica may survive for several days or weeks in water. In areas endemic for amoebiasis, heating or filtration techniques are more effective than chemical treatment of water.

Environmental measures should also include the protection of food and drink from flies and cockroaches and the control of these insects, although their role in spreading amoebiasis may not be as important as in shigella infections.

Practices aimed at avoiding or minimizing the contamination of food are more important, and theoretically easier, than destroying or denaturing the contaminants. Thus, carriers who pass cysts and are involved in handling food, whether at home, at street stalls, or in catering establishments, should be actively detected and treated since they are major transmitters of amoebiasis. Mechanisms to motivate healthy practices in food handlers must be developed and implemented. In all these efforts, food safety cannot be dissociated from ingrained socio-cultural habits, which present one of the major obstacles to success.

The high prevalence rates of amoebiasis are not adequately recognized by public health authorities as an indicator of deficient sanitation and poor general development.

3.2 Health education

In the long term a great deal can be accomplished in the prevention of amoebiasis through education of the public as well as all levels of health personnel. In endemic areas the latter should be reminded of the problem constantly, receive training in the specific diagnostic and therapeutic procedures, and participate actively in preventive measures.

Elementary hygienic practices should be propagated and constantly reinforced in schools, health care units, and the home through periodic campaigns using the mass media. The existing educational mechanisms developed for the national diarrhoeal diseases control programme should be used, and additional information (e.g., related to the safety of food) should be addressed to the adult population.

The long-ingrained cultural habit of purchasing and eating food from street vendors poses a constant threat in some countries, since they are a major source of infection which is not easy to control, nor is the habit easy to discourage.

3.3 Case management

The management of amoebiasis will differ according to whether clinical cases or persons with asymptomatic infections are being dealt with. It will also vary at different levels of the health services infrastructure.

3.3.1 Management of clinical cases

A community health worker is not able to do more than refer a clinically suspected case to the nearest health centre/physician/hospital. At the health centre level, symptomatic cases can be treated effectively with metronidazole and the clinical response in 48 hours may confirm the suspected diagnosis. Suspected cases of amoebic liver abscess with pain and tenderness in the right hypochondrium, along with other symptoms, should be referred to the nearest hospital.

Hospitals with a clinical laboratory and a properly trained technician should be able to diagnose acute amoebic dysentery correctly by detecting motile trophozoites with ingested red blood cells and by the presence of pus cells (usually less than 10 per high power field) in freshly voided stools. Such cases can be treated properly with metronidazole and their response to treatment observed. Cases of liver abscess can also be better diagnosed and managed.

3.3.2 Management of persons with asymptomatic infection

Generally, asymptomatic infections are diagnosed in a hospital equipped with a clinical laboratory. In an endemic area, the consensus is not to treat such persons because the probability of re-infection is very high. There may, however, be an epidemiological reason for treating them, e.g., high prevalence of potentially pathogenic strains in the area, or the carrier is a food handler by profession. In a non-endemic area, they are always likely to be treated.

3.4 Epidemic control

Amoebiasis characteristically occurs in endemic forms in areas of high prevalence, probably as a result of high levels of transmission and constant reinfection in crowded populations living in insanitary conditions. Epidemic outbreaks are rare and are usually associated with sewage seepage into the water supply. Prompt treatment of symptomatic cases and environmental hygienic interventions should help in combatting outbreaks.

3.5 Chemoprophylaxis and immunization

At present there is no acceptable chemoprophylaxis for amoebiasis, even for non-immune travellers. Mass examination followed by selective chemotherapy - i.e., treatment of all infected persons - cannot be considered a solution for the control of amoebiasis.

The induction of protective immunity is at an experimental stage. It has been shown that rodents can be immunized against intrahepatic challenge with pathogenic strains, using live trophozoites as well as crude or purified *E. histolytica* antigens. Furthermore, cellular immune responses have been induced in primates by the administration of purified *E. histolytica* antigen. No undesirable reactions have been registered in the different animal species immunized. These facts indicate that it should be possible to develop an antiamoebic vaccine[3].

4. CONCLUSIONS AND RECOMMENDATIONS

Despite the recognition of the problem caused by the high morbidity and mortality due to amoebiasis, and the serious need for knowledge in this field, there is a paucity of interested institutions and research workers. Support from national, international, and other funding organizations is minimal, and a reappraisal of this situation is sorely needed. In addition, laboratory facilities are often insufficient and the training of laboratory personnel inadequate for the diagnosis of amoebiasis. However, the activities related to parasitic diarrhoeas of the WHO Diarrhoeal Diseases Control and Parasitic Diseases Programmes offer new possibilities for improving both research and services in amoebiasis control.

4.1 Appropriate strategies currently applicable for control

Amoebiasis can be prevented and controlled both by non-specific and specific measures.

Non-specific measures deal with:

(i) improved water supply, excreta disposal, and food safety;

(ii) health education;

(iii) general social and economic development.

In areas endemic for invasive amoebiasis, all activities carried out at country, district, or community level related to intestinal infections should include amoebiasis. The implementation of individual and community preventive measures (e.g., washing hands, proper excreta disposal) should be an essential part of these activities. It should be realized, however, that measures such as the improvement of water supplies and sanitation are cost-intensive and are likely to be a long-term undertaking.

Specific measures that should be undertaken when possible are:

(i) community surveys to monitor the local epidemiological situation with regard to amoebiasis;

(ii) improvement of case management - i.e., rapid diagnosis and adequate treatment of patients with invasive amoebiasis at all levels of the health services including the community and health centre levels;

(iii) surveillance and control of situations that may be favourable for a wider spread of amoebiasis - e.g., refugee camps, contamined public water sources.

4.2 Intensification of training

Training is an essential component of all the specific interventions and should be provided for both medical and paramedical personnel. The areas in which training should be intensified are:

- clinical diagnosis and management of amoebiasis;
- laboratory diagnosis; and
- survey methodologies.

5. RESEARCH PRIORITIES FOR DEVELOPMENT OF IMPROVED STRATEGIES

5.1 Simplified reliable diagnostic and survey techniques

5.1.1 There is a need to develop, for general use, simple and reliable techniques for the identification of E. histolytica, and for the preservation and transportation of faecal samples to a reference laboratory for further examination.

5.1.2 In view of the recent developments in the immunology of amoebiasis, an evaluation should be made of the various immunodiagnostic techniques now available for the detection of serum antigen, faecal antigen, serum antibodies (especially IgM antibodies), and immune complexes. WHO should promote and support the development of a standardized diagnostic test for general use. Serious consideration should in particular be given to promoting a collaborative study, using standardized methods and reagents, to evaluate the radioimmunoassay and ELISA techniques as methods of detecting amoebic protein antigen in serum and to determine their usefulness for the diagnosis of invasive amoebiasis.

5.1.3 The production and evaluation of monoclonal antibodies for the detection of E. histolytica antigen in serum and faeces should be supported.

5.2 Community surveys

5.2.1 Community surveys, utilizing appropriate techniques, should be carried out in endemic foci to determine the clinical and epidemiological features of amoebiasis.

5.2.2 In particular, studies should be undertaken to confirm or refute the impression that illness is more severe in certain age-groups, geographical regions, and ethnic groups.

5.2.3 Longitudinal studies to assess the course of intestinal amoebiasis, the proportion of symptomatic and asymptomatic infections in defined communities, the mode of transmission and seasonality, and also possible host factors (e.g., immune status, under-nutrition, etc.) deserve consideration.

5.3 Studies on pathogenesis

5.3.1 Using the electrophoretic isoenzyme technique, E. histolytica isolates from asymptomatic and symptomatic individuals in various geographical areas should continue to be studied to confirm the relationship between the zymodeme pattern and the clinical expression of illness. These studies may be combined with community surveys (5.2).

5.3.2 Further studies are required on the pathogenesis of human invasive amoebiasis.

5.3.3 Studies of the role of immune complexes in amoebiasis should be encouraged.

5.3.4 Further efforts are needed to develop suitable experimental animal models simulating human disease.

5.4 Clinical management

The development of effective but inexpensive new drugs and/or new formulations for both invasive and luminal amoebiasis should be encouraged. A single-dose regimen will be particularly beneficial.

5.5 Immunological studies

5.5.1 Research aimed at the antigenic characterization of amoebae of different zymodeme groups should be promoted.

5.5.2 Basic studies on the role of humoral and cell-mediated immunity are essential.

5.6 Research strengthening

Efforts should be made to identify research workers and institutions in developing countries that could carry out operational and biomedical research on amoebiasis, and to provide adequate support to enable them to work independently or in collaboration with scientists in the developed world.

REFERENCES

1. WORLD HEALTH ORGANIZATION (1969) Amoebiasis. Report of a WHO Expert Committee. Geneva, WHO (Technical Report Series No. 421).

2. RAVDIN, J.I. & GUERRANT, R.L. (1982) A review of the parasite cellular mechanisms involved in the pathogenesis of amoebiasis. Rev. Inf. Dis. 4: 1185-1207.

3. SEPULVEDA, B. & MARTINEZ-PALOMO, A. (1984) Amoebiasis. In: Warren, K.S. & Mahmoud, A.A.F. (Eds): Trop. Geogr. Med., McGraw Hill, pp 305-318.

4. SARGEAUNT, P.G., JACKSON, T.F.H.G. & SLINJEE, A. (1982) Biochemical homogeneity of Entaemoeba histolytica isolates, especially those from liver abscesses. Lancet; i: 1386-1388.

5. SEPULVEDA, B. & MARTINEZ-PALOMO, A. (1982) The immunology of amoebiasis produced by Entamoeba histolytica. In: Cohen, S. & Warren K.S. (Eds): Immunology of Parasitic Infections, Oxford, Blackwell, pp 170-191.

6. WALSH, J.A. (1982) Epidemiology and magnitude of the problem of amoebiasis. A. Magnitude of the problem (morbidity and mortality on a global scale). In: Workshop on the World Problem of Amoebiasis: Current Status, Research Needs and Opportunities for Advancement. Prospect Hill, 16-18 June, 1982, pp 14-29.

7. DONTA, S.T. et al. (1977) Enterotoxigenic E. coli and diarrhoeal disease in Mexican children. J. Inf. Dis. 135: 482-486.

8. GUTIERREZ-TRUJILLO, G. (1980) Caracteristicas principales de la amibiasis invasora en el nino. Actualizacion de algunos conceptos clinicos y epidemiologicos. Arch.Invest.Med. (Mexico) 11, (Suppl. 1): 281-286.

9. ROMER, H. et al. (1978) La amibiasis intestinal en el nino. I. Estudio etiologico de las lesiones en el colon rectosigmoideo. Arch. Invest. Med. (Mexico) 9 (Suppl. 1): 375-380.

10. WORLD HEALTH ORGANIZATION (1981) Intestinal protozoan and helminthic infections. Report of a WHO Scientific Group, Geneva, WHO (Technical Report Series No 666).

11. GUERRANT, R.L. et al.(1981) Interaction between Entamoeba histolytica and human polymorphonuclear neutrophils. J. Inf. Dis. 143 : 83-93.

12. PILLAI, S. & MOHIMEN, A. (1982) A solid-phase sandwich radioimmunoassay for Entamoeba histolytica proteins and the detection of circulating antigens in amoebiasis. Gastroenterology 83: 1210-1216.

13. MARTINEZ-PALOMO, A. & MARTINEZ-BAEZ, M. (1983) Selective primary health care: Strategies for control of disease in the developing world. X. Amoebiasis. Rev. Inf. Dis. 5: 1093-1102.

14. FEACHEM, R.G. et al. (1983) Sanitation and disease. Health aspects of excreta and wastewater management, Washington, D.C. World Bank.

= = =