Special Report

INFECTIOUS DISEASES: A CHALLENGE TO DEVELOPMENT

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ABSTRACT: The 20th Anniversary of the Armauer Hansen Research Institute (AHRI) was commemorated by a symposium co-organized by AHRI, the Faculty of Medicine, Addis Ababa University and The Ethiopian Medical Doctors' Association. It was held on October 4 and 5, 1990 at the Tikur Anbessa (Black Lion) Hospital, Addis Ababa, Ethiopia. The two-day symposium was divided into six sessions which dealt with leprosy in general, control and prevention of leprosy and other communicable diseases, community health, malaria, leishmaniasis and schistosomiasis. The symposium invited scientists from Africa, Europe, Asia, the Americas and Australia who presented and discussed papers on various aspects of the above topics. This report will attempt to highlight the central theme of the symposium as seen by three young scientists from different countries connected to AHRI. Dr.Genene Mengistu (Ethiopia) - formerly Counterpart at AHRI - is a lecturer in the Department of Microbiology & Parasitology, Faculty of Medicine, and a Research scientist at the Institute of Pathobiology, Addis Ababa University, Dr.Yahya Ipuge (Tanzania) a lecturer in the Department of Microbiology/Immunology, Faculty of Medicine, University of Dar es Salaam is a holder of the AHRI African Fellowship and Dr.Tobias Rinke de Wit (Netherlands) is a Senior scientist at AHRI.

INTRODUCTION

The symposium was opened by welcome and opening addresses of the Director of AHRI, Dr.Dominique Frommel and the Minister of Health. Dr.Getachew Tadesse (Vice Minister of Health) gave the opening address on behalf of the Minster. He drew the attention of the audience to the fact that results of most research done in developing countries are published in journals in developed countries. He challenged the researchers to reverse this trend and publish their work in developing countries.

The keynote address was given by Prof. Morten Harboe, the first Director of AHRI, who underlined the activities of Dr.Gerhard Henrick Armauer Hansen as an epidemiologist.

Dr.Hansen, who first described *Mycobacterium leprae* in 1873, linked the bacilli to leprosy and demonstrated that the disease was acquired by an infectious process. It was noted that methods used by Dr.Hansen to study leprosy, such as learning from the people, are still applied today in the study of communicable diseases.

Dr.Tore Godal, the Director of WHO/TDR programme, discussed the challenges for tropical disease research in the 90's. Dr.Godal enlightened the researchers on the achievements and future research prospects in the six major tropical diseases given priority by the WHO - malaria, schistosomiasis,

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filariasis, trypanosomiasis, leishmaniasis and leprosy. Molecular biology techniques have made great contributions to research in these diseases. Between 1982 and 1988 about 100 genes encoding various proteins from the etiological agents of the six diseases have been cloned.

LEPROSY

This session covered subjects ranging from epidemiological patterns of leprosy in East Africa, clinical and immunological aspects of leprosy reactions, multi-drug therapy (MDT) and the search for anti-mycobacterial vaccines.

The trend of leprosy in East Africa was demonstrated by Dr. Debrezion Berhe, ALERT, with case studies from Ethiopia, Kenya and Tanzania. Demonstration of resistant *M. leprae* to dapsone - the mainstay of leprosy treatment since the 1940's - prompted the introduction of multiple drug therapy (MDT) regimens for treatment of leprosy. MDT regimens recommended by the WHO were gradually implemented in these East African countries from 1983 (Ethiopia and Tanzania) and 1985 (Kenya). The introduction of MDT has resulted in a substantial decline in the prevalence rate of the disease because a large number of patients are released from chemotherapy in a relatively short period. However, the fall in the case detection rate has been less dramatic. Implementation of MDT has also been accompanied by a fall in the proportion of lepromatous cases. These observations indicate a positive trend towards leprosy control. During the discussion, it was suggested that more time was needed to evaluate the effect of MDT on leprosy control. The role of other factors in leprosy control such as improvement in socio-economic status should be taken into consideration.

It was predicted that in the post-MDT period the incidence of leprosy would really decrease, but there would also be an increased chance of misdiagnosis due decreased awareness and suspicion for leprosy (Dr.G. Bjune, Oslo). The positive results in control programmes must not lead to decreased alertness. Emergence of *M. leprae* resistant to some of the drugs used in MDT may lead to an increased number of cases not responding to treatment.

With the introduction of short duration MDT regimens, leprosy patents are now susceptible to experience type 1 leprosy (reversal) reactions after completion of MDT. These late reversal reactions will occur at a time when the treated leprosy patient is susceptible to disease relapse. Dr.J. Ponninghaus (Malawi) defined relapse as renewed disease activity associated with the multiplication of *M. leprae* whereas a reversal reaction is

a type 1 hypersensitivity reaction. Since the appearance of a late type 1 reaction and a relapse can be very similar while the treatment differs there is an urgent need for a diagnostic tool to help clinicians in the field to make decisions.

A general outline of strategies to vaccinate against *M. leprae* and mycobacteria in general was given by Dr.M.J.Colston (MRC, London). These include immunisation with: (i) a related harmless cultivable bacterium, (ii) attenuated or killed mycobacteria, and (iii) specific antigens associated with protective immunity. Several *M. leprae* antigens have been defined. Most of them appear to belong to the family of heat shock proteins (12,18,28,36,65 and 70KD). A gene encoding a 180kD protein shared between *M. leprae* and a cultivate mycobacterium is being cloned in a shuttle plasmid. This construct will be used in the attempt to transform the non-protective cultivable mycobacterium into a protective vaccine against leprosy. Dr.R.Kiessling reported on his studies on the effects of intradermal injection of rIL2 in LL patients. This treatment resulted in activation of macrophages and other cells.

CONTROL AND PREVENTION OF LEPROSY AND OTHER COMMUNICABLE DISEASES

This session deliberated on the feasibility of integration of leprosy control in primary health care and prospects for new vaccines against tropical diseases. The experience of Tanzania in integrating tuberculosis and leprosy control programmes was presented and discussed (Dr.H.Chum, Dar es Salaam, Tanzania). In the discussion, a phased approach as that used in India was recommended.

Factors impending the development of new vaccines against tropical diseases were discussed in a paper presented by Dr.J.M. Dupuy (Lyon, France). It was observed that although almost all vaccines are produced in industrialised countries, most of the currently available vaccines are used in developing countries. Development of new vaccines is, however, not an attractive venture for industries since it is not economically rewarding. In addition, priorities for candidate vaccines in the developing versus industrialized countries at present differ. Developing countries lack financial resources and appropriate technology for development of new vaccines against tropical diseases. In an attempt to overcome these problems, WHO/TDR has embarked on a novel idea to integrate with the industry for financing of vaccine development and production. This may eventually solve the problem of lack of funds for development of new vaccines against tropical diseases.

COMMUNITY HEALTH

The role of availability of safe and adequate water in health programmes was discussed with reference to Ethiopia and experiences in the Gambia and Burkina Faso (Mr.Gebre-Emmanuel Teka, Addis Ababa). It was noted that although water is a basic need for life, it is also important in the control as well as in the spread of water-borne diseases. In order to be effective, provision of safe and adequate water should go hand in hand with improvement in sanitation and waste disposal. In Ethiopia, implementation of the WHO water and sanitation decade, 1980-1990 has improved the water coverage in rural areas from 25% in 1983 to 39-83% in 1990. However, sanitation coverage increased from 14% to 36% only.

The provision of safe water should also take into consideration that most of the water is contaminated after collection from the source. This was exemplified by observations from Burkina Faso (Dr.Frommel, AHRI) where modern technology was used for provision of water supplies to some villages. The quality of the water at most of the sources (88%) was within the WHO standards, but only 12-45% of the water collected for home use remained within the WHO quality standards.

MALARIA

This session began with an overview of the epidemiological pattern of malaria in Ethiopia by Dr.Assefa Nega (Addis Ababa). The role of mass migration associated with village settlement schemes, war, famine, droughts and floods in the extensive spreading of the disease was discussed. It was shown that, there is a gradual increase in the incidence of malaria in Ethiopia with relatively more *Plasmodium falciparum* (often chloroquine resistant) than *P.vivax*. The implication of the changing distribution pattern and the emergence of chloroquine-resistant *P.falciparum* were highlighted.

Bio-environmental strategies for malaria control were discussed with reference to experiences from the Gambia (Dr.S. Lindsay). It was emphasized that community participation is necessary for the success of any

control strategy. Very encouragingly, these studies from the Gambia showed that the use of impregnated bed nets not only decreased the incidence and mortality of malaria, but also decreased the overall mortality from other infectious diseases in children.

Presenting a paper on the chemotherapy of malaria, Prof.L.A.Salako (Nigeria) stressed the continued reliance on chloroquine as the first line drug despite the emergence of chloroquine resistant *P.falciparum* in many parts of Africa. It was emphasized that oral administration of chloroquine should be preferred over the parenteral route as it is cheaper and involves less risks for adverse drug effects and spread of human immunodeficiency virus (HIV). Bio-availability of chloroquine after a single oral dose is much higher than after intramuscular administration. However, in seriously ill patients who cannot swallow, intravenous infusion must still be used. Care should be taken to avoid over dosage in children with protein-energy malnutrition (kwashiorkor) since they have a very slow plasma clearance of chloroquine. Alternative drugs include Fansidar, Mefloquine and Halofantrine - now in clinical trials. The new Chinese drug, Quinghaosu was mentioned as a possible drug of choice for malaria in future.

The prospects for an anti-malaria vaccine were presented on the basis of ongoing studies in Senegal and elsewhere (Dr.Luiz Pereira da Silva, Paris, France). There is a difference in the response to malaria infection between children and adults. Whereas most children develop clinical disease, adults exhibit resistance. Passive transfer of IgG from adults to children has been shown to give resistance in vivo although no neutralizing activity is demonstrated in vitro. Proteins from protective sera have been purified and have been shown to confer protection in vivo, however, the use of recombinant proteins lead to development of auto-reactive antibodies in the recipient. In the discussion it was mentioned that attention should also be focused on the search for a vaccine against clinical disease rather than anti-parasite vaccines (Dr.R. Mashana, Fraceville, Gabon). The role of anti-tumor necrosis factor antibodies in the prevention of clinical disease are being studied.

LEISHMANIASIS

Dr.A.D.M Bryceson introduced leishmaniasis, which in the late 1950's was described as strange skin disease comparable to lepromatous leprosy. As in leprosy, the cell-mediated immune response determines the pattern and outcome of the disease. It has been shown that lipophosphoglycans which are among the surface molecules on the leishmania parasites have immunosuppressive properties in mouse models. The carbohydrate moieties of these molecules block antigen presentation with HLA class II molecules in a non-specific way. Studies on HLA and Leishmaniasis have not been performed yet. Dr.Tamas Laskay (AHRI) reported on the successful use of *L.m.mexican* oligonucleotide in the polymerase chain reaction (PCR) to amplify *L.aethiopica* specific DNA from sandfly specimens and paraffin embedded skin biopsies. In the near future the PCR technique will be used to detect parasite DNA on blood samples from (suspected) visceral leishmaniasis patients.

SCHISTOSOMIASIS

An overview of the magnitude of the epidemiology of schistosomiasis in Africa was presented highlighting the distribution patterns of *Schistosoma haematobium, S.mansoni* and *S.japonicum* (Dr.S.K. Chandiwana, Zimbabwe). The prevalence of infection in an endemic area is related to population density and the prevailing climatic conditions.

Prof.M.M.A Homedia (Khartoum, Sudan) discussed the control and treatment of schistosomiasis. A significant breakthrough in the control and treatment of schistosomiasis was the introduction of praziquantel. This drug, given as a single oral dose, is active against all species of schistosoma. However, in order to control the disease, there is a need for a change in the habits of the people. Developmental projects in agriculture, irrigation and livestock keeping if not properly planned are associated with an increase in disease transmission.

The last paper in this session discussed the role of Endod, a natural pesticide extracted from the *P.dodecandra* plant. This natural product can be used to replace expensive chemical molluscicides in the control of snail vectors in developing countries (Dr.L. Wolde-Yohannes). The probable mode of action of Endod is by interfering with Ca^{++} influx leading to destruction of the snail by osmosis. Since Endod was discovered in 1964, a careful selection program has resulted in the establishment of at least 10 stable

p.dodecandra subspecies that produce high yields. This plant originating from Ethiopia, has now been introduced in several African countries and abroad. A noted advantage of this natural product is its negligible toxicity to humans compared to the chemical agents.

On the prospects of a vaccine against schistosomiasis, Dr.T. Godal mentioned that, several antigens have been identified but they give only 30-60% protection in animal models.

CLOSING REMARKS

Prof. Asrat Woldeyes (Dean, Faculty of Medicine, Addis Ababa University) reminded the participants to learn from experience. Many of the so-called new strategies in disease control have been tried in the past. He also drew attention to the adage "in order to manage you must diagnose" to emphasize the need for a thorough study of a problem before institution of control measures. On community involvement in disease control Prof. Woldeyes posed a question: "The way we want or the community wants?"

CONCLUSION AND RECOMMENDATIONS

This was a meeting which invited researchers who are leading experts in various subjects under discussion as well as experts from the WHO. The selection of topics was very appropriate to the theme of the symposium. There is no doubt that most participants benefitted immensely from this symposium. The 40th anniversary of the institute will be after the year 2000. If one has to organize a similar symposium for the occasion, it would be appropriate to consider what has been achieved in relation to the theme "Health for all by the year 2000". The contribution of research at AHRI on improvement of basic health services will have to be underlined. Attempts should be made to obtain sponsorship for more young scientists to attend such symposia where they can gain experience from leading scientists in various fields of research.