BOOK REVIEWS

Lechat, M. F., Misson, C. B. and Walter, J. *OMSLEP. Recording and Reporting System for Leprosy Patients.* Geneva, Switzerland: World Health Organization, 1981, 75 pp. (available in English, French, and Spanish)

Planning of leprosy control activities should be based on a program or project formulation with an in-built evaluation component, as has been proposed, for instance, in the WHO document "The use of formulated plans of action for national leprosy control programmes" (LEP/79/1).

The process of continuous evaluation of control activities requires the use of a method for collecting, processing and analyzing information on clinical, epidemiological, and operational aspects of the program or project.

The need for such information systems has become even more urgent under present circumstances when leprosy control has reached a turning point, for the following two main reasons:

1) The control activities which, in general, have been carried out up to now through vertical programs, are to an increasing degree being integrated into the general health services, particularly within the primary health care approach, and it is accepted that this is the only way by which it will be possible to cope adequately with leprosy in countries which are also faced with many other health problems.
2) While the integration process calls for simplified methodologies, the increasing threat caused by resistance to drugs coupled with the problem of microbial persistence has made mandatory the use of combined chemotherapeutic regimens, which will result in greater operational complexity than the dapsone-based strategy.

The collection of data on leprosy control activities has been established in most countries, if not in all; guidelines on this aspect of monitoring control programs have been proposed by the WHO Expert Committee on Leprosy.

However, we are now facing a new requirement. In integrated programs the information compiled for processing should be as simple as possible, so that it can be collected at the farthest periphery by multipurpose health workers with the minimum of specific training. This requires the identification and selection of the minimum of information necessary to evaluate the progress of control activities. Obviously there are advantages if a single system of recording and reporting is used throughout any one country. And if the same system is applied in as many countries as possible, then there will be significant additional benefits: it will be possible, for example, to correlate epidemiological improvements with different methods for case-finding and case-holding.

Faced with this problem the WHO Leprosy Unit decided in 1976 that an attempt should be made to improve the situation, and requested the collaboration of the Epidemiology Unit of the School of Public Health in Louvain University, Brussels, Belgium, headed by Professor M. F. Lechat. The result of this collaboration is the information system called OMSLEP, which is presented in this booklet.

The first step in the development of OMSLEP was a detailed analysis of systems in use in some 80 countries or projects. After several revisions, the OMSLEP system in its present form has been tested in 16 countries.

It is not intended to propose that the OMSLEP system should be adopted without any modification. On the contrary, we fully expect that some adaptations will have to be made in individual countries, for example, in respect to the Individual Patient Form. However, before deciding on an adaptation at country level, the health authorities should keep in mind the essential principle that the information to be collected must only be information which will be utilized for decision making.

The OMSLEP system has been so designed that it is easy to transfer the data to a computer. This has been done because the development of low-cost mini-com-

puters makes it probable that they will increasingly come into use in the health services of endemic countries. It would then be possible to produce reliable, continuously updated information on the essential aspects of leprosy work.

From the time taken to develop the OMSLEP system, it is obvious that it has been the subject of many discussions and improvements. Here credit should be given to some of those who, besides the authors, have made important contributions to this effort, in particular, Dr. K. Seal, WHO consultant, Dr. S. K. Noordeen, Miss J. Gambke and Mr. M. O'Regan of the WHO Leprosy Unit; and moreover to all those, too numerous to be cited individually, who participated in the testing of the system in the various countries.

The essentials of this booklet were previously included in the WHO publication "A Guide to Leprosy Control" (1980), as well as in the WHO "Weekly Epidemiological Record" (1981, 56, 265–270, no. 34). This booklet represents an expanded version of the previous documents, with some amendments. We are indebted to the Damien Foundation which generously supplemented the WHO financial support for the development of OMSLEP.

Finally, we take pleasure in dedicating this booklet to all those who expend their time and energy in the fight against leprosy, in the hope that it may make the follow-up of their achievements easier and more reliable.—Foreword by H. Sansarricq

Michal, F., ed. *Modern Genetic Concepts and Techniques in the Study of Parasites*. Tropical Diseases Research Series: 4. Proceedings of a Symposium held in Geneva, Switzerland, 27–29 May 1980. Basel: Schwabe & Co. AG, 1981, 430 pp. SFr. 56.00/DM 67.00.

There has as yet been little exploitation of recent advances in molecular biology and molecular genetics in the study of parasites. A symposium on Modern Genetic Concepts and Techniques in the Study of Parasites was held in Geneva, 27–29 May 1980, by the Biomedical Sciences Scientific Working Group of the UNDP/WORLD BANK/WHO Special Programme for Research and Training in Tropical Diseases. The purpose was to identify possible applications of modern genetic concepts and techniques, including recent advances in molecular biology, to the study of tropical disease pathogens. The symposium brought together geneticists and molecular biologists as well as tropical disease specialists in a multidisciplinary search for better understanding of the problems and the ways to help develop strategies for improvements in disease control.

In the first two sessions the meeting was presented with current information on basic molecular biology and genetics, including the genetics of coexistence of parasites and man, the mechanisms of genetic adaptation by which different species selectively interact, and determinants of interaction between host and parasite. Genetic control of the host response and its relation to susceptibility or resistance to infection were also subjects of the meeting. The application of recent advances in molecular biology, including recombinant DNA technology, to parasite identification, diagnosis of disease, understanding of the pathogens and improved control of the diseases, was a major subject of discussion.

The two chapters of particular interest to leprosy workers are:

Chapter 7: The HLA System: Its Role in Disease Susceptibility and in the Immune Response by J. J. van Rood

In all mammalian species studied so far, a system of closely linked genes called the major histocompatibility complex (MHC) has been recognized. In humans this MHC system is called the human leukocyte antigens (HLA) system. It comprises genes coding for cell-surface determinants and complement factors (C_2 C_4 Bf). Two types of HLA coded cell-surface antigens can be recognized: 1) those present on all nucleated cells coded by the A, B, and C loci, and 2) those with limited tissue distribution and found most easily on B cells and macrophages, coded for by the D and DR loci. General characteristics are the large polymorphism and the phenomenon of linkage disequilibrium. Both phenomena most probably reflect natural selection.

Apart from the well-established involvement of the MHC products in the allograft rejection, a large number of reports indicate that the MHC has a pivotal position in the

immune response. It was shown in both the guinea pig and the mouse, that the ability to raise an immune response against a variety of antigens is dependent on the presence of genes located within the MHC, the so-called immune-response genes (Ir-genes). Since the homology of the MHC in different species is so striking, one might suspect that genes play a role in the preservation of the species by providing a selective advantage.

It seemed attractive to ascribe the association between HLA (the human MHC) and certain diseases to the involvement of human Ir-genes, at least in the association with those diseases in which the immune response plays a role in pathogenesis. Autoimmune disorders and infectious diseases are good examples. Experimental data indicate that Ir-gene products are, at least in part, identical to type I antigens (HLA-A, -B, -C and -DR antigens). For instance, in malaria patients it was shown that good humoral response after *Plasmodium vivax* infection was associated with A-locus antigens (Bradley, *et al.*, personal communication). De Vries and colleagues (1979) showed that B-locus antigens controlled resistance in yellow fever and/or typhoid fever. By *in vitro* experiments Greenberg showed that high responsiveness to streptococcal antigens was associated with HLA-B5. The specific cellular response *in vitro* after vaccination for smallpox was shown to be promoted by the absence of HLA-Cw3 (de Vries, *et al.*, 1979). Finally, it was found that in Indian families tuberculoid leprosy is associated with HLA-DR2.

In summary, although the actual function of the HLA system awaits definite elucidation, it seems more and more evident that one of its major tasks is to serve in the cell-to-cell collaboration in the immune response and in resistance against infectious diseases.

Chapter 20: Genetic Aspects of Leprosy by M. Harboe

Genetic factors may be decisive at several points on the chain of events occurring after infection with *Mycobacterium leprae* in man, leading to control of the infection without clinical symptoms or to leprosy, which shows a varying course between two polar groups: tuberculoid leprosy with few lesions with few bacilli, and lepromatous leprosy where the bacilli grow without inhibition due to defective cell-mediated immunity (CMI). Evidence from twin, family, and population studies indicate that genetic factors of the host play a role in determining susceptibility and/or type of response to the infection. The mechanisms and the extent of the genetic influence are unknown.

Additional knowledge on genetic factors should be sought both in man and in experimental models.

In man additional family studies are required to confirm and extend the current view that gene(s) linked to the HLA locus determine susceptibility to tuberculoid but not to lepromatous leprosy. Studies on patients and their HLA-D identical siblings permit experiments on mixtures of cells from lepromatous leprosy patients and normal individuals to determine if the defective CMI is due to a defect in lymphocyte or macrophage function and the importance of suppressor mechanisms. Many data indicate that a consistently negative lepromin reaction predisposes to development of lepromatous leprosy. Population and family studies should be explored to establish if there is a genetic basis for this characteristic and if it is linked with the HLA locus or markers on another chromosome.

The selection of experimental models is important at various levels. *M. leprae* in mice? *M. leprae* in armadillos? Or another, slowly growing mycobacterium (*M. lepraemurium*—MLM) in mice? We favor MLM in mice because it is a natural pathogen in mice. Various inbred mouse strains differ markedly in susceptibility to MLM. We have extensive knowledge on the immune system and how to manipulate it in mice. Several techniques permit localization of genetic defects in mice, and this is a new and very potent method to define the mechanisms of decreased resistance to infection. Resistance to various infections is known to be determined by genes in the H2 locus and on several other chromosomes. Several genes probably determine the degree of susceptibility and the course of MLM infection in mice. Localization of these genes would provide new means for studies of mechanisms of protective immunity and lack of resistance in mycobacterial infection. This is of immediate interest in prophylactic work, since the prospects for the suc-

cess of vaccination may depend to a great extent on the nature of the defect in susceptible strains and man. Selection of criteria for evaluation of the host response is more important than is generally realized. Ability to prevent growth of the infective microorganisms is essential to the host, but strong hypersensitivity reactions may have serious consequences for the host even with a modest bacterial load. Depending on the criterion used—counting of bacilli in the footpad after local inoculation, degree of local hypersensitivity reaction, time of death after intravenous injections of a large dose of MLM—the classification of strains as susceptible and resistance varies drastically. These variations should be carefully considered, explained, and controlled during experimental design, and related to important clinical features of leprosy in man.—RCH

Proposed International Guidelines for Biomedical Research Involving Human Subjects. A joint project of the World Health Organization and the Council for International Organizations of Medical Sciences. Geneva, Switzerland: CIOMS, 1982, 49 pp.

Over the past few years, the Council for International Organizations of Medical Sciences (CIOMS) has provided a forum for discussion of moral and ethical issues of the application of new scientific and technological knowledge to the practice of medicine.

The international guidelines for biomedical research involving human subjects that are now proposed are the results of a study initiated in 1976 by CIOMS in collaboration with WHO. They were drawn up after a series of extensive consultations with individual experts, representing a wide variety of backgrounds, and are based on the replies to a questionnaire received from national health administrations and medical faculties in many developing countries. The original version of the guidelines received, during 1980, the benefit of the comments of an *ad hoc* WHO/CIOMS working group, of the WHO Advisory Committee on Medical Research, and of a CIOMS Round Table Conference held in Mexico City.

The fundamental ethical principles that guide the conduct of biomedical research involving human subjects, and on which these guidelines are based, are embodied in the World Medical Association's Declaration of Helsinki, as revised by the 29th World Medical Assembly in Tokyo in 1975. The guidelines, which have been drawn up in the form of a general survey followed by specific recommendations, are intended to indicate how these principles can be effectively applied, particularly in developing countries, taking into account socio-economic circumstances, national legal provisions and administrative arrangements.

The guidelines, in their present form, were endorsed in September 1981 by the 56th Session of the CIOMS Executive Committee and in October 1981 by the 23rd Session of the WHO Advisory Committee on Medical Research, and recommended for wide distribution as a consultative document to ministries of health, medical research councils, medical faculties, relevant nongovernmental organizations, and medical journals as well as any other interested institutions, including research-based pharmaceutical companies.—Introduction by Z. Brankowski, Executive Secretary, CIOMS

Ramalingaswami, V. *Annual Report of the Director-General 1980–81, Indian Council of Medical Research.* Satyavati, G. V., ed. New Delhi: Cambridge Printing Works, 1982, 265 pp.

The following is that portion of the report dealing with the leprosy research activities:

The Council continued its studies on the clinical aspects, pathogenesis, immunology, chemotherapy and microbiology of leprosy, which continues to be a major communicable disease occurring in the country. These investigations are being undertaken at the Council's Central Jalma Institute for Leprosy (CJIL) at Agra and other centers.

The CJIL continued its service activities and facilities for patients in an area within a radius of about 200 km. With a view to involving the community in its activities, the Institute has set up a field unit in Bharatpur district of Rajasthan. This unit will serve a population of 100,000.

Chemotherapy of leprosy

Long-term results of rifampin therapy

In an attempt to study the magnitude of persister organisms following sequential

therapy of rifampin followed by dapsone (DDS), patients who had completed 2 years of regular treatment were investigated for viable organisms. The patients investigated were those who had received 300 mg rifampin daily for 3 months followed by DDS 100 mg daily for another 19 months. At the end of 2 years, bacillary inoculation from skin into mouse foot-pad resulted in multiplication in 3 of the 6 cases who had completed 2 years regular treatment, all the patients having shown good clinical and bacteriological improvement. The study highlights the fact that a short course of rifampin followed by DDS is not sufficient to kill a large majority of organisms. Similar investigations in patients who were given single dose rifampin and intermittent rifampin are in progress.

Persister organisms in patients under different drug regimens

Serial studies of the therapeutic effect of various drug combinations on bacillemia and bacteriological positivity of the nasal smears has been reported earlier. These cases have been followed up further. Nineteen cases have completed a period of 27.25 months and 26 cases a period of 19.5 months on an average. In those cases who had completed 2 years of treatment scrotal biopsies were performed in order to obtain information on the viability of the persister organism in the dartos muscle by animal inoculation. It was observed that among the combinations of drugs so far used, dapsone and rifampin combination is superior to the others. Dapsone and clofazimine and DDS and thiacetazone were equally effective. It has been found that in the control group on DDS alone, there was growth in all but one of the 5 subjects investigated.

Multidrug therapy in leprosy

In order to prevent the emergence of drug resistance and to obviate persistence of organisms in multibacillary forms of leprosy, different drug combinations are under trial. In experimental studies, prothionamide and ethionamide have been shown to be potent antileprosy drugs with bactericidal action. Studies in lepromatous patients using prothionamide alone are lacking. However, a study on the combination of this drug with rifampin (RFP), INH and DDS has been initiated. The patients are being given RFP 300 mg daily for the first month along with prothionamide (500 mg), INH (300 mg) and DDS (100 mg) daily. Prothionamide and INH are being discontinued at the end of 3 months. This combination has been undertaken to see whether the simultaneous administration of potent drugs initially, followed by DDS alone is in any way able to reduce the long-term twin problems of resisters and persisters. Early effect is also being monitored. Twenty cases have been included in the study. The results of this investigation will be compared with patients on daily RFP for 3 months followed by DDS. Since in the treatment of tuberculosis, pyrazinamide has been found to clear persister organisms, a study has been initiated with a view to investigate whether inclusion of pyrazinamide in drug combinations in leprosy would have a similar effect. Various combinations of DDS, clofazimine, thiacetazone, rifampin and pyrazinamide are under trial in this study.

Immuno-adjuvants in lepromatous leprosy

Treatment with levamisole was continued during the year in order to stimulate the immunological response in cases of lepromatous leprosy who had had long years of treatment but who were persistently bacteriologically positive. To the previous numbers more cases have been added and the earlier cases have been followed up.

It was found that 3 cases had become bacteriologically negative, and 8 cases had registered a decrease of over 50% in BI in 6 weeks. Clinical improvement was marked in all but two. Some lepromin response was obtained in 12 cases. However, frankly positive reactions were obtained only in six cases. These reactions were only temporary and were abolished after 4 months. The bacteriological improvement was maintained. Seven cases have become bacteriologically negative after one year. Animal inoculation had been performed in 3 cases where dapsone resistance was suspected. In one case there was growth but the organisms were found to be sulfone sensitive.

Fixed regimen therapy in non-lepromatous cases

An arbitrary period of treatment following a stage of clinical inactivity has been

the convention. While this may be justified to some extent in lepromatous cases, in non-lepromatous (T and BT) cases this may not be necessary. To investigate whether the treatment could be safely discontinued once the point of inactivity is reached in T/BT cases, "fixed regimen therapy" was initiated. A total of 100 cases were included in the study. In 43 cases treatment was discontinued at the point of their becoming inactive. Nine patients discontinued treatment on their own. These two groups are being followed up, with an aim to compare the relapse rates, if any, in these groups with a control group in whom treatment is being given in the conventional way. The study is in progress.

Sulfone resistance

The mouse foot pad model is being extensively applied in several laboratories to confirm sulfone resistance, which is now posing a major problem in the treatment and control of leprosy. A total of 44 patients have so far been investigated for this problem at CJIL. Of these, viable bacilli were present in the control animals in 36 cases. Fifteen cases were found to be fully resistant to sulfones, three being partially resistant. The remaining 18 were found to be sensitive to sulfones. Studies on sulfone resistance are also being undertaken at the Central Leprosy Teaching and Research Institute (CLTRI) at Chingleput.

Chemoprophylaxis against leprosy with acedapsone

A study on acedapsone prophylaxis was undertaken by the CLTRI, Chingleput, in 8 leprosy clinics in Madras city among 700 child contacts of 331 lepromatous and other multi-bacillary cases of leprosy attending the clinics. Sixty-four new cases of leprosy had occurred among the study subjects during the course of the study: 22 in the acedapsone prophylaxis group and 42 in the control group. Detailed analysis of the findings is in progress.

Another study on short-term chemoprophylaxis against leprosy with acedapsone has been started in Madras city to find out the effectiveness of a limited period regimen of acedapsone prophylaxis in contacts of lepromatous and other multi-bacillary cases of leprosy. Here three injections of acedapsone are to be given at intervals of 10 weeks. A total of 662 contacts below the age of 15 years, from the households of 315 lepromatous and other multi-bacillary cases of leprosy getting treatment in 8 leprosy clinics in Madras city, have already been screened. The subjects will be followed up at 10 week intervals during the first year and at intervals of 26 weeks for a further period of 3 years. If this long-term follow-up of the contacts treated for a limited period with acedapsone indicates its effectiveness, this will then be a method of chemoprophylaxis with a higher operational feasibility.

Ichthyosis due to clofazimine therapy

In an attempt to find the cause of the increased ichthyosis in patients on clofazimine therapy, a study was undertaken in 40 lepromatous cases, where clofazimine levels and granuloma index were compared in the ichthyotic and non-ichthyotic skin of the same patients. Levels of clofazimine were found to be significantly higher in the ichthyotic skin compared to non-ichthyotic skin. Likewise, the granuloma size as seen in histopathological sections was larger in the ichthyotic area as compared to the non-ichthyotic skin.

An attempt has been made to correlate the levels of clofazimine to those of vitamin A in the ichthyotic skin of leprosy patients treated with clofazimine. The levels of both vitamin A and clofazimine were also evaluated in the normal skin of the same patients. Thirteen lepromatous leprosy patients, 5 LL patients in reaction, 3 BT and 1 BL patient, have so far been studied. The results obtained indicate a decrease in vitamin A content and an increase in clofazimine content of ichthyotic skin as compared to those of normal skin of the patients under study. Further studies are in progress by administering vitamin A with clofazimine.

Clinical studies

Cardiovascular status in leprosy

The cardiovascular status was evaluated in 140 patients of lepromatous leprosy, 40 patients of borderline leprosy and 20 patients of tuberculoid leprosy. Family members of patients matched for age and sex

were also examined and investigated as controls for the different groups. The results show that there is higher frequency of involvement of the cardiovascular system in leprosy patients as compared to the controls. Most of the patients had ECG abnormalities which included rhythm disturbances and ventricular hypertrophies, and sometimes raised enzyme levels. The data are being analyzed.

Disabilities in leprosy patients

An assessment of disabilities among a random selection of 1057 cases out of 15,000 cases registered at CJIL was made. It was found that the ulnar nerve was the most commonly affected nerve. The radial nerve was the least affected (3 cases only). The involvement of other nerves was in the following order: posterior tibial, median, lateral popliteal and facial nerves, respectively. There were 44 cases of nasal deformities in LL cases only. The grading of deformities was done as per WHO criteria. Approximately 46.5% were grade I deformities, 16% grade II and 2% grade III. It was found that grade I was most predominant, indicating that intensive teaching of the care of hands and feet was necessary.

Surgical correction of deformities

While several reconstructive surgery units have been started in south India to provide facilities for correction of deformities in leprosy there are few such centers in northern India. Thus, a great need has been felt to develop a reconstructive surgery unit at the CJIL, Agra. A surgeon specially trained in reconstructive surgery has initiated efforts in this direction. There has been a steady progress of surgical operations and it has been possible to carry out during the year a total of 610 operations for correction of claw hand, opponens plasty, foot drop correction and nerve decompression, among others. The functional and cosmetic results of the operations have been very satisfactory and consequently there has been an increased demand for these operations.

Ulnar nerve decompression

Studies are being continued to establish the role of nerve decompression in the management of ulnar neuritis. The cases have been followed up for 12–88 weeks post-operatively. Relief from pain has been noted in practically all the cases. However, a few patients experienced pain in the operated nerve during reactive episodes. This pain was milder as compared to that occurring in non-operated nerves. There is no protection from pain in patients developing ENL lesions in the nerves. Sensory motor recovery was unpredictable but in a few cases who had paralysis of shorter duration (less than 2 months), the recovery was better. It is not clear whether the surgery helped in the recovery or the latter occurred spontaneously. Sensory recovery started earlier i.e., usually at the end of the second week following operation; whereas motor recovery took about 6 to 8 weeks to be appreciable.

Microbiological studies

Bacillary excretion in the milk of lepromatous patients

One of the causes of increased incidence of leprosy among the children of lepromatous patients is their exposure to a heavy dose of infection. An alimentary route of infection following the excretion of bacilli in breast secretions has been suggested. In a study conducted in the CJIL, Agra, 38 female leprosy patients were studied for bacilli in the breast milk. Twelve of the patients comprising 10 LL and 1 each of tuberculoid and borderline cases, showed bacilli in their milk; only 1 of these was on treatment. AFB count in 10 ml of milk was found to range from 4.3×10^4 to 15.3×10^4. While the possibility of the alimentary route of infection might be considered, the presentation of the antigen through the alimentary route might result in an altered immunological response.

Leprosy bacilli in the female genital tract

It is established that leprosy patients, particularly of lepromatous type, excrete large number of lepra bacilli through skin and mucous membranes. A study of female genital tract in leprosy patients has been undertaken with the object of finding the presence of acid-fast bacilli in the vaginal secretions and to establish whether these could be *M. leprae*. Of the 15 female lepromatous patients examined, acid fast bacilli were found in 5 (33.3%). However, *M.*

scrofulaceum was recovered on Dubos agar from 3 cases. On Lowenstein-Jensen medium, bacilli from two cases showed growth. In two cases, however, no growth was seen in either of the media. It is, therefore, concluded that acid-fast bacilli could be detected in the vaginal secretions but they could, in all probability, be saprophytic mycobacteria. The study is being pursued further.

Effect of clofazimine on the morphology of lepra bacilli

While carrying out routine investigations of the morphology, it was observed that in two cases on clofazimine therapy, there was sudden increase in the morphological index (MI) with very elongated solid bacilli. It was thought that clofazimine might possibly have some effect on septum separation of mycobacteria, particularly of *M. leprae* which might be responsible for such morphological alterations.

Ten other patients who were on clofazimine therapy were investigated for the possible effect of clofazimine on MI. Smears were taken by slit-smear technique and were stained by Ziehl-Neelsen method. No tinctorial or morphological alteration was observed in any of these patients and MI declined gradually in all those cases. No growth was observed on Lowenstein-Jensen medium. It appears therefore, that clofazimine does not produce any such morphological changes in *M. leprae*. It is likely that the highly elongated acid-fast bacteria originally observed were some aberrant forms or some different species of mycobacteria present in the skin.

Immunological studies

Complement catabolism and fibrinolytic activity in patients

With a view to determine an early parameter to identify patients going in for reactions, a study was undertaken in 60 patients both during reaction and the quiescent stage. The fibrinolytic activity was assessed by euglobulin lysis time, ethanol gelation test and plasma fibrinogen levels. The results indicated a general lowering of fibrinolytic activity during reaction. It is proposed to extend these investigations to establish the results in order to provide data which might possibly help in predicting lepra reaction.

Effect of chloroquine on the complement and the coagulation systems

Chloroquine is used to control certain types of reactions that occur in leprosy. As the complement system appears to play an important role in the pathogenesis of some of the reactions, the effect of chloroquine on the complement system was studied. Further, since it is known that the fibrinolytic activity is altered in patients during reaction, the effect of chloroquine on the coagulation system was also investigated.

Chloroquine was found to inhibit the complement mediated lysis of antibody coated sheep erythrocytes (for classical pathway) and normal rabbit erythrocytes (for alternative pathway). In addition, using two dimensional electrophoresis it was shown that the conversion of C3 to C3c by zymosan and aggregated IgG was inhibited by chloroquine. Chloroquine was able to inhibit thrombin-mediated clotting of normal plasma in a dose-dependent manner. This effect was, however, reversed on adding excess thrombin.

It is thus seen that chloroquine inhibits the activation of two acute phase systems *in vitro*. Since it has been shown by other investigators that chloroquine is able to prevent the release as well as action of various hydrolases which are tissue damaging, it could be postulated that chloroquine exerts its anti-inflammatory activity by inhibiting the action of hydrolases and proteases.

Identification of skin reactive component(s) from Dharmendra antigen

Dharmendra antigen when subjected to electrophoresis separates clearly into two different components—the anionic and cationic components. The anionic component does not form any visible precipitin line with antibody (leprosy sera), while the cationic component forms a distinct precipitin line with the antibody. These two components were eluted, purified and injected intradermally in tuberculoid leprosy patients. For a comparative study of skin reactions, Dharmendra antigen and leprosin A were also injected simultaneously. While the cathodal fraction did not exhibit any delayed type of hypersensitivity (DTH) reaction, the anodal fraction evoked a true DTH reaction which was almost akin to other lepromins.

Rather, this fraction evoked a stronger DTH than other standard lepromins. However, the cathodal fraction, while not showing any DTH evoked an early reaction after 6 hours of inoculation. These reactions were biopsied from a few cases and were studied histologically. While the anionic component mainly evoked a lymphocytic infiltration, the cationic component evoked predominantly a polymorphonuclear cell infiltration. Further studies are in progress for purification of the anionic component which might yield a true type IV reaction *in vivo*.

Isolation of soluble skin reactive component(s) from biopsies of tuberculoid and borderline tuberculoid patches

M. leprae is rarely noticed in skin smears or in biopsies of tuberculoid (TT) and borderline tuberculoid (BT) lesions. In spite of this low concentration of the organism the host tissue reaction is expressed for a long time and the reason for this is not known. The organisms present in the lesion might be continually destroyed by the host tissue reaction (CMI). If this hypothesis is true, one can envisage the presence of soluble antigens of *M. leprae* in these lesions. The presence of skin reactive antigens in TT and BT lesions was, therefore, looked for.

Biopsies were obtained from lesions of TT and BT patients. Biopsies were also taken from the normal skin of these patients which served as control. The tissue extracts were prepared and these materials were injected intradermally. In all the cases the early skin reactions were almost double with antigen extracts of lesions when compared to those obtained with normal skin extracts. However, no late reaction was noted with normal skin extracts. On the other hand, the extract from lesions evoked mostly a late reaction at the site of inoculation. Identification of *M. leprae* antigen in extracts of BT and TT lesions is in progress.

Continuous bacillemia in lepromatous leprosy

Hematogenous spread of leprosy has been an object of intense investigation from the turn of the century. Employing the hemolysis method bacillemia was studied in 45 leprosy patients of whom 27 were LL, 7 were BL type and 11 cases were of BT type. All of the 27 LL patients showed AFB. Out of 7 BL patients, 4 showed AFB and out of 11 BT patients, 8 showed AFB in blood.

For determining the occurrence of continuous bacillemia in leprosy cases, it was possible to examine the blood samples at 12 hour intervals for 3 days in 23 out of 45 cases. These included 16 LL cases, 2 cases of BL and 5 cases of BT. Out of 16 LL cases, 9 showed continuity of bacillemia; while out of two BL cases, one showed continuity. None of the BT cases showed continuous bacillemia. If during three days of blood sampling the blood was negative for AFB in two consecutive samples, the patient was not considered to be in the phase of continuous bacillemia.

Fluorescent leprosy antibody absorption (FLA-ABS) test for early serodiagnosis of leprosy

The FLA-ABS test has been standardized and found to be sensitive and specific. This test could be used to identify *M. leprae*. Further specific antibodies to *M. leprae* could be demonstrated in cases of leprosy. The FLA-ABS test has been found to give positive results in healthy contacts, indicating subclinical infection. FLA-ABS technique aided by lepromin test is being used for identifying the people at risk. A comparison of positivity of FLA-ABS test with lepromin in contacts is being continued.

Biochemical studies

Lipoprotein cholesterol analysis in the sera of leprosy patients

Male patients of three different age groups, i.e., 30–40, 40–50 and 50–60 years were studied. It was seen that the HDL cholesterol to total cholesterol ratio was significantly raised in both treated and untreated leprosy patients in all the three age groups, as compared to healthy controls. The data suggest that the risk of myocardial infarction due to atherosclerosis might be less in leprosy patients.

Beta-hydroxy methyl glutaryl CoA (HMG-CoA) to mevalonate ratio in the sera of leprosy patients

Earlier studies on lipid profile conducted at the CJIL, Agra, had revealed subnormal

levels of cholesterol in the blood of leprosy patients, especially in lepra reaction. Hence an attempt was made to study whether this decrease in cholesterol was due to utilization by the invading organism (*M. leprae*) or due to defective synthesis or increased catabolism of cholesterol by the host. The HMG-CoA to mevalonate ratio was taken as an index of the activity of HMG-CoA reductase, a key enzyme that regulates cholesterol biosynthesis. Healthy contacts of the patients served as controls. The results obtained so far tend to suggest a decreased activity of HMG-CoA reductase in the patients' sera. The study is in progress.—(*From* the report.)