CURRENT LITERATURE

This department carries selected abstracts of articles published in current medical journals dealing with leprosy and other mycobacterial diseases.

General and Historical

Awofeso, N. Appraisal of the knowledge and attitude of Nigerian nurses toward leprosy. Lepr. Rev. **63** (1992) 169–172.

The attitudes of nurses toward leprosy are studied and the findings show that their knowledge of leprosy is lacking and they also fear leprosy. This study recommends that leprosy should be included in the basic nursing curriculum in order to increase the awareness and to decrease the stigma of leprosy.—Author's Summary

Premkumar, R. and Dave, S. Relationship problems between doctors and paramedical professionals working in leprosy with reference to a possible solution. Lepr. Rev. **63** (1992) 173–182.

An empirical investigation was conducted on the in-group dynamics of health personnel working in leprosy. The sample populations were taken from the National Leprosy Eradication Programme (NLEP) employees of two state governments in India. They consisted of 21 doctors and 335 paramedicals, the former constituting a formal group and the latter a semiformal group. Two separate scales were developed for each of these groups to elicit information on five potential areas of intergroup relationships. The results indicated that there was very poor acceptance of the out-group and its roles, i.e., poor acceptance of the paramedicals by the doctors and vice versa. Three reasons were elicited from this study. First, doctors held their professional standing to be on a higher level than the paramedicals, leading to excessive social distancing between doctors and paramedicals. Second, multiprofessional involvement in NLEP work has increased the trend of professional overlapping, leading to a significant apprehension of the encroachment of skills. Third, there was a mutual lack of trust of each other's professional skills. Despite these problems, the otherwise more severe human relationship problems, such as domineering behavior and prejudiced perception against the out-group, were found to be significantly less in this study.

In order to improve working relationships between these groups a method that has been used at Karigiri is recommended. The method has two parts. The first is aimed at intrapersonal understanding and the second at the development of interpersonal skills. Role play that mimics their original work situation and an analysis of case histories were the methods of teaching that were found to be more advantageous in internalizing these skills.—Authors' Summary

Saha, S. P. and Das, K. K. Study of the characteristics and causes of relapse amongst leprosy cases in an urban area (Calcutta). Indian J. Lepr. **64** (1992) 169–178.

In this retrospective study of the 3737 cases of leprosy released from treatment and followed up during 1975 to 1990, 63 had relapsed giving an overall relapse rate of 1.69%. The relapse rate was significantly higher in the immunologically unstable N?L (borderline) cases (2.9%). It was also higher in those who had dapsone monotherapy (1.92%) compared to those who had multidrug therapy (1.01%). The relapse rate was higher in the 10 to 29 years age group and among those who became pregnant, suggesting puberty and pregnancy could be risk factors. Males had a significantly higher relapse rate (2.1%) than females (1.1%); 45.2% of relapses in N (nonlepromatous) cases occurred within 24 months and 71.4% within 36 months of stopping treatment. In those having monotherapy, 57.1% of relapses occurred within 24 months and 76.8% within 36 months. Regularity in treatment did not

seem to have much influence on relapse rates.—Authors' Abstract

Strobel, M., Gros de Beler, A., Arnaud, J. P. and Sibille, G. [Leprosy in Guadeloupe (FWI) 1980–1990: evolution and management in general hospital.] Bull. Soc. Pathol. Exot. Filiales **85** (1992) 22–25. (in French)

Twenty-seven leprosy patients (19 adults, 8 children) from Basse Terre (Guadeloupe, FWI) were referred to General Hospital from 1975 to 1989: for diagnostic purpose in half the cases, for starting or modifying treatment regimens, or for complications (ENL). Lepromatous type was predominant (16/27), whereas ENL was the most serious diagnosis and therapeutic problem (7/27). Some epidemiological and psycho-social aspects are discussed.—Authors' English Summary

Suite, M. and Gittens, C. Attitudes towards leprosy in the outpatient population of dermatology clinics in Trinidad. Lepr. Rev. **63** (1992) 151–156.

We interviewed a total of 92 dermatology clinic patients using a brief questionnaire to determine their knowledge, attitudes, and beliefs about leprosy. This small survey helped to confirm our suspicions that some knowledge of leprosy is lacking and that much stigma still remains.—Authors' Summary

Tekle-Haimanot, R., Forsgren, L., Gebre-Mariam, A., Abebe, M., Holmgren, G., Heijbel, J. and Ekstedt, J. Attitudes of rural people in central Ethiopia towards leprosy and a brief comparison with observations on epilepsy. Lepr. Rev. **63** (1992) 157–168.

To find out public attitudes toward leprosy a door-to-door survey was carried out in 1546 sampled households in the rural farming community of Meskan and Mareko in central Ethopia, where the prevalence of leprosy is estimated to be 1:1000. Attitudes toward leprosy were compared with attitudes toward epilepsy, studied in a previously performed survey in the same community. Eighty-seven% of the respondents were above the age of 25, and 59.5% were females. There were slightly more Muslims (54%) than Christians. The majority of the interviewees (87%) were farmers, with an illiteracy rate of 84%. Ninety-five% and 83%, respectively, were not willing to employ or work with a person having the disease. Seventy-five% would not allow their children to associate with a playmate suffering from leprosy. Comparative analysis of attitudes in the same community showed that negative attitudes toward leprosy were stronger than those toward epilepsy, particularly with regard to matrimonial associations, sharing of accommodation, and physical contact with an affected person. The reasons for these differences appear to be the community's deeply entrenched belief that leprosy is both hereditary and contagious, expressed respectively by 48% and 53% of the respondents. In order to minimize the perpetuation of negative attitudes, there is a need to educate and to impress on the population that leprosy is a treatable infectious disease which is not congenitally acquired. and that it is even curable if detected early. The study reinforces previously proposed suggestions that in developing countries, such as Ethiopia, leprosy care should be integrated into the general health services.—Authors' Summary

Terpstra, W. J. Mycobacterial research at the N. H. Swellengrebel Laboratory of Tropical Hygiene. Trop. Geogr. Med. **43** (1991) S3–S4.

The N. H. Swellengrebel Laboratory of Tropical Hygiene in Amsterdam has as its central research theme the analysis of genes and antigenes of agents of tropical diseases. This is in practice the development of simple and reliable methods for the early detection of tropical diseases ultimately in the interest of the control of these diseases. In the fields of leprosy and tuberculosis, monoclonal antibodies against specific epitopes were prepared allowing a quick and reliable identification, specific antibodies were detected in patients' sera, and with methods from the molecular genetics very small amounts of mycobacterial DNA could be detected in clinical specimens. The achievements of modern biotechnology offer novel approaches to the study of old and hard-to-solve clinical and epidemiological problems.—Author's Abstract

Chemotherapy

Forster, D. J., Causey, D. M. and Rao, N. A. Bull's eye retinopathy and clofazimine. (Letter) Ann. Intern. Med. **116** (1992) 876–877.

Clofazimine, a red phenazine dye used to treat dapsone-resistant leprosy, has now become part of the standard multidrug regimen for the treatment of patients with the acquired immunodeficiency syndrome (AIDS) who have disseminated *Mycobacterium avium-intracellulare* infection. Clofazimine has been found to accumulate in macrophages. Because retinal pigment epithelial cells have phagocytic properties similar to those of macrophages, clofazimine may accumulate in high concentrations in these cells and, like chloroquine, lead to degeneration of the retinal pigment epithelium and photoreceptors. We report a case of retinal pigment epithelial degeneration induced by clofazimine.

A 42-year-old man, diagnosed in 1983 as having AIDS, was having serial ophthalmologic examinations for cytomegalovirus retinitis. Approximately 10 months after beginning clofazimine therapy, the patient gradually developed bilateral retinal pigmentary changes in a "bull's eye" configuration. Several months before, a generalized darkening of the skin had begun. The maculopathy became more pronounced over several weeks and, although his visual acuity remained unchanged, he complained of slightly diminished peripheral vision and of altered light and dark adaptation. Color vision testing revealed a blue-yellow defect consistent with a toxic process.

Clofazimine-induced maculopathy has been previously reported in two patients. We recommend periodic (every 4 months) funduscopic examination and color vision testing of all patients who are receiving this medication.—From the Letter

Galal, S. M., Blaih, S. M. and Abdel-Hamid, M. E. Comparative spectrophotometric analysis of rifampicin by chelate formation and charge-transfer complexation. Anal. Lett. **25** (1992) 725–743.

Simple, rapid, and accurate spectrophotometric procedures for the determination of the antibiotic rifampin in capsules are presented. A chelate formation of the antibiotic with cupric ion and charge-transfer complexation with halogenated quinones were carried out. Linear correlations between absorbance and concentration over the range of 40–100 $\mu g\ ml^{-1}$ were computed. The reaction pathways were proposed. The utility of copper chelate as a stability indicating procedure as well as a method to determine rifampin in spiked urine samples is demonstrated.—Authors' Abstract

Gelber, R. H., Fukuda, K., Byrd, S., Murray, L. P., Siu, P., Tsang, M. and Rea, T. H. A clinical trial of minocycline in lepromatous leprosy. Br. Med. J. **304** (1992) 91–92.

Drugs for treating leprosy worldwide are limited to dapsone, clofazimine, and rifampin. This small number is of special concern because of the emergence of drug-resistant disease, the general recommendation of multiple drug treatment, and significant side effects and toxicities of each of these drugs, which at times preclude their use. We showed that minocycline at concentrations achievable in humans was active against *M. leprae* in mice and consistently bactericidal. We therefore initiated a clinical trial of minocycline in patients with lepromatous leprosy.

Eight consenting adults (seven men and one woman) with lepromatous leprosy (five patients) or borderline lepromatous leprosy (three) who had been previously untreated (six) or whose leprosy had relapsed (two) were treated with 100 mg minocycline alone once daily for 3 months. All of the pretreatment skin biopsy specimens consistently resulted in growth of the bacilli in mice. According to the findings of pooled harvests of foot pads no patient harbored any viable *M. leprae* at either two or three months after starting treatment. The clearance of viable *M. leprae* from the skin by minocycline was faster than that reported for dapsone or clofazimine, slower than that for rifampicin, and similar to that for pefloxacin and ofloxacin.—From the Article

Gidoh, M. and Tsutsumi, S. Activity of sparfloxacin against *Mycobacterium leprae* inoculated into footpads of nude mice. Lepr. Rev. **63** (1992) 108–116.

The antileprosy activity of a new quinolone, sparfloxacin, was examined in the nude mouse foot pad model. By serial dosing (once a day, 5 or 6 times per week, during the 3rd–5th months postinoculation), 10 mg/kg of sparfloxacin displayed bactericidal-type activity and bacteriostatic activity was present at daily doses of 5 and 2 mg/kg. By intermittent dosing (once a day, twice weekly at daily doses of 10 and 20 mg/kg or once weekly at a daily dose of 30 mg/kg, during the 3rd–5th months postinoculation), sparfloxacin markedly inhibited the growth of leprosy bacilli with slight remultiplication at later stages. Sparfloxacin seems to be worth studying clinically as a novel antileprosy drug.—Authors' Summary

Hastings, R. C. and Chehl, S. K. Chemotherapy of leprosy in multibacillary nude mice. Indian J. Lepr. **63** (1992) 350–355.

Most of the studies of the bactericidal action of rifampin, because of the tools available to measure *M. leprae* viability, have involved measurements of the rapidity of losses in viability of the first few logs of organisms. From a therapeutic point of view the rapidity of killing bacilli is not nearly so relevant in leprosy as the completeness of killing and the frequency of drug-resistant mutants of *M. leprae.* It is clear that in nude mice the killing of a large (multibacillary) population of leprosy bacilli does not follow the pattern of killing of the first few logs of organisms, the first few logs of organisms that can be measured with conventional mouse experiments. It may be necessary to discuss the effects of rifampin in leprosy in terms of a) the first few logs of easily and rapidly killed *M. leprae,* b) rifampin-resistant mutants and c) rifampin-sensitive bacilli which are not easily and rapidly killed by this drug.—From the Article

Kar, P. K., Jha, P. K. and Snehi, P. S. Indeterminate leprosy: a therapeutic evaluation. Indian J. Lepr. **64** (1992) 163–167.

Out of 50 cases of indeterminate leprosy, 46 were male and 4 were female. The only clinical finding was a single hypopigmented macule in 38 (76%) cases. Nine (18%) patients had two and three (6%) cases had three hypopigmented macules. All patients were treated with multidrug therapy for 1 year. At the end of 6 months, the lesions were still active in 12 (24%) cases. At the end of 1 year of treatment it was found that 33 (66%) patients became inactive and 3 (6%) cases were still active. The study shows that all indeterminate leprosy cases must be treated with multidrug therapy until all signs of activity are subsided.—Authors' Abstract

Kashyap, A., Sehgal, V. N., Sahu, A. and Saha, K. Anti-leprosy drugs inhibit the complement-mediated solubilization of pre-formed immune complexes *in vitro.* Int. J. Immunopharmacol. **14** (1992) 269–273.

Incubation of pre-formed immune complexes (IC) (^{125}I-HSA–anti-HSA) with normal human serum resulted in solubilization of IC. When various antileprosy drugs were added to human sera, solubilization of IC was fairly explicit with clofazimine, whereas this effect was marginal with dapsone. Rifampin hardly displayed this effect. Aspirin, chloroquine, and prednisolone, the drugs used in addition to multidrug therapy to control reactions in leprosy, were in a position to inhibit the solubilization of ^{125}I HSA–anti-HSA by normal serum only at a very high dose. From the current data of the inhibition of solubilization of pre-formed IC along with our earlier observations on the modulation of complement-mediated hemolysis by these drugs, it may be possible to postulate that clofazimine as well as chloroquine affect early complement components. This may in turn be responsible for preventing the deposition of C3 complement onto IC.—Authors' Abstract

Kaur, S., Sharma, V. K., Basak, P. and Kaur, I. Paucibacillary multidrug therapy in leprosy; 7½ years experience. Indian J. Lepr. **64** (1992) 153–161.

Three-hundred-twenty-three paucibacillary (PB) leprosy patients were treated with WHO-recommended multidrug therapy

(MDT) and followed up for over 7½ years. The paucibacillary MDT regimen (PBR) was well accepted and tolerated. Complete clinical regression was attained in 61.2% patients after 6 doses of PBR. Persistence of clinical activity after 6 months of therapy was associated with occurrence of type 1 upgrading reaction, presence of six or more patches and more than two thickened major nerve trunks. Reversal reactions were encountered in 15.9% of the patients, one third of which were accompanied by severe neuritis. Delayed upgrading reaction occurred in six patients, two patients had relapse 1 and 2 years after stopping of PBR. The WHO recommended MDT regimen for paucibacillary cases needs careful evaluation, and it may be necessary to extend the treatment beyond 6 months in certain situations.—Authors' Abstract

Krishnan, T. R., Abraham, I. and Vargha Butler, E. I. Wettability study of clofazimine and poly (vinyl methyl ether/maleic anhydride) copolymer coevaporates. Int. J. Pharmaceut. **80** (1992) 277–281.

Solid coevaporates of the antileprotic drug clofazimine with a poly (vinyl methyl ether/maleic anhydride) copolymer (PVM/MA, Mol Wt 20,000) were prepared by the solvent evaporation method. The drug/polymer carrier weight ratios in the coevaporates examined were 1:5, 1:10 and 1:20. The effect of the hydrophilic PVM/MA copolymer on the surface characteristics of the hydrophobic drug clofazimine was studied by performing contact angle measurements on tablets compressed from powders of both the pure components (drug and carrier) and their coevaporates. Contact angles, θ, of sessile drops of both distilled water and acidic, neutral and alkaline aqueous solutions, previously used as dissolution media for the coevaporates, were determined at 37°C. It was found that θ decreased (i.e., the wettability of the coevaporates increased) with increasing PVM/MA copolymer content. The increasing wettability of the coevaporates is consistent with the results obtained on dissolution for the relevant powder samples.—Authors' Summary

Noordeen, S. K. Recent developments in leprosy control. Trop. Geogr. Med. **43** (1991) S5-S12.

Leprosy continues to be a major problem in the developing world with over 3.9 million cases registered in 1989. The control of leprosy had been considerably handicapped by the widespread occurrence of resistance of *M. leprae* to dapsone, the most commonly used antileprosy drug. Together with problems of treatment compliance and social stigma this led to leprosy control losing considerable ground. In response to the situation and taking advantage of the availability of more potent drugs, in 1981 WHO recommended standard multidrug therapy (MDT) regimens for treatment of leprosy in control programs. The experience of implementating MDT all over the world over the last 8 years has shown the regimens to be highly effective and acceptable. By 1990, nearly 50% of all the registered leprosy cases in the world were benefitting from MDT. The future prospects for leprosy control appear bright with major reductions in prevalence foreseen in the coming years.—Author's Abstract

Pattyn, S. R., Bourland, J. and Kazeze. Ambulatory treatment of multibacillary leprosy with a regimen of 8 months duration. Lepr. Rev. **63** (1992) 36–40.

An ambulatory treatment regimen for multibacillary leprosy, of 34 weeks' duration composed of 8 weeks' daily supervised rifampin (RMP), ethionamide (ETH), dapsone (DDS) and clofazimine (CLO) followed by 26 weeks of unsupervised ETH, DDS and CLO, introduced in 1983 has been evaluated; 268 patients were followed for a mean of 4.4 years and a total of 1188 patient-years. The relapse rate was 0.33 per 100 patient-years of follow up. The reduction of the duration of the combined administration of RMP + ETH reduced the hepatotoxicity to 1.4%. It is possible that both phases of the regimen studied could still be reduced. However in the near future ETH will be replaced by alternative bactericidal drugs, avoiding the hepatotoxicity.—Authors' Summary

Pattyn, S. R., Groenen, G., Janssens, L., Kuykens, L. and Mputu, L. B. Treatment of multibacillary leprosy with a regimen of 13 weeks duration. Lepr. Rev. **63** (1992) 41–46.

In a prospective study 559 multibacillary patients in Zaire were treated for 13 weeks with twice weekly rifampin (600 mg) and daily ethionamide (500 mg) and dapsone (100 mg), 13-RED, or clofazimine (100 mg), 13-REC. The patients were followed for a total of 1418 person-years, mean 3.2 years. The incidence of hepatitis was 3.3%. The incidence of relapses was 0.28 per 100 person years. Relapses were due to drug-sensitive organisms. In patients who received the same drug regimens but with a reduced dosage of ethionamide to 5 mg/kg bodyweight, the incidence of hepatitis was significantly lower but the relapse rate was 7.8 per 100 person-years of follow up in the RED group; no relapses were diagnosed in the REC group. It is concluded that by the use of potent antileprosy drugs in suitable combinations and dosages, it will be possible to shorten the duration of antibacterial treatment in multibacillary leprosy to 3 months.—Authors' Summary

Ramu, G. Problems of multidrug therapy. Indian J. Lepr. **63** (1991) 435–445.

Experience with MDT, although by and large gratifying, has thrown up several problems. Clinical and therapeutic problems have been highlighted in this communication. Certain solutions have been suggested. However, research targeted to the problems is essential. They are: a) some measure of the bacterial load in paucibacillary leprosy is necessary; b) reversal reactions pose problems in many ways, (they are unpredictable, they portend nerve damage, silent neuritis is perhaps a microreversal reaction, it is difficult to differentiate relapse from reversal) and non-steroidal, acceptable and easily administrable therapy is a need of the hour. Multicentric studies on clinical, histopathological, immunological, and therapetuic aspects need to be taken up. Late reversal reactions are perhaps relapses with reactional signs. A paradoxical picture with highly bacillated lesions with BT histological findings are sometimes seen. c) Relapsed BL/LL lesions with or without resistance to rifampin and dapsone could be expected after 9 years of MDT in a given area. They need to the managed with alternative drug regimens. Ansamycin, ofloxacin, minocycline should be tried out in centers where facilities are available. d) Noncompliance to self-administered clofazimine is disturbing. The relationship between tissue reserves and blood levels needs to be studied so that spacing of doses could be worked out in order to save the drug and improve compliance. e) The danger of hemolytic effects of dapsone is very real. Iron therapy not only corrects the anemia caused by hemolysis but also seems to prevent it. This needs to be studied. f) The duration of therapy of multibacillary leprosy should be determined by regular monitoring using available tests for viability of *M. leprae.* g) A common very short course therapy for both paucibacillary and multibacillary leprosy would be ideal.—Author's Conclusions

Swart, K. J. and Papgis, M. Automated high-performance liquid chromatographic method for the determination of rifampicin in plasma. J. Chromatogr. **593** (1992) 21–24.

Due to the unstable nature of rifampin, a rapid automated high-performance liquid chromatographic method had to be developed for the analysis of a large number of plasma samples generated during a bioavailability trial. Extraction and injection of the samples were automatically done by a sample preparation system using C_2, 100 mg Bond Elut extraction columns. The extracts were chromatographed on a 4-μm reversed-phase C_{18} column with a citrate buffer and acetonitrile as mobile phase. The analytes were detected at 342 nm. Calibration curves were linear to at least 20 μg/ml and the limit of quantification was 0.16 μg/ml.—Authors' Abstract

Clinical Sciences

Balakrishnan, S. Clinical biochemical studies in leprosy. Indian J. Lepr. **63** (1991) 302–325. (137 ref.)

The objective of this review is to highlight the various possible alterations of functions observed in leprosy. Evidence has been ob-

tained for changes in liver, kidney and adrenocortical functions in LL and breakdown of connective tissues, liver and muscle tissues during reactive state. Awareness of these changes is expected to be helpful in the management of complications and adverse reactions to treatment with potentially hepatotoxic drugs like rifampin or prothionamide. An analysis of these findings points out the need for further investigations in the following directions: (a) A critical study of adrenocortical functions in leprosy patients. (b) A systematic follow up of liver and kidney functions in leprosy patients, particularly those under multidrug therapy. (c) A critical evaluation of the acute phase reactant proteins, like mucoprotein and fibrinogen, as biochemical parameters to follow the course of ENL in lepromatous leprosy. (d) A planned study to understand the role of zinc in leprosy.—From the Article

Baslas, R. G., Gupta, M., Arora, S. K., Mukhija, R. D. and Misra, R. K. Palmar involvement in histoid leprosy. Indian J. Lepr. **64** (1992) 193–195.

Our patient presented with multiple nodules which were highly positive for acid-fast bacilli (AFB), presumably *M. leprae.* Histopathological findings were compatible with histoid leprosy. We found nodules over the palmar aspect of the hand which were also positive for AFB on slit-smear examination. Histopathology of the palmar nodule also showed features of histoid leprosy. To the best of our knowledge no leprosy lesion has been reported over the palmar aspect of the hand in histoid leprosy cases. It is suggested that palms and soles should also be examined for lesions of histoid leprosy.—Authors' Discussion

Braga, F. J. H. N., Abreu, C. M., Abreu, P. R., Carmargo, E. E., Rivitti, M. C. M., Tedesco-Marchesi, L. C. M., Gambini, D. J. and Barritault, L. [Contribution to the study of two infectious granulomatous diseases (leprosy and cutaneous and mucous leishmaniasis) by scintigraphic methods.] Bull. Soc. Pathol. Exot. Foliales **85** (1992) 53–57. (in French)

Leprosy is a multiform chronic infectious granulomatous disease caused by *Mycobacterium leprae* that affects over 12 million people in the world. Cutaneous and mucous leishmaniasis (CML) is also a chronic granulomatous infectious disease, caused by *Leishmania brasiliensis* and transmited to man by the mosquitoes of the *Phlebotominae* family. It is a worldwide spread disease. We studied one case of borderline-virchowian leprosy and 2 cases of CML with Gallium-67 (GA-67) scintigraphy. Ga-67 is a radiopharmaceutical known for its property of concentrating in inflammatory sites. In the leprosy patient, Ga-67 accumulated in the skin in a moderate, homogeneous and disseminated way (outlined skin); in the area of the face, the uptake was important and homogeneous (image in beard). Several internal organs accumulated Ga-67. As for the 2 CML patients, Ga-67 accumulated focally, in different degrees, in the affected anatomical areas. The leprosy patient was not under treatment and the 2 CML were under treatment (20 and 40 days, respectively). In the 3 cases, all affected areas accumulated Ga-67. Intensity differences of uptake may be explained both by different degrees of inflammatory processes (between leprosy and CML) and by treatment lasting. It is possible that Ga-67 scintigraphy may be useful for the evaluation of these two diseases extent and also for the therapy follow up.—Authors' English Summary

Courtright, P. and Lewallen, S. Considerations in the integration of eye care into leprosy care services. Lepr. Rev. **63** (1992) 73–77.

Little attention has been directed to the development, management and evaluation of eye care programs for leprosy patients. This paper examines when an eye care program for leprosy patients is needed, methods for integrating eye care into leprosy control programs and lists of available ocular leprosy teaching materials.—Authors' Summary

Desikan, K. V. Clinico-pathological correlation in Indian Consensus Classification. Indian J. Lepr. **63** (1991) 329–333.

One cannot expect an absolute clinico-pathological correlation in the Indian consensus classification. Adoption of the Rid-

ley-Jopling classification, which is based on histology, is not feasible under field conditions where a very large number of patients are treated. The Ridley-Jopling classification also has its deficiencies. A nonspecific picture is termed "indeterminate," and as pointed out earlier, it could be "indeterminate," "macular borderline," or a healing lesion of any type. It would be impossible to find a suitable classification satisfying all needs. Despite the lack of perfect immunohistological correlation, the Indian Consensus Classification, which can easily be followed even by field workers, provides a broad base on which further embellishment and finer details can be worked out. Wherever necessary or possible a histological diagnosis and an immunological confirmation should be carried out, especially when carrying out a research study, but for routine clinical and epidemiological work the Indian Consensus Classification meets the required needs quite adequately.—Author's Conclusion

Dong, L., Li, F., Gu, Z., Zhang, J., Chen, J., Gu, D., Wang, Z. and Peng, J. Diagnostic exploration of enlarged peripheral nerves in suspected cases of leprosy; an analysis of 55 cases. Lepr. Rev. **63** (1992) 141–144.

In 55 cases presenting with enlarged peripheral nerves without any skin lesions, a rice-grain-sized biopsy of the nerve lesion was taken for histopathological examination. As a result definitive diagnoses could be established: leprosy was diagnosed in 32 cases. In 23 cases the cause of nerve enlargement was not leprosy: post-traumatic neuritis 9, cycts 5, hypertrophic neuritis 3, nonspecific 4, neurofibroma 1, and amyloidosis 1. In all of these cases there was a deficit of the nerve function and postoperatively there were no complications. The authors, as a result of this experience, believe that surgical exploration and biopsy is a harmless diagnostic tool for establishing a definitive diagnosis of leprosy in cases presenting with enlarged peripheral nerves without any skin lesions. In 23 out of 55 such cases the nerve enlargement was proved to be other causes than leprosy.—Authors' Summary

Girdhar, A., Venkatesan, K., Chauhan, S. L., Malaviya, G. N. and Girdhar, B. K. Red discoloration of the sputum by clofazimine simulating haemoptysis—a case report. Lepr. Rev. **63** (1992) 47–50.

A patient with lepromatous leprosy, who received a high dose of clofazimine as part of multidrug therapy, for chronic erythema nodosum leprosum (ENL) had frequent "hemoptysis." The hemoptysis was later found to be due to expectoration of clofazimine. This interesting and perhaps first case of such an occurrence is reported.—Authors' Summary

Lalwani, A. K., Tami, T. A. and Gelber, R. H. Lepromatous leprosy: nasal manifestations and treatment with minocycline. Ann. Otol. Rhinol. Laryngol. **101** (1992) 261–264.

Nasal involvement in lepromatous leprosy is universal and occurs early in the course of the disease. Nasal symptoms include obstruction, crusting, bleeding, and hyposmia. Traditional therapy with dapsone, rifampin, and clofazimine is limited by its cost and toxicity. Minocycline hydrochloride, a tetracycline antibiotic with limited side effects, is promising as a new treatment for leprosy. A case is presented that highlights the clinical presentation, diagnosis, and treatment of lepromatous leprosy.—Authors' Abstract

Lennon, J. L. and Coombs, D. W. An application of the LePSA methodology for health education in leprosy. Lepr. Rev. **63** (1992) 145–150.

This paper describes how the innovative LePSA technique can be used by community health workers to appropriately educate and increase compliance among leprosy patients. A lesson plan illustrating the interactive nature of the technique in a hypothetical Third World community is presented. The lesson plan, using MDT default, shows how the technique can elicit individual participation in a group setting and serve as both an educational and a behavior change tool.—Authors' Summary

Palande, D. D. and Bowden, R. E. M. Early detection of damage to nerves in leprosy. Lepr. Rev. **63** (1992) 60–72.

Methods of examining and diagnosing damage to nerves commonly involved in leprosy are described. The equipment used is inexpensive, gives reliable and repeatable results, and is useful in making objective assessments in terms of function in everyday living.—Authors' Summary

Patki, A. H. and Mehta, J. M. Hyperkeratotic and verrucous skin lesions on lower extremities of leprosy patients. Indian J. Lepr. **64** (1992) 183–187.

Three morphological varieties of hyperkeratotic and verrucous skin lesions on the anterior aspect of ankle joints in patients with leprosy are described: (i) verrucous lesions with thread-like horny projections similar to filiform warts; (ii) irregular compact hyperkeratotic lesions with deep fissures in between; and (iii) hyperkeratotic lesions with linear fissures corresponding to the transverse creases on the anterior aspect of the ankle. Chemical cautery was useful for the treatment of the first two varieties, and a potent topical corticosteroid with salicylic acid was useful for the third.—Authors' Summary

Porichha, D., Bramhne, H. G. and Samal, R. C. BI of patient vs BI of individual sites. Indian J. Lepr. **64** (1992) 179–182.

An analysis of 200 skin smear results from multibacillary patients showed that the average bacteriological index (BI) of a patient varied considerably from his site-wise highest BI. The average BI was equal to the site-wise highest BI only in 17.5% of cases and in the rest, it ranged from 99% to as low as 36% of the highest site-wise BI. In follow-up smears, site-wise consistency of the highest BI was found in 96% of cases. It is suggested that for follow-up purposes, repeating the smear from only one such site would be adequate.—Authors' Abstract

Valencia, L. B., Ventura, E. R., Paz, C. J., Darvin, A. C., Ortega, A. R. and Rosel, A. S. Society and leprosy: a study of knowledge, attitudes and practices of Philippine Ilocanos. Geneva: World Health Organization, 1988. Soc. Econ. Res. Proj. Rept. No. 2. (TDR/SER/PRS/2)

The integration of the social sciences and pure sciences has long been a global interest but very few have attempted to work on this existing gap in the field of research. This limitation is the predisposing factor behind the conceptualization of this ongoing investigation. This paper seeks to correlate the medical aspects (causation, transmission, symptomatology and treatment) of leprosy with the psycho-socio-linguistic facts (beliefs, knowledge, attitudes and practices) of the disease. The respondents for this study are divided into three sets, namely, the patients, the critical informants (who are close to the patients), and the key informants (who are unrelated to the patients but are occupying key positions in the community). Of the 213 respondents, 96 come from Barangay Guimod, Ilocos Sur, while 117 come from Tala, Novaliches. An analytical comparison of the data has, so far, yielded results stressing poverty-related circumstances as the major cause of leprosy prevalence in these areas. It has also been shown that the respondents have overlapping notions of causation and transmission, and of prevention and treatment. These, and the rest of the preliminary findings suggest that the present leprosy control programs be equipped with a stronger, concrete psycho-social foundation for greater efficacy.—Authors' Abstract

Vreeburg, A. E. M. Clinical observations on leprosy patients with HIV-1 infection in Zambia. Lepr. Rev. **63** (1992) 134–140.

The clinical observations carried out on 10 leprosy patients with HIV1-infection, admitted between 1/1/1986 and 1/5/1988 to the Salvation Army Hosptial at Chikankata, Mazabuka, Zambia, are described. A total of 8 of this group were newly diagnosed borderline leprosy patients. Their clinical data were compared with those of 34 newly diagnosed borderline leprosy patients admitted in the same period—50% were men, 50% women. The clinical presentation, with respect to leprosy, on admission did not differ very much in both groups. The incidence

of neuritis in both groups was 50% (respectively 5 and 17). The outcome of specific therapy of neuritis was worse in the HIV1 patients than in the other group: only partial recovery in 4 out of 5 and no response in 1, compared with a complete recovery in 10 cases, and a partial recovery in 7 cases in the other group. A total of 6 patients of the HIV1-group admitted to have had multiple heterosexual contacts, 5 had a history of sexually transmitted disease, 7 had generalized lymphadenopathy, and 4 presented with another disease in addition to leprosy. While in the hospital the group of 10 HIV1-infected patients suffered 17 episodes of intercurrent disease against none in the other group; 1 patient (male) died with generalized dermatitis and sepsis; 1 woman died with fulminant hepatitis.—Author's Summary

Immuno-Pathology

Chin-A-Lien, R., Faber, W. R., van Rens, M. M., Leiker, D. L., Naafs, B. and Klatser, P. R. Follow-up of multibacillary leprosy patients using a phenolic glycolipid-I-based ELISA. Do increasing ELISA-values after discontinuation of treatment indicate relapse? Lepr. Rev. **63** (1992) 21–27.

With the introduction of reproducible serological tests it was hoped that relapses in leprosy patients, after discontinuing treatment, could be detected before damaging reactions occurred and before the patients became infectious. The possible value of an ELISA using a semisynthetic analog of phenolic glycolipid-I to detect antibodies to this antigen in order to predict a relapse in multibacillary (MB) patients was investigated. In contrast to that reported for paucibacillary patients, this test was useful to detect early relapses in MB patients. In 3 out of 4 MB patients who relapsed, the ELISA-values were increased. The decreased ELISA-values in the one relapsed patient could be attributed to the corticosteroid therapy. In the MB patients who did not relapse after RFT, the ELISA-values were consistently low or decreased. In only one patient did the ELISA-values increase following his release from treatment and this patient was clinically suspected of developing a relapse.—Authors' Summary

Cho, S.-N., Kim, S.-H., Cellona, R. V., Chan, G. P., Fajardo, T. T., Walsh, C. P. and Kim, J.-D. Prevalence of IgM antibodies to phenolic glycolipid I among household contacts and controls in Korea and the Philippines. Lepr. Rev. **63** (1992) 12–20.

Phenolic glycolipid I (PGL-I) is a *Mycobacterium leprae*-specific antigen and the antibodies to the antigen may suggest an *M. leprae* infection. To compare the *M. leprae* transmission among the populations, we compared the prevalence of anti-PGL-I IgM antibodies among household contacts and controls between Korea and The Philippines. In Korea (prevalence of leprosy—0.04:1000), the prevalence of anti-PGL-I antibodies was 4.8% among controls and 8.0% among contacts, respectively. On the other hand, the seroprevalence rate was 10.8% among controls and 13.4% among contacts in The Philippines (prevalence of leprosy—0.70:1000). Interestingly, a marked difference was noted in the prevalence of anti-PGL-I antibodies among children between the countries; 10%–14% among children under 10 years old and 15%–18% among those aged between 10 and 19 in The Philippines compared to 0% and 2.9%–6.4% in Korea, respectively. This study, therefore suggests that a high prevalence of anti-PGL-I IgM antibodies among children may indicate an active transmission of *M. leprae*, resulting in a higher incidence of leprosy in the population.—Authors' Summary

Gidlund, M., Halapi, E., Cornelisse, Y., Ottenhoff, T., Wigzell, H. and Kiessling, R. Soluble CD4 suppress the antigen driven proliferative response of certain T cell clones specific for mycobacteria and for peptides by mycobacterial heat shock

proteins. Int. Immunol. **4** (1992) 355–360.

We have investigated the effect of soluble recombinant CD4 (sCD4) on the antigen-specific (BCG, peptides of mycobacterial 65-kDa hsp) response of T-cell lines or T-cell clones. The majority of the antigen-specific clones could be suppressed in their antigen-driven response by the addition of sCD4, while others, including the parental polyclonal T-cell line, were not. The suppression of the specific T-cell response was reversed by the addition of anti-CD3, did not affect the proliferative response to IL-2, and was independent of the amount of antigen. A decreased capacity to produce IFN-γ in response to the antigen by the addition of sCD4 was seen only with those clones that were also inhibited in their specific proliferative response. This model may be used to delineate further the interaction between T cells and the antigen-presenting cell, and the finding may limit the possible *in vivo* use of sCD4 in the therapy of human immunodeficiency virus (HIV) infections.—Authors' Abstract

Izzo, A. A. and North, R. J. Evidence for an α/β T cell-independent mechanism of resistance to mycobacteria. Bacillus Calmette-Guérin causes progressive infection in severe combined immunodeficient mice, but not in nude mice or in mice depleted of CD4+ and CD8+ T cells. J. Exp. Med. **176** (1992) 581–586.

Depleting thymectomized mice of CD4+ T cells, or CD4+ plus CD8+ T cells, rendered them incapable of resolving bacillus Calmette-Guérin (BCG) infection in their livers, spleens, kidneys, and lungs. However, it did not render them incapable of stabilizing infection in the latter three organs after an initial period of BCG growth. Athymic nude mice showed a similar capacity to control BCG growth in these organs after a certain stage of infection. In contrast, congenitally severe combined immunodeficient (SCID) mice appeared to offer no resistance to BCG infection, in that the organism grew progressively in all organs of these mice and was lethal for them beginning on day 55 of infection. The results suggest that, although CD4+ T cells are important for resolving BCG infection, an α/β T-cell-independent mechanism of resistance can be acquired at 2–3 wk of infection that is capable of inhibiting further BCG growth in all organs except the lungs. Because this mechanism is absent from SCID mice, it is likely that it depends on the functions of γ/δ T cells, B cells, or both types of cells. In keeping with this possibility is the additional finding that SCID mice engrafted with lymph node cells depleted of CD4+ or CD8+ T cells were capable of expressing an appreciable level of resistance against BCG infection.—Authors' Summary

Kaufmann, S. H. E. and Young, D. B. Vaccination against tuberculosis and leprosy. Immunobiology **184** (1992) 208–229.

The present paper has attempted to describe the major immune targets for vaccination against tuberculosis and leprosy. Furthermore, we tried to present information about currently known antigens of *M. tuberculosis* and *M. leprae* which might be considered for careful evaluation as vaccine candidates. Finally, we have stressed that antigen definition represents only one part of vaccine development and that identification of appropriate carrier systems is as important. Because complex T-cell mechanisms are responsible for both protection and pathogenesis in leprosy and tuberculosis, careful evaluation of the elements contributing to protective immunity is required. Whether a strictly synthetic strategy will indeed be successful in the near future remains unclear. Perhaps a combination of antigen definition and genetic manipulation may be better suited to solve the numerous obstacles toward a vaccine against tuberculosis and leprosy which has to be more effective than BCG.—Authors' Concluding Remarks

Laferte, J., Abreu, E. G., Robaina, R. and Verez, V. [UltramicroELISA assay for the detection of human IgM antibodies to *M. leprae*.] Rev. Inst. Med. Trop. São Paulo **33** (1991) 491–495. (in Spanish)

The availability of an ultramicroanalitic system (SUMA) and species-specific antigen of *M. leprae* obtained by chemical synthesis have made possible the standardiza-

tion and validation of an ultramicroELISA for detecting specific human IgM antibodies to this mycobacterium. The specificity of this test to demonstrate the infection with *M. leprae* was corroborated through a screening of 433 blood bank serum samples and other 265 from different groups (100 control group, 50 tuberculosis patients, 65 leprosy patients, 50 from households). The results obtained in the additional study of 140 household sera showed a high correlation ($r = 0.98$) with the conventional microELISA method. The use of SUMA allows saving reagents and time since sample handling, plate reading, print out and storing the data are computer assisted.—Authors' English Summary

Mahadevan, P. R., Robinson, P., Vermani, M., Pardhy, A. and Joshi, S. Delipidified cell components of *Mycobacterium leprae* and its applications. Indian J. Lepr. **63** (1992) 371–387.

Delipidified cell components (DCC) of *Mycobacterium leprae* obtained as an insoluble material consist of several proteins. This preparation, DCC, has the ability to differentially bind to sera from lepromatous leprosy patients and the antibodies to this complex get reduced as patients improve under chemotherapy. The antigenic complex has no ability to bind to proteins of sera from normal healthy individuals or tuberculoid leprosy patients. The DCC is antigenic and is recognized by immune deficient cells of lepromatous leprosy patients, leading to lymphocyte proliferation, production of interleukin 2 and interferon γ, and resulting in activation of the phagocytes to initiate killing of endocytosed *M. leprae* through reactive oxygen intermediates, primarily superoxide. The DCC has also immunomodulatory properties to protect mice against *M. leprae* infection. Experiments with mice and isolated peripheral blood cells from patients have indicated the probable molecular mechanism of immunomodulation by DCC.—Authors' Abstract

Mirando, W. S., Shiratsuchi, H., Tubesing, K., Toba, H., Ellner, J. J. and Elmets, C. A. Ultraviolet-irradiated monocytes efficiently inhibit the intracellular replication of *Mycobacterium avium intracellulare*. J. Clin. Invest. **89** (1992) 1282–1287.

The purpose of this study was to evaluate the effect of ultraviolet (UV) radiation on the antimicrobial activities of monocytes for the intracellular pathogen *Mycobacterium avium intracellulare* (MAI). UV radiation augmented monocyte antimicrobial activity for MAI in a dose-dependent fashion. UVB doses of ≥ 25 J/m^2 resulted in a 50–100-fold reduction in MAI growth 7 days after initiation of culture. The increased monocyte antibacterial effect could be blocked by a plate glass filter, indicating that wavelengths within the UVB were responsible for the effect. UV radiation did not stimulate monocyte phagocytosis, and enhanced inhibition of MAI growth was observed in populations of adherent mononuclear cells that were devoid of T cells. This suggested that UV radiation acted directly to augment intrinsic monocyte antimicrobial activities. The administration of 8-methoxypsoralen plus UVA radiation to monocytes also augmented their antimicrobial activities against MAI. UV radiation thus may serve as a unique agent by which to evaluate the mechanisms by which mononuclear phagocytes control the growth of MAI.—Authors' Abstract

Ramanathan, V. D. The pathophysiology of the complement system in leprosy. Indian J. Lepr. **63** (1992) 418–434.

The following are apparent: a) There is a hypercatabolism of the complement system in leprosy along with a reduction in the solubilization of IC through complement; b) *M. leprae* and its constituents can activate the complement system; and c) the complement system gets activated in leprosy by more than one stimulus. This can result in the generation of both acute and chronic inflammatory processes. Phagocytosis of complement-reacted *M. leprae* early in the course of the disease is of advantage to the host who is capable of initiating bactericidal mechanisms. On the other hand, this helps the organism to gain entry into an immunologically privileged site in a susceptible host.

Although a considerable amount of information regarding the pathophysiology of the complement system in leprosy is available now, there are still several areas of theoretical and practical importance to be covered in this field. The present review concludes with some of the lines of enquiry which need to be pursued in the next decade: a) Apart from its thick cell wall, does *M. leprae* get protected from the effects of complement in influencing the course of events in the early stages of host-parasite interaction? b) What is the role of complement in influencing the course of events in the early stages of host-parasite interaction? c) What is the reason for the dichotomy between the hemolytic function and the ability to solubilize IC? Are different polymorphic forms, especially those belonging to the class III products of the major histocompatibility region, responsible for the schism between two of the functions of the complement system? d) Do unsolubilized or partly solubilized immune complexes have the ability to modulate the immune system and also to initiate inflammatory processes? e) The status of complement receptors needs to be evaluated and its relationship to the disease and its manifestations established. —Author's Conclusions

Scollard, D. M., Bhoopat, L., Kestens, L., Vanham, G., Douglas, J. T. and Moad, J. Immune complexes and antibody levels in blisters over human leprosy skin lesions with or without erythema nodosum leprosum. Clin. Immunol. Immunopathol. **63** (1992) 230–236.

Erythema nodosum leprosum (ENL) is a serious complication of lepromatous leprosy, affecting skin and peripheral nerves in a large percentage of these patients, and is presumed to result from spontaneous immunologic changes. Its pathogenesis is poorly understood, although histopathologic features have suggested immune complex (IC)-mediated injury. Abundant circulating antibody is present but no convincing correlation has been established between circulating IC and ENL. We have examined cutaneous leprosy lesions *in vivo* using blisters induced by prolonged gentle suction to determine whether or not IC are demonstrable in lesions with or without ENL, using an IC assay based on monoclonal rheumatoid factor binding. We also examined whether antibodies involved in such IC are produced locally or reach the skin via the circulation. Surprisingly large quantities of IC were found in ENL lesions, and in some cases the quantities were significantly higher than in matching serum. Total IgG, IgA, and IgM in the skin were not higher than expected, however. Attempts to demonstrate increases in intracutaneous levels of specific anti-*Mycobacterium leprae* antibodies were unsuccessful. This is the first report of the demonstration of IC in suction blister fluid. The results indicate that large quantities of IC may be present in cutaneous leprosy lesions and are consistent with the hypothesis that they are formed *in situ* when circulating antibody combines with antigen in the skin. The nature of the antigen in these IC remains undefined. —Authors' Abstract

Sekar, B. and Anadan, D. Evaluation of *Mycobacterium leprae* particle agglutination test, using eluates of filter paper blood spots. Lepr. Rev. **63** (1992) 117–124.

A comparison of the ELISA test with the newly-developed MLPA test was carried out using eluates of blood spots from filter paper for the detection of the anti-PGL-I antibody. A very good positive correlation was observed between these two tests. The concordance rate was found to be 92.6%, ranging from 71.4% to 100%. This nonconcordance was not found when freshly collected samples were used. The MLPA test is simple and reliable. The use of eluates from blood spots collected on filter paper further simplifies the test in the collection and transportation of blood samples. This accurate and rapid method makes the MLPA test logistically feasible for large-scale screening. With our modification of MLPA with eluates more samples can be screened with the kit than with sera. —Authors' Summary

Shannon, E. J., Ejigu, M., Haile-Mariam, H. S., Berhan, T. Y. and Tadesse, G. Thalidomide's effectiveness in erythema nodosum leprosum is associated with a decrease in CD4+ cells in the peripheral blood. Lepr. Rev. **63** (1992) 5–11.

Thalidomide is well documented as being an effective drug in the treatment of erythema nodosum leprosum (ENL). The mechanism of action of thalidomide in ENL as well as the pathogenesis of ENL are yet to be fully determined. Lepromatous leprosy patients experiencing ENL have been reported to have an increase in the ratio of CD4+ to CD8+ cells in their blood and ENL skin lesions. Thalidomide has been shown to cause a decrease in the ratio of CD4+ to CD8+ lymphocytes in the blood of healthy males. This decrease was due to a significant reduction in the numbers of CD4+ lymphocytes and an apparent increase in the numbers of CD8+ lymphocytes. In this study, thalidomide's effectiveness in halting chronic ENL and arresting a relapse into ENL was consistently associated with a decrease in the numbers of CD4+ lymphocytes in the blood of two male lepromatous leprosy patients.—Authors' Summary

Sharma, V. K., Kaur, S., Vaishnavi, C., Agnihotri, N., Kaur, I. and Ganguly, N. K. Detection of a *Mycobacterium leprae* cell wall antigen in the urine of untreated and treated patients. Lepr. Rev. **63** (1992) 28–35.

A total of 90 leprosy patients, 12 household contacts, and 10 normal subjects were studied for the detection of *Mycobacterium leprae* cell-wall antigen in urine using monoclonal antibody ($ML30A_2$ IgG). In untreated multibacillary leprosy (BL-LL) the *M. leprae* cell-wall antigen could be demonstrated in the urine of 14 (64%) patients by immunofluorescence (IF) and 22 (100%) by ELISA. In untreated paucibacillary leprosy (TT-BT), it could be demonstrated in 3 (11.5%) and in 13 (50%) patients by IF and ELISA methods, respectively. All but 1 household contact (later confirmed to have BL leprosy) and all 10 normal subjects' urine was negative for *M. leprae* cell-wall antigen by both methods. The same antigen was, however, demonstrated in urine of 50% paucibacillary patients who had received 6 months of treatment and in 68% multibacillary patients who had received 24 months of WHO recommended multidrug therapy. *M. leprae* cell-wall antigen assays in urine will not be useful in the follow up of leprosy patients on multidrug therapy.—Authors' Summary

Shereef, P. H. Hypopigmented macules in leprosy—a histopathological and histochemical study of melanocytes. Indian J. Lepr. **64** (1992) 189–191.

A study of the number of melanocytes and amount of pigmentation in hypopigmented lesions and adjacent normal areas in 20 leprosy patients showed no differences in these parameters. It appears that hypopigmentation in leprosy lesions could be caused by defective transfer of melanin into keratinocytes.—Author's Abstract

Silva, C. L., Palacios, A., Colston, M. J. and Lowrie, D. B. *Mycobacterium leprae* 65hsp antigen expressed from a retroviral vector in a macrophage cell line is presented to T cells in association with MDH class II in addition to MHC class I. Microb. Pathogen. **12** (1992) 27–38.

Mycobacterium leprae lives free in the cytoplasm in infected macrophages. To test if an *M. leprae* antigen released into the cytoplasm would associate with major histocompatibility complex (MHC) class II, we introduced the gene encoding the 65-kDa heat-shock protein (ML65hsp) into a retroviral shuttle vector (pZIPNeoSV(X)) and transfected the murine macrophage cell line J774G8. S1 nuclease mapping and Western blot analysis of the transfected cell line (CJ11) showed that specific messenger RNA and ML65hsp antigen were stably expressed. Presence of antigen at the cell surface was demonstrated by flow cytometric analysis with specific monoclonal antibodies (mAb). Antigen-specific T lymphocytes were stimulated by CJ11 cells to proliferate and release interleukins (IL-2 and IL-3). These responses were blocked by mAbs specific for either MHC class II or for the mycobacterial antigen. The endogenous antigen was also recognized by MHC class I-dependent cytotoxic T cells; cytotoxicity was inhibited by mAbs against either MHC class I molecules or ML65hsp. Thus, production of ML65hsp within the host cytoplasm resulted in association of the antigen with both MHC class I and MHC class II antigen-presenting structures and evoked

both lymphocyte proliferation and cytotoxicity toward the antigen-presenting cell. These findings may be relevant to the development of recombinant subunit vaccines against intracellular pathogens.—Authors' Abstract

Sussman, G. and Wadee, A. A. Supernatants derived from CD8+ lymphocytes activated by mycobacterial fractions inhibit cytokine production; the role of interleukin-6. Biotherapy **4** (1991) 87–95.

Our study examined the effects of supernatants derived from CD8+ lymphocytes treated with high molecular weight components of *Mycobacterium tuberculosis* on cytokine production. Such suppressor but not control supernatants increased the production of IL-4 and IL-6 while suppressing IL-1β, TNF-alpha, IL-2 and IFN-γ production by monocytes and lymphocytes. The effects on cytokine production were time dependent, being observed as early as 4 hr with peak activity observed at 24 hr. The inhibition of IL-1β and TNF-alpha by monocytes appeared to be related to increases in IL-6 levels present in supernatants of nonadherent lymphocytes incubated with mycobacterial components. This was confirmed by studies demonstrating that the addition of recombinant IL-6 to cultures depressed the production of these cytokines. Furthermore, the addition of monoclonal anti-IL-6 to such cultures restored the production of IL-1β and TNF-alpha. The results suggest that mycobacterial components inhibit host cellular functions by manipulating the host's cytokine network.—Authors' Abstract

Turk, J. L., Curtis, J. and de Blaquiere, G. Immunopathology of nerve involvement in leprosy. Indian J. Lepr. **63** (1991) 483–491.

M. leprae is the only bacterium that penetrates the epineurium. In leprosy, axonal damage occurs as a result of the release of pharmacological mediators produced by infiltrating inflammatory cells. These cells come in as a result of either an immunological reaction or a para-immunological reaction, such as the activation of the alternative pathway of complement.—From the Article

Microbiology

Bruneteau, M., Perret, J., Vanlinden, F., Michel, G. and Cocito, C. Composition and immunogenicity of the polysaccharide components of the thermostable macromolecular antigen group of mycobacterial antigens. Med. Microbiol. Immunol. **181** (1992) 13–23.

The thermostable macromolecular antigen (TMA) group includes major components of the mycobacterial cell envelope and cytoplasm, which elicit humoral and cellular immune reactions, and seems to play important roles in infectious diseases. The best known member of this group, antigen A60 of *Mycobacterium bovis* BCG, was previously shown to contain three moieties of polysaccharides, free lipids, and polypeptides. In this work, the TMA polysaccharides of three pathogenic mycobacteria (*M. avium, M. bovis* and *M. paratuberculosis*) have been analyzed by coupled gas chromatography-mass spectrometry. In all cases the cores of the TMA complexes were represented by branched glucans of high molecular mass (about 10^6 daltons), for which structural models have been proposed. The immunogenicity of the polysaccharide components from the three TMA was verified with several immunological procedures (immunodiffusion and immunoelectrophoresis of the antigen, and immunoblotting of the corresponding electrofocused immunoglobulins). All tests tallied in showing a negligible immunogenicity of the glucans examined (inability to produce, upon injection, the synthesis of specific immunoglobulins), thus pointing to the protein moiety of TMA as the one responsible for the high immunoreactivity of the complexes.—Authors' Abstract

Franzblau, S. G., Biswas, A. N., Jenner, P. and Colston, M. J. Double-blind evalu-

ation of BACTEC and Buddemeyer-type radiorespirometric assays for *in vitro* screening of antileprosy agents. Lepr. Rev. **63** (1992) 125–133.

Two radiorespirometric assays, the BACTEC 460 and Buddemeyer-type $^{14}CO_2$ detection systems, were evaluated in a double-blind manner for their ability to discriminate between authentic antileprosy agents and inactive compounds. Freshly harvested, nude-mouse-derived *Mycobacterium leprae* were incubated in axenic media in the presence of coded test solutions prepared in a remote laboratory. Activity was assessed by comparing the rate of $^{14}CO_2$ evolution from [1-^{14}C]palmitic acid to controls. Breaking the code revealed that both systems demonstrated a dose response to ethionamide, pefloxacin and rifampin as well as sensitivity to dapsone. Most of the water, ethanol, sucrose, dabsyl chloride and riboflavin negative-control samples failed to effect a significant reduction in radiorespirometric activity. This study confirms the ability of the radiorespirometric assays to function as a primary drug-screening system in leprosy.—Authors' Summary

Katoch, V. M. Recent advances in the development of techniques for diagnosis and epidemiology of leprosy. Indian J. Lepr. **63** (1991) 362–370.

This review shows that significant progress in developing these techniques has been achieved. Already some gene probes with a potential role in identification and characterizing of *M. leprae* have become available. In addition, a few gene amplification techniques directly applicable to clinical specimens of leprosy have also been published. These techniques need to be further optimized and evaluated in different situations, e.g., isolates from different regions and different clinical types, relapse/reaction, active/inactive cases, correlation with chemotherapy, drug resistant isolates, etc. The gene sequences used for designing the abovementioned probes or primers for gene amplification represent a very small part of the *M. leprae* genome, and it is possible that as further information about genes of *M. leprae* becomes available more probes/amplification systems will be developed. Also, it would be better for easy application if nonradioactive detection systems are also standardized. At the present stage, it will not be proper to speculate which probe(s) or gene amplification system(s) will be suitable to answer a particular question about diagnosis or epidemiology of leprosy. However, it would be reasonable to be optimistic and conclude that chances of developing such techniques are very bright.—Author's Conclusions

Kikuchi, S., Rainwater, D. L. and Kolattukudy, P. E. Purification and characterization of an unusually large fatty acid synthase from *Mycobacterium tuberculosis* var. *bovis* BCG. Arch. Biochem. Biophys. **295** (1992) 318–326.

Fatty acid synthase was purified from *Mycobacterium tuberculosis* var. *bovis* BCG. The method developed gave a 23% yield of the synthase and also yielded purified mycocerosic acid synthase. The fatty acid synthase is of unusually large size and composed of two 500-kDa monomers. The amino acid composition of the two synthases was not identical; the N-terminus of the fatty acid synthase was blocked, whereas that of the mycocerosic acid synthase was not. Western blot analysis of crude mycobacterial extracts with polyclonal antibodies prepared against each synthase showed a single band in each case with no crossreactivity with the other synthase. Fatty acid synthase required both NADH (K_m, 11 μM) and NADPH (K_m, 14 μM). The K_m for acetyl-CoA and malonyl-CoA were 5 and 6 μM, respectively. Fatty acids were released from the synthase as CoA esters. A bimodal distribution of fatty acids was obtained at around C_{16} and C_{26}. The primer utilization also reflects the *de novo* synthesis and elongation capabilities of the enzyme; acetyl-CoA was the preferred primer but CoA esters up to C_8 but not C_{12} and C_{14} could serve as primers, whereas C_{16} was readily used as a primer for elongation. Addition of CoA and CoA ester-binding oligosaccharides caused enhanced release of C_{16}. Since this mycobacterial fatty acid synthase is twice as large as other multifuctional fatty acid synthases, it is tempting to suggest that this synthase represents a head-to-tail fusion of two fatty acid synthase genes coding for a

double size protein with one-half producing C_{16} acid and the other elongating the C_{16} acid to a C_{26} acid. The monomer of fatty acid synthase from *M. smegmatis* was immunologically similar and equal in size to the synthase from *M. tuberculosis.*—Authors' Abstract

Moudgil, K. D., Williams, D. L. and Gillis, T. P. DNA hybridization analysis of mycobacterial DNA using the 18-kDa protein gene of *Mycobacterium leprae.* FEMS Microbiol. Immunol. **89** (1992) 165–174.

DNA hybridization studies using a 611-base pair (bp) probe, encoding the entire 18-kDa protein of *Mycobacterium leprae,* demonstrated that *M. simiae, M. intracellulare, M. kansasii, M. terrae,* ADM-2, *M. avium, M. scrofulaceum, M. gordonae* and *M. chelonei* appear to possess DNA sequences homologous to the 18-kDa protein gene of *M. leprae.* RFLP analysis revealed that the restriction sites in the *M. leprae* 18-kDa gene were not conserved in the putative gene homologs of *M. simiae* and *M. intracellulare.* The restriction patterns observed with the 611-bp probe were useful in differentiating *M. intracellulare, M. simiae,* and *M. leprae* from each other, as well as in distinguishing strains of *M. simiae* serovar 1. Finally, the presence of homologous sequences in various mycobacteria did not affect the specificity of a previously described PCR test for detection of *M. leprae,* based on the *M. leprae* 18-kDa protein gene.—Authors' Summary

Prabhakaran, K., Harris, E. B. and Randhawa, B. A unique type of GABA binding by *Mycobacterium leprae.* Microbios **70** (1992) 139–144.

Neurotropism is one of the unusual properties of *Mycobacterium leprae.* The organism contains glutamic acid decarboxylase that generates gamma-amino-butyric acid (GABA) which is an inhibitory neurotransmitter. The binding of GABA by *M. leprae in vitro* was studied by using ^{3}H-GABA as substrate. The bacteria had high-affinity binding sites for the amino acid. The uptake was a specific saturable process with a K_m of 66.7 pM, pH optimum of 7.3 and a temperature optimum of 37°C. The binding did not seem to be time-dependent, being complete in about 5 min. None of the known antagonists and agonists of GABA uptake by neurons showed any significant effect on *M. leprae*; the receptors in the bacteria are apparently of a non-neuronal type, and different from those reported in spermatozoa and *Pseudomonas.*—Authors' Abstract

Rinke de Wit, T. B., Bekelie, S., Osland, A., Miko, T. L., Hermans, P. W. M., van Soolingen, D., Drijfhout, J.-W., Schöningh, R., Janson, A. A. M. and Thole, J. E. R. Mycobacteria contain two *groEL* genes: the second *Mycobacterium leprae groEL* gene is arranged in an operon with *groES.* Mol. Microbiol. **6** (1992) 1995–2007.

In contrast to other bacterial species, mycobacteria were thus far considered to contain *groEL* and *groES* genes that are present on separate loci on their chromosomes. Here, by screening a *Mycobacterium leprae* λgt11 expression library with serum from an Ethiopian lepromatous leprosy patient, two DNA clones were isolated that contain a *groEL* gene arranged in an operon with a *groES* gene. The complete DNA sequence of this *groESL* operon was determined. The predicted amino acid sequences of the GroES and GroEL proteins encoded by this operon are 85%–90% and 59%–61% homologous to the sequences from previously characterized mycobacterial GroES and GroEL proteins. Southern blotting analyses with *M. leprae groES*- and *groEL*-specific probes demonstrate that similar *groESL* homologous DNA is present in the genomes of other mycobacteria, including *M. tuberculosis.* This strongly suggests that mycobacteria contain a *groESL* operon in addition to a separately arranged second *groEL* gene. Using five T-cell clones from two leprosy patients as probes, expression of the *M. leprae* GroES protein in *Escherichia coli* after heat shock was demonstrated. Four of these clones recognized the same *M. leprae*-specific GroES-derived peptide in a DR2-restricted fashion. No expression of the *groEL* gene from this operon was detected in *E. coli* after heat shock, as tested with a panel of T-cell clones and monoclonal an-

tibodies reactive to previously described GroEL proteins of mycobacteria.—Authors' Summary

Shannon, E. J., Harris, E. B., Haile-Mariam, H. S., Guebre-Xavier, M. and Frommel, D. Competency of human-derived *Mycobacterium leprae* to use palmitic acid in the synthesis of phenolic glycolipid-I and phthiocerol dimycocerosate and to release CO_2 in axenic culture. Lepr. Rev. **63** (1992) 101–107.

Insufficient numbers of viable *Mycobacterium leprae* have hampered metabolic studies using human-derived *M. leprae.* In this study, sufficient numbers of *M. leprae* were obtained from an untreated lepromatous patient to titrate the effects of pH on the metabolism of ^{14}C-palmitic acid by *M. leprae.* Catabolic metabolism (oxidation of ^{14}C-palmitic acid and release of $^{14}CO_2$) was maximal when *M. leprae* were incubated at 33°C and suspended in Middlebrook 7H9, ADC supplemented medium that had been buffered to maintain a pH of 4.8. Anabolic metabolism (synthesis of ^{14}C-phenolic glycolipid-I and its precursor, ^{14}C-phthiocerol dimycocerosate) was maximal when the pH was maintained at 6.8.—Authors' Summary

Sinha, S. Heat-shock proteins and leprosy. Indian J. Lepr. **63** (1991) 466–475.

The heat-shock proteins (HSPs) have acquired a unique status by virtue of their abundant and ubiquitous presence in living beings—hosts and pathogens alike. Therefore, not surprisingly, these proteins have been the prime target of biomedical research in recent years. The physiological functions of HSPs are now reasonably well understood but many of their immunological activities which have been reported so far appear controversial and, at times, paradoxical. The role played by HSPs in host-parasite interactions in leprosy is beginning to be understood only now. We shall have to learn a lot more about these proteins before considering the use of this knowledge for the benefit of leprosy patients.—Author's Conclusion

Experimental Infections

Job, C. K. Nine-banded armadillo (*Dasypus novemcinctus*) as an animal model for leprosy. Indian J. Lepr. **63** (1992) 356–361.

Although the armadillo develops a typical lepromatous disease, it also has a spectrum of susceptibility to the disease. Now that typical, untreated, lepromatous leprosy patients are becoming rare, lepromatous armadillos can serve as suitable subjects for drug trials. Drug-resistant strains and persistors can be easily isolated in this animal model. The ability of a reagent to convert lepromin reaction from negative to positive in humans is widely used to choose a candidate vaccine for leprosy. The armadillo can easily be used for such a study instead of humans. The study can be taken to its successful conclusion by experimentally infecting the lepromin-tested animals to find out the efficacy of their acquired resistance. Such a study can be done quickly and with less expense as compared to vaccine studies involving human subjects.—From the Article

Job, C. K., Drain, V., Truman, R., Deming, A. T., Sanchez, R. M. and Hastings, R. C. The pathogenesis of leprosy in the nine-banded armadillo and the significance of IgM antibodies in PGL-I. Indian J. Lepr. **64** (1992) 137–151.

Twenty-seven nine-banded armadillos captured from the wild and tested free of wild *Mycobacterium leprae* infection were distributed into four groups. They were injected at the right hind foot pad with saline suspensions of *M. leprae* at doses of 10^3, 10^4, 10^5 and 10^6. PGL-1 antibody levels were estimated using an ELISA test, twice during 6 months before the infection and every 2 months after the infection. One an-

imal from each group was sacrificed at 6, 12, 18, 24, and 30-month intervals and another eight at unspecified intervals. A thorough autopsy and histopathological examination were conducted on all of them. Of the 27 animals, 18 developed the infection. In 10, there were granulomas at the site of inoculation and in 17 the regional lymph nodes were infected. The disease spread extensively to other lymph nodes and to the liver and spleen and then to the other organs. Peripheral nerves were invaded by *M. leprae* in only five animals. PGL-1 antibody levels registered a positive reading in only 6 of the 18 animals with the infection. In armadillo leprosy, the lesions did not persist at the site of entry in all animals. *M. leprae* multiplied in the macrophages at the site of inoculation and the reticuloendothelial cells of the lymph nodes before they spread to other organs. There was evidence of invasion of endothelial cells of capillaries and possible bacteremia even at an early phase of the infection. Peripheral nerves were not the preferred sites of entry or multiplication of *M. leprae*. Progressive increase in PGL-1 antibodies was recorded in five lepromatous armadillos with disseminated infection and high bacterial load. However, PGL-1 antibodies response was not sensitive enough to detect early disease.—Authors' Abstract

Rees, R. J. W. Evolution and contribution of animal models in leprosy. Indian J. Lepr. **63** (1991) 446–456.

It is interesting to reflect that all of the remarkable advances in the field of leprosy during the last 30 years have been achieved without a single leprosy bacillus having been cultured *in vitro*. Finally, it is fascinating that the armadillo has not only made a major contribution to leprosy research but has now been confirmed as the first and only known natural host of leprosy. It is already an occupational risk to those handling armadillos in South American countries where the animals are used for preparing food or ladies' handbags.—From the Article

Epidemiology and Prevention

Ganapati, R. Control of leprosy in India in the background of urbanization. Indian J. Lepr. **63** (1991) 334–341.

With increasing MDT coverage of the country by the National Leprosy Eradication Programme, more cities are already under the umbrella of chemotherapy. Moreover, a massive vertical program by the German Leprosy Relief Assocation, specializing in urban leprosy since 1971, has adopted nearly a 10 million population (40% in Bombay alone) in 12 cities and claims to have brought down the prevalence rate of leprosy from 15.2 to 2.0 per thousand. In addition, a few other voluntary agencies also are doing commendable work. It should, however, be mentioned that urban leprosy control does not just mean administration of MDT alone. It implies total leprosy care including disability care and elimination of stigma. If one has to reach this tall objective, the problem ahead is truly gigantic and calls for extensive coordinated effort with intersectoral cooperation particularly between multiple voluntary agencies and the government and municipal programs. Nonleprosy agencies and the medical profession at large also have to be reckoned with. Conflicting areas and ego problems will have to be resolved by common understanding, and only purely scientific attitudes in relation to leprosy should prevail in the urban atmosphere, so that an united effort may be put up to "eliminate" leprosy as per the WHO goal.—Author's Conclusion

Gupte, M. D. Vaccines against leprosy. Indian J. Lepr. **63** (1991) 342–349.

Information on the three candidate vaccines had been discussed extensively in the Indian Council of Medical Research, by the Indian Association of Leoprologists, as well as at the last Pre-Congress Workshop on leprosy vaccine trials in The Hague in 1988. It was uniformly agreed that all these vaccines deserve to be tested for their prophy-

lactic efficacy. The recently launched trial in South India is providing an unique opportunity to compare them together. It is to be accepted that the available parameters of animal studies, sensitization to *M. leprae* antigens following vaccination and immunotherapy are only indirect measures of probable prophylactic efficacy of the candidate vaccines. The extensive information available on armadillo-derived *M. leprae* in combination with BCG is very convincing with respect to these proxy measures. For *M.w* and ICRC vaccines also the evidence is somewhat similar, though limited. If ultimately ICRC and or *M.w* are found to be sufficiently effective in preventing leprosy, these vaccines from cultivable mycobacteria will naturally be preferred for general use. As ICRC and *M.w* bacilli are cultivable, their characteristics can be monitored and their availability will be easy and abundant. But if these vaccines fail and the *M. leprae* and BCG combination turns out to be effective, a technology for leprosy prevention will have become available. It is economical and scientifically very sound to compare all the available candidate vaccines in the same given population during the same time span. The South Indian trial has been launched with precisely these objectives. It will take 8 years to get the first results on the prophylactic efficacy of these vaccines. It is impossible to predict which of the three vaccines or whether any of them will prove to be effective in preventing leprosy in the Indian context. The trial has been launched optimistically because of the potential merits of each of the candidate vaccines.—Author's Concluding Remarks

Noordeen, S. K. Elimination of leprosy as a public health problem. Indian J. Lepr **63** (1991) 401–409.

In conclusion, I would like to point out that there is still an immense amount of work that needs to be done if the target of elimination of leprosy as a public health problem is to be achieved by the year 2000, as envisaged by the World Health Assembly in its resolution adopted in May 1991. The target can be achieved provided that further substantial intensified efforts are made in terms of both action and mobilization of adequate resources. Such intensification is important, particularly during the next few years. For the leprosy-endemic countries like India, it is an important opportunity that cannot be missed. It remains to be seen how we exploit this opportunity and thus solve a major public health problem.—From the Article

Smith, P. G. Recent trends in the epidemiology of tuberculosis and leprosy. Trop. Geogr. Med. **43** (1991) S22–S29.

Recent advances in the study of the epidemiology of tuberculosis and leprosy are reviewed with special reference to the impact of BCG vaccination against both diseases and to serological tests for the early diagnosis of leprosy.—Author's Abstract

Rehabilitation

Gershon, W. and Srinivasan, G. R. Community-based rehabilitation: an evaluation study. Lepr. Rev. **63** (1992) 51–59.

Leprosy gives rise to two types of stigmatization, one from the disease and its neuropathetic manifestations, with their resultant disability and handicaps, and the other due to social ostracism. The process of rehabilitation should begin from the moment the disease is diagnosed, and the earlier its detection the better the prognosis for patients. The family unit to which the patient belongs plays a vital role in his social life, ensuring and enhancing his self-respect and dignity in society, and this fact must be recognized when evolving a strategy for rehabilitation. In no circumstances should a patient be removed from his natural home environment. It is important that the community is made leprosy conscious and gets more involved in hastening the social assimilation of patients. Communication plays an important role throughout the rehabilitation process. One of the major functions is the removal of the social stigma in the

family and in the community, and this involves communication skills to ensure interaction between the staff and patients' families and the education of the community. A highlight of community-based rehabilitation is the excellent rate of repayment of loans by the patients to whom they were made. Also of note is the extent to which former defaulters make repayments due to the continuous rapport and good interpersonal relationship between the staff and patients. Most of the subjects of this study were drawn from the lower economic strata of society and for them the most essential consideration is to make a living, however meager. This problem is augmented in the case of leprosy sufferers, not only because of the fear and hostility which their disease excites in others, but because of their deformity and handicap. No rehabilitation program can afford to ignore these factors which so seriously disturb the normal life of patients.—Authors' Summary

Other Mycobacterial Diseases and Related Entities

Bessis, D., Guillot, B., Monpoint, S., Dandurand, M. and Guilhou, J. J. Thalidomide for systemic lupus erythematosus. Lancet **1** (1992) 549–550.

We report 3 patients with SLE, confirmed according to the American Rheumatism Association 1982 criteria. In all 3 patients a good clinical response of cutaneous and articular symptoms to thalidomide was seen within the first month of treatment, being greatest after 3–4 months. Moreover, in corticodependence, doses were lowered substantially by instituting thalidomide therapy combined with glucocorticoids. Despite the low doses, drowsiness was reported by 2 patients, leading to discontinuation of treatment in 1, and sensitive neuropathy was seen in 1 case, but this disappeared 4 months after stopping treatment. Nevertheless we believe that thalidomide treatment at moderate doses combined with glucocorticoids, under strict contraceptive measures, is helpful for SLE because it improves cutaneous and articular control, and steroid use can be reduced. Although thalidomide probably has an immunomodulator role, its mode of action has not yet been established.—From the Letter

Prevention and control of tuberculosis among homeless persons; recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR **41** (1992) 13–23.

Because tuberculosis (TB) is a major problem among homeless persons, the Advisory Council for the Elimination of Tuberculosis has developed recommendations to assist health-care providers, health departments, shelter operators and workers, social service agencies, and homeless persons prevent and control TB in this population. TB should be suspected in any homeless person with a fever and a productive cough of more than 1–3 weeks' duration, and appropriate diagnostic studies should be undertaken. Confirmed or suspected TB in a homeless person should be immediately reported to the health department so that a treatment plan can be decided upon and potentially exposed persons located and examined. Patients with TB should be counseled and voluntarily tested for human immunodeficiency virus (HIV) infection because TB treatment recommendations are different for HIV-seropositive and HIV-seronegative persons. TB therapy should be directly observed whenever possible. This may require the establishment of special shelters or other long-term-care arrangements for homeless persons with TB. For each person with an infectious case, an investigation should be conducted to identify exposed persons, and those found to be infected should be considered for preventive therapy. Shelter staff should receive a tuberculin skin test when they start work and every 6–12 months thereafter. Those with positive skin test results should be considered for preventive therapy according to current guidelines. Shelters for the homeless should be adequately ventilated. The installation of ultraviolet lamps also may be

useful to further reduce the risk of TB transmission.—Summary of Recommendations

Prevention and control of tuberculosis in U.S. communities with at-risk minority populations; recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR **41** (1992) 1–11.

Tuberculosis (TB) is an increasing public health problem in the United States, particularly among racial/ethnic minorities. In 1990, the number of reported TB cases increased 9.4% compared with 1989 and 15.5% compared with 1984. In 1990, almost 70% of all TB cases and 86% of those among children ages <15 years occurred among racial/ethnic minorities. Compared with non-Hispanic whites, the 1990 TB case rate was notably higher for racial/ethnic minorities. Adverse social and economic factors, the human immunodeficiency virus epidemic, and immigration of persons with tuberculous infection are contributing factors to the increase in TB cases. Other contributing factors include physician nonadherence in prescribing recommended treatment regimens and patient nonadherence in following prescribed recommended treatment regimens.

To eliminate TB in U.S. communities with at-risk racial/ethnic minorities, the Advisory Council for the Elimination of Tuberculosis recommends a) initiating public awareness campaigns to alert these communities about the increasing TB problems; b) training and educating public and private health-care providers in the skills needed to relate effectively to the at-risk communities being served, and empowering at-risk populations with knowledge and other resources needed to influence the TB programs directed toward their communities; c) building coalitions to help design and implement intensified community TB prevention and control efforts; d) intensifying the screening of at-risk populations for TB and tuberculous infection and providing appropriate treatment and preventive therapy; e) increasing the speed and completeness with which all health-care providers report confirmed and suspected TB cases to appropriate health departments; and f) improving the availability and quality of TB health-care services in socioeconomically disadvantaged areas.—Summary of Recommendations

Selvakumar, N., Kumar, V., Acharyulu, G. S., Rehman, F., Paramasivan, C. N. and Prabhakar, R. Susceptibility of south Indian strains of *Mycobacterium tuberculosis* to tuberactinomycin. Indian J. Med. Res. [A] **95** (1992) 101–104.

A total of 114 strains of *Mycobacterium tuberculosis* isolated from sputum samples of 114 patients of pulmonary tuberculosis in south India, were coded and tested for their *in vitro* susceptibility to tuberactinomycin (Tum) incorporated in Löwenstein-Jensen (LJ) medium. Of these strains, 95 (83.3%) and 15 (13.2%) were susceptible to Tum at 25 and 50 mg/l, respectively. Only 4 (3.5%) strains were inhibited at 100 mg/l or more. Of the 37 drug-sensitive strains, 2 (5.4%) were not susceptible to Tum at 25 mg/l compared to 17 (22.1%) of 77 strains resistant to one or more antituberculosis drugs ($p < 0.02$). The drug susceptibility pattern of the strains revealed that there was no significant association of resistance between Tum and streptomycin or rifampin or ethambutol or ethionamide or isoniazid. However, 15 (53.6%) of 28 kanamycin (K) resistant strains were not susceptible to Tum at 25 mg/l. This crossresistance between Tum and K was further studied in 24 and 15 K sensitive and resistant strains, respectively, by correlating their proportion resistance at 16 mg/l, and it was found to have a significant positive correlation ($r = 0.55$; $p < 0.001$).—Authors' Abstract

Yamada, T., Mizuguchi, Y., Isono, S. and Isono, K. Genetic and biochemical analysis of ribosomal proteins of minocycline-susceptible and -resistant *Mycobacterium smegmatis*. Microbiol. Immunol. **36** (1992) 139–148.

A minocycline (MINO)-resistant mutant was isolated from *Mycobacterium smegmatis* strain Rabinowitschi. Polypeptide synthesis in the cell-free system prepared from the mutant was resistant to MINO because of alterated 30S ribosomal subunits. Upon two-dimensional gel electrophoresis, two proteins of 30S subunit were found to be altered. MINO-resistant phenotype was

transferred by mating to the recipient strain P-53. MINO-resistant phenotype of a recombinant thus obtained was transferred by a different mating system to the recipient strain, Jucho, once again. Ribosomal proteins of each of the donors, recipients and recombinants were analyzed and compared on two-dimensional (2D) electrophoresis. Approximately 50 ribosomal proteins were observed in 70S ribosomes. Some proteins were differently electrophoresed in different strains. The 30S ribosomal subunits contained at least 19 proteins and 50S ribosomal subunits contained at least 23 proteins. Some proteins were easily washed off during dissociation of subunits in sucrose gradients. At least one protein (designated F) in both subunits was observed at the same position. One protein designated C in 30S subunits could be co-transferred to the recipient cells together with resistance phenotype at the frequency of 100% in the 30 recombinants examined so far. The other protein designated D in 30S subunits could be transferred at the frequency of 86%–88%. Three other proteins in 50S subunits could be co-transferred to the recipient strain at a lower frequency. Minocycline resistance, therefore, could be mapped close to genes encoding the structure of ribosomal proteins in *M. smegmatis.*—Authors' Abstract