CURRENT LITERATURE

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

General and Historical

Findlay, G. H. Samuel Patton Impey, M.D. (Aberdeen) (1856–1928), Cape Town's primordial leprologist, dermatologist, radiotherapist and rock-art enthusiast. S. Afr. Med. J. **71** (1987) 381–385.

Samuel Impey was a noteworthy medical pioneer of the Cape Colony. He was the author of what was probably the first medical textbook of note to be written in South Africa, a *Handbook of Leprosy,* published in London in 1896. He carried much of the frontier spirit into the medical life of the time, entering vigorously into controversy and fresh developments. As an amateur artist, he also put forward some individual views on rock paintings.—Author's Summary

Naudin, J. C., Detoeuf, G., Diouf, B. and Millan, J. [Practical problems of multidrug therapy management in Senegal.] Acta Leprol. **4** (1986) 479–489. (in French)

The authors make an inventory of the difficulties they have met while realizing the different stages of multidrug therapy treatment programs in Senegal. Main problems were: a) necessity of complementary training on theoretical but even more on practical techniques for all the staff: Ridley and Jopling classification, neurological examination, bacteriological examination, data collection; b) difficulty to maintain a true supervision; c) necessity to settle a quality control of slit-skin smears; d) necessity to settle a system to trace irregular patients; e) heaviness of centralized management, but its necessity to maintain "tightness" of the drug distribution network; f) difficulty to obtain a regular follow up of patients who are released from treatment. The evolution of antileprosy activities makes it necessary to adapt the "Service des Grandes Endemies."—Authors' English Summary

Reich, C. V. Leprosy: cause, transmission, and a new theory of pathogenesis. Rev. Infect. Dis. **9** (1987) 590–594.

Leprosy is generally accepted as being caused by *Mycobacterium leprae,* an acid-fast organism often present in great numbers in certain forms of leprosy. However, it has not been possible to confirm with scientifically acceptable evidence that this entity is the cause of leprosy; laboratory cultivation, an essential factor in the proof, has not been accomplished with the acid-fast bodies seen in leprotic tissue. The mechanisms of transmission of the disease also remain conjectural; prolonged, close contact and transmission by nasal droplet have both been proposed and, while the latter fits the pattern of disease, both remain unproved. It is proposed that the causative agent of leprosy is not a difficult-to-transmit agent but, rather, an organism that has evolved a highly efficient state of parasitism in stable types of populations and that everyone in the population harbors the leprosy parasite at some time. The majority of the population incubate subclinical infections at various levels; clinical leprosy arises from within the pool of subclinical infection in the endemic population rather than by transmission from an index case. A theory of complete infection of endemic populations is consistent with the rate of development and distribution of positive lepromin reactions among healthy persons in endemic regions and provides an explanation for the difficulty in controlling leprosy in endemic populations by isolation of patients or by therapy for clinical cases.—Author's Abstract

Chemotherapy

Deng, Y., Qian, A., Hui, D., *et al.* [Relapse of leprosy among 599 arrested cases in the city of Baoji.] Chin. Lepr. J. **3** (1986) 12–13. (in Chinese)

There were accumulatively 599 arrested cases of leprosy in the city of Baoji, Shanxi Province, in the years of 1955–1985, of which 328 cases were reexamined in 1985 and 28 relapsed cases were found among them. The rate of relapse is 8.54%. A lot of the factors which could bring about relapse are discussed, and the authors point out that shorter course of treatment and lack of compliance in treatment for preventing relapse are the major causes of relapse.—Authors' English Abstract

Dousset-Faure, I., Millan, J., Decazes, J. M. and Languillon, J. [Clinical and bacteriological evaluation 8 years after triple drug chemotherapy for multibacillary leprosy in Senegal.] Acta Leprol. **4** (1986) 465–472. (in French)

Increasing resistance to dapsone (DDS) leads to recommend triple-drug chemotherapy (TCT) in multibacillary leprosy. To determine long-term evolution, we evaluated patients who received TCT 8 years ago. Between 1974 and 1976, 30 patients with multibacillary leprosy received TCT (rifampin, prothionamide and DDS) for 6 or 12 months. At this time, satisfactory clinical and bacteriological findings were reported, and from then DDS was given alone. Twelve of the 30 patients were evaluated in 1983. Six patients had a bacterial index $\geq 2+$; three of them had clinical relapse. Seven of the 12 patients did not take DDS regularly; the six relapses belong to this group.—Authors' English Summary

Girdhar, A., Girdhar, B. K., Ramu, S. G., *et al.* Effect of prothionamide on the infectivity of lepromatous leprosy. Indian J. Dermatol. Venereol. Leprol. **51** (1985) 198–201.

To study the effect of prothionamide on the infectivity of untreated lepromatous patients, 20 cases were randomly given either 250 mg or 500 mg prothionamide monotherapy daily for 2 months. All patients tolerated the drug well. Clinical improvement with healing of mucosal ulcers was seen in 13 of the 16 cases. Nasal smears became negative in all the cases within 2 months. Mouse foot pad inoculation done from biopsy specimens/skin scrape suspensions became noninfective to mice in all the cases within the trial period. There was a substantial reduction in the morphological index, and histopathology showed complete fragmentation of the bacilli with a significant increase in the lymphocyte content. The findings suggest a rapid bactericidal effect and a similar usefulness of both the doses of the drug for the treatment of multibacillary leprosy.—(*From* Excerpta Medica)

Grillone, S. and Pattyn, S. R. [New plan of the war against leprosy in Anjouan; preliminary results.] Acta Leprol. **4** (1986) 453–460. (in French)

Treatment of paucibacillary leprosy patients with 10 weekly doses of rifampin 600 mg gave a cure rate of 88% or more at 3 years as judged by histopathology. There were no severe neurological complications. The future will show if this regimen also prevents relapses. In multibacillary leprosy, a 2-month regimen of daily rifampin, ethionamide, and dapsone followed by 10 months of daily ethionamide and dapsone with weekly rifampin gave excellent clinical and bacteriological results. There were no relapses for 2–3 years after the end of therapy among 111 newly diagnosed and previously treated patients (95% confidence interval 3.3%) of whom 67 were new patients (95% confidence interval 5.3%). The hepatotoxicity of this regimen has to be followed closely. The results illustrate the possibility to cure multibacillary leprosy by a treatment of finite duration.—Authors' English Summary

Husser, J. A., Baquillon, G. and Pattyn, S. R. [Comparison of three therapeutic regimens for paucibacillary leprosy; prelim-

inary note.] Acta Leprol. **4** (1986) 447–452. (in French)

Between 1980 and 1983, all paucibacillary patients presenting at the Institut Marchoux, Bamako, took part in a prospective randomized therapeutic trial and were allocated to one of the following regimens: Dapsone 100 mg 7/7 3 years, rifampin 900 mg 1/7 8 doses, rifampin 900 mg 7/7 12 doses. At this moment, 24, 29, and 22 patients, respectively, have been followed for periods of 24–56 months. With the exception of some irregular drug intake in the dapsone patients followed either by relapse or delay in improvement, the efficacy as judged by histopathological examination did not reveal any difference between the regimens. The study continues.—Authors' English Summary

Liu, W., *et al.* [Relapse of leprosy in Jinju hospital for old-disabled patients.] Chin. Lepr. J. **4** (1986) 27–28. (in Chinese)

There are 357 arrested leprosy cases in Jinju hospital for disabled leprosy patients in Guangdong Province, of which 36 cases have relapsed in 1964–1985 and 26 recurred in 1980–1985 with a relapse rate of 10.1%. Among 246 arrested multibacillary leprosy patients, 35 cases have relapsed (14.2%), and among 123 arrested paucibacillary patients only one case relapsed. Among 12 cases that recurred in 1984, five cases showed positive results on bacteriological examination without clinical expression.—Authors' English Abstract

Miao, Z. and Xiong, S. [Effect of multibacillary leprosy patients taking multidrug therapy on the population around them.] Chin. Lepr. J. **3** (1986) 10–11. (in Chinese)

Twenty-one multibacillary cases of leprosy have been treated with the multidrug regimen of dapsone (DDS), rifampin (RMP), and clofazimine (B663) at their homes. After 1–3 years of treatment, their bacterial index decreased from 2.8 to 0.6–1.1 on an average. The 726 contacts with the patients, living in their houses or in the same villages, were examined two times a year for 3 years and no case was found suffering from leprosy.—Authors' English Abstract

Pattyn, S. R., Husser, J. A. and Saint-André, P. [Efficacy of combined treatments involving 6 months' administration of rifampin in multibacillary leprosy.] Acta Leprol. **4** (1986) 445–446. (in French)

Ten patients infected with mouse-proven dapsone-resistant bacilli were treated with the following combined regimen: rifampin 600 2/7 6 months, ethionamide 500 7/7 6 months, and dapsone 100 7/7 12 months. Follow up was for 27–54 months without relapses. Added to patients from previous study (Int. J. Lepr. **52**:297–303, 1984), the 95% confidence limit decreases from 12% to 9%.—Authors' English Summary

Prabhakaran, K., Tsutsumi, S. and Harris, E. B. Effect of 2-mercapto-3-hydrazinoquinoxaline (MHQ) on diphenoloxidase and growth of *Mycobacterium leprae*. Microbios Lett. **34** (1987) 139–142.

Strains of *Mycobacterium leprae* resistant to the antileprosy drugs presently in use have already emerged. MHQ (2-mercapto-3-hydrazinoquinoxaline) is a compound with broad antimicrobial (including antituberculous and antimycotic) activity. Among mycobacteria, diphenoloxidase is an *M. leprae*-specific enzyme reported to be essential for the growth of the organism in the host. The effect of MHQ was tested on diphenoloxidase of *M. leprae* and on multiplication of the bacteria in mouse foot pads. The drug did not inhibit the enzyme and showed no antibacterial effect on the growth of the bacilli.—Authors' Abstract

Wang, Z. and Chen, J. [Report on four cases with acute DDS intoxication.] Chin. Lepr. J. **3** (1986) 17–20. (in Chinese)

The authors reported four cases of leprosy with acute intoxication from dapsone (DDS). These patients had swallowed 66–130 tablets of DDS containing 50 mg per tablet and clinically showed methemoglobinemia, hemolytic anemia, icterus, hepatic function disturbance, fever, and psychosis. Two cases died and two recovered. The pathological mechanism and treatment of DDS intoxication are discussed.—Authors' English Abstract

Wu, Y. [First year's results of multidrug therapy of leprosy.] Chin. Lepr. J. **4** (1986) 16–17. (in Chinese)

Eighty-five cases of multibacillary leprosy who have been treated with dapsone in the hospital without good results on the single dapsone regimen were transferred to three-drug (dapsone, rifampin and clofazimine) therapy. One year after the combined treatment, the skin lesions have partly disappeared in 90.6% of the patients, the bacterial index has decreased by an average of 0.41 in 84.2%, and leprosy reactions (especially type 2) have been mostly controlled. No side effects were observed.—Authors' English Abstract

Xu, R., *et al.* [Treatment of leprosy with two multidrug regimens for one year.] Chin. Lepr. J. **4** (1986) 17–18. (in Chinese)

Thirteen cases of leprosy have been treated with combined regimens containing dapsone, rifampin, and clofazimine or dapsone plus rifampin for 1 year and showed that there are no differences in clinical effects and toxicities between the two regimens, but the bacteriological and pathological improvements in the group with clofazimine are better than those without clofazimine.—Authors' English Abstract

Yang, T.-T. and Swarbrick, J. Sustained-release delivery systems, I: Phase diagram studies of dapsone and selected derivatives. J. Pharm. Sci. **75** (1986) 53–56.

In order to develop slowly dissolving particles containing the antileprotic drug dapsone (4,4′-sulfonylbisbenzamine, 1) that would be suitable for a sustained-release intramuscular injection, the dilauryl (2) and monolauryl (3) derivatives of dapsone, *N,N′*-didodecanoyl - 4, 4′ - sulfonylbisbenzamine and *N*-dodecanoyl-4,4′-sulfonylbisbenzamine, respectively, were studied for their ability to form solid dispersions with the parent compound. The 1:2 binary phase diagram showed these two compounds were partially miscible in the liquid state, leading to the coexistence of a monotectic and a eutectic system in the phase diagram. The 1:3 phase diagram showed that these compounds were completely miscible in the liquid state and formed discontinuous solid solutions in the solid state. At a cooling rate of 2.5°C min^{-1}, eutectic mixtures lying on the dapsone side of the eutectic point formed glass solutions. Taken as a whole, the results demonstrate that the molecular interactions between 1 and 3 are stronger than those between 1 and 2. Accordingly, 3 would appear to be the better carrier for reducing the rate of dissolution of dapsone from a solid dispersion.—Authors' Abstract

Yang, T.-T. and Swarbrick, J. Sustained-release delivery systems, II: *In vitro* dissolution of 4,4′-sulfonylbisbenzamine (dapsone)—*N*-dodecanoyl-4,4′-sulfonylbisbenzamine comelts. J. Pharm. Sci. **75** (1986) 264–270.

An approach under investigation in our laboratory is the development of slowly dissolving particles containing an active drug, mixed or coated with a less-soluble derivative or derivatives, that may hydrolyze back to the active drug following solution. Such particles have potential for sustained release by a number of routes of administration, including intramuscular injection. In the present work, the *in vitro* dissolution of particles of 4,4′-sulfonylbisbenzamine (dapsone) (1) and various comelts of 4,4′-sulfonylbisbenzamine (dapsone) (1) and *N*-dodecanoyl-4,4′-sulfonylbisbenzamine (the monolauryl derivative of dapsone) (3) was studied using a continuous flow-through cell under laminar flow conditions. Dissolution of particles of dapsone showed a biphasic pattern when plotted according to the Hixson–Crowell cube root equation. Dissolution rates of dapsone (1) from the comelts were found to correlate with the physical state of 1 in the solid binary dispersion. Comelts of 1:3 with a content higher than 36.5% w/w 1 (the eutectic mixture) had initial rates of dissolution which appeared to be dependent on the porosity of the particles. However, once this initial phase passed, the total amount dissolved increased as the amount of noneutectic 1-rich solid solution in the comelt increased. This suggests that 1 in the eutectic mixture has a slower dissolution rate than when present in the noneutectic, or excess 1-rich solid solution form. The comelts with a content of dapsone at

or below the eutectic mixture dissolved more slowly and their dissolution rates were less dependent on concentration of 1. The mechanism of release of 1 from 1:3 comelts appeared to be matrix diffusion-controlled.—Authors' Abstract

Ye, S., Tang, M. and Lu, W. F. [II. *M. lepraemurium* in cell culture, possibly useful for screening antileprosy drugs.] Chin. Lepr. J. **3** (1986) 23–28. (in Chinese)

The anti-*Mycobacterium lepraemurium* activity of several drugs was determined by using the model of *M. lepraemurium* cell culture. The result showed that the multiplication of *M. lepraemurium* was inhibited by rifampin (10 μg/ml) and streptomycin (100 μg/ml), but not by dapsone (10 μg/ml). These results were consistent with that in the animal infection model. Also a new drug, R-773 (10 μg/ml and 5 μg/ml), could inhibit the multiplication of *M. lepraemurium*. Therefore, the model of *M. lepraemurium* cell culture showed promise for use in screening antileprosy drugs.—Authors' English Abstract

Clinical Sciences

Balybin, E. S. [Iodine metabolism in leprosy patients (examination with a method of total body radiometry)]. Med. Radiol. (Mosk.) **2** (1986) 36–39. (in Russian)

A method of total body radiometry was used to study iodine metabolism in 47 patients with lepromatous leprosy. Disorders were found in ⅓ of the cases. The level of organic iodine in the body was the most informative of all iodine metabolism indices. In the active stage of leprosy it was twice as low, on an average, as the normal one, in the stage of incomplete and stable regression it rose not reaching, however, the values of healthy persons. The lowest mean value of an organic iodine level in the body was observed in patients with noticeable specific polyneuritis. The content of iodine in the thyroid of leprosy patients showed a tendency to rise starting from the active stage, however it was only in the stages of incomplete and stable regression that it significantly exceeded the normal level. The data obtained should be considered during therapy of leprosy patients to predict and control an unfavorable complication like specific polyneuritis.—Author's English Summary

Bucci, F., Jr., Mesa, M., Schwartz, R. A., McNeil, G. and Lambert, W. C. Oral lesions in lepromatous leprosy. J. Oral Med. **42** (1987) 4–6.

A case of lepromatous leprosy presenting with characteristic oral lesions is reported. The literature related to oral manifestations of leprosy is reviewed. The pattern and sequence of involvement of the oral tissues suggest that a mechanism of self-inoculation and/or direct extension may be operating in the spread of these infections.—Authors' Summary

Immuno-Pathology

Abe, M., Miyaji, I., Okushita, T., Minagawa, F., Yoshino, Y., Sakamoto, Y. and Saikawa, K. Anti-mycobacterial antibodies in saliva. Lepr. Rev. **57** Suppl. 2 (1986) 213–223.

Modified techniques for the fluorescent leprosy antibody absorption (FLA-ABS) test and the enzyme-linked immunosorbent assay (ELISA) using phenolic glycolipid-I (PGL-I) antigen of *Mycobacterium leprae*

were employed for detecting anti-*M. leprae* antibodies in sera and saliva from the patients with leprosy, household contacts and inhabitants in leprosy endemic areas. The FLA-ABS test with saliva was positive in 20 (58.8%) of the 34 household contacts, 92 (39%) of the 236 schoolchildren, and 37 (38.1%) of the 97 adults who had social contacts with leprosy, but negative in the 23 patients with pulmonary tuberculosis. Serological specificity of salivary anti-*M. leprae* antibodies detected in the specimens of saliva from the schoolchildren was checked by crossreactions and additional absorption tests. Only 7 out of the 55 specimens of saliva showing a positive FLA-ABS test were crossreactive with some species of mycobacteria. Positive reactions against *M. leprae* were not influenced at all by additional absorptions with crossreacting mycobacteria, but became negative after an additional absorption with *M. leprae*. Therefore, the modified technique of FLA-ABS test was found specific to *M. leprae* and useful for detecting subclinical leprosy infection. The PGL-I-ELISA activity was most frequently found in the serum and salivary IgA from the patients with leprosy, the percentage of positive reactions in saliva being comparable to that of FLA-ABS test. The PGL-I-ELISA using anti-IgA-enzyme conjugate was negative in the specimens of saliva from the patients with tuberculosis and the schoolchildren who had no suspicious symptom or FLA-ABS reactivity, but was positive in 3 (11.1%) of the 27 specimens of saliva from the schoolchildren who had suspicious symptoms and/or FLA-ABS reactivity and in 17 (17.5%) of the 97 specimens of saliva from the adults who had social contacts with leprosy. Therefore, the PGL-I-ELISA with saliva was also found specific to *M. leprae* and useful for detecting the secretory type of anti-PG antibodies. A significant difference in the percentage of positive reactions between FLA-ABS and PGL-I-ELISA was discussed from a point of view concerning specific epitopes of *M. leprae*.—Authors' Summary

Aguado Sanchez, G., Malik, A., Tougne, C., Lambert, P. H. and Engers, H. D. Simplification and standardization of serodiagnostic tests for leprosy based on phenolic glycolipid-I (PGL-I) antigen. Lepr. Rev. **57** Suppl. 2 (1986) 83–93.

In this report we present data from our laboratory related to: a) the standardization of the microplate ELISA for the detection of anti-PGL-I IgM antibodies using the D-BSA synthetic antigen; b) the simplification of sample collection techniques; c) the development and evaluation of a modification of the rapid, sensitive, visual "dot ELISA" using the synthetic D-BSA antigen and nitrocellulose filters as the solid phase; and d) preliminary results concerning the detection of PGL-I antigen in the urine of leprosy patients using a rapid, simple, nonisotopic "dot ELISA" detection technique.—(*From* the Article)

Anderson, D. C., Young, R. A. and Buchanan, T. M. Solid phase peptide synthesis of epitopes that react with monoclonal antibodies to the 65,000 dalton protein of *Mycobacterium leprae*. Lepr. Rev. **57** Suppl. 2 (1986) 169–175.

The gene coding for the 65,000 dalton protein of *Mycobacterium leprae* has recently been sequenced. Subclones of this gene which expressed a peptide that reacted with monoclonal antibodies (MOAbs) IIC8 or IIIC8 were compared to subclones that expressed nonreactive peptides. From these comparisons it was predicted that the epitopes recognized by MOAb IIC8 and IIIC8 would be contained within separate domains of 12 and 13 amino acids, respectively. The capabilities of solid phase peptide synthesis made it possible to synthesize these peptides and variants thereof to test the accuracy and specificity of the predictions made by DNA sequencing. In addition, as part of a collaborative study of all known monoclonal antibodies to the 65,000 dalton protein, MOAb F67-2 was found to be closely related but different from MOAb IIC8. The IIC8 peptide and its variants were therefore also tested against the F67-2 MOAb. This article reports the peptides synthesized and the results of tests of their antigenicity.—(*From* the Article)

Brett, S. J., Kingston, A. E. and Colston, M. J. Limiting dilution analysis of the human T cell response to mycobacterial

antigens from BCG vaccinated individuals and leprosy patients. Clin. Exp. Immunol. **68** (1987) 510–520.

The number of peripheral blood T lymphocytes responding to soluble mycobacterial antigens from *Mycobacterium tuberculosis* purified protein derivative (PPD) and *M. leprae* (MLS) was estimated by limiting dilution analysis. Antigen-induced lymphocyte activation was measured by means of [^{3}H]TdR incorporation on day 10 of culture in the presence of suboptimal concentrations of interleukin 2 (IL-2). In the peripheral blood of BCG-vaccinated individuals from the U.K., the frequency of T lymphocytes responding to PPD was 1.5 to 4 times greater than to MLS. Frequencies between 1/1970 and 1/13,982 were observed in response to PPD and between 1/4097 and 1/24,717 in response to MLS. A proportion of cells in the peripheral blood was also observed to respond to IL-2 only. The frequency of cells observed in limiting dilution analysis for PPD and MLS reflected the relative amounts of proliferation to these two antigens in bulk culture lymphocyte transformation tests. Use of PPD-specific T-cell lines suggested that the responsiveness observed to *M. leprae* antigens in BCG-vaccinated individuals was due to crossreactivity with antigens shared with *M. bovis* BCG. In tuberculoid leprosy, the frequency of peripheral blood T lymphocytes responding to *M. leprae* antigens was either greater than or similar to the frequency of T cells responding to PPD. In contrast, limiting dilution analysis of T lymphocytes from the peripheral blood of lepromatous leprosy patients revealed the complex regulatory heterogeneity of this group. In some patients, *M. leprae*-responsive T cells were detected in the presence of exogenous IL-2.—Authors' Summary

Britton, W. J., Garsia, R. J., Hellqvist, L., Watson, J. D. and Basten, A. The characterization and immunoreactivity of a 70 kD protein common to *Mycobacterium leprae* and *Mycobacterium bovis* (BCG). Lepr. Rev. **57** Suppl. 2 (1986) 67–75.

A 70 kD protein antigen has been identified in sonicates of *Mycobacterium leprae* and *M. bovis* (bacillus Calmette-Guerin) (BCG) with murine monoclonal antibodies (Mabs). The antigen was readily radiolabeled and was immunoprecipitated by the Mab L7, or leprosy sera. On two-dimensional electrophoresis, it had a pI of 5.1. The protein, after purification from BCG, stimulated proliferation and lymphokine secretion in lymphocytes from Mantoux-positive subjects and elicited skin test reactivity *in vivo*. The sequence of N-terminal residues of the BCG protein was determined. Two DNA clones encoding the Mab-defined epitopes have been isolated from the genome of *M. leprae*.—Authors' Summary

Brown, W. B., Larrabee, W. A. and Kim, P. S. Analysis of a leprosy-specific antibody epitope. Lepr. Rev. **57** Suppl. 2 (1986) 157–162.

The epitope recognized by the monoclonal antibody IIIE9 is the only epitope in the 65 kD antigen that is known to be specific for *Mycobacterium leprae*. Previous work localized a linear epitope recognized by IIIE9 to a 15-residue region of the 65 kD antigen and DNA sequencing of the *M. tuberculosis* homologue indicated that there were only three amino acid substitutions in this 15-residue region. These amino acid substitutions occur at positions 1, 4, and 8.

Our results indicate that the amino acid substitutions at positions 4 or 8 are individually capable of eliminating binding of IIIE9 to peptides when ELISA is used. The amino acid substitution at position 1 appears to be less important. The results suggest that it will be possible to localize further the linear epitope recognized by IIIE9. Our conclusions are preliminary: it is possible but unlikely that the amino acid substitutions have abolished the ability of the peptides to stick to the microtiter wells. We plan to measure binding of the peptides to the antibody in solution (e.g., using radioimmunoassays or competitive ELISA).

If the 15-residue antibody epitope studied here is also found to be a T-cell epitope, then it will be interesting to see how the amino acid changes studied here affect T-cell recognition. The helical wheel representation of Schiffer and Edmundsom indicates

that this sequence is capable of forming an amphipathic α-helix. It has been suggested that T-cell antigenic sites tend to be amphipathic helices. All three amino acid substitutions found in the *M. tuberculosis* sequence are on the same face of this presumptive helix.—(*From* the Article)

Buchanan, T. M., Nomaguchi, H., Anderson, D. C., Young, R. A., Gillis, T. P., Britton, W. J., Ivanyi, J., Kolk, A. H. J., Closs, O., Bloom, B. R. and Mehra, V. Characterization of mycobacterial species specificity of 14 separate epitopes which reacted with monoclonal antibodies to the 65,000 molecular weight protein molecule of *Mycobacterium leprae*. Lepr. Rev. **57** Suppl. 2 (1986) 63–66.

This study examined the number of different epitopes recognized by 23 monoclonal antibodies known to recognize the 65 kD protein of the leprosy bacillus, and the mycobacterial species specificity of those 14 monoclonal antibodies shown to recognize different epitopes.—(*From* the Article)

de Vries, R. R. P., Ottenhoff, T. H. M., Li, S.-G. and Young, R. A. HLA class II restricted helper and suppressor clones reactive with *Mycobacterium leprae*. Lepr. Rev. **57** Suppl. 2 (1986) 113–121.

More than 10 years ago we decided to start a search for HLA-linked factors controlling the course of *Mycobacterium leprae* infections. We chose an infectious disease because—in contrast to the diseases known to be associated with HLA at that time—there the etiological agent is known. We chose leprosy because of its remarkable spectrum of clinical symptoms paralleling the cell-mediated immune reactivity of the host to the bacillus. This choice appeared to be an extremely lucky one for two reasons. The first is that HLA molecules were shown to regulate antigen presentation to T cells which, apart from being important in leprosy, appeared to be easy to clone *in vitro*. The second reason is that recently a remarkable progress has been made in the characterization and synthesis of *M. leprae* antigen. Thus, we and others are now in a rather privileged position to be able to study in detail the role of HLA products in the presentation of well-defined medically relevant antigens. Such studies may contribute to the definition of both mechanisms and potential epitopes involved in protective immunity, immunopathology, and suppression following an infection with *M. leprae*.

In this paper we review our recent studies and present new data on restriction and antigen specificity of *M. leprae*-reactive helper and suppressor clones.—(*From* the Article)

Fine, P. E. M., Ponnighaus, J. M. and Maine, N. P. The relationship between delayed type hypersensitivity and protective immunity induced by mycobacterial vaccines in man. Lepr. Rev. **57** Suppl. 2 (1986) 275–283.

The prominent position of skin testing in the literature on BCG against tuberculosis and leprosy and in the design of mycobacterial vaccine trials implies a belief that skin test results are informative with regard to the protective action of such vaccines. This review of the literature and analysis of data from Malawi have failed to find evidence of the usefulness of skin tests in this context. In particular: a) There is little evidence that either prevaccination or postvaccination skin tests, e.g., with tuberculin, are predictors of vaccine efficacy against either leprosy or tuberculosis. b) The observation that natural strong tuberculin sensitivity was associated with "protection" against leprosy in Uganda has not been confirmed elsewhere, and may have been an artifact attributable to other characteristics of the tuberculin-positive group in the Uganda trial. c) There is no evidence that the waning of post-BCG vaccination tuberculin sensitivity is associated with waning protective immunity. Thus, there is no justification for repeating a BCG vaccination solely on the basis of waning tuberculin sensitivity.—(*From* the Article)

Gigg, J., Gigg, R., Payne, S. and Conant, R. The allyl group for protection in carbohydrate chemistry. Part 19. The coupling of allyl 2,3-di-*O*-methyl-4-*O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside to bovine serum albumin. Preparation of a diagnostic reagent for antibodies to the major glyco-

lipid of *Mycobacterium leprae* (the leprosy bacillus) in human sera. J. Chem. Soc. Perkin Trans. **1** (1987) 1165–1170.

Epoxidation of allyl 4-*O*-(2,4-di-*O*-benzyl-3,6-di-*O*-methyl-β-D-glucopyranosyl)-2,3-di-*O*-methyl-α-L-rhamnopyranoside and subsequent alkaline hydrolysis of the epoxide and hydrogenolysis of the benzyl groups gave 2′,3′-dihydroxypropyl 2,3-di-*O*-methyl-4-*O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside which was cleaved with sodium metaperiodate to give the corresponding formylmethyl glycoside. Two other routes to the latter compound, via allyl 2,3-di-*O*-methyl-4-*O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside, were also developed. The formylmethyl glycoside was coupled to bovine serum albumin using "reductive amination" in the presence of sodium cyanoborohydride to give a glycoconjugate useful for the serodiagnosis of antibodies to the major glycolipid of *Mycobacterium leprae* in the sera of leprosy patients. 5′,6′-Dihydroxyhexyl and 10′,11′-dihydroxyundecyl 3,6-di-*O*-methyl-β-D-glucopyranosides were also prepared as intermediates for the synthesis of the 4-formylbutyl and 9-formylnonyl glucosides, respectively, which are also suitable for coupling to bovine serum albumin by the "reductive amination" technique.—Authors' Abstract

Gill, H. K., Mustafa, A. S., Ivanyi, J., Harboe, M. and Godal, T. Humoral immune responses to *M. leprae* in human volunteers vaccinated with killed, armadillo-derived *M. leprae*. Lepr. Rev. **57** Suppl. 2 (1986) 293–300.

In a trial of a leprosy vaccine consisting of killed, armadillo-derived *Mycobacterium leprae*, four groups of healthy human volunteers residing in a leprosy nonendemic country were given 1.5×10^7, 5×10^7, 1.5×10^8 and 5×10^8 bacilli intradermally. The antibody responses to *M. leprae* in these volunteers were measured before and up to 1 year after vaccination using two assays: a serum antibody competition (SAC) test and an enzyme-linked immunosorbent assay (ELISA). Both assays revealed similar antibody profiles in the vaccinees. The two groups which received the lower doses of vaccine were observed to have very low levels of antibody before and up to 1 year after vaccination. The two groups which received the higher doses of vaccine showed low antibody titers before and up to 3 months after vaccination, with a discernible rise in antibody titers 6 months after vaccination which increased even further 1 year after vaccination.—Authors' Summary

Harboe, M. and Wiker, H. G. Immunological and biochemical characterization and classification of mycobacterial antigens. Lepr. Rev. **57** Suppl. 2 (1986) 33–37.

A combination of biochemical techniques and studies of the reactivity with polyvalent, precipitating antibodies in systems providing high resolving power like crossed immunoelectrophoresis presents powerful tools for reliable identification of individual constituents of mycobacteria before further detailed studies of their immunological reactivity at epitope level towards B and T cells.—(*From* the Article)

Hokama, Y., Dayaon, E., Iwamoto, L., Yanagisawa, R., Reichert, E., Sato, D. and Ching, C. Y. Significant enhanced superoxide anion (O_2^-) monocytes of lepromatous leprosy patients stimulated with liposome and suppression by C-reactive protein (CRP). J. Med. **17** (1986) 299–311.

Peripheral blood monocytes (PBM) from normal individuals, infectious mononucleosis (IM) and leprosy patients were stimulated with liposome. The mean and standard error of superoxide anion (O_2^-) generated in nm/1.5×10^5 PBM/well for 5 normal subjects and 3 IM patients was 2.9 ± 0.5 and 3.1 ± 0.2, respectively. Monocytes stimulated with 100 ng C-reactive protein (CRP) incorporated into liposome gave values of 3.3 ± 0.3 and 2.7 ± 0.1 nm $O_2^-/1.5 \times 10^5$ PBM/well for normals and IM, respectively. No significant differences in O_2^- production between liposome and liposome with incorporated CRP were shown. PBM from lepromatous patients demonstrated a significant ($p < 0.01$) increase in O_2^- production with liposome alone compared with tuberculoid patients (3.5 ± 0.4 vs 1.8 ± 0.3). The most dramatic

suppression of O_2^- was shown when purified CRP was added to the mixtures in all groups examined 0.4 ± 0.1 (500 ng), 0.3 ± 0.0 (500 ng), 1.5 ± 0.1 (100 ng), and 1.3 ± 0.6 (100 ng) nm $O_2^-/1.5 \times 10^5$ PBM/well for normals, IM, lepromatous, and tuberculoid, respectively. Results of O_2^- formation with incorporation of CRP into liposome as compared with liposome alone had no significant effect on PBM of lepromatous or tuberculoid patients. It is suggested that CRP may play a significant role in regulation of oxygen-free radicals formed during acute and chronic inflammatory episodes.—Authors' Abstract

Hussein, Y. M., Kerr, M. A. and Beck, J. S. The mechanism of action of the factor in leprosy serum that inhibits the growth of mitogen-stimulated normal human lymphocytes. Immunology **61** (1987) 125–129.

A factor found in the serum of patients with leprosy that inhibits the growth of mitogen-stimulated, normal, peripheral blood lymphocytes has been studied. The inhibitor, previously identified as an IgG, has been shown to act by blocking the recruitment of lymphocytes into growth. It was not cytotoxic and did not inhibit the rate of growth of those lymphocytes that had been stimulated. The inhibitory activity was less potent if the serum was added after mitogen stimulation. The inhibitor, which could be absorbed by activated but not resting lymphocyte cultures, appeared to act by inhibition of an early event preceding the release of IL-2. The inhibition of mitogen stimulation was overcome by the addition of purified IL-2, although the inhibitor did not block the action of IL-2 on a long-term cultured IL-2-dependent cell line.—Authors' Summary

Ivanyi J. and Praputpittaya, K. Analysis of idiotypes expressed by anti-mycobacterial mouse monoclonal antibodies using rabbit antisera. Lepr. Rev. **57** Suppl. 2 (1986) 53–61.

Rabbit antisera against 12 mouse monoclonal antibodies to mycobacterial antigens showed idiotype-specificity following cross-absorption with normal mouse globulin. The functional aspects have been partly evaluated so far with two of these reagents. The representation of ML04 idiotype appeared to be associated with Igh alleles. Injection of mice with Rb04 anti-Id in incomplete Freunds adjuvant induced Id+ serum levels but without corresponding antigen binding specificity. In contrast, Rb71 anti-Id revealed internal image properties corresponding to the homologous 38 kD protein antigen of tubercle bacilli. This was demonstrated by the potency of Rb71 to sensitize mice *in vivo* and to elicit T-cell proliferative and DTH responses.—Authors' Abstract

Kaldany, R.-R. J. and Nurlign, A. Development of a dot-ELISA for detection of leprosy antigenuria under field conditions. Lepr. Rev. **57** Suppl. 2 (1986) 95–100.

A dot-ELISA using nitrocellulose paper as the support has been developed to detect phenolic glycolipid-I (PGL-I) under field conditions. Urine from healthy individuals and those diagnosed as having leprosy were concentrated 100 times using a combination of ultrafiltration and lyophilization; 100 μl aliquots were treated with 5% TCA, or extracted with chloroform/methanol (2:1), or directly applied to the nitrocellulose filter. The antigen was detected using a mouse monoclonal antibody. PGL-I was most easily detected in the urine of lepromatous leprosy patients following extraction with chloroform/methanol. PGL-I was detected in patients' urine for up to 2 months after the onset of multidrug therapy.—Authors' Abstract

Kaplan, G. and Cohn, Z. A. Regulation of cell-mediated immunity in lepromatous leprosy. Lepr. Rev. **57** Suppl. 2 (1986) 199–202.

Patients with lepromatous leprosy demonstrate a selective T-cell unresponsiveness to *Mycobacterium leprae* and fail to mobilize appreciable numbers of T cells—particularly of the T4 (helper) phenotype—into their dermal lesions. In the absence of lymphokine production, cutaneous macrophages serve as permissive hosts for the bacilli and extensive intravacuolar replication

takes place. In our studies, we wished to examine the factors leading to T-cell and monocyte emigration into the skin and the role of interferon-γ. For this purpose we generated delayed hypersensitivity reactions in the dermis of control and lepromatous patients and examined the nature and host-parasite interactions of the cells accumulating at these sites. In addition, we have administered recombinant, human interferon-γ into the skin of patients with lepromatous leprosy. The nature of these reactions at the local and systemic level are presented.—(*From* the Article)

Kaplan, G., Nusrat, A., Witmer, M. D., Nath, I. and Cohn, Z. A. Distribution and turnover of Langerhans cells during delayed immune responses in human skin. J. Exp. Med. **165** (1987) 763–776.

The generation of a delayed immune reaction in the skin involves a large number of complex events leading to the emigration and activation of blood-borne and local elements. This laboratory has over the past 2 years been involved in the analysis of such reactions in the context of leprosy. The lepromatous state is characterized by a lack of specific responsiveness to *Myobacterium leprae* antigens, the absence of the T-helper subset from dermal lesions, and the unrestricted proliferation of *M. leprae* in dermal macrophages. To analyze the striking emigratory defects in these patients, we have generated a second-party immune response in the skin with purified protein derivative of tuberculin (PPD). In many sensitized individuals this has led to a massive influx of monocytes and T cells, largely of the helper phenotype, with subsequent changes in epidermal thickness and Ia expression.

In the course of these immunocytochemical studies, we noted alterations in the number and distribution of T6+ Langerhans' cells (LC)[1] in both the epidermis and dermis. These cells play important accessory roles in initiating T-cell replication and lymphokine formation. Their distribution and turnover in the skin is poorly understood. For this reason we have carried out a combined light- and electron-microscope study, sampling PPD reactions in leprosy patients at short intervals from 1–14 days after the administration of antigen. This has allowed us to quantify the number of LC, evaluate their directional flux into and out of the dermis and epidermis, determine nearest neighbors, and make predictions as to their fate.—(*From* the Article)

Kaufman, S. H. E., Chiplunkar, S., Flesch, I. and de Libero, G. Possible role of helper and cytolytic T cells in mycobacterial infections. Lepr. Rev. **57** Suppl. 2 (1986) 101–111.

The data summarized in this article demonstrate that T cells of both the CD4 and CD8 phenotype are generated after immunization with *Mycobacterium leprae* and *M. tuberculosis*. It is shown that *M. tuberculosis*- and *M. leprae*-reactive CD4 T-cell clones recognize mycobacterial antigens in the context of self class-II molecules and that this recognition triggers the secretion of lymphokines, including IFN-γ. Our experiments with r-IFN-γ and T-cell derived lymphokines reveal that these molecules can indeed render macrophages capable of limiting growth of *M. bovis* and *M. tuberculosis* H37Rv. *M. tuberculosis* Middelburg, however, proved resistant against IFN-γ activated macrophage functions. In addition, our study demonstrates that CD8 T cells are capable of lysing macrophages expressing mycobacterial antigens. Cytolytic activity was, however, not unique to CD8 T lymphocytes since CD4 T cells were also able to lyse macrophages primed with mycobacterial antigens provided the latter expressed sufficient amounts of Ia antigens. Furthermore, not only CD4 but also CD8 T-cell clones produced IFN-γ after appropriate stimulation. From these studies, we conclude that mycobacteria-reactive T-cell clones of CD4 and CD8 phenotype are functionally similar and that they primarily differ in their antigen reactivity pattern. This difference may have consequences for the capacity of these lymphocytes to detect mycobacteria-infected host cells: unlike CD4 T cells which are restricted to Ia-bearing cells, CD8 T cells should be able to detect infections in virtually all nucleated host cells.—(*From* the Article)

Kerr, M. A., Hussein, Y. M., Potts, R. C., Beck, J. S. and Sheriff, M. M. Characterization of a factor in leprosy serum that

inhibits the growth of mitogen-stimulated normal human lymphocytes. Immunology **61** (1987) 117–123.

A factor that inhibits the growth of mitogen-stimulated lymphocytes from normal donors has been detected in the sera of patients with chronic leprosy. The inhibitory activity was detected with similar frequency in patients with tuberculoid or lepromatous leprosy, although higher levels of activity were detected in the latter. The factor reduced the growth in volume of the lymphocytes in the first 24 hr after stimulation, the synthesis of RNA during the first 3 days of culture, and the replication of DNA in 72-hr cultures. All the inhibitory activity co-purified with IgG on gel filtration, ammonium sulfate fractionation and ion exchange chromatography. The activity was stable to heating at 56°C but labile at 100°C and was absorbed from serum or from purified IgG preparations by staphylococcal protein A. On gel filtration of the sera on Sephadex G-200, none of the activity appeared in the void volume, indicating that it is not due to immune complexes. We conclude that the activity is due to an IgG antibody and suggest that it is an autoantibody since the sera inhibited the growth of all donor lymphocytes tested.—Authors' Summary

Kikuchi, I., Ozawa, T., Hirayama, K. and Sasazuki, T. An HLA-linked gene controls susceptibility to lepromatous leprosy through T cell regulation. Lepr. Rev. **57** Suppl. 2 (1986) 139–142.

Genetic control of the clinical manifestation of leprosy was investigated in 66 unrelated patients with leprosy and eight multiplex families. In 32 lepromatous leprosy (LL) patients, both phenotype frequency of HLA-DR2 and haplotype frequency of HLA-B35-DR2-DQwl were significantly increased. Our family data combined with other investigators' showed that the distribution of shared HLA haplotypes differed significantly from the random distribution, thereby suggesting the existence of an HLA-linked major gene for lepromatous leprosy. To investigate the function of this major gene, the cellular mechanism of nonresponsiveness of LL that is strictly specific to *Mycobacterium leprae* (ML) antigen was analyzed using panning technique and monoclonal antibodies. We have tested 30 LL patients for their suppressive activity of T8 cells on the T-cell response to ML of tuberculoid leprosy (TT) patients. T8 cells from two LL patients abrogated the response of TT patients. None of the LL patients tested showed proliferative response to ML antigen even when we removed the T8 cells from the culture. Therefore, we concluded that nonresponsiveness to ML antigen of LL patients *in vitro* was generated by the elimination of responding T cells. In the minor population of LL, T8 suppressor T cells were still active in peripheral blood. The T8 suppressor T cells might play some role in the elimination of responding T cells to ML antigen.—Authors' Abstract

Klatser, P. R., Hartskeerl, R. A., van Schooten, W. C. A., Kolk, A. H., van Rens, M. M. and de Wit, M. Y. L. Characterization of the 36 K antigen of *Mycobacterium leprae*. Lepr. Rev. **57** Suppl. 2 (1986) 77–81.

Our *Mycobacterium leprae*-specific MCAb F47-9 recognizes a 36K protein, one of the antigens previously identified using patients' sera. We have employed this MCAb for the development of an ELISA competition test for serological investigation of patients with leprosy. Furthermore, the 36K antigen has been shown to play a role in the cellular immune-response of leprosy patients. Several T-cell clones from tuberculoid leprosy patients recognized common as well as specific epitopes on this antigen. Continuation of the study of the antigen at the molecular level should further elucidate its role in evoking an immune response against *M. leprae*. Since genes for the major protein antigens of *M. leprae* recognized by mouse MCAbs have been isolated, it has become feasible to isolate large amounts of protein comprising the antigenic determinant recognized by our MCAb F47-9.—(*From* the Article)

Lamb, J. R., Ivanyi, J., Rees, A., Young, R. A. and Young, D. B. The identification of T cell epitopes in *Mycobacterium tuberculosis* using human T lymphocyte clones. Lepr. Rev. **57** Suppl. 2 (1986) 131–137.

Strategies for the design and development of subunit vaccines to protect against infectious disease depend upon the identification and characterization of immunodominant epitopes of important biological function and specificity present in the pathogen. Since effective immunity during mycobacterial infection appears to be mediated predominantly by the cellular arc of the immune response, this necessitates the detailed analysis of the specificity of T-cell recognition of mycobacterial antigens. In this report we review some of the recent advances that have been made in this area of mycobacterial research.—(*From* the Article)

Longley, B. J., Haregewoin, A., de Beaumont, W., Smith, K. A. and Godal, T. Lepromin stimulates interleukin-2 production and interleukin-2 receptor expression *in situ* in lepromatous leprosy patients. Lepr. Rev. **57** Suppl. 2 (1986) 189–198.

The finding of Langerhans' cells, IL-2-producing cells, and IL-2R-bearing cells shows that lepromatous patients are capable of mustering these basic cell types in response to lepromin A. The presence of the latter two cell types offers some evidence for a functional antigen-presenting mechanism. Yet, for some reason, these cells fail to persist at lepromatous patient test sites, and the patients fail to form tuberculoid granulomas. These results could be seen with pathologic suppression, natural decay (down-regulation or attrition) due to lack of effective stimulation, or a combination of these factors. The results of our study are consistent with any of these possibilities. Although active suppression seems likely at least somewhere in the response, it is not clear that it is pathological, and documenting it will require techniques for following cellular control at the molecular level, prior to mRNA transcription. It is clear that to understand the relevance of these mechanisms we must be able to establish a time frame and identify the earliest stage at which they differ in lepromatous and tuberculoid patients.—(*From* the Article)

Modlin, R. L., Gersuk, G. M., Nelson, E. E., Pattengale, P. K., Gunter, J. R., Chen, L., Cooper, C. L., Bloom, B. R. and Rea, T. H. T-lymphocyte clones from leprosy skin lesions. Lepr. Rev. **57** Suppl. 2 (1986) 143–147.

Cloned suppressor T cells derived from lepromatous leprosy skin lesions can be triggered by lepromin to suppress the ConA response of normal PBMC. These suppressor T-cell clones can suppress the proliferative response of helper T-cell clones to lepromin. This suppression is probably restricted by class II MHC antigens. Therefore, the unresponsiveness of lepromatous leprosy patients to antigens of *Mycobacterium leprae* may be related to the presence of these suppressor T cells within lesions, perhaps by inhibiting IL-2 production.

These methods provide a new means to study the immune response of patients to infection, neoplasia and autoimmune disease at the tissue level. In addition, the helper and suppressor clones from leprosy skin lesions can be used to elucidate the range of cloned antigens and epitopes recognized by the T-lymphocyte repertoire in leprosy.—(*From* the Article)

Mustafa, A. S., Oftung, F., Gill, H. K. and Natvig, I. Characteristics of human T-cell clones from BCG and killed *M. leprae* vaccinated subjects and tuberculosis patients; recognition of recombinant mycobacterial antigens. Lepr. Rev. **57** Suppl. 2 (1986) 123–130.

A total of 121 human T-cell clones from 9 BCG vaccinated healthy subjects, 42 T-cell clones from 6 normal volunteers vaccinated with killed *Mycobacterium leprae*, and 52 T-cell clones from 4 tuberculosis patients were raised from peripheral blood mononuclear cells (PBMC). Irrespective of the group of subjects, all the proliferating clones were CD4+ CD8−. Some clones were specific to the antigens against which they were raised, and others were limited to broadly crossreactive in proliferative assays. Antigen specificity of three *M. leprae*-specific T-cell clones tested was also maintained in lymphokine and cytotoxicity assays. Responses of the clones to BCG and *M. tuberculosis* H37Rv paralleled closely. Although 68% and 63% of *M. leprae* raised T-cell clones responded to BCG and *M. tuberculosis*, respectively, only 9% BCG raised

T-cell clones and 23% *M. tuberculosis* raised T-cell clones responded to *M. leprae*. Twenty-four T-cell clones from BCG-vaccinated subjects, 22 T-cell clones from *M. leprae*-vaccinated volunteers, and all the 52 T-cell clones from tuberculosis patients were tested for their reactivity to recombinant antigens of *M. leprae* and *M. tuberculosis* identified by monoclonal antibodies. Five specific clones from two *M. leprae*-vaccinated subjects recognized an epitope on the *M. leprae* 18 kD protein, and one nonspecific clone from a third individual reacted to both the *M. leprae* and *M. tuberculosis* 65 kD proteins. From tuberculosis patients, one specific clone responded to the *M. tuberculosis* 65 kD protein while another limited cross-reactive clone proliferated to the *M. tuberculosis* 19 kD protein. None of the 24 BCG induced T-cell clones responded to the recombinant antigens.—Authors' Summary

Nath, I. Reversal of T cell unresponsiveness in lepromatous leprosy. Lepr. Rev. **57** Suppl. 2 (1986) 207–212.

During ENL reactions many LL patients show transient but definitive evidence of circulating functional T cells which produce lymphokines. In addition, activated T cells with helper phenotype enter dermal lesions and may secrete interferon-γ at the local site, thereby inducing Ia on keratinocytes and possible enhanced microbicidal activity in bacilli-laden phagocytes.

Both the natural emergence of T cells during reactional phases and modulation of *in vitro* cellular interactions indicate that responsiveness to *Mycobacterium leprae* antigens and thereby reversal of the anergic state is possible in lepromatous leprosy. The initiating causes of the emergence of reactive T cells *in vivo* and the reasons for the nature of this phenomenon are not yet clear and may need sequential studies. Of the various protocols used to trigger T-cell responsiveness *in vitro*, addition of exogenous IL-2, deletion of monocytes, and presentation of antigen by dendritic cells showed impressive results.—(*From* the Article)

Nilsen, R., Mshana, R. N., Negesse, Y., Menigistu, G. and Kana, B. Immunohistochemical studies of leprous neuritis. Lepr. Rev. **57** Suppl. 2 (1986) 177–187.

Biopsies from 44 patients with a diagnostic histology of leprosy in either the nerve or the skin biopsy were used to study different aspects of leprous neuritis. Biopsy specimens from 14 out of 44 patients showed histologically a diagnostic picture of leprosy in the nerve lesions but not in the skin. Eight of 11 patients had a paucibacillary (BI = 0) skin lesion and a multibacillary (BI > 3) nerve lesion. The immunohistochemical studies revealed that the nerve lesions of this group had low T helper/suppressor ratio, low number of IL-2-receptor positive cells and low number of IL-2-containing cells, corresponding to the findings in nerve at the lepromatous part of the scale. This emphasized the importance of developing good methods for proper classification and, thus, appropriate treatment of the patients. The paucibacillary nerve lesions in patients with borderline tuberculoid skin lesions had higher numbers of IL-2-receptor positive cells, T-helper lymphocytes and Th/Ts ratios than those from lepromatous leprosy patients. The expression of the transferrin receptor was equal. An evident number of B lymphocytes (Leu14+ cells) were found in all lesions studied, showing that the humoral immune system may be more involved in the pathogenesis of the leprous lesions than previously thought. Schwann cells in all types of lesions showed a strong staining for the anti-HLA-DR and HLA-DQ antigens in contrast to Schwann cells in normal nerves. Much deposits of complement factor C9 and C3 and almost no Clq were found on Schwann cells, suggesting an activation of the alternative pathway of the complement system.—Authors' Abstract

Ohkawa, S., Martin, L. N. and Gormus, B. J. Lepromin-induced lymphoproliferative response of experimental leprosy monkeys: regulatory role of monocyte and lymphocyte subsets. J. Immunol. **138** (1987) 3943–3948.

We investigated the immunological status of seven normal, control mangabey monkeys and 23 mangabey monkeys experimentally inoculated with mangabey-origin *Mycobacterium leprae*.

Clinically, these monkeys were divided into three broad groups: a recently inoculated group, a resistant group, and a sus-

ceptible group. The resistant group included 11 monkeys, 7 of which showed no clinical sign of disease to date and 4 of which had shown local disease that partially regressed spontaneously. The susceptible group included 8 monkeys, 5 of which have disseminated disease and 3 with local but stable disease. When peripheral blood mononuclear cells of these monkeys were cultured with Dharmendra-type human lepromin, 1 of 7 normal monkeys, 4 of 4 of the recently inoculated group, 7 of 10 resistant monkeys, and 3 of 8 susceptible monkeys showed significant responses.

In this experimental monkey model, we studied possible regulatory mechanisms by using OKT4- and OKT8-enriched lymphocytes, and Fc receptor-positive (FcR+) and FcR− monocyte (Mϕ) subsets. The OKT4+ subset was the main lepromin-responsive cell type. High percentages of OKT8+ cells showed a good negative correlation with the lymphoproliferative responses of T-enriched cells supplemented with unfractionated Mϕ. But the depletion of OKT8+ cells could not increase the response of nonresponding monkeys' lymphocytes. The resistant group and susceptible group did not differ in their percentages of OKT8+ cells. Because OKT8+ cells negatively regulate the response of lymphocytes and OKT4+ cells are the main responding cells, OKT8+ cells are phenotypically and functionally suppressor cells and OKT4+ cells are the helper/inducer cell population in this system.

The FcR− Mϕ population mainly includes antigen-presenting activity, but high percentages of FcR− Mϕ showed a significant negative correlation with lymphoproliferative responses in the resistant group. A weak but significant lymphocyte response to Dharmendra lepromin was obtained by depleting FcR+ Mϕ from cultures of some susceptible monkeys; whereas lymphocytes of other susceptible monkeys remained unresponsive to lepromin. By these criteria, we could find an array of immunological defects in monkeys with experimental leprosy. The data suggest that some immunological defects may exist in the OKT4+ lymphocytes or FcR− Mϕ of leprosy monkeys.—Authors' Abstract

Patarroyo, M. E., Parra, C. A., Pinilla, C., del Portillo, P., Torres, M. L., Clavijo, P., Salazar, L. M. and Jimenez, C. Immunogenic synthetic peptides against mycobacteria of potential immunodiagnostic and immunoprophylactic value. Lepr. Rev. **57** Suppl. 2 (1986) 163–168.

The great chemical complexity of this microorganism is seen when analyzing the *Mycobacterium tuberculosis* sonicates on Coomassie-blue stained SDS-PAGE. A large number of protein bands of different sizes can be observed, with molecular weights ranging from 175 kD (kilodaltons) to peptides of 6,000 daltons. Despite the numerous studies on the composition of the *M. tuberculosis* bacilli, little is known about the chemical structure of its proteins mainly due to the fact that only a few have been isolated and characterized in detail. To understand the biology of *M. tuberculosis,* our laboratory started working on the isolation and chemical and immunological characterization of a series of these molecules, centering its interest in the molecules capable of inducing an immunogenic specific response in human beings. This research is the purpose of this report.—(*From* the Article)

Ridley, D. S. The pathology of leprosy as a reflection of the host parasite relationship. In: *Leprosy, A Problem of Mankind in Transition.* Part II. Würzburg: Deutschen Aussätzigen-Hilfswerk, 1986, 345–352.

The histology of leprosy remains a subject of research in its own right in addition to its role as an adjunct to other aspects of research. In the last 5 years, much progress has been made with the application of immunological methods to histological specimens taken from the sites of disease. This is much more relevant for the evaluation of the disease process than similar tests applied to the cells of the blood, which has been the usual method in the past and which is still of value. It becomes possible, for example, to see microscopically the types of lymphocytes which are at work, and to observe the interaction of cells, immunological agents and leprosy bacilli, all appropriately stained. The results are proving of value

not only to leprosy but in the study of related diseases.—(*From* the Chapter)

Samuel, N. M., Mirsky, R., Grange, J. M. and Jessen, K. R. Expression of major histocompatibility complex class I and class II antigens in human Schwann cell cultures and effects of infection with *Mycobacterium leprae*. Clin. Exp. Immunol. **68** (1987) 500–509.

Recent experiments on rats have raised the possibility that Schwann cells can present antigens to T lymphocytes. We have investigated whether this mechanism might be relevant in leprosy by determining under what conditions human Schwann cells express class I and class II antigens, and whether infection with *Mycobacterium leprae* affects this expression. The distribution of these antigens was examined on human Schwann cells in dissociated cell cultures derived from human fetal peripheral nerves. We find that both Schwann cells and fibroblastic cells in these cultures normally express class I antigens but not class II antigens. When Schwann cells are infected with live *M. leprae* for 48 hr, 73% of Schwann cells phagocytose the bacteria. *M. leprae* prevents ^{3}H-thymidine incorporation into cultured human Schwann cells, but does not affect class I expression in these cells. Treatment of normal and *M. leprae*-infected cultures with gamma-interferon for 72 hr induces class II expression on most Schwann cells but not on the majority of fibroblastic cells. The fact that human Schwann cells infected with *M. leprae* can be induced by gamma-interferon to express class II antigens suggests that they may be able to present *M. leprae* antigens to T lymphocytes and thus initiate immune responses against the bacteria. We suggest that a failure of this response, such as that seen within nerve trunks in lepromatous leprosy, is caused by deficient class II expression on Schwann cells. This deficiency in class II expression, in turn, may be caused by the reduced gamma-interferon production characteristic of lepromatous leprosy.—Authors' Summary

Shinnick, T. M. Peptides as potential immunodiagnostic reagents to detect mycobacterial infections. Lepr. Rev. **57** Suppl. 2 (1986) 149–155.

Chemically synthesized peptides have been shown to be able to elicit immunologic reactions useful in the laboratory. These results suggest that clinically useful peptide or peptide-elicited antibody-based assay systems to detect mycobacterial antigens or anti-mycobacterial antibodies are feasible. Peptides are also excellent candidates for a new generation of skin test reagents to detect a T-cell response elicited by the infecting mycobacterium. The potential advantages of such a reagent are that it is easy to manufacture, stable at room temperature, chemically defined, and, perhaps, more specific than tuberculin for detecting a particular mycobacterial infection. What needs to be done in the immediate future is the identification of the optimal peptide by a series of *in vitro* assays of immunologic reactivity and specificity and then an analysis of its potential clinical usefulness. Two candidates to focus our current attention on are the 65 kD antigens of *Mycobacterium leprae* and *M. tuberculosis*. Of a much more speculative nature is the possibility that a peptide corresponding to a portion of the highly conserved 65 kD antigen that elicits a strong DCH reaction might also be a good candidate for a synthetic peptide vaccine against tuberculosis or leprosy. A great deal of work remains to be done before we know if such a vaccine is even feasible. Nonetheless, it seems clear that the synthetic peptide immunogen and antigen approach should generate new, clinically useful reagents for the immunodiagnosis of tuberculosis and leprosy.—Author's Summary

Tung, K. S. K., Umland, E., Matzner, P., Nelson, K., Schauf, V., Rubin, L., Wagner, D., Scollard, D., Vithayasai, P., Vithayasai, V., Worobec, S., Smith, T. and Suriyanond, V. Soluble serum interleukin 2 receptor levels in leprosy patients. Clin. Exp. Immunol. **68** (1987) 10–15.

Soluble interleukin 2 receptors (IL-2R) in sera of leprosy patients from Chiang Mai, Thailand, were quantified with a solid-phase enzyme immunoassay using two monoclonal antibodies to the IL-2R. The IL-2R

levels of untreated lepromatous, borderline lepromatous or midborderline patients and treated lepromatous and borderline lepromatous or treated borderline tuberculoid and tuberculoid patients were comparable to those of the Thai household or nonhousehold contacts, and they were significantly higher than the levels of U.S.A. control subjects. In contrast, IL-2R of untreated tuberculoid or borderline tuberculoid patients were significantly reduced. Patients with ongoing reversal reaction had very high circulating IL-2R, the levels of which correlated with fever and extent of skin lesions. Although erythema nodosum leprosum (ENL) patients also had elevated IL-2R levels, they were significantly below those of patients with reversal reaction. When treated with corticosteroid, precipitous reduction of IL-2R was noted in all patients with reversal reaction but not in patients with ENL.—Authors' Summary

Wu, Q., *et al.* [Preliminary study of serologic activity of phenolic glycolipid deacetylate of *M. leprae*.] Chin. Lepr. J. **4** (1986) 19–22. (in Chinese)

An enzyme-linked immunosorbent assay (ELISA) with deacetylated phenolic glycolipid (D-PG) was performed. Sera were collected from 59 leprosy patients and 102 healthy individuals from a nonendemic area of leprosy. The results (at 1:200 serum dilution) showed that the activity of D-PG against sera from leprosy patients is very high. The classes of antibody in sera of the patients were detected. The rates of positivity with IgM are 100% in multibacillary patients (LL, BL, BB) and 75%–83% in paucibacillary patients (BT, TT). With IgG and IgA, the rates of positivity are also 100% in LL, BL and BB, but their levels in BT and TT are lower than those of healthy controls. Results of comparison of A plates (made in China) with B plates (imports) indicated that the B plates can be replaced by A plates in D-PG-ELISA. The results of comparison of EA (egg albumin) with BSA (bovine serum albumin) indicated that the BSA can be replaced with EA. The authors suggest that D-PG-ELISA with IgM is highly sensitive and specific for the detection of infection with *Mycobacterium leprae*.—Authors' English Abstract

Xie, Y. and Dong, X. [Comparative investigation on two modified techniques of acid-fast stain.] Chin. Lepr. J. **3** (1986) 34–40. (in Chinese)

A comparative observation on the specificities of the oil Ziehl-Neelsen (ZN) and in deparaffinized ZN stains which were considered to have identical staining mechanism and of the various pre-oxidized ZN stains for demonstrating mycobacteria was performed. Twenty-five species of non-acid-fast microorganisms were tested, and a classical ZN stain and four species of mycobacteria used as controls. Wade-Fite's oil ZN and Harada's in deparaffinized ZN stains were a specific acid-fast stain for mycobacteria, and consistent with classical ZN. A variety of pre-oxidized ZN stains, particularly the various periodic acid-oxidized ZN stains, were of less specificities. The acid-fast properties, induced by the oxidation, are relative and conditional on differential agents and differentiated time, and they are different in their natures.—Authors' English Abstract

Zhu, W., Xia, M., Gu, G., Lou, H., *et al.* [The foamy cells in skin lesions of arrested lepromatous patients.] Chin. Lepr. J. **3** (1986) 28–31. (in Chinese)

The pathologic changes of foam cells in regressive skin lesions of nine arrested lepromatous leprosy patients, who have been treated by dapsone for 15–30 years, are reported. The cells varied in number around the small dermal vessels in six of nine cases, but no bacilli were found in them. The cells were stained red by Sudan IV. The activity of succinic dehydrogenase disappeared or markedly decreased in the cells. Direct immunofluorescent examination showed that there was no deposition of IgG, IgA, IgM, and C3 in the cells. IgM could be determined at the dermo–epidermal junctions of two cases and in the capillary walls of one case. Electron-microscopic study of the cells showed that there were vacuoles of varying sizes within their cytoplasms from which large vacuoles contained many small vacuoles of varying sizes, and each of them was surrounded by a unit membrane. Some vacuole walls were discontinuous. The foam cell contained numerous fatty drops and a

few cell organs but no *Mycobacterium leprae*. The rough endoplasmic reticula were well developed and markedly dilated in proliferating fibroblast cells. They looked like foamy structures. It is concluded that these foam cells possess much lower metabolism and may persist for a long time because they are degenerated cells which are not able to clean away the foamy structures. On the other hand, a few macrophages around the foam cells also could not dispose of them.—Authors' English Abstract

Microbiology

Brennan, P. J. The carbohydrate-containing antigens of *Mycobacterium leprae*. Lepr. Rev. **57** Suppl. 2 (1986) 39–51.

The overt antigenicity of *Mycobacterium leprae*, as for all mycobacteria, is dominated by carbohydrate-containing entities. We now know sufficient of the immunochemistry of *M. leprae* to realize that its carbohydrate-based antigens are relatively simple; perhaps, the *in vivo* setting of *M. leprae*, prior to its isolation, ensures limited autolysis. The dominant carbohydrate-containing epitopes of *M. leprae* are contained within but three classes of structures: the phenolic glycolipids, the lipoarabinomannan, and the insoluble cell wall skeleton. Our work over the past few years has addressed each of these complexes and herein is presented a brief review of our studies.—(*From* the Article)

Chakrabarty, A. N., Das, S. and Dastidar, S. G. Isolation of a nocardia-like chemoautotroph from clinically proven multibacillary cases of leprosy. J. Exp. Biol. **24** (1986) 663–665.

A nocardia-like organism was isolated from 22 multibacillary cases of leprosy on inorganic mineral salt minimal medium supplemented with simple carbon sources (e.g., liquid paraffin, tetradecane, etc.) and nitrogen sources (e.g., ammonium salts, urea, asparagine, gelatin, etc.). Complex organic substances, i.e., casein, tyrosin, peptone, meat extract, blood, serum, yeast extract and medium 199 totally, and agar considerably, inhibited the growth of this organism. Na-metasilicate was a useful solidifying base, which also appeared to provide an additional energy source to the bacteria. Paraffin-urea minimal or paraffin-gelatin minimal liquid media selectively allowed luxuriant growth of this organism which could be easily serially propagated. On the basis of a multi-parameter study, these were found to be indistinguishable from the causative agent of leprosy.—Authors' Abstract

Dhariwal, K. R., Yang, Y.-M., Fales, H. M. and Goren, M. B. Detection of trehalose monomycolate in *Mycobacterium leprae* grown in armadillo tissues. J. Gen. Microbiol. **133** (1987) 201–209.

Trehalose-6-monomycolate (TMM) was isolated from the lipids of armadillo-derived *Mycobacterium leprae*. Only meager amounts of this glycolipid were recovered, but its structure was unequivocally established. Only α-mycolates were detected in the TMM by ^{252}Cf plasma desorption mass spectrometry. Electron impact mass spectrometry showed the alpha branch to be principally C_{20}. Trehalose dimycolate (cord factor) was not detectable. Since we have also found TMM in *M. lepraemurium* and in every *Mycobacterium* species so far examined, we suggest that this glycolipid is truly ubiquitous among mycobacteria.—Authors' Abstract

Draper, P. Enzymes and other biochemically active components of mycobacteria. Lepr. Rev. **57** Suppl. 2 (1986) 21–32.

Most pathogenic mycobacteria can grow in a variety of culture media, using a variety of carbon or nitrogen sources which may be available. Even the difficult-to-grow *Mycobacterium lepraemurium* and so far uncultivated *M. leprae* can use a variety of

these substrates when they are supplied to suspensions of the bacteria. Many of the substrates—organic acids, amino acids, sugars and purines, for example—would be available inside the host so perhaps this metabolic versatility is a factor which enables the bacteria to obtain nutrients during changing conditions in the host.

However, in one sense, the picture of what nutrients mycobacteria acquire when inside the host is intriguingly incomplete. They have to compete for nutrients so some nutrients which isolated organisms take up readily may not be taken up by mycobacteria in the host tissues. What is needed is information on transport; for what substrates are there permeases with high enough affinity, or capable of rapid uptake to enable mycobacteria to scavenge the substrates from the host? Information, in mycobacteria grown in the host, is restricted to one activity, tryptophan uptake in *M. tuberculosis*. Otherwise, it is known that mycobacteria produce siderophores with high enough affinity for iron to abstract iron from host iron-proteins. The ferri-siderophores are then taken up by a specific mechanism. It is possible that mycobacteria have the ability to become dormant (=persister?) when essential nutrients are not available in the host. *In vitro,* this can occur when oxygen is limiting.

Inside host cells, most of the potential nutrient molecules would be phosphorylated. Purine nucleotides are certainly present at concentrations at least an order of magnitude higher than their bases of nucleosides, and free glycerol (readily utilized by mycobacteria *in vitro*) is unavailable—all glycerol is present in glycerophosphate (or in glycerides). Hardly anything is known about the uptake of phosphorylated intermediates into mycobacteria. However, most mycobacteria have high phosphatase activity, and might take up intermediates after dephosphorylation. The exception is *M. leprae*—over 99% of the phosphatase associated with isolated even highly purified *M. leprae* is derived from the host. Whether this is an artifact of isolation from host tissue, or represents acquisition of the activity for the purposes of the bacteria is not known, but there is no doubt—stated previously—that for *M. leprae* to acquire the purine base from extracellular nucleotides, they must first dephosphorylate the nucleotide molecules and this could represent a role for host-derived phosphatase.

From all the foregoing, it would seem that in general pathogenic mycobacteria are not specialized parasites in the sense of being dependent on the host for any substrates. However, *M. leprae* may be an exception. If analogies can be drawn between other host-grown mycobacteria and *M. leprae,* then it seems unable to synthesize its own purines and is thus dependent on the environment for purines. In the meantime it would seem sensible to include a source of the purine ring in any potential media for cultivation of leprosy bacilli.—(*From* the Article)

Draper, P. Structure of *Mycobacterium leprae.* Lepr. Rev. **57** Suppl. 2 (1986) 15–20.

The two current requirements—for new antileprosy drugs and for a vaccine—should more easily be fulfilled if some of the remaining puzzles about the structure of *Mycobacterium leprae,* and particularly its capsule, wall and membrane, are solved. Some of the solutions will be reached by inference from knowledge of other mycobacteria, but the unique nature of this pathogen makes it likely that important structural features are also unique, and that the organism itself, as well as models, must be studied.—Author's Conclusion

Draper, P., Kandler, O. and Darbre, A. Peptidoglycan and arabinogalactan of *Mycobacterium leprae.* J. Gen. Microbiol. **133** (1987) 1187–1194.

The arabinogalactan and peptidoglycan of armadillo-grown *Mycobacterium leprae* were examined. Within the limits defined by the small amount of material available, the resemblance of these polymers to those of other mycobacteria was confirmed. The polymers were linked by a highly acid-labile bond and the arabinogalactan was itself acid-labile, free arabinose and a variety of oligosaccharides containing both arabinose and galactose, as well as polysaccharide and peptidoglycan, were released by dilute acid. The resonances from anomeric protons in the proton NMR spectrum of the arabinogalac-

tan were similar to those from the arabinogalactan of *M. tuberculosis*. The composition and structure of the peptidoglycan resembled those of other mycobacteria. The only major difference was the specific replacement of L-alanine by glycine in the peptide of the peptidoglycan.—Authors' Abstract

Vejare, S. and Mahadevan, P. R. Importance of determining viability of *Mycobacterium leprae* inside macrophages—an *in vitro* method using uracil. J. Biosci. **11** (1987) 455–463.

It has been demonstrated that *Mycobacterium leprae* are capable of taking up uracil and incorporating it into trichloroacetic acid-insoluble materials, both as a free suspension of bacteria as well as when they are inside the macrophages, a host cell for their *in vivo* survival. The same amount of bacteria shows better incorporation inside macrophages than as a free bacterial suspension. Both types of incorporation are inhibited by rifampin, an antileprosy drug and an RNA synthesis inhibitor. Thus, uracil uptake by *M. leprae* inside macrophages has been used for standardizing a rapid *in vitro* viability assay for the leprosy-causing bacteria.—Authors' Abstract

Experimental Infections

Bach, M.-A. and Hoffenbach, A. Strain-dependent protective effect of adult thymectomy on murine infection by *Mycobacterium lepraemurium*. Clin. Exp. Immunol. **68** (1987) 521–527.

C57BL/6, DBA/2, BALB/c, and CBA mice were thymectomized as adults, or sham-thymectomized, and infected subcutaneously with 10^6 *Mycobacterium lepraemurium* (MLM). The number of MLM in the spleen and in the inoculated foot pad was measured after 1 year of infection as well as the DTH reactions and the IgM and IgG antibody levels to MLM. Non-thymectomized mice exhibited a broad spectrum of resistance to MLM infection and of T-cell-mediated immunity grading from the highly resistant C57BL/6 strain to the highly susceptible CBA strain. In between, DBA/2 was found more resistant than BALB/c mice. Adult thymectomy reduced by 100 times the MLM number in the spleen of infected DBA/2 mice, without affecting that measured in the inoculated foot pad, and significantly decreased DTH reaction in the same strain. No effect of adult thymectomy was observed in any other strain, except for an increase of anti-MLM antibodies in BALB/c mice. These results may suggest that the medium-resistant DBA/2 strain developed after MLM infection suppressor T cells which favor MLM dissemination and are sensitive to adult thymectomy.—Authors' Summary

Juscenko, A. A. and Vishnevetsky, F. E. [Histochemical study of reverse reactions in *M. leprae*-infected armadillos.] Biull. Eksp. Biol. Med. **3** (1987) 376–380. (in Russian)

Morphological and histochemical characteristics of reversal reactions in *Mycobacterium leprae*-infected armadillos are reviewed. The reversal reactions develop in generalized lepromatous disease and are characterized by a dramatic decrease in mycobacterial macrophage load and the appearance of lymphocytes, epithelioid and giant multinuclear cells with peripheral nucleus distribution. Histochemical investigation has shown a decrease in the activity of redox enzymes and alpha-naphthyl acetate esterase and an increase in β-glucuronidase activity. The reversal reactions in the liver are accompanied by hepatic granuloma and hepatocyte destruction.—Authors' English Summary

Liu, X., Lin, Z., *et al.* [Study on DDS resistance using the mouse foot pad tech-

nique.] Chin. Lepr. J. **3** (1986) 32–34. (in Chinese)

The authors report the results of mouse foot-pad tests with ten strains of *Mycobacterium leprae* isolated from ten suspected dapsone (DDS)-resistant cases. Nine of them are positive: 2 strains are completely sensitive to DDS, 3 strains had a moderate degree of resistance (secondary) and 4 strains low-degree resistance (primary). One strain did not infect the animals. In this test the sensitivity of the C57BL mouse to *M. leprae* was demonstrated.—Authors' English Abstract

Epidemiology and Prevention

Blake, L. A., West, B. C., Lary, C. H. and Todd, J. R., IV. Environmental nonhuman sources of leprosy. Rev. Infect. Dis. **9** (1987) 562–577.

Leprosy has been considered to occur only after exposure to a human case. However, evidence has been accumulating that this conventional view is wrong and that an environmental nonhuman source is critical to some human infections with *Mycobacterium leprae*. Observations, some of which date back to the 19th century, support soil, vegetation, water, arthropods, and armadillos (*Dasypus novemcinctus*) as environmental sources of leprosy. Disparate clinical, epidemiologic, and microbiologic evidence has been critically reviewed in light of the fact that 50%–70% of sporadic cases of leprosy in well-studied populations occur in persons who have had no known contact with human leprosy. Historical data and current information alike substantiate the concept of nonhuman sources of the disease; recent observations with monoclonal antibody have shown that phenolic glycolipid-I antigen, which is unique to the *M. leprae* cell wall, is present in soil. In the absence of a technique for *in vitro* cultivation, indirect methods and the body of observations reviewed here persuasively favor but do not prove the existence of environmental nonhuman sources of *M. leprae*.—Authors' Abstract

Du, J. [Survey of leprosy in Dali Bai Autonomous Prefecture, Yunnan.] Chin. Lepr. J. **3** (1986) 1–3. (in Chinese)

The author reports a clue investigation for finding leprosy cases made in 1983 in Dali Miao Autonomous Prefecture, Yunnan Province, through which it was proved that there are 1929 cases of active leprosy in the prefecture distributed as small foci with the prevalence of 0.71 to 1.45 per thousand and in 1963 and multibacillary form accounts for 54.84% of the patients, 65.57% of them under age 30 years. There is no difference between the nationalities there according to the prevalence of leprosy. The incidence of leprosy did not decrease in the last 10 years.—Author's English Abstract

Hu, Y., *et al.* [Epidemiological survey of leprosy in Ankang Prefecture, Shanxi Province.] Chin. Lepr. J. **4** (1986) 10–11. (in Chinese)

There have been accumulatively 1054 cases of leprosy since 1949 in Ankang Prefecture of Shanxi Province among a population of about 2.6 million, but now the number of active patients is only 124 and the prevalence is 0.5‰. In the area of Qinling in this prefecture, there were more leprosy patients, probably a result of the activities of the armies from Guangdong and Guangxi Provinces during the War of Resistance against Japan.—Authors' English Abstract

Jiang, C., *et al.* [Comprehensive study of household gathering of leprosy with probability model of negative binomial and Poisson distributions.] Chin. Lepr. J. **4** (1986) 12–15. (in Chinese)

Because leprosy has a lower prevalence rate, the comprehensive analysis of 3054 families in Baoying County, Jiangsu Province, People's Republic of China, was per-

formed with the function models of negative binomial distribution and probability density for distribution coordinating. The results showed that the distribution of leprosy as a unit of the family conformed with the negative binomial distribution and did not with Poisson distribution. Therefore, the distribution of leprosy has a highly significant relationship to familial aggregation.—Authors' English Abstract

Lu, Z. [Investigation of leprosy endemic foci in Nandan County.] Chin. Lepr. J. **3** (1986) 5–9. (in Chinese)

The activity of endemic foci of leprosy in Nandan County, Guangxi Zhuang Autonomous Region, People's Republic of China, is in two forms: a) development of new foci with leprosy patients and b) the occurrence of new cases in existing endemic foci, with the former being of main importance. The occurrence of new endemic foci is positively correlated with the incidence rate of leprosy; the activity of the endemic foci would be considered as one of the indexes for assessment of the endemic trend of leprosy. In a high-endemic area or in the early phase of leprosy control, the activity of new endemic foci is more common, but in a low-endemic area or when leprosy control is more successful, existing endemic foci are more active. This is because new endemic foci are more rapidly brought under control and then case finding to examine household contacts with leprosy patients and to survey the foci are feasible and economical. The author finds that new cases would only arise in about 1.84%–10.23% of leprosy endemic foci in a year. The more recent the activity of an endemic focus was found to be, the more possibility there would be of new cases, especially where multibacillary patients have existed. If there have been no new cases appearing there over 15 years, the endemic focus can be cancelled.—Author's English Abstract

Pan, R. [Leprosy control in 30 years in Hechi Prefecture.] Chin. Lepr. J. **3** (1986) 3–5. (in Chinese)

One thousand four-hundred forty-five cases of leprosy have been accumulatively found in Hechi Prefecture, Guangxi Zhuang Autonomous Region, up to 1985. The incidence of leprosy has decreased from 5.58 per hundred thousand in the years of 1956–1960 to 0.44 in 1981–1985, and the prevalence has fallen from 2.24 per thousand in 1971–1975 to 0.49 per thousand in 1981–1985. At the same time, the duration of the disease in the patients newly found was shortened, the rate of lepromatous type decreased, the number of endemic foci were reduced, and the incidence among the family members of leprosy patients evidently was reduced by taking preventive therapy.—Author's English Abstract

Wang, C., *et al.* [Effects of leprosy control in Yulin Prefecture.] Chin. Lepr. J. **4** (1986) 8–9. (in Chinese)

Yulin Prefecture, Guangxi Autonomous Region, has 8 counties with a population of 7.76 million where, since 1956, 3 counties have treated all leprosy patients at home while the other 5 counties have treated and isolated the patients in leprosy hospitals. After 30 years, the comparison between the two groups showed that the control effects on leprosy are very similar.—Authors' English Abstract

Wang, Q., *et al.* [Investigation and analysis of leprosy epidemiology in Lufeng County of Guangdong Province.] Chin. Lepr. J. **4** (1986) 1–4. (in Chinese)

There are accumulatively 3640 leprosy cases up to 1985 in Lufeng County, Guangdong Province, among which 2583 cases have been cured while 71 relapsed, 709 died, and 181 moved away. In 1985 there are 207 active leprosy patients there, of which 39 cases are hospitalized and 168 are receiving treatment at home. The prevalence has decreased from 3.49 per thousand in 1959 to 0.18 in 1985 and the incidence from 46.25 per hundred thousand in 1955 to 0.6 in 1985.—Authors' English Abstract

Wei, A. [Epidemical state of leprosy in Shannan Prefecture of Tibet.] Chin. Lepr. J. **4** (1986) 8–9. (in Chinese)

Shannan Prefecture with 13 counties, Xizang (Tibet) Autonomous Region, has a total of 296 leprosy patients; the prevalence is 1.14‰, decreasing with increasing height above sea level. The patients are mostly

people 20–50 years of age. The ratio of male and female patients is 1 to 0.73. Tuberculoid type accounts for 56.42%; lepromatous, 34.80%. Endemics of leprosy have nothing to do with the nationalities of the area.—Author's English Abstract

Xiong, D., *et al.* [Outpatient treatment of leprosy patients for 4 years in Luding County, Sichuan Province.] Chin. Lepr. J. **4** (1986) 6–7. (in Chinese)

Since 1982 in Luding County, Sichuan Province, People's Republic of China, outpatient treatment has been given to 155 cases of leprosy who account for 81.2% of all patients registered. Dapsone (DDS) and rifampin (RMP) were delivered monthly to the patients' homes. Of 131 patients treated for over 1 year, 80 cases have been cured (61.1%), while the unimproved cases comprise only 1.5%. Most new patients reported by themselves or by others to leprosy control workers, and among them, most patients were in an earlier stage of the disease with less deformities. The relapse rate of leprosy is 0.8% in the county. At present, there are 80 active leprosy patients and the prevalence is 1.23%; in 1982, it was 2.5%. The cost of outpatient treatment only comes to 8% of the cost of hospitalization.—Authors' English Abstract

Rehabilitation

Chen, Q. and Jing, X. [Effects of orthopedic and conservative therapies on paralytic lagophthalmus.] Chin. Lepr. J. **3** (1986) 14–16. (in Chinese)

Ninety-seven leprosy patients with paralytic lagophthalmus have accepted various reconstructive surgical treatments or conservative therapies and were followed up 17 months later. The authors found that the conditions of the patients in the two groups with surgical and conservative treatment all showed some improvement. The significance and operation methods of treating lagophthalmus are discussed.—Authors' English Abstract

Pan, X., *et al.* [Psychosis of leprosy patients from social discrimination and somatic deformities.] Chin. Lepr. J. **4** (1986) 29–30. (in Chinese)

The authors report on the mental state of 200 leprosy patients. Among them, 39 patients have complicated psychogenesis with the incidence rate of 19.5% being higher than that reported in India. The rate between the leprosy psychogenesis and the incidence of leprosy is inverse. The main cause of leprosy psychogenesis is social discrimination and physical deformities. To overcome the social discrimination against leprosy patients and prevent the deformities, the doctors should have a strong sense of responsibility and enthusiasm.—Authors' English Abstract

Shu, H., *et al.* [A survey of persons living in leprosaria after leprosy cured.] Chin. Lepr. J. **4** (1986) 23–25. (in Chinese)

In Baoying County's leprosarium in Jiangsu Province, there are 72 cases of cured leprosy patients, accounting for 10.3% of all of the cured cases, who continue to stay there. Of these, 54.2% belong to those who have no home to go back to, and 41.6% are those who cannot return to society because of discrimination by society. Among them, 87.5% have deformities from leprosy, of which 81% have I or II degree disability, and 69.4% have totally lost their labor ability. Among the married ones, 31.3% have been divorced—this being 51.3 times more than the rate for normal persons in the county. The authors call upon society to remove the prejudice against leprosy patients so as to make it possible for them to return to their home and social life. The authors also suggest that the legislative body of the state must revise the provision for-

bidding leprosy patients to marry in the marriage law of the People's Republic of China, so that the leprosy patients could enjoy their due civil right as ordinary persons.—Authors' English Abstract

Shu, W., *et al.* [Loss of labor ability and social economics from leprosy deformities.] Chin. Lepr. J. **4** (1986) 25–27. (in Chinese)

The authors surveyed the disabilities of 3234 leprosy patients and the economic loss brought about by them in Baoying County of Jiangsu Province. Among these patients, 1442 cases have had various disabilities, of which 925 patients lost their abilities to work. The average output value from labor for a year per peasant in the locality is RM 634.24 yan. Therefore leprosy deformities bring about some 7,221,430.30 yan of economic loss. The disabilities from leprosy might not only bring the difficulty to the patients, but also an extremely large economic loss to the society.

Therefore it is necessary for early efforts to prevent the disabilities and to launch the rehabilitative treatment for recovering labor abilities of leprosy patients as far as possible.—Authors' English Abstract

Tan, D. and Zhang, Z. [On the mental care of leprosy patients.] Chin. Lepr. J. **3** (1986) 20–22. (in Chinese)

The authors discuss the most basic requirement and general state of mind in leprosy patients, and they propose some measures for caring for mental health. The authors point out that leprosy patients need not only medical care for their somatic recovery but also psychotherapy for their mental health, and that the doctors and nurses must make them feel satisfied.—Authors' English Abstract

Other Mycobacterial Diseases and Related Entities

Averbakh, M. M., Eremeev, V. V. and Khomenko, I. S. [Regulatory subpopulations of T lymphocytes in patients with pulmonary tuberculosis.] Probl. Tuberk. **2** (1986) 50–54. (in Russian)

The paper deals with investigation of the immune response regulation in patients with destructive tuberculosis of the lungs at various stages of the process. It was shown that at the phase of infiltrative outbreak of tuberculosis and during the disease progress there was a significant decrease in the subpopulation of T-helper (T_μ) cells and a relative increase in the proportion of T-suppressor (T_γ) cells in the patients which was evident from a decrease in T_μ/T_γ. It is concluded that T_μ/T_γ may serve as an additional index in estimation of the disease activity.—Authors' English Abstract

Berezousky, B. A., Mostovoi, Y. M., Pukhlik, B. M. and Mikhei, L. V. [Testing of the hypothesis of multifactorial type inheritance of predisposition to pulmonary tuberculosis.] Probl. Tuberk. **2** (1986) 24–26. (in Russian)

The hypothesis of the multifactorial type inheritance of pulmonary tuberculosis was tested. The testing was based on comparison of the data obtained by the authors and the literature data with the criteria of multifactorial diseases. The necessity for more active popularization of the clinical genetics among phthisiologists is discussed.—Authors' English Abstract

Doga, J., Lal, B. B. and Misra, S. N. Dapsone in the treatment of cutaneous leishmaniasis. Int. J. Dermatol. **25** (1986) 398–400.

Fifty patients with cutaneous leishmaniasis were treated with dapsone (DDS) approximately 2 mg per kilogram body weight per day for 21 days. Forty patients (80%) were declared cured on the basis of clinical

and pathologic criteria. Follow-up examination after 6 months revealed no recurrences. No major side effects were noted. In the control group of 15 patients not receiving the drug, no significant change was seen in the lesions. Dapsone thus was used successfully for the first time.—(*From* Excerpta Medica)

Fox, W. and Kee, T. S. Long-term follow-up of a clinical trial of six-month and four-month regimens of chemotherapy in the treatment of pulmonary tuberculosis. Am. Rev. Respir. Dis. **133** (1986) 778–783.

In a study in Singapore, patients of Chinese, Malay, or Indian ethnic origin with sputum-smear-positive pulmonary tuberculosis received 2 months of daily treatment with streptomycin, isoniazid, rifampin, and pyrazinamide followed by daily isoniazid and rifampin, either with or without pyrazinamide, allocated at random. Both regimens were given for a total duration of either 6 or 4 months by random allocation. As previously reported, all 330 patients with drug-susceptible strains of tubercle bacilli pretreatment had a favorable bacteriologic response during chemotherapy, and only 2 (1%) of 158 in the 6-month series, compared with 15 (10%) of 156 in the 4-month series, relapsed bacteriologically during the 30 months after the start of chemotherapy. A long-term follow-up assessment has been conducted 5 to 8 years after admission to the study. The excellent results in the 6-month series were maintained; only 1 of the 138 patients assessed relapsed after 30 months, compared with 5 of the 131 in the 4-month series. Of 33 patients with bacilli resistant to isoniazid, streptomycin, or both drugs pretreatment, 1 had an unfavorable response during treatment, and none of 9 in the 6-month series and 2 of 22 in the 4-month series relapsed bacteriologically by 30 months, but none of the nine 6-month and eighteen 4-month patients assessed relapsed subsequently.—(*From* Excerpta Medica)

Frehel, C., Ryter, A., Rastogi, N. and David, H. The electron-transparent zone in phagocytized *Mycobacterium avium* and other mycobacteria: formation, persistence, and role in bacterial survival. Ann. Inst. Pasteur Microbiol. **137B** (1986) 239–257.

After phagocytosis by bone-marrow macrophages, *Mycobacterium avium* was surrounded by a thick electron-transparent zone (ETZ). The use of various fixation and embedding procedures showed that ETZ did not seem to be an artifactual structure. A quantitative assessment of ETZ frequency was performed at different times after infection of macrophages with SmD and SmT colony variants of *M. avium*. For SmT-variant-infected macrophages, a higher percentage of ETZ+ bacilli paralleled a higher percentage of intact bacilli than was the case for SmD-infected macrophages.

Macrophages were also infected with bacteria killed with ultraviolet or gamma rays, H_2O_2, heat, or glutaraldehyde. About 50% of bacilli killed with any of these treatments were found ETZ+ instead of 80%–85% with live bacteria. Unlike live bacilli, for which the percentage of ETZ frequency remained stable throughout incubation time, ETZ frequency for killed bacilli decreased with time. ETZ assessment performed on *M. tuberculosis* H37Rv for comparison showed that, despite a very low ETZ frequency (8%–15%), the percentage of intact bacteria was identical to that observed with *M. avium*. In contrast, three rapidly growing nonpathogenic species (*M. smegmatis, M. phlei,* and *M. fallax*) presented a low ETZ frequency after phagocytosis and were rapidly degraded.

The process of ETZ formation and its role in bacterial survival are discussed.—Authors' Summary

Gunich, L. A., Vishnevsky, B. I. and Volkon, V. M. [Chlorprothixen efficacy in combined treatment of patients with pulmonary tuberculosis.] Probl. Tuberk. **64** (1986) 35–39. (in Russian)

Combined use of chlorprothixen and antituberculous drugs in treatment of patients with destructive tuberculosis of the lungs increased the bacteriostatic activity of blood and accelerated elimination of the disease clinical signs, discontinuation of tubercle bacilli isolation and cavern closing.—(*From* Excerpta Medica)

Karachunsky, M. A., Dorozhkova, I. R., Chukanov, V. I., Balta, Y. E. and Kyazimova, L. M. [Rifampicin effect on L-transformation of mycobacterial population in patients with destructive tuberculosis of the lungs.] Probl. Tuberk. **2** (1986) 31–34. (in Russian)

The effect of rifampin on the time course of isolation of L-forms of tubercle bacilli was studied in two identical groups of patients subjected to comparative clinical and bacteriological examinations. The frequency of the L-forms in both groups was the same. Inhibition of L-transformation of the mycobacterial population was observed in the patients treated with rifampin along with other drugs at the first stage of the treatment. At the second stage of the treatment, i.e., on the 4th–8th month, the intensity of this process increased.—Authors' English Abstract

Khor, M., Lowrie, D. B., Coates, A. R. M. and Mitchison, D. A. Recombinant interferon-gamma and chemotherapy with isoniazid and rifampicin in experimental murine tuberculosis. Br. J. Exp. Pathol. **67** (1986) 587–596.

Viable bacterial counts in the lungs and spleens of mice infected intravenously with *Mycobacterium tuberculosis* strain H37Rv were reduced by intravenous recombinant murine interferon-γ (IFN-γ) 1000–5000, but not by 200 μ. Reduction in counts was greatest when IFN-γ was given 1 day before infection and was not increased by additional doses in the preceding 2 days. The effect was complete in 1 day and was not increased by successive doses during the next week. Giving IFN-γ in multilamellar liposomes further reduced the spleen viable counts, but this appeared due to the liposomes themselves and not to encapsulation of IFN-γ within them. Only a minimal reduction in organ viable counts, not statistically significant, occurred when IFN-γ was given 5 days after infection. Although IFN-γ alone and isoniazid 25 mg/kg alone reduced the organ viable counts, combined treatment with IFN-γ and isoniazid was no more bactericidal than isoniazid alone. Similarly, the bactericidal activity of rifampin 25 mg/kg was not increased by simultaneous administration of IFN-γ. There seems little likelihood that IFN-γ would increase the efficacy of the early stages of the chemotherapy of tuberculosis.—(*From* Excerpta Medica)

Koronelli, T. V. and Fadeeva, N. I. [Cultivation of tubercle and opportunistic mycobacteria on medium with N-alkanes.] Probl. Tuberk. **2** (1986) 44–46. (in Russian)

The growth of tubercle and opportunistic (atypical) mycobacteria on the medium with a mixture of N-alkanes C_{12}–C_{18} as the sole source of carbon and energy, ammonium sulfate as the source of nitrogen and without growth additives was satisfactory. The growth appeared in 3 days. In 5 days it was abundant. The cell morphology remained typical and acid resistance was preserved.—Authors' English Abstract

Kostina, Z. I., Pokhodzei, I. V., Kotenko, T. V., Gerasimova, E. V., Obrosova, T. I. and Tsareva, O. I. [Significance of certain biochemical and immunological indices in estimation of activity of limited tuberculosis of the lungs.] Probl. Tuberk. **2** (1986) 18–23. (in Russian)

Ceruloplasmin activity, levels of copper, histamine and products of lipid peroxidation (dienic conjugates), serum general antioxidation activity and immunological indices were studied in 140 new cases of active limited tuberculosis of the lungs. Focal, infiltrative and disseminated tuberculosis of the lungs was detected in 45, 50, and 30 patients, respectively; 15 patients had tuberculosis of the intrathoracic lymph nodes. The above indices and in particular the activity of ceruloplasmin and the levels of dienic conjugates were shown to be highly informative in the estimation of activity of the specific process with or without clinical manifestations.—Authors' English Abstract

Levi, D. T., Yablokova, T. B., Lebedeva, L. V., Altynova, M. P., Tikhomirov, A. F., Sokolnikova, G. M. and Klyuev, B. V. [Study of new method for the application of tuberculin ointment for cutaneous use in comparison with the Mantoux test.] Zh. Mikrobiol. Epidemiol. Immunobiol. **1** (1987) 52–55. (in Russian)

The method for the applications of tuberculin ointment for the skin test by means of special aluminum chambers (Finn Chambers, obtained from Epitet Ltd. OY, Finland) was approved after trial. For control, the Mantoux test (intracutaneous tuberculin test) was used. The results of these two tests, made in parallel, were found to coincide in children with clinical symptoms of tuberculosis, or infected with *Mycobacterium tuberculosis,* in 84% of cases. The tuberculin skin test with the use of Finn Chambers proved to be more sparing, painless, and safe. At the present stage of investigation, the new skin test may be recommended for children of preschool age.—Authors' English Abstract

Petrashenko, A. I. [Rosette-forming T lymphocytes of different types in patients with pulmonary tuberculosis.] Probl. Tuberk. **2** (1986) 26–28. (in Russian)

The counts of T and B lymphocytes were investigated in 30 patients with active tuberculosis of the lungs and in 10 healthy subjects. Separate subpopulations of T lymphocytes were characterized quantitatively and the suppressor activity of T lymphocytes induced by concanavalin A (ConA) was estimated. A significant decrease in the count of T cells, impairment of the proportion of separate subpopulations of the rosette-forming cells (E-RFC) and an increase in the ConA-induced suppressor activity of lymphocytes in cell cultures in phytohemagglutinin were observed.—Authors' English Abstract

Ridley, D. S. and Ridley, M. J. Rationale for the histological spectrum of tuberculosis; a basis for classification. Pathology **19** (1987) 186–192.

There is need to re-appraise the cellular response to *Mycobacterium tuberculosis.* Histological analysis of 54 untreated patients with established disease demonstrated a continuous spectrum of tissue responses in which six groups correlated with evidence of resistance to bacterial multiplication. A predominance of cases in the two middle groups (82%) signified an immunological equilibrium in middle-grade resistant patients that is absent in related diseases such as leprosy and cutaneous leishmaniasis.

The dominant feature was necrosis, which increased progressively across the spectrum. Its form varied from minimal fibrinoid change, through fine eosinophilic necrosis, to basophilic necrosis characterized by neutrophil karyorrhexis, and finally to an almost acellular lesion with many bacilli. Cytological differentiation of the granuloma was of subsidiary significance, mature epithelioid cells being found only in high-resistant cases. No correlation was found for the number of lymphocytes.

This classification is thought to be an accurate reflection of the immune state in relation to antigenic load. It raises a hitherto unconsidered possibility that "caseation," a loosely applied macroscopic term, may embrace immunologically distinct states. The classification of multiple lesions was consistent. Histology offers a promising basis for further immunopathological investigation.—Authors' Summary

Ridley, M. J. and Ridley, D. S. Histochemical demonstration of mycobacterial antigen, specific antibody and complement in the lesions of tuberculosis. Histochem. J. **18** (1986) 551–556.

Lesions were studied histochemically for mycobacterial antigen, its specific antibody, and complement in 31 patients with recently diagnosed tuberculosis. The results were related to a histological spectrum that correlated with bacterial load. The form, localization, and persistence of antigen were found to be as significant as the amount. In high-resistant cases, the antigen was mainly soluble, a form which was nontoxic when ingested by macrophages but associated with tissue damage when bound to connective tissue. There was no close contact between plasma cells and antigen. However, in cases with moderate resistance, where plasma cells and antigen intermingled freely, necrosis with karyorrhexis and polymorph infiltration was associated with deposition of antigen, antibody, and complement at the same sites, indicating the probability of immune complex formation in these lesions. In low-resistant cases, extensive necrosis was attributed partly to high levels of extracellular antigen.

The correlation between immunological circumstances and the manifold forms of necrosis validated these forms as the basis for a histological spectrum in tuberculosis.—Authors' Summary

Wilkins, E. G. L. and Roberts, C. Management of non-respiratory tuberculosis. Lancet **2** (1986) 458–459.

The success of short-course regimens depends on combining highly bactericidal agents (such as isoniazid), which kill large numbers of actively metabolizing bacilli, with drugs exhibiting high sterilizing activity (such as rifampin and pyrazinamide) which kill slow or intermittently metabolizing bacilli. The importance of pyrazinamide in these regimens must be stressed. This drug is unique among available antituberculosis agents in being active on semidormant mycobacteria. It should therefore be considered in all schedules for treating nonrespiratory tuberculosis, e.g., tuberculous meningitis. *Mycobacterium bovis* strains account for up to 12% of all significant mycobacterial isolates from extrapulmonary sites. *M. bovis* is pyrazinamide resistant. Several features of the browning reactions of glycosylated proteins are consistent with a free-radical-mediated process. This lends further support to the suggestion that free-radical processes may be implicated in the pathogenesis of diabetic microangiopathy.—(*From* Excerpta Medica)

Yablokova, T. B., Pisarenko, N. N., Levi, D. T., Kazachkova, T. E., Nesterenko, L. A., Ozeretskovsky, N. A., Mitinskaya, L. A., Ejimova, A. A., Litseva, O. A., Kogan, E. S. and Zhukova, L. N. [Method of immunization with BCG-M vaccine with reduced antigenic content.] Probl. Tuberk. **2** (1986) 41–45. (in Russian)

Experimental and clinical investigations on the possibility of reducing the antigenic content of the vaccine intended for the immunization of newborn infants have been made. Experiments on guinea pigs and white mice have demonstrated that the reduced dose of the preparation, twice as low by weight (0.025 mg), produces the same level of protection against tuberculosis as the full dose (0.5 mg). A new preparation with reduced antigenic content, vaccine BCG-M, has been developed. The technical specifications for this preparation have been approved, and its serial production has been allowed. Clinical tests have revealed that the use of the new preparation makes it possible to decrease the occurrence of unusual postvaccinal reactions and complications (lymphadenitis, ulceration) threefold and, at the same time, to increase the coverage of infants by primary immunization against tuberculosis by 7%–8% annually. Since January 1986 this vaccine has been introduced into medical practice.—Authors' English Abstract

Yajko, D. M., Nassos, P. S. and Hadley, W. K. Therapeutic implications of inhibition versus killing of *Mycobacterium avium* complex by antimicrobial agents. Antimicrob. Agents Chemother. **31** (1987) 117–120.

Patients with the acquired immune deficiency syndrome (AIDS) with disseminated *Mycobacterium avium* infection have responded poorly to treatment with rifabutine (ansamycin) and clofazimine, in spite of the good *in vitro* response of *M. avium* to these antimicrobial agents. We compared the ability of these and other antimicrobial agents to kill versus the ability to inhibit the growth of strains of the *M. avium* complex isolated from patients with AIDS. Killing curve experiments showed that the concentrations of rifabutine and clofazimine needed to kill two log units of *M. avium* are at least 32 times greater than the concentrations needed to inhibit growth. Little or no killing occurred at concentrations of these antimicrobial agents that are achievable in serum. In contrast, 5 of 7 strains tested were killed by ciprofloxacin at concentrations that can be achieved in serum. Ciprofloxacin should be studied further for possible use in the treatment of *M. avium* infections.—Authors' Abstract

Young, L. S., Inderlied, C. B., Berlin, O. G. and Gottlieb, M. S. Mycobacterial infections in AIDS patients, with an emphasis on the *Mycobacterium avium* complex. Rev. Infect. Dis. **8** (1986) 1024–1033.

Serious infections caused by the *Mycobacterium avium* complex (MAC) have been

increasingly recognized over the last three decades. However, the epidemic of the acquired immunodeficiency syndrome (AIDS) has increased interest in these infections. Disseminated mycobacterial disease is common in patients with AIDS, and MAC is the predominant bacterial isolate. Indeed, at U.C.L.A. Medical Center, MAC organisms are now the predominant isolates in both AIDS- and non-AIDS-associated mycobacterial disease. MAC lung infections have been difficult to treat. Complex regimens employing four to six drugs are not clearly effective and are usually associated with considerable toxicity. Treatment of MAC infections in patients with AIDS has been particularly frustrating, and evidence that treatment can either eradicate disease or prolong life is limited. MAC organisms are invariably resistant to traditional antituberculosis medications. We have examined a variety of other compounds, and our findings, based on both *in vitro* and animal-model studies, have identified drugs which, when used in combination, are potentially of therapeutic utility.—Authors' Abstract

Zawar, P. B., Pol, J. T., Bulakh, P. M. and Chawhan, R. N. Serial estimation of serum lactic dehydrogenase & its isoenzymes in active pulmonary tuberculosis. Indian J. Med. Res. **85** (1987) 244–248.

Serial estimations of serum total lactic dehydrogenase (LDH) and its isoenzymes were done in 30 untreated patients of active pulmonary tuberculosis on the day of admission and on the third and eighth week of antitubercular chemotherapy. Thirty healthy individuals matched for age and sex served as controls. The mean level of serum total DLH in healthy individuals was 100.00 ± 10.00 IU/l. The mean LDH activity and isoenzyme LDH_4 in patients were significantly higher than that in the controls ($p < 0.001$). A progressive fall in the values of serum total LDH and isoenzyme LDH_4 was observed after 3 and 8 weeks of treatment. The changes in the levels of LDH and its isoenzymes were consistent with that found in other prognostic parameters, i.e., radiological improvement, fall in ESR, sputum negativity, and improvement in clinical status of the patient.—Authors' Abstract

Zosimov, A. N. and Khodzitskaya, V. K. [Asymmetry of dermatoglyphical indices and topics of tuberculosis process in the lungs.] Probl. Tuberk. **2** (1986) 40–43. (in Russian)

Characteristic features of the dermatoglyphical indices were studied in 150 patients at the age of 8 to 30 years with unilateral pulmonary tuberculosis. Relationship between the asymmetry of the dermatoglyphical indices and the topics of the tuberculosis process in the lungs was observed, which indicated participation of genetic mechanisms in localization of the pathological process. The correlation analysis permitted one to detect a more pronounced relationship with respect to the affected side. The curvature of the proximal flexion fold which was more pronounced at the side of the affection is the most informative parameter of the relationship between the asymmetry of the dermatoglyphical indices and the topics of the pathological process in pulmonary tuberculosis.—Authors' English Abstract