CURRENT LITERATURE

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

General and Historical

Bedi, B. M. S. Presidential Address, Indian Association of Dermatologists, Venereologists & Leprologists, Problem of Leprosy. Indian J. Dermatol. Venereol. Lepr. **46** (1980) 1–5.

"In conclusion I shall like to sum up by emphasizing that:

1. Medical education must cater to the needs of community and country to provide the essentials of the subject of leprosy at the level of teaching and examinations. Leprosy medical officers and general practitioners should need periodic refresher courses in the subject.
2. The National Leprosy Programme must be periodically reassessed at its various control units with a view to improve upon its performance.
3. It is essential that the survey should include all the risk population, especially children.
4. All cases must be detected and treated early. Testing of the risk population by skin test to find out the resistance or susceptibility shall be very useful for taking up further protective measures.
5. Attempts must be made to make available the newer drugs at cheaper rates. This can be done by encouraging their manufacture in our own country.
6. Lastly, no program for leprosy control can be successful unless and until it has the backing of the public and community. It is important to educate the public on the subject to remove their prejudice and ignorance about the disease. The social stigma must be removed by imparting necessary education at all levels. We celebrate Mahatma Gandhi's birthday as anti-leprosy day."—(*Adapted from* the address)

de Maar, E. W. J. The new policies of WHO in research for new tools to control six major tropical diseases. Trans. R. Soc. Trop. Med. Hyg. **73** (1979) 147–149.

A collaborative international research and development program for improved and new tools to control tropical diseases, the Special Programme for Research and Training in Tropical Diseases, has been developed along the following lines:

1. To determine where the need is greatest and to select diseases and technical approaches;
2. To focus on the problems and to identify priorities for research and development, for training and for strengthening institutions—improved or new means of control, not the supply of those currently in use, are the objectives;
3. an annual budget of US$15–19 million provided by the cooperating parties and co-sponsors.

Six chronic debilitating diseases—malaria, schistosomiasis, filariasis, trypanosomiasis, leprosy, and leishmaniasis have been selected. After careful consideration, tuberculosis and diarrheal diseases were not included. Technical approaches include chemotherapy, immunology, vector biology, epidemiology, biomedical, socio-economic, and operational research.

Groups of scientists from academia and industry, chosen on a world-wide basis for their competence in the diseases and/or the approaches, have been formed for each disease and for several technical approaches. Scientific Working Groups comprise all the scientists who plan, carry out, and review research on a specific aspect. Members of the group meet regularly. After defining the objectives, they devise a strategic plan to achieve them and review the research as the work progresses. Members participate according to their individual interests and expertise. A Steering Committee of up to ten members considers the relevance of project submissions and judges their sci-

entific quality before funding. Research proposals are being sought to fill knowledge gaps identified in priority research areas. The need to have broad input on an international scale and to strengthen research capabilities to create self-reliance are prime considerations in the organization of the program.

The Special Programme can be helped if all those interested will study the reports of the Scientific Working Groups and communicate their views, opportunities, and needs to the secretaries. Some may wish to apply for research support under the plan, and some may be able to offer training opportunities. University-industry linkages can be created for the development of drugs, vaccines, and diagnostic tests for tropical diseases.—(*Adapted from* the article)

Grove, D. I. Leprosy. In: *Antimicrobial Therapy*. 3rd ed. Kagan, B. M., ed. Philadelphia: Saunders, 1980, pp. 335–339.

This chapter provides a brief review of leprosy. The classification of leprosy is explained with emphasis on the clinical presentation, bacteriologic findings, and biopsy picture. The major drugs utilized in the treatment of leprosy are briefly discussed and include dapsone, acedapsone, rifampin, and clofazimine. A paragraph deals with the reactions in leprosy, and mention is made of the possible value of BCG in leprosy prophylaxis.—RCH

Lew, J. The integration of handicapped people due to Hansen's disease into the community. J. Formosan Med. Assoc. **78** (1979) 899–900.

In 1945, there were more than 5000 patients with leprosy in Korea, who were begging on the streets. There were additionally some 10,000 inpatients in four leprosaria. At that time, it was thought desirable to gather these 5000 patients together. Beginning in 1948, the Korean Leprosy Association, through volunteers and Sung-Jua-Hoi (The Federation of Hansenarian), set about to accomplish this goal. From 1948 until the outbreak of the Korean War in 1950, 16 villages were established to accommodate these patients. This movement was named the Hope Village movement. In the summer of 1955, the Korean Leprosy Association began to combat leprosy problems in the country once more. The new chemotherapeutic agent, DDS, and new concepts of leprosy were introduced, and a leprosy outpatient clinic was established. Approximately 20,000 institutionalized leprosy patients were examined. Physically fit and arrested patients were given the options of discharge or settling in "resettlement villages." Presently, there are about 100 such resettlement villages where about 20,000 victims are managing their daily lives. These resettlement villages are now very rapidly merging with ordinary villages after becoming prosperous and developing a normal relationship with their neighbors.—(*Adapted from* the article)

Michael, J. M. The Public Health Service Leprosy Investigation Station on Molokai, Hawaii, 1909–1913—An opportunity lost. Public Health Reports **95** (1980) 203–209.

In this article the author details the events surrounding the establishment of the hospital and laboratory facilities of the Leprosy Investigation Station on Molokai, Hawaii. The project had its inception through the efforts of Walter Wyman, Surgeon General of the Public Health and Marine-Hospital Service, from 1891–1911, who was zealous in his determination to end the problem of leprosy. The author points out that during 1904–1905 the U.S. government appropriated generous sums for this project and subsequently that excellent research facilities and beautiful personal residences were built for station personnel. However, during the early years of the Station, an outstanding "opportunity" was lost to utilize these facilities because of the attitudes of the chief personnel. For example, the Station's first director declined even to come to Molokai, preferring instead to work in Honolulu; additionally, so concerned was this gentleman with the possibility of leprosy infection that "he allowed his good sense to be overwhelmed to the point where his precautions became offensive, as well as ridiculous." Thus, in the author's opinion, although the persons ap-

pointed to the Leprosy Investigation Station during its first years had a genuine interest in the scientific problems of leprosy, their insensitivity and lack of concern with the human needs of leprosy victims "led to wasted resources and inadequate treatment."—G. Gordon

Rotberg, A. The Brazilian Phase III of prevention of hanseniasis. Int. J. Dermatol. **18** (1979) 655–659.

Phase I in the prevention of hanseniasis (a half-century of compulsory isolation of patients) and Phase II (30 years of case finding, ambulatory treatment, integration and education on "lepra," and attempts at social rehabilitation of "leprosy patients") have failed. The endemic and the stigma are rising in most developing countries; social rejection of patients and contacts continue; ignorance and counter-education prevail everywhere. Phase III is inaugurated in Brazil with the frank admission that "lepra is not a disease like any other" but rather an exceptional "psychosocial-somatic phenomenon" to be handled in an exceptional way.

In 1976, a completely new program for the prophylaxis of hanseniasis was inaugurated by the Brazilian Ministry of Health, which was to be in accordance with the recommendations of the "National Conference to Assess the Policies of Hanseniasis Control" (Brasilia, March 1976) and with an 8-year-old satisfactory experience in the Brazilian state of S. Paulo. This new program is practially an official admission that the two previous phases have failed to control the epidemic in the country. It is based on the concepts that: 1) the worst of the patients' and their contacts' suffering is not physical but social and psychological; 2) the removal of the psychosocial factors, besides solving the greater part of the patients' problems, ends their hiding and opens the way to medical measures essential to preventing the aggravation of the physical disease and of the endemic; 3) the psychosocial cultural factor is intimately and inextricably bound to the term "lepra," a "label of primary force," whose ancient and continuously reinforced stigmatizing and degrading connotations by all communications media will never be erased by any amount of educational effort.

By removing the social stigma and the problems psychologically related, which often lead to psychopathy, most of the problems of the disease will be solved, as only a relatively small fraction of patients are victims of seriously deforming and debilitating conditions. This is the new angle from which the whole question is seen in Phase III.

Furthermore, most physical and epidemiologic consequences of the disease are expected to be averted as soon as patients really feel that their disease is "like the others" and that they—and their contacts—may seek examination and treatment totally fearless of social ostracism. Only when early "service finding" and "doctor finding" occur in massive proportions, as in other diseases, and replace the peculiar and painstaking "leprosy case finding," will the disease begin to be clinically and epidemiologically controlled.

Proven by the failure of Phase II and by the inquiries cited, this cannot be achieved with the term "lepra" or equivalent appellations. In Brazil, a new name was found necessary to gradually disentangle the physical disease from the enormously heavy load of stigma and disgrace carried by a term whose pejorative connotations are being constantly reinforced by all mass communications media. Neither Brazil nor any other developing endemic country will ever have the means to resist such massive daily counter-education.

As international organizations have not yet substituted a better terminology, the eponymic "hanseniasis," previously tested with reasonable success in São Paulo and other Brazilian states, was nationally adopted. The destigmatizing and preventitive programs of Brazil—and other countries which might adopt similar measures—would certainly acquire a new impulse everytime an English- or French-speaking author substituted "hanseniasis," "hansenosis," "Hansen's disease," or "maladie de Hansen" for the demoralizing "leprosy" or "lèpre," whose connotations in Latin-American dictionaries are those of "filth," "vice," "loathsomeness," "foulness"—or worse.—(*Adapted from* the article)

Chemotherapy

Baehner, R., Ismail, G., Allen, J. and Boxer, L. The oxidative effects of a dapsone derivative on normal and chronic granulomatous disease polymorphonuclear function. Infection (Suppl. 1) **6** (1978) S129–S135.

To evaluate the potential use of dapsone (4,4′-diaminodiphenyl sulfone) to restore oxidative metabolism and bactericidal potency to polymorphonuclear (PMN) leukocytes from patients with chronic granulomatous disease (CGD), the active derivative of dapsone, 4-amino-4′-hydroxylaminodiphenyl sulfone (DDS-NOH) was evaluated for its ability to generate reduced products of oxygen. In a cell free system, DDS-NOH reduced the redox dye, nitroblue tetrazolium (NBT), and the reaction was ablated by superoxide dismutase (SOD), an enzyme specific for inhibiting superoxide anion mediated reactions. Addition of catalase, a scavenger of hydrogen peroxide (H_2O_2), and sodium benzoate or mannitol, both scavengers of hydroxyl radical, had no effect on the reduction of NBT by DDS-NOH. In an acellular system, high concentrations of DDS-NOH were bactericidal for *Staphylococcus aureus* 502A, and the effect was enhanced by SOD. Catalase, but not benzoate or the singlet oxygen scavenger, beta carotene, elminated the bactericidal effect of DDS-NOH in the presence of SOD. Incubation of CGD PMNs with 0.2 and 1.0 mM DDS-NOH for 30 min improved the rate of glucose 1-^{14}C oxidation and the rate of iodination of ingested zymosan particles to activities observed in control leukocytes. However, the bactericidal response was only partially restored. Washed leukocytes previously incubated with DDS-NOH failed to show enhancement of bactericidal activity in CGD PMN, supporting the idea that DDS-NOH does not enter the cell. Exposure of normal and CGD PMN to 0.02 mM DDS-NOH promoted capping of Concanavalin A (Con A) on the plasma membrane and improved the translocation of the granular enzyme, myeloperoxidase into phagocytic vesicles. Both responses depend upon the disassembly of cytoplasmic microtubles confirmed directly by ^{3}H colchicine binding. These studies indicate that DDS-NOH generates superoxide anion and H_2O_2, which are bactericidal, but the oxidative properties of DDS-NOH are toxic toward the sulfhydryl containing microtubules, allowing only partial restoration of CGD PMN phagocytic function.—Authors' Summary

Belda, W., Margarido, L. C., Marlet, J. M., Martínez, E. A. L. W., Kliemann, T. J. A. E., Lombardi, C. and Belda, Jr., W. Estudo comparativo das médias móveis, dos índices baciloscópico e morfológico, em pacientes de Hanseníase virchoviana tratados pela rifampicina e pela diaminodifenil-sulfona. (A comparative study of the variable averages of the bacilloscopic and morphologic indexes in virchowian hanseniasis patients treated with rifampin and with diaminodiphenyl sulfone.) Rev. Saúde Pública **13** (1979) 80–91. (in Portuguese)

The clinical and bacilloscopic results obtained in a comparative study of the therapeutic action of rifampin and DDS in the treatment of the virchowian form of Hansen's disease are presented. Two relatively homogenous groups of 24 and 23 patients were observed during periods ranging from 12 to 24 months. The results demonstrated the superiority of the action of rifampin during the first months of treatment both in clinical aspects and in relation to the reduction of viable bacilli. Rifampin is recommended for treatment of the virchowian form of Hansen's disease, at least at the beginning of treatment.—Authors' Summary

Brodie, M. J., Boobis, A. R., Dollery, C. T., Hillyard, C. J., Brown, D. J., MacIntyre, I. and Park, B. K. Rifampicin and vitamin D metabolism. Clin. Pharmacol. Ther. **27** (1980) 810–814.

A 2 week course of rifampin orally (600 mg/day) in eight male subjects resulted in a consistent fall in plasma 25-hydroxycholecalciferol (25-OHD) levels of around 70%, accompanied by increased oxidation of antipyrine and 6 β-hydroxycortisol (indicative of hepatic enzyme induction). Plasma

levels of 1,25-dihydroxycholecalciferol, parathyroid hormone, and calcitonin were not altered. The fall in 25-OHD may represent the earliest lesion of drug-induced osteomalacia.—Authors' Summary

Das, P. K., Klatser, P. R., Pondman, K. W., Huikeshoven, H., Landheer, J. E., Leiker, D. L. and Rees, R. J. W. Dapsone and anti-dapsone antibody in circulating immune complexes in leprosy patients. Lancet **1** (1980) 1309–1310. (Letter to the Editor)

Dapsone binds to serum proteins and could, as a hapten in association with serum protein, elicit an antibody response. Such an antibody response in a leprosy patient taking dapsone might lead to the formation of dapsone/anti-dapsone complexes, complement activation, and consequently erythema nodosum leprosum (ENL). Such complexes might also neutralize dapsone and therefore play a role in drug resistance. As a first step to test this hypothesis, we looked for dapsone or antibodies to it in circulating immune complexes (CIC) of patients taking the drug.

Both the Clq binding and Clq deviation tests were used to screen for CIC in serum samples from 48 patients. Almost all the patients showed abnormal Clq binding regardless of their classification. Only eight patients showed abnormal Clq deviation tests, and these were in the lepromatous range. Only eight patients had values greater than normal in both tests; no difference was found in CIC levels between lepromatous patients with and without ENL.

Two patients (both lepromatous without ENL) had both dapsone and anti-dapsone in their CICs. One patient with borderline tuberculoid leprosy had only dapsone in his CIC but not antibody.

The other four samples examined were negative for both dapsone and its antibody. Three sera (not including any of the three with dapsone in their CICs) contained anti-dapsone. Neither dapsone nor antibody could be detected in sera or isolated CICs of six patients not taking the drug nor in five sera of normal individuals. Thus the authors have shown that immune complexes containing dapsone antibody can occur in leprosy patients being treated with the drug. However, there is no evidence that such complexes play any role in ENL.—(*Adapted from* the letter)

Dobek, A. S., Klayman, D. L., Dickson, Jr., E. T., Scovill, J. P. and Tramont, E. C. Inhibition of clinically significant bacterial organisms *in vitro* by 2-acetylpyridine thiosemicarbazones. Antimicrob. Agents Chemother. **18** (1980) 27–36.

Antibacterial activity of 65 2-acetylpyridine thiosemicarbazones and related compounds was determined by using clinical isolates of nine bacterial genera. Minimal inhibitory concentrations (MICs) of 0.002 to 0.062 μg/ml were obtained with 23% of the compounds for *Neisseria gonorrhoeae* and 0.016 to 0.062 μg/ml with 17% of the compounds for *N. meningitidis*. *Staphylococcus aureus* was inhibited in the MIC range of 0.125 to 0.5 μg/ml by 18% of the thiosemicarbazones, whereas 26% inhibited group D enterococcus with an MIC of 0.25 to 2.0 μg/ml. Poor antibacterial activity was shown toward the gram-negative bacilli, i.e., *Pseudomonas, Klebsiella-Enterobacter, Shigella, Escherichia coli,* and *Proteus*.—Authors' Summary

Gidoh, M., Tsutsumi, S., Funazu, T., Koide, S. and Narita, M. On characteristic antiinflammatory effects of several antileprosy drugs. Jap. J. Lepr. **48** (1979) 7–18. (in Japanese)

The authors made use of several procedures now available in an attempt to determine and in some cases to quantify the antiinflammatory action, long-suspected but not demonstrated precisely, of several drugs used in the treatment of leprosy, including drugs used empirically for their alleged antiinflammatory action. In addition to the carrageenan-induced acute edema observed in rats, they employed such investigations as Pontamine Sky Blue skin diffusion, carboxymethyl cellulose pouch, adjuvant-induced arthritis, etc.

By comparing and contrasting the diverse results obtained with these various methods of assessing the antiinflammatory action of several standard drugs used in leprosy, the authors were able to demonstrate a strong action in the case of dapsone in some tests but weak in other tests; similar-

ly, with clofazimine and thalidomide the antiinflammatory effect seemed to vary with the method used for the investigation.

Obviously, more work needs to be done on the suspected antiinflammatory action of antileprosy drugs since the mechanisms may vary from drug to drug, and no single test will show positive results with all drugs having somewhat similar clinical results.—S. G. Browne (*from* Trop. Dis. Bull.)

Griciute, L. and Tomatis, L. Carcinogenicity of dapsone in mice and rats. Int. J. Cancer **25** (1980) 123–129.

Dapsone (4,4′-diaminodiphenyl sulfone) has been tested for possible carcinogenicity in long term animal experiments. BDIV rats and C57BL mice received a 3.5% aqueous suspension of dapsone by intragastric intubation. Treatment was started in pregnant females during the last part of pregnancy, continued during lactation, and then given to the offspring after weaning five times a week for 104 weeks. The dose administered was 100 mg/kg to both rats and mice; total doses ranged from 10–16 g per rat and 1.2–1.4 g per mouse. Separate groups of animals received a combined treatment of dapsone with urethane or benzo(α)pyrene to investigate the possible additive or synergistic action of dapsone with known carcinogens as well as the possible inhibiting effect of dapsone on carcinogenesis. Unusual tumors, e.g., spleen sarcomas (related to severe fibrosis of the spleen) were detected in male rats, and higher morbidity from C-cell thyroid carcinomas was observed in treated rats of both sexes than in control rats. There was no evidence that dapsone can modify the action of other chemical carcinogens. It was noted that: 1) although the increase in the incidence of tumors in dapsone-treated animals over that observed in untreated controls is statistically significant, the increase is relatively low; 2) the tumors appeared after a lifetime treatment with the maximum tolerated doses; 3) in rats, spleen sarcomas were observed mostly in males; this may indicate a possible hormone-dependence of the observed carcinogenic effect. The present results therefore provide only limited evidence of carcinogenicity of dapsone in rats.—Authors' Summary

Ji, B. H., Tang, Q. G., Wang, S. Y. and Ni, G. X. Chemotherapeutic studies against experimental leprosy infection in the mouse foot pad model. Chinese J. Dermatol. **13** (1980) 20–28. (in Chinese)

This paper reports the results on chemotherapeutic studies of 11 drugs and four drug combinations in mouse foot pads infected with *M. leprae*. The kinetic method of Shepard was used. Jin Qiao, Nei Hong Xiao (two Chinese herb medicines), DDC (diethyldithiocarbamate), and Antabuse showed no effect. Clindamycin revealed definite bactericidal action although the activity was slightly lower than an equal dose of rifampin. DDS, B663, B628, rifampin, "phenylthiazole rifamycin" (R-75-1), and prothionamide showed marked bactericidal activity under certain dosages. Four different drug combinations did not reveal any antagonistic action. The effect of the combinations of DDS plus prothionamide, DDS plus rifampin, and rifampin plus B628 showed an effect slightly better than any of the compounds given singly.—(Authors' Summary translated by Y. T. Chang)

Lew, J. The review of chemotherapeutic trials on leprosy and its present states in Korea. Yonsei Med. J. **20** (1979) 52–55.

Leprosy was described in what is now Korea in 13 A.D. Chaulmoogra was advocated for treatment in 1613. Promin was introduced in 1947 and dapsone in 1955. The value of dapsone as chemoprophylaxis for leprosy contacts was established in Korean trials published in 1966–1969. A thiocarbanilide compound designated as L-4 has been studied in chemotherapeutic trials. L-4 appears to be safe and effective. Clofazimine use has been limited because of skin colorization. More recently, trials of rifampin, alone or in combination with dapsone, have shown good results, particularly with the combination of rifampin and dapsone. Since 1967, the Korean chipmunk has been used as an experimental animal for the growth of *M. leprae*. After a lag period of approximately 7 months, *M. leprae* multiply in both foot pads and ears of these animals. Yields as high as 2.0×10^{10} acid-fast bacilli per foot pad have been obtained. Korean chipmunks were found susceptible to a variety of mycobacteria and therefore

can be used in research with various mycobacterial species other than *M. leprae*.—(*Adapted from* the article)

Meisel, S., Pupkoff, R. and Svaan, J. *In vitro* effect of rifampin on serum bilirubin determinations. Antimicrob. Agents Chemother. **18** (1980) 206–207.

An *in vitro* study demonstrated interference with the total serum bilirubin assay by toxic rifampin levels. This interference was not observed with therapeutic rifampin levels.—Authors' Summary

Neuvonen, P. J., Elonen, E. and Mattila, M. J. Oral activated charcoal and dapsone elimination. Clin. Pharmacol. Ther. **27** (1980) 823–827.

The effect of orally given activated charcoal on the elimination of therapeutic and toxic doses of dapsone was studied in five healthy subjects and in two intoxicated patients. In a randomized crossover study the subjects took a total dose of 500 mg dapsone over 4 days; 10 hr after the last 100 mg dose of dapsone 50 g activated charcoal as a water suspension (or water) was taken, followed by four consecutive doses of 17 g at 12 hr intervals. The half-life ($t_{1/2}$) of serum dapsone was 20.5 ± 2.0 hr during the control period and 10.8 ± 0.4 hr during the charcoal period ($p < 0.01$). The $t_{1/2}$ of serum monoacetyldapsone (MADDS) was shortened from 19.3 ± 1.2 hr to 9.5 ± 0.7 hr ($p < 0.01$) by charcoal. The $t_{1/2}$s of dapsone and MADDS, calculated on the basis of urinary excretion rate, were shortened by charcoal. Two patients had taken large doses of dapsone in suicide attempts. The use of activated charcoal, 80 g/day for 1 or 2 days increased (3 to 5 times) the rate of elimination of both dapsone and MADDS, as reflected in serum concentration and urinary excretion data. The use of multiple doses of charcoal seems to be indicated as supplementary treatment of certain intoxications during the postabsorption phase if the drugs have a long $t_{1/2}$ and if they are secreted into the gut with subsequent reabsorption.—Authors' Summary

Pattyn, S. R., Baquillon, G., Ferracci, C. and Saint-André, P. Premier cas de lèpre à résistance secondaire à la dapsone en Afrique occidentale. (First case of leprosy with secondary resistance to dapsone in West Africa.) Méd. Afr. Noire **26** (1979) 687–691. (in French)

On the occasion of the diagnosis of the first proven case of dapsone resistance in West Africa, the authors review the mechanism of the appearance of resistance, its importance, and the different stages of diagnosis.—Authors' Summary

Poupon, R. Y., Meyniel, D., Petit, J., Gustot, P. and Darnis, F. Hépatite cholestatique au cours d'un traitement par l'I. N. H. et la rifampicine: arguments en faveur de l'hépatoxicité de la rifampicine. (Cholestatic hepatitis during treatment with INH and rifampin: Arguments in favor of the hepatotoxicity of rifampin.) Ann. Méd. Interne **130** (1979) 371–375. (in French)

It is generally accepted that hepatitis occurring during treatment with INH and rifampin results from the hepatotoxicity of INH metabolites.

A case is reported of cholestatic hepatitis occurring during such treatment in which there was a previous history of an isolated hepatic affection. The administration of INH and rifampin caused cholestasis alone, which reoccurred after rifampin administration only.

No immuno-allergic phenomenon was shown to be involved in this case of rifampin toxicity. This observation suggests that rifampin may be hepatotoxic itself, especially in patients with previous hepatic disease.—Authors' Summary

Terencio de las Aguas, J., Gervazoni, B. and Ravioli, R. Conclusiones sobre la rifampicina en la lepra a los siete años de tratamiento. (Conclusions concerning rifampin in leprosy after seven years of treatment.) Rev. Fontilles **12** (1980) 425–436. (in Spanish)

Fourteen patients with lepromatous leprosy were treated with rifampin for periods ranging between 5 and 7 years. The dose of rifampin was 600 mg daily. Seven of the patients (50%) discontinued treatment. Of the remaining seven patients, 76% became negative for acid-fast bacilli in nasal mu-

cous smears by 29 months, and during this same period 24% achieved considerable morphologic improvement. In the skin, 71% improved morphologically, and 29% became bacteriologically negative.

Lepra reactions were seen in five of the seven patients. Those patients having reactions experienced an average of ten such episodes. An additional 12 patients were treated with Isoprodian and rifampin for periods of time ranging between 2 and 6 years. The results were better with this combination than with rifampin as monotherapy. Tolerance to rifampin was very good.—RCH

Clinical Sciences

Bourne, A. J., Dymock, R. B., Parry, W. D. H. and Turner, T. W. Leprosy in Indo-Chinese refugees. Med. J. Aust. **1** (1980) 275–276.

Five cases of leprosy, four borderline tuberculoid and one indeterminate, which were recently diagnosed in Indo-Chinese refugees in Adelaide are reported. This diagnosis should be kept in mind when dealing with skin lesions in Indo-Chinese refugees.—Authors' Summary

Carrillo Casaux, D. and Carillo Montesinos, J. M. Lepra neural. (Neural leprosy.) Rev. Fontilles **12** (1980) 415–423. (in Spanish)

The paper consists of a case report of lepromatous leprosy without any specific cutaneous lesions, which would suggest the diagnosis. There was a predominantly neural presentation with painful paralysis of the "cubital-medium" nerves, at times acute, and atrophic changes in the hands. There was no visceral involvement detected.

No definite source was discovered for the patient's infection in the patient's household. The patient resided in a small village, containing nine known cases. Thus he came from an endemic area for leprosy.

The patient was treated with dapsone 50 mg daily together with intramuscular B_{12} and B_1 vitamins.

It is pointed out that the prognosis is guarded because of the irreversibility of the existing paralysis and that 10–12 years of treatment will be required.—(*Adapted from* authors' summary)

Chiron, J.-P., Maupas, Ph. and Denis, F. Infection par le virus de l'hépatite B chez les hanséniens. IV. Recherche de nouveaux marqueurs (HB_eAg, anti-HB_e, anti-HB_c) dans le sérum. (Hepatitis B virus infection in patients with Hansen's disease. IV. Detection of further markers (HB_eAg, anti-HB_e, anti-HB_c) in the blood.) Dakar Méd. **24** (1979) 79–84. (in French)

The "new markers" of the hepatitis B virus were searched for in the serum of 553 leprosy patients. The antigen HB_eAg is present in 15% of these sera of the subjects HB_sAg positive, and anti-HB_e is detectable in approximately 50% of these sera from the same subjects.

Thirty-three percent of these sera of leprosy patients did not contain markers for the envelope (HB_sAg negative, anti-HB_s negative) and possessed anti-HB_e or anti-HB_c. This new class of "infected patients" by hepatitis B virus, rare in Europe and America, exists in Africa in the population without leprosy but with a frequency much less than that observed with leprosy patients.—(*Adapted from* the article)

Duncan, M. E. Babies of mothers with leprosy have small placentae, low birth weights and grow slowly. Br. J. Obstet. Gynecol. **87** (1980) 471–479.

One hundred and sixteen women with leprosy and 31 healthy controls were studied throughout 155 pregnancies, and their babies were observed for a period of up to 2 years. Babies of mothers with leprosy weighed less than those of healthy mothers; the placental weights and coefficients followed the same trend. The babies of the mothers with leprosy grew more slowly than those of healthy mothers, and these

findings were most marked in the babies of mothers with lepromatous leprosy. The cause of the reduced feto-placental weight is thought to be related to the immune status of the mother.—Author's Summary

Goiriena de Gandarias, F. J., Monge Jodra, V. and Perez Perez, B. Presencia del Hb_sAg en una población de enfermos leprosos. (Detection of Hb_sAg in a group of leprosy patients.) Rev. Sanid. Hig. Publica (Madr.) **52** (1978) 1467–1478. (in Spanish)

The presence of Hb_sAg in 206 sera from leprous patients (173 inpatients and 33 outpatients) has been studied. The frequency of positive in the first group was higher in lepromatous patients of both sexes in 8.27%, and in tuberculoid patients the frequency descended to 2.63%, a figure very close to that found in the healthy population (1.66%). In outpatients the only case occurred among the lepromatous patients with a frequency of 6.25%. These facts seem to show that there is a series of factors favoring the appearance of the disease: 1) blood transfusions are more frequent in lepromatous patients; 2) there are more contacts in hospitalized patients; and 3) probably the higher persistence of Hb_sAg in lepromatous patients is due to the higher incidence among them of hepatic disease.—Authors' Summary

Hentschel, B. Lepra und Nervensystem. (Leprosy and the nervous system.) Nervenarzt **50** (1979) 346–351. (in German)

Three cases of leprosy are described. They were diagnosed during a period of 6 years in the Mannheim Clinic of the University of Heidelberg. A short review of the clinical manifestations of leprosy is given with special emphasis on neurological symptoms. It is necessary in Germany today to keep the possibility of leprosy in mind in the differential diagnosis of neurological disturbances.—Author's Summary

Herrerias, J. M., Ariza, A. and Garrido, M. Laparoscopic aspects of lepromatous leprosy. Endoscopy **12** (1980) 121–123.

The authors performed laparoscopy on eight patients (six females and two males) with lepromatous leprosy. The findings showed that *goose flesh* hepatomegaly (100% of the cases) and red or gray splenomegaly (75% of the cases) can be considered as laparoscopic hallmarks of lepromatous leprosy.—Authors' Summary

Ishihara, S. *Calcinosis cutis* occurred in leprosy patients. Jap. J. Lepr. **48** (1979) 67–70. (in Japanese)

I have observed six cases of *calcinosis cutis* in leprosy patients. The patients had lepromatous leprosy, and all had been hospitalized in a leprosarium for over 20 years. All of them were detected by X-ray, and all showed deposits of calcium in the skin. In all cases, serum calcium, phosphorus, and alkaline phosphatase were normal. Two cases were examined histologically. Both specimens were taken from the forearm, which contained bone-like masses which were too hard to cut with a knife. Histological studies were done after decalcification of the specimens with trichloroacetic acid. In histologic sections the collagen bundles were replaced by amorphous material showing faintly basophilic on H & E stains. By Kossa's stain, there were scanty, dark brown granules in the same collagen fibers. These cases could be suspected as being dystrophic *calcinosis cutis*. The calcium probably deposited in previously damaged tissues in which prolonged lepromatous lesions existed, or erythema nodosum leprosum occurred repeatedly.—(*Adapted from* author's summary)

Jerez, J., Quintanilla, E., Martin-Gil, D., Ayesa, C. and Oehling, A. Lepromatous leprosy and contact dermatitis. Dermatologica **160** (1980) 31–36.

The rare association of lepromatous leprosy and allergic contact dermatitis due to chromium in cement was confirmed clinically and biologically in a male patient. The apparent lack of influence of lepromatous leprosy on the development and maintenance of this dermatitis dependent upon cell-mediated immune mechanisms is discussed.—Authors' Summary

Johnson, A. C., James, Jr., A. E., Reddy, E. R. and Johnson, S. Relation of vas-

cular and osseous changes in leprosy. Skeletal Radiol. **3** (1978) 36–41.

Bilateral lower limb angiography was performed on 58 patients with leprosy. Ischemia to the anesthetic feet with delay in circulation and constricted vessels was demonstrated. Further compromise of the restricted blood flow, due to abnormal arteriovenous shunting in thigh and calf muscles or to the inflammatory granulomas of the foot sole, was noted. These vascular abnormalities associated with abnormal granulomatous areas in the sole were seen to precede and influence the pathologic skeletal changes of the lower extremities and feet.—Authors' Summary

Koya, G. and Arakawa, I. Pathology of the spinal cord in leprosy. Jap. J. Lepr. **48** (1979) 27–36. (in Japanese)

Such limited damage cannot account for the dissociated deficit of the sensory system. The selective involvement of the posterior funiculi in our patients with leprosy may be a better explanation of the neurologic deficit following neuropathy.—Authors' Summary

Kuntz, J. L., Meyer, R., Vautravers, Ph., Kieffer, D. and Asch, L. Polyarthrites au cours de la lèpre. (Polyarthritis in leprosy.) Sem. Hosp. Paris **55** (1979) 1889–1892. (in French)

Inflammatory polyarthritides simulating rheumatoid arthritis belong in the manifestations of reactions in leprosy. The pathogenesis of these arthritides vary with the type of reaction. In the present observation, it most probably was the transition from a tuberculoid leprosy to a lepromatous form in which the immunological state looked like that seen with lupus.—(*Adapted from* authors' summary)

Lynch, P. and Johnston, J. H. The greater auricular nerve in presumably non-leprous British soldiers. Trans. R. Soc. Trop. Med. Hyg. **74** (1980) 136.

One hundred seventy-five soldiers recruited in Britain were examined to assess the frequency with which great auricular nerves were visible or palpable, and it was found that the nerves were palpable in 152 (87%) and were both palpable and visible in 68 (39%). The subjects with palpable nerves were significantly lighter in weight than those whose nerves could not be felt. The authors conclude that in the diagnosis of leprosy, a finding of palpable great auricular nerves has limited significance.

[In palpating peripheral nerves in normal subjects the abstracter has been impressed by the range of nerve sizes in different individuals, but in nearly all cases the nerves have felt equal on both sides of the body. Early leprosy can be suspected if a nerve is found to be thicker on one side of the body than on the other and in addition to be harder; the suspicion of leprosy is strengthened if there is tenderness on palpating the nerve or if there is a history of pain or discomfort in the nerve. The authors of this paper have performed a valuable service in emphasizing that palpable nerves per se are of no clinical significance.]—W. H. Jopling (*from* Trop. Dis. Bull.)

Mahapatra, S. B. Significance of infiltration of lower abdominal skin in lepromatous leprosy. Indian J. Dermatol. **22** (1977) 130–133.*

The area of the abdomen below a horizontal line passing through the lower border of the umbilicus and joining both anterior superior iliac spines does not show clinically appreciable lesions in polar lepromatous leprosy in the author's experience in India. Twenty typical or polar lepromatous patients and ten atypical lepromatous patients were studied for bacterial densities by skin scrapings from areas of the abdomen above and below the umbilicus. Supraumbilical sites yielded higher bacterial indexes than sub-umbilical sites in the typical lepromatous cases, but this difference was not seen in atypical lepromatous cases. Skin biopsies from similar supra- and sub-umbilical abdominal sites were taken in five patients with typical lepromatous leprosy and seven cases with atypical lepromatous disease; similar find-

* Editor's Note: It may be that patterns of habitually worn clothing may affect skin temperature and result in different patterns in other areas of the world.—RCH

ings were obtained.—(*Adapted from* the article)

Nigam, P., Dayal, S. G., Sriwastava, P. and Joshi, L. D. Serum calcium and magnesium in leprosy. Asian J. Infect. Dis. **3** (1979) 81–83.

Serum calcium and magnesium were studied in 70 leprosy patients and 25 normal healthy individuals. An attempt has been made in this study to find out if there is any correlation between the clinical and pathological status of the disease and serum calcium and magnesium levels in the blood. Serum calcium was found to be significantly decreased in lepromatous leprosy (Ca = 8.42 ± 0.7 mg%, $p < 0.001$) and dimorphous leprosy (Ca = 8.68 ± 0.94 mg%, $p < 0.05$) while it was normal in tuberculoid leprosy (Ca = 9.14 ± 2.12). The decrease in serum magnesium level was highly significant in all clinical types of leprosy (Mg = 1.08 ± 0.29, $p < 0.001$).—Authors' Summary

Sehgal, V. N., Koranne, R. V., Nayyar, M. and Saxena, H. M. K. Application of clinical and histopathological classification of leprosy. Dermatologica **161** (1980) 93–96.

A simultaneous clinical and histological study in 82 new, untreated leprosy patients was undertaken, using the criteria of Ridley and Jopling. The disparity between the clinical and histological diagnoses was abundantly clear because in only 35 patients did the two conform with each other while in others there was a shift of one step towards either the tuberculoid or the lepromatous end of the spectrum. In 18 patients from other groups of leprosy, histologic delineation had features of indeterminate leprosy.—Authors' Summary

Thyagarajan, S. P., Subramaniam, S., Solomon, S., Panchanadam, M. and Madanagopalan, N. Antigenic subtypes of HB_sAg: Their distribution and pattern of occurrence among blood donors and patients with liver diseases and leprosy in Tamil Nadu, India. J. Trop. Med. Hyg. **82** (1979) 62–66.

One hundred and seventy hepatitis B surface antigen positive sera derived from blood donors, patients with liver diseases, and leprosy were antigenically subtyped by Rheophoresis and 107 of them by agar-gel diffusion. For the time in India, HB_sAg/adr as a predominant subtype (64%) is documented.

Of the two methods adopted, Rheophoresis showed a greater sensitivity of typing, namely 82.3% in contrast to 39.2% only by agar-gel diffusion ($p < 0.001$).

Analysis of the hepatitis B_e antigen and antibody (anti-HB_e) positive sera for subtype predeliction revealed the same pattern as in HB_e system negative sera.—Authors' Summary

Wirawan, R., Sardi, F., Latu, J. and Wirjadi, B. Investigation of coagulation abnormalities in patients with erythema nodosum leprosum. Southeast Asian J. Trop. Med. Public Health **10** (1979) 393–397.

Twenty erythema nodosum leprosum (ENL) patients were examined. Coagulation studies were carried out in 13 of them during their active stage and seven in the latent stage. Of these 13 patients, six were re-examined when the disease became latent. From these observations a conclusion can be drawn that there are coagulation abnormalities in the majority of ENL patients in the active stage, and these abnormalities will return to normal values when the disease becomes latent.—Authors' Summary

Immuno-Pathology

Anderson, R., Gatner, E. M. S., Imkamp, F. M. J. H. and Kok, S. H. *In vivo* effects of propranolol on some cellular and humoral immune functions in a group of patients with lepromatous leprosy. Lepr. Rev. **51** (1980) 137–148.

Certain functions of blood neutrophils and lymphocytes were investigated at varying time intervals after the addition of propranolol to standard therapy in a group of patients with lepromatous leprosy. A control group of patients received standard therapy only. The leucocyte functions tested were neutrophil chemotaxis, phagocytosis and NBT reduction and lymphocyte mitogen induced transformation, leucocyte inhibitory factor production and number of spontaneous E, E and EAC rosettes. Serum immunoglobulins, complement components, and total hemolytic complement were also measured in both groups. Over a 3-month period neutrophil chemotaxis, numbers of active-E and E rosettes, lymphocyte transformation, and lymphokine production improved on standard therapy alone. However, although the propranolol group had the highest mean responses, there were no significant differences between the two groups of patients after 1 month and 3 months. Likewise there was no difference between the two groups with respect to other cellular or humoral investigations. Neutrophil chemotaxis appeared to be the best functional correlate of clinical improvement.—Authors' Summary

Bjune, G. Significance of immune reactions in leprosy. J. Oslo City Hosp. **30** (1980) 81–100.

The author provides a review of the disease, leprosy. The parasite, *Mycobacterium leprae*, has several traits that together make it a unique pathogen in human disease: it has a specific affinity for Schwann cells. It has a very slow multiplication rate. It is extremely nontoxic. Most of the bacilli in the leprosy patient are dead. It has not yet successfully been grown in artificial medium. The host response to infection with *M. leprae* is discussed. Three types of "reactions" are generally distinguished: reversal reactions, erythema nodosum leprosum, and Lucio reactions. A number of hypotheses are discussed regarding the possible mechanisms by which *M. leprae* avoid immune responses of the host and thus favor the development of chronic infection. An interesting thought is that antigens introduced through the nasal mucosa (presuming that *M. leprae* often infect the body via the respiratory tract) will follow a different path from antigens introduced through the skin. The significance of different lymphatic drainage patterns from the nose as opposed to the skin as well as the high proportion of IgD producing cells associated with lymphoid tissue in this area may be important in suppressing host responses. It is pointed out that recent research suggests that IgD positive cells, by stimulation with specific antigen, can produce IgD-Fab-antigen complexes, which in turn elicit the production of anti-idiotype antibodies and thereby have an important immunoregulatory effect, e.g., by inducing suppressor cells. Other "protected" sites for *M. leprae* may be in muscle cells and other cells which have a weak phagocytic potential but lack Ia antigens on their surface, which are necessary for collaboration with lymphocytes. Schwann cells may also be "protected sites" for bacillary multiplication. The various possible mechanisms by which infection with *M. leprae* may suppress the immune response are considered. Inhibitory plasma factor(s) and suppressor cells are considered. A possible defect in lepromatous macrophages is discussed. The evidence for and against genetically determined susceptibility to leprosy is presented and discussed. After discussing the purposes of immunologic testing in leprosy and outlining the present status of leprosy control, the article brings up a number of intriguing questions regarding the *in vitro* lymphocyte stimulation tests in leprosy: 1) are the cells which incorporate thymidine in the *in vitro* lymphocyte stimulation test identical with cells responsible for the *in vivo* resistance to bacillary multiplication?; 2) are circulating lymphocytes representative for the cell-mediated response to *M. leprae* in host tissues?; 3) does a given

batch of human-derived *M. leprae* present the relevant antigen(s) to the lymphocytes *in vitro*?; 4) is the *in vitro* response modified by immune regulatory mechanisms in the host? The article concludes that the *in vitro* lymphocyte response to *M. leprae* in healthy individuals has been shown to indicate sensitization and probably subclinical infection with leprosy bacilli. The implication that it reflects acquired resistance to developed clinical disease must await further clarification. There is evidence for a disassociation between clinical and histologic correlation of hypersensitivity and the ability to control the infection. The features with which the *in vitro* lymphocyte responses to *M. leprae* correlate best are those of hypersensitivity (not immunity). This finding as well as the finding of antigenic specificities of the lymphocyte responses, modification of the response by plasma factors, and other immunoregulatory mechanisms working *in vitro* make the use of the test for the measure of the individual patients' resistance to bacillary multiplication difficult.—RCH

Dastur, D. K. and Porwal, G. L. Lepromatous leprosy as a model of Schwann cell pathology and lysosomal activity. In: *Clinical and Experimental Neurology*. Proceedings of the Australian Association of Neurologists. Vol. 16. Tyrer, J. H. and Eadie, M. J., eds. Baltimore: University Park Press, 1979, pp. 277–293.

A brief illustrated account is presented of the light microscopic pathology, histochemistry of lysosomal enzymes, and fine structural changes in the nerves of patients with untreated or treated lepromatous leprosy. Predominant bacillation of the Schwann cells of unmyelinated fibers, degeneration of their axons, prominence of phagolysosomes, and disappearance of these cells with endoneural collagenosis were observed on electronmicroscopic examination of the index branch of the radial cutaneous nerve. Although there were changes in the blood vessels and proliferation of perineurium, bacillation of endothelial or perineural cells was much less conspicuous. Intact and degenerating forms of *M. leprae* were found in both treated and untreated patients, fragmenting or crumpled forms being more frequent in the treated. Both groups of patients also showed increased lysosomal enzyme activity, evidenced by single or paired paranodal spots of acid phosphatase and β-glucuronidase in Schwann cells in histochemical preparations of the nerve. There was lesser activity and activity in fewer cells in the case of β-glucuronidase than of acid phosphatase. Diffuse β-glucuronidase activity was found in the wall of empty-looking oval chambers in the Schwann cells, and acid-fast bacilli were seen in these chambers. In teased fiber preparations, both axonal degeneration and segmental demyelination were found. In semi-thin araldite sections, the myelinated fiber density was either preserved or reduced; large diameter fibers were more frequently depleted, with tall peaks of smaller fibers seen on plotting diameter spectra.—Authors' Summary

Department of Dermatology, Nanjing Medical College, *et al.* A study of cellular immunity and phagocytic activity of macrophages in 63 cases of leprosy. Chinese J. Dermatol. **13** (1980) 88–91. (in Chinese)

Immunological studies were made of 63 leprosy patients, including 21 LL, 26 TT, 7 BL, and 9 BT patients. For statistical convenience the patients were classified into the following three groups: BL/LL, TT/BT, and TT with treatment less than 1 year. Five immunological tests were performed, i.e., PHA test, three different rosette tests, and phagocytosis. Lower response (lower percentage than normal) to the PHA test was observed in patients in all the three groups. Lower response to the E rosette test was observed in patients of the BL/LL and TT/BT groups. Lower response to the active rosette test was observed in patients of the BL/LL group. There was no deviation from normal to the $FcR^{+}T$ (T cells with Fc receptors for IgG) rosette test in patients of all three groups. For the phagocytic test, TT/BT patients revealed a lower phagocytic rate and lower phagocytic index for leukocytes while BL/LL patients showed a higher phagocytic rate for monocytes.—Y. T. Chang

Fumarola, D., Jirillo, E., De Santis, A., Monno, R. and Munno, I. Leukocyte in-

hibiting factor (LIF) production from human lymphocytes of healthy donors stimulated by armadillo's lepromin. Ann. Sclavo **20** (1978) 33–40.

Armadillo lepromin (AL) was used to stimulate normal human lymphocytes, cultured *in vitro* at different temperatures, and the production of leukocyte inhibiting factor (LIF) was measured. AL caused LIF release from the cells at 37°C, and this effect was less marked at 35°C and 30°C. The occurrence of lepromatous leprosy lesions in cooler areas of the body and the appearance of lepromatous-like lesions in armadillos with a cool body temperature may be related to the effect of these cooler temperatures to depress lymphocyte metabolic activity and thereby reduce effective cell-mediated immunity.—(*Adapted from* the article)

Han, S. H., Chang, Z. N., Tsai, L. C. and Hsu, K. H. Factors contributing to impairment of the mixed lymphocyte reaction in leprosy. Chinese J. Microbiol. **12** (1979) 35–42.

Whereas the mixed lymphocyte reaction was essentially normal in inactive lepromatous leprosy and tuberculoid leprosy, it was severely impaired in active lepromatous leprosy. The impairment was found to be contributed by certain unknown factors in their plasma and subnormal reactivity of their T lymphocytes. The plasma derived from active lepromatous leprosy patients depressed the reaction of normal cells, and normal plasma enhanced the reaction of active lepromatous lymphocytes. The cellular factor was studied using a one-way reaction in which one of the two lymphocyte preparations was inactivated with mitomycin C. The impairment of blastogenesis of active lepromatous lymphocytes was partially reversed by substituting inactivated normal cells for similarly treated leprous cells, and conversely the response of normal allogeneic lymphocytes was depressed by substituting inactivated leprous lymphocytes as the stimulator cells.—Authors' Summary

Hirschberg, H. and Bergh, O. J. Defective T cell-macrophage interaction in leprosy. In: *Cell Biology and Immunology of Leukocyte Function*. Vol. 12. Quastel, M. R., ed. New York: Academic Press, Inc., 1979, pp. 893–899.

The results presented here indicate a significant role for macrophages in the activation of T cells by *M. leprae* antigens *in vitro*. T cells from all the three groups of individuals tested (low and high responding patients and high responding normal contacts) failed to respond to *M. leprae* in the presence of macrophages from low responding individuals. On the other hand, T cells from all three donor groups reacted significantly in the presence of macrophages from high responders (i.e., T patients or normal healthy contacts). These findings might be analogous to those demonstrated previously in the guinea pig where T cells from an F1 hybrid between a responder and a non-responder could only be stimulated to proliferation by antigen coated responder macrophages but not by macrophages from the non-responding strain. If this analogy is correct, the response to *M. leprae* might well be controlled by the human equivalent of the Ir genes, explaining the fact that genetic host factors influence the susceptibility to leprosy and the clinical manifestation of the disease. On the other hand, acquired macrophage defects due to the disease state, such as the inability of the macrophages to phagocytose or digest *M. leprae*, or the existence of suppressor macrophages would also explain our experimental findings. In addition, the existence of a mixed lymphocyte macrophage allogeneic response makes the interpretation of the experimental results difficult. Clearly, further studies employing HLA-D compatible macrophage lymphocyte donors are required and are now in progress.—(*Adapted from* the article)

McGee, M. P., Myrvik, Q. N. and Leake, E. S. Organization of allergic granulomas and dependence on insoluble antigen. J. Reticuloendothel. Soc. **24** (1978) 253–262.

Insolubilized tuberculoprotein was found to induce a typical granulomatous response in the lungs of Bacillus Calmette-Guerin (BCG)-sensitized rabbits upon intratracheal (i.t.) challenge. Histologically, the granulomas were composed of macrophages, ep-

ithelioid cells, and giant cells surrounded by lymphocytes. Electron microscopic examination of the epithelioid cells demonstrated ultrastructural characteristics indistinguishable from those of the epithelioid cells present in typical hypersensitivity granulomas. Granulomas were not induced when control animals were injected with the insolubilized tuberculoprotein or when BCG-sensitized animals were challenged i.t. with insolubilized albumin. Furthermore, soluble tuberculoprotein did not induce granulomas in BCG-sensitized animals. The insolubilized tuberculoprotein elicited specific dermal delayed reactions; however, the induration persisted longer than in reactions elicited with comparable doses of soluble purified protein derivative (PPD). These results indicated that typical dermal delayed hypersensitivity reactions are produced by soluble tuberculoprotein with minimal granuloma formation. However, if the same antigen was introduced in an insoluble form, a typical allergic granulomatous response was elicited. Accordingly, the local persistence of antigen can explain the development of highly organized allergic granulomas.—Authors' Summary*

Melsom, R. and Duncan, M. E. Demonstration of antibodies against *Mycobacterium leprae* both in immunoglobulin G and M in sera from pregnant and nonpregnant lepromatous leprosy patients. Lepr. Rev. **51** (1980) 125–135.

Antibodies against *M. leprae* antigen 7 have been shown to consist of both immunoglobulin G and M in a lepromatous leprosy serum pool and in individual sera from patients with active lepromatous leprosy. Various implications of the occurrence of anti-*M. leprae* antibodies in several immunoglobulin classes are discussed, particularly their use as an indicator of transfer of *M. leprae* antigens or of live leprosy bacilli to the fetus during pregnancy. With the present techniques, no IgM antibodies against *M. leprae* antigen 7 could be detected in several cord sera from babies born of mothers with active lepromatous leprosy.—Authors' Summary

Mukoyama, M. and Sasaki, N. Peripheral nerve involvement in leprosy: Neuropathological study of autopsy cases. No to Shinkei (Brain and Nerve) (Tokyo) **31** (1979) 403–408. (in Japanese)

Sciatic, tibial, and peroneal nerves were neuropathologically investigated on four autopsy cases of leprosy. Loss of myelinated nerve fiber with proliferation of connective tissue was observed in each peripheral nerve, prominently in two cases and moderately in the other two cases. Differences in the grade of pathological alterations among the sciatic, tibial, and peroneal nerves were not demonstrated.

Lymphocytic infiltration was found in two cases in epi- and perineural areas of the nerves. Lepra bacilli were detected in one case with a special staining method (methenamine silver staining).

Thickening and hyaline degeneration of the wall of perineural blood vessels were observed in all cases. Multinuclear giant cells, abscesses, or amyloid substances were not found in the peripheral nerves in this study.

In morphometric studies performed on the sural nerves of two cases, the total fiber myelinated density was decreased to 10,400/mm^2 and 7300/mm^2, respectively. A histogram showed a unimodal distribution with loss of larger myelinated nerve fibers.

In a nerve teasing study, variation in internodal length was seen in each sural nerve in two cases, which was interpreted to mean segmental de- and remyelination. At the same time, nerve fibers with small internodal length, regardless of fiber diameter, were found in one of these cases, which demonstrated the coexistence of Wallerian degeneration.

The pathological alterations observed in the peripheral nerves of the leprosy patients are considered to be provided by various factors, such as the disease type (L or T type), the therapy given to the patient during the clinical course, the disease stage at the time of pathologic examination, and the effect of aging.—(*Adapted from* authors' summary)

Podoplelov, I. I. and Selezneva, S. P. Study of lymphocyte sensitization to lepromin in patients with the polar types of leprosy. Zh. Mikrobiol. Epidemiol. Immunobiol. (6) (1980) 82–84. (in Russian)

* Editor's Note: The analogy to lepromin skin testing seems striking.—RCH

In the presence of lepromin, the lymphocytes of patients with the tuberculoid type of leprosy had a pronounced cytotoxic effect on target cells (line HEP-2) whereas the lymphocytes of patients with the lepromatous type of leprosy showed no such effect. The data obtained in this study suggest that the severe lepromatous form of leprosy is accompanied by a functional insufficiency of the T cell immune system.—Authors' Summary

Rea, T. H. and Terasaki, P. I. HLA-DR antigens in tuberculoid and lepromatous leprosy. Lepr. Rev. **51** (1980) 117–123.

The frequencies of distribution of six histocompatibility antigens of the HLA-DR locus were determined in 38 Mexican patients with lepromatous leprosy and in 19 Mexican patients with tuberculoid leprosy. These were compared with antigen frequencies of 174 Mexicans who did not have leprosy. No evidence of an association between HLA-DR antigens and leprosy could be found. In tuberculoid subjects HLA-DRW2 was more common than in controls, 32% and 15% respectively. Although this difference was not statistically significant, it was in accord with another report of a significant increase in HLA-DRW2 among patients with tuberculoid leprosy. Furthermore, frequencies for 16 HLA-A, 23 HLA-B, and five HLA-C antigens did not differ significantly in the two groups of patients as compared with controls.—Authors' Summary

Ridley, M. J., Badenoch-Jones, P. and Turk, J. L. Ultrastructure of cells of the mononuclear-phagocyte series (MPS) across the leprosy spectrum. J. Pathol. **130** (1980) 223–227.

A systematic ultrastructural study of cells of the mononuclear-phagocyte series (MPS) across the spectrum of leprosy has been carried out. Graded changes in macrophage ultrastructure from the lepromatous to the tuberculoid poles have been shown. Mycobacteria-filled macrophages in lepromatous leprosy are characterized by long cell processes whereas in borderline tuberculoid leprosy these cells have a rounded appearance and are mainly characterized by numerous intracellular vacuoles. In borderline leprosy, macrophages have an intermediate appearance. Cells of the MPS containing abundant endoplasmic reticulum were only seen in typical "epithelioid cell" tuberculoid granulomas, in "BT in reaction" and in the Mitsuda reaction. Epithelioid cell granulomas in other forms of BT leprosy contained activated macrophages.—Authors' Summary

Saha, K., Whittingham, S., Ray, D., Mittal, M. M. and Beohar, P. C. Impairment of Jones-Mote hypersensitivity and specific antibody response against depolymerized flagellin in lepromatous leprosy. Scand. J. Immunol. **10** (1979) 31–38.

Cutaneous hypersensitivity and antibody-producing capacity were assessed in patients with lepromatous leprosy with defective immunity by immunizing them with monometric flagellin from *Salmonella adelaide*. Results were compared with those of controls, matched for age and sex, derived from a similar socioeconomic stratum, but without any defect of the immunological system. In contrast to the normal individuals, who showed Jones-Mote type of hypersensitivity, no lepromatous type of patient could mount any "delayed-in-time" cutaneous hypersensitivity reaction against an intradermal challenge of monometric flagellin. However, when immunized through the subcutaneous route, both groups could produce adequate amounts of specific serum antibody. In addition to this unique split tolerance found in all lepromatous patients, some patients showed low levels of "natural" IgM antibody, reduced formation of specific antibody when immunized through the subcutaneous route, and incomplete maturation of IgG class of anti-flagellin antibody. When immunized by the intradermal route, however, production of both anti-flagellin antibody and maturation of IgG antibody was significantly inhibited in normal adults but not in lepromatous patients. Thus, contrary to the earlier concept of hyperactivity of the humoral immune apparatus in lepromatous leprosy, the present study detected B-cell hypofunction in some patients.—Authors' Summary

Singh, S. and Nath, I. Reduction of a subset of T cells bearing Fc receptors for IgG in

lepromatous leprosy. Int. Arch. Allergy Appl. Immunol. **62** (1980) 81–85.

Enumeration of a subpopulation of T cells with receptors for the Fc portion of IgG (Tγ) in the peripheral blood of 14 normal subjects and 43 patients with leprosy was undertaken. Tuberculoid leprosy patients showed normal levels of Tγ cells. In contrast, bacillary positive patients with lepromatous leprosy revealed a significant reduction of circulating Tγ cells ($p < 0.001$).

Our data indicate that in lepromatous leprosy there is a significant depletion of spontaneously occurring Tγ cells in the peripheral blood. On the other hand, tuberculoid patients had a normal range of these cells. It would thus appear that in the low-resistant form of infection where poor cellular immunity is observed, there is a decrease in regulator cells. It would further seem that the loss of these cells correlates with a lack of control over humoral responses, leading thereby to excessive antibody production to nonprotective mycobacterial antigens and self-components. The situation is analogous to systemic lupus erythematosus and the autoimmune phenomenon noted in NZB/W mice where loss of suppressor function is related to the development of autoantibodies. Earlier data from our laboratory using another parameter indicates that concanavalin A induced suppressor cells are also reduced in patients with lepromatous leprosy. It would thus appear that in the spectrum of leprosy, regulator T cells are observed where cellular immune responses are good (e.g., tuberculoid leprosy). However, in patients showing a failure of cellular responses and the presence of irrelevant antibodies, there is a concomitant loss of regulator T cells.—(*Adapted from* the article)

Microbiology

Cao, S. N., Wu, Q. X., Liu, Q. and Jiang, B. L. An attempt in cultivation on *M. leprae in vitro*: I. A summary of 23 positive cultures from 13 cases of leprosy. Chinese J. Dermatol. **13** (1980) 12–19. (in Chinese)

This is the summary of our studies on the cultivation of *M. leprae* over a period of 15 months from October 1970 to December 1971. A total of 91 cultures were performed from 44 biopsies obtained from 36 lepromatous or borderline leprosy patients. All cultures were observed for a period of more than 6 months. Successful growth was based on the appearance of bacterial colonies in cultures. Growth of acid-fast organisms was observed in 13 out of 36 patients (36.1%), in 19 out of 44 biopsies (43.2%), and in 23 out of 91 cultures (25.3%). We found that our Jing 4 liquid medium and the Tai 31 and Tai 33 bi-phase media gave definite growth of organisms and that Jing 4 might become an important medium. In Jing 4 medium, we used fresh egg white, two neurotropic substances (acetylcholine and norepinephrine), and freshly prepared homogenate of rat peripheral nerves. In the solid phase of the bi-phase medium, we included a comparatively high concentration of glucose. As far as we are aware, the use of these substances for *M. leprae* cultivation studies has not appeared in the literature. Preliminary discussion of certain specific properties of our cultivated organisms was made. Discussion of the relationship between our cultivated organisms and *M. leprae* was made. Further studies on differentiation of our cultivated organisms are in progress, and the results will be reported later.—(Authors' Summary translated by Y. T. Chang)

Colston, M. J. and Hilson, G. R. F. The effect of freezing and storage in liquid nitrogen on the viability and growth of *Mycobacterium leprae*. J. Med. Microbiol. **12** (1979) 137–142.

The effects of rapid and slow rates of freezing in liquid nitrogen, storage in liquid nitrogen for 12 months, and the rate of subsequent thawing on the viability and growth of *M. leprae* in the mouse foot pad were studied. Some loss of viability of *M. leprae* was detected, and this was found to be associated with the freezing process rather than with storage or thawing. Slow freezing was less deleterious than quick freezing, with a loss of viability of 90% compared with 98%. The growth pattern of *M. leprae* was unaffected except for a delay in the appearance of growth caused by the loss of viability though there was some evidence of an increased lag phase of one strain, possibly due to the repair of sub-lethally damaged organisms.—Authors' Summary

Wang, H. Y. and Huang, H. S. Study on viability of *Mycobacterium leprae*: Effect of ultraviolet rays and sunlight. Chinese J. Dermatol. **13** (1980) 85–87. (in Chinese)

This paper reports the bactericidal effect of ultraviolet rays and sunlight on *M. leprae*. The mouse foot pad model was used to test bactericidal activity. Suspensions of *M. leprae*, 10^6 and 10^7/ml, were exposed to ultraviolet (30 W) rays at different distances for a period of 30 or 60 min. All organisms were killed. There was no growth of organisms in the mouse foot pads. After exposure to the sunlight for 1 hr, the survival of *M. leprae* was markedly reduced. All organisms were killed after exposure to sunlight for 2 hr.—Y. T. Chang

Experimental Infections

Navalkar, R. G., Patel, P. J. and Kanchana, M. V. Studies on immune response to *Mycobacterium lepraemurium*. Evaluation of the cell-mediated immune response in mice. Int. Arch. Allergy Appl. Immunol. **62** (1980) 423–432.

Evaluation of the cell-mediated immune response (CMI) in mice infected with *Mycobacterium lepraemurium* revealed a disturbance in the nonspecific components of the CMI. Expression of delayed-type hypersensitivity (DTH) in skin test studies indicated that the organism is capable of inducing skin reactivity in mice. This begins at a very early stage of infection and subsequently decays as the infection becomes disseminated. At this stage, gross pathological changes are noticed, followed by a high rate of mortality. An *in vitro* correlate of DTH, namely lymphocyte transformation, was in concordance with the observation of DTH. The suppression of CMI appears to be due to extensive multiplication of the infecting pathogen within the host system.—Authors' Summary

Epidemiology and Prevention

Abreu, A., Werthein, L. J. and Ruiz de Zarate, S. Doce años de vacunación BCG y lepra infantil en Cuba. (Twelve years of vaccination with BCG vaccine and infant leprosy in Cuba.) Rev. Cub. Hig. Epidemiol. **16** (1978) 63–72. (in Spanish)

Since 1963, every infant born in institutions has been systematically vaccinated with BCG vaccine. From 1970 on, and on the basis of studies performed between March and April 1969 (Sevy-Warner), revaccination at 5 years was eliminated; it was maintained in the fifth grade of primary education centers, i.e., approximately 10 years after the first vaccination. The total number of persons with leprosy under 15 years old between 1965–1976 (180 patients) was analyzed, and 133 (73.9%) were surveyed. All patients with a positive diagnosis were born between 1951–1970, and no new case from that date on was reported. The highest number of patients (79) belonged to the 11–14 year age group. Thirty-one patients (32.3%) with positive bacillary studies and 102 (76.7%) with negative bacillary studies had a positive diagnosis. The anesthetic spot was the most frequently reported clinical symptom. Ninety-five patients (71.4%) were diagnosed with the aid of contact examinations, and 38 (28.6%) did not refer to any contact with disabled people. Among nonvaccinated children, 34 had lepromatous leprosy, and two had dimorphous leprosy (81.3%); among vaccinated children, only four had lepromatous leprosy, and two had dimorphous leprosy (18.7%).—Authors' Summary

Ahmed, H. A., Belehu, A., Stoner, G., Touw, J. and Reitan, L. Leprosy and ABO blood groups in Ethiopia. Ethiop. Med. J. **17** (1979) 37–40.

The blood group distribution among 308 leprosy patients has been determined. The results are analyzed in relation to the previously reported blood group distribution among 2161 volunteer blood donors in Addis Ababa. No significant differences were found between the leprosy patients as a whole and the general population nor between the tuberculoid or lepromatous leprosy groups and the general population.—Authors' Summary

Guarneri, B., Randazzo, S. D. and Giardina, A. A proposito di alcuni casi di lebbra autoctona in Sicilia. (Some cases of indigenous leprosy in Sicily.) Minerva Dermatol. **112** (1977) 541–543. (in Italian)

The prevalence of registered leprosy cases in Sicily since 1913 is reported. Three outstanding epidemiological features were identified. A constant high incidence was noted in three provinces, Messina, Catania, and Syracuse, which are situated on the

same longitude along the eastern coast of the island. The clinical onset of the disease was of recent origin, and there was a high prevalence of multiple cases within families. The authors suggest these features reflected an indigenous origin of the disease.—C. D. Enna

Lombardi, C. Situaçáo da endemia da hanseníase no município de São Paulo, Brasil (1976–1977). (The situation of endemic Hansen's disease in the county of São Paulo, Brazil [1976–1977].) Rev. Saúde Públ. (São Paulo) **13** (1979) 281–298. (in Portuguese)

The situation of endemic Hansen's disease in the county of São Paulo, Brazil during 1976 and 1977 is described and analyzed and also characterized as a public health problem through the presentation and discussion of prevalence and incidence rates according to the location of the homes in the different districts and subdistricts of the city, including central, intermediary, and outlying zones of the city/county. The specific medical resources available are described and evaluated according to the same criteria. An attempt was made to relate the distribution of the resources to the distribution of the endemic rates found.—Author's Summary

Martínez Domínguez, V., Gallego Garbajosa, P., Gyi, M. M., Tamondong, C. T., Sundaresan, T., Bechelli, L. M., Lwin, K., Sansarricq, H., Walter, J. and Noussitou, F. M. Epidemiological information on leprosy in the Singu area of Upper Burma. Bull. WHO **58** (1980) 81–89.

In the course of a WHO trial designed to evaluate the possible protective action of BCG vaccine against leprosy, a longitudinal epidemiological study of the whole population was carried out in an area of very high endemicity in Burma from 1964 to 1976. Two mass surveys of the whole population with an interval of 4 years and annual re-examination of the 28,000 children (0–14 years) in the BCG trial were carried out. The data collected yielded important information about general prevalence and yearly incidence of the disease as well as on sex, age, and classification of cases. The general prevalence rate declined from 32.6 per 1000 in the first survey to 25.2 per 1000 in the second. The number of cases among males was significantly higher than among females. Incidence rate among contacts of already known cases was 9.8 per 1000 person-years. The estimated yearly incidence among noncontacts was 5.9 per 1000. Prevalence rates reached a peak in the 20–39-year age group. The prevalence rate of multibacillary patients also reached a peak in the same age bracket. It is stressed that a further period of epidemiological surveillance will be essential in order to have a correct estimate of the expected number of new infections, especially multibacillary cases in the 20–39-year group. The value of this information is considered unique for planning and programing of future control activities.—Authors' Summary

Matthews, C. M. E., Selvapandian, A. J. and Jesudasan, M. Health education and leprosy. Lepr. Rev. **51** (1980) 167–171.

In the context of effective health education in leprosy, various theories from the behavioral sciences are reviewed. In a project carried out near Vellore in South India over a period of 1½ years, the three main stages included information, motivation, and action. The objectives were to make the patients come for early and regular treatment, to make the public willing to employ patients and not to avoid harmless contact with them, and to make patients take proper care of their hands and feet. The techniques employed are described and the results analyzed—indicating a considerable improvement in knowledge, attitude, and reported practice.—Authors' Summary

Sebai, Z. A. An epidemiological study of leprosy and leprosy care in Saudi Arabia. Saudi Med. J. **1** (1980) 133–140.

An analysis of the 144 inpatients in the only leprosarium in Saudi Arabia has been made; an assessment of the attitude of the local population to afflicted patients was considered and recommendations made for the future management of patients suffering from leprosy.—Author's Summary (*from* Trop. Dis. Bull.)

Texier, L., Maleville, J., Géniaux, M., Sarrat, Ph. and Guillaume, A. Etude épidémiologique de 82 cas de lèpre suivis à la clinique dermatologique de Bordeaux de 1947 à 1979. (Epidemiologic study of 82 cases of leprosy managed at the dermatological clinic in Bordeaux from 1947 to 1979.) Bordeaux Méd. **13** (1980) 873–875. (in French)

The authors report their observations concerning 82 cases of leprosy managed at the dermatological clinic at Bordeaux. Over the last 15 years, the authors have chiefly observed Hansen's disease which is imported and affects a high percentage of West Indians and Africans from south of the Sahara. Lepromatous forms are observed especially in city populations but are also seen in the West Indian and Portuguese populations. It is noteworthy to mention that the percentages observed in Bordeaux are close to those observed in the country of origin. Lepromatous forms are often diagnosed very late in the disease, and this diagnostic delay is longer among the city population than in noncity dwellers. The delay in the diagnosis of this disease is accompanied by numerous misdiagnoses.—Authors' Summary

van Eden, W., de Vries, R. R. P., Mehra, N. K., Vaidya, M. C., D'Amaro, J. and van Rood, J. J. HLA segregation of tuberculoid leprosy: confirmation of the DR2 marker. J. Infect. Dis. **141** (1980) 693–701.

Families with multiple cases of leprosy were tested for HLA (histocompatibility leukocyte antigen)-linked control of susceptibility to tuberculoid leprosy and association with HLA-DR2. Thirty-one non-HLA genetic markers were also examined for indications of non-HLA-linked genetic factors that might control susceptibility to tuberculoid leprosy. A significant ($p = 0.002$) preferential inheritance of HLA-DR2 by siblings affected with tuberculoid leprosy but not by healthy siblings nor by siblings affected with lepromatous leprosy, was observed. In addition, combined family data showed a significant ($p < 0.0025$) excess of identical HLA haplotypes inherited from healthy parents by siblings affected with tuberculoid leprosy. Segregation of non-HLA polymorphisms did not deviate significantly from what would have occurred randomly. These data are compatible with a recessive inheritance of HLA-linked susceptibility to tuberculoid leprosy. The preferential segregation of DR2 observed in children with tuberculoid leprosy ($p < 0.001$ for the combined data from India) indicates that the HLA-linked susceptibility gene is either DR2 or in linkage disequilibrium with it.—Authors' Summary

Wolf, E., Fine, P. E. M., Pritchard, J., Watson, B., Bradley, D. J., Festenstein, H., Chacko, C. J. G. and Stevens, A. HLA-A, B and C antigens in South Indian families with leprosy. Tissue Antigens **15** (1980) 436–446.

Seventy-two families, selected for having at least two children affected with leprosy, were HLA typed for 57 A, B, and C locus antigens recognized by the WHO Nomenclature Committee. In addition, 20 possible new "splits" were investigated. The distribution of A, B, and C locus antigens in affected and unaffected family members was similar irrespective of the type of leprosy in the family. Gene frequencies (derived by direct gene counting from 253 haplotypes), haplotype frequencies, and delta values were calculated. There is evidence for heterogeneity of B5, B15, B17, Bw16, and Bw35 and for the existence of at least one A locus and one B locus antigen not previously detected. The value of the HLA system for detecting expaternal children in a highly inbred population and the effect of inbreeding on the HLA system are discussed.—Authors' Summary

Rehabilitation

Keeler, R. F. and Ryan, M. A. The incidence of disabilities in Hansen's disease after the commencement of chemotherapy. Lepr. Rev. **51** (1980) 149–154.

Of 529 patients diagnosed as having Hansen's disease during the period 1 January 1971 to 31 December 1976 in the tropical twin island nation of Trinidad and Tobago, 473 (89%) were free of disabilities at the time of diagnosis. Of these, 335 (71%) were re-evaluated in 1978 in an attempt to determine the incidence of disabilities during the first few years of chemotherapy. Only two patients (0.6%) in this group were found to have developed disabilities. We concluded that disability occurs very infrequently in Trinidad after the diagnosis of Hansen's disease and the commencement of chemotherapy.—Authors' Summary

Smith, W. C. S., Antin, U. S. and Patole, A. R. Disability in leprosy: a relevant measurement of progress in leprosy control. Lepr. Rev. **51** (1980) 155–166.

Nine hundred thirty-one patients have been detected in a Leprosy Control Project in Karnataka, India, giving a prevalence of 4.86/1000. Two hundred ninety-two of these cases have disability, and these are analyzed in detail using the WHO Disability Index DI-2. The effects of different forms of treatment on this Index are examined. It is suggested that incidence of disability is a more relevant measurement of the effectiveness of leprosy work than the incidence of cases. Secondary preventative measures are unlikely to prevent new cases whereas primary preventative measures for disability should affect the incidence of disability. This study forms the baseline of a prospective study of the incidence of disability.—Authors' Summary

Other Mycobacterial Diseases and Related Entities

Bhaskaram, P. Macrophage function in severe protein energy malnutrition. Indian J. Med. Res. **71** (1980) 247–250.

Peripheral blood monocytes from nine normal children and 11 children suffering from kwashiorkor were cultured *in vitro*, and the morphological features of the transformed macrophages were studied. Their bactericidal capacity was assessed. The results showed that macrophage function is unaltered by severe malnutrition.—Author's Summary

Burkhardt, K. R. and Nel, E. E. Monitoring regularity of drug intake in tuberculosis patients by means of simple urine tests. S. Afr. Med. J. **57** (1980) 981–985.*

A study was undertaken to evaluate simple, reliable urine spot tests suitable for detection of the major anti-tuberculosis (TB) drugs, rifampin, isoniazid, and pyrazinamide. The discrepancy between the actual ingestion of anti-TB tablets and prescribed medication was investigated in 234 hospitalized male and female patients as well as in 85 male and female outpatients with pulmonary tuberculosis. Several factors implicated in patient noncompliance are discussed, namely the degree of supervision, the independent administration of rifampin before the other TB medication, and patient preference for certain TB medicines because of tablet size.—Authors' Summary

Kazda, J. *Mycobacterium sphagni* sp. nov. Int. J. Syst. Bacteriol. **30** (1980) 77–81.

From the sphagnum vegetation of moor biotopes in northwestern Germany and Scandinavia, 183 strains of a new type of rapidly growing, scotochromogenic *Mycobacterium* have been isolated. Of these, 50

* Editor's Note: The color test for urinary rifampin and desacetylrifampin consists of merely mixing 10 ml urine with 2 ml n-butanol, mixing by inverting two times, and allowing the tube to stand to allow the butanol layer to separate again. In positive urine, a salmon-pink to cherry-red color appears in the butanol layer. False positives can occur if the urine contains an excess of urobilinogen.—RCH

were randomly selected and subjected to a taxonomic analysis. The tested strains split urea and pyrazinamide (37 strains), hydrolyzed Tween 80, had phosphatase activity, and possessed putrescine, oxidase, and nitrate reductase. They produced acid from glucose, fructose, inositol, mannitol, and mannose and usually from sorbitol. Their internal similarity is 98.23 ± 2.29%. A comparison of their properties with those of strains of 22 taxa (clusters) of rapidly growing mycobacteria was made. The mycolic acid production and the micromorphology of these strains confirmed that the strains belong to the genus *Mycobacterium*. They have unique lipid and immunodiffusion patterns and form special sensitins. Hence they are considered as belonging to a new species of nonpathogenic, rapidly growing mycobacteria for which the name *Mycobacterium sphagni* is proposed. Sph 38 is the type strain, a culture of which has been deposited in the American Type Culture Collection under the number 33027.—Author's Summary

Kazda, J. and Müller, K. *Mycobacterium komossense* sp. nov. Int. J. Syst. Bacteriol. **29** (1979) 361–365.

Strains of a new type of rapidly growing, scotochromogenic mycobacterium have been isolated repeatedly from sphagnum vegetation of moors in south Sweden and the Atlantic coastal area of Norway. These strains split urea and succinamide, hydrolyze Tween 80, produce acid from glucose, fructose, mannitol, rhamnose, sorbitol, and trehalose and grow on a medium with fumarate, succinate, citrate, malonate, oxalate, propanol, or hippurate as the single carbon source. Furthermore, they possess acid phosphatase and putrescine oxidase activities, degrade salicylate, and metabolize iron. Additional properties of these strains are presented. The internal similarity of the strains, as determined by numerical taxonomy methods, is 94.97 ± 3.42%. A comparison with 21 species (clusters) of rapidly growing mycobacteria is also presented. The production of mycolic acid by these strains and their micromorphology confirm that they belong to the genus *Mycobacterium*. The strains have unique lipid and immunodiffusion patterns and form special sensitins. These strains are considered as belonging to a new species of nonpathogenic, rapidly growing mycobacteria for which we propose the name *Mycobacterium komossense*. Strain Ko 2 is the type strain of *M. komossense*; a culture of this strain has been deposited in the American Type Culture Collection under the number 33013.—Authors' Summary

Steele, R. W., Myers, M. G. and Vincent, M. M. Transfer factor for the prevention of varicella-zoster infection in childhood leukemia. New Engl. J. Med. **303** (1980) 355–359.*

Sixty-one patients with leukemia and no immunity to chickenpox were given dialyzable transfer factor or placebo and followed for 12 to 30 months in a double-blind trial designed to examine the clinical efficacy of transfer factor. Sixteen patients in the transfer factor group and 15 in the placebo group were exposed to varicella zoster, and most of them had a rise in antibody titer. Chickenpox developed in 13 of 15 exposed patients in the placebo group but in only one of 16 in the transfer factor group.—Authors' Summary

Tandon, A., Saxena, R. P., Saxena, K. C., Jamil, Z. and Gupta, A. K. Diagnostic potentialities of enzyme-linked immunosorbent assay in tuberculosis using purified tuberculin antigen. Tubercle **61** (1980) 87–89.

Delayed hypersensitivity tests with tuberculin or purified tuberculin (PPD) have been used for detection of tuberculosis infection. The present paper describes an enzyme-linked immunosorbent assay (ELISA) for detection of PPD-antibodies in tuberculosis patients. The ELISA test was positive in nearly 80% of cases having bacteriological evidence of tuberculosis. The test could also detect PPD-antibodies in 66% of the cases not showing bacteriological evidence of tuberculosis. The potentiality of the test in the immunodiagnosis of tuberculosis is discussed.—Authors' Summary

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* Editor's Note: Transfer factor for high-risk household contacts of multibacillary leprosy cases?—RCH

ten Dam, H. G. and Hitze, K. L. Does BCG vaccination protect the newborn and young infants? Bull. WHO **58** (1980) 37–41.

In recent years, BCG vaccination has been applied to the newborn in many immunization programs at the time of the changeover from mass vaccination to an integrated program. Whereas the efficacy of BCG vaccination in adolescents and adults has been studied in a number of controlled trials, there is very little direct evidence of the efficacy of BCG vaccination against infant tuberculosis. This article reviews the evidence that is available concerning vaccination of the newborn from both controlled and retrospective studies. Further controlled prospective studies and epidemiological surveillance of BCG vaccination in infancy are highly indicated.—Authors' Summary

Third East African/British Medical Research Council Study. Controlled clinical trial of four short-course regimens of chemotherapy for two durations in the treatment of pulmonary tuberculosis. Second report. Tubercle **61** (1980) 59–69.

Four short-course chemotherapy regimens for pulmonary tuberculosis have been compared: 1) streptomycin, isoniazid, rifampin, and pyrazinamide daily for 2 months followed by daily thiacetazone plus isoniazid; 2) the same four drugs daily for 1 month followed by thiacetazone plus isoniazid; 3) the same four drugs daily for 1 month followed by twice-weekly streptomycin, isoniazid, and pyrazinamide; 4) the first regimen but without pyrazinamide in the initial intensive phase. Each regimen was given for 6 and 8 months, and patients were followed up to 30 months.

When given for 6 months, the regimen with a 2-month, four-drug intensive phase had a bacteriological relapse rate of 13%, and when given for 8 months there were no relapses. When pyrazinamide was omitted in the first 2 months, the relapse rates were 18% for the 6 month and 6% for the 8 month series. The regimen with the four drug initial phase shortened to 1 month had relapse rates of 18% and 7% respectively if the continuation phase was thiacetazone plus isoniazid. However, the relapse rates were lower, 9% and 2% respectively, when the continuation phase was twice-weekly streptomycin, isoniazid, and pyrazinamide.—Authors' Summary