CURRENT LITERATURE

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

General and Historical

Bayliss, J. H. Domus leprosae—community care in mediaeval England. Nurs. Times **75** (1979) 62–67.

The author traces the spread of leprosy from its ancient origins in India and the Far East. The disease was probably carried back to Macedonia by the armies of Alexander the Great around 312 B.C. From there it was spread by the army of Pompey to Roman Italy and then extended through Europe as Imperial Rome extended its conquests and control. Leprosy then spread during the Middle Ages into northern Europe, Iceland, and Greenland, following Norse invasions, and became widespread after Moorish conquests of southern Europe during the latter Crusades. After 1500 A.D., the disease appeared to die out in Europe except in Scandanavia and Russia. It apparently was carried to America by the slave trade and into the Pacific area by Chinese immigrants.

The author traces social attitudes towards leprosy, including ancient attitudes of expulsion and isolation of leprosy victims. The development of a more compassionate attitude in England is traced from the activities of ecclesiastical orders. The founding of a large number of houses in England for the care of leprosy victims beginning in the 11th century A.D. is described. The gradual decline in the number of such houses being built occurs by the 14th century, and their virtual disappearance occurs by the 16th century. From old records the author speculates regarding epidemiological considerations existing in medieval England and on the cause of the decline of the disease in that country. The article is a useful illustration of the complex relationships among various presumed ecologic factors governing the equilibrium of a disease balance during a period in history.—RCH

Beson, C. A. Leprosy: A modern enigma. J. Am. Med. Technol. **40** (1978) 273–277.

Immunological defects specific for *Mycobacterium leprae* provide a wide clinical spectrum that chemotherapy can usually control but not with any certainty cure. Studies of the pathogenesis in mouse foot pads, T/900 R mice, hamsters, and nine-banded armadillos provide clues that may well lead to a cure for this enigma of antiquity. The clinical bacteriologist has available various techniques that can identify *M. leprae*. These techniques, used in diagnosis and follow-up, provide an accurate, definitive picture of the stage of the disease and an accurate evaluation of the patient's immune status.—Author's Summary

Garrigue, R. Leprosy in China. Lepr. Rev. **51** (1980) 29–33.

An account is given of a personal visit to China in early 1978. A list of 14 questions concerning the extent, classification, and treatment of leprosy was submitted, and the answers are recorded in this article, concluding with some recommendations for the promotion of Franco-Chinese exchanges in leprosy.—Author's Summary

Kansky, A. Lepra. Kratak pregled novijih dostignuća. (Recent developments in leprosy research. A brief survey.) Acta Dermatovenerolog. Iugosl. **5** (1978) 115–123. (in Serbo-Croatian)

In the field of leprosy, many new facts were established during recent years. As part of the cooperation between Yugoslavia and the developing countries, a number of Yugoslav doctors could find themselves in the position of facing a possible case of leprosy. The primary purpose of this short review is to keep doctors informed of new developments and also to arouse the inter-

est of young physicians in the problems of leprosy. Etiology, epidemiology, immunology, histology, laboratory tests, clinical symptoms, classification, early diagnosis, differential diagnosis, treatment, and social aspects are discussed.—(*Adapted from* author's summary)

O'Connor, R. J. J. Evaluation of an interactive instructional television program in Hansen's disease. J. Continuing Ed. Nurs. **11** (1980) 47–49.

To determine the effectiveness of a media-oriented continuing medical education program in Hansen's disease, a target population of 47 nurses was randomly divided into two treatment and one control groups. Treatment groups viewed two 16 minute instructional videocassettes on Hansen's disease with one of the two programs incorporating a learner response mechanism. Approximately two weeks later, all participants completed a 25 item multiple-choice examination based on program content, and a statistical analysis was performed. Results indicate that both treatment groups performed significantly better on the posttest than the control group and that the treatment group viewing the response feature version performed significantly better than the group viewing the programs in a conventional manner. Implications of the study were discussed.—Author's Summary

Saint André, P. The Marchoux Institute. Lepr. Rev. **51** (1980) 35–42.

An account is given of the origin and development of the Marchoux Institute in Bamako and of its present-day activities as a center of research in dermatology, leprology, tropical epidemiology and as a collaborating center with WHO. Thanks to the collective efforts of the eight member states of OCCGE (Organisation de Coordination et de Coopération pour la Lutte Contre les Grandes Endémies) together with financial assistance from ILEP (The International Federation of Anti-Leprosy Associations), the Institute has intensified its activities in the fields of research, training of personnel, and the organization of control work in the field.—Author's Summary

Chemotherapy

Acocella, G. and Arioli, V. Pseudomembranous colitis and rifampicin. Lancet **1** (1980) 827–828. (Letter to the Editor)

This Letter to the Editor is in response to a Letter to the Editor by Fournier, *et al.* (Lancet **1** [1980] 101; abstracted in Int. J. Lepr. **48** [1980] 222–223), who diagnosed pseudomembranous colitis (PMC) and associated it with rifampin. The authors contend that this association is not causal because 1) the diagnosis was not substantiated by demonstrating *Clostridium difficile*, the etiologic agent of PMC or its toxin; 2) this has never been reported before despite hundreds of thousands of patients being treated with rifampin; 3) rifampin is very active against *Cl. difficile*, resembling vancomycin (used to treat PMC) and metronidazole; and 4) the causal relationship of rifampin to the alleged PMC was not established by rechallenge with rifampin.—RCH

Girdhar, B. K., Sreevatsa, and Desikan, K. V. Intermittent rifampicin therapy in lepromatous leprosy. Lepr. India **52** (1980) 89–96.

A double blind trial involving intermittent administration of rifampin in addition to daily dapsone (DDS) has been undertaken in order to evaluate the efficacy as well as the potential dangers of such a regimen.

Twenty untreated LL cases who were otherwise healthy were included in the study. Ten cases received weekly 900 mg rifampin for six weeks in addition to 100 mg daily DDS while the rest were treated likewise but were given similar looking placebo capsules instead of RFP.

A nine month follow-up as well as mouse foot pad results indicate that the efficacy of this regimen was found to be better than that with DDS alone, and this compares favorably with trials involving 600 mg

rifampin administration daily. No major untoward side effects were encountered in the trial group though the incidence of ENL was slightly higher in the trial group.—Authors' Summary

Girling, D. J. and Hitze, K. L. Adverse reactions to rifampicin. Bull. WHO **57** (1979) 45–49.

This summary of adverse reactions to rifampin has been prepared with the intention that it will be made available to all those involved in the administration of rifampin in tuberculosis and leprosy programs. The reactions covered comprise those to both daily and intermittent administration, namely cutaneous and gastrointestinal reactions, hepatitis, and thrombocytopenic purpura, and those to intermittent administration only, namely "flu" syndrome, shock, shortness of breath, hemolytic anemia, and renal failure.—Authors' Summary

Mani, M. Z., Rajan, M. V., Mathew, M. and Singh, C. M. Lichen planus-like lesions caused by thiacetazone. Indian J. Dermatol. Venereol. Lepr. **45** (1979) 455–458.

Thiacetazone has been used as a standard antituberculous drug in several countries. Side effects, which include various types of skin eruptions, have been observed in about 10% of patients taking thiacetazone. We are reporting two cases of lichen planus-like lesions presumably due to thiacetazone. Of these, one case had preexisting lichen planus hypertrophicus, but the other one did not have any past history of lichen planus.—Authors' Summary

Nwude, N. and Ebong, O. O. Some plants used in the treatment of leprosy in Africa. Lepr. Rev. **51** (1980) 11–18.

Thirty-four species of plants reported used in the treatment of leprosy in Africa are reviewed. The botanical and vernacular names, localities, and comments on the plants are given. The importance of research into herbal medicine to establish the efficacy and toxicity of plants used is discussed.—Authors' Summary

Pershin, G. N. Development of chemotherapy of infectious diseases in the Soviet Union. Russ. Pharmacol. Toxicol. **40** (1977) 190–195.

A brief review of the achievements of Soviet pharmacologists in the fight against infectious diseases is presented to celebrate the 60th anniversary of the founding of the Soviet Union. Special sections are devoted to reviews of the chemotherapy of protozoal infections, spirochetosis, tuberculosis, leprosy, mycosis, and viral infections.

There is only a rather restricted range of drugs suitable for the treatment of leprosy. The most useful among them are derivatives of diphenylsulfone (diaphenylsulfone, solusulfone, acesulfone). As an adjunct to the therapy of leprosy, use is made also of sulfonamides, some antitubercular preparations (ethoxid, thiacetazone), and of a number of other chemotherapeutic preparations.—(*Adapted from* the article)

Saint-André, P., Louvet, M., Giraudeau, P., Discamps, G. and Schlecht, B. Bilan actuel du traitement de la lèpre par chimiothérapie et immunostimulation associées. (Present evaluation of leprosy treatment by association of chemotherapy and immunostimulation.) Méd. Trop. **38** (1978) 331–349. (in French)

The authors report a series of uncontrolled pilot trials of nonspecific immunostimulation of patients suffering from various types of leprosy from borderline-tuberculoid (BT) to lepromatous (LL).

The immunostimulants included BCG, given intradermally every fortnight in gradually increasing dosage, commencing with 0.1 ml of 1/100 dilution, progressing by steps of 0.1 ml to 1.0 ml, and repeating the process first with a 1/10 dilution and then with undiluted BCG suspension; levamisole, 100 mg on two days per week; and a lysate of *Neisseria perflava* (Ducton), 5 ml given intramuscularly, three times per week. Chemotherapy routinely consisted of dapsone (DDS) 50 mg daily, six days per week, although occasionally it was changed to clofazimine or to a long-acting sulfonamide, especially in patients in reaction.

The patients were divided into five main groups: 1) six previously untreated patients, consisting of three suffering from

lepromatous (LL) and three from borderline (BT/BB or BB) leprosy, of whom half received combined BCG and dapsone, and half received initial therapy with BCG alone for six to 23 months before commencing combined dapsone and BCG; 2) ten lepromatous patients, who had received previous treatment with dapsone monotherapy for one to ten years (seven patients), or rifampin for one year followed by dapsone for three to four years, were given combined BCG and dapsone; 3) 22 previously untreated patients (16 LL, one BL, four BB and one BT) received immunostimulation alone for varying periods with BCG, levamisole, or *N. perflava* lysate (12, five and five patients respectively). Subsequently they were treated with chemotherapy plus BCG, save for three patients who received dapsone alone; 4) ten previously untreated patients (nine LL, one BB) received combined therapy for 18 months with dapsone and *N. perflava* lysate, and then BCG plus dapsone for approximately a further 18 months. Three other patients (two LL, one BL) after varying periods of combined dapsone and *N. perflava* lysate therapy, were continued on clofazimine; 5) a further 16 previously untreated patients (13 LL, three borderline) received 17 months' treatment with dapsone and *N. perflava* lysate.

It is claimed that immunostimulation when given alone to previously untreated patients resulted in marked clinical improvement but had little or no effect on the bacterial index (BI) or the morphological index (MI) whether in skin smears or nasal mucus. Bacterial improvement occurred after giving chemotherapy (with or without immunotherapy). By and large neuritis improved and did not deteriorate on immunostimulation. Patients who received initial immunostimulation usually did not develop neuritis when chemotherapy was added. Weak positive Mitsuda reactions occurred temporarily in a number of patients receiving BCG, levamisole, or *N. perflava* lysate; and a few underwent mild reversal type reactions.

As the authors have reported that their nonspecific immunotherapies, when given alone before commencing chemotherapy, had little or no effect on the nasal and skin BI and MI and therefore presumably none also on the infectivity of lepromatous patients, the withholding of chemotherapy during an initial course of immunostimulation would undoubtedly appear to be contraindicated. There is, however, considerable interest in investigating whether immunotherapy given as an adjunct to chemotherapy, has any effect on the small numbers of persisting drug-sensitive bacilli detected after many years of therapy, whether with dapsone, clofazimine or rifampin. Professor Saint-André and his colleagues have shown that immunotherapy may be a relatively safe procedure. Further carefully controlled studies would appear indicated.—M. F. R. Waters (*from* Trop. Dis. Bull.)

Clinical Sciences

Barton, R. P. E., Hogerzeil, L. M. and McDougall, A. C. Borderline tuberculoid leprosy with a "lepromatous" nodule of the nasal mucosa: A case report. Lepr. India **52** (1980) 114–118.

An 18-year-old Indian presented with a two year history of cracked, swollen feet and tingling in the hands and feet. On examination he had skin and neural lesions typical of borderline-tuberculoid (BT) leprosy, and this was confirmed by biopsy of one of the skin lesions. He also complained of left-sided nasal obstruction of ten days' duration, examination revealing a nodule on the anterior end of the inferior turbinate, from which area smears were positive for acid-fast bacilli. Smears from other areas of the nose and from various skin sites were all negative for acid-fast bacilli. Histopathological examination of the nodule showed a highly active cytology, with numerous closely-packed cells resembling fibroblasts together with large numbers of acid-fast bacilli, all of which were in granular form; the cellular picture suggested histoid leproma.

This unexpected finding in a patient with well-defined features of borderline leprosy cannot be explained on the data available, but it is recorded in order to emphasize the importance of nasal examination in leprosy, aided by biopsy in selected cases. The rarity of histoid lesions in the nose is also discussed.—Authors' Summary

Busch, S. and Korting, G. W. Lepra lepromatosa. (Lepromatous leprosy). Med. Welt **28** (1977) 1561–1563. (in German)

The authors stress the well known fact that in dermatology, leprosy plays the role of the great imitator and that there is danger in not recognizing it when one does not think of the possibility of its occurrence. They point to the fact that in Europe leprosy still exists in Portugal, Spain, Italy, Greece, and Malta.

Population movements in Europe in connection with the hiring of guest workers should increase the level of awareness of leprosy. The authors describe lepromatous leprosy in a 41 year old mason from Portugal who since 1971 has lived in France, Switzerland, and for the last two and one-half years in Germany. The patient had some dermatological symptoms for the last one and one-half to two years, which appeared to him not important enough to seek medical advice. Eventually, on account of a persistent sore throat, he consulted a general practitioner, who referred him to a dermatologist, who referred him to the Dermatology Hospital of the University of Mainz where the diagnosis of lepromatous leprosy was made. The patient was hospitalized, and specific chemotherapy was initiated. (This case does not seem to underline unawareness of leprosy in physicians as much as it underlines the failure of persons to be sensible about their health. It could have been something worse.)—W. F. Kirchheimer

de Castro, I. M. Um instrumento para investigação de sensibilidade térmica da pele. (An instrument to investigate the thermal sensitivity of skin.) Hansenologia Int. **3** (1978) 165–167. (in Portuguese)

A simple, safe, precise, and fast-working electrical apparatus (thermoesthesic discriminator) for the measurement of skin thermic sensitivity was planned and developed by the author under the sponsorship of WHO. Details are described.—Author's Summary

Gatner, E. M. S., Glatthaar, E., Imkamp, F. M. J. H. and Kok, S. H. Association of tuberculosis and leprosy in South Africa. Lepr. Rev. **51** (1980) 5–10.

In a study of the simultaneous occurrence of pulmonary tuberculosis and leprosy it was found that 13.4% of leprosy patients were also suffering from tuberculosis on admission to hospital. This figure is considered to accurately reflect the prevalence of the association of these two diseases in South Africa. Tuberculosis occurred throughout the leprosy spectrum and in general responded well when appropriate therapy was added to standard leprosy treatment. There is potential danger in that rifampin resistant strains of *M. tuberculosis* may be selected for if the clinician fails to recognize the simultaneous condition.—Authors' Summary

Hans, G. Saggio sull'uso delle Fitostimoline garze nelle ulcere trofiche nella lebbra. (Trial on use of Fitostimoline gauzes in leprous trophic ulcers.) Rassegna Internazionale di Clinica e Terapia (Naples) **58** (1978) 278–283. (in Italian)

The author treated 25 patients with Fitostimoline, suffering from trophic ulcerations on the lower limbs. The results were very satisfactory, and the practical use of the medication was appreciated.—Author's Summary

Kaur, S., Kumar, B. and Gupta, S. K. Study of bacteriological and morphological indices in lymph node by needle aspiration. Indian J. Dermatol. Venereol. Lepr. **45** (1979) 425–429.

Bacillary index (BI) and morphological index (MI) in lymph nodes have been studied in 30 patients with various types of leprosy by lymph node aspiration and impression smears. This comparatively safer, less traumatizing outpatient procedure, already established for the study of malignant cytology, is recommended as a better alternative to the more time-consuming and

painful lymph node excision biopsy technique for the study of viability of lepra bacilli (MI) in patients undergoing anti-leprosy treatment.—Authors' Summary

Koch, U., Pau, H.-W. and Klingmüller, G. Lepromatöse Lepra im Kopf-Hals-Bereich. (Lepromatous leprosy in the head-neck region.) Therapiewoche **28** (1978) 4122–4127. (in German)

The authors present pictures of changes in the head-neck area, typical of lepromatous leprosy. These include facies leontina with loss of eyebrows (sign of Lucio), changes of the external and inner nose, of oral and pharyngeal mucosa, and of radiographs of the maxilla showing the Møller-Christensen syndrome (atrophy of the alveolar process and loosening of the teeth). They also show a section of a tongue biopsy stained with Fite's modification of the Ziehl-Neelsen stain. The authors point out that as in this patient the diagnosis of leprosy is frequently missed in the absence of a high level of suspicion and that leprosy also can occur in nonendemic areas.—W. F. Kirchheimer

Koranne, R. V., Singh, R. and Iyengar, B. Liver function tests in tuberculoid leprosy. Indian J. Dermatol. Venereol. Lepr. **45** (1979) 430–435.

A total of 24 patients with untreated tuberculoid leprosy were taken up for study. They were the same group of patients in whom the authors had earlier reported involvement of liver in 85% of cases. The five healthy controls studied also belonged to the same series. Liver function tests included prothrombin time, serum bilirubin, zinc sulfate turbidity, serum proteins, and serum transaminases. No significant alterations in the liver function were observed. This is because the changes in the liver were so minimal and focal that they were not reflected in the various liver function tests.—Authors' Summary

Lauer, B. A., Lilla, J. A. and Golitz, L. E. Leprosy in a Vietnamese adoptee. Pediatrics **65** (1980) 335–337.

We report here the case of a ten year old Vietnamese adoptee with tuberculoid leprosy, diagnosed in Denver, Colorado, U.S.A. Our purpose is to remind physicians that leprosy is a common infection in Vietnam and that clinical symptoms may not appear for several years because of the long incubation period.—(*Adapted from* authors' summary)

McAdam, K. P. W. J. Leprosy, filariasis and malaria as causes of secondary amyloidosis in the tropics. Papua New Guinea Med. J. **21** (1978) 69–78.

In Papua New Guinea, amyloidosis has been shown to be a significant health problem. In 7% of one autopsy series, amyloid was demonstrated histologically, and in a rural point prevalence study in one high incidence area, 7% of the population had amyloidosis. Special histochemical stains were performed on tissue sections from a representative selection of patients diagnosed as having amyloidosis during the course of a two and one-half year survey in Papua New Guinea. In all 40 cases, the amyloid was characteristic of the secondary amyloid protein AA, thus confirming previous chemical studies which had demonstrated AA protein to be the major fibril protein in eight patients with amyloidosis. These findings suggest an unusual predisposition to amyloidosis in Papua New Guinea since the prevalence is much higher than has been observed in other tropical countries. The studies reviewed here sought to answer the following questions: Which individuals with lepromatous leprosy develop amyloidosis? Why do so many patients with amyloid protein AA have no obvious cause for secondary amyloidosis, and could malaria or filariasis be implicated as causes of amyloidosis in this group? Is there a genetic basis for amyloidosis in Papua New Guinea?

Lepromatous leprosy patients who developed amyloidosis were those who suffered from immune complex mediated reactions. During these recurrent erythema nodosum leprosum (ENL) reactions, there was inflammation, fever, neutrophil leukocytosis, and elevation of the serum protein (SAA) related to amyloid fibril protein AA. Colchicine therapy did not abolish the ENL reactions, and the height of the acute SAA response correlated with the severity of the inflammatory reaction.

A high incidence of geographic localization of juvenile amyloid goiter with renal failure was identified in the upper Watut Valley. A point prevalence study utilizing abdominal wall aspiration biopsy in 55 adults identified eight cases of amyloidosis in a population of 113 (7.1%). Some of the patients were related, but no simple genetic trait could be established. Malaria was suggested as the cause of secondary amyloidosis in this area of mesendemic transmission. Not only was SAA concentration shown to rise during malarial attacks, but a comparative survey in a nonmalarious area inhabited by the same tribal group showed a lower prevalence of amyloidosis.

Filariasis was also identified as a cause of secondary amyloidosis in six out of 224 villagers from the Upper Fly River. Two of these patients in particular were remarkable as they suffered from recurrent attacks of adenolymphangitis. SAA concentration was shown to rise during a typical attack of lymphadenitis.

There appears to be a genetic factor underlying the high prevalence of AA amyloidosis in Papua New Guinea, although this has not been proved. Those who suffer from adequate stimuli have elevated concentrations of the putative serum precursor (SAA) of the fibril protein AA. It is unknown whether these individuals produce excessive SAA for the normal catabolic processing of this protein or lack catabolic enzymes or even produce SAA having amino-acid-sequence micro-heterogeneity. Each of these possibilities might lead to fibril formation, which is thought to occur first within the lysosome following partial enzymic cleavage of SAA.

Therapy of amyloidosis can be aimed at several different areas. The underlying disease should be treated. Antiinflammatory agents might decrease the inflammation and concurrent SAA elevation. Colchicine has been shown to be effective in preventing amyloid formation, and this appears to act at the lysosomal level and not by preventing SAA elevation. Early reports suggest that the dissolution of established amyloid fibril deposits has been successfully achieved with the solvent dimethylsulfoxide (DMSO). Thus this relatively common and fatal complication of several tropical infections in Papua New Guinea ought to be preventable and treatable as awareness of the condition and better medical surveillance allow earlier diagnosis. It may well be that awareness of the condition in other tropical countries will lead to its being identified there more frequently. This was certainly our finding in Papua New Guinea.—Author's Summary

Pacin, A. and Fliess, E. L. Estudios enzimáticos en pacientes hansenianos. I. Actividad de las transaminasas glutámico pirúvica y glutámico oxalacética. (Enzymatic studies in hanseniasis patients. I. Activity of glutamic pyruvate transaminase and glutamic oxaloacetic transaminase.) Hansenologia Int. 3 (1978) 151–159. (in Spanish)

The enzymatic activity of SGOT and SGPT was studied in 130 hanseniasis patients who were classified in four groups: 1) quiescent Virchowian hanseniasis; 2) quiescent tuberculoid hanseniasis; 3) reactional Virchowian hanseniasis; 4) reactional tuberculoid hanseniasis. Significant differences between quiescent and reactional forms were observed but not among the quiescent cases themselves. Differences between reactional Virchowian (the highest values) and reactional tuberculoid patients were observed, but these differences were of low significance or not significant at all. Hypersensitivity mediated either by immune complexes or by cells would stand at the basis of these variations.—Authors' Summary

Reação dimorfa com comprometimento ósseo nas extremidades superiores em paciente com endocardite-bacteriana. (Seções anátomo-clínicas). (Dimorphous reaction with bone involvement of the upper extremities in a patient with bacterial endocarditis. (Clinical-pathologic conference.)) Hansenologia Int. 3 (1978) 232–239. (in Portuguese)

A 54-year-old patient with a diagnosis of dimorphous hanseniasis, interned in the hospital for physical therapy, presented with systemic infectious involvement of sub-acute evolution associated with acute inflammatory manifestations in the upper limbs with bone involvement. This involve-

ment was characterized by periostitic lesions of the phalanges and metacarpus and by areas suggesting bone erosions. He died of toxic-infectious shock and congestive heart failure. The autopsy indicated bacterial endocarditis with thrombotic ulcerations and the involvement of skin, peripheral nerves, and bone tissue by tuberculoid granulomas with a positive (+) BI. Cicatricial fibrosis, disorganization, and bone neoformations were also noted in the bone tissue, principally in sub-periosteal locations. The relationship between bacterial endocarditis and dimorphous hanseniasis reactivations is discussed.—Authors' Summary

Sebille, A. The Hoffmann reflex of the soleus muscle. J. Neurol. Sci. **45** (1980) 373–378.

The Hoffmann reflex of the soleus muscle was used to investigate the monosynaptic reflex arc of two groups of leprosy patients (12 with BT and 18 with LL) compared with a similar group of 30 normal subjects.

Although the tendon reflex was preserved in leprosy, the H reflex recordings showed two abnormalities:

1) An increase in the latency of the reflex without difference between lepromatous and borderline patients, probably due to demyelination of the larger fibers.
2) A decrease of the H_{max}:M_{max} amplitude ratio more pronounced in the lepromatous group, related to Ia fiber axonal degeneration.

The discrepancy between these results and the commonly described preservation of the deep tendon reflexes in leprosy is discussed, and the hypothesis that leprosy neuropathy would affect all nerve trunks related to blood vessel changes is suggested.—Author's Summary

Tello, E. E. Condiciones socio-economicas y hanseniasis. Comparación durante 30 años entre la consulta privada y un dispensario especializado. (Socio-economic conditions and hanseniasis. Comparison during a 30 year period between a private office practice and a public outpatient clinic). Hansenologia Int. **3** (1978) 160–164. (in Spanish)

During a 30 year period, 308 and 916 hanseniasis patients were observed by the author in his private office (middle, upper-middle, and upper class) and in a public outpatient clinic of Cordoba, Argentina, respectively. No significant differences were found in comparing the percentages of Virchowian, tuberculoid, and dimorphous cases in any class, a fact which shows an evident failure in early diagnosis. In contrast, indeterminate hanseniasis was diagnosed in 19.48% of private patients against only 9.06% of public clinic patients, which may be due to the higher economic and educational levels of the former group.—Author's Summary

Immuno-Pathology

Anders, R. F. Amyloid fibril proteins found in Papua New Guinean and other amyloidoses. Papua New Guinea Med. J. **21** (1979) 79–85.

Recent studies have established that amyloid fibrils found in different clinical conditions differ in the nature of their constituent proteins. In primary amyloidosis and in amyloidosis associated with multiple myeloma or macroglobulinemia, the amyloid fibrils are usually largely composed of fragments of immunoglobulin light chains. In secondary amyloidosis, protein AA, a unique protein unrelated to immunoglobulins, is the major component of the fibrils. Other chemical types of amyloid have been described in primary medullary carcinoma of the thyroid and in senile cardiac amyloidosis.

In Papua New Guinea, amyloidosis is seen secondary to chronic infections such as leprosy and tuberculosis as well as in patients without an apparent predisposing disease. The amyloid proteins obtained

from a representative range of Papua New Guinean patients have been characterized, and in all cases examined the amyloid was found to be of the protein AA or secondary type.

Current research into the pathogenesis of secondary amyloidosis centers on the mechanisms whereby protein AA is derived from the presumed precursor molecule, protein SAA, which is a normal acute phase reactant.—Author's Summary

Antia, N. H., Shetty, V. P. and Mehta, L. N. Study of evolution of nerve damage in leprosy. Part IV—An assessment. Lepr. India **52** (1980) 48–52.

This study demonstrates the evolution of nerve damage in leprosy in the earliest stage of involvement.

It reveals that the early lesions in human as well as mouse leprosy follow a definite and almost similar pattern and also that the pattern of early nerve involvement is similar in the tuberculoid as well as the lepromatous spectrum of the disease.

The unmyelinated fibers and their Schwann cells are the earliest to be involved, followed by small myelinated, and only lastly by the large myelinated fibers.

The fiber damage is predominantly of segmental demyelination in the early stages of this disease in both the lepromatous as well as the tuberculoid forms and occurs even without the presence of bacilli in the nerve.

The earliest lesions cannot be detected on light microscopy and can be demonstrated only on electron microscopy.

The definite and typical nerve changes can be demonstrated not only in the uninvolved nerves in early clinical leprosy but also in the contacts of leprosy patients.

The semi-quantitative methods of sensory testing and nerve conduction studies as described by us can help to detect nerve changes at an earlier stage than by the routine methods.

Finally, this study indicates the presence of diffuse peripheral neuropathy not only in the earliest stages of clinical leprosy but also in otherwise healthy contacts of leprosy patients. Such changes may occur as early as four months after infection if any analogy can be drawn from the mouse model.—Authors' Summary

Bjune, G. *In vitro* lymphocyte stimulation in leprosy; simultaneous stimulation with *Mycobacterium leprae* antigens and phytohaemagglutinin. Clin. Exp. Immunol. **36** (1979) 479–487.

Peripheral blood lymphocytes from 105 subjects with different forms of leprosy and healthy contacts of leprosy patients were stimulated *in vitro* with different preparations of mycobacterial antigens alone or in combination with a suboptimal dose of phytohaemagglutinin (PHA). In nearly all individuals, sonicated leprosy bacilli and PHA together gave a lower ^{3}H-thymidine incorporation than did the same dose of PHA alone. There was no difference in the degree of inhibition seen in the different patient groups or the healthy contacts. High doses of whole, washed *Mycobacterium leprae*, combined with PHA, led to an increased thymidine incorporation in borderline tuberculoid leprosy patients who had experienced a reversal reaction and in healthy contacts with more than six months of exposure while most lepromatous patients and contacts with less than six months exposure did not show an augmentation of the PHA-induced thymidine incorporation. The inhibition exerted by sonicated *M. leprae* was dose-dependent, seen even with very low doses of antigen, and was not due to direct cytotoxicity. *M. bovis*, strain BCG, was weakly suppressive in combination with PHA, and sonicated *M. duvalii* had a very marked suppressive effect. There was no correlation between the suppressive effect of *M. leprae* antigens and the other mycobacteria; neither was there any correlation with the responses to the mycobacterial antigens alone. Many lepromatous leprosy patients showed significant suppression of background incorporation with the addition of *M. leprae* antigens. This paper discusses whether the apparent "non-responsiveness" in lepromatous leprosy could be due to active suppressor mechanisms operative *in vivo*.—Author's Summary

Closs, O., Mshana, R. N. and Harboe, M. Antigenic analysis of *Mycobacterium leprae*. Scand. J. Immunol. **9** (1979) 297–302.

About 20 distinct antigenic components have been demonstrated in *Mycobacterium*

leprae (*M. leprae*) by crossed immunoelectrophoresis against a rabbit antiserum produced by immunization with concentrated *M. leprae* antigen. This system allows a more detailed analysis of the antigenic relationship between *M. leprae* and other mycobacteria and a better characterization of the antigenic content of various *M. leprae* preparations than with previously available antisera which reacted with far fewer components. The antibody activity in sera of patients with lepromatous leprosy was studied by incorporating the sera into the intermediate gel of the *M. leprae* reference system. Antibodies were found against only seven of the components. Since those compared are all known to be cross-reacting widely with antigens of other mycobacteria, it is speculated that cross-immunization may influence the antibody response in lepromatous leprosy.—Authors' Summary

Convit, J., Monzón, H., Pinardi, M. E., Aránzazu, N. and Ulrich, M. The development of an active vaccine against leprosy. Acta Cient. Venez. **30** (1979) 491–493.

The development of an effective vaccine against leprosy will be directed to obtain a product which can modify the immunological response of the population susceptible to develop the disease and to avoid the occurrence of lepromatous, infecting forms. This action would interrupt the transmission chain, producing an important decrease in the incidence of the disease.

The measures used at present for antileprosy campaigns such as early diagnosis, control of contacts, outpatient treatment, and prevention of disabilities can be effective if applied with a high degree of efficiency and during extended periods of time. If to these measures we could add a vaccine, we would be able to reduce considerably the expense and time needed for keeping the disease under control.

The development of a vaccine against leprosy is based on the assumption that the disease is due to an immunological defect of the host which is specific against this particular bacterium. Previous work done by us, where we have obtained highly favorable immunological modifications in prelepromatous, indeterminate patients and in Mitsuda negative contacts and, partially, in lepromatous patients, using an injection of a mixture of armadillo *M. leprae* and BCG, serves as a basis for our proposal to use this same type of preparation as an anti-leprosy vaccine in susceptible persons, where it would evoke a positive immunological change which would prevent the onset of infecting forms of the disease.—Authors' Summary

Fliess, E. L. Posible origen de la inmunodeficiencia en la hanseniasis virchowiana. (Possible origin of the immunodeficiency in Virchowian hanseniasis.) Hansenologia Int. **3** (1978) 141–150. (in Spanish)

Clinical manifestations and some studies of cell-mediated immunity (CMI) demonstrate a graduate response, from the Virchowian polar form with a poor CMI response to the tuberculoid polar form with exacerbated phenomena of CMI. The possibility of a genetic-controlled IMC response to *M. leprae* is reviewed. A hypothesis is suggested that the susceptibility to any type of hanseniasis is controlled by an operon linked to the K or D regions of the HLA system. This operon would act as a trigger to the heteroantigen-detecting fraction of the T cells receptors.—Author's Summary

Kliemann, T. A. E., Ferri, R. G., Chaves, J., Irulegui, I. and Coppi Vaz, C. A. Detecção de complexos imunes circulantes na hanseníase utilizando C_1q humano e eqüino. (Detection of circulating immune complexes in hanseniasis patients using human and equine C_1q.) Hansenologia Int. **3** (1978) 135–140. (in Portuguese)

The presence of soluble immune complexes (IC) was observed in sera of Virchowian hanseniasis patients; some of these patients presented with active erythema nodosum. These IC were detected by their reactivity with the C_1q component of complement. The IC were previously precipitated by polyethylene-glycol (PEG) and dissolved in borate buffer. The presence of IC was confirmed by reduction of 2-mercaptoethanol and alkalation with 2-iodoacetamide, followed by new C_1q reactions, and no precipitin lines were obtained.—Authors' Summary

Lai A. Fat, R. F. M., Chan Pin Jin, J., Van Furth, R. and Harboe, M. *In vitro* synthesis of anti-mycobacterial antibodies in biopsies from skin lesions of leprosy patients. Infect. Immun. **27** (1980) 297–301.

To demonstrate local synthesis of anti-*Mycobacterium leprae* antibodies, biopsies from skin lesions of leprosy patients were cultured *in vitro* in a medium containing ^{14}C-labeled lysine and isoleucine, and the culture fluids were analyzed by crossed immunoelectrophoresis with intermediate gel and autoradiography. The results show that anti-*M. leprae* antibodies were synthesized *in vitro* in the biopsies from the skin lesions of leprosy patients and that the specificity of the locally produced antibodies varied from patient to patient.—Authors' Summary

Mehta, L. N., Antia, N. H., Lakhani, R. and Srinivas, H. V. Study of thickened nerves in a leprosy endemic area. Part II—Ultrastructural and tease fibre study. Lepr. India **52** (1980) 65–73.

Ten out of 16 cases of thickened nerves labeled as having idiopathic neuropathy showed hypertophic changes when their peripheral nerves were observed under light microscopy. Electron microscopy of seven nerves revealed more details. The reactions in various parameters of nerves were recorded. The significant observation was of one case harboring lepra bacilli as seen under electron microscope and having other changes similar to changes seen in early cases of leprosy. Two cases were also thought to have leprosy on the basis of the ultrastructural observation of their nerves. These could have been missed otherwise.—Authors' Summary

Melsom, R., Duncan, M. E. and Bjune, G. Immunoglobulin concentration in mothers with leprosy and in healthy controls and their babies at time of birth. Lepr. Rev. **51** (1980) 19–28.

Immunoglobulins were quantitated in sera from 52 matched mothers at delivery and in the corresponding cord blood samples. The cord IgA concentration was significantly increased in babies from mothers with active lepromatous leprosy compared to a control group and a group where the mothers suffered from tuberculoid leprosy. The cord IgM concentration was normal both in babies from mothers with active lepromatous leprosy, the control group, and the group of mothers suffering from tuberculoid leprosy. Since IgA does not cross the placenta, this increase reflects an active increased production of IgA in the fetus of mothers suffering from active lepromatous leprosy. This could indicate transfer of *M. leprae* or *M. leprae* antigens across the placenta into the fetus.—Authors' Summary

Nath, I., Narayanan, R. B., Mehra, N. K., Sharma, A. K. and Gupte, M. D. Concanavalin A induced suppressor activity in human leprosy. J. Clin. Lab. Immunol. **2** (1979) 319–324.

Peripheral blood lymphocytes from nine normal subjects and 40 patients with leprosy were pretreated *in vitro* with Concanavalin A (Con A). Cells from normal subjects pretreated for 24 hr showed consistent and effective generation of suppressive activity which inhibited mitogen induced transformation of autologous lymphocytes. Prolongation of Con A pretreatment to 40 hr resulted in maximal suppressive activity. Tuberculoid leprosy patients had lymphocytes in their blood which on 24 hr pretreatment with Con A exerted suppressive effects markedly greater than the maximal suppression noted with 40 hr pretreated normal lymphocytes. In contrast, untreated patients with polar lepromatous leprosy showed a decrease in suppressive activity which could not be altered by prolongation of Con A pretreatment: the loss of suppressive activity noted in this form of leprosy was restored during erythema nodosum leprosum.—Authors' Summary

Negassi, K., Closs, O. and Harboe, M. Cross-reactions between serum proteins and water soluble liver tissue antigens of the nine-banded armadillo (*Dasypus novemcinctus* Linn.) and man. Clin. Exp. Immunol. **38** (1979) 135–147.

Cross-reactions between serum proteins and water soluble liver antigens of the nine-banded armadillo (*Dasypus novemcinctus*

Linn.) and man were studied by crossed immunoelectrophoresis (CIE). Armadillo serum tested with rabbit antiserum against human serum proteins gave 12 components in CIE. Nine of these cross-reacting proteins were identified and showed partial identity with the corresponding human proteins. The electrophoretic mobility of α_2-macroglobulin and Gc-globulin differed in the two species. An ultrasonicate of normal armadillo liver gave 28 anodic and eight cathodic components in CIE. By absorption experiments with armadillo serum, 20 of the former and seven of the latter were shown to be liver tissue components. A combination of CIE and crossed-line immunoelectrophoresis (CLIE) revealed the presence of 12 anodic and six cathodic liver tissue components cross-reacting with man. A cathodic armadillo liver antigen called (CALA-17) showed partial identity with that of man both in tandem and fused rocket immunoelectrophoresis. The implications of the findings are discussed in relation to the use of armadillo-grown *M. leprae* for skin testing and other purposes in man.—Authors' Summary

Pedley, J. C., Harman, D. J., Waudby, H. and McDougall, A. C. Leprosy in peripheral nerves: histopathological findings in 119 untreated patients in Nepal. J. Neurol. Neurosurg. Psychiatry **43** (1980) 198–204.

From a series of 342 nerve biopsies taken by one clinician over a period of 12 years in Nepal, this paper describes the histopathological findings in 153 biopsies from 119 patients suffering from tuberculoid, borderline (dimorphous), or lepromatous leprosy, who were untreated at the time of first presentation and diagnosis. They were taken during the course of other studies, mainly concerned with the mode of transmission of leprosy, and which included biopsies of skin, dartos muscle, nasal mucous membrane, and nipple, results of which have already been published. Examinations of serial sections by light microscopy revealed a density of cellular infiltration in non-lepromatous cases or of bacilli in macrophages and Schwann cells in lepromatous cases, which was marked in degree and usually widespread from one end of the biopsy to the other. Intraneural caseation was recorded in four patients with tuberculoid or borderline-tuberculoid leprosy, and many others in this part of the spectrum showed extensive disruption of perineurial and endoneurial structure. In lepromatous patients the numbers of bacilli in the endoneurial area not infrequently exceeded 1000 per oil immersion field. Although well known to histopathologists familiar with this disease, it is considered that the significance of these findings in patients presenting for the first time is not well appreciated by those working in general medicine, neurology, epidemiology, or even in leprosy control.—Authors' Summary

Rotberg, A. "N-Factor/Anergic Margin" or resistance/susceptibility to hanseniasis. III. The general acceptance of the theory under other names, a few pending questions and the related researches ahead. Hansenologia Int. **3** (1978) 122–134.

In this third and final article of a series, the general acceptance of the "N-Factor/Anergic Margin" theory, under other names, is reported. "Constitutional capacity to react," "genetical aptitude," and "potential immunity" are some of the numerous synonyms for the old (1937) "natural" N-Factor. "Lepromatous macrophage defect" and "specific defect of cell-mediated immunity" are pathogenetical explanations for the "Anergic Margin" (AM). However, "depression" and "impairment" of immunity are not included among the synonyms for AM since according to the theory, anergy precedes and conditions Virchowian hanseniasis and is not caused by it.

Secondary unspecific depression of cell-mediated immunity possibly exists in moderately advanced cases of Virchowian hanseniasis but has no relationship with the primary genetical incapacity to react with *Mycobacterium hansenii*, which characterizes the AM of the general population.

Studies with homozygotic twins and HL-A antigens support the theory of a genetical conditioning of types of hanseniasis. Many works on the immunogenetics of the disease were inconclusive, partly due to the fact that Mitsuda-negative persons were wrongly considered a homogenous group,

not a heterogeneous group ranging from total anergy (the AM) to the highest grades of Mitsuda responsiveness (only needing stimulation by mycobacteria, especially Hansen's and Koch's).

"N-Factor" bearers (reactors) and AM members (nonreactors) exist worldwide, both in endemic and nonendemic areas, and constitute an ample field for research. Further investigations to clarify unanswered questions are suggested.—Author's Summary

Serjeantson, S. and Dry, P. Lymphocytotoxins in leprosy and in asymptomatic hepatitis B virus infection. Clin. Exp. Immunol. **39** (1980) 289–296.

Serum lymphocytotoxic antibodies (LCAs) were detected in 67% of Papua New Guinean lepromatous leprosy patients who were persistent carriers of hepatitis B surface antigen (HBsAg). Lymphocytotoxins were not associated with asymptomatic HBsAg in either healthy controls or tuberculoid leprosy patients. It was apparent that, although HBsAg itself is a poor indicator of *in vitro* lymphocytotoxicity, when the antigen occurred in a host with impaired immune response, lymphocytotoxicity was enhanced. In contrast to this finding, lepromatous leprosy patients without HBsAg had significantly depressed LCA production in comparison with tuberculoid patients and controls. The interaction between leprosy and hepatitis B virus was highly significant ($p = 0.001$) in an analysis of variance of cytotoxicity scores. It is proposed that the previously reported equivocal results regarding autoantibodies in leprosy patients may be explained by this unusual interaction between lepromatous leprosy and hepatitis B virus infection.—Authors' Summary

Shetty, V. P., Mehta, L. N., Irani, P. F. and Antia, N. H. Study of the evolution of nerve damage in leprosy. Part I—Lesions of the index branch of the radial cutaneous nerve in early leprosy. Lepr. India **52** (1980) 5–18.

A total of six index finger branch of the radial cutaneous (IRC) nerves from three BL, two BB and one BT cases of leprosy with less than six months history of disease were subjected for nerve conduction velocity (NCV) studies followed by biopsy. The biopsy was divided into three parts and subjected for light microscopy quantitative histology, electronmicroscopy, and fiber tease studies.

The nerves revealed a slight reduction in NCV and a varying degree of segmental demyelination, ranging from 10% to 35%. The earliest changes observed were the thickening and proliferation of Schwann cell processes of the unmyelinated fibers and degeneration of their axons regardless of the type of leprosy.—Authors' Summary

Shetty, V. P., Mehta, L. N., Irani, P. F. and Antia, N. H. Study of evolution of nerve damage in leprosy. Part II—Observations on the index branch of the radial cutaneous nerve in contacts of leprosy. Lepr. India **52** (1980) 19–25.

A total of 35 contacts from 20 families of lepromatous index cases were screened clinically. All of them were subjected for nerve conduction velocity (NCV) studies of both left and right index branch of the radial cutaneous (IRC) nerve. Fifteen of these nerves were biopsied.

Out of 15 IRC nerves biopsied, ten had slightly reduced average NCV values, and five were normal. Four nerves out of ten where average NCV was reduced and one nerve out of five where NCV was normal showed significant ultrastructural changes and higher percentage of segmental demyelination (10%–13%). There was a striking similarity between the changes seen in the IRC nerves of early cases of leprosy and of contacts.—Authors' Summary

Shetty, V. P., Vidyasagar, P. B. and Antia, N. H. Study of evolution of nerve damage in leprosy. Part III—Sciatic nerve lesions in mice inoculated with *M. leprae* with nerve conduction velocity correlates. Lepr. India **52** (1980) 26–47.

Non-immunosuppressed Swiss white mice inoculated with 5000 *M. leprae* in each hind foot pad were subjected to nerve conduction velocity studies followed by light and electron microscopy and fiber tease of both sciatic nerves at sequential time intervals from the fourth to the 24th month.

The conduction velocity was standardized for basal temperature of 35°C, and uninoculated mice were used as controls.

Progressive changes were noted in conduction velocity from the sixth post inoculation month and correlated with the ultrastructural changes which were first observed at the fourth month. Fiber teasing showed predominant segmental demyelination.—Authors' Summary

Skinsnes, O. K. Lysosomal contrasts in the immunological polar dichotomy of leprosy. Front. Biol. (Amsterdam) **48** (1979) 131–148.*

Leprosy may be regarded as a unique model for the study of polar immunologic concepts as related to humoral antibody immunity (HAI) versus cell-mediated immunity (CMI) and associated cell functions reflected by their lysosomal activity. It is the only single pathogen/single host infectious disease model, presently recognized, which apparently presents the full spectrum of this immunologic dichotomy from CMI to HAI with interlying gradations and intermixtures of response. As such, it presents opportunities for comprehensive study of relationships between immunologic mechanisms and cell enzymology that have been minimally exploited.

Leprosy is reviewed from the points of view of its immunological and morphological polarity, the role of T cells in the immunological defect of lepromatous leprosy, the evidence for a macrophage functional defect, the evidence for a macrophage lysosomal defect in lepromatous leprosy, and the significance of the lysosomal defect in the relationship of lysosomal polarity to other infectious granulomas.—(*Adapted from* the article)

* Editor's Note: Dr. Skinsnes' chapter is a scholarly review of present day concerns in the immunopathology of leprosy. It contains a large amount of useful information and well-reasoned perspectives, which preclude adequate summation.—RCH

Srinivas, H. V., Lakhani, R., Mehta, L. N. and Antia, N. H. Study of thickened nerves in a leprosy endemic region. Part I—Clinical and histological study. Lepr. India **52** (1980) 53–64.

Sixteen patients with thickened peripheral nerve/nerves with clinical features of mononeuropathy/multineuropathy/polyneuropathy were included in the study. Leprosy was excluded by careful clinical examination and by nasal and ear lobe smears for AFB. A history of chronic alcoholism and/or chronic smoking was obtained in seven patients. There were two patients with severe diabetes. A detailed histopathological examination of the nerve biopsies helped in diagnosing tuberculoid leprosy in three patients and borderline leprosy in one patient. There was no evidence of leprosy in the remaining 12 patients. Though no definite diagnosis could be made in these 12 patients, the role of chronic trauma, friction, drugs, and diabetes has been discussed. It is suggested that a diagnosis of leprosy should be withheld unless there is some other positive proof besides thickened nerves. The etiological factors in nearly 50% of cases of peripheral neuropathy remain undetermined in spite of extensive investigations. Similarly, it may not be possible to give an etiological diagnosis in every case of thickened nerve with neuropathy, but this is better than labeling them as leprosy in view of the severe psychological trauma, besides the prolonged treatment with dapsone with its attendant hazards.

Out of five cases of leprosy diagnosed by this study, only one had been previously diagnosed as leprosy and was taking DDS while in the other four the diagnosis had been missed. Two cases of diabetic neuropathy had been treated with DDS. Two cases of idiopathic neuropathy were on DDS before the present investigations were performed when the diagnosis of leprosy was made.—Authors' Summary

Microbiology

Harahap, M. and Nasution, A. H. The Harada's staining method for leprosy bacilli. Asian J. Infect. Dis. **3** (1979) 41–44.

The Ziehl-Neelsen stain is universally used for demonstrating mycobacteria. This paper describes the use of a modified allochrome Harada's staining method to stain leprosy bacilli from smears taken from skin lesions of leprosy patients and compares it with the Ziehl-Neelsen stain.

It has been suggested that mycobacteria may exist in two phases, either in the metabolically active, acid-fast form or in the inactive chromophobic form, depending on the environment.

Leprosy bacilli stained with Harada's method were more intensely colored and numerous. It appears that with Harada's stain that some strains which stained weakly with Ziehl-Neelsen were solidly stained while some chromophobic forms were rendered stainable.

It has been observed that in preparations containing a high proportion of acid-fast bacilli, the number of stained bacilli could not be improved with periodate treatment. However, in preparations with a high proportion of chromophobic forms, the number of stainable bacilli could be significantly increased with periodate treatment. Such chromophobic bacilli could be seen only by staining with periodic acid carbol pararosaniline.—(*Adapted from* the article)

Marchiondo, A. A., Smith, J. H. and File, S. K. Naturally occurring leprosy-like disease of wild armadillos: ultrastructure of lepromatous lesions. J. Reticuloendothel. Soc. **27** (1980) 311–325.

An independent survey of leprosy-like disease in wild armadillos was undertaken in the French Acadiana section of Louisiana in order to arbitrate the controversy over the existence of this entity. As part of this study, material from lepromas was prepared for electron microscopy. Bacilli were concentrated in macrophages and were also found in capillary endothelial cells and fibroblasts, but they were not observed in lymphocytes or plasma cells. Bacilli consisted of electron-dense fibrillogranular material limited by a pentalaminar membrane (inner trilaminate plasma membrane and outer bilaminate cell wall). Bacillary division was common and was manifested as irregularly coiled nuclear strands and transverse septation by ingrowth of the plasma membrane. Degenerating bacilli were numerous in large multinucleate macrophages. The host inflammatory infiltrate was comprised of active plasma cells, untransformed lymphocytes, and macrophages originating from circulating monocytes. Monocytes recently emerging from capillaries were small and had a relative paucity of bacilli and lysosomes. These monocytes increased in size, plasma membrane complexity, bacillary burden, numbers and varieties of heterophagic and autophagic lysosomes, numbers of nuclei, and nucleolar activity. Replicating, interphase, and degenerating bacilli were found within macrophage phagolysosomes or free in the cytoplasmic matrix often aggregated in ranks forming "cigar bundles." Bacilli were variably surrounded by an electron-lucent substance comparable to the "gloae" or "schleim layer" described in human leprosy. Aggregates of bacilli in "gloae" formed "foamy bodies" and rarely observed opaque droplets. Thus, the ultrastructural features of this disease in wild armadillos are identical to those seen in human leprosy and armadillos experimentally infected with *Mycobacterium leprae* from human lesions. The findings suggest that B lymphocyte-macrophage interaction may be the predominant mechanism of leproma formation.—Authors' Summary

Epidemiology and Prevention

Beiguelman, B. Genética na Hanseníase. (The genetics of hanseniasis.) Hansenologia Int. **3** (1978) 179–193. (in Portuguese)

The research lines which have been explored to evaluate the importance of human genetic constitution on the determination of resistance and susceptibility to *Mycobacterium leprae* were reviewed.

A critical analysis was presented of the investigations of the familial recurrence of hanseniasis, familial association of the polar types of hanseniasis, intrafamilial contagion risks, population distribution of hanseniasis, concordance of hanseniasis manifestations in twin pairs, Mitsuda reaction in families and in twin pairs, *in vitro* reaction of blood macrophages to killed *M. leprae*, selected pedigrees, dermatoglyphics, associations of genetic polymorphisms to hanseniasis, and chromosomal aberrations.—Author's Summary

Beylot, C., Moretti, G., Beylot, J., Bioulac, P. and Doutre, M.-S. La lèpre en France. Problèmes épidémiologiques, diagnostiques et thérapeutiques. Notre expérience bordelaise. (Leprosy in France. Epidemiologic, diagnostic, and therapeutic problems. Our experience in Bordeaux.) Bord. Méd. **10** (1977) 1423–1432. (in French)

Concerning some 17 cases of leprosy observed in Bordeaux over ten years, the authors consider the particular problem caused by this disease in continental France.

On the epidemiologic plane, there has been an increase in the number of cases of the illness, but the origin of the disease has altered over the last ten years due to political and sociological factors. Since the end of the colonial era, there have been fewer and fewer cases among Frenchmen of metropolitan France who had lived in overseas countries. On the other hand, because of the constantly increasing need for labor, there are more and more cases among Frenchmen of the overseas departments and among immigrant workers. Such cases are above all lepromatous and therefore contagious.

The diagnosis can prove to be difficult because of the very particular psyche of these patients, who are still imbued to a greater or lesser extent with the terror of leprosy dating from the Middle Ages and who often seek to conceal all or part of this illness from those around them and from their doctors.

For the same reasons, it is very difficult to get such patients to follow regularly the prolonged treatment necessary for their recovery. Persons with leprosy are difficult to follow since they may be treated at one health service only to appear at another one a year or two later. This fact is detrimental to therapy.

Using the cases they have treated, the authors treat classification of leprosy and reactional conditions, which at present are defined above all according to immunologic criteria.—(*Adapted from* authors' summary)

Davey, T. F. New dimensions in our understanding of the transmission of leprosy and their impact on priorities in leprosy control. Lepr. India **52** (1980) 104–113.

Older thinking was that leprosy was mildly contagious and was spread by prolonged intimate contact with bacteriologically positive cases. In the early 1970s, it became clear that leprosy is rather freely transmissible to individuals with far less than intimate contact and that the relatively low attack rates among contacts are due to host factors. Skin to skin contact is no longer felt to be important in transmitting leprosy. Attention is given to the large numbers of viable *M. leprae* discharged from the nose in untreated lepromatous leprosy as a major source of infectious organisms. Additional sources or routes of exit of viable *M. leprae* from lepromatous leprosy patients include the mouth, ulcerated lepromatous skin lesions, infected blood (with transmission by biting insects), and breast milk. Newer work showing that *M. leprae* may remain viable outside the body for up to 46 days in

moist soil means that opportunities for transmission via common insects and contaminated fomites as well as direct contact with infected noseblows and saliva could well play roles. More and more evidence points to the importance of transmission by inhalation.

These new insights provide additional reasons for the importance of early diagnosis and continuous effective chemotherapy of lepromatous leprosy patients to reduce or eliminate their infectivity. Local efforts to achieve early diagnosis must be tailored to local situations. In general, specific mass surveys for leprosy are inadequate in achieving the early diagnosis of lepromatous leprosy. Health education supplemented by school surveys, contact surveys, etc., are generally more effective in the early diagnosis of lepromatous cases. The possible involvement of insect vectors immediately sets leprosy control in a wider setting of community health and hygiene. Comprehensive community health approaches may be the optimum methods to achieve leprosy control.

In conclusion, leprosy control will indefinitely be delayed unless the quality of service rendered to patients respects and understands the profound psychological, social, and economic effects of the disease and is able to win their confidence and sustained cooperation. There is no other way.—(*Adapted from* the article)

Figueiredo, A. A. and Sudo, L. Observações sobre a freqüência da hanseníase em Hospital Universitário. (Observations on the frequency of hanseniasis in a university hospital.) Hansenologia Int. **3** (1978) 194–202. (in Portuguese)

The authors made a survey of hanseniasis cases (139 patients) in the University Hospital of the City of Rio de Janeiro during the period between January 1975 and March 1978. Data are presented concerning the epidemiologic aspects of the metropolitan area. The authors emphasize the considerable increase of hanseniasis incidence in the hospital and the importance of the latter as a screening center for the metropolitan area of Rio de Janeiro; they recommend better material and technical preparations to fight the endemics.—Authors' Summary

Grainger, C. R. Leprosy in the Seychelles. Lepr. Rev. **51** (1980) 43–49.

The early history and possible origins are outlined and an account given of the more recent trends in the development of leprosy, based on a brief analysis of records available in the Department of Public Health.

Although the total number of patients is not high, leprosy continues to be a public health problem in the Seychelles, which is going to require a much higher level of awareness if it is to be eradicated from this country.—Author's Summary

Irgens, L. M. Leprosy in Norway. An epidemiological study based on a national patient registry. Lepr. Rev. **51** (1980) (Supplement 1) 130 pp.*

The study was based on The National Leprosy Registry of Norway, established in 1856 and in operation until the last patients were registered in the 1950s. Information on all 8231 patients was transferred to a computer file, which, together with the original sources, formed the basis for an evaluation of the material. Diagnostic criteria with respect to the disease and the type of disease, and principles as well as practical aspects of case finding in the field substantiated the Leprosy Registry as a satisfactory basis for an epidemiological study.

Leprosy was frequent in West and North Norway and particularly in the coastal health districts. The disease was infrequent in towns and was almost unknown in East Norway. The top of the endemic was reached in the middle of the 19th century with prevalence (per 10,000) and incidence (per 100,000 per year) rates of 16.7 and 16.6 for the whole country (mean population: 1,984,791), 101.1 and 97.5 for the top frequency county (mean population: 87,074), and 253.0 and 318.3 for the top frequency district (mean population: 2,609).

Sex ratio, based on age-adjusted sex-specific incidence rates of patients taken ill during the observation period 1851–1920,

* Editor's Note: This 130 page monograph is a storehouse of information on leprosy epidemiology. It is an authoritative work of immense scope, meticulously done, with intriguing implications. It defies summation and should be studied in its entirety.—RCH

was 142.6. Sex ratio was highest in the age group 30–49 years (187.1) and increased from the first decade of the observation period (136.4) to the last (160.3). Highest average annual incidence rates were found in the age group 15–29 years (13.5) in females and in the age group 30–49 years (19.9) in males. Mean age at onset by year of *onset* in males and females increased through the observation period from 33.0 and 32.9 to 45.9 and 43.9 respectively, with a total mean of 34.3 and 33.0 in males and females. Mean age at onset by year of *birth* in males and females decreased through the observation period from 23.1 and 22.9 for patients born 1841–50, to 15.1 and 10.7 for patients born 1891–1900. The relative frequency of lepromatous cases was 53.8%. In the age group 25–60 years, lepromatous cases were more frequent in males than in females. In the top frequency health district, compared with the low frequency areas, mean age at onset and sex ratio were low while the relative frequency of lepromatous cases was high.

The association between mean age at onset, sex ratio, and relative frequency of lepromatous cases on one hand, and *level* of incidence rates on the other was high (r = 0.74), and so was the association between the same variables and *time trend* in incidence rates (r = 0.70). A high association was also found to exist between degree of *isolation* and relative fall in incidence rates when prevalence rates exceeded 15.0 (r = 0.81).

In *families*, relative frequency of lepromatous cases increased by number of patients per family. In sibships, patients tended to be more concordant with respect to the type than expected except in sibships of patients taken ill after the age of 30 years. Secondary attack rate among spouses was 5.3%. Degree of concordance with respect to type in spouses did not differ from what was expected.

In the top frequency health district, the occurrence of leprosy at *farm level* was associated with a low production of oats and milk, and favorable conditions in the surroundings for growth of mycobacteria in sphagnum vegetation.—Author's Summary

Marlet, J. M. Efeito da terapêutica sulfônica na sobrevida dos doentes de hanseníase. (Effect of sulfone therapy on the outliving of hanseniasis patients.) Hansenologia Int. **3** (1978) 203–231. (in Portuguese)

By utilizing the technique of outliving, modified to follow-up chronic diseases, the accumulated probabilities of outliving of 5000 hanseniasis patients of the presulfone era and of 5000 of the sulfone era were studied. The probabilities of outliving were calculated according to the initial classification and the patient's age at the time of diagnosis.

It was observed that: 1) sulfone therapy increases the hanseniasis patients' accumulated probabilities of outliving; 2) Virchowian patients are those who benefit most regarding outliving by sulfone therapy; 3) the growth of outliving supplied by sulfones to tuberculoid patients is practically the same as to indeterminate patients.—Author's Summary

Mohan Das, M. G. Prevention and control of leprosy. J. Indian Med. Assoc. **72** (1979) 37–40.

The author begins this study by pointing out the well known fact that leprosy frequently has a particularly high prevalence rate in endemic pockets of a country. For example, in India, the overall prevalence rate in 1976 was five per 1000, but in selected areas of Tamil Nadu, the prevalence rate was 11–20 per 1000.

Prevention may be classified as primary and secondary. Primary prevention involves the use of chemoprophylaxis and immunoprophylaxis. The author mentions the possibility in discussing chemoprophylaxis that providing small doses of dapsone on a mass scale may give rise to sulfone resistance and that the use of BCG vaccination as part of leprosy control measures has not as yet been proven to be effective. Secondary prevention consists of isolation and mass treatment. The author carefully details the social problems of isolation and points out that mass treatment programs have been estimated to be $^1/_{40}$ the cost of isolation.

Control involves dealing with 1) the source of infection, 2) the routes of transmission, and 3) the promotion of resistance of new hosts. In dealing with sources of

infection, the author reviews the uncertainty that exists about the possibility of acquiring the disease except from an infected case. Under routes of transmission the author mentions the suggestions that droplet infection, breast feeding, gastro-intestinal infection, flies, and mosquitoes may all create infection as well as prolonged close contact with an infected case but does not suggest them as definite routes. As part of the promotion of resistance of new hosts, the author discusses BCG injection, lymphoid cell transfer, injection of sensitized lymphoid cell extracts, and thymus transplantation as well general health measures such as good personal hygiene, environmental sanitation, avoidance of overcrowding, and health education. The author concludes by discussing the history of the leprosy control program in India since 1955 through its use of 1) an intensive special service approach in both urban and rural areas; 2) an integrated service approach through survey, education, and treatment (SET) centers; and 3) use of voluntary agencies.—G. Gordon

Noordeen, S. K., Neelan, P. N. and Munaf, A. Chemoprophylaxis against leprosy with acedapsone. An interim report. Lepr. India **52** (1980) 97–103.

The Central Leprosy Teaching and Research Institute, Chingleput, has carried out through the years a number of studies on chemoprophylaxis and has established the value of oral dapsone as a chemoprophylactic against leprosy. The need to administer dapsone orally among healthy subjects as frequently as twice a week for prolonged periods has limited its operational feasibility to a considerable extent. However, with the advent of acedapsone (DADDS), a long-acting parenteral sulfone, the possibility of an operationally more feasible chemoprophylactic has emerged, resulting in the study under report.

The major objective of the study was to determine through a controlled trial the effectiveness of acedapsone as a prophylactic against leprosy among child contacts of multi-bacillary cases of leprosy. The study subjects, numbering 700, were contacts of 331 index cases attending various leprosy clinics in the city of Madras. The study was carried out double-blind, and the contacts received more than 90% of the expected treatment.

The study has been under progress for over two years and has so far yielded 50 cases of leprosy, 32 from the control group and 18 from the prophylaxis group. The difference between control and prophylaxis groups is statistically significant and shows that acedapsone prophylaxis in this study has an efficacy rate of about 47%. Analysis of the protection by age, sex, duration, etc., has also given certain interesting findings. The study is to continue further.—Authors' Summary

Saikawa, K. The report on leprosy survey in Okinawa. 2. Leprosy in Yonaguni island. Therapeutics (Tokyo) **31** (1977) 407–408 and 475–478. (in Japanese)

Yonaguni island is located in the southwesternmost part of Okinawa, near Taiwan. The island is 520 km from the main island of Okinawa. The island is the most endemic in Okinawa with a prevalence rate of 17.65% and an incidence rate of 0.93% in 1975. The average prevalence rate in Okinawa is 1.34% and the average incidence rate is 0.59%.

Leprosy contact tracing and school surveys were performed in June 1973 to investigate the epidemiological situation on the island. Two hundred fifty-eight students in two middle schools and 430 in primary schools were examined, and two tuberculoid leprosy patients (two female students in primary school) were newly detected. The case detection rate was 4.65% in the primary schools and 2.91% in the whole school survey, which was quite higher than our school survey on a different island. No newly detected case was found in the contact tracing program in 20 leprosy household contacts.

Since 1970, the migration of persons on the island to urban areas on the main island has been observed, and the epidemiological situation on the island has changed as follows: before 1970 the leprosy endemic pattern on Yonaguni island was such that leprosy infection and onset occurred on the island, but since 1970 the infection has occurred there but the disease has developed in the urban areas of the main island. During the five years between 1966–1970, three new patients have been detected on Yona-

guni island, and seven new cases, born on the island, were detected in cities on the main island. The recent leprosy endemic situation on Yonaguni island has improved, but still more leprosy cases who were infected there could be detected in urban areas in the future.—(*Adapted from* author's summary)

Saikawa, K. The report on leprosy survey in Okinawa. 6. Leprosy in Irabu island. Therapeutics (Tokyo) **32** (1978) 537 and 647–649. (in Japanese)

Irabu island has been one of the most leprosy endemic islands of Okinawa. In 1968, the population was 10,211, and the incidence rate was 1.47%. The rate decreased to 0.11% in 1976, and the incidence rate for lepromatous leprosy also decreased. In 1967, the school survey case finding program had a detection rate of 0.68% and in 1970 had a rate of 0.99%. In 1973, no leprosy cases were detected by school surveys. The epidemiological situation has improved, and the endemic peak has passed. However, the lepromatous rate and the incidence in children are still high, and it is still necessary to employ household contact examinations.—(*Adapted from* author's summary)

Samsoen, M., Basset, A. and Grosshans, E. Contribution a l'étude épidémiologique de la lèpre en France métropolitaine. (Contribution to the epidemiologic knowledge of leprosy in continental France.) Bull. Soc. Pathol. Exotique **72** (1979) 295–304. (in French)

Three hundred twenty-two new cases of leprosy in France were registered by a postal survey of 11 towns from 1970–1978. Two hundred seventeen were detected in Paris and 105 in other parts of France. One hundred thirty-seven were foreigners, 104 came from overseas French territories, and 45 were repatriated French nationals; 39.7% were lepromatous cases, 43.6% were tuberculoid cases, and 13.9% were indeterminate cases. Of 35 cases in Alsace, 16 were diagnosed in Strasbourg.—(*Adapted from* authors' summary)

Terencio de las Aguas, J. La lepra regresa a Europa. (Leprosy returns to Europe.) Rev. Leprol. (Fontilles) **12** (1979) 285–289. (editorial) (in Spanish)

Just as leprosy spread throughout Europe during ancient history through wars, commerce, and migrations, Dr. Terencio de las Aguas points out that similar events are bringing about an increase in imported cases of leprosy in contemporary Europe both in formerly endemic areas and in countries previously free of leprosy. This is due in great part to the influx of people from highly endemic Third World countries, and the rise in morbidity is most visible in the highly industrialized areas of Europe. Present day programs aimed at eradicating leprosy concentrate their efforts in Third World countries, and rightly so, because of their high incidence of leprosy, but because of the influx of imported leprosy, there will be a rise in the incidence of leprosy secondary to imported cases. Thus in a few years the epidemiology of leprosy in Europe may be changed. Currently, leprosy in Europe is localized in the southernmost countries bordering the Mediterranean, with small endemic areas and low rates of morbidity. For example:

1) Portugal—2500 cases, some of whom are patients who have returned from former colonies within the last four years.
2) Spain—5100 cases, including 1356 inactive. There are an estimated 2000–3000 imported cases in Spain. With regard to classification, 65% are lepromatous, 24% tuberculoid, 10% indeterminate, and 1% dimorphous.
3) France—1800, the majority imported.
4) Italy—514 cases, an endemic country with some imported cases from Latin America.
5) Greece—3000, Turkey—4796, Romania—101 (endemic in all 3 countries); Bulgaria—31, Russia—6000.
6) The Netherlands—leprosy had disappeared but the country is now experiencing a large number of imported cases both among Dutch who have returned from former colonies and contracted the disease there as well as a great number of immigrants from Indonesia, Surinam, etc. Leiker has indicated that there were 1200 leprosy

patients in the Netherlands between 1945–1977, with 600 still living.

7) Other European countries with imported cases—England—200, West Germany—53, Belgium—38, Norway—3, and Switzerland—1.

It is imperative therefore that the European countries with endemicity and a large influx of immigrants from the Third World should revise their strategies in the fight against leprosy because there is now a third source of cases to be considered: leprosy secondary to imported cases.—I. Ellis

Rehabilitation

Bourrel, P. La chirurgie de la lèpre à 25 ans. (Surgery in leprosy after 25 years.) Médecine et Armées **6** (1978) 157–162. (in French)

The author summarizes the surgical accomplishments in leprosy during the past 25 years by pointing out initially that the emphasis during this period has changed from amputation of severe deformities to corrective procedures geared towards helping the patient achieve a rehabilitated state.

The two principal types of surgery in leprosy treated by the author are reconstructive surgery and surgery involving the nerves. Under reconstructive surgery of the hand, the author discusses the operations of Zancolli, Brand, Giraudeau, Srinivasan, and Thompson and under reconstructive surgery of the foot, the operations of Carayon, Srinivasan, Andersen, Giraudeau, and Brand. Under advances dealing with surgery involving the nerves, the author discusses the work of Carayon, Lassièra, Granberg, Réginato, Callaway, and Palande. The author stresses that these surgical procedures require the services of highly trained personnel but that under these conditions the success rate is very high.—G. Gordon

Ghosh, P. K. Leprosy among factory workers. J. Occup. Med. **19** (1977) 500–501.

Leprosy is prevalent in Asia, Africa, and South American countries. There are two types—lepromatous (infectious) and nonlepromatous (noninfectious). Eighty percent of leprosy cases are noninfectious. Leprosy carries a social stigma. In offices and in factories, fellow workers look down upon leprosy patients and avoid them. The problems facing the employer are discussed. An enlightened management will not rehabilitate the victim but encourage him to take treatment. As soon as he is certified as noninfectious by a specialist, he should be permitted to return to work.—Author's Summary

Kelman, H. R. and Kavaler, F. Socio-medical characteristics of patients with Hansen's disease. Milit. Med. **144** (1979) 462–464.

We have presented a statistical study of a sample group of 56 patients with Hansen's disease who were treated as inpatients at the U.S. Public Health Service Hospital, Staten Island, New York, between 1962 and 1977. Medical care characteristics and socio-demographic characteristics of the disease in this group of patients are analyzed and briefly discussed.—Authors' Summary

Lerner, R. D. and Margarido, L. C. Ectrópio-lagoftalmo: correção cirúgica da paralisia hansênica da região orbitária. (Ectropion-lagophthalmos: surgical correction of the paralysis caused by hanseniasis in the orbital region.) Hansenologia Int. **3** (1978) 168–178. (in Portuguese)

The functional changes of the orbital region are studied, especially ectropion and lagophthalmos in hanseniasis patients. The surgical techniques of Kuhnt, Szymanowski (modified), and Gillies-Andersen were performed in 26 patients. The results are reported.—Authors' Summary

Linois, H. and Sebille, A. Electrophysiological evidence for motor unit impairment during the treatment of leprosy. J. Neurol. Sci. **45** (1980) 57–63.

Although neuropathy is the most striking feature in leprosy, the effects of various

drugs are usually assessed by dermatological and bacteriological improvement. This short term electrophysiological study shows that both antileprosy drugs, DDS and Sulforthomidine, do not affect the insidious deterioration of motor unit condition in lepromatous and borderline patients. Differences observed in the results of the two groups were discussed.—Authors' Summary

Palande, D. D. Surgery on ulnar nerve in leprosy. Lepr. India **52** (1980) 74–88.

Surgery on 64 ulnar nerves in leprosy was done for the treatment of ulnar nerve paralysis of less than one year's duration. The initial treatment, indications for surgery, clinical findings, the operation procedures, and findings are described in detail. Factors shown to have statistically significant bearing on nerve function before and after surgery are discussed. The results were: improved 32, further nerve damage stopped in 11; worsening in six while in the remaining 15 nerves there was no nerve function recovery. The main conclusions are that the earlier the duration of paralysis and the lesser the initial nerve function deficit the better is the result. Lepromatous cases showed better results than nonlepromatous cases.—Author's Summary

Other Mycobacterial Diseases and Related Entities

Mahfouz, M. O., Fraser, C. E. O. and MacDonald, A. B. An immunofluorescence test for detection of antibodies to *Mycobacterium tuberculosis*. Tubercle **61** (1980) 1–9.

An immunofluorescence (I.F.) test for detection of antibodies to *M. tuberculosis* has been developed. The antigen utilized in this test is polymerized tuberculin which is obtained by treating acidified old tuberculin with ethylchloroformate. In tuberculin negative non-human primates it was found that 98% were negative at 1:2, and 100% were negative at 1:10 by I.F. In experimentally infected rhesus monkeys the I.F. titers rose as the disease progressed and in general were higher in the animals with severe disease and lower in less affected animals. In humans it was found that 100% skin negative persons were negative at 1:10 and that 100% tuberculin skin test positive persons without active disease were negative at 1:20. Sera from actively infected patients were tested, and the titers ranged from 1:64 to 1:256. The test was shown to be sensitive and appears to distinguish infected individuals with active disease from those infected cases without active disease. In addition, the test may be of value in monitoring chemotherapy.—Authors' Summary

Tsukamura, M. *In vitro* antimycobacterial activity of minocycline. Tubercle **61** (1980) 37–38.

Minocycline has been shown to exhibit *in vitro* antimycobacterial activity against almost all slowly growing, pathogenic mycobacteria, including *Mycobacterium intracellulare* strains. Strains of *M. intracellulare* were inhibited in the presence of 6.3 μg/ml minocycline.—Author's Summary

van den Broek, H. Treatment of prurigo nodularis with thalidomide. Arch. Dermatol. **116** (1980) 571–572.

A 57-year-old man with prurigo nodularis unresponsive to conventional therapy was successfully treated with thalidomide. The pharmacology and side effects of the drug are briefly reviewed. Why thalidomide is effective for prurigo nodularis is unclear, but possible mechanisms of action are discussed.—Author's Summary

Zierski, M. and Bek, E. Side-effects of drug regimens used in short-course chemotherapy for pulmonary tuberculosis. A controlled clinical study. Tubercle **61** (1980) 41–49.

An analysis is presented of the side effects which occurred in 530 patients treated

with six months chemotherapy for newly detected pulmonary tuberculosis. Five treatment regimens were used. The initial phase of treatment consisted of daily isoniazid, rifampin, and ethambutol (HRE) or isoniazid, rifampin, streptomycin, and pyrazinamide (HRSZ) given for two months. The second phase of treatment consisted of isoniazid and rifampin given twice weekly (H_2R_2) or isoniazid, rifampin, and ethambutol given daily (4HRE) or intermittently ($H_1R_1E_1$ or $H_2R_2E_2$) for four months.

Side effects were detected in 66 (12.4%) patients. Hepatotoxic reactions occurred in 48 (9%) patients, mainly of a mild and transient nature, and the majority were attributable to isoniazid. The "flu like" syndrome occurred in only two patients, both during the daily phase of treatment, and it was not encountered in patients taking rifampin intermittently (dose 600 mg).

Inclusion of pyrazinamide in the initial phase of one regimen did not result in an increase of frequency of side effects. In 56% of patients on pyrazinamide the serum uric acid concentration was elevated, but there was no arthralgia.

Drug toxicity leading to alteration or withdrawal of treatment occurred in only ten (1.8%) patients. This study shows that with these six month regimens the overall risk of drug toxicity was low and less than that associated with more conventional treatment regimens.—Authors' Summary