CURRENT LITERATURE

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General and Historical

Gatti, Juan Carlos and Cardama, Jose Esteban. Inmunoterapia en lepra. [Immunotherapy in leprosy.] Rev. Leprol. **11** (1978) 357-370. (In Spanish)

The article discusses the following points: results of inoculation of *M. leprae* into the mouse foot pad and the nine-banded armadillo and the usefulness of these inoculations in the field of leprosy; usefulness of the Morphologic Index and the more important drugs in treatment of leprosy; comments on the deficient immunological capacity of lepromatous patients; and the known principal immunotherapeutic technics (e.g., diphtheria toxoid, BCG, levamisol and isomers, allogenic leukocytes, transfer factor, etc.), their results and side effects.—(*Adapted from* English summary)

Clinical Sciences

Applebaum, P. C. and Bowen, Annette J. Opportunistic infection of chronic skin ulcers with *Pseudomonas putrefaciens*. Br. J. Dermatol. **98** (1978) 229-231.

Heavy growth of *Pseudomonas putrefaciens* was isolated repeatedly in mixed culture with other Gram-negative rods from chronic ulcers on the extremities of an elderly patient with burnt-out leprosy. Treatment was with systemic cotrimoxazole, topical framycetin and general supportive therapy, and the ulcers gradually healed over a period of four weeks.—Authors' Summary

Barrett-Connor, Elizabeth. Latent and chronic infections imported from Southeast Asia. JAMA **239** (1978) 1901-1906.

This review is intended to remind physicians of exotic infections with latency of at least one year that could cause illness in refugees or U.S. citizens exposed in Southeast Asia. Tuberculosis, melioidosis, and leprosy are the major chronic infections of bacterial origin. Intestinal protozoa, roundworms, and flatworms are considered with regard to pathogenic potential and duration of infection. Malaria, filariasis, and schistosomiasis may be seen on occasion. Paragonimiasis and Chinese liver fluke infections are more common and may simulate other less exotic diseases.—Author's Abstract

Chovet, M., Metge, P., Fauxpoint, B. and Saint-Andre, P. Uvéite postérieure lépreuse. Incidence de la réaction lépromateuse. [Posterior lepromatous uveitis. Lepromatous leprosy reaction as an etiologic factor.] Bull. Soc. Ophthalmol. Fr. **76** (1977) 1215-1217. (In French)

Among 79 patients with lepromatous leprosy, 55 developed lepra reactions. Six of these patients presented pathologic aspects of the fundus, i.e., aveopapillitis (1), localized perivasculitis (3), and hemorrhagic lesions (2). The authors consider that *erythema nodosum leprosum* is the major etiologic factor operating in these cases.—(*Translation by* M. F. Lechat)

Harris, Ruth C. Leprosy in a child. Pediatrics **61** (1978) 330. (Letter)

Recently, a ten year old child who had been in this country for 19 months after the "baby-lift" in Vietnam was discovered to have a granulomatous lesion on her right index

finger. Biopsy and histologic examination failed to reveal the exact diagnosis except that it was a "granulomatous process." Recurrence of a similar lesion on the palm of the hand and referral of the patient to a large medical center identified the process as mild tuberculoid leprosy.

While this is a rare and exotic problem in the United States, those children who have been brought into this country since 1975 and who have unusual skin lesions or areas of anesthesia should be evaluated from this standpoint. Early identification and treatment are important for the well-being of the child and the family if the leprosy should be of the infectious variety. Since this is a disease that most of us pediatricians never dream of seeing, we should be sure that we put it in the back of our minds for evaluation in overseas patients from the tropics.—Author's Letter

Huikeshoven, H., and Bijleveld, I. Encouraging results from DDS urine analysis among registered leprosy patients in the Wangas, Kenya: an exception that challenges the rule. Lepr. Rev. **49** (1978) 47-52.

From previous research among the Wangas (Kenya), it appears to be the standard of medical services, and in particular the leprosy fieldworker's approach, rather than sociocultural factors, which accounts for failure of leprosy control.

The present investigation adds weight to these findings. Urine samples were taken from 39 patients of one highly reputable leprosy fieldworker, and analyzed for DDS/creatinine ratios. Comparison with data from elsewhere demonstrates their scrupulousness in weekly DDS-taking at home.—Authors' Abstract

Huikeshoven, H., Landheer, J. E., Denderen, A. C. v., Vlasman, M., Leiker, D. L., Das, P. K., Goldring, O. L. and Pondman, K. W. Demonstration of dapsone in urine and serum by ELISA inhibition. Lancet **1** (1978) 280-281. (Letter)

Conventional methods for demonstrating dapsone are either insensitive or not practicable for general use in leprosy endemic areas. We have developed an immunoassay that is both simple and sensitive.

Diazotised dapsone was conjugated to bovine serum albumin, and 10 mg of conjugate emulsified in Freund's complete adjuvant was injected into rabbits. Booster injections of 10 mg of conjugate in Freund's incomplete adjuvant were given after three weeks. Anti-dapsone antibody was demonstrated by microscale diazotised dapsone/horseshoe-crab hemocyanin conjugate (DDS-HCH) to coat the wells of polystyrene microtiter trays, and horseradish-peroxidase-conjugated antirabbit IgG antiserum (Institut Pasteur, Paris). Sera positive for anti-dapsone antibody were identified by adding a solution of 5-amino-salicylic acid/H_2O_2 and looking for development of a brown color. Addition of as little as 0.1 μg dapsone to each well inhibited positive reactions by two doubling dilutions. Ten micrograms of sulphadiazine, a structural analogue of dapsone did not inhibit the ELISA response to the same extent. A test for inhibition of ELISA (ELISIT) was then developed to detect dapsone in urine and sera from leprosy patients. Urine was collected from 44 leprosy patients in Kenya, 40 of whom were supposed to be taking 300 mg of the drug once a week, while the other 4 were taking lower doses.

The urine was collected two days after a scheduled dose. It was preserved by adding hydrochloric acid. Before testing the urine its pH was adjusted to 7.2. In addition urine taken six hours after the intake of 300 mg dapsone was obtained from one Dutch volunteer. Urine from 16 healthy individuals not taking dapsone was also tested. Sera of three leprosy patients taking 100 mg daily and one volunteer whose blood sample was taken six hours after a single dose of 300 mg dapsone was examined too. Control sera from four healthy people not taking dapsone was treated in the same way.

The wells of the tray were first coated (30 minutes, 37°C) with 100 μg of carbonate-buffered solution (pH 9.6) containing 0.2 μg DDS-HCH. After the normal washing cycle, 50 μg of 1/500 diluted antidapsone rabbit serum was added. After incubation, washing, conjugate addition and so on, the tests were read and yielded the following results:

1. Dapsone solutions containing 0.3 μg/ml can be detected by ELISIT.

2. A positive result for one of the Kenyan urine samples may be questionable. In two other samples the quantity of dapsone is very low (around 0-3 μg/ml). Six other samples contained not more than 1 μg/ml. The remaining 35 Kenyan urine samples all contained more than 1 μg/ml.

3. Six hours after a single dose of 300 mg dapsone, urine diluted 1/250 was positive.

4. Positive and negative sera can be clearly distinguished when diluted 1/100.

The urine samples were used to compare ELISA inhibition with two conventional spectrophotometric procedures. Out of ten samples, negative on one or both spectrophotometric procedures, nine were positive and one equivocal on ELISA inhibition testing.

Sera from patients taking dapsone, which would be expected to contain 1-3 gm/ml were dapsone positive by ELISIT even when diluted a hundredfold. A sensitivity of ELISIT and its simplicity may be of practical value in leprosy-endemic countries with limited laboratory services.—(*Adapted from* authors' letter)

Li, W. M. and Wong, C. K. Leprosy found in a dermatology clinic in Taiwan. Mod. Med. Asia **14** (1978) 45-46.

During the last five years, 45 cases of leprosy were discovered in a dermatology clinic in Taiwan. The number of leprosy patients has increased gradually year by year. A description of the prevalence of leprosy is given and discussed with specific reference to age, sex and type.—Authors' Abstract

Matsumoto, Toshiko and Sasaki, Norisuke. A case report of seborrheic keratosis with an exacerbated leproma. Jap. J. Lepr. **46** (1977) 73-77. (In Japanese)

The patient was a 52 year old male. Even though long-term chemotherapy for leprosy was carried out, the skin smear test for the detection of leprosy bacilli never showed a negative result. While the exacerbation of leproma sometimes reoccurs, a small multiple black tumor appeared in the skin on various parts of the body, e.g., the chest, back, upper arm, abdomen and breech, etc. In the upper left arm a black tumor, which measured 13 × 10 mm, was the largest compared to other areas, therefore it was removed for microscopic observation. The results showed that the nature of this tumor was seborrheic keratosis (verruca senilis) without a melanoma or pigment cell nevus. This seborrheic keratosis was presented together with the nodular exacerbated leproma, which showed abundant rod-shaped bacilli and many globi in the star-shaped or spindle-shaped lepra cells. There were no leprous foamy cells and nerve thickening in the dermis. The epidermis in the center of the seborrheic keratosis was very thin due to the pressure of the developing leproma. The epidermis of the center demonstrated macroscopically a slight reddish color and thickening in its surroundings. One characteristic was that minimal lepromas formed in the thickening epidermis.

We have discussed the correlation between seborrheic keratosis and exacerbated leproma, and although we have considered the possibility that stimulation of the leproma might have developed the seborrheic keratosis, we do not have clear evidence at this time.—(*Adapted from* English summary)

Naafs, B. and Wheate, H. W. The time interval between the start of antileprosy treatment and the development of reactions in borderline patients. Lepr. Rev. **49** (1978) 153-157.

One hundred patients who developed a reversal reaction were analyzed with respect to the time lapse between the start of treatment and the start of the reaction. It was found that in nearly all cases BT and BB patients developed reaction in the first half year of treatment. For BL patients such an obvious relationship could not be found. The authors express the opinion that the reversal reaction is a natural occurrence in the course of untreated borderline leprosy and that although sulfone treatment may accelerate the reaction it certainly does not cause it.—Authors' Abstract

Pandya, Narendra J. and Antia, Noshir H. Elective surgical decompression of nerves in leprosy—technics and results: a preliminary study. Lepr. Rev. **49** (1978) 53-62.

Elective surgical decompression by extraneural and medial longitudinal epineurotomy was carried out in 45 patients. The ulnar nerve was the commonest, followed by the lateral popliteal, median and posterior tibial which comprised 69 nerves which were biopsied. The maximum period of follow-up was up to three years with a mean of 25 months.

Thirty-three patients showed sensory recovery, three failed to recover and only one deteriorated. Motor recovery was less predictable and seen in 26 patients. Seven failed

to show any improvement and one deteriorated. Six patients with no sensory and nine with no motor loss showed no adverse effects when followed for three years. The recovery was better seen in the group seeking early treatment and at an earlier age.

It is felt that the beneficial effects may have resulted from the increased vascularity and improved venouse return due to relief from the extraneural and intraneural compression.—Authors' Abstract [*A manuscript apparently covering the same procedures on the same group of patients was published by Dr. Pandya virtually simultaneously in the IJL* **46** *(1978) 47-55. This* JOURNAL *was not aware of simultaneous manuscript submission.—Ed.*]

Rea, Thomas H. and Levan, Norman E. Lucio's phenomenon and diffuse nonnodular lepromatous leprosy. Arch. Dermatol. **114** (1978) 1023-1028.

The records of ten patients with Lucio's phenomenon showed clinical and histopathologic changes similar to those described by others. Lucio's phenomenon is a syndrome distinct from *erythema nodosum leprosum* as indicated by an absence of fever, leukocytosis and tenderness, a failure to respond to thalidomide, and a restriction to patients with a diffuse nonnodular lepromatous leprosy. Lymphopenia associated with splenomegaly in three patients and glomerulonephritis in one patient were unexpected findings of unknown relevance.—Authors' Abstract

Reddy, B. S. N., Chandra, S., Jha, P. R. and Singh, G. Waardenburg's syndrome with leprosy. Indian J. Dermatol. Venereol. Leprol. **44** (1978) 24-26.

A rare association of Waardenburg's syndrome and tuberculoid leprosy in a 13 year old male patient is described. This is an unrecorded feature in the literature. These two disorders were quite unrelated entities and their occurrence in the same patient is a casual one. All the classical features of Waardenburg's syndrome except deafness were present and the disease was manifest as an isolated case in the family. The pertinent literature is briefly reviewed.—Authors' Summary

Rietschel, Robert L. and Lewis, Charles W. Invisible dermatoses. Cutis **21** (1978) 213-217.

An invisible dermatosis is defined as a skin disease manifesting no clinically apparent lesion but histologic changes of a characteristic nature. An example of an invisible form of transient acantholytic dermatosis is presented. Invisible forms of pseudoxanthoma elasticum, sarcoidosis, lepromatous leprosy, and lichen planus are reviewed. Dermal deposits may also be found on biopsy of clinically normal skin in amyloidosis, Hunter's and Hurler's syndromes, and thyroid disease.—Authors' Abstract

Rimon, D., Machtey, I., Himelstein, M. Hand pain in the early diagnosis of lepra. Athritis Rheum. **21** (1978) 282-283. (Letter)

Lepra reaction (type 2) is characterized by one or more of the following: *erythema nodosum leprosum,* intermittent fever, nerve swelling and pain, bone pain, swollen joints, acute iridocyclitis, epistaxis, edema of the glottis, lymphadenitis and mental depression. Also, polyarthritis, myositis, and immune-complex glomerulonephritis have been described in a patient with lepromatous leprosy (Iveson, JMI, McDougall, AC, Leathem, AJ, Harris, HJ: Lepromatous leprosy presenting with polyarthritis, myositis and immune-complex glomerulonephritis. Br. Med. J. 3:619-621, 1975).

We had the opportunity to diagnose lepra reaction in a very bizarre case: a 48 year old woman, who came to Israel from Poland in 1957, was hospitalized because of paroxysmal atrial fibrillation and symmetrical convulsions of short duration in all extremities. History included bronchial asthma since 1959 and allergic reaction to different drugs. In 1969 there was one episode of edema of the larynx. In 1970 she underwent explorative laparotomy because of acute pain in the abdomen, and acute pancreatitis was found. Since then, she has been hospitalized six more times because of pain in the right hypochondrium, vomiting and fever, but no definite diagnosis could be made. During one hospitalization elsewhere (in 1974) she also had a maculopapular eruption all over the body. In 1974 she underwent drainage of a perianal abscess, and thereafter she was hospitalized for prolonged fever of unknown origin with abdominal pain. A short time after

this she was admitted to a psychiatric hospital for depression. In the last month she suffered pain in both hands, and these complaints prevailed during this last entire hospitalization. On examination her general condition was good, blood pressure was 130/80. Her temperature was subfebrile (37-38°C) during many weeks. Occasional expiratory wheezing was heard over both lungs. The main complaint during this hospitalization was pain in both hands accompanied by fever. There were no signs of arthritis, and x-rays of the joints were normal. A complete laboratory examination on admission to the rheumatology department showed no special changes, except for a transient leukopenia (3000/mm^3) and thrombocytopenia (60,000/mm^3). A connective tissue disorder was suspected, but no definite diagnosis could be made.

Later on, during her hospitalization peripheral neuropathy appeared. A thorough checkup ruled out many causes of peripheral neuropathy, including metal poisoning, vitamin deficiency, and diabetes. Repeated neurological examinations disclosed bilateral distal hypoalgesia of the hands (gloveform, without sharply defined borders). The ulnar nerves on both sides and the greater auricular nerve on the right side seemed to be thickened and were tender on palpation. On the forehead a faint reddish infiltrate was visible; the right earlobe was slightly reddish and swollen, and there was partial alopecia of the eyebrows. In both legs and forearms there was an inability to discriminate sharp from blunt and changes of temperature or touch. Both optic discs were normal. X-ray of skull and EEG were normal. A skin biopsy of the ear lobule and a nasal smear did not reveal acid-fast bacilli. EMG revealed decreased conduction in the right ulnar nerve at the elbow region. Surgical decompression of the right ulnar nerve at this site was performed. During this procedure, a biopsy was done from a minor branch of this nerve, which microscopically showed signs of nerve fiber degenerations (including hydropic degeneration) and groups of acid-fast bacilli.

Thus, lepra reaction of Hansen's disease could be diagnosed. After a short course of thalidomide therapy her pain disappeared. Later she was transferred to a leprosarium for further treatment. She was seen again, one year after the treatment with thalidomide was started; she felt generally well, had no more pain, though she complained again of paresthesia in both hands.

One can wonder whether all the details of her past medical history belong to lepra, and in fact, without doubt, many symptoms and signs were similar to those of lepra; for example, edema of the glottis, intermittent fever, typical neurological findings and bone pain. There was fever and pain in her hands which, eventually, led us to the diagnosis of lepra.—(*Adapted from* authors' letter)

Takizawa, Hideo. Studies of clinical course and prognosis of Hansen's disease during chemotherapy. 3. Acute infiltration reaction (Tajiri) in lepromatous leprosy. Jap. J. Lepr. **46** (1977) 139-143. (In Japanese)

This is a report of lepromatous cases with acute infiltration reaction (Tajiri) in the clinical course during chemotherapy. All patients were male, among whom one case showed localized skin lesions and the other two cases had generalized lesions on admission. Skin biopsies revealed all borderline-lepromatous features (Ridley-Jopling's classification). Reactions developed 1.5 to 4 months after beginning treatment and lasted 9 months to 2 years intermittently. After this reaction the Mitsuda test gave the same result as before in one case, but the other two cases became weakly or moderately positive. Bacterial clearance time (Takizawa) was 2.7, 4.3, and 5.9 years, respectively. The nomenclature and nature of this reaction are discussed, especially in relation to chemotherapy.—(*Adapted from* English summary)

Thawerani, H., Sanchez, R. L., Rosai, J. and Dorfman, R. F. The cutaneous manifestations of sinus histiocytosis with massive lymphadenopathy. Arch. Dermatol. **114** (1978) 191-197.

Ten patients with sinus histiocytosis with massive lymphadenopathy (SHML) also had cutaneous involvement. Seven of the ten were children. The skin lesions were solitary in three patients and multiple in seven. They were papular or nodular, up to 4 cm in diameter, and often had a xanthomatous appearance. Microscopically, they were constituted by a dermal infiltrate made up predominantly of histiocytes, plasma cells and lymphocytes. Some of the histiocytes contained phagocytosed lymphocytes in their cytoplasm. The microscopic differential diagnosis includes

dermatofibroma, xanthoma, Tangler disease, histiocytosis X, reticulohistiocytoma, juvenile xanthogranuloma, and leprosy.—Authors' Abstract

Vaidyanathan, E. P. and Anthony, P. Extensor pollicis brevis transfer to flexor digitorum sublimis in Hansen's disease. Follow-up study for four years. Lepr. Rev. **49** (1978) 63-68.

Five cases of tuberculoid leprosy with paralysis of thumb were studied. Extensor pollicis brevis was anastomosed with ring finger, flexor sublimis at different levels, and cases were assessed. Case reports, assessments and advantages of the operation are presented.—(*Adapted from* authors' abstract)

Vaidyanathan, E. P. and Vaidyanathan, S. I. Superficial peroneal nerve thickening as an early diagnostic sign in leprosy. Lepr. Rev. **49** (1978) 149-151.

Clinical examination of 1,020 persons in a region of India in which leprosy is endemic revealed thickening of *one or both* superficial peroneal nerves in 54 persons, 19 having previously received treatment for leprosy, whether full or incomplete (old cases), and 35 never having been treated (new cases). Biopsies of thickened superficial peroneal nerves showed that of 33 symptom-free new patients, 18 had diagnostic histologic changes (54.5%). A plea is made that screening examinations for leprosy should always include palpation of superficial peroneal nerves, for subsequent nerve biopsies are likely to provide early diagnostic evidence in more than 50% of cases.—Authors' Abstract

Chemotherapy

Colston, M. J., Ellard, G. A. and Gammon, P. T. Drugs for combined therapy: experimental studies on the antileprosy activity of ethionamide and prothionamide, and a general review. Lepr. Rev. **49** (1978) 115-126.

The activity of ethionamide and prothionamide against *Mycobacterium leprae* has been evaluated using the mouse foot pad model. The minimum effective doses of both drugs were found to be approximately 0.01%, and their minimal inhibitory concentrations were estimated to be about 0.05 μg/ml. Both compounds were found to be bactericidal against *M. leprae* at dietary concentrations of 0.1%. These findings indicate the importance of studies to evaluate the potential role of ethionamide and prothionamide in clinical practice. The available experimental evidence concerning the relative antileprosy activities of drugs that might be used in the combined treatment of lepromatous patients is reviewed.—Authors' Abstract

Colston, M. J., Hilson, G. R. F. and Banerjee, D. K. The "proportional bactericidal test": a method for assessing bactericidal activity of drugs against *Mycobacterium leprae* in mice. Lepr. Rev. **49** (1978) 7-15.

A new method for assessing the bactericidal activity of antileprous drugs against *Mycobacterium leprae* using the mouse foot pad technic is described. This approach, referred to as the "proportional bactericidal test," has been devised to overcome some of the problems of interpretation caused by drug persistence or prolonged bacteriostasis after drug administration has ended. The bactericidal activity of several drugs against *M. leprae* has been determined using this approach and the results obtained compared with those previously reported using alternative methods.—Authors' Abstract

Colston, M. J., Hilson, G. R. F., Ellard, G. A., Gammon, P. T. and Rees, R. J. W. The activity of thiacetazone, thiambutosine, thiocarlide and sulphamethoxypyridazine against *Mycobacterium leprae* in mice. Lepr. Rev. **49** (1978) 101-113.

The mouse foot pad model has been used to evaluate the activity of thiambutosine, thiocarlide, thiacetazone and sulphamethoxypyridazine against *Mycobacterium leprae.* The minimum effective doses of thiambuto-

sine and thiocarlide were found to be approximately 0.05% and of thiacetazone 0.03%, although different strains of *M. leprae* displayed varying sensitivity to all three drugs. The minimal inhibitory concentrations of thiambutosine, thiacetazone and sulphamethoxypyridazine were estimated to be about 0.5 μg/ml, 0.2 μg/ml and 30 μg/ml, respectively. Evidence was obtained indicating that the antileprosy activity of thiambutosine, thiocarlide and thiacetazone was essentially bacteriostatic. The clinical relevance of these findings is discussed.—Authors' Abstract

Cottenot, F. and Pennec, J. Poussée évolutive de lèpre lépromateuse. Action favorable du Lamprène. [Favorable effect of clofazimine in lepromatous leprosy.] Bull. Soc. Fr. Dermatol. Syphiligr. **83** (1976) 269. (In French)

One case of lepromatous leprosy of the histoid type is described. The treatment consisted of long-acting sulfones and rifampicin, intradermal BCG, dapsone and clofazimine. A considerable improvement has been observed, both clinically and bacteriologically. The patient, however, is still slightly positive. The red coloring of the skin due to clofazimine is reported.—(*Translation by* M. F. Lechat)

Delville, J. and Jacques, P. J. Death and intracellular degradation of *Mycobacterium leprae* after exposure *in vitro* to enzymatic free-radical generators. Biochem. Soc. Trans. **6** (1978) 394-395.

Fresh suspensions of *M. leprae* were exposed *in vitro* at pH 5 and 36°C in aerobic conditions to a mixture of fungal glucose oxidase, glucose, plant peroxidase and iodide or to a similar mixture lacking peroxidase and iodide, for either a few seconds or one hour. The controls were incubated for one hour in the same conditions, except that iodide and both enzymes were omitted. After washing the microbial preparation in the cold and resuspension, hind foot pads of normal mice were inoculated with this resuspended preparation. At various times, ranging from 180 to 424 days after inoculation, the foot pads were collected and processed for enumeration of total acid-fast bacteria and for differentiation between granular and solid-stained bacteria.

Contact *in vitro* of *M. leprae* with the complete oxidase mixture for only a few seconds resulted in a considerable decrease of the number of solid-stained (live) and granular (dead) mycobacteria that could be observed in mouse foot pads up to 14 months after the treated microbial suspension had been transferred to that growth system *in vivo*. Since not a single acid-fast bacterium could be detected when treatment with the complete oxidase mixture had been applied for one hour, we conclude that a true bactericidal action of the oxidative "cocktail" has been observed. In addition, tissue concentration of the dead mycobacterium was considerably decreased in the case of treated compared with control preparations, presumably through an acceleration of intralysosomal biodestruction of acid-fast bacteria.

Exposure for one hour to peroxidase- and iodide-depleted "cocktail" produced the same effect as exposure for a few seconds to the complete oxidase "cocktail." When the concentration of glucose oxidase was increased 100-fold in that depleted "cocktail," results similar to those after exposure for one hour to the complete glucose oxidase mixture were obtained.—(*Excerpted from* authors' article)

Delville, J. and Jacques, P. J. Effect of treatment *in vivo* with Triton WR-1339 and Macrocyclon on infection of the mouse foot pad by *Mycobacterium leprae*. Biochem. Soc. Trans. **6** (1978) 395-396.

Reported studies and the urgent need for new and more adequate therapeutic procedures against human leprosy prompted us to test the effect of Triton WR-1339 and of Macrocyclon on the experimental disease that follows the injection of human leprosy bacilli into foot pads of mice.

An incipient rather than established infection was chosen for the assay to improve accuracy in the detection of possible decreases in solid-stained (viable) mycobacteria. At one month after inoculation of *M. leprae* into the foot pads of TB/Gif mice, Triton WR-1339 or Macrocyclon dissolved in 0.9% NaCl were injected intraperitoneally at the dose of 4 mg/animal; this injection was repeated weekly. At regular time intervals ranging from 41 to 96 days after onset of treatment, foot pads were collected for enumeration of acid-fast bacteria. To dis-

tinguish live from dead mycobacteria, the criterion of granular against solid staining was adopted. Both detergents significantly decreased the count of acid-fast bacteria and those of granular and solid-stained mycobacteria. The proposed greater effect of Macrocyclon compared with Triton WR-1339 was also statistically significant.—(*Excerpted from* authors' article)

Freerksen, Enno and Rosenfeld, Magdalena. Die therapeutische Aktivität von Chemotherapeutika und ihre klinisch-experimentelle Bestimmung. [Clinical and experimental evaluation of the activity of chemotherapeutic agents.] Prax. Pneumol. **32** (1978) 41-55. (In German)

1. The view has repeatedly been expressed that a purely clinical evaluation of the therapeutic efficacy of a chemotherapeutic agent is not sufficiently reliable. Because of these doubts attempts have been made to refine and increase the accuracy of the clinical observations by controlled studies with a statistical evaluation of the results.

2. Although these technics can be made increasingly more detailed and precise they do not make the end results more reliable because the degree of accuracy of the data used in the analysis has not changed. The patient and his disease represent statistically a conglomeration of symptoms and pathologic processes too many of which, and many of them of greatest importance, cannot be specified numerically with any degree of certainty.

3. The evaluation of the efficacy of chemotherapeutic agents can be made more precise and more objective if "therapeutic activity" is estimated as an independent factor directly related to the clinical results. This is also advantageous for the patient in that it greatly reduces the unpleasantness attendant on clinical trials.

4. The most suitable method available at present is determination of serum activity; it is the link between experimental and clinical tests.

5. Laboratory experiments and clinical studies should be regarded as an interconnected system for jointly planning the appropriate therapy of infectious diseases, assessing its efficacy and making such adjustments to the mode of treatment as may become necessary.—(*Adapted from* authors' summary)

Freerksen, E., Rosenfeld, M., Bonnici, E., Depasquale, G., and Kruger-Theimer, M. Combined therapy in leprosy: background and findings. Chemotherapy **24** (1978) 187-201.

This report is based on data obtained from 64 lepromatous cases. Despite many years of DDS monotherapy, the homogenates from biopsies of these patients revealed 10^4 or more bacteria. From the beginning of combination therapy with synergistic acting substances (rifampicin + isoprodian (INH + PTH + DDS) the logarithms of the number of bacteria in the homogenates decreased, both during the treatment period and the treatment-free observation period. During the whole time biopsies were taken almost monthly. A considerable regression of the bacterial mass or even "negativity" could be observed within a relatively short time. Once started, the process of reduction of bacteria continued also after termination of therapy. In order to evaluate medication, therapy-free observation periods (for a minimum of five years) are indispensable.—(*Adapted from* authors' abstract)

Noordeen, S. K. and Neelan, P. N. Extended studies on chemoprophylaxis against leprosy. Indian J. Med. Res. **67** (1978) 515-527.

The role of dapsone as a chemoprophylactic was studied among: a) 955 household contacts of lepromatous leprosy when the drug was administered once a week in a dose schedule equal to about 1 to 2 mg per kg body weight per week, and b) 2,000 household contacts of nonlepromatous leprosy when the drug was administered twice a week in a dose schedule equal to about 4 mg per kg body weight per week. The study was double blind with comparable controls. The contacts received about 90% of the expected treatment. The results showed that chemoprophylaxis with dapsone was effective, the protection received by the contacts of lepromatous cases varying between 37% and 40%, the protection received by the contacts of nonlepromatous cases being about 35%. The protective value of chemoprophylaxis in preventing the occurrence of lepromatous cases

could not be studied as no new lepromatous cases occurred, even in the control group. Although the protection from chemoprophylaxis was moderate, certain subgroups were found to be associated with higher protection. These subgroups, in general, had a higher risk of getting leprosy as observed from the occurrence of the disease in the relevant control groups.—(*Adapted from* authors' abstract)

Orlowski, E. H. Klinischer Bericht über die Anwendung einer fixen Kombination von Isoniazid, Prothionamid und 4,4-Diamino-Diphenyl-sulfon (DDS) bei der Behandlung der Lungentuberkulose Erwachsener. [Clinical report on the administration of a combination of isoniazid, prothionamide and 4,4-diaminodiphenylsulfone (DDS) in the treatment of pulmonary tuberculosis in adults.] Prax. Pneumol. **30** (1976) 224-229. (In German)

1. Results are reviewed which were obtained with Isoprodian, a combination containing 175 mg of isoniazid, 175 mg of prothionamide, and 50 mg of 4,4-diaminodiphenylsufone per tablet.

2. The radiologic changes and the time of sputum conversion observed with Isoprodian therapy in 214 patients were approximately the same as those seen with a combination of isoniazid, ethambutol and rifampicin.

3. The drug was well tolerated. In some cases it caused a transient fall in hemoglobin and erythrocyte count, followed by a rapid return to normal despite continuation of the therapy. Exceptional decrease in hemoglobin could be counteracted by administration of ascorbic acid.

4. The special advantages of Isoprodian are: a) Treatment is simplified because less tablets need be taken. b) There is greater certainty that even in domicilliary treatment a highly efficacious antituberculous drug is being taken. c) It offers the possibility to alternate between rifampicin and ethambutol as part of a combination therapy. d) It offers a new approach to the treatment of tuberculosis including difficult cases. e) The fact that the combination of Isoprodian with rifampicin currently represents the most effective therapy of leprosy opens up new possibilities for the simultaneous treatment of tuberculosis and leprosy.—Author's English Summary

Terencio de las Aguas, J. and Gatti, C. F. Asociacion clofazimina-sulfonas en el tratamiento de la lepra. [The association of clofazimine and sulfones in the treatment of leprosy.] Rev. Leprol. **11** (1978) 357-370. (In Spanish)

Fifteen cases of lepromatous leprosy were treated with sulfones and clofazimine consisting of a dosage of 100 mg clofazimine three times per week, alternating with 50 mg dapsone three times per week in some cases, and in other cases using three injections of promin. For the best clinical and bacteriological activity and the minimum of side effects, the authors believe that this is the ideal treatment for lepromatous patients over a two year period.—(*Adapted from* English summary)

Venkatesan, T. V. Treatment of lepromatous leprosy with clofazimine (B663 Lamprene). Indian J. Dermatol. Venereol. Leprol. **44** (1978) 16-19.

The present clinical study is comprised of 11 lepromatous leprosy patients. In all these patients lepra reaction was noticed. These patients were previously taking sulfones. Patients were followed for two years and the results are given.—(*Adapted from* author's summary)

Waters. M. F. R., Laing, A. B. G. and Rees, R. J. W. Proven primary dapsone resistance in leprosy. A case report. Lepr. Rev. **49** (1978) 127-130.

A patient is described who at the age of ten years developed tuberculoid leprosy; during the next two years while on oral dapsone therapy, his condition deteriorated and he became lepromatous. Both clinically and experimentally by drug sensitivity testing in mice, his strain of *Mycobacterium leprae* was found to be fully resistant to dapsone. His father was a known case of secondary (acquired) dapsone resistance. The potential medical and economic importance of primary sulfone resistance is discussed.—Authors' Abstract

Waters, M. F. R., Rees, R. J. W., Pearson, J. M. H., Laing, A. B. G., Helmy, H. S. and Gelber, R. H. Rifampicin for lepromatous leprosy: nine years' experience. Br. Med. J. **1** (1978) 133-136.

Over 100 patients with lepromatous leprosy were treated with rifampicin in a series of pilot, uncontrolled, and controlled trials in 1968-1977. The rapid bactericidal effect of rifampicin on *Mycobacterium leprae* was confirmed. Clinical improvement became apparent sometimes as early as 14 days after the start of treatment. Nevertheless, a few persisting viable *M. leprae* were detected as long as five years after the start of treatment with rifampicin either by itself or in combination with the bacteriostatic drug thiambutosine. Treatment with rifampicin and dapsone for six months reduced the number of persisting leprosy bacteria more than treatment with dapsone alone.

Although rifampicin proved more effective than dapsone, it is unlikely that used by itself it can significantly shorten the length of treatment in lepromatous leprosy. Therefore initial intensive combined treatment with two or more bactericidal drugs (including rifampicin) warrants further investigation in both untreated leprosy and lepromatous leprosy resistant to dapsone.—Authors' Summary

Immuno-Pathology

Bullock, Ward E. Leprosy: A model of immunological perturbation in chronic infection. J. Infect. Dis. **137** (1978) 341-354.

It is abundantly clear that our knowledge of the biological complexities embodied in the paradigm of leprosy is fragmentary at best. Nevertheless, progress has been made, and projections for the future are very exciting indeed. The recent conceptualization and demonstration of immunoregulatory control systems that inhibit immune responses in mammals is potentially of great importance to the students of chronic progressive intracellular infections. Heretofore, many of us have viewed such infections as examples of a failure or deficiency of the cell-mediated immune defense mechanism. Now it becomes imperative that we explore an alternate hypothesis, namely, that suppression of the host reponse to these infections may result at least in part from intense stimulation of immunosuppressor regulatory mechanisms. The implications of such research for future approaches to immunotherapy may well be considerable; if it is regarded as desirable to augment T cell helper activity by giving transfer factor or thymic hormones, it may be of equal importance to interdict the immunosuppressor function of other cell subpopulations. In any event, future forays into the hinterland between the activities of lymphocytes and macrophages are likely to be most rewarding.—Author's Conclusion

Campailla, E. and Martinelli, B. Il piede lebbroso. [Leprosy of the foot.] Clin. Ortop. **26** (1975-76) 119-126. (In Italian)

The more frequently occurring bone lesions of leprosy of the foot are described with illustrations from patients with leprosy seen some years previously in Sardinia. These cases are classified into groups depending on the presence of osteoporosis, osteitis, lesions with predominantly inflammatory manifestations, those with a spindle-shaped appearance, and lastly those with pathologic fractures. The anatomical relationship between cutaneous and bone lesions is outlined.—Authors' English Summary

Chen, Li-Tsun. Microcirculation of the spleen: an open or closed circulation? Science **201** (1978) 157-158.

By injecting plastic microspheres of a specific size (3 or 4 micrometers) into the circulation and following their movement and distribution in the spleen, it was revealed how blood travels from the arterial capillaries to the venous sinuses. This method demonstrated that both open and closed circulation exist in the spleen and that about 90% of the blood takes the open route of

circulation in the normal unanesthetized rabbit.—Author's Abstract

Cottenot, F. and Pennec, J. Lèpre tuberculoïde majeure avec hypertrophies nerveuses particulièrement marquées. [Major tuberculoid leprosy with important nervy hypertrophy.] Bull. Soc. Ophthalmol. Fr. Syphiligr. **83** (1976) 269. (In French)

A case of tuberculoid leprosy in regression is described in which ulnar, external popliteal, median and transverse cervical nerves were grossly enlarged.—(*Translation by* M. F. Lechat)

Ellis, B. P. B. Leprosy and the rheumatoid factor. Cent. Afr. J. Med. **24** (1978) 8-10.

This investigation was designed to establish the incidence of rheumatoid factor in three groups, namely a) leprosy patients, b) patients with dermatological conditions, and c) healthy persons; and secondly, to observe the effects of treatment on seropositivity in leprosy reactional states.—(*Excerpted from* author's article)

Fumarola, D. and Jirillo, E. Leukocyte migration inhibition with armadillo lepromin in human lymphocytes of healthy donors. Infection **6** (1978) 5-7.

Armadillo lepromin activates human lymphocytes from normal donors to release leukocyte inhibiting factor. The above activity was expressed optimally when leukocytes were incubated with lepromin at 37°C, and only partially when incubation was carried out at 30°C or at 35°C. The possible mechanism of the *in vitro* production of lymphokine from lymphocytes stimulated by armadillo lepromin is discussed.—Authors' Summary

Harboe, M., Closs, O., Bjune, G., Kronvall, G. and Axelsen, N. H. *Mycobacterium leprae* specific antibodies detected by radioimmunoassay. Scand. J. Immunol. **7** (1978) 111-120.

A radioimmunoassay was developed for demonstration of antibodies against *M. leprae* specific antigenic determinants. The specificity of the assay was tested with hyperimmune rabbit antisera against other mycobacteria and shown to be very high. The titer of *M. leprae* specific antibodies in a lepromatous serum pool was 10^5. Sixty-one of 62 lepromatous sera, all of 12 borderline sera, and 20 of 48 tuberculoid sera were positive in the assay; whereas all of 38 control sera from tuberculin positive individuals from a leprosy nonendemic area were negative. Application as a diagnostic test for subclinical infection with *M. leprae* is discussed. The principle of the test appears promising for serological distinction between pulmonary infection with *M. tuberculosis* and other mycobacteria.—Authors' Abstract

Johnson, A. C., Reddy, R., Johnson, S. and James, A. E., Jr. Lower limb angiography in leprosy. Radiology **126** (1978) 327-332.

Bilateral lower limb angiography was performed on 58 patients with leprosy and compared with bilateral lower limb angiography performed on 63 nonleprosy patients. The vessels in leprosy were narrow and constricted. Decreased blood flow through arteries in the distal third of the lower limb was present. Abnormal AV fistula formation in the thigh and calf muscles and in trophic ulcers of the feet was also seen. Deep inflammatory granulomatous reaction surrounding the arteries as a result of leprosy is a possible explanation for these angiographic findings and is felt to be related to trophic ulceration. These findings were specific for leprosy, precede clinical manifestations, and are helpful in management.—Authors' Abstract

Klingmuller, Von Georg. Nervenänderungen bei lepra. [Nerve changes in leprosy.] Wiener Symposium, Vienna, April 29-30, 1977. (In German)

The nerves are affected first in leprosy and therefore it is better to speak of leprosy as a nerve rather than a skin disease. Many investigations have been made in this field with EM methods, and it is now possible to give a summary of the cytopathology of nerve alterations. In lepromatous leprosy *Mycobacterium leprae* are found in histiocytes around the nerves, in endothelial cells of vessels near them, in perineurial cells, in the endoneurial endothelial cells, in cytoplasm of Schwann-cells, and also in axons of myelinated and nonmyelinated nerves. The alterations of Schwann-cells and axons

are not very marked and the mycobacteria are mostly of good structure. An interesting point is that the well-structured *M. leprae* lodge in cells which are surrounded by basal lamina. These alterations of nerves greatly change with the type of disease in the immunologic spectrum. On the tuberculoid side we see the full picture of epithelioid cell granuloma mostly with destruction of the whole nerve and development of abscesses. It is possible that drugs cannot reach the bacteria in the nerves. The spread of bacteria can be by the blood or by the nerves, perhaps by axonal transport up to the ganglion. Whether or not drugs can reach the bacteria within the Schwann-cells and axons, like in the keratinocytes of outer root hair sheath and nevus cells, is discussed. This could be an explantion of the bad therapeutic results in this disease.—(*Adapted from* author's English summary)

Melsom, R., Naafs, B., Harboe, M. and Closs, O. Antibody activity against *Mycobacterium leprae* antigen 7 during the first year of DDS treatment in lepromatous (BL-LL) leprosy. Lepr. Rev. (1978) **49** 17-29.

A specific radioimmunoassay was developed for demonstration and quantitation of antibodies against *Mycobacterium leprae* antigen 7 which cross-react extensively with a similar antigen in many species of mycobacteria including BCG-antigen-60.

The antibody activity against *M. leprae* antigen 7 showed only a slight tendency to decrease in 15 patients with lepromatous leprosy during their first year of treatment with dapsone associated with marked clinical improvement.—Authors' Abstract

Nirmala, V., Chacko, C. J. G. and Job, C. K. Tuberculoid leprosy and tuberculosis skin —a comparative histopathological study. Lepr. India **49** (1977) 65-69.

Since it has been found hard to differentiate tuberculoid leprosy from tuberculosis of the skin histopathologically, a study of 20 biopsies from each of these conditions was undertaken to identify, if possible, some of their characteristic features.

In tuberculoid leprosy along with tuberculoid granulomata there is always selective involvement and destruction of nerves, lack of fibrosis, absence of caseous necrosis, and often epidermal atrophy. On the other hand, in cutaneous tuberculosis in addition to tuberculois granuloma there is often a proliferative reaction of the epidermis, areas of ulceration, absence of nerve destruction, marked increase in the reticulin, significant fibrosis and occasionally caseous necrosis. —(*Adapted from* Trop. Dis. Bull.)

[*The interested reader is reminded of the detailed, related manuscript of Wiersema, J. P. and Binford, C. H. in Int. J. Lepr.* **40** *(1972) 10-32.—Ed.*]

Park, Jang Kue and Lee, Yoo Shin. Clinical and histopathologic observation in patients with *erythema nodosum.* Korean J. Dermatol. **15** (1977) 379-388. (In Korean)

Erythema nodosum is a clinical entity defined easily but, because of the variable histopathologic findings showing involvement of the vessels, septa and fat lobules, the histopathologic features often are not compatible with the clinical diagnosis.

We present the results of clinical and histopathologic findings in 26 patients with *erythema nodosum* observed at the Department of Dermatology, Seoul National University Hospital, from January 1973 to August 1976.

1. Clinical findings: *erythema nodosum* is characterized by painful erythematous nodosum lesion occurring symmetrically (92%), on shins (50%), or shins and calves (50%) of women (M:F = 4:2), chiefly between 16-25 years of age (58%). In the laboratory study, leukocytosis (1/17) was rare but increased titers of antistreptolysin (64%) and elevation of E.S.R. (88%) were found frequently.

2. Histopathologic findings: even though hemorrhage (73%), perivascular (100%) and periadnexal (85%) inflammatory cell infiltration were frequently seen in histopathologic changes of *erythema nodosum,* these changes were nonspecific. Moreover, granulomatous change (38%), thrombophlebitis (35%) and necrosis of fatty tissue (38%) were observed not infrequently in *erythema nodosum.*

We concluded that there were no specific histopathologic findings in *erythema nodosum* which differentiated it from the other erythematous nodosum disease on the legs consisting of panniculitis, thrombophlebitis

or granulomatous changes.—(*Adapted from* Korean Med. Abstr.)

Ridley, M. J., Ridley, D. S. and Turk, J. L. Surface markers on lymphocytes and cells of the mononuclear phagocyte series in skin sections in leprosy. J. Pathol. **125** (1978) 91-98.

E, EA and EAC rosetting technics and Ig fluorescence were used in a study of receptor sites in cryostat sections of lesions through the spectrum of leprosy, and for comparison in some other mycobacterial and granulomatous lesions. Anti-C_3 and trypsin were used as blocking agents.

Lymphocytes in borderline lepromatous leprosy produced EA adherence and IgG fluorescence indicating B type cells. Lymphocytes in tuberculoid leprosy produced neither E or EA adherence and no fluorescence; these cells were presumed to be T cells.

EAC and EA adherence was more marked in areas of macrophage infiltration, where there were few lymphocytes, than over the lymphocytes themselves. Two distinct patterns emerged: 1) EA binding together with IgG fluorescence was seen in active lepromatous leprosy and could be localized to the surface of individual macrophages, and 2) EAC binding together with IgM fluorescence was seen in the granuloma of tuberculoid leprosy and sarcoidosis, but could not be definitely related to cell surface; rather it was diffusely spread over the whole granuloma; EAC adherence was diminished by anti-C_3 serum. Trypsin removed EA binding completely, but only diminished EAC adherence. It is suggested that the EA pattern indicates immunoglobulin receptors on macrophage and lymphocyte surfaces: and that the EAC binding (which is stronger than EA) involves C_3 and IgM receptors at extracellular sites as well as C_3 receptor sites on epithelioid cell surfaces.

EA and EAC binding were enhanced in borderline tuberculoid leprosy in reaction and *erythema nodosum leprosum,* suggesting that immunoglobulin and complement receptor sites increase in number with enhanced hypersensitivity.—Authors' Summary

Saha, K., Mittal, M. M. and Maheswari, H. B. An attempt at passive transfer of immunity to leprosy patients by transfusion of allogeneic lymphocytes inactivated with mitomycin C. Vox Sang. **34** (1978) 104-110.

An attempt was made to repair cell-mediated immunity in seven patients suffering from lepromatous leprosy and severe *erythema nodosum leprosum* by intravenous infusion of 400 million allogeneic blood lymphocytes on three occasions. The lymphocytes were obtained from lepromin and tuberculin-positive subjects and were inactivated *in vitro* by treatment with mitomycin C. Immunotherapy with inactivated lymphocytes only modifed the severity of *erythema nodosum leprosum,* without altering other aspects of the disease.—Authors' Abstract

Serjeantson, S. and Woodfield, D. G. Immune response of leprosy patients to hepatitis B virus. Am. J. Epidemiol. **107** (1978) 321-327.

The immune responses of 323 Melanesian leprosy patients and 290 controls to hepatitis virus type B were examined by analyzing prevalence rates of hepatitis B antigen (HBsAg) and its antibody (anti-HBs) in an area of Papua New Guinea hyperendemic for the virus. By use of multivariate technics, extraneous variables known to be correlated with both leprosy severity and HBsAg prevalence, such as institutionalization, age, sex and place of residence, could be statistically controlled. In multivariate analysis of HBsAg rates, after removal of the variation due to age, which was the most important single factor contributing to HBsAg carrier-status, lepromatous leprosy was a significant determinant of antigenemia. Similarly, when the series was grouped into three immune-response categories of HBsAg, anti-HBs or no serologic evidence of exposure to the virus, disease severity was a significant factor in determining immune response. For lepromatous and borderline lepromatous patients, the probability of responding antigenically to the virus, given that some measurable response has occurred (HBsAg/[HBsAg + anti-HBs]) was 0.42. The corresponding probability for tuberculoid patients was 0.25 and for healthy controls 0.29. These probabilities indicate that lepromatous patients have an impaired immune response that not only predisposes them to the most severe form of leprosy but may also decrease their effi-

ciency in terminating HBsAg infection with anti-HBs.—Authors' Abstract

Sharma, S., Sarin, R. C. and Parkash, S. Secondary amyloidosis in leprosy (a case report). Indian J. Dermatol., Venereol. Leprol. **44** (1978) 31-33.

A case of amyloidosis secondary to lepromatous leprosy is discussed. The patient had proteinuria, Congo red retention 64% (first hour), hyperglobulinemia and renal biopsy revealed amyloid depositis. Factors responsible for amyloidosis are highlighted.—Authors' Summary

Takata, H., Sada, M., Ozawa, S. and Sekiguchi, S. HLA and mycobacterial infection: increased frequency of B8 in Japanese leprosy. Tissue Antigens **11** (1978) 61-64.

A total of 60 leprosy patients, 28 of lepromatous and 32 of tuberculoid form, and 70 active tuberculosis patients were compared with a control of 184 persons for 34 HLA specificities. The most interesting finding was an increased frequency (10.0%) for HLA-B8 (corrected $P = 0.062$, relative risk = 20.3) in the leprosy patients as compared with the control group, despite the fact that B8 had leprous member(s) in their family.—Authors' Abstract

Thyagarajan, S. P., Subramanian, S., Solomon, S., Panchanadam, M. and Madanagopalan, N. Incidence of hepatitis B surface antigen and antibody in patients with liver diseases, blood donors and leprosy patients—a preliminary report. Indian J. Med. Res. **67** (1978) 528-534.

Preliminary observations are presented on the incidence of hepatitis surface antigen (HBsAg) and antibody (anti-HBs) in voluntary and professional blood donors, patients with liver disease and leprosy screened by CIEOP. It was noted that 4.9% of the professional blood donors and 1.6% of the voluntary blood donors were carriers of the HBs antigen; 4% of the voluntary and 1.6% of the professional blood donor had anti-HBs. The HBsAg positivity among 281 patients with viral hepatitis was 23.1%. The sera of 18.3% of the patients with CALD, 20% of the patients with primary carcinoma of the liver, and 10% with established cirrhosis of the liver were positive for HBsAg. Antigen positivity was also noted in a few patients with proven extra hepatic billiary tract obstruction, amoebic liver abscess and thalassemia with infantalism. Of the lepromatous leprosy patients, 10.4% had HBsAg while only 1.3% had anti-HBs in their serum. The incidence of HBsAg and anti-HBs was equal (5.05%) in patients with tuberculoid leprosy. Fifty-nine HBsAg positive cases were subtyped while 33 of these were not typable. Of the typables, 18 were of the "adr" subtype and 8 of the "ay" subtype. —(*Adapted from* authors' abstract)

Verma, K. C., Kumar, R. and Bhargava, N. C. Histopathologic study of liver in leprosy. Indian J. Dermatol. Venereol. Leprol. **44** (1978) 108-109.

Fifty patients with lepromatous leprosy were studied. Involvement of the liver was observed in 90% of the cases. Fatty degeneration was seen in only two cases; amyloid deposit was not seen in any of them. —(*Adapted from* authors' summary)

Yadav, S. S. Arteriographic evaulation of vascular changes in leprosy. Angiology **29** (1978) 17-21.

A large number of arteriograms (284) were performed in the hands and feet of 178 leprosy patients. Narrowing and tortuosity of the digital vessels, especially in the presence of bone absorption, were constant features. Digital tufts revealed signs of ischemia. However, in the presence of infection hyperemia was a definite observation. Diminution in the caliber of the digital arteries and thinning or absence of the vascular end loops prove that ischemia plays a vital role in the production of various lesions in leprosy. —(*Adapted from* author's summary)

Experimental Infections

Biswas, S. K. Growth of *Mycobacterium leprae* in thyroxine treated culture medium. A preliminary report. Lepr. India **50** (1978) 57-63.

A new approach in cultivation of *Mycobacterium leprae* in thyroxine treated Lowenstein-Jensen media is reported. The method has been proved to be successful as the organisms multiplied and remained viable in the thyroxine solution added at the bottom of the culture vial, for a period of 18 to 20 weeks of incubation at 37°C. This has been possible due to metabolic stimulating action of thyroxine sodium solution as well as diffusion of nutrients into this solution from the medium.

Intracutaneous inoculation of culture fluid on the surface of the foot pad in cortisone treated mouse helped in rapid appearance of the specific lesion at the site within 20 days after injection. Both the intracutaneous method of inoculation and treatment of mouse with high doses of cortisone may play some role in shortening the period of development of such lesion.—Author's Abstract

Campo-Aasen, I., and Convit, J., Host-parasite relationship between *Mycobacterium leprae* and hamster cheek-pouch cells. Acta Cient. Venez. **23** (1977) 150-154.

Optical and electron microscope studies were made of the pathology produced in the superficial lax connective tissue of the cheek-pouch of the golden hamster by inoculation of 1×10^6 *Mycobacterium leprae* taken from the nodules of human patients having active cases of lepromatous leprosy. The optical microscope showed bacilli in phagocytes and a lepromatous reaction more or less differentiated toward the tuberculoid type. The electron microscope revealed the presence of autophagic vacuoles, dense bodies, multivesicular bodies and mitochondrial alterations; foamy structures, leprous inclusions, together with degenerating bacilli within the phagocytic cells. In the adjacent muscle, there was peripheral myopathy consisting of edema, protrusion of the sarcolemma, disorganization of the myofibrils, and vacuolar increase in the reticulo-sarcoplasmic system. Since the contralateral pouches utilized as controls showed no significant alterations, the observed pathologic changes were attributed possibly to the presence of *Mycobacterium leprae*—although it is known to be incapable of producing toxins—or to the lymphokines produced by the lymphocytes of the granulomatous reaction.—Authors' Abstract

Kunigoshi, U., Fukushi, K. and Kawatsu, K. The effect of *E. coli*-12 treated with liquid paraffin against the development of experimental murine leprosy in mice. Jap. J. Lepr. **46** (1977) 79-84. (In Japanese)

Mice were divided into two groups: a control group and a treated group. One tenth mg of *E. coli*-12 cells, was frozen and dried and emazol-liquid-paraffin (10%) was added at once until it was easily dispersed and penetrated thoroughly by the cells and then water was added. This mixture was heated in warm water (less that 50°C) and diluted 1,500-fold or 4,000-fold. This constituted an oil-in-water-in-oil-in-water emulsion and was referred to as A-emulsion. The A-emulsion was kept at 4°C until used. Its characteristic feature was that it never separated into separate components, even when it was kept quiet. Then a preparation of water-in-oil-in-water emulsion was made and kept by means of the above mentioned process except without freezing and drying the *E. coli*-12 cells (referred to as B-emulsion). Its striking characteristic was that the cells were more swollen so the 10% Emazol-paraffin was little dispersed and penetrated into them, and therefore it was easily separated into components when it was kept quiet.

The treated mice had previously been given subcutaneous and intraperitoneal injections of 0.1 mg either of the A or B-emulsion simultaneously twice a week for one month. One week later all the animals were subcutaneously injected with 0.1 mg of *M. lepraemurium*. At the end of the experiment all survivors were killed for macroscopic and microscopic studies. Pathologic appearance was as follows: severe destructive leprous lesions were recognized in the control groups. Multiplication of histiocytes accompanied multiplication of the bacilli becoming a specific nodular mass of histiocytes with the formation of murine lepromas accompanied by slight perivascular infiltration of inflammatory cells. Formations called globi could be found in the control groups. In marked contrast there was regression of active lesions in the A-emulsion treated groups with the formation of epithelioid granulomas sometimes containing Langhans type giant cells, and including granular shaped degenerative acid-fast bacilli. There were inflammatory cells surrounding the granulomas.

It is concluded that the A-emulsion treated

groups revealed more protective power against the development of progressive leprosy as determined by the clinical, macroscopic and microscopic examinations. The principle utilized here can be applied not only to the treatment of inflammatory diseases but also can probably be on the high road of paving the way for the immunotherapy of malignant tumors.—(*Adapted from* English summary)

Lampe, David. The armadillo blunders on. Natl. Wildlife Feb.-Mch. (1977) 35-37.

Farmers and gardeners in Texas curse it for uprooting their seedlings. Hunters in the Lone Star State insist that it wantonly plunders eggs from the nests of wild turkeys and quail. And Texas ranchers blame its countless burrows for crippling their livestock. The party in question is the nine-banded armadillo, a nearly deaf, blind and dumb living fossil that for years has endured the kind of calumny and vituperation that Texans normally reserve for pests.

A holdover from the age of the dinosaurs some 75 million years ago, the armadillo looks like a creature from another planet—or a science fiction screenwriter's version of one. About two feet long (including the tail), the armadillo weighs up to 17 pounds. Its greatest asset is its heavy armor. Small animals can't bite through its protective shell, so when the armadillo is attacked, its first reaction is to roll into a tight ball. Unfortunately, because of the armor's configuration such a feat is virtually impossible. Unlike its three-banded South American cousin, the nine-banded armadillo cannot draw in its head—which appears to be armored but is, in fact, easily crushed. Most animals that attack it, however usually go for its hairless, unprotected underbelly. If it escapes [from being caught] the armadillo heads for the dirt, burying itself completely in about two minutes. And if caught by the tail while in the act of burrowing, the animal swells its flanks until its "shell" plates wedge into the earth like a partially opened umbrella.

Researchers in at least three different scientific disciplines are currently taking a look at the Texas armadillo. Geneticists are intrigued by the fact that the armadillo's births are always of identical quadruplets, right down to the same number of hairs on each body. Climatologists suspect that fluctuations in its population and range can help measure long-range climatic changes. Medical researchers studying leprosy use it as a "guinea pig." Researchers at the U.S. Public Health Services's leprosy center in Carville, Louisiana have managed to keep more than 100 nine-banded armadillos captive for long periods, but so far they have been unable to breed them.

The armadillo's alleged bad habits [e.g., uprooting seedlings on farms, burrowing holes in suburban lawns and golf courses] are much easier to understand than is its propensity for "suicide" on Texas highways. Unquestionably, the automobile is the most dangerous enemy that the armadillo has had to cope with throughout its long history. Venturing ontò roadways at dusk to enjoy the last lingering sun rays, dozens of armadillos are run down by cars each day. Many would probably survive such encounters quite easily by standing still, crouching down and letting the machines pass right over them. But armadillos are biologically unable to control the reflexes that cause them to leap several feet straight up when startled. It is as if they choose to leap to their deaths rather than take the easy way out. But then, any animal with so many odd habits is bound to act a little weird in the face of adversity.—(*Excerpted from* author's article)

Minagawa, F., Yoshino, Y. and Abe, M. Early immune responses in nude mice following intravenous injection of *Mycobacterium leprae.* Jap. J. Lepr. **47** (1978) 37-42.

For the purpose of elucidating the immune mechanism in the early stage of leprosy, three strains of mice, conventional BALB/c, SPF BALB/c-nu/+ and BALB/c-nu/nu mice, were injected intravenously with a mixture of 10^7 *M. leprae* and 10^8 sheep red blood cells. All of these mice showed a similar degree of antibody response to *M. leprae,* as demonstrated by indirect immunofluorescence, the antibody-titer reaching the maximum within a week after the injection of antigens. The production of IgG antibodies was somewhat delayed and the titer reached a plateau within two or three weeks. No decline of antibody-titer was observed till at least five weeks after the injection of antigens. The transfer of thymocytes from immunized nu/+ donors to nu/nu recipients did not in-

fluence the antibody-titer in the recipient.

Both agglutinins and hemolysins to sheep red blood cells were less produced in nu/nu mice than in nu/+ and conventional mice. After the transfer of thymocytes followed by a second injection of antigens, nude mice showed a low level of antibody response which was sensitive to mercapto-ethanol treatment. *In vitro* transformation of spleen cells to *M. leprae* antigens did not occur in any of the mice, except for a positive response by one nude mouse into which thymocytes from immunized donor and a second injection of antigens were given.

From these observations it may be concluded that the production of anti-*M. leprae* antibodies is thymus-independent and that this immune response can be induced at an early stage of leprosy infection without induction of cell-mediated immunity.—(*Adapted from* authors' summary)

Patel, P. J. and Lefford, M. J. Induction of cell-mediated immunity to *Mycobacterium leprae* in mice. Infect. Immun. **19** (1978) 87-93.

The immune response of mice to armadillo-derived, irradiation-killed *Mycobacterium leprae* (I-ML) was investigated. Following injection of 100 μg of I-ML into the left hind foot pads of mice, a state of cell-mediated immunity (CMI) was engendered to antigens of *M. leprae*. The evidence for CMI was as follows: (i) development of delayed-type hypersensitivity to both human tuberculin purified protein derivative and soluble *M. leprae* antigens; (ii) T- lymphocyte-dependent macrophage activation at the inoculation site; (iii) specific systemic resistance to the cross-reactive species *M. tuberculosis;* and (iv) immunopotentiation of the delayed-type hypersensitivity response to an unrelated antigen. The CMI induced by I-ML in aqueous suspension was greater than that obtained with the same antigen in water-in-oil emulsion, even though the latter generated a more severe reaction at the site of immunization. I-ML also induced a stronger CMI response than the corresponding dose of heat-killed BCG.—Authors' Abstract

Shepard, C. C., Walker, L. L. and Van Landingham, R. M. Immunity to *Mycobacterium leprae* infections induced in mice by BCG vaccination at different times before or after challenge. Infect. Immun. **19** (1978) 391-394.

Viable suspensions of BCG, an attenuated strain of *Mycobacterium bovis,* have been previously shown to immunize mice against infections with *M. leprae.* Usually the mice have been vaccinated about one month before challenge. Experiments have now been carried out with single intradermal injections of BCG given before or after the *M. leprae* challenge. Approximately equal immunizing effect was seen in one experiment when the BCG was given at -168, -119, -70, and -28 days relative to challenge. Approximately equal protection was observed in another experiment when the vaccine was given at -28, +28, and +56 days. In the latter experiment, however, vaccine given at +91 days appeared to be somewhat less effective. Enlargement of the lymph nodes regional to the intradermal vaccine site persisted for at least the duration of the experiment, approximately 400 days. Thus, antigenic stimulation appears to have continued throughout the period of observation.—Authors' Abstract

Epidemiology and Prevention

Filice, Gregory A. and Fraser, David W. Management of household contacts of leprosy patients. Ann. Intern. Med. **88** (1978) 538-542.

The authors describe an approach to the management of household contacts of leprosy patients and the rationale on which it is based. Initially, all household contacts should be interviewed and examined for symptoms and signs consistent with leprosy and appropriate diagnostic measures taken. Contacts of untreated lepromatous and dimorphous (borderline) leprosy patients are at relatively high risk of disease and should be examined annually for at least five years. Dapsone prophylaxis has been shown to prevent secondary cases in contacts up to 25 years old and should be used in these and possibly in older persons. Insufficient data

exist to support a recommendation for the use of BCG at present.—Authors' Abstract

Ganapati, R., Revankar, C. R., Christina and Romano. Associated cases in the families of school children with leprosy. Lepr. Rev. **49** (1978) 43-46.

The screening of 190 families in which children suffering from leprosy discovered through school surveys were present, yielded a total of 41 cases. Though the prevalence rate among the contacts was 44 per thousand, only in 14% of the families visited could another associated case be found, and only in 2 instances out of 27 families did the associated case belonged to L type. The school surveys as well as contact examination yielded predominantly cases belonging to non-lepromatous type mostly with single lesions whose contribution to the pool of infection in the community is questionable.—(*Adapted from* authors' abstract)

Honey, Norman R. Leprosy in Hong Kong, past present and future. Soc. Community Med. H.K. Bull. **9** (1978) 22-28.

During the past two decades, the incidence of leprosy declined from a peak of 16.2 per 100,000 population in 1956 to a low level of 1.7 per 100,000 population in 1976. The decline appears to be associated with the use of specific antileprotic drugs, improved socio-economic conditions and migration patterns. During the period segregation of patients has almost ceased and management of patients is now based on the knowledge that bacteriologically positive patients become non-infectious after a short period of treatment.—Author's Summary

Kaur, Paramjit. Prevention of leprosy. Indian J. Dermatol. Venereol. Leprol. **44** (1978) 12-15.

Leprosy evolves over a long period and after the time of contact it takes a long time before pathologic changes become evident. Prevention may be achieved by increasing the level of detection and controlling the risk factors. In this paper the methods of prevention of leprosy are described. Primary prevention, or prophylaxis is of prime importance and can be achieved by reducing an individual's susceptibility as well as by reducing his/her exposure to susceptible individuals. The former needs general health promotion, immunoprophylaxis and chemoprophylaxis. The latter is achieved by isolation and early detection of cases. A critical review of merits and demerits of these measures is presented. Secondary prevention is through early detection of cases and their prompt treatment. Tertiary prevention is the prevention of deformities and rehabilitation of those who are already disabled.—(*Adapted from* author's summary)

McDougall, A. C. and Rose, P. Integrated leprosy control in Guyana. Bull. Pan Am. Health Org. **12** (1978) 11-17.

Guyana's leprosy problem is small compared to that of some South American countries. On the other hand, there is a nagging incidence of new cases, despite adequate treatment and diagnostic facilities, which is similar to the situation found in portions of the neighboring Caribbean and in some other parts of the world.

After more than a century of leprosarium-based treatment, a "find and treat" program using existing outpatient facilities was initiated in 1971. This has proved successful and has been well accepted by patients, medical staff members, and the general public.

Particular attention is now being paid to the yearly incidence of new cases in assessing the continuing effectiveness of this program. It is possible that reduced incidence and further impetus toward eradication may be achieved through improved health education (including the definitive closure of the existing leprosarium), prolonged periods of regular treatment (particularly for bacillipositive patients), and intensive examination of schoolchildren and household contacts. On the other hand, it may be helpful to consider a more detailed analysis of the situation if the incidence does not fall. In fact, there may be a case for conducting a detailed epidemiologic study of all new cases diagnosed since 1971. Such a study might contribute toward the eradication of leprosy not only in Guyana, but also in other countries with a small yearly incidence where the disease is potentially—but not actually—under control.—Authors' Summary

Nigam, P., Verma, B. L. and Srivastava, R. N. Leprosy—a clinico-epidemiologic study in a rural population of Bundelkhand. Lepr. India **49** (1977) 349-359.

The present study was carried out in three villages viz. Kochha Bhanwar, Kargawan and Pichhore, situated within a three kilometer radius of the M.L.B. Medical College, Jhansi, U.P. About 91% (91.7%) of the population was surveyed. Out of the 3,362 individuals studied, 18 cases of leprosy were detected, giving a prevalence rate of 5.41/1,000 population. No association between the size of the village and the prevalence of leprosy cases was observed. The highest prevalence rate (7.40/1,000) was seen in the 15-49 years age group with a male to female ratio of 2.6:1. The disease was not prevalent in the preschool age group. Comparatively, the poor class of people contributed to a greater extent (6.37/1,000). The size of the family also did not seem to be associated with the prevalence of the disease. More than one case of leprosy in a family was observed in 30.7% of the families. Early cases of leprosy remained acceptable in rural society whereas advanced cases were not acceptable. The disease seemed to manifest itself at all ages except the preschool age group. The majority of the cases (66.56%) were of an early stage with a duration of the disease of less than two years. Possibilities of arresting the disease by early diagnosis and prompt and proper treatment are emphasized.—(*Adapted from* authors' summary)

Rampen, Frans. The dermatological clinic in a leprosy control scheme: Ten years' experience in Malawi. Lepr. Rev. **49** (1978) 141-147.

A few years after starting a leprosy control scheme in the southern part of Malawi, it became clear that increasing numbers of patients with general dermatological conditions were being referred to the leprologist for diagnosis and treatment. Weekly clinics were therefore established in the two urban centers of the control area, and between 1968 and 1975 over 9,000 new patients were seen. This paper describes the main conditions diagnosed during these years, listing those of one recent year (1975) in detail. Many curable conditions were seen and the clinics were also a valuable source of new cases of leprosy. The role of the general skin clinic within a leprosy control program (and in a country with nearly five million people and no dermatologist) is discussed, and it is concluded that it may be of considerable diagnostic, therapeutic and research value.—Author's Abstract

Ratard, R. C. and Bravo, L. L. The epidemiology of leprosy in the New Hebrides. Lepr. Rev **49** (1978) 31-42.

The epidemiologic study of leprosy in the New Hebrides was based on a survey of the population (41% coverage), and the results of 20 years of case finding. The annual incidence of new cases is 0.45 per thousand. Thirteen percent are of the lepromatous type. Leprosy predominates among males. The incidence of leprosy cases increases with age until the age group 30 to 44. Leprosy is concentrated in families, in villages and in foci in which the prevalence is high. The prevalence is also very high among contacts. Most of the foci are well under control but some are still developing. In some areas there is a possibility of a small outbreak occurring. Leprosy being one of the major public health problems in the New Hebrides, a careful and selective control program is indispensable.—Authors' Abstract

White, S. J., Stone, M. M. and Howland, C. Genetic factors in leprosy: a study of children in Uganda. J. Hyg. (Camb.) **80** (1978) 205-216.

A group of 20,990 children in Uganda was examined for leprosy over a period of eight years. There was no evidence that the incidence of leprosy varied according to a child's genetic relationship to a leprosy patient, once allowance had been made for the grade of physical contact.

The present study aimed to examine the occurrence of leprosy in a large group of children with differing family (genetic) histories of leprosy, to see if the effect of a genetic factor could be shown. The data on family history and degree of exposure to the disease were necessarily limited, but should have been sufficient to reveal any important genetic influence. That such an influence was not shown was due partly to the difficulty of distinguishing genetic from environmental

effects for many of the children. However, for the children for whom the effects could be separated no evidence of a genetic factor was found. Thus the conclusion is that, if a genetic component of susceptibility existed, its influence was small. The large apparent differences according to genetic relationship may therefore be attributed to the differing degrees of physical contact.

In this study it was unfortunately not possible to examine the occurrence of leprosy in only those children with a lepromatous contact, since the numbers were small. Since the ability to develop lepromatous leprosy may be a genetically transmitted character (Beiguelman, 1972; Newell, 1966), it would be of interest to study this in a population with a higher proportion of lepromatous cases.—(*Excerpted* from text)

World Health Organization. Strategy of leprosy control. WHO Chronicle **32** (1978) 193-199.

Use of the primary health care approach with active community participation should be possible in leprosy control programs provided that the primary health care workers are adequately trained to make a tentative diagnosis of leprosy and are given full support from higher levels of the health service. A suitable strategy for leprosy control must take into account case detection and bacteriology, contact surveillance, classification of patients and their disabilities, treatment, rehabilitation measures, management of relapse, and prophylaxis. The most recent (fifth) report of the WHO Expert Committee on Leprosy dealt with this subject and the article is based on this section of the report. —Author's Abstract

Rehabilitation

Mehendale, M. S. and Shriyan, S. K. Prospects of rehabilitation of leprosy patients through self-employment. NLO Newsletter **6** (1978) 103-114.

Long-term hospitalized leprosy patients were selected for this project. Many had lost contact with their families and had lost their previous jobs, if any. The main condition was that the patients must work in their own villages. They were to be given initial financial assistance in the form of loans. This article describes the work done with respect to the 18 patients included in the project during the first year.

Some general observations are as follows:

1. Eagerness on the part of the elder patients to go home and get resettled is manifest from this experience.

2. Patients are generally well received in the family and the village leaders do not raise objections. They remain content with certificates, etc. given by the hospital authorities. In some cases, however, some members of the family of the patient (viz. brothers and in-laws) did not welcome the patient. This was due to vested interests. The patient's property and resources had been used by his relatives for long periods of time and the latter did not easily give up such resources to the patient.

3. Readmissions to the leprosy hospital are few. The patients do take care of themselves and take regular treatment. Even the two patients who had to be admitted for two and four to five months, respectively, were anxious to return at the earliest possible opportunity.

4. The patients cooperate eagerly with authorities of the hospital whenever they are invited for follow-up or in meeting the visitors to Bandorawalla Leprosy Hospital.

5. The initial response to this scheme from the patients was quite slow, guarded and reserved. Some patients even thought that this was a scheme to drive them out of the hospital. However, once they saw that money was actually received by the patients and that the patients did go home, many patients came forth to seek help.

6. Later, a tendency was observed among the patients to mutually help their fellow patients. Thus they offered surety, use of their house for work, etc. to other patients.

7. The scheme has created a deep impact on the existing patients in our hospital, resulting in greater morale and increased effort on their part to get rehabilitated.

8. Bad debts: it is too early to assess whether there will be cases of bad debts. However, judging from the trend observed so far, it is reasonable to expect none. Only time will prove or disprove this aspect.—(*Adapted from* authors' article)

Mutatkar, R. K. Health education in leprosy. An evaluation. Lepr. India **49** (1977) 234-239.

This is an evaluation by the University of Poona of health education programs related to leprosy pioneered in that city by the Gandhi Memorial Leprosy Foundation, and undertaken on behalf of the Foundation. Two areas are compared and random sampling methods employed. The study indicates that the methods employed have effectively changed both attitudes and behavior of the people towards leprosy, but the process is slow and needs repeated contact between educator and people in a continuous program.—T. F. Davey (*From* Trop. Dis. Bull.)

Other Mycobacterial Diseases and Related Entities

Edlin, G. P. Active tuberculosis unrecognized until necropsy. Lancet **1** (1978) 650-652.

Twelve of the 24 cases of active tuberculosis which came to necropsy in Dundee hospitals from 1968 to 1975 were diagnosed after death. The overall distribution of anatomical types was similar to that in previous surveys, but in those diagnosed at necropsy there was an excess of psoas abscess and miliary, colonic, and adrenal lesions. Class-IV patients and a history of steroid therapy were also more common in cases diagnosed at necropsy. None of these differences is statistically significant.—Author's Abstract

Panitch, Martha L. and Levy, Louis. The action of dapsone on a susceptible strain of *Mycobacterium kansasii.* Lepr. Rev. **49** (1978) 131-140.

Because studies of the action of dapsone on *Mycobacterium leprae* have been obstructed by the need to conduct the studies in infected animals, a study of the action of the drug has been carried out on a strain of *M. kansasii* shown to be inhibited by 0.3 μg dapsone per ml, a concentration 100 times larger than the minimal inhibitory concentration of the drug for *M. leprae.* In stationary broth cultures, dapsone was bactericidal in concentrations of 1.0 μg per ml or larger; populations of *M. kansasii* as small as 1.7×10^6 organisms appeared to contain individuals resistant to 1.0 and 10 μg dapsone per ml. The organisms were shown to bind the drug against a concentration gradient. The action of the drug was antagonized by 4-amino-benzoic acid (PABA) in a mole ratio (PABA:dapsone) of 2:1. PABA itself, in a concentration of 10 μg per ml, inhibited multiplication of this strain of *M. kansasii.* —Authors' Abstract

Peters, Manfred and Kazda, Jindrich. Vergleichende tierexperimentelle Untersuchung mit Mykobacterium intracellulare Serotyp Davis zur Frage der Pathogenität und Virulenz. [Comparative experiments in animals with *Mycobacterium intracellulare* Serotype Davis with particular reference to pathogenicity and virulence.] Zentralbl. Bakteriol. [Orig. A] **239** (1977) 70-86. (In German)

Histogenesis and structure of tuberculous inflammation has been well studied. Histopathologic research of infection with atypical mycobacteria is not very often done and the results are doubtful. Comparative histologic examinations in the different groups of atypical mycobacteria cannot be found. In the case of differentiating atypical mycobacteria the lack of histopathologic findings is very important, because pathogenicity and virulence are the main criteria in this field. In our own animal experiments with rabbits, guinea pigs and mice we examined the pathogenicity and virulence of a strain of atypical mycobacteria of group III, *M. intracellulare* Serotype Davis with special reference to histopathologic examination. After intracutaneous, subcutaneous and intramuscular injection of different doses of the mycobacteria, we saw localized abscess-formations in rabbits and guinea pigs, but never after intramuscular injection of rabbits. A repeated oral infection was ineffective in these ani-

mals. Only one rabbit died after intravenous injection of different doses. The infection of the intraperitoneal route in guinea pigs led to an intensive tuberculous inflammation of the abdominal cavity and only three of the animals survived. After subcutaneous, intracutaneous, intramuscular, intravenous and intraperitoneal infection we saw in some animals in the liver, spleen and kidney a localized abscess-formation, consisting of necrotic leukocytes surrounded by a tuberculous-like granuloma of epithelioid cells and multinucleated giant cells. In some animals we found additional scanty tuberculous granulomas of epithelioid cells and giant cells in the liver. We never found in this study a generalized tuberculous inflammation.

The foot pad infection of the mouse was localized in the hind foot pad without any extension. A comparative histologic examination in rabbits, guinea pigs and mice showed in a week a localized suppuration of the skin consisting of a decay of leukocytes. During a six-week period we found in this initial leukocytic inflammation the development of a granulation tissue consisting of mononuclear cells, macrophages, epithelioid-like cells, multinucleated giant cells of the Langhans type, and foreign body giant cells. We never saw typical tuberculous granulomas in the skin. In the mouse foot pad there was an intensive leukocytic inflammation with suppuration, later developing nonspecific granulation tissue. After intracutaneous injection of dead mycobacteria of the same strain, we found in the skin of rabbits and guinea pigs a tuberculous granuloma with epithelioid cells arranged in a palisade manner and giant cells of the Langhans type as well as foreign body giant cells. The cause of this different kind of tissue reaction after injection of living and dead mycobacteria of the same strain is not yet clear. The nontuberculous character of the inflammation after injection of living mycobacteria, the abscess-formation in the skin and the organs, and the incomplete tuberculous granulation tissue may be due to the following reasons: a quick elimination of the causative germ, a massive infection, a reaction to metabolic processes of the mycobacteria, a low toxicity to macrophages and a low activation of the monocyte-macrophage system or a species-specific reaction of the host.

We have to do research in this field especially by electron microscopy and enzyme-histochemistry. The virulence of this mycobacterium is very low for rabbits, guinea pigs and mice because we saw only in a few cases propagation of the mycobacteria in the place of injection. The pathogenicity of this strain was demonstrated in a localized suppuration in the skin and organs in the place of settlement of the mycobacteria. This tissue reaction to the invasion of living mycobacteria seems to be a typical characteristic of this strain.—(*Adapted from* author's English abstract)