

CURRENT LITERATURE

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Clinical Sciences

✓ **Bergtholdt, Harry T. and Brand, Paul W.** Thermography: an aid in the management of insensitive feet and stumps. *Arch. Phys. Med. Rehabil.* **56** (1975) 205-209.

Infrared thermography contributes to the care of insensitive limbs. The inflammatory response of near damaged or damaged tissue presents areas of increased heat on the surface which can be detected and followed. Thermography was found to be a valuable aid to the established management methods used for insensitivity problems including management of healing and freshly healed ulcerations, management of neuropathic bone and joint problems and fitting of prosthetic devices and custom shoes. The most important contribution thermography offered was the detection of irritated tissue prior to frank breakdown, often in time to prevent permanent injury if quick and effective management followed.—Authors' Abstract

✓ **Cooper, Carlos. T., Jr.** Hansen's disease: a podiatrist's experience. *J. Am. Podiatry Assoc.* **65** (1975) 300-309.

This article discusses podiatric complications of Hansen's disease, which the author treated during a trip to Nigeria. The nature and mode of transmission of Hansen's disease is briefly discussed. The author also describes various ways in which the disease affects the foot, and the methods used to treat the disorders. These methods include reduction of excrescences, debridement of tissue, redistribution of weight by padding, treatment of ulcers and surgical intervention. The author stresses the importance of educating the patient with Hansen's disease in proper foot care. Finally, the author discusses the fabrication of molded foot gear to afford the patient greater mobility and comfort.—Author's Abstract

✓ **Crawford, C.L.** Nerve grafting in leprosy. *Lancet* **II** (1975) 326. (Letter to Editor)

Sir: In your annotation (Aug. 2, p 216), you describe McLeod *et al*'s work on nerve grafting in leprosy to correct sensory loss leading to "burns, trophic ulcers, cellulitis, osteomyelitis, and bone absorption." These operations would have a rational basis if such sensory complications were caused by a localized lesion of an individual nerve such as the median, ulnar or posterior tibial, i.e., a mononeuritis or mononeuritis multiplex. But they are not. Instead they are due to a sensory polyneuritis as clinical examination of patients with these complications would reveal. Multiple mononeuropathies from other causes are not associated with these sensory complications. McLeod *et al* do not give details of the distribution of sensory loss in their patients before operation. For these reasons, nerve grafting operations should not be performed in leprosy patients. The question of sensory loss in leprosy has previously been ventilated in your correspondence columns, and it is surprising that you have ignored these facts.—Author's Letter to Editor

✓ **Fasal, Paul.** But it was not leprosy. *Cutis* **15** (1975) 499-508.

Leprosy is known to be a great imitator and is able to imitate most diseases of the skin and some diseases of the peripheral nerves. It is essential that a high index of suspicion be maintained in order not to miss diagnosis of the disease. However, if the index of suspicion for the disease is too high, then there is an increased chance that patients will be considered afflicted with leprosy, when in fact they do not have the disease. This article describes a number of such patients who are arranged in four

groups: 1) patients presenting clinical manifestations very suggestive of leprosy; 2) patients whose manifestations were not truly characteristic or suggestive of leprosy, but who were suspected of suffering from the disease because they showed mutilations and disfigurements; 3) contacts of patients with leprosy, usually family members; and 4) individuals seen during leprosy surveys in endemic areas.

To misdiagnose a person as having leprosy can cause great mental suffering for the individual involved and can also cause hardship by depriving him of the treatment indicated for his condition. Both situations should and can be avoided by combining a high index of suspicion of leprosy with stringent diagnostic criteria, which must include histopathologic examination of skin biopsy specimens. [There are very nicely illustrated color, and black and white photographs of clinical entities resembling leprosy.]—(Adapted from author's article)

Jagadeesan, K., Visweswaran, M.K. and Iyer, K.H. Acute abdomen in a patient treated with Lamprene. *Int. Surg.* **60** (1975) 208–209.

Patients receiving Lamprene may develop acute abdominal symptoms which simulate an abdominal emergency. Withdrawal of the drug relieves these symptoms. The absorption of Lamprene can be increased and deposition in the reticuloendothelial system as crystals can be avoided if it is administered in an alcoholic medium.—Authors' Summary

Kenzhebaev, A.Ia. Impairment of intestinal absorption of vitamin B₁₂ in leprosy. *Vestn. Dermatol. Venerol.* **8** (1974) 67–70. (In Russian)

Investigations of intestinal absorption of vitamin B₁₂ were conducted in 50 patients with leprosy of different types using vitamin B₁₂ Co 58. The rate and degree of impairment of vitamin B₁₂ intestinal absorption was found to be influenced most greatly by the severity of the clinical course, type and duration of leprosy.—English Summary

Lal, Sardari and Gupta, A.K. Lenticular deposits associated with chloroquine keratopathy. *Indian J. Ophthalmol.* **22** (1974) 34–35.

A case of a 30 year old male suffering from lepromatous leprosy, who showed lenticular deposits along with chloroquine keratopathy, is reported. Corneal as well as lenticular deposits decreased on discontinuing chloroquine therapy.—Authors' Summary

Miner, K.M., Shipley, D.E. and Enna, C.D. Rehabilitation of the paralytic drop foot in Hansen's disease. *Phys. Ther.* **55** (1975) 378–381.

Drop foot, resulting from paralysis of the deep branch of the common peroneal nerve, is a frequent complication of patients with Hansen's disease. Specific routines have been established at the U.S. Public Health Service Hospital in Carville, Louisiana to deal with the drop foot which has been managed by a tendon transfer procedure. These routines are supplemented by careful monitoring of tissue temperatures, volume, and joint mobility which serves as a guide for progressing treatment programs and determining the time when concentrated physical therapy can be discontinued.—Authors' Introduction

Nebout, Max. Observation d'un cas de lèpre tuberculoïde nodulaire consécutive à des scarifications rituelles. [Report of a case of nodular tuberculoid leprosy following ritual scarification.] *Med. Afr. Noire* **21** (1974) 867–870.

In 1945, three years after ritual scarifications were made with an unsterile metal instrument on a male aged 15 years of the Central African Republic, large nodules began to appear in the resulting cheloid scars on the face. Nearly 25 years later, similar nodules developed in a symmetrical pattern on the thoracic wall and afterwards on the limbs. Some loss of sensation was demonstrable in the skin over the lesions. No other signs were present (the state of the peripheral nerves is not recorded) and the chest x-ray was normal. Although no *Mycobacterium leprae* were seen, the histological diagnosis of "typical tuberculoid leprosy" was made. After a year's standard treatment, the nodular lesions had completely disappeared. The author suggests that leprosy bacilli must have been introduced at the time of the ritual scarifications through a breach in the skin.

He summarizes usefully the nine recorded

cases in which percutaneous introduction of leprosy bacilli is presumed largely on anecdotal history.

[The present report leaves many crucial questions unanswered (and unasked). A very rare form of nodular tuberculoid leprosy, which disappeared spectacularly after a year's treatment, requires better substantiation than the author provides before it can be admitted as another instance of an inoculated leprosy infection.]—S. G. Browne (*From Trop. Dis. Bull.*)

✓ **Palande, Dinkar D.** Opponensplasty in intrinsic-muscle paralysis of the thumb in leprosy. *J. Bone Joint Surg. (Am.)* **57-A** (1975) 489-493.

For 86 cases of leprosy paralysis of the intrinsic muscles of the hand, a modified Bunnell opponensplasty (transfer of a finger flexor) was done. Good results were seen in 18 and fair results in 63. The five poor results occurred because of infection, weakness or deformity. Adjuvant procedures, as needed, were interphalangeal arthrodesis of the thumb, capsulorrhaphy of the wrist, and additional tendon transfers.—Author's Abstract

✓ **Rose, Patricia and McDougall, Colin.** Adverse reactions following pregnancy in

patients with borderline (dimorphous) leprosy. *Lepr. Rev.* **46** (1975) 109-114.

Following pregnancy, adverse reactions are described in seven patients suffering from borderline (dimorphous) leprosy. The reactions in most cases were sudden and severe; nerve damage often occurred within the space of a day or so, with resultant paralysis and anesthesia. Some of these patients were seen in remote areas, and on clinical signs alone it was not possible to distinguish between immunologically beneficial (upgrading, reversal) and immunologically detrimental (downgrading) reactions. However, their spontaneous occurrence following pregnancy, and the fact that cell-mediated (not humoral) immune factors are known to be involved in this type of reaction, raise the possibility that they may have been precipitated by a return of cell-mediated competence following pregnancy. These reactions frequently cause tissue damage, and this is most important in peripheral nerves; their pathogenesis is as yet poorly understood. The possible significance of their occurrence in or following the puerperium is discussed in relation to recent research on depression of cell-mediated immune responses in pregnancy, and in women taking the contraceptive pill.—Authors' Summary

Chemotherapy

✓ **Azulay, R.D.** Personal experience with clofazimine in the treatment of leprosy. *Br. J. Dermatol.* **93** (1975) 13-14. (Summary of paper only)

We have treated 20 cases of advanced lepromatous leprosy with clofazimine. They were adults, predominantly male (all Brazilian except for one Portuguese) who had been afflicted with leprosy for 1 to 28 years, most of them being long-standing cases (16 for over ten years); 15 of the 20 were sulfone resistant cases. They were treated during five years with the initial daily dose being 200 mg which was later decreased to 100 mg.

Eighteen cases had a complete regression of the skin and mucosal lesions; in the other two the regression was marked. All cases became negative. The lepromatous infiltra-

tion practically disappeared; brownish pigmentation was observed in both the epidermis and dermis.

Before treatment, 11 of 20 cases had a positive reaction which disappeared with the treatment. The side effects were minor: reddish and dark pigmentation and ichthyosis-like lesions were observed as well as some infrequent dyspeptic symptoms.—(*Adapted from author's summary*)

✓ **Beiguelman, B., Pinto, W., Jr., El-Guindy, M. and Krieger, H.** Factors influencing the level of dapsone in blood. *Bull. WHO* **51** (1974) 467-471.

The level of dapsone in the blood four and six hours after the ingestion of the seventh daily dose of 100 mg of the drug was investigated in 36 adult males with leprosy who

had normal renal function and were free of diarrhea and emesis. The bimodal distribution of the dapsone levels at six hours was shown by multiple regression analysis to be due to a negative correlation between this trait and the hematocrit value. Among the patients with high dapsone blood levels, 81.8% presented hematocrit values under 36%, whereas only 20% of those with low levels showed low hematocrit values. Partial regression coefficients, calculated for the dapsone level on the age, weight of the patient, estimated number of years since the onset of leprosy, number of years under sulfone treatment, and blood levels of hemoglobin, albumin, and globulins, did not show statistical significance.—Authors' Abstract

Biggs, J. T., Jr., Uher, A. K., Levy, L., Gordon, G. R. and Peters, J. H. Renal and biliary disposition of dapsone in the dog. *Antimicrob. Agents Chemother.* 7 (1975) 816-824.

Dapsone (DDS) was administered intravenously to anesthetized dogs; urine was collected, heparinized venous blood was obtained, and bile was collected from some of the dogs. A constant infusion of inulin was maintained, and isosmotic or hyposmotic fluids were administered. Dogs were studied under conditions of standardized, increased or decreased urine flow, and before and after plasmapheresis. Plasma, urine, and bile samples were analyzed for DDS and DDS conjugates; the degree of binding of DDS by plasma proteins was also determined. The renal clearances of inulin and DDS were calculated. No monoacetyldapsone (MA DDS) was detected in the plasma, and only negligible quantities were found in the urine. Small quantities of DDS and DDS conjugates were detected in the bile in four hours following the dose. Between 10% and 30% of the administered drug could be identified as DDS plus DDS conjugates in the urine in eight hours after the dose. Renal clearance of unbound DDS was proportional to the urine flow rate, and the clearance ratio of DDS to inulin approached the same maximal value as that for urea. Although the rate of urinary excretion of DDS conjugates was the same in the dog as in man, the rates of excretion of DDS and of DDS plus DDS conjugates were greater in the dog than in man; suggesting that the acetylation of DDS to

MADDS by man but not by the dog and the greater degree of plasma protein binding of DDS and MADDS by man account for the longer half-time of disappearance of DDS in man compared to that in the dog.—Authors' Summary

Cochran, M., Moorhead, P. J. and Platts, M. Permanent renal damage with rifampicin. *Lancet* 1 (1975) 1428. (Letter to Editor)

Acute renal failure has been associated with intermittent rifampicin therapy, or reintroduction of the drug. In two cases, circulating antibodies to rifampicin were found. These patients had an attack of vomiting, diarrhea, malaise and rigors one to four hours after ingestion of the drug. Anuria then followed and maintenance dialysis was usually required, but full recovery was the rule. Renal biopsies showed acute tubular necrosis with normal vasculature and glomeruli and there was no evidence of immune complex deposition. We report here two further cases, one with permanent renal damage. . . .

It is clearly important that patients should not be restarted on rifampicin therapy after a lapse without careful consideration. Although renal side-effects have so far only been described with intermittent therapy, there should perhaps be an awareness of the possibility of these complications occurring with continuous treatment.—(From Letter to Ed.)

Gordon, G. R., Ghoul, D. C. and Peters, J. H. Identification and quantitation of impurities in dapsone preparations. *J. Pharm. Sci.* 64 (1975) 1205-1207.

Chromatographic and fluoremetric procedures were developed to isolate and quantitate small amounts of 2,4'-diaminodiphenyl sulfone and 4-aminodiphenyl sulfone in pharmaceutical preparations of the antileprosy drug 4,4'-diaminodiphenyl sulfone (dapsone). Identification was accomplished by comparison with authentic compounds employing UV absorption, fluorometry, and mass spectrometry in addition to TLC (thin layer chromatography) and high pressure liquid chromatography.—Authors' Abstract

Levy, Louis. The activity of chaulmoogra acids against *Mycobacterium leprae*. *Am. Rev. Respir. Dis.* 111 (1975) 703-705.

The activity of the crude sodium salts of the fatty acids of chaulmoogra oil and of hydnocarpic and chaulmoogric acids against *Mycobacterium leprae* was studied in mouse foot pad infection. Multiplication of the organisms was inhibited when the salts were administered intraperitoneally and subcutaneously three times per week, and when chaulmoogric acid was administered intraperitoneally five times per week in half the equivalent dose. Dihydrochaulmoogric acid was also active, whereas palmitic acid was not. Hydnocarpic acid administered intraperitoneally once per week in a dose equivalent to half that of the sodium salts of the chaulmoogra fatty acids was not effective. The demonstration that chaulmoogra fatty acids possess activity against *M. leprae* lends weight to our earlier suggestion that a study of compounds analogous to these acids may yield effective antimicrobial agents with a unique mechanism of action.—Author's Summary

✓ **Murray, J. F., Jr., Gordon, G. R., Gullidge, C. C. and Peters, J. H.** Chromatographic-fluorometric analysis of antileprotic sulfones. *J. Chromatogr.* **107** (1975) 67–72.

Modifications to the power supply system of a spectrophotofluorometer are described. These modifications stabilize the output of the xenon arc lamp and permit the determination of nanogram quantities of antileprotic sulfones. The sulfones are removed from plasma by a single extraction with ethyl acetate, then separated by high pressure liquid chromatography on silica, and detected in the effluent by their fluorescence. The method is specific, rapid and reproducible.—Authors' Summary

✓ **Murray, J. F., Jr., Gordon, G. R. and Peters, J. H.** Determination of rifampin and desacetyl-rifampin in plasma. Paper presented at meeting of American Society Pharmacol. Exp. Therap., Davis, California, 17–21 August 1975.

Bioassay methods that rely on uridine-2-¹⁴C uptake or zone inhibition are currently used to determine the antibiotic rifampin (RFM). Although sensitive (0.002–0.2 µg/ml plasma), the methods are not specific for RFM because its metabolite desacetyl-rifampin (DRFM) also inhibits growth. To overcome this difficulty, we have developed

a high pressure liquid chromatographic system that separates RFM and DRFM. CHCl₃ was employed to extract RFM and DRFM from plasma at pH 5 in the presence of 0.025 M ascorbic acid and 4 M urea. Interfering materials in the extract were removed via an aqueous alkaline wash in the presence of piperidine. After ascorbate retreatment and solvent evaporation, we dissolved RFM and DRFM in benzene:methanol (95:5). The solution was injected onto a 2 × 500 mm 5-µm Lichrosorb Si-60 column and elution was accomplished using ethyl acetate:piperidine:methanol (85:10:5). By monitoring the effluent liquid at 485 nm, we quantitated both compounds at levels of 0.1–10 µg/ml of plasma. Recoveries of RFM and DRFM from plasma were 105 ± 5.5% (SD) and 114 ± 6.8%, respectively. RFM quinone was converted quantitatively to RFM by this procedure.—Authors' Abstract

✓ **Pattyn, Stefaan and Saerens, E. J.** Minimal inhibitory dosage of rifampicin in intermittent treatment of *Mycobacterium leprae* infection in mice. *Zentralbl. Bakteriell.* [Orig. A] **231** (1975) 503–507.

The total minimal inhibitory dose of rifampicin determined in the experimental mouse model, was found to be 10 mg/kg body weight, administered once a week for six weeks or once every two weeks for twelve weeks.

From these and other results it is suggested that administration of RMP in human treatment can be reduced to a total amount of 7.2 gm either as a 600 mg dose once a week for 12 weeks or as a 900 mg dose once a week for 8 weeks.

At present these regimens can only be used as an introductory treatment for multibacillary cases and are still too expensive for developing countries, but their efficacy should be evaluated in the field as sole treatments in tuberculoid cases, since they could signify a substantial economy for the management of the majority of leprosy infections.—Authors' Summary

✓ **Peters, J. H., Gordon, G. R. and Karat, A. B. A.** Polymorphic acetylation of the antibacterials, sulfamethazine and dapson, in South Indian subjects. *Am. J. Trop. Med. Hyg.* **24** (1975) 641–648.

A group of South Indian subjects was studied for their capacities to acetylate sulfamethazine (SMZ) and dapsone (DDS) and to clear DDS from the circulation. An apparent trimodal distribution of acetylator phenotypes was found in 49 subjects (51% slow, 12% intermediate, and 37% rapid acetylators) from measurements of the percentage acetylation of SMZ in six-hour plasma samples after administration of 10 mg SMZ/kg. The intermediate phenotype was not discernible from either the percentage acetylation of SMZ in urine (collected concurrently with the plasma after SMZ) or that of DDS in plasma after the ingestion of 50 mg DDS by the same subjects. The latter two measurements yielded a bimodal distribution of 59% slow and 41% rapid acetylators, nearly identical to earlier reported distributions of isoniazid inactivator phenotypes in larger numbers of South Indian tuberculosis patients. In the current group, acetylation of DDS and SMZ was positively correlated. The half-time of disappearance ($T_{1/2}$) of DDS, an expression of the rate of clearance from the plasma, ranged from 13 to 40 hours. No correlation was found between the subject's capacity to acetylate DDS and the $T_{1/2}$ value for DDS. These results were generally consistent with earlier observations made during similar studies of American and Filipino subjects.—Authors' Abstract

Russell, D. A., Shepard, C. C., McRae, D. H., Scott, G. C. and Vincin, D. R. Acedapsone (DADDS) treatment of leprosy patients in the Karimui of Papua New Guinea: status at six years. *Am. J. Trop. Med. Hyg.* 24 (1975) 485-495.

Acedapsone (DADDS), a repository sulfone given by injection five times a year, has been used since 1967 for the treatment of all leprosy patients in the Karimui, an area of difficult access. More than 460 patients have been treated, 336 beginning in November 1967 and continuing through the latest assessment six years later. The injections have been well received and they have been administered very regularly. Clinical observations were begun before 1967, so a base line of assessments was available for the patients whose disease appeared before that time. The response to DADDS therapy has been satisfactory except in 5 of 28 multi-

bacillary patients in whose smears solid-staining *M. leprae* have reappeared. *M. leprae* was isolated in mice from three of these patients; one strain has been proven to be completely susceptible to dapsone (DDS) and the other two very probably are. DDS levels in the plasma of these five patients were normal and well above the minimal inhibitory concentration. The most probable explanation is that a few viable *M. leprae* survived in the presence of inhibitory concentrations of DDS for the four to six years during which dead bacilli were disintegrating and disappearing from the tissues. The other 23 multibacillary patients responded satisfactorily. The decrease in the number of *M. leprae* in the skin smears has been most prompt in patients with low initial bacterial loads and in those with borderline lepromatous diagnoses. A high initial bacterial load and a fully lepromatous diagnosis were associated with a slow initial loss of *M. leprae* in the first year, followed by a more rapid loss the next year. All of the multibacillary patients have now been treated by the addition of a 90 day course of rifampicin.—Authors' Abstract

Sheskin, Jacob. Therapeutische Erfahrungen über den Einfluss des Thalidomids bei der Lepra-Reaktion. [Therapeutic experiences concerning the influence of thalidomide on lepra reaction.] *Hautarzt* 26 (1975) 1-5. (In German)

In November of 1964 suppression of lepra reaction by administration of thalidomide in lepromatous leprosy patients was observed. The present report is concerned with the results.

Summaries of the courses of 4,522 patients from 62 worldwide institutes were obtained and favorable results were observed in 99% of the patients. Thalidomide alone is not, however, effective for the treatment of leprosy. A combination of thalidomide and sulfone made the treatment of leprosy patients suffering from reaction possible. This combination so far has not caused any untoward effect. The optimal beginning dosage of thalidomide was 400 mg daily or 6 mg per kg of body weight. The favorable maintenance dosage was 100 mg daily. Resistance against thalidomide has not yet been observed. The patients under long-time steroid therapy had their

steroid doses reduced slowly with the beginning of full doses of thalidomide. Electromyographic observations concluded that thalidomide can play a role in overcoming the neural, muscular or bone changes occasioned by neuritic process resulting from reaction. Reaction presenting as iridocyclitis or iritis responds favorably to thalidomide therapy like the other symptoms of reaction. Although it is not severe enough to stop thalidomide therapy some side effects were observed. Repeated various laboratory examinations during therapy caused no noticeable pathologic changes. Due to its teratogenic activity thalidomide should not be used for the treatment of pregnant patients.—(Translated from summary)

✓ **Steenbergen, G.J. and Pfaltzgraff, R.E.**

Treatment of neuritis in borderline leprosy with rifampicin and corticosteroids. A pilot trial. *Lepr. Rev.* **46** (1975) 115-118.

Upon the premise that rifampicin in conjunction with corticosteroids may be of value in the treatment of neuritis in borderline leprosy, a full scale trial was planned. But the rapid appearance of an increasing peripheral neuropathy in three of the patients made cessation of the trial imperative. The combination of clofazimine with a similar scheme of administration of corticosteroids was found to produce far superior results even after rifampicin had caused an exacerbation of the neuritis.—Authors' Summary

U.S. Leprosy Panel and Leonard Wood Memorial. Rifampin therapy of lepromatous leprosy. *Am. J. Trop. Med. Hyg.* **24** (1975) 475-484.

Patients with borderline-lepromatous (BL) or fully lepromatous (LL) leprosy were treated in the sanitarium for approximately one year with oral rifampin (600 mg daily) or with oral dapsone (100 mg daily). They were then treated as outpatients with intramuscular acedapsone (225 mg every 12 weeks) or oral dapsone (50 mg daily). They have now been followed for a total of 28 to 34 months. Death of *M. leprae* during the initial 24 weeks was monitored by mouse inoculation with *M. leprae* from skin punch biopsy specimens. With rifampin therapy, death of *M. leprae* occurred rapidly, and viable *M. leprae* were nearly undetectable by the time the first specimen was taken after the start of treatment at four weeks. With dapsone therapy death of *M. leprae* was slower, and in some cases the inoculation results were still positive at 12 weeks. The therapeutic response during the period of outpatient treatment has been satisfactory. The number of dead *M. leprae*, as measured by the BI in skin smears and the number of acid-fast bacteria in skin specimens, has continued to decrease and clinical progress has been satisfactory. The measured drug-induced death of *M. leprae* occurred at about the same rate in BL patients as in LL patients. Disappearance of dead *M. leprae* from the tissues was much more rapid in BL patients than in LL patients.—Abstract

Immuno-Pathology

✓ **Agarwal, D.P., Srivastava, L.M., Goedde, H.W. and Rohde, R.** Biochemical, immunological and genetic studies in leprosy. I. Changes in serum lactate dehydrogenase isoenzymes, creatine phosphokinase and aldolase activity in different forms of leprosy. *Tropenmed. Parasit.* **26** (1975) 207-211.

Serum lactate dehydrogenase isoenzymes, creatine phosphokinase and aldolase activity were determined in healthy control subjects and in lepromatous and tuberculoid leprosy

patients from Ethiopia. Sera from lepromatous patients showed a higher total LDH activity compared with control subjects. The values for tuberculoid leprosy patients were similar to those of controls. Sera from normal healthy controls showed a higher proportion of LDH-H form (72%) while lepromatous leprosy patients' sera exhibited a higher proportion of LDH-M form (55%). Tuberculoid leprosy patients showed a pattern similar to that of healthy controls. A possible significance of these observations is discussed. No significant variations were observed in fructose-1,6-diphosphate aldolase activity with-

in the different types of disease and controls. Although creatine phosphokinase levels in different types of leprosy decreased significantly from those of normal healthy individuals, it fell within reported variation of the activity in normal sera.—Authors' Summary

✓ **Closs, Otto.** *In vitro* lymphocyte response to purified protein derivative, BCG and *Mycobacterium leprae* in a population not exposed to leprosy. *Infect. Immun.* **11** (1975) 1163-1169.

Lymphocytes from 14 BCG-vaccinated donors, seven tuberculin positive and seven tuberculin negative by skin testing, were stimulated *in vitro* with four mycobacterial antigens, purified protein derivative (PPD), PPD/BCG, whole BCG bacilli, and whole *Mycobacterium leprae* and also with *Candida* antigen and phytohemagglutinin. The response was measured by incorporation of H-labeled thymidine. The response to PPD, PPD/BCG, and BCG was found to correlate with the result of skin testing with tuberculin. The tuberculin-positive group also responded more strongly to *M. leprae*, whereas the two groups did not differ significantly in their response to *Candida* antigen or phytohemagglutinin. These findings indicate a certain degree of cross-reactivity between BCG and *M. leprae*. The use of the lymphocyte transformation test to measure antigenic cross-reactivity is discussed.—Author's Summary

✓ **Date, Anand and Johny, K.V.** Glomerular subepithelial deposits in lepromatous leprosy. *Am. J. Trop. Med. Hyg.* **24** (1975) 853-856.

The presence of subepithelial humps seen in the glomeruli on electron microscopy in a case of lepromatous leprosy with *erythema nodosum leprosum* is described. Negative cultures and normal antibody titers for streptococci suggest a nonstreptococcal etiology for this finding. Further studies in this immune complex nephritis are required to establish its relationship to lepromatous leprosy.—Authors' Abstract

✓ **Doumanova, Lyuba.** Changes in the electrophoretic mobility of antigen-stimulated macrophages. *J. Reticuloendothel. Soc.* **17** (1975) 262-266.

Guinea pig macrophages were isolated

and stimulated with *Bacillus subtilis*. The electrophoretic mobility of stimulated and unstimulated (resting) macrophages was determined. Another series of experiments was aimed at determining the electrophoretic mobility of stimulated and unstimulated macrophages treated with formaldehyde. It was established that the antigenic stimulation of macrophages increases their electrophoretic mobility by 22% and the increase after treatment with formaldehyde is two to six times greater. The influence of antigenic stimulation of macrophages on plasma membrane conformation is discussed.—Author's Summary

✓ **Edwards, Rosa P.** Long-spacing collagen in skin biopsies from patients with lepromatous leprosy. *Br. J. Dermatol.* **93** (1975) 175-182.

In the course of evaluating the effect of different drugs on the morphology of *Mycobacterium leprae* and on the phagocytic cells containing these organisms, an unusual feature was observed in the dermal connective tissue of skin biopsies obtained from some of the patients. Variable amounts of an extracellular, cross-striated osmiophilic material were present in the dermis.

The purpose of this communication is to describe the banded substance observed in the extracellular space of the lepromatous skin and to compare it briefly with similar substances and structures reported to occur elsewhere.—Author's Summary

✓ **Goedde, H.W., Benkmann, H.-G., Hirth, L., Rohde, R., Rougemont, A. and Delbruck, H.** Phenotypes of Gc and Tf in leprosy patients of Mali and Ethiopia. *Hum. Hered.* **24** (1975) 383-386.

The distribution of Gc and Tf phenotypes of leprosy patients from the districts of Mali and Ethiopia was investigated in respect to different forms of leprosy. In Mali we observed a significant difference in the Gc system between leprosy patients and healthy persons. In Ethiopia no association was observed.—Authors' Abstract

✓ **Goihman-Yahr, Rodriguez-Ochoa, G., Aranzazu, N. and Convit, J.** Polymorphonuclear activation in leprosy. I. Spontaneous and endotoxin-stimulated reduction of nitroblue tetrazolium: effects of serum and

plasma on endotoxin-induced activation. Clin. Exp. Immunol. 20 (1975) 257-264.

Spontaneous nitroblue tetrazolium (NBT) reduction was evaluated in neutrophils from patients with the different types and forms of leprosy, and compared with reduction obtained from cells from normal controls. Leukocytes from the same subjects were stimulated *in vitro* by endotoxin, and the rise in percentage of cells reducing NBT was determined.

Patients of all groups, with the exception of those with reactional lepromatous leprosy (RLL) had an essentially normal proportion of reducing cells. Neutrophils were normally activated by endotoxin. This indicates that while *Mycobacterium leprae* does not by itself stimulate leukocytes from leprosy patients, there is no overall anergy of neutrophils in lepromatous or other forms of leprosy. In RLL the proportion of reducing cells was significantly raised. Stimulation with endotoxin was able further to enhance this proportion, but not above levels reached by stimulation of normal cells.

Neutrophil activation could not be reproduced by mixing serum from highly activated RLL patients with normal leukocytes.

An inhibitory effect of serum and plasma over *in vitro* endotoxin activation of neutrophils was found.—Authors' Summary.

Ivanova, N.N. The results of parallel investigation of the content of xanthurene and 5-oxiindolylacetic acids in the urine of patients with leprosy. Vestn. Dermatol. Venerol. No. 2 (1975) 16-19. (In Russian)

Parallel studies were carried out to determine the content of xanthurene acid (XA) according to the method of G. Ya. Vilenkina (1965), and of 5-oxiindolylacetic acid (OIA) by the method of Udenfriend *et al* (1955), in the daily urine of 17 apparently normal subjects of the control group and of 57 patients with leprosy (42 [41?] with lepromatous, 12 undifferentiated, 3 with tuberculoid, and 1 with dimorphic borderline forms). In 28 out of 42 patients with lepromatous leprosy the content of XA in the urine was found to be increased considerably (76.95 ± 7.68 mg/day, $p < 0.001$), as compared to that in the subjects of the control group (21.15 ± 1.96 mg/day). As the disease regressed the XA content showed a trend to normalization (46.16 ± 11). The XA content was increased

also in 5 of 12 patients with undifferentiated leprosy, in some patients with tuberculoid and borderline leprosy. Increased excretion of 5-OIA in the urine was observed in 21 of 42 patients with lepromatous leprosy (4.27 ± 0.3 mg/day, $p < 0.001$ against 2.38 ± 0.189 mg/day in the controls), in 6 out of 12 patients with undifferentiated leprosy (5.13 ± 0.948 mg/day, $p < 0.011$), and in one patient with dimorphic leprosy (5.8 mg/day).

The increase in the content of XA and 5-OIA acid in the urine of the patients with leprosy attests to disorders of kinurenine and serotonin ways of tryptophane metabolism.—English Summary (From Trop. Dis. Bull.)

King, G. W., Para, M. F., LoBuglio, A. F. and Sagone, A.L., Jr. Human monocyte metabolism: male vs. female. J. Reticuloendothel. Soc. 17 (1975) 282-289.

Rates of glycolysis, Krebs cycle and hexose monophosphate shunt (HMPS) were established for normal human monocytes on the basis of sex, age and menstrual status. Monocytes from menstruating women demonstrated enhanced HMPS activity when compared to monocytes from men of comparable age. Postmenopausal women and men over the age of 40 had identical HMPS activity intermediate between that of menstruating women and young men. No significant differences were noted in Krebs cycle activity and glycolysis among any of the groups studied. These data are important in evaluating comparative studies of monocyte metabolism and may correlate with known differences in male-female reticuloendothelial function in animals.—Authors' Summary

Kirchheimer, W. F., Prabhakaran, K., Harris, E. B., Sanchez, R. M. and Shannon, E. J. Preparation of protein from *Mycobacterium leprae* and skin test responses of vaccinated animals. Lepr. India 47 (1975) 142-150.

Mycobacterium leprae protein was prepared by trichloroacetic acid precipitation from ultrasonicates of leprosy bacilli obtained from leprosy armadillo liver. From 62 gm wet weight of infected liver, 1.8×10^{11} *M. leprae* were recovered with a yield of 1.16 mg protein. Armadillos vaccinated with heat-killed *M. leprae* gave positive delayed-type hypersensitivity reactions to intracutaneous tests with 29 and 170 μ g of this pro-

tein but not to tuberculin. Nonvaccinated armadillos were nonreactive. In all but one of the hypersensitive armadillos increased blast transformation of cultured lymphocytes was observed in the presence of *M. leprae*. The use of delayed-type sensitivity tests for predicting resistance or susceptibility of armadillos to infection with *M. leprae* is discussed.—Authors' Summary

✓ **Kronvall, G., Husby, G., Samuel, D., Bjune, G. and Wheate, H.** Amyloid-related serum component (protein ASC) in leprosy patients. *Infect. Immun.* **11** (1975) 969-972.

The presence of amyloid-related serum component, protein ASC, in serum samples from 63 leprosy patients was investigated. Protein ASC was detected in 38% of the patients. A correlation to the disease spectrum of leprosy was apparent: polar lepromatous cases, 64% positive; borderline lepromatous, 50%; borderline tuberculoid, 36%; subpolar tuberculoid, 17%; and polar tuberculoid, negative. Antibody activity against the a antigen of *Mycobacterium leprae* was also determined, showing a similar correlation to the disease spectrum. Serum samples from 23 apparently healthy Ethiopians serving as controls showed a protein ASC incidence of 22%. This figure is significantly higher than the frequency found by others among healthy Norwegian blood donors. Immunoglobulin M levels among patients were elevated in the borderline lepromatous and polar lepromatous groups. The three tuberculoid groups did not differ in this respect from the control group but were all elevated as compared to a normal Caucasian serum pool. Although raised immunoglobulin M levels seemed to parallel increased frequencies of protein ASC in the patient groups as well as in controls, this correlation might be only secondary to a primary derangement in T cell function.—Authors' Summary

✓ **Kwapinski, J. B. G., Bechelli, L. M., Haddad, N. and Simao, E. T.** Impairment of reactivity to lepromin by mycobacterial antigens related to, or identical with *Mycobacterium leprae*. *Can. J. Microbiol.* **21** (1975) 896-901.

Young children, totaling 320, were injected with BCG saline, or with one of the mycobacterial cytoplasmic antigens related with *Mycobacterium leprae*. At an appropriate time thereafter they were tested for

dermal hypersensitivity to the antigens and for reactions to lepromin.

Whereas all the antigens induced cell-mediated immunity, the incidence and intensity of late response to lepromin were significantly reduced in children preinjected with the cytoplasmic mycobacterial antigens, as contrasted with increased lepromin reactivity in the BCG group and with the findings, in saline injected children—Authors' Abstract

✓ **McDougall, A. C., Rees, R. J. W., Weddell, A. G. M. and Wadji Kanan, M.** The histopathology of lepromatous leprosy in the nose. *J. Pathol.* **115** (1975) 215-226.

On the basis of clinical, histologic and bacteriologic assessments, thirty-one patients in central India were selected and classified as having active but early lepromatous leprosy and four patients as having early borderline leprosy. From the nose of each patient an average of four biopsies were taken from particular sites of the septum and turbinates either by punch biopsy or dissection with a scalpel. The nasal tissues from all the lepromatous patients contained many acid-fast bacilli; no bacilli or abnormalities were seen in the nasal tissues from the borderline patients.

The histopathology of these highly bacilliferous tissues is described. Bacilli were universally seen in macrophages, but they were also seen in blood monocytes and polymorphs, fibroblasts, squamous and pseudo-columnar epithelium, keratin, peri- and endoneurial cells of tiny nerve bundles, erectile tissue, vascular plain muscle, perivascular histiocytes, and frequently and abundantly in the cytoplasm of endothelial lining cells of lymphatics and of small blood vessels and free within the lumina of these vessels.

Five basic mechanisms of escape of bacilli from the submucosa onto the surface, and thus into the external environment, are described. Secondary infection, in the presence of an expansile lepromatous infiltrate, together with simple trauma to the surface epithelium, are the main factors in the discharge of bacilli. These histopathologic observations are consistent with the findings from other recent studies on the nose in leprosy regarding 1) the large numbers of morphologically intact and viable *M. leprae* excreted in the nasal mucus of lepromatous

patients; 2) the clinical changes observed in the nose of such patients; and 3) the similar nasal involvement and excretion of *M. leprae* from the nose of mice inoculated with leprosy bacilli of human origin.

Of particular interest was the frequency and intensity of bacilli within the endothelial lining cells of small blood and lymph vessels and the presence of bacilli free within the lumina of these vessels or within monocytes and polymorphs. The possible dynamic significance of these observations in the pathogenesis of leprosy is discussed.

The significance of all these observations in relation to 1) the spread of leprosy; 2) local factors in the nose which might favor the growth of *M. leprae*, and 3) the nose as a portal of entry, are discussed.—Authors' Summary

✓ **Meyers, W. M., Kvernes, S. and Staple, E. M.** Failure of levamisole to alter the lepromin reaction. *Am. J. Trop. Hyg.* **24** (1975) 857-859.

In a study of 37 leprosy patients, the oral administration of levamisole failed to provoke an increase in both the Fernandez and Mitsuda reactions to lepromins of human and armadillo origin. We interpret this as evidence against an effective specific immunostimulatory capability of levamisole in leprosy patients under the conditions of the study. Current knowledge of the mechanism of levamisole action supports the concept that the fundamental immunologic defect in lepromatous leprosy may reside in the lymphocyte and not the macrophage, or the respective related functions of these two cell forms.—Authors' Abstract

✓ **Myrvang, B., Negassi, K., Lofgren, M. and Godal, T.** Immune responsiveness to *Mycobacterium leprae* of healthy humans. *Acta. Pathol. Microbiol. Scand. [C]* **83** (1975) 43-51.

Immune responsiveness to *M. leprae* was studied in various groups of healthy humans. Contacts of leprosy patients responded significantly more than noncontacts by the methods of leucocyte migration inhibition, lymphocyte transformation and early and late lepromin testing. By classifying responses of strengths found in noncontacts as negative, 71.2% of medical attendants,

the main category of contacts, were responders by the leucocyte migration inhibition test, 44.2% by the lymphocyte transformation assay and 50% by the early lepromin reaction. On the other hand, no degree of the late lepromin reaction was found solely in *M. leprae*-exposed people. While the assays of leucocyte migration inhibition, lymphocyte transformation and early lepromin testing thus may be considered useful for detection of healthy individuals exposed to *M. leprae*, the late lepromin reaction appears unsuitable as a measure of exposure. Besides the association of negative responses by leucocyte migration inhibition, lymphocyte transformation and early lepromin tests, there was in the group of noncontacts a significant quantitative correlation between early and late lepromin reactions. In the group of medical attendants significant correlations were observed between the results of all tests employed.

—Authors' Summary

✓ **Navalkar, R. G., Patel, P. J. and Dalvi, R. R.** Immunological studies on leprosy: separation and evaluation of the antigens of *Mycobacterium leprae*. *J. Med. Microbiol.* **8** (1975) 319-324.

Chromatographically separated antigens of *Mycobacterium leprae* were tested for their ability to elicit skin reactions in guinea pigs sensitized with homologous and heterologous mycobacteria. Of the three antigen-positive fractions obtained, one showed specific activity and the other two cross-reactivity, as indicated by studies of hypersensitivity and passive cutaneous anaphylaxis.

The fraction exhibiting specificity contained only one antigen, which was protein in nature, whereas the other two fractions contained more than one antigen and possessed both protein and polysaccharide constituents. Because the single-antigen-containing fraction showed both positive skin and PCA reactivity, the suggestion is made that this fraction may contain either an antigen with two determinants or may contain two antigens that are not easily distinguishable by immunodiffusion methods.—Authors' Summary

✓ **Padma, M. N. and Desikan, K. V.** Bacillema in leprosy. *Indian J. Med. Res.* **63** (1975) 888-892.

The presence of acid-fast bacilli in the blood stream of leprosy patients provides direct evidence of the mode of spread of the disease. Venous blood of 114 cases of lepromatous leprosy was examined for presence of bacilli. Techniques were evolved to eliminate contamination of the blood sample by bacteria from the overlying skin. Seventy-seven cases showed bacilli in the blood. The bacilli were found mainly in monocytes, and less frequently in polymorphs. No correlation was found between the degree of bacillary positivity in the skin and in blood. These findings are discussed with reference to their bearing on the dissemination of the disease, lepra reactions and possible bacillemia in other clinical types of the disease.—Authors' Abstract

✓ **Parks, D. Elliot and Weiser, Russell S.** The role of phagocytosis and natural lymphokines in the fusion of alveolar macrophages to form Langhans giant cells. *J. Reticuloendothel. Soc.* **17** (1975) 219-228.

Pulmonary lavage fluid from immunized rabbits mounting a secondary pulmonary response to i.v. administered, heat-killed BCG is capable of promoting the fusion of cultured normal alveolar macrophages to form multinucleate giant cells of the Langhans type. The factor responsible for the fusion-inducing activity of the immune lavage fluid is presumed to be the lymphokine designated macrophage fusion factor (MFF). Pulmonary lavage fluids from both normal and immune rabbits enhance the survival of normal macrophages in culture and promote their phagocytic activity for heat-killed *Candida albicans*, polystyrene latex beads and *Staphylococcus aureus*. Apparently the particulates observed within giant cells in such preparations did not represent materials engulfed by the giant cells themselves but, instead, materials initially present in the macrophages that fused to form the giant cells. Normal macrophages cultured for 24 hours in immune lavage fluid exhibited greater intracellular inactivation of *Staph. aureus* than macrophages cultured in normal lavage fluid or in medium alone.—Authors' Summary

✓ **Paul, R. C., Stanford, J. L. and Carswell, J. W.** Multiple skin testing in leprosy. *J. Hyg. (Camb.)* **75** (1975) 57-68.

Groups of patients with lepromatous and tuberculoid leprosy and hospital staff from six leproseries in East Africa and "noncontact" groups of villagers or staff from general hospitals have been skin tested with ten reagents. These were prepared by ultrasonic disintegration from *M. tuberculosis*, *M. duvalii*, *M. chelonae* and seven other species identified in the Ugandan environment. Comparisons were made of the percentages of positive reactors in each study group for each reagent. The specific defect of lepromatous patients was found to apply to a variable extent to six of the species tested, but not to *M. tuberculosis*, *M. avium*, or *M. A**. The defect applied most noticeably to *M. nonchromogenicum* and *M. vaccae*, suggesting that they are more closely related to *M. leprae* than are the other species tested. The reagent Chelonin produced unexpected and anomalous results in the lepromatous group. It is suggested that this was due to an unusually slow clearing of Arthus' reaction.—Authors' Summary

✓ **Pearson, J. M. H. and Weddell, A. G. M.** Perineurial changes in untreated leprosy. *Lepr. Rev.* **46** (1975) 51-67.

Perineurial changes were studied by light microscopy in biopsies of skin and nerve from 64 patients covering the full range of the leprosy spectrum. In all types of leprosy a multilayered appearance of the perineurium could be observed: in lepromatous cases the layers tended to consist of swollen cells which contained more leprosy bacilli than the Schwann cells; in borderline and tuberculoid biopsies they took on a thinner, more fibrotic appearance, and bacilli were scanty or absent. Epithelioid changes were seldom observed in this site. The possible effects of perineurial damage in the endoneurium, and of endoneurial damage on the perineurium, are discussed.—Authors' Summary

✓ **Purtilo, David T. and Pangi, Charles.** Incidence of cancer in patients with leprosy. *Cancer* **35** (1975) 1259-1261.

Individuals with congenital immunodeficiencies and patients who are immunosuppressed for maintenance of organ allografts experience a marked increase in the occurrence of malignancy. Patients with lepromatous leprosy also have depressed cellular immunity, but our study of 195 autopsied

subjects with leprosy did not reveal an increase in the occurrence of cancer. Thirty-three of the 195 subjects with leprosy or 16.9% died of cancer, which is comparable to an age-matched group of individuals.—Authors' Summary

✓ **Rao, B. N., Satyanarayana, B. V., Venkatarathnam, G. and Reddy, C. R. R. M.** "Isopathic phenomenon" in leprosy. *Dermatologica* **150** (1975) 169-175.

Isopathic phenomenon of Sagher was elicited in 21 proved leprosy patients (consisting of 7 lepromatous, 7 tuberculoid, 3 neuritic, 2 borderline, and 2 indeterminate types). The substances used to elicit the isopathic phenomenon were BCG lepromin, India ink and staphylococcal vaccine. Isopathic phenomenon was elicited in most of the cases and BCG was the substance which produced the most responses. The phenomenon could be used to classify difficult cases of leprosy.—Authors' Abstract

✓ **Ridley, Dennis S.** Histological classification and the immunological spectrum of leprosy. *Bull. WHO* **51** (1974) 451-465.

The clinical and histologic manifestations of leprosy are known to be closely correlated with the immunologic state of the patient, which determines prognosis and constitutes the natural basis for the classification of this disease. A classification based on this correlation has come to be widely used but needs to be brought up to date and expanded in the light of more recent experience. The author of the present paper presents a much fuller account of the histologic side of the classification, taking into account the results of recent experience. This histologic classification has been found to provide a workable and widely applicable system, different histologists achieving remarkably good agreement with one another.—Author's Abstract

✓ **Saha, K., Mittal, M. M. and Maheshwari, H. B.** Passive transfer of immunity into leprosy patients by transfusion of lymphocytes and by transfusion of Lawrence's transfer factor. *J. Clin. Microbiol.* **1** (1975) 279-288.

About 1,200 million viable lymphocytes from normal but lepromin and tuberculin positive human beings were transfused in four patients of lepromatous and one of tu-

berculoid leprosy three times at monthly intervals. Three patients with lepromatous leprosy suffered from *erythema nodosum* whereas the other two developed severe reaction whenever put on the smallest dose of dapsone. In one patient with lepromatous leprosy, minimal improvement or none was observed, whereas in the remaining three cases with lepromatous and one with tuberculoid leprosy, clinical, bacteriologic, as well as histologic improvement occurred. Two of the five patients started to tolerate the dapsone during the period of study. The present study indicates that immunotherapy might have a definite role in the management of the disease especially in cases with *erythema nodosum*. Lawrence factor, prepared from leucocytes of normal donors, was transfused three times into four lepromatous leprosy patients who were intolerant to antileprosy drugs. The donors were healthy but were tuberculin and lepromin (Mitsuda) positive. The clinical, histologic, bacteriologic (Morphologic Index), and immunologic assessments of the patients were performed before and five months after starting the immunotherapy. In two patients conversion of Mitsuda reaction occurred, but there was no appreciable improvement in the clinical, histologic and bacteriologic status of these patients.—Authors' Summary

✓ **Saxena, H., Ajwani, K. D., Pradhan, S., Chandra, J. and Kumar, A.** A preliminary study on bacteremia in leprosy. *Lepr. India* **47** (1975) 79-84.

The present work deals with demonstration of lepra bacilli in peripheral blood in 32 cases of leprosy. The evidence of bacteremia was seen in only two cases of lepromatous leprosy, wherein the bacilli were seen in intracellular as well as extracellular location; indicating that the remaining 30 cases of the tuberculoid type of leprosy are noninfectious and could be socially adjusted as normal people. The findings are interesting and the authors hope that this important aspect of transmission of leprosy will be investigated by a larger number of workers.—(Adapted from authors' summary)

✓ **Smith, G. S., Walford, R. L., Shepard, C. C., Payne, R. and Prochazka, G. J.** Histocompatibility antigens in leprosy. *Vox Sang.* **28** (1975) 42-49.

Results of HL-A typing are presented in 82 patients with leprosy and 50 normal Filipinos from Cebu, and 144 normal Filipino immigrants from the Luzon area. Comparisons of HL-A antigen frequencies among the total patients and normals of Cebu showed no statistically significant differences; however, HL-A10 was increased in frequency among the patients with lepromatous disease compared to the normals, and HL-A5 was increased among the tuberculoid patients compared to the lepromatous patients. None of these comparisons was statistically significant when corrected for the number of antigens tested. Comparisons of HL-A antigen frequencies between normal Filipinos of the Cebu and Luzon regions showed increased W-5 in the Luzon population (corrected $p < 0.025$).—Authors' Abstract

✓ **Srivastava, L. M., Agarwal, D. P., and Goedde, H. W.** Serum lactate dehydrogenase and other enzymes in different forms of leprosy. Presented at Joint Meeting, Biochemical Societies of Belgium, the Federal Republic of Germany and the Netherlands. Hoppe-Seyler's Z. Physiol. Chem. **355** (1974) 1258.

The observed changes in serum enzymes and their isoenzymes are in most cases an established criteria for the assessment of various diseases and their clinical course. In an attempt to clarify a possible role played by certain key enzymes in different forms of leprosy, a chronic granulomatous disease, serum levels of lactate dehydrogenase (EC 1.1.1.27) types, aldolase (EC 4.1.2.13) and creatine kinase (EC 2.7.3.2) were studied in samples from Ethiopia.

For the determinations of these enzymes the kits supplied by Boehringer Mannheim were used. The H and M forms of lactate dehydrogenase (LDH) were quantitated by utilizing the temperature sensitivity of the two forms. Although small differences in the total lactate dehydrogenase and aldolase levels (mean average) were observed between the groups of normal healthy, lepromatous leprosy and tuberculoid leprosy subjects, they were not statistically significant. In contrast, a marked shift between M and H subunits of lactate dehydrogenase was noted. Serum of normal healthy subjects showed a preponderance of H type while lepromatous leprosy subjects possessed a

higher proportion of M type. Tuberculoid leprosy subjects showed intermediate values.

LDH-M type favors the pyruvate \rightleftharpoons lactate reaction more towards the lactate while H type favors pyruvate formation. An increased proportion of M type in lepromatous leprosy would therefore signify certain early physiologic changes that might have been caused in such subjects as a result of the infection by *Mycobacterium leprae*. Higher blood lactate levels in lepromatous leprosy subjects over those of controls have been reported. As M and H subunits of lactate dehydrogenase are controlled by two different genes, it might be possible that such a shift symbolizes certain changes in genetic setup of the enzyme in leprosy subjects. Creatine kinase levels and modifications of other enzymes would be discussed.—Authors' Abstract

✓ **Srivastava, L. M., Agarwal, D. P., Goedde, H. W. and Rohde, R.** Biochemical, immunological and genetic studies in leprosy. II. Profile of immunoglobulins, complement components and C-reactive protein in sera of leprosy patients and healthy controls. Tropenmed. Parasit. **26** (1975) 212-218.

Various classes of immunoglobulins (IgA, IgM, IgG, IgD and IgE), complement components (C3 and C4), and C-reactive protein (CRP) were estimated in sera from normal healthy controls and leprosy (lepromatous and tuberculoid) patients from Ethiopia. Higher levels of IgA, IgM, IgG and IgD were found in lepromatous leprosy compared with normal healthy people, while in tuberculoid leprosy only IgM, IgG and IgD levels were increased. Borderline leprosy patients showed increase in IgG level only.

Although an increase in IgE was noted in lepromatous leprosy, it was not significant; the variations in IgE levels could be due to different socio-economic backgrounds and exposure to intestinal parasites.

C3 component was significantly reduced in leprosy patients compared with healthy controls, while no difference in C4 component was observed. The results point towards an involvement of the "alternate pathway." A positive test against C-reactive protein antiserum was given by about 20% of the normal healthy controls while more

than 60% lepromatous and tuberculoid leprosy patients were CRP positive.

The results are discussed in relation to the status of immunoglobulins and complement components in leprosy and possible factors (environmental and genetic) which might affect them.—Authors' Summary

✓ **Van Ginckel, R. F. and Hoebeke, J.** Carbon clearance enhancing factor in serum from levamisole treated mice. *J. Reticuloendothel. Soc.* **17** (1975) 65-72.

Levamisole increased the carbon clearance in CD₁ male mice. From sera of levamisole treated mice, a substance was prepared which is capable of enhancing carbon clearance. This substance was dialyzable and heat-labile and could be isolated by molecular sieving on Sephadex G-10 in one of the fractions absorbing at 280 nm.—Authors' Summary

✓ **Wisniewski, Henryk M. and Bloom, Barry R.** Primary demyelination as a nonspecific consequence of a cell-mediated immune reaction. *J. Exp. Med.* **141** (1975) 346-359.

Primary demyelination occurs in a variety of human and experimental diseases known to be associated with the presence of inflammatory cells. However, the mechanism of demyelination remains unclear. The possibility that myelin can be damaged as a non-

specific consequence of a specific delayed type of hypersensitivity reaction directed at nonnervous tissue antigens was investigated.

Guinea pigs were sensitized to tuberculin with Freund's complete adjuvant, and were challenged in the central and peripheral nervous system either with live or killed sonicated tubercle bacilli, Old Tuberculin, or tuberculin purified protein derivative (PPD). Local inflammatory reactions were invariably produced and primary demyelination was a constant feature of the lesions. The morphological picture was rather similar to that observed in human neurotuberculosis and early tuberculoid leprosy, and in experimental allergic encephalomyelitis and distemper encephalitis in animals. The infiltrates consisted predominantly of mononuclear cells with some polymorphonuclear cells as well. Vesicular disruption of the myelin sheath in the immediate vicinity of the inflammatory cells and stripping of the myelin lamellae by the histiocytes without axonal damage were the leading features of the lesion. The results indicate that cell-mediated immune reactions to a variety of nonbrain antigens could be responsible for a component of the demyelination seen in some inflammatory demyelinating conditions, and suggest that this system may serve as a useful model for studying the immunopathology of demyelinating disease.—Authors' Summary

Microbiology

✓ **Delville, J. and Pichel, A.M.** Microbiology of leprosy. Does an *in vitro* cultivable phase of Hansen bacillus exist? *Ann. Soc. Belg. Med. Trop.* **55** (1975) 109-118. (In French, English summary)

Non acid-fast bacilli are present alone or in association with classical acid-fast bacilli in leprosy lesions.

These two types of bacilli behave similarly by fluorescent antibody technics. Twenty-six non acid-fast strains have been isolated from biopsies and blood of leprosy patients. The same strains are regularly isolated from the foot pad, but only in mice inoculated with leprosy material. All strains are antigenically related with each other and with *M. leprae*.

These observations suggest that *M. leprae* could be cultivable as non acid-fast bacilli.—Authors' Summary

✓ **Kato, Laszlo and Ishaque, Muhammad.** Oxidation of reduced nicotinamide adenine dinucleotide by particles from *Mycobacterium lepraemurium*. *Cytobios* **12** (1975) 31-43.

Particles from *Mycobacterium lepraemurium* catalysed the oxidation of NADH with oxygen as the terminal electron acceptor. The preparation contained cytochromes of the *a + a₃*, *b* and *c* types, as well as CO-binding pigments. The NADH oxidase activity was sensitive to inhibitors of the flavoprotein system as well as to HQNO and antimycin A. In addition, a cytochrome oxidase sensitive to cyanide was also present. The system was inhibited by the thiol-binding agent, PCMB, and thus indicated the involvement of sulphhydryl group in the enzymatic oxidation of NADH. The sensitiv-

ity of the NADH oxidase system to all the inhibitors of the respiratory chain and the effect of these inhibitors on the absorption spectra suggested that cytochromes of the *b*, *c*, *a* + *a*₃ types are involved in the transfer of electrons in NADH oxidation.—Authors' Abstract

✓ **Nakamura, M., Itoh, T. and Yoshii, Z.** A mode of the growth of *Mycobacterium lepraemurium* in a cell-free liquid medium (38501). *Proc. Soc. Exp. Biol. Med.* **148** (1975) 183–186.

The first report regarding *in vitro* growth patterns of *M. lepraemurium* was presented. Evidence is indicated that a growth mode of a single cell of *M. lepraemurium in vitro* is similar to that of culturable mycobacterium, especially atypical mycobacterium. This finding has added one property to characteristics of *M. lepraemurium* which have been already known.—Authors' Summary

✓ **Navalkar, R. G., Dalvi, R. R. and Patel, P. J.** Antigenic evaluation of *Mycobacterium lepraemurium*. *J. Med. Microbiol.* **8** (1975) 177–181.

Immunodiffusion analysis of *M. lepraemurium* indicated the presence of at least six antigens. Comparative analysis of the *M. lepraemurium* antigen-antibody system with similar systems established for other mycobacterial species, showed that *M. lepraemurium* shared up to two antigens with other species.

Although our observations are in accord with some of the studies on the antigenic mosaic of *M. lepraemurium*, they are in disagreement with the observations of Stanford (1973) concerning a close serologic relationship of this organism to *M. avium*. This incompatibility cannot be explained satisfactorily at present.—Authors' Summary

✓ **Olitzki, A. L. and Muller, S.** Further investigations on *M. leprae*. Growth promotion and inhibition by organic substances and

observations on antagonistic and synergistic effects. *Boll. Ist. Sieroter. Milan.* **54** (1975) 5–12.

The multiplication of two strains of *M. leprae* on a medium containing a sonic extract (SE), prepared from *M. smegmatis*, was promoted by cysteine, tryptophane and dimethylsulfoxide (DMSO), while glutamic acid, glutamine and histidine exerted variable effects. The final effects of glutamic acid and glutamine were determined by the total concentration of both compounds together. The presence of cysteine and glutamic acid alone or together with DMSO abolished all inhibitory effects. Desferal did not enable the multiplication of *M. leprae* on media devoid of SE prepared from *M. smegmatis*. However with SE and 0.005% and 0.002% concentrations of Desferal its initial growth was accelerated. Its final counts, noted after an eight month incubation, did not exceed those observed without Desferal.

Purine and pyrimidine compounds promoted markedly the multiplication of *M. leprae* (counts $> 3 \times 10^7$ /ml.). The highest counts were observed with pyrimidines (thymine, thymidine, cytosine) applied single or combined.—Authors' Summary

✓ **Prabhakaran, K., Harris, E. B. and Kirchheimer, W. F.** *o*-Diphenoloxidase of *Mycobacterium leprae* separated from infected armadillo tissues. *Infect. Immun.* **12** (1975) 267–269.

We reported earlier the occurrence of a unique *o*-diphenoloxidase in *Mycobacterium leprae* recovered from lepromatous human tissues. No other source of *M. leprae* for biochemical studies was available at the time. In the present report, properties of phenoloxidase in *M. leprae* separated from infected armadillo tissues are presented. The results show that the *o*-diphenoloxidase remains unaltered in the passage of the bacilli from the human to the animal host, indicating that the enzyme is an intrinsic characteristic of the leprosy bacteria.—Authors' Summary

Experimental Infections

✓ **Collins, F. M., Auclair, L. and Montalbaine, V.** Effect of T cell depletion on the growth of BCG in the mouse foot pad. *Int. Arch. Allergy Appl. Immunol.* **48** (1975) 680–690.

The growth of *Mycobacterium bovis* (BCG Montreal) and *M. tuberculosis*, Erdman was determined in normal and T cell depleted (THXB) mice when injected subcutaneously into a hind foot pad. The bacilli multiplied

only to a limited extent within the foot pad itself but the infection quickly spread to the draining popliteal lymph node to eventually reach the liver, spleen and lung. The amount of systemic growth seen in the THXB mice was 10–100 times greater than in the normal controls, all of which developed a tuberculin hypersensitivity and an immune response in 14 to 18 days. T cell depletion completely inhibited the expression of tuberculin sensitivity by the infected host as well as ablating the antituberculous response against both the vaccinating BCG population and a super-infecting Erdman challenge inoculum. Incorporation studies in the THXB mice indicated a striking reduction in cell division within the draining lymph node but there was an unexpected elevation in the level of incorporation by the lung cells as the BCG infection progressed. The significance of these findings is discussed in relation to the possible use of the BCG foot pad model for studies of leprosy immunity.—Authors' Abstract

- ✓ Job, C.K., Chacko, C.J.G., Verghese, R. and Singh, S. Padam. Leproma of the mouse foot. *Lepr. Rev.* **46** (1975) 39–49.

Leproma of the foot in six T 900r CBA mice produced by local injection with *M. leprae* is reported in this paper. Organisms numbering 10^4 multiplied to the order of 10^9 in 10 to 12 months. The original inoculum of *M. leprae* was obtained from a lepromatous patient and the bacilli were first passaged through a group of T 900r Swiss albino mice and later were subcultured three times successively in T 900r CBA mice. One or more of the animals used in each of the subcultures developed erythematous swelling of both inoculated hind feet which on microscopic examination showed typical lepromatous nodules. None of the other 23 strains of bacilli studied from different lepromatous patients showed this reaction. It is possible that this particular strain of *M. leprae* had undergone certain variations producing lesions characteristic of lepromatous leprosy.—Authors' Summary

- ✓ Kirchheimer, W.F. and Sanchez, R.M. Survival of *M. leprae* in cutaneous inoculation sites of armadillos. *Lepr. India* **47** (1975) 5–8.

Fifteen armadillos were infected by simul-

taneous cutaneous inoculation of 10^7 *M. leprae* from the same human patient. After 1,095 days ten armadillos were alive and five had died with disseminated leprosy (death rate 33.3% in 1,095 days). Of the ten survivors six had no signs of disseminated leprosy while four had such signs. Survival of leprosy bacilli and their presence in the infection site for more than 400 days signalize dissemination of the infection later on. The time of death ranged from 397 days to 1,016 days after infection. This, together with the other findings, shows that there are great differences in susceptibility to infection with *M. leprae* among nine-banded armadillos.

The importance of making susceptibility studies in relation to dose of infection with simultaneous inoculation with leprosy bacilli from the same source is stressed.—Authors' Summary

- ✓ Levy, Louis. Superinfection in mice previously infected with *Mycobacterium leprae*. *Infect. Immun.* **11** (1975) 1094–1099.

Previous studies of the protection of mice by prior infection with *M. leprae* in one hind foot pad against challenge with *M. leprae* in the opposite hind foot pad had produced conflicting results; therefore, the problem was restudied. In several experiments, BALB/c mice were inoculated first in the right hind foot pad with 5,000 *M. leprae* and then challenged in the left hind foot pad with 5,000 *M. leprae* of the same strain at intervals after primary infection, at the same time that uninfected mice were inoculated. Multiplication of the *M. leprae* of the secondary challenge inoculum occurred at the same rate and to the same level as multiplication in uninfected mice when challenges were made soon after primary infection. Multiplication was slowed but proceeded to the same level in previously infected as in uninfected mice when the challenges were administered between 76 and 106 days after primary infection (47 to 17 days before the *M. leprae* of the primary inoculum had multiplied to the level of 10^6 organisms per foot pad). Finally, the *M. leprae* of a secondary challenge administered at the time that the organisms of the primary inoculum had multiplied to 10^6 per foot pad or later not only multiplied more

slowly in previously infected than in control animals, but multiplication in the previously infected animals reached a lower maximum. These results are similar to those observed when mice previously infected with *M. bovis* (BCG), *M. marinum*, *Toxoplasma gondii*, or *Besnoitia jellisoni* were challenged with *M. leprae*.—Author's Summary

✓ Levy, L., Ng, H., Evans, M.J. and Krahenbuhl, J.L. Susceptibility of thymectomized and irradiated mice to challenge with several organisms and the effect of dapsone on infection with *Mycobacterium leprae*. Infect. Immun. 11 (1975) 1122–1132.

B6C3F₁ mice that had been thymectomized at 8 to 12 weeks of age, subjected to 950 R of whole-body X irradiation, and transfused with syngeneic bone marrow were challenged in a foot pad with *M. leprae* or *M. marinum*, or intravenously or intraperitoneally with *Listeria monocytogenes*. Also, mice inoculated with *M. leprae* in a hind foot pad were administered dapsone in the mouse chow. The thymectomized-irradiated (T+R) mice did not survive as well as nonthymectomized mice when housed in the vivarium with no special precautions, but survived sufficiently well to permit the completion of some long-term experiments. *M. leprae* multiplied to a higher "ceiling" and survived longer in the T+R mice than in the nonthymectomized controls. But a ceiling to multiplication of *M. leprae* was imposed, and finally the organisms were killed. The histopathologic appearance of the foot pad tissues, studied by electron microscopy, was consistent with the measurements of bacterial numbers and viability. Swelling of the foot pad after local inoculation with *M. marinum* was greater in T+R mice than in nonthymectomized controls. Similarly, the number of *L. monocytogenes* following intravenous challenge was greater in the spleens of T+R than of nonthymectomized mice, and the survival of the T+R mice after intraperitoneal challenge with *L. monocytogenes*, was striking, suggesting that these T+R mice had retained or regained some immune competence. The effects of dapsone treatment of T+R mice inoculated with *M. leprae* were much the same as those of treatment of nonthymectomized mice. Because these T+R mice

were not greatly immunosuppressed, they would not have provided a model of human lepromatous leprosy suitable for chemotherapeutic studies.—Authors' Summary

✓ Levy, Louis and Ullman, Nancy M. Inhibition of multiplication of *Mycobacterium leprae* by several antithyroid drugs. Am. Rev. Respir. Dis. 111 (1975) 651–655.

Multiplication of *Mycobacterium leprae* in the mouse foot pad was inhibited when mice were fed, mixed in their diet, 0.05% methimazole, 0.066% USP thyroid powder, methimazole plus thyroid powder, 0.15% 5-*n*-heptyl-2-thioxo-4-thiazolidinone, 0.1% propylthiouracil, and 0.1% thiambutosine for 154 days, beginning on the day of inoculation. All of the treatment regimens except for the two containing thyroid powder, decreased the plasma concentrations of thyroxide and protein-bound iodine. It is suggested that the two antithyroid drugs, methimazole and propylthiouracil, and the two antimicrobial agents, heptylthioxo-thiazolidinone and thiambutosine, all of which possess structural features in common, may exert the antithyroid and antimicrobial effects through a common mechanism.—Authors' Summary

✓ Prabhakaran, K., Harris, E.B. and Kirchheimer, W.F. Hairless mice, human leprosy and thymus-derived lymphocytes. Experientia 31 (1975) 784–785.

The authors found that there is no significant increase in proliferation of *M. leprae* in hairless mice as compared to normal mice. Despite their proven T cell deficiency, the nude mice do not promote generalized infection with *M. leprae*. Immune deficiency disorders are usually accompanied by high incidence of malignancies. However, Rygaard and Povlsen (1974) found that hairless mice do not develop spontaneous tumors. These authors propose a third (as yet unknown) expression of immunological surveillance in nude mice, separate from cell-mediated and humoral immunity. Our observations suggest that deficient T lymphocyte function alone might not provide a satisfactory explanation for excessive susceptibility to leprosy.—(From authors' results and discussion)

✓ **Purtilo, D. T., Walsh, G. P., Storrs, E. E. and Gannon, C.** The immune system of the nine banded armadillo (*Dasypus novemcinctus*, Linn.). *Anat. Rec.* **181** (1975) 725-733.

The armadillo is rapidly emerging as an animal for biomedical research. A morphologic study of the immune system of the armadillo was undertaken to try to demonstrate a possible defect in the morphogenesis of the lymphoid organs that could account for their susceptibility to leprosy. Blood from 20 domesticated adult armadillos revealed lymphocytes predominated among circulating leukocytes in the majority of animals, whereas in wild animals neutrophils predominated. Necropsies revealed well-developed thymus glands and the thymus-dependent areas in lymph nodes and spleens contained abundant lymphoid cells. Hence, we conclude that the susceptibility of the armadillo to leprosy cannot be explained on a morphologic basis.—Authors' Abstract

✓ **Rees, R. J. W., McDougall, A. C. and Weddell, A. G. M.** The testis in mice infected with *Mycobacterium leprae*. *J. Pathol.* **115** (1975) 73-79

Following inoculation either locally or intravenously with *M. leprae* of human origin, the histopathology and bacteriology of the testis in experimental mice is described. Normal mice, and mice rendered immunologically deficient by thymectomy and whole-body irradiation, were studied.

Attention is drawn to a heavy bacillation of the testis in mice from both groups. Bacilli were found in and beneath the tunica albuginea, but mainly in interstitial cells and in macrophages surrounding the tubules. The percentage of solidly staining bacilli was high, and globi were frequent.

The study showed that the testis in mice is particularly favorable for the lodgment and multiplication of *M. leprae* following either local or intravenous inoculation.

The significance of this in relation to the

metabolism of the leprosy bacillus and to the frequent occurrence of testicular damage in the lepomatous male patient is discussed.

This work was supported by grants to A.G.M. Weddell and A.C. McDougall from the Medical Research Council and the British Leprosy Relief Association.—Authors' Summary

✓ **Watson, S. R., Sljivic, V. S. and Brown, I. N.** Defect of macrophage function in the antibody response to sheep erythrocytes in systemic *Mycobacterium lepraemurium* infection. *Nature* **256** (1975) 206-208.

The results presented indicate that the antibody response to SRBC is depressed in mice systemically infected with *M. lepraemurium*. Furthermore, the defect was associated particularly with the macrophages of infected animals and not with their lymphocytes at the stages of infection studied. Our experiments do not indicate a direct contact effect by heavily infected macrophages or the release of a suppressive factor. The nature of the defect has yet to be established. Two possibilities are being considered in our immediate experiments. First, that overloading of macrophages with mycobacteria may interfere with their ability to ingest, process and present other antigens in a normal manner and second, a possibility associated with the massive antibody production against *M. lepraemurium* antigens during infection, that antigen-antibody complexes are formed and become bound to the surface of macrophages, thus blocking the sites for binding of the factor(s) produced by T lymphocytes which may be required for antibody production to SRBC. Whether or not macrophage defects of a similar nature occur in diseases of man where macrophage involvement is extensive, for example, leprosy, leishmania and malaria, requires further study. If they do, they could account, at least in part, for the immunosuppressed state often associated with such infections.—(Excerpted from article, no summary)

Epidemiology and Prevention

✓ **Hertroijis, Adrianus, R.** Defaulters and non-defaulters. *East Afr. Lepr. Bull.* **3** (1975) 25-34.

The high-risk group concerning treatment

defaulting is characterized by persons who are: in the lower age group under 20 years old, especially males; single rather than married; of the indeterminate or tuberculoid

type of leprosy; not deformed or disabled; free of reactions; only under treatment for a short time (less than one year); and registered relatively early or after a survey.

The main reason for defaulting is mobility (67%). The reasons for this mobility are not known or whether they are different from the reasons of mobility in the general population. Until we know more about the reasons for mobility of the leprosy patient it will be difficult to state anything specifically about the real reason for defaulting.

Although numerically the defaulting problem is a big one, it is epidemiologically a lesser problem because only a small portion of the defaulters are potentially infectious (6.4% lepromatous or borderline lepromatous, against 21.9% in the nondefaulter population).

It must be possible to visit all the potentially infectious patients who have recently registered and who have dropped out of treatment for one month only, and to make this the first priority of the field workers. A nationwide coverage of leprosy field programs is required to determine the migration problem. Further investigation is needed on the mobility problem, and the reasons of the leprosy patients compared with those of the general population, which are to be accompanied with an accurate investigation for the reasons of defaulting. This may require a very enthusiastic sociologist.—*(Adapted from author's conclusions)*

Kurian, P. V., Victor, Smt. V. and Devanbu, D. School survey as an effective method for leprosy control in rural areas. *Lepr. India* 47 (1975) 75–78.

During the school year June 1973 to April 1974, 85% of the pupils attending 380 schools in Gudiyatham Taluk of Tamil Nadu were examined for evidence of leprosy. Among the 76,891 children examined, 217 new cases of leprosy were detected. There was no case of lepromatous leprosy in this group. All except two borderline cases were either indeterminate or tuberculoid. In endemic areas repeated annual examination of the school population will help considerably in the control of the disease and in educating the people. The results of school surveys carried out in some Indian cities are also included for comparison.—*Authors' Summary*

Lechat, M. F., Misson, J. Y., Vellut, C. M., Misson, C. B. and Bouckaert, A. Un modèle épidémiométrique de la lèpre. [An epidemic model of leprosy.] *Bull. WHO* 51 (1974) 361–373. (In French)

The authors describe an epidemic model of leprosy elaborated with the aim of evaluating the long-term efficacy of control measures (systematic case-finding and mass ambulatory treatment) and simulating the effects of other control methods on incidence. The model was based on data concerning 35,262 cases observed during the period 1955–1970 in the Polambakkam region of India. One of the main difficulties encountered was the lack of epidemiologic data indicating the relative importance of different forms of leprosy as sources of infection. Furthermore, the prevalence and the duration of subclinical disease could not be determined. In order to overcome these problems, a method was developed for estimating the infectivity of the lepromatous and tuberculoid forms of leprosy according to the duration and assiduity of treatment, as well as the distribution of the incubation period. The evolution of incidence over the past 20 years was simulated on the computer. The forecast indicates that, if the current control measures were maintained without change, a 60% reduction in the incidence of both forms of leprosy would be achieved in 20 years. Various control measures were simulated—vaccination with a vaccine preventing the development of lepromatous leprosy or with a hypothetical specific vaccine; intensification of case finding; a reduction in the rate of treatment default; and selective segregation of lepromatous patients. The results obtained are discussed with a view to establishing priorities in leprosy research and defining the strategies to be adopted in future control programs.—*Authors' English Summary*

Noordeen, S. K. Evolution of tuberculoid leprosy in a community. *Lepr. India* 47 (1975) 85–93.

The paper is based on a longitudinal study of a geographically limited rural community highly endemic for leprosy. The entire population in the community numbering about 8,000 was followed up every year for over six years, including cases of leprosy that occurred. The mean incidence of tuberculoid

leprosy was found to be 10.6 per 1,000 per year. Intensive follow-up of newly detected cases revealed that regression of disease among tuberculoid leprosy cases was a very common feature, the mean inactivation rate being 10.9% per year. Inactivation rates were not influenced by either age or sex. Inactivation rates were comparatively low when more than one part of the body was affected, or when the patient had more than two patches, or when he had involvement of nerve trunks. Inactivation rates were not influenced by treatment, the bulk of inactivation being spontaneous. The epidemiologic significance of the findings with regard to leprosy control is reviewed.—Author's Summary.

- ✓ **Otsyula, Y. and Chum, H. J.** A comparative study in attendance rates where dapsone (DDS) is given to outpatients at variable intervals. *East Afr. Lepr. Bull.* 3 (1975) 18-23.

An attempt was made to assess if using various treatment intervals attendance rates would improve (keeping all other factors constant). Attendance rates of patients re-

ceiving treatment once monthly was significantly better than the twice weekly, once weekly, or once a fortnight.

Short interval treatment regimens did not improve the attendance rates.—(*Adapted from authors' summary*)

- ✓ **Rodriguez, Jose N.** The trend of leprosy in Cebu Province, Philippines. *Lepr. Rev.* 46 (1975) 9-13.

Although covering different periods of time and different sections of the population, four studies are presented which establish the fact that there had been a downward trend of leprosy, at least of the lepromatous type, in the province of Cebu, Philippines. This decline occurred during a period when the administrative procedures for the control of leprosy consisted of compulsory segregation of bacteriologically positive cases and the outpatient treatment of paucibacillary cases at skin clinics. Moreover, the downward slope occurred during the presulfone era. Possible causes of the decline of leprosy in this province are discussed.—Author's Abstract

Other Mycobacterial Diseases and Related Entities

- ✓ **Gee, B. R., Schiefer, B. and Ward, G. E.** Disease resembling feline leprosy. *Can. Vet. J.* 16 (1975) 30. (Letter to Editor)

We would like to draw to the attention of veterinary practitioners in Canada the presence of lesions in cats resembling leprosy.

Evidence of feline leprosy was first encountered in 1971 during examination of suspect skin tumors submitted as formalin-fixed specimens to the Department of Veterinary Pathology, WCVN. To date nine specimens have been submitted from British Columbia and one from Alberta. The lesions at presentation were described as single or multiple skin nodules located in a variety of sites including the elbow, flank, ventral abdominal wall, back and tail. Ulceration was reported in three cases.

Two cats were examined retrospectively and both were free of cutaneous lesions. The right superficial inguinal lymph node was enlarged in one cat and the node was surgically removed for histological and bacter-

iological investigation.

Histologically, there was extensive granulomatous inflammation involving the dermis and the subcutaneous tissue. The lesions were composed principally of histiocytes and in some areas they resembled foam cells. The numbers of neutrophils, plasma cells and lymphocytes varied. Large numbers of acid-fast stained bacteria were scattered throughout the lesions. A granulomatous lymphadenitis was found in the surgically removed lymph node but acid-fast staining failed to demonstrate any bacteria in that lesion. Bacteriological study of lymph node tissue was not rewarding.

As far as the public health aspect is concerned, there appears to be no reason for excessive concern at this time. Firstly, it still remains to be proven that the spontaneous feline leprosy cases are caused by the same agent that is responsible for the disease in man.... We are soliciting the referral of cats with suspicious lesions and the

submission of fixed and unfixed tissue specimens to facilitate this needed study.—(From Letter to Ed.)

Havel, A. and Pattyn, S. R. Activity of rifampicin on *M. ulcerans*. Ann. Soc. Belg. Med. Trop. **55** (1975) 105–108.

The minimal inhibitory concentration of RMP for *M. ulcerans* is 5 mcg/ml. The MED of RMP on the experimental *M. ulcerans* infection in mice is 10 to 15 mg/kg body weight, administered five days a week.

The known active drugs against *M. ulcerans* are enumerated. It is concluded from the experimental data available that human chemotherapy of *M. ulcerans* infections will be comparable to that of tuberculous infections, both in terms of cost of drugs and duration of treatment.—Authors' Summary

✓ **Meyers, Wayne M. and Connor, Daniel H.** *Mycobacterium ulcerans* infections in leprosy patients. Lepr. Rev. **46** (1975) 21–27.

In a population of 1,061 patients with leprosy and 180 patients with *M. ulcerans* infections, we recorded a history of both diseases in six individuals. There was no

evidence that either infection altered the tissue response or clinical course of the other.—Authors' Summary

Stanford, J. L., Revill, W. D. L., Gunthorpe, W. J. and Grange, J. M. The production and preliminary investigation of Burulin, a new skin test reagent for *Mycobacterium ulcerans* infection. J. Hyg. (Camb.) **74** (1975) 7–16.

The preparation of a skin test antigen from *Mycobacterium ulcerans* by ultrasonic disintegration and filtration is described. The reagent, called Burulin, was tested in Africa in normal schoolchildren, and in patients with leprosy, tuberculosis or *M. ulcerans* disease. Those with tuberculosis or *M. ulcerans* disease were simultaneously tested with Tuberculin PPD. Burulin was found to be highly specific for patients in the reactive stage of *M. ulcerans* disease, and there was no cross-reaction in patients with other mycobacterioses. On the other hand, the majority of patients with *M. ulcerans* disease reacting to Burulin also produce positive reactions to Tuberculin PPD.—Authors' Summary