

## CURRENT LITERATURE

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## General and Historical

**Kalisch, Philip A.** Tracadie and Penikese leprosaria: a comparative analysis of societal response to leprosy in New Brunswick, 1844-1880, and Massachusetts, 1904-1921. *Bull. Hist. Med.* **17** (1973) 480-512.

This extended recapitulation of the lives of the colonies in Canada and Massachusetts is drawn effectively from contemporaneous "Annual Reports" originating within the institutions. The article is not without its own bias that "superstition and medievalism ran their course." There is little doubt that the selection of the areas for the two institutions was unimaginative, and that the spots were at times mighty dreary places, borne of middle 19th century concepts of leprosy in the case of the institution at Tracadie, scarcely advanced in the Penikese Island hospice, which was in effect a small and unimportant refuge. The article provides much insight into the thinkings that instigated establishment of these inadequate asylums in the historical sense.—G. L. Fite

**Klafstad, Jacob.** Et leprakranium fra middelalderens Oslo. [A leprosy cranium from medieval Oslo.] *Tidsskr. Norske Legeforen.* **93** (1973) 1483-1485. (In Norwegian)

This paper describes the osseous findings in the cranium of a female skull at the University of Oslo, on the basis of which a diagnosis of leprosy is made. The changes de-

scribed are those previously noted by Glück, Möller-Christensen, Hjørting-Hansen and others.—O. K. Skinsnes

**LEPROLOGIA**, **18**, No. 2 (1973) 99-213.

The second issue of 1973 of this publication begins with an editorial by Dr. Luis M. Balina which questions the scientific developments of leprology in a "scientific" era. Dr. Balina wonders if the logistics of apportionments of funds to patient care, and of assignments of patients to institutions, are really in accord with modern concepts of the disease. Then, Dr. Pascual B. Arcuri reports on the development of epidemiological studies of leprosy and their practical application in the province of Tucuman in northwestern Argentina. Frontera Vaca and four colleagues follow with a review of nerve histopathology, especially as studied by Dr. Florencio Castoldi (pp 109-115). Manzi and colleagues (pp 116-122) report on the clinical and anatomical changes in the ulnar nerve in leprosy, emphasizing the value of electromyography. In an autopsy study of three cases of hepatic cirrhosis found among 63 autopsied cases of leprosy, one showed bacilli in portal vacuolated cells, but the writers concluded that the cirrhosis was incidental and not directly related (Bernard and Brounstein, pp 124-134). Gatti and others treated 44 patients in reaction with imipramine. Results were favorable in 19 cases; the drug was well tolerated in all but six (pp 141-146).—G. L. Fite

## Clinical Sciences

**Antia, Noshir H.** The significance of nerve involvement in leprosy. *Plast. Reconstr. Surg.* **54** (1974) 55-63.

This nicely illustrated article presents an overall view of the neurosurgical approach to the handling of treatment of nerve damage in leprosy.—G. L. Fite

**Barton, R. P. E.** Olfaction in leprosy. *J. Laryngol. Otol.* **88** (1974) 355-361.

The sense of smell was assessed in a group of 150 leprosy patients. The methods used and the results obtained are presented. Overall, 38% of patients showed some degree of hyposmia, and this was shown to be related to the severity of the lepromatous involvement of the nose, to the amount of sensory loss in the nose and to the systemic clinical state. The possible reasons for the loss of olfaction are discussed.—Author's Summary

**Enna, Carl D.** Neurolysis and transposition of the ulnar nerve in leprosy. *J. Neurosurg.* **40** (1974) 734-737.

Neurolysis of the ulnar nerve is an accepted surgical procedure for the treatment of leprosy neuritis. The indications for this procedure in leprosy differ from those in other conditions; the basis for performing the specific steps are explained, and the general results discussed.—Author's Abstract

**Giraudeau, P.** Transferts (36) du seul jambier postérieur pour réactiver la dorsiflexion chez les lépreux. (Nouvelle technique personnelle d'amarrage pluri-tendineux.) [Transposition of the tibialis posterior muscle to restore dorsiflexion in 36 leprosy patients. A new technic of multiten-dinal attachment.] *Med. Trop.* **33** (1973) 377-383. (In French, English summary)

The transfer of the tendon of the tibialis posterior muscle alone, variant of the Carayon's double transposition, is of a special interest in the treatment of the paralysis of Hansenian lateral popliteal nerve.

This transfer allows the reanimation of the dorsal flexion of the foot. It can also be done in the treatment of traumatic paralysis, of lesions of sciatic nerve following an injection of quinine, and sometimes of poliomyelitis paralysis.

Its technic is easy but a postoperative functional reeducation is always necessary.—(From *Trop. Dis. Bull.*)

**Hasan, S.** A survey of plantar ulcers among the inmates of the Leprosy Home and Rehabilitation Center, Moula Ali, Hyderabad, A.P. *Lepr. India* **46** (1974) 99-102.

On surveying plantar ulcers among the patients of the leprosy home and rehabilita-

tion center at Hyderabad, it was found that: 1) The first metatarsal head was the most frequent site for plantar ulceration. The chances of ulceration at this site are double those at the fifth metatarsal head. 2) Proximal phalanx of the great toe is the next frequent site of ulceration. 3) Clawing or damage of toes increases the chances of ulceration over forefoot area. 4) A large number of anesthetic feet do not ulcerate.—(Adapted from author's summary)

**Heinz, C.** Die Grundlagen der chirurgischen Behandlung von Leprapatienten. [Basis for the surgical treatment of patients with leprosy.] *Praxis* **62** (1973) 1285-1287. (In German)

Surgery has assumed an important place in the therapy of leprosy and its complications. We recognize three groups of complications: 1) the disease itself, 2) primary lesions, and 3) secondary lesions. As a result of the invasion of peripheral nerves by leprosy bacilli, there are frequently irreversible losses of motor or sensory functions, i.e., paralysis or anesthesia. These primary lesions and not the disease itself, cause contractures, penetrating ulcers, and osteomyelitis of the fingers and toes producing serious mutilations of the hands and feet. Paralysis of the eyelids causes keratitis leading to corneal opacities and blindness.

Surgery plays a definite role in the prevention of primary lesions: by transposing and decompressing the ulnar nerve leprosy neuritis may be terminated. Surgery is particularly useful in the prevention of secondary lesions. For example, tendon transfers restore muscle balance to weakened hands and feet, and temporal muscle transfers may prevent blindness by aiding eye closure.—(Adapted from author's French summary)

**Palande, D. D.** A review of twenty-three operations on the ulnar nerve in leprosy neuritis. *J. Bone Joint Surg. [Am.]* **55-A** (1973) 1457-1464.

Ulnar neurolysis and transposition operations were done on 23 patients with leprosy neuritis. The pain was relieved in all cases and motor recovery of various degrees was evident. Follow-up of up to two years showed that most of the motor recovery occurred between six and twelve months after the operation. The extent of damage and

recovery were related to the type and duration of neuritic involvement.—Author's Abstract

**Powell, Sheila and McDougall, Colin.** Clinical recognition of leprosy: some factors leading to delays in diagnosis. *Br. Med. J.* **1** (1974) 612-613.

The case histories of eight patients in the United Kingdom admitted to hospital for the diagnosis of leprosy are examined in detail. Review of their early symptoms and signs showed that there had been delays in diagnosis, ranging from a few months to many years. Possible reasons for delay are discussed, and attention is called to the importance of nasal symptoms in the early diagnosis of lepromatous leprosy.—Authors' Summary

**Ramu, G. and Ramanujam, K.** Relapse in borderline leprosy. *Lepr. India* **46** (1974) 19-25.

1. One hundred seventy cases of subsident borderline leprosy were followed up for from 3-9 years and presented a relapse rate of 4.4% per year.

2. The category of cases belonging to the middle of the borderline spectrum possessed the most chances of relapse.

3. No relapses have been seen after the fifth year of follow-up therapy after subsidence; hence, six years of regular therapy following subsidence might be deemed necessary. The study emphasizes the fact that gratifying early subsidence should not make one complacent of the final outcome and that an arbitrary period of discharge of cases from treatment is unsafe.

4. The mild grades of lepromin positivity in the majority of the cases perhaps indicate that the tissue reactivity to *M. leprae* is weak enough to allow some other factors to gain the upper hand in determining the onset of relapses in the face of regular therapy.—(Adapted from authors' summary)

**Sehgal, V. N. and Manerkar, A. N.** Significance of sweat response in diagnosis of leprosy. Part 1. *Lepr. India* **46** (1974) 43-45.

Local intradermal "carbachol" (carbaminoyl choline) injections were given in 50 cases of leprosy comprising 38 tuberculoid and 12 dimorphous. The sweat response was recorded and the results compared to that

of the contralateral side which acted as a control. The result of the sweat response in de novo leprosy patients was poor, as compared to those on antileprosy therapy for variable periods of time. Diagnostic value of this test in the presence of equivocal clinical features is brought out. Its probable objective value in the assessment of leprosy after treatment is mentioned.—(Adapted from authors' summary)

**Selby, Roy C.** Neurosurgical aspects of leprosy. *Surg. Neurol.* **2** (1974) 165-177.

The classification, clinical manifestations and indications and methods of neurosurgical diagnosis and treatment of leprosy have been reviewed. The role of surgery for the management of nerve abscess, some entrapment syndromes and methods to establish diagnosis have been indicated. Further improvements in medical management of the disease and its complications will lessen the therapeutic role of surgery. Increasing knowledge of the pathogenesis of leprosy and *erythema nodosum leprosum* (ENL) probably will shed light on the mechanisms involved in the production of other neuropathies, particularly those associated with collagen diseases.—Author's Summary

**Senechal, G. and Neveu, M.** Perforations septales et rhinoplasties. [Septal perforations and rhinoplasties.] *Ann. Otolaryngol. Chir. Cervicofac.* **90** (1973) 659-664. (In French)

This article presents a general discussion of various types of nasal septal perforations, and the authors' technics for their repair are described. Preexisting and post-rhinoplasty perforations are considered.—W. M. Meyers

**Watson, R. A., Gangai, M. P. and Skinsnes, O. K.** Genitourinary leprosy. *Urol. Int.* **29** (1974) 312-326.

The genitourologic aspects of leprosy are reviewed. 1. Renal complications are widespread and clinically significant. Amyloid degeneration is common in leprosy, particularly in the West. 2. Adrenal involvement is also seen. Clinical consequences, although not thoroughly evaluated, do not seem significant. 3. Testicular and epididymal involvement, universal in lepromatous leprosy, is of diagnostic and therapeutic importance, particularly in association with

lepromatous gynecomastia, a clinical model of "acquired Klinefelter's syndrome." 4. The existence of venereal leprosy, postulated through the ages in folklore, is not borne out by scientific investigation. 5. The external genitalia are generally spared, although occasional involvement has been reported. 6. The ureters, bladder and urethra are spared as are the prostate and seminal vesicles. 7. Abnormal urinalyses, reflecting renal impairment, are frequently seen. The frequency and significance of mycobacteriuria remain unsettled.—Authors' Abstract

**Wyss, T.** Wiedereingliederung der Lepra-kranken durch Korrektur der Nasendefor-

mitäten. Neue Wege zur Korrektur der Sattelnase. [Rehabilitation of the leprosy patients by correction of the nasal deformities. New ways in the correction of the saddle nose.] *Praxis* 62 (1973) 1305-1306. (In German, English summary)

A simple and riskless alloplastic operation for saddle nose reconstruction is described. It has been especially devised for the rehabilitation of leprosy patients, removing their saddle nose deformity. Soft polyethylene has been proven to be the optimal material for the alloplastic inlay, avoiding internal decubitus and having ideal long-term tolerance in the tissue.—English Summary

## Chemotherapy

**Barranco, Vincent P.** Inhibition of lysosomal enzymes by dapsone. *Arch. Dermatol.* 110 (1974) 563-566.

The possible inhibition of lysosomal enzymes by dapsone (diaminodiphenylsulfone) was studied. Experimentally induced hypervitaminosis A in rabbits results in loss of chondroitin sulfate from cartilage matrix through the release of lysosomal enzymes.

In this study, thinning and decreased toluidine blue and Alcian blue staining of tracheal and articular cartilage produced by the administration of 500,000 international units of vitamin A daily were inhibited by the administration of dapsone. These findings strongly suggest that dapsone inhibits lysosomal enzyme activity. Inhibition of lysosomal enzyme activity may play a role in the therapeutic effects of dapsone on certain diseases such as dermatitis herpetiformis.—Author's Summary

**Edwards, O. M., Courtenay-Evans, R. J., Galley, J. M., Hunter, J. and Tait, A. D.** Changes in cortisol metabolism following rifampicin therapy. *Lancet* II (1974) 549-551.

A patient with Addison's disease required increased corticosteroid dosage whilst receiving rifampicin. The pharmacological half-life of cortisol was reduced, but returned to normal when rifampicin was stopped. Cortisol-production rates in four patients with pulmonary tuberculosis rose during treatment with rifampicin, as did

urinary D-glucuronic-acid excretion, an index of liver microsomal-enzyme activity. The alteration of the corticosteroid requirement in the patient with Addison's disease and the elevation of the cortisol-production rates were attributed to increased cortisol catabolism following hepatic microsomal-enzyme induction by rifampicin.—Authors' Summary

**Ellard, G. A., Gammon, P. T., Helmy, H. S. and Rees, R. J. W.** Urine tests to monitor the self-administration of dapsone by leprosy patients. *Am. J. Trop. Med. Hyg.* 23 (1974) 464-470.

Three qualitative and one simple quantitative urine test methods are described for monitoring the self-administration of daily doses of dapsone (DDS) by leprosy patients. The qualitative methods can be employed for monitoring the taking of daily doses of 50 mg DDS or more. In the quantitative method the ratio of DDS plus its diazotizable metabolites to creatinine in the urine is determined using simple colorimetric methods. This method is considerably more sensitive and efficient than the qualitative methods and is capable of monitoring the taking of daily doses of DDS of as little as 10 mg.—Authors' Abstract

**Gupta, S., Grieco, M. H. and Siegel, I.** Immunosuppression by rifampin in tuberculosis. *Am. Thorac. Soc./Am. Lung Assoc. Annu. Mtg. Sci. Community Health Abstracts*, May 13-15, 1974, p 44.



Immunosuppressive property of rifampin has been reported in various animal systems both *in vivo* and *in vitro*. Rifampin appears to inhibit lymphocyte stimulation *in vitro* to phytohemagglutinin (PHA) and purified protein derivative (PPD) and suppresses delayed cutaneous hypersensitivity to PPD in man. The current study was designed to observe the effect of rifampin on circulating T and B lymphocytes in patients with tuberculous infections. Circulating T and B lymphocytes were assayed by the rosette-forming technic of Wybran and associates (1972) and Bianco and associates (1971). Results of the study are summarized in table form.

Rosettes		Normal control (n=13)	Patients with tuberculosis on rifampin (4-32 weeks) (n=11)
T cells	Mean	27.1	19.5
	SD	3.8	5.1
B cells	Mean	12.1	10.4
	SD	2.5	3.0

These data suggest that rifampin significantly suppressed circulating T lymphocyte rosettes in patients with tuberculosis receiving rifampin therapy for more than four weeks ( $p=0.005$ ). No significant effect was seen on circulating B lymphocyte rosettes.—Authors' Abstract

**Holmes, I. B. and Hilson, G. R. F.** The rate of bactericidal action of rifampin on *Mycobacterium leprae* in the mouse foot pad (38021). *Proc. Soc. Exp. Biol. Med.* **145** (1974) 1395-1400.

The rate of bactericidal action of rifampin on *Mycobacterium leprae* in the mouse foot pad was determined by the kinetic technic of Shepard and a serial dilution subinoculation technic. In kinetic experiments, rifampin (0.01%) in continuous dietary administration, produced a delay in bacillary growth, the extent of which was dependent on the period of drug administration. The estimated survival half-life of *M. leprae* was 0.5 day. This was confirmed by the subinoculation technic, by which a survival half-life of 0.6 day was obtained.

Drug administration for 14 days rendered an inoculum of  $10^4$  *M. leprae* noninfective for mice.—Author's Summary

**Pandey, S. and Singh, A. K.** Treatment of neural involvement in leprosy. *Lepr. India* **46** (1974) 83-88.

A trial of clofazimine dye along with INH and local hydrocortisone acetate was carried out on 25 cases of leprosy, of both lepromatous and nonlepromatous types. The response was assessed clinically and through the Bacterial Index. On the whole, the early results are quite encouraging.—Authors' Summary

**Pattyn, S. R., Rollier, R., Saerens, E. J. and Rollier, M. R.** Initial three months continuous and intermittent therapy in lepromatous leprosy. A controlled clinical trial. Preliminary data. *Ann. Soc. Belg. Med. Trop.* **54** (1974) 43-49.

Preliminary data are presented on a controlled clinical trial of three months introductory treatment of leprosy, comparing standard daily dapsone (100 mg) with rifampicin daily (450 mg), rifampicin (900 mg) once weekly and clofazimine, once weekly (300 mg) regimens. Present results on 54 patients show a rapid bactericidal effect of the two rifampicin regimens, already evident after one month of drug administration. No serious adverse effects due to intermittent administration of rifampicin were observed. A short-term introductory rifampicin treatment of leprosy, rapidly bactericidal and easy to administer and to supervise followed by a long-term intermittent, supervisable aedapsone treatment might provide fool-proof treatment of the disease.—Authors' Summary

**Pattyn, S. R. and Saerens, E. J.** Results of intermittent treatment with dapsone and rifampicin of mice inoculated with *Mycobacterium leprae*. *Ann. Soc. Belg. Med. Trop.* **54** (1974) 35-41.

Dapsone administered continuously in the food at a 0.01% concentration during six months was bactericidal for *M. leprae* in the mouse foot pad test.

When the same dose was given once a week or less frequently the effect was bacteriostatic. The MID for once weekly regimens of rifampicin is situated between 0.125 mg and 0.062 mg. In a dose of 1.5 mg once a

week and once every two weeks this drug had a bactericidal effect. A dose of 0.5 mg once a week and once every two and four weeks was bactericidal. A dose of 0.25 mg was bactericidal when given once a week and once every four weeks, bacteriostatic only when given once every eight weeks.

Such experiments should provide information on the possibility to use low doses of rifampicin as an introductory treatment in lepromatous leprosy.—Authors' Summary

**Peters, J. H., Gordon, G. R., Levy, L., Storckan, M. A., Jacobson, R. R., Enna, C. D. and Kirchheimer, W. F.** Metabolic disposition of dapsone in patients with dapsone-resistant leprosy. *Am. J. Trop. Med. Hyg.* **23** (1974) 222-230.

To investigate the question of whether dapsone (DDS) resistance in leprosy patients is related to the metabolic disposition of DDS, we studied a group of 22 patients who had relapsed with DDS-resistant disease after approximately 19 years of sulfone therapy. Tests for acetylator phenotype with sulfamethazine (SMZ) showed that this group of patients contained a lower percentage of slow and a higher percentage of intermediate and rapid acetylators than had been observed previously in other populations. Acetylation of SMZ and DDS were directly related. In addition, plasma clearance of DDS for the DDS-resistant group was significantly faster than that found previously in any other population. These observations suggest that the emergence of DDS resistance may be associated with the rapid or intermediate acetylator phenotype and an ability to clear DDS from the circulation at a fast rate. Combining the two parameters into a multirisk factor yielded a significantly higher mean value in DDS-resistant patients than that of any other group studied previously. The implications of these findings for the large-scale treatment of leprosy patients are discussed.—Authors' Abstract

**Riley, R. W. and Levy, L.** Characteristics of the binding of dapsone and monoacetyl-

dapsone by serum albumin (37200). *Proc. Soc. Exp. Biol. Med.* **142** (1973) 1168-1170.

The characteristics of binding of DDS and MADDS by HSA and of DDS by MPA have been studied by means of an equilibrium dialysis technic and analyzed by means of the Scatchard relationship. The plot of  $v/A$  vs  $v$  for each of the three studies yielded a straight line, suggesting only one species of binding site. Each molecule of HSA was found to possess one binding site for MADDS. Each molecule of MPA and HSA possessed 1/2 binding site for DDS, suggesting that DDS behaved as a bivalent molecule, and that one molecule of DDS was bound to two albumin molecules. The binding constant of HSA binding of MADDS was ten times greater than the constant of HSA binding of DDS. The binding constants for DDS binding by both HSA and MPA were the same.—Authors' Summary

**Verhagen, A. R.** Die Anwendung einer neuen antimykobakteriellen Kombinations-therapie bei der Lepra in Ostafrika. [The effect of a new combined antimycobacterial treatment of leprosy in East Africa.] *Z. Tropenmed. Parasitol.* **24** (1973) 36-39.

The present drugs available in leprosy have to be given for years, which makes control of the disease ineffective. Excellent results have recently been reported in the treatment of leprosy with rifampicin. On the basis of experimental research with *M. marinum*, two combinations of rifampicin, 300 mg, and isoniazid, 200 mg twice daily and 200 mg sulfanil-amido-methoxy-pyrazine once daily was tried in ten untreated cases: eight diffuse-lepromatous and two borderline-lepromatous. Clinical results were excellent and there was only one case with a severe reversal reaction, liver function tests, blood and urine showed no severe abnormalities.

It is concluded that the treatment is well tolerated in leprosy and gives excellent results, but its superiority over rifampicin alone remains to be proved.—Author's Summary

## Immuno-Pathology

**Abe, M., Minagawa, F. and Yoshino, Y.** Therapeutic effect of rifampicin (RFP) on

leprosy. IV. Serological examination. *Lepro* **43** (1974) 45-51. (In Japanese)

In order to know the effect of rifampicin (RFP) on the immunological state of leprosy, the sera of lepromatous patients treated with the combined use of RFP and DDS were examined at three month intervals for a period of one year using the following tests: fluorescent leprosy antibody absorption test (FLA-ABS); lepro agglutination, i.e., an agglutination of kaolin particles coated with cardiolipin-lecithin (1:1) and electrophoresis on cellulose-acetate membrane.

The antibody-titer of the FLA-ABS test dropped temporarily during treatment and then tended to rise at the twelfth month. Such a fall of antibody-titer was more conspicuous in the patients who had ENL under treatment than in the cases without ENL. The titer of the lepro agglutination test showed a similar temporary fall in the latter cases but not in the ENL cases. In two cases of patients who had borderline reaction under treatment, the FLA-ABS titer was on the decline after the reaction subsided. Immunoglobulins M and G were found to participate in this test and the titer of respective immunoglobulins underwent similar changes to those described above.

Among serum protein fractions only  $\alpha_2$ -globulin showed a temporary drop in level in cases without ENL. No significant difference was found in lepromin reactions examined before and after treatment. The implications of these findings are discussed from a viewpoint of the immunology of leprosy.—(Adapted from English summary)

**Adams, Dolph O.** The structure of mononuclear phagocytes differentiating *in vivo*. I. Sequential fine and histologic studies of the effect of BCG. *Am. J. Pathol.* **76** (1974) 17-39.

Although the differentiation of mononuclear phagocytes is fundamental to their multifarious activities, their differentiation is incompletely understood—particularly *in vivo*. The development of an epithelioid granuloma may be hypothesized to represent such differentiation *in vivo*. To test this, the sequential ultrastructure of developing epithelioid granulomas was examined. Viable bacilli Calmette-Guerin (BCG) injected into the subcutaneum of guinea pigs produced epithelioid granulomatous inflammation, which was sampled for light and electron microscopy on alternate days until

the 33rd day after injection. Initially, monocytes invaded the tissues and then coalesced, enlarged and formed small granulomas which ultimately evolved into epithelioid granulomas. The monocytes, ultrastructurally very simple cells, developed increased nuclear euchromatin, prominent nucleoli, extensive cytoplasm, free ribosomes, abundant Golgi profiles, many mitochondria and numerous large lysosomes and became macrophages. The macrophages in turn underwent further enlargement and became closely intertwined with one another to form epithelioid cells—large polygonal macrophages, containing euchromatic nuclei, numerous lysosomes, plentiful mitochondria and prominent synthetic apparatus. These changes undergone by monocytes during their development into epithelioid cells, which may be divided into five stages, are interpreted as differentiation *in vivo* of the mononuclear phagocytes. The observations demonstrate directly the differentiation of these cells *in vivo* and suggest some, if not all, characteristic features of granulomatous inflammation result from such differentiation.—Author's Summary

**Agarwal, D. P., Benkmann, H. G., Goedde, H. W., Rohde, R., Delbruck, H. and Rougemont, A.** Levels of serum  $\beta_1C/\beta_1A$  globulin (C3) and its polymorphism in leprosy patients and healthy controls from Ethiopia and Mali. *Humangenetik* **21** (1974) 355-359.

The distribution of C3 variants in leprosy patients and healthy controls from Ethiopia and Mali are reported. Significantly lower concentration of  $\beta_1C/\beta_1A$  globulin was observed in sera of affected individuals as compared to healthy controls. Possible association between C3 levels and leprosy is discussed.—Authors' Summary

**Axelsen, N. H., Harboe, M., Closs, O. and Godal, T.** BCG antibody profile in tuberculoid and lepromatous leprosy. *Infect. Immun.* **9** (1974) 952-958.

In sera from 12 patients with polar tuberculoid leprosy, 12 with subpolar tuberculoid leprosy, and 16 with lepromatous leprosy there were demonstrated a total number of 125 anti-BCG precipitins by means of crossed immunoelectrophoresis with intermediate gel. Up to 14 different precipitins

were found in individual sera, and the complexity in antibody response was higher than previously realized. The specificity of 69% of the antibodies was defined, and these antibodies were titrated in three arbitrary titer units. A highly significant difference ( $p < 0.002$ ) was found in antibody response between the tuberculoid and the lepromatous group. Due to simplicity, sensitivity, and high resolution, the method used is a promising tool for providing exact data to be used as guidelines for purification of important individual mycobacterial antigens. The need for reference antisera is emphasized.—Authors' Summary

**Bellossi, A., Languillon, J. and Duclos, M.**

Effet d'un champ magnétique uniforme sur les leucocytes. Étude du test de migration des leucocytes chez les lépreux. [Effect of a uniform magnetic field on leukocytes. Study of a test of leukocyte migration in leprosy patients.] Bull. Soc. Pathol. Exot. 67 (1974) 25-30. (In French)

If a uniform magnetic field leads to an increase of cellular energy, it is hoped that after a stay in such fields, the lymphocytes of lepromatous leprosy patients, anergic subjects, will be able to react like the lymphocytes of allergic tuberculoid leprosy patients. The leukocyte migration test, a reflection of cellular immunity, is chosen as a parameter.

In fact, it can be stated that leukocyte migration is inhibited, whether these cells come from tuberculoid or lepromatous leprosy patients, and irregardless of whether the antigen used is nonspecific (phytohemagglutinin) or specific (lepromine). Nevertheless, after exposure of white cells in a uniform magnetic field the results appear more homogenous and do not go against the initial assumption about an increase of cellular energy.—(Adapted from English summary)

**Boddingius, Janny.** The occurrence of *Mycobacterium leprae* within axons of peripheral nerves. Acta Neuropathol. (Berl.) 27 (1974) 257-270.

*Mycobacterium leprae* were found within axons of peripheral nerves in patients with lepromatous leprosy and in mice with leprosy.

In the human radial and superficial peroneal nerve biopsies examined, intra-axonal (IA) bacilli were found in one to five percent of the myelinated axons. The bacilli usually occurred in groups situated near the core of the axon, but single organisms were sometimes located more peripherally.

In mouse sciatic nerves, IA bacilli were predominantly found in unmyelinated axons, and the organisms occurred singly. The number of IA bacilli per unit area of the nerve was positively correlated with the number of bacilli occurring in Schwann cells of unmyelinated axons.

Some IA bacilli in both man and mice occurred free in the axoplasm, some were invested by a phagosomal membrane, whereas others were surrounded by an electron-transparent zone and by a phagosomal membrane.

Morphologically, the IA bacilli in mice and in one patient appeared to be viable. In other patients, however, half of the IA bacilli were fragmented (nonviable) and these were found within lysosome-like structures.

There was no histological evidence that IA bacilli were causing pathologic changes in the axoplasm.—Author's Summary

**Carranza Goycochea, C. E., Frontera Vaca, J. L., Temporini, A., Rosati, A. A. and Rugieri, F.** Anatomia radiologica vascular del territorio tibial posterior y tecnica arteriografica. [Vascular anatomy radiography of the posterior tibial territory and arteriography technic.] Leprologia 18 (1973) 27-31. (In Spanish)

This article is a summary of the area supplied by the posterior tibial nerve revealed by radiography and selective arteriography of the lower limb in utilizing a tri-iodic compound. The importance of arterial implants especially to enhance collateral circulation through tibial posterior artery decompression, is pointed out.—(Adapted from English summary)

**Convit, J., Pinardi, M. E. Ochoa, G. R., Ulrich, M., Avila, J. L. and Goihman, M.** Elimination of *Mycobacterium leprae* subsequent to local *in vivo* activation of macrophages in lepromatous leprosy by other mycobacteria. Clin. Exp. Immunol. 17 (1974) 261-265.



This investigation studied the possibility of activating lepromatous macrophages by a local *in vivo* test.

Lepromatous macrophages have an evident incapacity for clearing *M. leprae*. This is demonstrated by injecting lepromatous patients with an antigen containing *M. leprae* from human tissue at a concentration of  $640 \times 10^6$  bacteria per ml. This produces a nodule which, at a 30-day biopsy, shows a macrophagic granuloma<sup>1</sup> with numerous bacteria inside the macrophages, proving that these cells are unable to remove *M. leprae*. This incapacity is specific for *M. leprae*, and all other mycobacteria produce a different reaction.

Local *in vivo* stimulation of the lepromatous macrophage was obtained by injecting *M. leprae* in the same concentration as above but mixed with other mycobacteria (*M. lepraemurium* or BCG).

The mixed antigens produced a tuberculoïd granuloma with abundant lymphoid cells. Fite-Faraco stains showed almost no acid-fast bacteria. Therefore, our mixture of antigens had activated the macrophages locally and made them competent for clearing *M. leprae*.—Authors' Summary

<sup>1</sup>Leproma (IJL 38 [1970] 203-206)—Editor.

**Cottenot, F. and Pennec, J.** Baisse du taux des anticorps circulant dans la lèpre aux cours des poussées réactionnelles. [Reduction in circulating antibody levels in leprosy during reactional episodes.] Ann. Med. Interne. 124 (1973) 405-407. (In French)

A total of 14 leprosy patients were studied. Antibody levels were determined by an immunofluorescent technic using the Stefansky bacillus.

During the first few days of reactions, the antibody levels drop in all patients and then return to initial levels 5-6 weeks after the episode is finished. These findings are consistent, signify a reactional state, and suggest that therapy should be diminished or an antireactional drug administered, e.g., thalidomide. Unchanged antibody levels are symptomatic of advancing disease and either another antileprotic should be used or the dosage of the present drug increased. These alterations are of physiopathologic interest since they are immunologic expres-

sions of the local deposition of antibodies in the reactional foci. Turk, in 1970, demonstrated histologically by immunofluorescence that ENL lesions contained deposits of IGG antibodies and complement. The drop in circulating antibody levels seems to precede or accompany the local deposition of antibodies in the lesions.—(Translated from French conclusion)

**Dutta, R. N. and Saha, Kunal** Australia antigen and lepromatous leprosy: its incidence, persistence and relation to cell-mediated immunity. Indian J. Med. Res. 61 (1973) 1758-1765.

A high incidence of Au-antigen has recently been reported in cases of leprosy from South India and Bombay. In this paper, an attempt has been made to study the incidence of the Au-antigen in various types of leprosy. The present study shows a high incidence of Au-antigen in the lepromatous leprosy as opposed to the tuberculoïd variety which is found to be negative for Au-antigen. Au-antigen positive leprosy cases from the civilian population have been followed up for a period of two and half years and were found to be persistently positive for Au-antigen without any clinical manifestations. It is suggested that they are carriers of hepatitis associated virus. Lepromatous leprosy is known to have a depression of cell-mediated immunity. The present study also suggests that the higher incidence of Au-antigen in lepromatous leprosy is probably correlated to the depression of cell-mediated immunity in the lepromatous variety. It also suggests that a good physical health and nutritive diet help in resisting the development of lepromatous variety of leprosy.—Authors' Summary

**Enna, Carl D. and Zimny, Marilyn.** A scanning electron microscopy study of cartilage obtained from contracted joints of denervated hands. Hand 6 (1974) 65-69.

Samples of articular cartilage obtained from joints with flexion contractures, in denervated hands of patients with leprosy were studied with the scanning electron microscope.

Varying degrees of degenerative changes were noted affecting the surface and all levels of the cartilage. In advanced degradation there was a decrease in total thickness

with loss of identity of the three zones.

A decrease in the porosity of the matrix was especially evident in the midzone, and the lacunae with chondrocytes were smaller and lacked the morphological appearance of the chondrocyte in normal cartilage.

Areas of increased density, suggesting calcification of the matrix, varied in extent. With lesser involvement, it was usually localized to raised areas, at the edge of exposed lacunae, whereas generalized involvement was observed less frequently.

It is our opinion that these findings indicate degenerative processes produced by a combination of factors including increased intrinsic forces and joint incongruity compression with immobilization. The relatively extensive degrees of degradation are attributed to lack of pain perception in denervated extremities.—Authors' Summary

✓ **Gelber, R. H., Drutz, D. J., Epstein, W. V. and Fasal, P.** Clinical correlates of Clq-precipitating substances in the sera of patients with leprosy. *Am. J. Trop. Med. Hyg.* **23** (1974) 471-475.

*Erythema nodosum leprosum* (ENL) is often interpreted as a manifestation of immune complex deposition in patients with lepromatous leprosy. We used a Clq precipitin assay technic to demonstrate directly the presence of immune complexes in sera from patients with leprosy. Seven of 15 patients with ENL had serum Clq precipitin activity; serial tests often showed continued Clq precipitin activity. Only 3 of 27 lepromatous patients without ENL had positive tests; multiple positive tests were not seen in these patients. Single positive tests were encountered in patients with borderline (dimorphous) leprosy, especially those with downgrading reactions. There was no relationship between Clq precipitin activity and serum levels of C3, CH<sub>50</sub>, or cryoglobulins. Single positive Clq precipitin tests may occur sporadically in patients with leprosy, but repeatedly positive tests are closely associated with occurrence of ENL, supporting the concept that ENL is a complication related to the presence of circulating immune complexes.—Authors' Abstract

✓ **Hamburger, R. N., Fernandez-Cruz, E., Arnaiz, A., Perez, B. and Bootello, A.** The relationship of the P-K titer to the serum

IgE level in patients with leprosy. *Clin. Exp. Immunol.* **17** (1974) 253-260.

Fifty patients with leprosy were found to have P-K titers inversely related to their serum IgE levels. Patients with leprosy react in a manner similar to normal individuals and to patients with other diseases. Serum IgG, IgM, IgA and complement were measured in 25 of the leprosy patients in addition to the serum IgE and only the IgG significantly positively correlated with the serum IgE. All of these leprosy patients were shown to react to exogenous histamine and they released endogenous histamine when chemically stimulated. Two patients had absent flare responses with normal weals, the remaining 48 had complete weal and flare responses. Higher serum IgE levels were noted in those patients with recent institution of chemotherapy.—Authors' Summary

✓ **Jacob, T., Vijayarathnam, P., Verghese, R. and Krishnamurty, S.** Lymphoblast transformation in leprosy. *Indian J. Med. Res.* **62** (1974) 696-698.

Phytohemagglutinin-M induced lymphoblast transformation of peripheral lymphocytes in cell cultures was studied in 21 lepromatous and 7 tuberculoid leprosy patients and in 9 control subjects. There was no appreciable difference in the range or mean of the proportion of blasts in the cultures among the three groups. This indicates that thymus-dependent lymphocytes are basically normal in number and function in lepromatous leprosy in our locality.—Authors' Summary

✓ **Jones, Thomas C.** Macrophages and intracellular parasitism. *J. Reticuloendothel. Soc.* **15** (1974) 439-450.

Interactions of mammalian host cells with various viral, bacterial, fungal and protozoan parasites serve to constantly reemphasize the marvels of the biologic process. Most fascinating is the interaction of these parasites with cells of the system specifically differentiated by the host organism to deal with foreign microbes, i.e., cells of the monocyte-macrophage system. What phylogenetic adjustments must have occurred to allow microbes not only to evade this defense system, but in some instances, to enter into it, alter it and create within it a micro-

environment ideal for survival! In this discussion, I would like to focus on several examples of those facultative and obligate intracellular parasites which have accomplished this feat. Not to be outdone by such phylogenetic ingenuity, the macrophage has countered with equally clever mechanisms which, in an amazingly worldly way, have often led not to ultimate victory, but to negotiated peace; a tolerant symbiosis. The microbe is allowed to persist; in exchange the host achieves lasting immunity against similar organisms in the environment. I will discuss the entry of parasites into host cells, survival within the vacuolar system and the effects of immunity on intracellular parasitism, with particular reference to studies we have done on the interaction between the protozoan, *Toxoplasma gondii*, and mouse peritoneal cells.—Author's Abstract

**Krishnan, A. D. and Talwar, G. P.** Cultivation of human peripheral blood monocytes *in vitro*. Indian J. Med. Res. **62** (1974) 313-316.

A simple method requiring minimal processing is described for obtaining and culturing macrophages derived from monocytes of human peripheral blood. Essentially, heparinized venous blood is obtained from fasting subjects and allowed to settle for 45 minutes at 37° C, using siliconized glassware. The plasma along with the buffy coat is transferred to a test tube.

The monocytes thus obtained are cultured in Leighton tubes with 0.5 ml of medium 199 preadjusted to pH 7.8 to which has been added 0.5 ml of enriched plasma. Tubes are incubated at 37° C and the cultures fed on the second or third day, depending on the rate of metabolic activity as gauged by the change in color of the medium towards yellow, with 0.3 ml of medium 199 containing 50% heat inactivated (56° C—30 min) autologous serum adjusted to a pH of 8. The medium is changed usually on the sixth day when macrophages are developed.

Twenty ml of blood can furnish about 15 culture tubes with good yields of cells. Macrophages can be maintained for prolonged periods under the conditions indicated. The cells give reactions for lysosomal enzymes and are competent to phagocytose intracellular parasites such as *Mycobacterium leprae*.—O. K. Skinsnes

**Lim, S. D., Kizskiss, D. F., Jacobson, R. R., Choi, Y. S. and Good, R. A.** Thymus-dependent lymphocytes of peripheral blood in leprosy patients. Infect. Immun. **9** (1974) 394-399.

Study of the numbers of thymus-derived lymphocytes by the rosette assay (T-RFC) in patients with leprosy reveals that lower than normal numbers of T-RFC are regularly seen in those patients with the active lepromatous form of this disease. Essentially normal numbers of T-RFC were found in inactive lepromatous, borderline, and indeterminate types of leprosy. The lowest percentages and lowest absolute numbers of T-RFC were encountered in patients with lepromatous leprosy resistant to chemotherapy. Patients with lepromatous leprosy complicated by *erythema nodosum leprosum* show numbers of T-RFC that are more nearly normal than the numbers of T-RFC in patients with uncomplicated lepromatous leprosy. These findings are discussed with respect to the pathogenesis of lepromatous leprosy and the T-RFC deficiency demonstrated in this disease. The possibility that transient defects in T-RFC numbers or function may predispose to lepromatous leprosy is proposed.—Authors' Summary

**Louie, J. S., Koransky, J. R. and Cohen, A. H.** Lepra cells in synovial fluid of a patient with *erythema nodosum leprosum*. N. Engl. J. Med. **289** (1973) 1410-1411.

Acute arthritis may occur in association with *erythema nodosum leprosum*, an exacerbation of lepromatous leprosy characterized by fever, nodular skin eruptions and occasionally iritis, orchitis, neuritis, nephritis and lymphadenopathy. The pathogenesis of this arthritis is not clear. Though direct infiltration from overlying skin has been reported, usually no organisms are described either in the synovial fluid or in synovial tissue, and immunologic phenomena are postulated.

Lepra organisms, free and within foamy macrophages (lepra cells), are reported within the synovial fluid of the patient with *erythema nodosum leprosum*.—(Adapted from authors' introduction)

**Mendes, E., Raphael, A., Mota, N. G. S. and Mendes, N. F.** Cell-mediated immunity in leprosy and transfer of delayed hypersen-

sitivity reactions. *J. Allergy Clin. Immunol.* **53** (1974) 223-229.

Eighty-nine patients with leprosy, 65 classified as lepromatous and 24 as tuberculoid, were examined in this study. Skin test responses to protein antigens and dinitrochlorobenzene (DNCB) were depressed in lepromatous patients compared to controls. Tuberculoid patients did not exhibit a significant depression to microbial antigens, but they showed a definite depression in the ability to be sensitized with DNCB. The transfer of delayed hypersensitivity reactions to tuberculin, trichophytin, and lepromin (Fernandez and Mitsuda reactions) was accomplished in lepromatous and indeterminate leprosy patients using viable lymphocytes from donors presenting positive reactions to these antigens. The lepromin reaction was also transferred to patients with South American blastomycosis and cutaneous leishmaniasis. The positive reactions of adoptive immunity were confirmed by histologic examination of skin biopsies.—Authors' Summary

**Mendes, N. F., Kopersztych, S. and Mota, N. G. S.** T and B lymphocytes in patients with lepromatous leprosy. *Clin. Exp. Immunol.* **16** (1974) 23-30.

The percentages of T and B peripheral blood lymphocytes were established in 36 patients with lepromatous leprosy. T lymphocytes were detected by rosette formation with sheep erythrocytes (E) and B lymphocytes were detected by rosette formation with human erythrocytes sensitized with antibody and complement (HEAC). The mean percent values for both T and B lymphocytes were significantly lower in these patients as compared to mean values from 30 normal subjects ( $0.05 > p > 0.01$ ). Lymph node sections treated *in vitro* with E or HEAC from two lepromatous patients which were examined, showed marked depletion of T cells in the paracortical areas and the follicles were slightly reduced in size, but still presenting B cells. Establishing the percentages of T and B peripheral blood lymphocytes and their distribution in lymph nodes may represent an additional method of evaluating the immunologic status of leprosy patients.—Authors' Summary

**Minjat, Marguerite.** Données immunologiques dans la maladie de Hansen. Place

de la réaction d'immuno-fluorescence indirecte. [Immunologic data on Hansen's disease. Role of the indirect immunofluorescent reaction.] Doctoral thesis in pharmacy of Dr. Minjat, University of Claude Bernard, Lyon, France, 1973. (In French)

In this 208-page thesis the author presents an extensive review of the literature on the immunology of leprosy (307 references) and describes the results of 1) her detailed three to six year clinical immunologic follow-up study of 18 leprosy patients, and 2) more than 2,000 sera of various origins. The salient findings were: 1) a drop in total serum antibodies prior to reactions in lepromatous patients, and 2) the usefulness of mycobacterial antigens (especially the well-known *M. marinum* and Stefansky bacillus) in the immunofluorescent sero-diagnosis of leprosy. Positive reactions in sera of grouped lepromatous patients varied from 84-100% while those of active tuberculoid patients reached 65%. Contacts of leprosy patients gave 53% positive reactions and 40 normal sera were all negative—W. M. Meyers (Summarized from French)

**Myrvang, Bjorn.** Immune responsiveness to *Mycobacterium leprae* of healthy humans. Application of the leukocyte migration inhibition test. *Acta Pathol. Microbiol. Scand. [B]* **82** (1974) 707-714.

Immune responsiveness to *Mycobacterium leprae* was studied, by the method of leukocyte migration inhibition, in 90 healthy adults allocated into four groups according to previous contact with leprosy patients. Groups working or living in close relationship with leprosy patients responded significantly more strongly to *M. leprae* than a group without such contact. With a selected concentration of *M. leprae* 71.2% of medical attendants dealing with leprosy patients, 22.2% of administrative staff of a leprosy hospital, and 50% of household contacts of leprosy patients showed migration indices  $< 0.800$ , but none of the group without known contact with leprosy patients showed indices below the threshold value. Since the inhibition of migration to BCG was similar in all groups, and no evidence was found that other mycobacteria had provoked the positive responses elicited by *M. leprae*, the above figures appear to represent indi-



viduals immunologically stimulated with *M. leprae* itself. The study, therefore, showed that the method of leukocyte migration inhibition may be used as an assay for specific detection and enumeration of immune responses mounted by *M. leprae*. The results lend strong support to the view that leprosy bacilli are frequently transmitted from patients to contacts. The introduction of *M. leprae* into the human body is, however, rarely accompanied by development of clinical signs of leprosy.—Author's Summary

**Myrvang, B., Feek, C. M. and Godal, T.** Antimycobacterial antibodies in sera from patients throughout the clinico-pathological disease spectrum of leprosy. *Acta Pathol. Microbiol. Scand.* [B] **82** (1974) 701-706.

Sera from one hundred and thirty-nine leprosy patients, clinico-pathologically classified into seven groups, were examined for precipitating antimycobacterial antibodies by double diffusion in gel analyses. As the source of antigen, *Mycobacterium duvalii* tended to be superior to *Mycobacterium bovis* (BCG) and revealed precipitins in 57 of the sera. Throughout the leprosy spectrum, the proportion of precipitin-positive sera increased from the tuberculoid to the lepromatous end giving a maximum of 73.6% positive sera in the polar lepromatous (LL) group. Similarly, the number of precipitin lines also increased and in some lepromatous sera five lines were deciphered. The presence of precipitins was closely related to the density of *Mycobacterium leprae* in the skin of the patients. This suggests that the antigenic load is the main factor in determining the antibody formation in leprosy.—Authors' Summary

**Myrvang, B., Godal, T., Feek, C. M., Ridley, D. S. and Samuel, D. R.** Immune response to *Mycobacterium leprae* in indeterminate leprosy patients. *Acta Pathol. Microbiol. Scand.* [B] **81** (1973) 615-620.

Immune responsiveness to *Mycobacterium leprae* was examined in 31 histologically classified indeterminate leprosy patients. Fourteen of the patients were also classified as indeterminate clinically (strictly indeterminate group), while the other 17 patients were clinically classified as tuberculoid or borderline leprosy. The strictly indeterminate group appeared to be quite

homogeneous in their immune reactivity to *M. leprae*. All patients revealed a lymphocyte transformation of less than 3% (mean  $0.57 \pm 0.88$ ) and only one out of seven patients tested by the leukocyte migration technic revealed a migration index of less than 0.80 (mean  $0.91 \pm 0.16$ ). Only one patient gave a positive early lepromin reaction. None of the patients revealed a positive reaction in gel precipitation to mycobacterial antigens. These findings are in agreement with the view that the immune response to *M. leprae* has not been triggered off in strictly indeterminate leprosy. On the other hand, the clinically tuberculoid and borderline patients with an indeterminate histological picture responded on average more strongly to *M. leprae*, and by and large according to their clinical diagnosis. It is concluded that in classifying patients as indeterminate leprosy, the clinical picture may give more information than histopathology.—Authors' Summary

**Myrvang, B., Godal, T., Ridley, D. S., Froiland, S. S. and Song, Y. K.** Immune responsiveness to *Mycobacterium leprae* and other mycobacterial antigens throughout the clinical and histopathological spectrum of leprosy. *Clin. Exp. Immunol.* **14** (1973) 541-553.

Immunological responsiveness was studied throughout the clinical and histopathological spectrum of leprosy (Ridley-Jopling scale) by the methods of lymphocyte transformation, leucocyte migration inhibition and delayed skin hypersensitivity.

The response to *Mycobacterium leprae* showed by all methods a continuous decrease from strong responses in the polar tuberculoid (TT) group to virtually negative responses in the polar lepromatous (LL) group. There was a good agreement between the *in vitro* methods and the lepromin skin test, giving support to the latter as a useful tool in the evaluation of immune responsiveness to *M. leprae* in leprosy patients.<sup>1</sup>

The immune response to BCG and PPD on the other hand, decreased only slightly towards the lepromatous pole of the spectrum, confirming the high degree of specificity of the immune defect in lepromatous

<sup>1</sup>Or vice-versa, lepromin being a long-established useful tool in such evaluation!—Editor

leprosy. Patients grouped histologically as subpolar tuberculoid (TT/BT) reacted particularly strongly to BCG and PPD.

As it is likely that the methods used mainly measured T lymphocyte function, the clinicopathological manifestations of leprosy appear to reflect the strength of the cellular immune response against *M. leprae*. Thus the findings give strong support to the concept of a host-determined, immunological disease spectrum as expressed in the Ridley-Jopling classification.—Authors' Summary

**Oon, B. B., Khong, K. Y., Greaves, M. W. and Plummer, V. M.** Trophic skin ulceration of leprosy: skin and serum zinc concentrations. *Br. Med. J.* 2 (1974) 531-533.

Skin and serum zinc measurements have been made in patients with leprosy with and without trophic skin ulceration and in several other groups. Serum zinc concentrations were decreased in leprosy irrespective of the presence or absence of skin ulceration. Serum zinc concentrations in leprosy were also unrelated to smears positive for *Mycobacterium leprae* and to the clinical type of leprosy. Since a decrease of the serum zinc was also found in patients with dermatitis herpetiformis and pulmonary tuberculosis it seems likely that the decreased serum zinc in leprosy is a nonspecific metabolic consequence of chronic skin and internal disease. The mean skin zinc concentration in leprosy did not differ significantly from the corresponding value in control subjects, the lack of agreement between serum and skin concentrations being possibly related to the presence of nonexchangeable keratin-bound zinc in skin. Though the clinical significance of lowered serum zinc concentrations in leprosy is uncertain, therapeutic trials of zinc treatment in leprosy with trophic skin ulceration seem justifiable.—Authors' Summary

**Page, R. C., Davies, P. and Allison, A. C.** Participation of mononuclear phagocytes in chronic inflammatory diseases. *J. Reticuloendothel. Soc.* 15 (1974) 413-438.

The presence of mononuclear phagocytic cells is a constant feature of chronic inflammatory lesions of the diffuse and granulomatous types. These cells are beneficial to the host since they have the capacity to seques-

ter and destroy necrotic debris, microorganisms, foreign cells and other noxious materials. Cells engaged in these activities frequently exhibit many features characteristic of stimulated or activated cells, including increased cell size and granularity, elevated levels of lysosomal and other cellular enzymes and increased rates of membrane synthesis and metabolism. Normally acid hydrolase activity is confined to lysosomes and is not released into the cell cytoplasm or the extracellular environment. In addition to these protective functions, mononuclear phagocytes appear to be responsible, at least in part, for the pathogenesis of chronic inflammatory lesions. Exposure of these cells in culture to substances which induce chronic inflammatory lesions *in vivo* results in the production and selective release of large amounts of hydrolytic enzymes into the extracellular environment. The releasing cells remain viable for a long time and the continuous discharge of these enzymes into the extracellular compartment may be an important factor in the tissue destruction and fibrosis associated with chronic inflammatory reactions.—Authors' Summary

**Papageorgiou, P. S., Sorokin, C. F., Kouzoutzakoglou, K., Bonforte, R. J., Workman, P. L. and Glade, P. R.** Host responses to Epstein-Barr virus and cytomegalovirus infection in leprosy. *Infect. Immun.* 7 (1973) 620-624.

A study was undertaken in patients with leprosy to assess the contribution of cell-mediated immunity to the host response to Epstein-Barr virus (EBV) and cytomegalovirus (CMV) infection. Sixteen of 72 patients (22%) with lepromatous leprosy, with impaired cellular immunity, had anti-EBV titers of 1,640 or higher. Only 4 of 49 patients (8%) with tuberculoid leprosy, with intact cell-mediated immunity, attained the level of 1:640. The anti-EBV antibody titers were significantly higher in patients with lepromatous leprosy ( $P \approx 0.025$ ). No significant differences were found in the level of anti-CMV antibody titers in patients with the two types of leprosy. The presence of high anti-EBV antibody titers in lepromatous leprosy suggests that cell-mediated immunity is a significant factor in host response to EBV infection. Host immune

responses should be taken into consideration when assignment of an etiological role to EBV is based upon seroepidemiological data.—Authors' Summary

**Parikh, A. C., Souza, N. G., Chaulawala, R. and Ganapati, R.** Leprosy lesions in the scalp. *Lepr. India* **46** (1974) 39-42.

The few references on the incidence of leprosy lesions on the scalp are pointed out. The case histories of two patients, one with borderline leprosy showing raised anesthetic lesions on the scalp, and another with lepra reaction showing lesions resembling ENL on the scalp are described.

It is concluded that, though in the vast majority of lepromatous patients the bacilli cannot be demonstrated in the smears from the scalp, there is evidence to show that the scalp is a site where *M. leprae* do thrive and produce lesions, though rarely.—Authors' Summary

**Periaswami, V.** A modified technic for staining paraffin sections for acid-fast bacilli. *Lepr. India* **46** (1974) 94-98.

An attempt to improve the technic of staining paraffin sections for the demonstration of *M. leprae* is reviewed. A modified technic by the author is described where hot vegetable oil is used to remove the paraffin, 5% sulfuric acid for decolorization, Weigert's acid iron chloride for nuclear staining and picro-methyl blue for differentially staining the muscle and the nerve of the skin in the same section. By this technic a larger number of bacilli were seen than in methods where hot oil is not used for deparaffinization and sulfuric acid for decolorization. When present, they can easily be demonstrated because of yellow, green and blue backgrounds in any structure of the skin. The color contrast pattern is good for color photomicrography of the bacilli. Presence of bacilli in the tissues and their relationship to cellular response can also be studied.—Author's Summary

**Petchclai, B., Chutanondh, R., Prasongsom, S., Hiranras, S. and Ramasoota, T.** Complement profile in leprosy. *Am. J. Trop. Med. Hyg.* **22** (1973) 761-764.

We investigated complement in leprosy to detect its possible role in pathogenesis. Complement components, C3 proactivator (C3PA), CH<sub>50</sub> and anticomplementary ac-

tivity (AC) were determined in sera collected from lepromatous and tuberculoid leprosy. C3 was found increased in lepromatous leprosy and highly increased C3PA was found in both groups. Changes in other components lacked specific pattern. Increases in C3PA levels are believed to be due to aggregation of the increased serum immunoglobulins. C3 levels and CH<sub>50</sub> levels in the present study agree with those in other reports. Development of AC occurred in lepromatous sera even during two days of storage at -80° C. AC found among freshly collected sera was probably due to aggregated immunoglobulins. The present study serves as a groundwork for future investigations.—Authors' Summary

**Spielmann, V. W., Teixidor, D. and Matznetter, Th.** Blutgruppen und Lepra bei angolanischen Völkern. [Blood groups and leprosy in Angola people.] *BLUT (München)* **27** (1973) 426-431. (In German, English summary)

When testing more than 900 aborigines from Angola, approximately 50% suffering from leprosy, no significant relations were found between blood group frequencies and leprosy in general or its different clinical forms. This is demonstrated in detail by the results of the ABO- and Rhesus-system. There was not even a uniform trend of deviations detectable in gene frequencies, neither in the different populations nor in the different clinical forms of leprosy.—English Summary

**Sunderland, Sydney.** The internal anatomy of nerve trunks in relation to the neural lesions of leprosy. *Brain* **96** (1973) 865-888.

The internal anatomy of peripheral nerve trunks has been studied and discussed in relation to some features of the neural lesions of leprosy.

Special significance is attached to the perineurium, funicular structure and the intraneural funicular plexuses.

The perineurium controls the spread of the microorganisms confining them, for some time, to the affected funiculi and promoting their movement centrally along the bundles. By the time the outlines of the perineurium have been lost and the epineurium involved at any level, the microorganisms

are likely to have advanced considerable distances up the bundles.

Because of the elastic resistance of the perineurium, the pressure inside the bundle builds up as the products of the inflammatory reaction slowly accumulate. Compression and ischaemia of the contents of the bundle introduced in this way add to the involvement and destruction of nerve fibers due directly to the activity of the *M. leprae*.

The manner in which funicular plexuses control the funicular distribution of the *M. leprae* as they ascend along the nerve are described.

The intraneural arrangement is such that:  
a) The clinical signs and symptoms are initially sensory in nature. There can be no motor involvement in the absence of sensory changes. b) The appearance of motor signs is evidence of involvement of funiculi at levels where motor and sensory fibers are mixed in the funiculi. The levels at which this can be expected are discussed for the major peripheral nerve trunks.

The genesis of the conspicuous enlargements of the affected nerves which are limited to certain regions has been analyzed in relation to the variations in the internal structure of nerve trunks which have been shown to occur along their lengths.

The significance of the internal anatomy of nerve trunks has been discussed in relation to the surgical treatment of nerve trunk lesions in leprosy. The reasons for using restraint when contemplating desheathing the nerve, funicular neurolysis or nerve grafting are given. All remain questionable procedures.—Author's Summary

**Wall, J. R. and Wright, D. J. M.** Antibodies against testicular germinal cells in lepromatous leprosy. *Clin. Exp. Immunol.* **17** (1974) 51-59.

Testicular germinal cell antibodies were found in 44 out of the 59 patients with lepromatous leprosy and in 4 out of 10 patients with tuberculoid disease. A similar pattern was found in 12 out of 262 control patients and normal subjects.

The antibody was found to be of the IgG class and 40 out of 49 of these antibodies were shown to be complement fixing. Spermatozoal antibodies were detected in 12 patients, but no ovarian antibodies were found in any specimen. There was no close

correlation between *erythema nodosum leprosum* (ENL) and testicular antibodies. It was found that the characteristic of the testicular antibody in leprosy was its ability to be absorbed by *Mycobacterium* BCG suspension suggesting that this is another antibody induced by infection. A similar fluorescent pattern was seen in some patients who did not have leprosy, but in these cases it could not be abolished with BCG. It is concluded that autoimmunity may be one of the factors involved in the pathogenesis of orchitis in leprosy.—Authors' Summary

**Wright, D. J. M.** The significance of the fluorescent treponemal antibody (FTA-ABS) test in collagen disorders and leprosy. *J. Clin. Pathol.* **26** (1973) 968-972.

A test is described to distinguish the immunofluorescence seen on *T. pallidum* in syphilis from that due to antibodies against DNA.

The method consists of comparing the results of the fluorescent treponemal antibody (FTA-ABS) test with the staining obtained with *T. gondii* and *T. cruzi* using an indirect fluorescent technic. The ability of a particular serum to stain other organisms, in addition to *T. pallidum*, at a significant titer indicates that the treponemal fluorescence is not specific, and the loss of this staining property when organisms are pretreated with deoxyribonuclease suggests that the common microbial antigen is DNA. The isolated treponemal fluorescence found in syphilis is unaffected by pretreatment of *T. pallidum*.

When 123 sera from patients with collagen disorders were examined, nonspecific bacterial fluorescence was observed in six sera, while in 95 sera from patients with lepromatous leprosy, a positive FTA-ABS reaction was obtained in 14. There was no accompanying immunofluorescence on other protozoa. Therefore the antibody reacting in the FTA-ABS test in leprosy is likely to be treponemal in origin. A mitochondrial antibody was found in seven out of the fifteen sera from patients with lepromatous leprosy.—Author's Synopsis

**Yantorno, C. E., Vazquez, C. A. and Riera, C. M.** Reacciones anómalas auto y hetero-inmunes en enfermos hansenianos y convivientes clínicamente sanos. [Anomalous reactions, auto- and heteroimmune, in



leprosy patients and their healthy cohabitants.] *Rev. Leprologia* 9 (1974) 471-482. (In Spanish)

In the experimental part of this study 40 rabbits were subjected to different treatments. It was proven that tissue injury provoked by a unique or repetitive cryogenic treatment was able to induce antinuclear antibodies (AAN) in approximately one-third and one-half of the cases, respectively. The auto- and heteroimmunization using complete Freund's adjuvant (*Mycobacterium butyricum* incorporated to mineral oil) proved to be procedures capable of inducing the same phenomenon.

In the clinical part, leprosy patients and their healthy cohabitants were studied. It was demonstrated that in the two polar forms of leprosy there was a significant incidence of antinuclear, heterophile, and antihuman IgG antibodies. Thirty-six cohabitants belonging to nine families were studied. AAN were detected in 13, heterophiles in 6, and antihuman IgG in 2 cases.

It is proposed as a working hypothesis, that the serologic alterations observed in healthy cohabitants are produced by coadjuvant action of the bacillus during incubation of the disease.—(Adapted from English summary)

Yata, J., Gatti, R. A., Klein, G., Good, R. A. and Tsukimoto, I. Lymphocyte subpopulations in immunodeficiency disorders. *Clin. Immunol. Immunopathol.* 2 (1974) 519-525.

Peripheral blood lymphocytes from 25 normal persons and 47 patients with immunodeficiency diseases were studied for the presence of human thymus-lymphoid tissue antigen (HTLA) and their responsiveness to PHA. Whereas in normal persons, HTLA values were consistently around 36%, 17 immunodeficient patients had low numbers of HTLA-positive lymphocytes in their peripheral blood. In general, HTLA values corresponded with PHA responsiveness (36/47), however, a number of discordant situations were observed. These results suggest that HTLA may be a useful marker in evaluating an immunologically relevant lymphocyte population in clinical situations. This population is most likely of thymus origin and appears to be associated with PHA responsiveness in most situations. On the

other hand, the dissociation of these markers in 11 patients suggests that they detect either distinct but overlapping populations, different phases of differentiation of a single lymphocyte population or that the cells involved may be perturbed independently by exogenous factors, such as infections.—Authors' Summary

Yokomura, E-iti, Shimizu, Yoriko and Seno, Satimaru. Studies on the mechanism of phagocytosis. II. Analysis of the adhesion phase. *Jap. J. Med. Sci. Biol.* 27 (1974) 191-204.

To clarify whether electrostatic interaction contributes to the adhesion of red blood cells to monocytes, the first phase of phagocytosis was studied *in vitro* in ion-deficient environments compared to that in ionic environments. Monocytes from mouse tumor ascites and chicken and mouse red cells were used. In isotonic sucrose aqueous solution, glutaraldehyde-fixed red cells did not adhere to monocytes, whereas in Hank's solution they did. In Hank's solution adjusted to pH 5.8 or 6.95, the fixed red cells adhered to monocytes to the same degree as in Hank's solution, but not in a sucrose solution of pH 5.8, 6.95 or 7.4. Addition of calcium and magnesium ions to the isotonic sucrose solution to the same concentration as those in Hank's solution did not induce adhesion of the red cells to monocytes. The percentage of monocytes adhering to the fixed red cells increased in direct proportion to the logarithm of the ionic strength in mixtures of Hank's solution and isotonic sucrose aqueous solution at various ratios. The red cells fixed with glutaraldehyde and further methylated adhered to monocytes even in ion-free sucrose solution, but the fixed, deaminated red cells did not. From these results the mechanism of the adhesion is discussed from the viewpoint of lyophobic mechanisms. In adhesion of the glutaraldehyde-fixed red cells to monocytes, Van der Waals' interaction may act between the cell surfaces in a short range and electrostatic interaction in a long range. On the other hand, the fixed, methylated red cells may adhere to monocytes by electrostatic interaction in ion-free sucrose solution.—(Adapted from authors' summary)

Yoshizumi, Marc O. and Asbury, Arthur K. Intra-axonal bacilli in lepromatous lepro-

sy. Acta Neuropathol. (Berl) 27 (1974) 1-10.

*M. leprae* bacilli in nerves of three patients with lepromatous leprosy were found in the axoplasm of myelinated and unmyelinated nerve fibers. Axonal bacillation occurred in as much as 2% of myelinated axons. Bacilli within Schwann cells were a

more common finding in lepromatous leprosy than intra-axonal bacilli. Intra-axonal bacillation probably represents a late stage phenomenon in lepromatous leprosy. Intra-axonal bacilli may contribute to the dissemination of leprosy by migration of bacilli within the axon, and may contribute directly to nerve fiber destruction.—Authors' Summary

## Microbiology

Beaman, B. L., Kim, K. S., Laneelle, M. A. and Barksdale, L. Chemical characterization of organisms isolated from leprosy patients. J. Bacteriol. 117 (1974) 1320-1329.

Chemical analyses of the cell walls of organisms isolated in various parts of the world from cases of lepromatous and tuberculoid leprosy make possible their assignment to one of the three genera: *Corynebacterium*, *Mycobacterium*, or *Propionibacterium*. One, bacterium 22M, remains unassigned. The combined chemical and enzymatic properties attributed to leprosy bacilli freshly harvested from lepromata are found collectively, but not individually, in these three genera.—Authors' Summary

Bhatt, P. V. and Antia, N. H. Study of viability of *M. leprae* from multiple tissue biopsies of ten leprosy patients using the mouse foot pad technic. Lepr. India 46 (1974) 73-82.

Bacilli obtained by homogenization of biopsies from skin, lymph node, dartos muscle, nasal mucosa, nerve and striated muscle, were inoculated into the mouse foot pad to study viability. The ten patients included in this study consisted of four BT, four BL and two LL cases under various durations of treatment. The inoculates of nerves showed consistent and most significant growth as compared to the other tissues.—Authors' Summary

Dhople, Arvind M. and Hanks, John H. Energetics (adenosine 5'-triphosphate) of *Mycobacterium lepraemurium* in diffusion chambers incubated *in vitro* and in mice. Infect. Immun. 8 (1973) 907-910.

Adenosine 5'-triphosphate (ATP) measurements and the processing of samples have

been refined to a point where the energetics and growth potential of microscopic samples of unwashed host-grown, host-dependent microbes can be investigated. *Mycobacterium lepraemurium*, the noncultivated agent of murine leprosy, was employed to examine three reports of the slow microscopic growth of this organism in the absence of host cells. A few million bacterial cells were enclosed in Rightsel- and Ito-type diffusion chambers, which were incubated *in vitro* and in the peritoneal cavities of mice. In the *in vitro* experiments, a complex medium containing bovine serum and mouse brain extracts, renewed three times a week, did not sustain the energetics of the bacilli. The microscopic counts declined to 72% and the ATP per culture to 9% of the original values. Very different results were obtained from chambers incubated in the peritoneal cavities of mice. The bacterial biomass increased 2.7-fold and the ATP per culture increased 2.5-fold. Because the ATP per cell was 93% of the original, this system is regarded as the first to permit the extracellular growth of a so-called "obligate intracellular microbe." The results obtained with only  $1 \times 10^6$  host-grown cells per assay demonstrate a significant biochemical tool for investigating the growth potential of host-grown microbes during the progression, regression and therapy of disease.—Authors' Summary

Gangal, Sudha, G. and Khanolkar, Saroj R. Delayed hypersensitivity *in vivo* to an acid-fast mycobacterium cultivated from human lepromatous leprosy. Indian J. Med. Res. 62 (1974) 290-296.

Guinea pigs and mice were sensitized with heat-killed sonicated and frozen and thawed acid-fast mycobacteria, isolated from human

lepomatous leprosy and grown *in vitro*. The inhibition of migration of macrophages from sensitized animals in presence of antigens was studied. The antigens used for the studies were two strains of acid-fast bacilli, isolated from lepomatous leprosy patients, lepromin prepared from fresh lepra bacilli, human serum, H<sub>37</sub>Rv and PPD. The results showed cross-reactivity between cultivated acid-fast bacilli, lepromin and H<sub>37</sub>Rv. No cross-reactivity was seen with PPD and human serum components. The cross-reactivity between cultivated bacilli, lepromin and H<sub>37</sub>Rv indicates shared antigens either specific to leprosy bacillus or to the mycobacteria group.—Authors' Summary

**Kohsaka, K., Mori, T., Tanaka, M. and Nishimura, S.** Consideration on the origin of natural murine leprosy infection. Acid-fast bacillus present in the goldfish and inoculation of the bacilli into SPF mice reared under aseptic conditions using the vinyl-isolator system. *Lepro* 42 (1973) 210-217. (In Japanese)

It is important to clarify the source of natural infection of murine leprosy since we have found in a previous experiment that the murine leprosy bacillus is present in apparently healthy mice. An attempt was, therefore, made to isolate acid-fast organisms from the organs of fresh-water fish bred and reared in a pond closely related to the earth, and then inoculate the organisms isolated to SPF (specific pathogen free) mice reared under aseptic conditions in the vinyl-isolator system.

For examination of bacilli in fish, stamp smears were prepared from liver, spleen, kidney and gills. The slides were stained by the Ziehl-Neelsen method, examined closely under the microscope, and the organ showing bacilli was emulsified in Hank's solution, centrifuged lightly, and a small quantity of India ink was added to the supernatant. A part of the prepared material was inoculated subcutaneously into the backs of SPF mice and the remainder was cultivated. The inoculated mouse was carefully examined by the method of spread preparation from connective tissue surrounding the site of inoculation which was marked by India ink.

The organs of 3 carp and 280 goldfish were examined for the presence of acid-fast bacilli and bacilli were found in the organs of three

goldfish. In two of six primary inoculated mice (origin, No. 243), though a leproma was not formed, there was pronounced bacterial proliferation at the site of injection. The material from the subcutaneous tissue showing the proliferation of bacilli was then inoculated into the next generation of SPF mice. Four of six animals in the second generation showed bacterial proliferation and a mild leproma, and, moreover, three of four animals showed pulmonary lesions with lepromas. All animals inoculated with material from the second passage mouse developed subcutaneous lepromata of murine leprosy in the third generation (C3H mouse reared conventionally).

In the controls, proliferation of the acid-fast bacillus was not found in animals of both groups inoculated with heat-killed material and untreated, and there was no growth on the usual media for acid-fast bacteria at 33°C or 37°C.

As a result of the findings in this study it was shown that acid-fast bacilli were found in organs of fish grown in fresh-water ponds and the typical leproma of murine leprosy was produced at the site of inoculation in mice inoculated with living material. It seems that these findings are important in considering the origin of natural infection of murine leprosy, but it is difficult to obtain the conclusion from only the present data because there are several questions at the present time. It will be possible to clarify these difficult problems by the development of culture techniques for *M. lepraemurium* in the future.—(Adapted from English summary)

**Nakamura, Masahiro.** Quantitative multiplication of *Mycobacterium lepraemurium* in a cell-free liquid medium (NC-5). *J. Gen. Microbiol.* 82 (1974) 385-391.

*Mycobacterium lepraemurium* multiplies in a cell-free liquid medium, referred to as NC-5, which is enriched Kirchner medium plus goat serum,  $\alpha$ -ketoglutaric acid, cytochrome *c*, hemin and L-cysteine. At 30°C the bacilli gradually elongated before multiplying 100- to 1000-fold. The maximum number of bacilli is reached after eight weeks' incubation. The generation time of *Mycobacterium lepraemurium* is between 8 and 14 days, depending upon the size of inoculum. Bacilli grown in NC-5 medium maintain their capac-

ity to produce leprosy in mice. Optimum growth was with the basal medium at pH 7.3 using a small number of bacilli in the inoculum.—Author's Summary

**Ogawa, Tatsuji and Hiraki, Minako.** Studies on the murine leprosy bacillus. VIII. Reproduction test of the disease in mice using graded doses of the sixth subculture of the supposed Hawaiian strain of *Mycobacterium lepraemurium* Lepro 42 (1973) 218-227. (In Japanese)

The bacillus used in the test was the sixth subculture, two month's old, on 1% egg yolk medium, of the supposed Hawaiian strain. Male mice of ddN strain were divided into six groups of ten each and the groups were inoculated either subcutaneously or intravenously with three different doses each ( $2 \times 10^{-1}$ ,  $2 \times 10^{-2}$ ,  $2 \times 10^{-3}$  mg and  $10^{-1}$ ,  $10^{-2}$ ,  $10^{-3}$  mg). The inoculated mice were sacrificed at the end of 4, 6, 9 and 11 months.

Observations of gross disease were made at necropsy. Spleens were weighed and their weights per gram of body weight were recorded. The internal organs, superficial lymph nodes and local lesions were removed, homogenized and then submitted to microscopic examination and cultural recovery. The Ziehl-Neelsen stained smears were rated not only for the number of acid-fast bacilli under oil immersion but also for relative numbers and maximum and minimum sizes of globi under low magnification. In some instances histopathologic examinations were also performed. The results obtained indicated that in the mice inoculated with each of the doses subcutaneously or intravenously there was gross and bacteriologic evidence of infection, supported in some by histopathologic evidence. The findings were more pronounced in the animals intravenously inoculated than in those subcutaneously inoculated. In either case, however, they showed a tendency to become more marked in the course of infection. It seems reasonable to conclude that the disease in mice was fairly consistently reproduced with the test organisms, even when small inoculum doses such as  $10^{-1}$ ,  $10^{-2}$  and  $10^{-3}$  were used.—(Adapted from English summary)

**Ogawa, Tatsuji and Hiraki, Minako.** Studies on the murine leprosy bacillus. IX. Reproduction test of the disease in mice using

graded doses of the second subculture of the supposed Keishicho strain of *Mycobacterium lepraemurium*. Lepro 42 (1973) 228-237.

The bacillus used for the test was the second subculture, three month's old, on the 1% egg yolk medium, of the supposed Keishicho strain. Male mice of ddN strain were divided into six groups of 12 each and the groups were inoculated either subcutaneously or intravenously with three different doses ( $10^{-1}$ ,  $10^{-2}$  and  $10^{-3}$  mg) of the bacillus. The mice subcutaneously inoculated were sacrificed at the end of 3, 6, 8, 10 and 13 months and the intravenously inoculated mice at the end of 3, 6 and 8 months.—(Adapted from English summary) [The remainder of this abstract was identical to the last paragraph of the preceding abstract.—Editor]

**Olitzki, A. L.** Effect of inorganic and organic substances containing sulfur or nitrogen and of vitamins on the growth of *Mycobacterium leprae*. Isr. J. Med. Sci. 10 (1974) 519-524.

*Mycobacterium leprae* was grown in media enriched with mycobacterial extracts. Growth was found to be enhanced by dimethyl sulfoxide, cysteine and cytine. No additive effect of these substances was observed. Sodium thiosulfate and thiamine pyrophosphate had the same effect. The growth of *M. leprae* was promoted by sodium nitrite and nitrate, urea and uric acid, but was slightly inhibited by histidine. Growth was accelerated by ascorbic acid, biotin, folic acid, guanosine, inositol, nicotinamide and pyridoxal hydrochloride.—Author's Abstract

**Olitzki, A. L., Levy, L., Sheskin, J. and Groszowicz, N.** Effect of surface active agents and semisolid agar media on the growth of *Mycobacterium leprae*. Isr. J. Med. Sci. 9 (1973) 150-154.

The *in vitro* culture of *Mycobacterium leprae* remains a crucial problem requiring sustained studies, states WHO TECH. REP. SER., No. 459, 1970 (Trop. Dis. Bull. 68 [1971] abstr. 1007). In this respect Olitzki and his colleagues in Israel have been very active and their further experimental work is recorded in this paper. They have observed that *M. leprae* as far as bacillary counts *in vitro* are concerned, when inoculated in a basic medium of physiological saline en-



riched by phospholipids from BCG, mycobactins, ethanol extracts and sonic products of *M. smegmatis*, could be shown to be favorably affected by: a) semisolid media (0.1% to 0.2% agar); b) dimethyl sulphoxide (2.5% and 5.0%); and c) dilute Eagle's medium (1 in 20), in comparison with liquid media, other surface active substances, namely propylene glycol (0.5%) and sodium dodecyl sulphate (0.01%), and undiluted Eagle's medium.

[It is recommended that interested readers read previous works by these authors in order to put this paper into a proper perspective (Trop. Dis. Bull. 63 [1966] 411 and 765; 64 [1967] 264; 65 [1968] abstrs. 573 and 574; 69 [1972] abstr. 1397; and Israel J. Med. Sci. 8 [1972] 1940)—E. E. Vella (Adapted from Trop. Dis. Bull.)

**Pattyn, Stefaan R.** Conservation of *Mycobacterium leprae* in liquid nitrogen. Ann. Soc. Belge. Med. Trop. 53 (1973) 645-650.

Suspensions of *M. leprae* can be successfully preserved if they are slowly frozen in buffered dimethylsulfoxide 7.5% final concentration, and maintained in liquid nitrogen.—Author's Summary

**Pattyn, Stefaan R.** The problem of cultivation of *Mycobacterium leprae*. Bull. WHO 49 (1973) 403-410.

Some criteria are presented to help evaluate papers appearing in the literature claiming successful cultivation of *M. leprae* either in the absence or in the presence of tissue-cultured cells. Recently, electron microscopic studies have definitely shown *M. leprae* to belong to the genus *Mycobacterium* and its division to occur through transverse section. A survey is given of the mycobacterial strains isolated in the last ten years from leprosy lesions. These strains belong to taxonomically different species and cannot be considered to be *M. leprae*. No substantiated claim was made concerning the *in vitro* growth of *M. leprae* and the application of the tissue culture technic has been equally disappointing. The view is expressed that progress towards the *in vitro* cultivation of *M. leprae* can be made only as a result of increased knowledge about the intracellular environment and the metabolic activities of this organism, to be obtained by the application of modern biochemical and histochemical technics.—Au-

thor's Summary

**Stanford, J. L. and Grange, J. M.** The meaning and structure of species as applied to mycobacteria. Tubercle 55 (1974) 143-152.

In an attempt to determine the nature of species amongst mycobacteria, analyses at both interspecific and intraspecific levels have been performed. Over 1,000 strains were examined in immunodiffusion analysis, and the majority were allotted to 20 named species on the basis of from two to eight species specific (group iv) antigens. In no case were any of these antigens shared by other species and the other the fast-growing species, on the basis of two other groups (ii and iii) of antigens.

Twenty-eight strains of *Mycobacterium fortuitum* (*ranae*) were analyzed by a multiplicity of methods to determine the extent of naturally occurring variation within this species. By picking off single colonies, certain variants could be selected from other variants indicating that genetically more complete strains throw off deleted mutants which may be most successful in surroundings different from those favoring the parent strain. Another mechanism of intra-specific variation, lysogeny with mycobacteriophage, was also demonstrated. The nature of species as determined by the two methods of approach are discussed, and the need for strict adherence to the rules of taxonomic nomenclature explained.—Authors' Summary [Addendum: *Mycobacterium leprae* was not studied, perhaps because the necessary technic of growing the organism on a nonantigenic medium is not available. However, *M. lepraemurium* is reported as being classified under the species designated as *M. avium*. In the absence of the requisite culture technic, *M. leprae* together with *M. ulcerans*, was studied by special methods.—Editor.]

**Talwar, G. P., Krishnan, A. D. and Gupta, P. D.** Quantitative evaluation of the progress of intracellular infection *in vitro*: incorporation of <sup>3</sup>H-thymidine into deoxyribonucleic acid by *Mycobacterium leprae* in cultivated blood monocytes. Infec. Immun. 9 (1974) 187-191.

Growth of intracellular parasites such as *Mycobacterium leprae* in macrophages derived from human peripheral blood monocytes can be assessed by selective incorpora-

tion of [*methyl*-<sup>3</sup>H] thymidine into deoxyribonucleic acid of the bacterial cells. The radioactive precursor is not taken up by the host cells, and evidence has been presented

for its incorporation into bacteria. The procedure is sensitive, reproducible, and highly quantitative.—Authors' Abstract

### Experimental Infections

✓ **Amborski, R. L., LoPiccolo, G. and Amborski, G. F.** Development of an established cell line derived from *Dasyurus novemcinctus* (armadillo), a laboratory animal susceptible to infection by *Mycobacterium leprae*. *Experientia* **30** (1974) 546-548.

Kidney derived fibroblastic cells from the nine banded armadillo are reported as growing on Eagle's minimal essential medium (MEM) supplemented with 15% fetal calf serum, 0.1 M Hepes buffer, 50 units/ml penicillin and 50 µg/ml dihydrostreptomycin. The cell lines were grown at 37°C, 33°C and 31°C. The latter two temperature growths were erratic and inconsistent, whereas growth at 37°C was accompanied by excess acid production as compared with growth at 33°C. It is as yet undetermined what effect this might have on the interaction between the leprosy bacillus and the cultured armadillo cells.—O. K. Skinsnes

✓ **Cohn, D. A., Athanassiades, T. J. and Speirs, R. S.** Inflammatory cell responses to antigen in thymus-deprived mice: reduced eosinophils and mononuclear cells. *J. Reticuloendothel. Soc.* **15** (1974) 199-212.

The influence of the thymus on inflammatory cell responses was studied in intact, thymus-deprived and thymus-grafted mice. Changes in the population of peritoneal exudate cells were determined quantitatively following infections of tetanus toxoid, pertussis vaccine or carbon.

Thymectomy resulted in reduced inflammatory cell responses to the antigens tested but not to carbon. The cells most affected were mononuclear cells and eosinophils. Marked reductions in mononuclear and eosinophil responses occurred when thymectomized mice were more drastically depleted of their peripheral T cells by lethal irradiation and reconstitution with bone marrow cells. Subcutaneous implants of whole thymus restored the capacity of T cell-deprived mice to produce normal mononuclear and eosinophil responses to antigen.

Quantitative studies showed that the bone

marrow of thymectomized mice contained normal numbers of eosinophils but, following reinjection of antigen, the proportion of mature eosinophils was far greater than that seen in intact mice. The diminished eosinophil response in thymus-deprived mice was, therefore, not caused by bone marrow insufficiency but probably by an absence of factors which trigger the release of mature eosinophils and stimulate their accumulation at the inflammatory site.—Authors' Summary

✓ **Kwapinski, J. B. G., Kwapinski, E. H. and McClung, N. M.** The growth of *Mycobacterium leprae* in snakes. *Can. J. Microbiol.* **20** (1974) 420-422.

*Mycobacterium leprae*, obtained from a human case of lepromatous leprosy, was successfully grown in newborn snakes, within five to six weeks, and it was transferred from snake to snake, upon intramuscular injection.—Authors' Abstract

✓ **Ng, H., Jacobsen, P. L. and Levy, L.** Analogy of *Mycobacterium marinum* disease to *Mycobacterium leprae* infection in foot pads of mice. *Infect. Immun.* **8** (1973) 860-867.

Because it appeared likely that the disease process that follows inoculation of foot pads of mice with *Mycobacterium marinum* might serve as a useful model of mouse foot pad infection with *M. leprae* for immunological studies, an attempt was made to establish an analogy between the two processes. As a second objective, the adequacy of measurements of mouse foot pad thickness as an index of the total number of *M. marinum* and of the number of viable *M. marinum* was determined. The evolution of *M. marinum* disease in the foot pads of BALB/c mice was observed, and the influences of mouse age and sex and of inoculum size were measured. Mice were challenged with *M. marinum* in one foot pad at several intervals after inoculation of the contralateral hind foot pad with the same organism. In all of these experiments, mouse foot pad thickness was noted to parallel multiplication of *M.*

*marinum* during the phase of increasing foot pad swelling. Cessation of bacterial multiplication was noted to occur just before maximal swelling had been achieved, and was followed by rapid loss of viable *M. marinum*. The total number of organisms and mouse foot pad thickness decreased only slowly and incompletely. Analogy between *M. marinum* disease and *M. leprae* infection of the mouse foot pad was established by the self-limited nature of both processes, and by similar patterns of protection against homologous and heterologous challenge conferred by the two processes.—Authors' Summary

**Purtilo, D. T., Walsh, G. P., Storrs, E. E. and Banks, I. S.** Impact of cool temperatures of human and armadillo lymphocytes (*Dasypus novemcinctus*, Linn.) as related to leprosy. *Nature* **248** (1974) 450-452.

Marked reduction of transformation of lymphocytes from armadillos at 33°C and 28°C occurred as compared with transformation at 37°C. Similar temperature related differences in lymphocyte transformation are reported in human subjects. The authors concluded that cool temperatures probably depress cell-mediated immunity *in vivo* and that such a depression of CMI could explain the susceptibility of armadillos to infection with *M. leprae*.

The authors apparently do not take into account the possibility that their findings may be due to slower *in vitro* reaction at lower temperatures—a not uncommon finding generally in chemistry and biology. Whether or not this has any relation to depressed cellular immunity seems, therefore, not to be established.

The term "lepromatous leprosy" is replete with clinical and laboratory as well as historical connotations, very few of which have relevance to what is currently known about disseminated infection in the armadillo. Therefore, the authors' designation of "lepromatous leprosy" in the armadillo seems inappropriate. It has previously been suggested that the term "lepromatoid" leprosy is more appropriate.—O. K. Skinsnes

**Storrs, E. E. and Greer, W. E.** Maintenance and husbandry of armadillo colonies. *Lab. Anim. Sci.* **23** (1973) 823-829.

Housing, diets, and medical care suitable for three species of armadillos (*Dasypus novemcinctus*, *Dasypus hybridus*, and *Chaetophractus villosus*) were examined. Three types of housing facilities which had proved satisfactory for housing animals in outdoor, semioutdoor, and indoor pens were described. A diet satisfactory for adults of all three species consisted of softened Cat Chow plus vitamin, mineral, and protein supplements. Diets most satisfactory for young animals were mixtures of a soybean base milk substitute, cereal, Cat Chow, and vitamin, mineral and protein supplements. For adaptation of animals from the wild, all food was withheld for two days and water was supplied *ad libitum*. Food, when first supplied, was added to the water to make a soupy mix to adapt the armadillos to the laboratory diet. Medical problems most often encountered were tail and foot infections which could usually be treated with a pyoktatin blue-phenol base product. Tail amputations were sometimes required. Surgery was performed using ketamine hydrochloride and ether as anesthetics.—Authors' Summary

**Storrs, E. E., Walsh, G. P., Burchfield, H. P. and Binford, C. H.** Leprosy in the armadillo: new model for biomedical research. *Science* **183** (1974) 851-852.

Eight of twenty armadillos (*Dasypus novemcinctus* L.) developed severe lepomatous leprosy 3 to 3.5 years after inoculation with viable *Mycobacterium leprae*. A total of 988 grams of lepomas containing an estimated 15 to 20 grams of leprosy bacilli has been harvested from these animals. The large amounts of material now available will permit indepth studies of the biochemistry and metabolism of the leprosy bacillus, and the animal model should make possible definitive studies on the immunology, chemotherapy, and epidemiology of the disease.—Authors' Abstract

## Rehabilitation

**Ranney, D. A. and Aiyappa, N. S.** A realistic appraisal of the value of microcellular

rubber sandals for ulcer prevention in South India. *Lepr. India* **46** (1974) 65-72.

A definite preference was shown for new kinds of footwear which are functionally satisfactory and cosmetically superior. Issuing such footwear, however, failed to materially influence the actual wearing of microcellular rubber footwear. This is simply because customs in our part of South India are such that villagers, who are largely agriculturists, do not wear any kind of footwear in and around the home and few use any footwear at work.—Authors' Summary

**Sharma, R. S.** Agricultural rehabilitation at Dattapur Leprosy Colony, Wardha. *Lepr. India* **46** (1974) 89-93.

Agricultural occupation is the most suitable vocation for rehabilitation of leprosy patients, though not all can undertake the work without risk of injury to their limbs. Those not found suitable for agricultural work could be engaged in some allied lighter

work as indicated above. Modern methods along with the use of mechanized methods, chemical fertilizers and insecticides have a good wage-giving capacity. Agriculture also helps in removing isolation from the nearby community where healthy persons also become interested in learning new methods and purchase agricultural products from the patients. Experience at Dattapur has shown that this can be multiplied easily without much per capita investment and training to benefit a large number of patients. If financial assistance is rendered to the institution, we plan to open a training center in new techniques of farming for patients and others interested in modern technology, with our goal being to rehabilitate the leprosy patients on their own farms allotted to them by the government or other philanthropists.—*(Adapted from author's summary)*

## Epidemiology and Prevention

**Browne, Stanley G.** Leprosy in Southeast Asia: present position and prospects. *Southeast Asian J. Trop. Med. Public Health* **5** (1974) 65-69.

The countries of Southeast Asia have a huge leprosy problem. Some success has attended determined local efforts, and voluntary agencies have made much-appreciated contributions, but two-thirds of leprosy sufferers still lack treatment.—Author's Summary

**Di Martino, M., Gualdi, G. and Marracino, F.** Attualta' sulla lebbra: aspetti epidemiologici e preventivi. [The present position of leprosy: epidemiological and preventive aspects.] *Nuovi Ann. Ig. Microbiol.* **23** (1972) 361-391. (In Italian, English summary)

This is an extremely interesting report on the recent incidence of leprosy throughout the world. The authors point out that the true incidence is not known but give figures of registered and estimated cases by continents and countries; in 1965 these were 2.8 million and 10.8 million, and by 1970 it was not thought that they had altered greatly. However, the chronicity of the disease, the difficulty in the diagnosis of early cases and the costs of treatment and prevention multiply

the problems. The authors discuss the diagnosis of stained films by the light microscope and the presumed difference in pathogenicity of fully stained, presumably live bacilli and partly stained, possibly dead bacilli; they feel that this subject is still obscure and are uncertain whether any prophylactic significance can be ascribed to this difference. The immunological state will have repercussions on the type of the disease and there may even be persons who are relatively resistant (see also abstract 83, *Trop. Dis. Bull.* **71** [1974] 50). For treatment, thalidomide and B663 for leprotic reactions are mentioned, and also the various and numerous antileprosy drugs in current use, particularly rifampicin, although dapsone still seems the general maid-of-all-work. For prevention, the infectivity of the leprotic forms makes it especially important that children should be removed from such patients (but what of the indeterminate forms?) and the value of BCG vaccination of children is extensively discussed. Here the three great BCG campaigns in Uganda, New Guinea and Burma are mentioned, the success of the first being balanced by the failure in Burma, while the results in New Guinea are equivocal to say the least; so here also the position is still by no means clear.

The authors conclude that, in spite of all the efforts of those interested throughout the



world, leprosy still retains some as yet undiscovered secrets.

[This paper is very well worth reading in the original for its extremely well balanced views.]—W. K. Dunscombe (*From Trop. Dis. Bull.*)

**Ekambaram, V.** Absenteeism for treatment, their causes and suggested remedial measures. *Lepr. India* 46 (1974) 46-48.

The common causes of absenteeism for treatment as analyzed by the author in Tirukoilur and in the ELEP area are as follows:

1. Daily labor: many of the patients being poor daily laborers can ill-afford to spare even half a day to attend the clinic.

2. Minimal lesions: quite a few with minimal lesions which do not cause them bodily suffering do not think it necessary to go for treatment.

3. Disbelief that they are suffering from leprosy: many of those with minimal lesions do not believe they have leprosy despite advice by the staff to take treatment.

4. Dissatisfaction with prolonged treatment: a few are not satisfied with only tablets for a big disease for which they feel injections are needed. Yet a few who are receiving regular treatment at the beginning become dissatisfied at the slow pace of improvement under sulfone therapy and later stop their treatment.

5. Social stigma: some of the rich and prominent persons of the locality are unwilling to come for treatment at the public clinics for fear of losing their prestige. These are the people who feel they can get better treatment from private doctors but ultimately fall into the hands of quacks. This is the most difficult section of the community to deal with.

6. Religious functions account for only occasional absence from treatment. Similarly, general ailments and complications of leprosy account for a few absentees. In addition to the above major causes, inexperienced medical officers in charge of these units and lack of facilities for hospitalization undermine the confidence of the patients in the units where they take treatment, which ultimately leads to irregularity in treatment.—(*Adapted from text*)

**Loaiza, W. O.** Lepra en el Ecuador. [Leprosy in Ecuador.] *Medna Cutanea* 6 (1972) 447-

450. (English summary)

The author mentions that the Andean Cordillera divides the country into three zones: a) a coastal zone which has a hot and humid climate and where most of the cases of leprosy occur; b) the sierra which is cold and dry; c) the lower eastern zone consisting of tropical forest.

Historically, leprosy is thought to have arrived in the country with the Conquistadores but there are certain curious features as in the lower eastern zone and in the Galapagos Islands where no autochthonous cases have been detected. The national antileprosy campaign began in 1963 although there had been attempts at leprosia before then. Between 1963 and June 1971 over 770,000 persons had been examined out of a total population of just over six million, and 1,894 new cases detected. Of 1,862 cases classified, the numbers were: lepromatous 765, tuberculoid 436, indeterminate 618 and dimorphic 43 (no details are given of the missing 32). Of the new cases 152 were in children under the age of 15 years, most of whom had the indeterminate form. In general, more males were affected than females and this was particularly the case in those over the age of 15 years. Over the 17 provinces of the country the incidence ranged from 0.02 to 1.21 per mille. The author stresses that there are important foci of the disease in six provinces, two of which border Peru, and he regards the degree of infection as of moderate intensity.—W. K. Dunscombe (*From Trop. Dis. Bull.*)

**Medford, F. E.** Leprosy in Vietnam veterans. *Arch. Intern. Med.* 134 (1974) 373.

Only 76 cases of leprosy contracted during active duty in endemic areas have been reported from the Spanish-American War through 1968. This may be the first report of such a case in a Vietnam veteran who contracted tuberculoid leprosy while on active duty in that country. American physicians must be alert to other cases of leprosy that may develop in veterans in the future.—(*From JAMA*)

**Rees, R. J.W. and Meade, T. W.** Comparison of the modes of spread and the incidence of tuberculosis and leprosy. *Lancet* I (1974) 47-49.

It has been assumed in the past that attack rates for leprosy are lower than those for tuberculosis, that leprosy is spread by direct person-to-person contact, and that in leprosy the skin is the most likely route of infection. However, the numbers of *Mycobacterium tuberculosis* in sputum from open cases of tuberculosis and of *M. leprae* in the nasal secretions of patients with lepromatous leprosy are similar; in addition, attack rates in family or household contacts for the two diseases in comparable populations in South India are of the same order. While these findings do not prove that modes of spread and routes of infection are identical for the two diseases, they are consistent with this possibility.—Authors' Summary [It could be remembered that Mouritz (Hawaii, 1916) thought that infection might take place by inoculation at broken skin surfaces or inhalation through mucous surfaces as did Leloir (1886) and Goldschmidt (1891); that Klingmuller (1930) wrote of nasal lesions and their bacilli rich secretions; that Rogers and Muir (1946) wrote of "The commonly held view that the organism may find access through abrasions of the skin or the nasal mucous membrane"; that Muir (1948) wrote that "As in tuberculosis, droplet transmission from the nose and mouth is probably one of the most common methods." Jeanselme (1934) (free translation) noted "That every author quoted noted the significance of nasal involvement and admitted that inoculation can be effected by the nasal discharge." Muir expressed the wish to know whether or not such discharged bacilli are alive and we now know that they are. The subject has been widely discussed and the present authors join a distinguished coterie of leprologists. It is unfortunate that none of the references cited go back before 1960.—Editor]

✓ **Saikawa, Kazuo.** An epidemiological study of leprosy on Okinawa Island. First report: on the newly-detected patients for each year. *Lepro* 43 (1974) 52-62. (In Japanese)

In 1931, the leprosy control program requiring segregation was initiated by the local government according to the Leprosy Prevention Law in Japan. Since that time, in 1961, the Ryukyu government issued a new law changing the leprosy control policy and, in 1962, began outpatient treatment for patients

at several places.

From 1931 to 1972, about 3,735 leprosy cases have been detected and controlled. On the number of newly-detected patients for each year the analysis was done epidemiologically by leprosy incidence rate, lepromatous incidence rate, age and sex.

The conclusions are as follows: 1) During the first five years when the outpatient treatment began its operation in 1962, the number of newly-detected patients increased from 70 cases in 1962 to 173 cases in 1967. The number then decreased from 173 to 70 in 1972 during the second five years. The increase during the first five years was mainly due to the policy change on leprosy control. The patients were willing to go to OPD for treatment. The decrease during the second five years was due to the success of the leprosy control policy because many slight and early cases were detected in OPD or other medical institutions, public health units, centers, general hospitals and private practitioners. 2) The outpatient treatment of leprosy patients in Okinawa Island for ten years has proved to be successful due to leprosy control.—(Adapted from English summary)

✓ **Walter, J., Seal, K. S., Sansarricq, H. and Engler, V.** Random sample surveys in leprosy control programs. Are they a nuisance? *Z. Tropenmed. Parasitol.* 25 (1974) 89-95.

An attempt is made to demonstrate the advantages and possibilities of random sample surveys in the assessment of leprosy control. The need for reliable random sample surveys is emphasized. Methods are recalled by which an estimation and the prediction of the endemic level over periods of five to ten years is feasible, and which permit comparison of the survey results with the predicted development of the disease in the population.

The epidemiological results of control measures or other factors influencing disease levels in leprosy, are frequently labeled either as "good" or "bad." Such judgements appear to be superficial and premature: quantitative objectives of programs are feasible after findings of several random sample surveys, planned and carried out for evaluation purposes, have become available.—Authors' Summary

## Other Mycobacterial Diseases and Related Entities

**Feldman, Roger A. and Hershfield, Earl.**

Mycobacterial skin infection by an unidentified species. *Ann. Intern. Med.* **80** (1974) 445-452.

Twenty-nine patients from a geographically limited area, predominantly in Minnesota and Southern Manitoba, had mycobacterial skin infection. Acid-fast bacilli were found in biopsy specimens of the lesions but could not be cultured. The patients presented most frequently in winter months and most often had lymph node swelling and an associated positive tuberculin test. They responded to local excision or antituberculous therapy, or both. It is suggested that these patients had primary skin infections, with a single species of mycobacterium, and they represent a previously undescribed clinical problem.—Authors' Summary [Sporadic examples of mycobacterial infections (occasionally generalized) similar to those within this group have puzzled more than an occasional pathologist. A striking feature of the lesions, nicely illustrated in this report, is the large number of intracellular organisms in the granulomas—G. L. Fite]

**Judson, Franklyn N. and Feldman, Roger A.**

Mycobacterial skin tests in humans 12 years after infection with *Mycobacterium marinum*. *Am. Rev. Resp. Dis.* **109** (1974) 544-547.

Forty-four persons were studied 12 years after clinical infection with *Mycobacterium marinum* to determine the pattern of skin sensitivity to *M. marinum* and other mycobacterial skin test antigens. The individuals all lived in an area in Colorado with little reported tuberculosis. None had received BCG vaccine. No skin test pattern distinctive for previous *M. marinum* infection was demonstrated, using purified protein derivatives from *M. marinum*, *M. tuberculosis*, *M. kansasii*, and *M. intracellulare*. Twenty-three persons, infected at least 12 years earlier with *M. marinum*, had skin test sensitivity to PPD-S compatible with earlier infection with *M. tuberculosis*. These persons might have been considered for isoniazid prophylaxis if the probable source of their skin test results were not known.—Authors' Summary

**Meyers, W. M., Shelly, W. M. and Connor,**

**D. H.** Heat treatment of *Mycobacterium ulcerans* infections without surgical excision. *Am. J. Trop. Med. Hyg.* **23** (1974) 924-929.

Eight patients from Zaire with *Mycobacterium ulcerans* infections were treated by the local application of heat to maintain a temperature of approximately 40°C in the ulcerated area. All lesions healed without surgical intervention and without local recurrences during follow-up periods of up to 22 months. This study shows that local heat promotes healing of *M. ulcerans* lesions. We postulate that the mechanism is primarily by direct inhibition of multiplication of *M. ulcerans*. Other possible contributory effects are discussed.—Authors' Abstract

**Meyers, W. M., Shelly, W. M., Connor, D. H.**

**and Meyers, E. K.** Human *Mycobacterium ulcerans* infections developing at sites of trauma to skin. *Am. J. Trop. Med. Hyg.* **23** (1974) 919-923.

In Zaire we studied 180 patients with *Mycobacterium ulcerans* infections and found 14 with a history of antecedent trauma at the site of the lesion (e.g., gunshot and land mine injuries, penetrating wood splinters and scorpion stings). Two patients developed lesions following hypodermic injections. We believe that trauma is an important mode of transmitting *M. ulcerans* infections, or of introducing the etiologic agent into the dermis or subcutaneous tissue from superficially contaminated skin.—Authors' Abstract

**Oelerich, S., Büttner, D. W. and Mannweiler,**

**E.** Kreuzreaktionen in der Immundiagnostik der Chagaskrankheit und der Kala Azar unter Einbeziehung von Seren Tuberkulöser und Lepröser. [Cross-reactions in the serological diagnosis of Chagas' disease and kala azar including sera of tuberculous and leprosy patients.] *Zentralbl. Bakteriol.* [Orig. A] **226** (1974) 283-290. (In German, English abstract)

Twenty-nine sera from patients with leprosy (12 borderline and 17 lepromatous cases) and 75 sera from patients with tuberculosis

reacted with varying titers in the complement fixation test with a *Mycobacterium smegmatis* antigen. The highest titers were observed with sera from patients with lepromatous leprosy. Only 2 out of the 104 sera from patients with mycobacterial infections gave a positive reaction with *Leishmania donovani* antigen and both sera showed low titers.

Compared with this, out of 30 sera from patients with Chagas' disease and 6 sera from kala azar a high percentage reacted with the heterologous *Trypanosoma cruzi* and *Leishmania donovani* antigen also in the complement fixation test. With regard to the kala azar sera the antigen from *Mycobacterium smegmatis* was as sensitive as the antigen from *Leishmania donovani*. Sera from patients with Chagas' disease reacted also well with the antigen from *Mycobacterium smegmatis*.

The double gel diffusion test proved to be the best one for the identification of homologous reactivities. In this test, sera from patients with Chagas' disease reacted nearly exclusively with antigens from *Trypanosoma cruzi*, while kala azar sera gave stronger reactions and more abundant precipitates with the homologous antigen than with the heterologous one. The significance of the double gel diffusion test, however, needs further investigations, because some of the sera from Chagas' patients did not react with their homologous antigen.—English Abstract

**Purtilo, D. T., Meyers, W. M. and Connor, D. H.** Fatal strongyloidiasis in immunosuppressed patients. *Am. J. Med.* **56** (1973) 488-493.

Cell-mediated immunity is a major bulwark of defense against certain viruses, intra-

cellular bacteria, fungi and protozoa. Cell-mediated immunity against helminthic infections is inadequately understood. Thirty-two patients with strongyloidiasis who were studied at autopsy had underlying diseases characterized by depressed cell-mediated immunity, including lepromatous leprosy, malignant tumors, protein-calorie malnutrition, burn, radiation, advanced tuberculosis, tertiary syphilis or pancytopenia. At autopsy defective cell-mediated immunity against strongyloides was manifested by a lack of a granulomatous immune response to larvae in the tissues. Depletion of lymphocytes in thymus glands and in the thymus-dependent areas of lymph nodes and spleens in the hosts indicated an inadequate capacity of cell-mediated immunity for preventing *Strongyloides stercoralis*.—Authors' Abstract

**Verma, I. C., Gupta, M. L. and Ghai, O. P.**

*In vitro* lymphoblastoid transformation with purified protein derivative (PPD) as a diagnostic test in tuberculosis. *Indian J. Med. Res.* **62** (1974) 615-620.

Lymphoblastoid transformation with PPD was studied in 25 patients diagnosed to have tuberculosis. Transformation was observed in  $27.93 \pm 12.36\%$  of cells from 15 patients in whom a positive Mantoux reaction was recorded, and in  $16.6 \pm 5.38\%$  of cells from 10 patients with a negative Mantoux reaction. These mean values are significantly greater than the values obtained in unstimulated cultures ( $p$  values less than 0.001). Lymphoblastoid transformation is a useful test to detect sensitization to tuberculin in patients suffering from tuberculosis but showing a negative Mantoux reaction.—Authors' Summary