CURRENT LITERATURE

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Clinical Sciences

Papageorgiou, P. S., Sorokin, C., Kouzoutzakoglou, K., and Glade, P. R. Herpes-like Epstein-Barr virus in leprosy. Nature **231** (1971) 47-48.

Twenty-two serum specimens from patients with leprosy (eleven each of the lepromatous and tuberculoid types), diagnosed by identification of the microorganism in pathologic specimens and by skin testing in the leprosarium "Aghia Barbara" in Athens, Greece, were studied.

Seven of the eleven patients with lepromatous leprosy had anti-HLV antibody titres of 1:640 or higher, but only three of eleven patients with tuberculoid leprosy attained the concentration of 1:640. Using a Mann-Whitney U test, the concentrations of anti-HLV antibody were found to be significantly lower in patients with tuberculoid leprosy (one-tail test: $P=0.016$) than those with lepromatous leprosy.

The findings reported here add to the evidence for an antibody escape mechanism as indicated by the increased concentrations of IgG immunoglobulins in our patients with lepromatous leprosy. — EXCERPTED.

Pearson, J. M. H., and Weddell, G. Changes in sensory acuity following radial nerve biopsy in patients with leprosy. Brain **94** (1971) 43-50

Histologically successful biopsies from the radial nerve at the wrist were taken before and at various intervals following treatment in 52 patients with different forms of leprosy. Two consecutive biopsies were taken from the same nerve close to the same site in 23 patients and three consecutive biopsies from 2 patients. The sensory acuity of the skin served by the radial nerve was determined before and at intervals after operation using a series of nylon bristles of graded thickness and within a defined framework of rules.

The following observations were made: (1) The sensory acuity test if performed in the manner described is sensitive, reliable and consistent. (2) The test objects are cheap, the technic is not time-consuming and can be used successfully even in the face of a language barrier. (3) The removal of small radial nerve biopsies at the wrist does not lead to any permanent loss of tactile sensory acuity and this is so for as many as three consecutive biopsies. (4) Biopsies from nerves affected with leprosy do not accelerate the progress of nerve damage. (5) Nerve biopsy is a safe and ethical method of obtaining material for studying the etiology of the neurohistopathological changes which occur in leprosy.—Authors' Summary

Sehgal, V. N. Inoculation leprosy appearing after seven years of tatooing. Dermatologica **142** (1971) 58-61.

A case of inoculation leprosy resulting after 7 years of tatooing in a female aged 25 years is described. This conforms to high resistant tuberculoid leprosy and illustrated an inoculation by lepra bacilli as an alternative route for the transmission of leprosy.—Author's Summary

Slem, G. Clinical studies of ocular leprosy, Amer. J. Ophthal. **71** (1971) 431-434.

Investigation of the eyes of 388 Turkish patients suffering from leprosy revealed some rare and interesting ocular lesions, including Melkersson-Rosenthal syndrome, acute diffuse plastic iridocyclitis, miliary

leproma of the iris, an unique type of iris atrophy that produces iris holes and hypopigmented patches in the fundus and choroiditis leprosa praecox.

Histopathologic studies of the orbicularis oculi muscle in patients with lagophthalmos suggested that myositis rather than facial nerve paralysis was responsible for the clinical picture.

Tonometric examination of 38 eyes showed abnormally low pressures, and tonographic studies of 49 eyes demonstrated that both aqueous production and drainage were diminished in leprosy patients.—Author's Summary

Sehgal, V. N., Rege, V. L., and Vadiraj, S. N. Inoculation leprosy subsequent to small-pox vaccination. Dermatologica **141** (1970) 393-396.

A case of high resistant tuberculoid leprosy in a 25-year-old female, developing after small-pox vaccination is described. This case supports the hypothesis of inoculation leprosy.—Authors' Abstract

Schmidt, H. Serologische Untersuchungen bei Leprösen. (Serological investigations in leprosy.) Hautarzt, **20** (1969) 271-273.

A significant number of leprosy sera, especially from patients with the lepromatous type of the disease contained antibodies which reacted with a lecithin-free "Lipid-Antigen."

These should not be counted in the same terms as the biological false positive results seen with tests for treponemal reactions, because the results indicate that the lecithin-free antigens serve to distinguish the results from those in syphilis. However, the reactions are not specific for leprosy, and seem to show a relationship between the serum findings and the duration of the disease, and, together with the lepromin test to provide a little information on prognosis.—Author's Summary

Garner, M. F., Backhouse, J. L., Collins, C. A., and Roeder, P. J. Serological tests for treponemal infection in leprosy patients. Brit. J. vener. Dis. **45** (1969) 19-22.

Serological tests for treponemal infection were carried out on 270 patients with lepromatous leprosy and 250 normal controls, from the Philippines. All sera were subjected to the Cardiolipin Wassermann reaction, the Veneral Disease Research Laboratory test, the Reiter protein complement-fixation test, the fluorescent treponemal antibody test, the fluorescent treponemal antibody absorption test, and the *Treponema palidum* immobilization test. A reactive TPI test result was taken as evidence of treponemal infection and all other test results were compared with it.

Sera from 5.6% of the leprosy patients showed evidence of treponemal infection. BFP reactions occured with 8.1% of leprosy sera, the VDRL slide flocculation test being responsible for the majority of these. Non-specific reactive results to the RPCF and FTA-200 tests are discussed. Special attention was given to evaluating the FTA-ABS test against the TPI test. They were found to be of almost equal specificity and of equal sensitivity.

It is concluded that, where the TPI test is not available, the FTA-ABS test can replace it in detecting BFP and non-specific reactions to serological tests for treponemal infection in sera from patients with the lepromatous form of leprosy.-Authors' Summary

Emiru, V. P. Ocular leprosy in Uganda. Brit. J. Ophthal. **54** (1970) 740-743.

The incidence of the ocular complications of leprosy in Uganda is reported. Iris pearls and subepithelial punctate keratitis were found to be uncommon and this agrees with similar findings in Tanganyika, Ghana, and Malawi, but the reason for this regional variation is not known.

Complications were rare in young people who had been treated from the early stage of the disease. Moreover, the incidence of blindness, which was reported to be high in other countries before sulphone treatment, was found to be only 1.3%—Author's Summary

Chaudhury, S. D., and Ahuja, I. S. Tissue lipids in leprosy. J. Indian Med. Assoc. **56**(1971) 196-198.

This article is a review of histochemical studies of lepra cells by various technics.—Authors' Summary

Mittal, M. M., Saha, K., Shali, P. L., and Shivpuri, D. N. A study of Prausnitz-Küstner reaction in leprosy. Clin. exp. Immunol. **8** (1971) 657-661.

The P-K reaction was studied in twenty biopsy-proven leprosy cases who denied any personal histories of atopic diseases and exhibited no reaction to antigenic extracts or homologous serum. The reaginic sera used were obtained from well-documented cases of asthma, which gave highly positive (+ + to + + +) P-K reaction in normal individuals. The P-K reactions were positive in 20% of leprosy cases. The intensity of weal and erythema was depressed even in these cases. Type and stage of the disease did not seem to influence the weal and flare of P-K reaction. In the light of these findings a possible mechanism of P-K reaction has been discussed.

It is now nearly half a century since Prausnitz & Küstner (1921) first described the passive transfer of weal and erythema reactivity in the skin of normal individuals by means of serum from an atopic donor. This phenomenon has been commonly referred to as the 'P-K reaction', and the antibodies as the reagins. Although there are several procedures available for the detection of human reagins, the P-K test is still one of the most acceptable technics in many laboratories. It is interesting to note that, despite its universal application, its mechanism is still little understood. The demonstration of negative P-K reaction in 80% of the leprosy cases in the present study may be an important turning point in discovering the mechanism of the P-K reaction.—Authors' Summary

Moschella, S. L. Unusual clinical expressions of leprosy. Lahey Clinic Foundation Bulletin **20** (1971) 143-149.

An unusual case of Charcot's joints involving the proximal interphalangeal joints of the hands and feet, associated with sensory and minimal motor changes and leprous osteitis, is described. Among the lepra reactions, attention is drawn to a distinctive, reactive lesion—the so-called red leg—seen in an adult woman. The histoid leproma, a clinicopathologic variety of lepromatous and rarely of borderline leprosy (BL type), is briefly discussed with a presentation of a case.—Author's Summary

Bechelli, L. Leprosy today. World Health, Oct 1971, 10-17.

This is a well illustrated presentation to the layman of current methods and approaches to the handling of leprosy problems and treatment of the disease.—G. L. Fite

Taube, E. and Ellis, B. P. B. An unusual case of leprosy with pathological features common to Lucio's phenomenon. Central African J. Med. **17** (1971) 119-122.

A long-standing case of lepromatous leprosy with many clinical and histological similarities to Lucio's phenomenon, is described.

There are many fundamental clinical and histological similarities between the case under review and the Lucio's phenomenon, but the diagnosis is more likely to be an ulcerating borderline reaction, particularly as the final biopsy showed an absence of vasculitis and suggested a healing borderline type.

No case of this kind has ever been reported in Rhodesia before, although extensive trophic ulceration and sometimes leprotic ulceration have been noted by Mostert.—Authors' Summary

Chemotherapy

Sloan, N. R., Worth, R. M., Jano, B., and Fasal P. Repository acedapsone in leprosy chemoprophylaxis and treatment. The Lancet **2** (1971) 525-526.

This study was carried out on Pingelap Island of the Ponape District of Micronesia.

The use of repository acedapsone, 225 mg once every 75 days for three years, in approximately 1400 people highly exposed to and susceptible to leprosy led in the first year to a reduction of the number of new cases to half the expected figure. In the following two years no new cases appeared. No problems with toxicity were encountered. Sixty-six of the 68 active cases of leprosy in this population have improved satisfactorily during three years of acedapsone therapy.—Authors' Summary

Molavi, A. and Weinstein, L. *In vitro* susceptibility of atypical mycobacteria to rifampin. Applied Microbiol. **22** (1971) 23-25.

Atypical mycobacteria (209 strains) were examined for susceptibility to rifampin by the proportion method by using Middlebrook 7H-10 agar. All strains of *Mycobacterium kansasii* and tap-water scotochromogens were inhibited by 0.25 to 1 ug of the drug per ml. Seventy-six per cent of *M. scrofulaceum* and 61% of *M. intracellulare* strains were susceptible to 4 ug/ml or less; 5% of the former and 8% of the latter were resistant to 16 ug/ml. All strains of *M. gastri* and *M. triviale* and most strains of *M. terrae* were sensitive to 1 to 4 ug/ml. Two strains of *M. borstelense* were both inhibited by 8 ug/ml. Nearly all strains of *M. fortuitum* were resistant to the drug. The results of this study suggest that rifampin may be a valuable agent for the treatment of many atypical mycobacterial infections.—Authors' Summary

Shronts, J. S., Rynearson, T. K., and Wolinsky, E. Rifampin alone and combined with other drugs in *Mycobacterium kansasii* and *Mycobacterium intracellulare* infections of mice. Amer. Review of Respiratory Disease **104** (1971) 728-741.

The effects of rifampin alone and in combination with other drugs were investigated in mice infected intravenously with the Brownell strain of *Mycobacterium kansasii* and several strains of *Mycobacterium intracellulare*. Evaluation of therapeutic results was based mainly on changes in serial counts of viable bacilli in the kidney, as well as on cultures of blood from the heart, extent of gross lesions, microscopic morphologic examination, and mortality. Rifampin and all other drugs except streptomycin were administered by the drug diet method starting seven days to ten days after infection and continuing for 28 days to 49 days.

Rifampin alone was effective in the *Mycobacterium kansasii* infection; the response was directly related to the dosage in the range of 1.0 mg to 40 mg per kg per day. The addition of streptomycin markedly enhanced the response, which was not improved by the further addition of isoniazid. The next best combination was rifampin plus isoniazid, with or without ethionamide. The *Mycobacterium intracellulare* infection was more resistant to treatment; the only effective regimens were those containing the combination of rifampin plus streptomycin.

No evidence for the emergence of significant drug resistance was found when cultures recovered from treated mice were tested by the proportion method. These results offer encouragement for the use of drug regimens containing rifampin and streptomycin in the treatment of *Mycobacterium kansasii* and *Mycobacterium intracellulare* infections in man. — Authors' Summary

Waters, M. F. R. An internally-controlled double blind trial of thalidomide in severe *erythema nodosum leprosum*. Leprosy Rev. **42** (1971) 26-42.

A double-blind, internally-controlled, clinical trial of thalidomide in severe,

chronic, histologically-proven *erythema nodosum leprosum* (ENL) is reported. A total of ten adult male patients were admitted to the trial, all of whom were receiving continuous treatment with steroids and whose minimum daily requirement just to suppress the reaction was in no case less than 15 mg of prednisolone or 18 international units of corticotrophin. The trial was divided into four equal parts (of either four or six weeks' duration) consisting of an initial control period, first and second trial periods, and a final control period. Throughout the trial all patients received DDS, 100 mg twice weekly; thalidomide, 300 mg daily, was given during one trial period and identical placebo tablets during the other. As judged by the reduction in their steroid requirements, nine of the ten patients showed a very significant improvement while they were receiving thalidomide, although seven subsequently relapsed after stopping the drug. There was no dose-for-dose relationship between thalidomide and prednisolone. Two patients developed a mild allergic dermatitis. —Authors' Summary

Bergel, M. Actividad antioxidante biologica de la diaminodifenilsulfona (D.D.S.). Arch. argent. dermat. Tomo XVIII (1968) 5-30 (See Abstracts Ninth International Leprosy Congress. Internat. J. Leprosy **36** (1968) 653.)

Biggs, J. T., and Levy, L. Binding of dapsone and monoacetyldapsone by human plasma proteins (35647). Proc. Soc. Exp. Biol. and Med. **137** (1971) 692-695.

Binding of dapsone and monoacetyldapsone to human plasma proteins has been investigated by means of an ultrafiltration technic. When binding was studied *in vivo* or *in vitro* at therapeutic concentrations of the drugs, dapsone was 70 to 80% bound, and monoacetyldapsone 98 to 100%. Rapid and slow acetylators of dapsone bind both compounds to the same degree. Protein binding of monoacetyldapsone may well account for the limited excretion of this compound in the urine. The contribution of protein binding to the long plasma half-lives of these compounds must be evaluated in the light of future studies.—Authors' Summary

Gelber, R., Peters, J. H., Gordon, G. R., Glazko, A. J., and Levy, L. The polymorphic acetylation of dapsone in man. Clin. Pharmacol. Ther. **12** (1971) 225-238.

The characteristics of the acetylation of dapsone (avlosulfon) were found to parallel those of isoniazid and sulfamethazine in 19 subjects, thereby establishing the genetic polymorphism for the acetylation of dapsone. This polymorphism was revealed by the distribution of the ratios of the plasma concentration of acetylated to parent drug. The acetylation capacity for dapsone was shown to be a reproducible, individual characteristic. Acetylation of dapsone and deacetylation of monoacetyl dapsone occurred concurrently. Constant plasma ratios of acetylated to parent drug characteristic for the individual were attained immediately after administration of dapsone but only after several hours following administration of monoacetyl dapsone. The available data suggest that acetylation rather than deacetylation is the primary determinant of these ratios. Rates of disappearance of dapsone and monoacetyl dapsone from the plasma were the same regardless of which of the two was administered or of the acetylator phenotype of the subject. After dapsone, no differences between rapid and slow acetylators were found in the 24 hour urinary excretion of dapsone and its conjugates hydrolyzed by mild or strong acid treatment. Rapid acetylators excreted significantly more monoacetyl dapsone and its acid labile conjugates than slow acetylators. Because these compounds accounted for only a very small fraction of the dose, it was not possible to phenotype individuals by these measurements. More dapsone and acid-hydrolyzable conjugates of dapsone were found in 120 hour urine collections after monoacetyl dapsone than after dapsone in both phenotypes.—Authors' Summary

Microbiology

Lefford, M. J. The effect of inoculum size on the immune response to BCG infection in mice. Immunology **21** (1970) 369-381.

In mice infected with BCG the rate of development of resistance to *L. monocytogenes* was related, and the growth of BCG in the liver and spleen was inversely related, to the size of the infecting inoculum. The rate of elimination of BCG after the onset of immunity was independent of the infecting dose. The effect of dose on the growth of BCG *in vivo* was abolished by immunosuppressants, and was restored by certain categories of lymphoid cells. Spleen and thymus cells, but not bone marrow cells, were able to confer immunity on X-irradiated recipients. There was no evidence of cooperation between thymus and bone marrow cells.

It is concluded that the inoculum effect in BCG infections has an immunological basis. With increasing doses of BCG there is progressive reduction of the latent period prior to the induction of immunity.—Author's Summary

Choi, C. S., Royal, W. A., and Francis, J. The anti-complement fluorescent antibody technique for the identification of mycobacteria Tubercle **52** (1971) 148-150.

An anti-complement fluorescent antibody technic has been evaluated for the identification of mycobacteria.

M. tuberculosis, *M. avium*, *M. intracellulare*, *M. marinum*, *M. kansasii*, *M. scrofulaceum* and *M. fortuitum* could readily be differentiated from each other, using the reference serum of each species.

It may become possible to carry out the procedure directly on sputum samples.—Authors' Summary

Jansson, E., Tuuri, S., and Ridley, D. S. Isolation of a mycoplasma from three patients with lepromatous leprosy. Int. J. of Dermatology **10** (1971) 175-178.

Using a modified cell-free culture medium and modern microscopic equipment, a mycoplasma was isolated from scrapings of skin lesions of three patients with lepromatous leprosy. Three specimens were taken from the first patient. All five isolates were arginine-positive and their antibiotic sensitivity was identical with only one slight exception.—Authors' Summary

Smithwick, R. W., and David H. L. Acridine orange as a fluorescent counterstain with the auramine acid-fast stain. Tubercle **52** (1971) 226-231.

Evidence is presented to show that acridine orange is an effective counterstain when used with the auramine-O acid-fast stain. The non-acid-fast material is stained orange to red and the acid-fast bacilli fluoresce yellow to yellow-green.

When 133 sputum specimens were examined by the new method and by other fluorescence acid-fast methods, no significant difference in the number of acid-fast positive smears was found. Furthermore, more acid-fast positive smears were found by fluorescence acid-fast microscopy than by the Ziehl-Neelsen method. Culture on Lowenstein-Jensen medium was used as a control on 100 of the specimens.—Authors' Summary

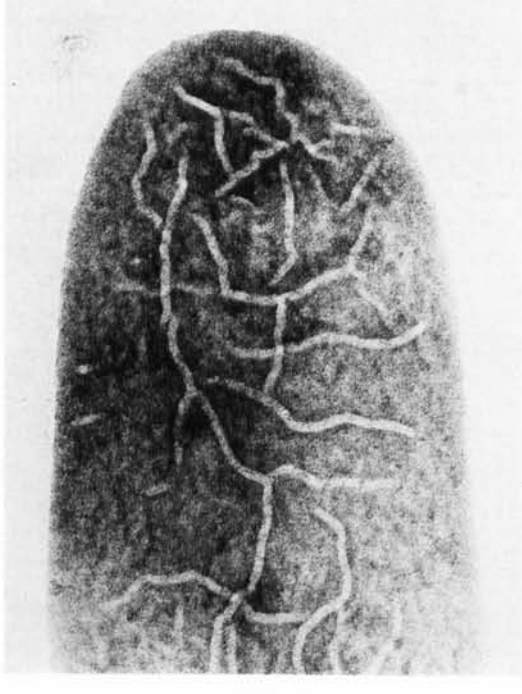
Gordon, J., and White, R. G. Surface peptido-glycolipid filaments on *Mycobacterium leprae*. Clin. exp. Immunol. **9** (1971) 539-547.

Mycobacterium leprae was shown to possess a superficial network of filaments fundamentally identical with the adjuvant active peptido-glycolipid filaments present on all other mycobacteria, and in biologically active wax D derived from *Mycobacterium tuberculosis* and related organisms. Differences between the filaments seen on *M. leprae* recovered from human lepromatous tissue and those demonstrated on mycobacteria grown in artificial culture are attributed to the effect of prolonged intracellular existence in a host phagocyte and are given as evidence of sensitivity of peptido-glycolipid to the action of intracellular enzymes.

The immunological phenomena common to leprosy and tuberculosis are largely dependent upon the biological activity of the mycobacterial peptido-glycolipid and its ability to resist the action of host enzymes is thought to be of fundamental importance for its functions as an immunological adjuvant. It is therefore of interest that the study has provided evidence that at least the macromolecular arrangement of the surface network is susceptible to attack by human tissues. It is at present not known whether the released substances retain an adjuvant effect or possess any other biological activity which may contribute to the pathogenesis of the disease.—Authors' Summary

This is a nicely illustrated article, which in its original form will interest all students of the anatomy and immunologic properties of *M. leprae*.—(Fite)

An original illustration from this paper is here reproduced with the permission of Dr. Gordon. A similar illustration for *M. tuberculosis* will be found in: Imaeda, T. Electron microscopy. Approach to leprosy research. Internat. J. Leprosy **33** (1965), 669-683, Figure 8.—OKS.



Levy, L. The effect of several rates of freezing and thawing on the viability of *Mycobacterium leprae*. Cryobiology 6 (1969) 42-44.

The influence on the viability of the organisms of various rates of freezing and thawing of suspensions of *M. leprae* in 10% glycerol and 0.1% bovine serum albumin was investigated, employing Shepard's mouse foot pad technic as a measure of viability. Freezing and thawing produced some loss of viability. Rapid freezing was less deleterious than slow freezing, and approximately 75% of the organisms survived rapid cooling to —60°C and overnight storage at this temperature, followed by slow warming. Study of the additional effect of prolonged storage on the viability of *M. leprae* is planned.—Author's Summary

Levy, L. and Merigan, T. C. Failure of an interferon inducer to inhibit multiplication of *Mycobacterium leprae* (34734). Proc. Soc. Exp. Biol. and Med. **134** (1970) 87-89

Treatment of mice with the interferon inducer polyinosinic:polycytidylic acid failed to inhibit multiplication of *Mycobacterium leprae* in the mouse foot pad. This same treament has recently been shown to inhibit multiplication *in vivo* of several intra- and extracellular pathogenic microorganisms.—Authors' Summary

Prabhakaran, K. Unusual effects of reducing agents on *o*-diphenoloxidase of *Mycobacterium leprae*. J. Bacteriology **107** (1971) 787-789.

Reducing agents had no effect on the oxidation of 3, 4-dihydroxy-phenylalanine (DOPA) to quinone by *Mycobacterium leprae*; no quinone formation by *o*-diphenoloxidase of mammalian or plant origin was detected under similar experimental conditions. Ascorbic acid and reduced glutathione prevented further oxidation and polymerization of the quinone to melanin by *M. leprae;* cysteine was less effective. In the presence of reducing agents, the quinon (indole-5,6-quinone) formed from

DOPA by *M. leprae* was not reduced back to diphenol. On the other hand, the quinone (dopachrome) produced from DOPA by mammalian or plant phenolase was rapidly decolorized by reducing agents. Oxidized glutathione and cystine had little effect on *o*-diphenoloxidase from all of the three sources. Cyanide, which completely inhibited mammalian and plant phenolases, had only a partial effect on the enzyme in the bacilli. Various lines of evidence suggest that the properties of *o*-diphenoloxidase in *M. leprae* are different from those of similar enzymes obtained from other sources.—Author's Summary

Rees, R. J. W. Immunological aspects of experimental leprosy in the mouse. Proc. Royal Soc. Med. **63** (1970) 1060-1062.

Using a pure-line strain of mice, various experimental models have been developed from which it should now be possible to unravel the immunological processes associated with infections with *M. leprae*. Thus, in normal mice, there is only limited multiplication of *M. leprae* confined to the first six months of infection and then a further 14 months until an epithelioid-type granuloma is established at the site of inoculation, resembling borderline leprosy. Such a prolonged incubation period would suggest either a weak antigen or that the operative antigen was released only after a long interval of time. However, when the mice are thymectomized and irradiated – treatment known to suppress cell-mediated immune responses—*M. leprae* multiply for a much prolonged period, spread throughout the body and produce a disease resembling lepromatous-type leprosy. Moreover, multiplication of *M. leprae* in the immunologically deficient mice can be inhibited and the lepromatous form changed to the borderline form of the disease by the inoculation of syngenic lymphoid cells from normal mice. These findings not only demonstrate the role of cell-mediated immunity in determining the outcome of infections with *M. leprae*, but that a deficiency in this type of immunity could determine those individuals who will develop lepromatous type leprosy. The experimental models using *M. lepraemurium* also show that heavy infections of macrophages with this organism nonspecifically depress a wide range of cell-mediated immune responses, thus increasing further the individual's susceptibility to infection.—Author's Summary

Immuno-Pathology

Weddell, A. G. M., Palmer, E., and Rees, R. J. W. The fate of *Mycobacterium leprae* in CBA mice. J. Pathology **104** (1971) 77-92.

A series of experiments was designed to follow, systematically, the fate of inoculated *M. leprae* histologically and to relate this to the number present, in a pure-line strain of mice (CBA). After local inoculation *M. leprae* rapidly entered striated muscle fibres, wherein they survived and multiplied. For the first 15 months this site provided the main yield of bacilli. From the 15th month onwards increasing numbers of bacilli were found in perineural and Schwann cells; at first in local dermal nerves, and later in dermal nerves at other sites and in peripheral nerves, particularly the sciatic and median nerves. At all times throughout the infection *M. leprae* were found in the lining cells of capillaries in muscles and nerves. Exactly the same intracellular distribution of bacilli was seen in mice inoculated intravenously. There were, however, sites of predilection, including foot pads, ears and nose. From 20 months onwards all mice showed increasing histologic and clinical evidence of nerve destruction.

The late cellular and bacteriological patterns of response to *M. leprae* in the mouse are similar to those seen in leprosy in man, and the relevance of the earlier responses in the mouse to the pathogenesis of human leprosy is therefore discussed. – Authors' Summary

Sainte-Marie, G., and Sin, Y. M. Structures of the lymph nodes and their possible function during the immune response. Rev. Can. Biol. **27** (1968) 191-207.

The lymph node has a heterogeneous constitution that remains to be clarified. This paper reports the observations from a three-dimensional analysis of the rat lymph node carried out as an attempt to elucidate its architecture. We studied the reticular-fiber pattern, the blood vascular pattern as well as the follicles and nodules of the node. We studied also the pseudofollicle, a rarely mentioned nodal structure. We placed emphasis on the topographical relations existing between the various nodal structures. It was found that the node has a well-organized architecture in spite of the variable appearance of random sections of nodes. Hence, the observations led us to elaborate a pattern illustrating its architecture. Finally, an explanation of the functioning of the various structures during the immune response was proposed, taking into consideration their definite topographical relations.-Authors' Summary

Nelson, D. S., Nelson, M., Thurston, J. M., Waters, M. F. R., and Pearson, J. M. H. Phytohaemagglutinin-induced lymphocyte transformation in leprosy. Clin. exp. Immunol **9** (1971) 33-43.

Blood lymphocytes from Malay, Indian and Chinese patients with leprosy, and from race-matched controls, were cultured in the presence of phytohaemagglutinin. Cells from Malays and Indians with lepromatous leprosy and from Malays with tuberculoid leprosy transformed, as well as cells from normal controls, when cultured in normal (reference) serum. Cells from lepromatous Malays and Indians transformed significantly less well than cells from normal controls when cultured in autologous serum. Normal lymphocytes transformed significantly less well when cultured in serum from lepromatous or tuberculoid Malays or from lepromatous Indians than when cultured in serum from normal controls.

Lymphocytes from lepromatous Chinese transformed significantly more extensively than those from normal Chinese, whether cultured in normal (reference) or autologous serum. The ratio of transformation in autologous serum to transformation in reference serum was significantly depressed for lepromatous Chinese. Although lepromatous Chinese serum, compared with normal Chinese serum did not depress the response of lymphocytes from one donor, there was evidence of depression when cells from another donor were used. Cells and sera from Chinese patients biopsied for suspected nasopharyngeal carcinoma behaved similarly to those from lepromatous Chinese, and not to those of normal Chinese, whether or not nasopharyngeal carcinoma was found.

Lymphocytes from patients with disease classified as stable, regardless of other criteria, transformed significantly less well in either normal or autologous serum than did cells from patients with downgrading (rapidly progressive) disease. This was true of all races. In the case of Malays and Indians with stable disease the cells also transformed less well than normal cells in reference serum.—Authors' Summary

Saha, G., and Mittal, M. M. A study of cell mediated immunity in leprosy: changing trends in the immunological spectrum of the disease. Clin. exp. Immunol. **8** (1971) 901-909.

Skin tests of delayed hypersensitivity were performed on thirty-eight patients with leprosy with a bacterial antigen (tuberculin), a hapten (dinitrochlorobenzine) and allogenic lymphocytic transplantation. The results have indicated that leprosy is associated with a generalized depression of delayed allergic response. The depression is of greater severity in patients with lepromatous leprosy and less among tuberculoid patients. The depression of cell mediated immunity in these cases is not absolute but is relative and depends upon the dose and potency of an antigen and the severity of the disease.—Authors' Summary

Mittal, M. M., and Saha, K. A. A study of delayed hypersensitivity in patients with leprosy. Indian J. Med. Sci. **25** (1971) 464-466.

Sixteen patients with leprosy were tested with a bacterial antigen (tuberculin) and a hapten (dinitrochlorobenzene) for signs of delayed hypersensitivity. The results indicate that leprosy in general is associated with depression of delayed allergic response, the depression being of greater severity in patients with lepromatous leprosy and of less severity among tuberculoid patients. The depression of delayed hypersensitivity in these cases is not absolute but is relative and depends upon the dose and potency of the antigen used and the immunological status of the patients.—Authors' Summary

Caspary, E. A., and Field, E. J. Lymphocyte sensitization in sarcoidosis. British Med. Jour. **17** (1971) 143-145.

Nineteen patients with sarcoidosis have all been shown to have lymphocytes in their blood sensitized to several antigens, including purified protein derivative of tuberculin and Kveim agent, though they had negative or greatly reduced Mantoux reaction. Two patients who repeatedly failed to "convert" after BCG inoculation showed the same cell sensitization phenomena. No explanation can be offered for this anomaly.—Authors' Summary

Bonomo, L., and Dammacco, F. Immune complex cryoglobulinemia in lepromatous leprosy. Clin. exp. Immunol. **9** (1971) 175-181.

Cryoglobulins isolated from the sera of six patients with lepromatous leprosy were extensively studied by various immunochemical technics.

Immunoelectrophoresis and analytical ultracentrifugation revealed, in all cases, the presence of two components only, which were identified as IgG and IgM respectively. The IgG component of all six cryoprecipitates and the IgM component of five of them were polyclonal, whereas the remaining IgM component was monoclonal as it produced a narrow-banded electrophoretic spike and contained kappa light chains only.

Anti-y-globulin activity, detected in all sera and isolated cryoglobulins, was consistently found to be associated with the IgM fraction of the mixed cryoglobulins and were present at very high titres in the IgM monoclonal component. B1A serum levels were decreased in all cases.

The cryoglobulins that appear to be immune complexes of the IgG/anti-IgG type may play a role in the pathogenesis of some clinical features of leprosy patients. — Authors' Summary

Bullock, W. E., Jr., and Fasal, P. Studies of immune mechanisms in leprosy III. The role of cellular and humoral factors in impairment of the *in vitro* immune response. J. Immunology **106** (1971) 888-899.

Phytohemagglutnin (PHA)- and antigen-induced DNA synthesis was measured in leukocyte cultures from 16 patients with lepromatous leprosy, 12 with tuberculoid leprosy, and 20 normal persons. In cultures containing 20% autologous plasma, the responses of lepromatous leukocytes to PHA, purified protein derivative (PPD), streptolysin O (SLO) and antigens of *Mycobacterium leprae* were significantly below those of the control group. Simultaneous culture of lepromatous leukocytes washed and suspended in normal homologous plasma (20%) resulted in significantly increased SLO-induced DNA synthesis and a modest increase in response to PPD. The response to PHA and antigens of *M. leprae* remained unchanged. Except for PPD, the responses of tuberculoid leukocytes in autologous or homologous plasma were not significantly lower than normal. Nine of 14 lepromatous plasmas were found to contain a factor that depressed the response of normal leukocytes to PPD and SLO but not to PHA. The depressor factor is nondialyzable, stable after prolonged storage at −20°C, and resistant to heating at 56°C; its activity is lost at relatively low dilutions. It is concluded that the *in vitro* demonstration of impaired cellular immune function in patients with leprosy may reflect a primary cellular defect, the depressive effect of a humoral factor, or both, to varying degrees.—Authors' Summary

Costello, R., Izumi, T., and Sakurami, T. Behavior of attenuated mycobacteria in organs of neonatal and adult mice. J. Exp. Med. **134** (1971) 366-380.

The consequences of Calmette-Guérin bacillus (BCG) vaccination were followed in newborn and adult mice.

BCG failed to multiply in the organs of adult mice when administered peritoneally. In contrast, extensive multiplication occurred in both splenic and pulmonary tissue after its peritoneal administration to newborn mice. This absence of tuberculostasis occurred during the period when the animal's spleen, lung, and thymus were rapidly growing.

Although neonatal infection with BCG was severe, as shown by the large numbers of organisms recovered from the animals' tissues, the animals suffered no mortality or overt signs of disease. Neonatal vaccination did not signficantly affect either the animal's growth rate or the gross development of its organs.—Authors' Summary

Nopajaroonsri, C., and Simon, G. T. Phagocytosis of colloidal carbon in a lymph node. American J. Path. **65** (1971) 25-42.

Colloidal carbon, injected intramuscularly, migrates rapidly and selectively to a corresponding lymph node by lymphatics, in which the carbon travels as free particles. In the lymph node, carbon particles are mainly phagocytosed and stored by macrophages, which exhibit morphologic changes in the plasma membrane and the tubules of endoplasmic reticulum. The subsequent migration of these cells results in wide distribution of carbon in the lymph node. Cytoplasmic changes also occur in sinusoidal macrophages, in which no carbon is seen. A possible relation of these macrophages to macrophage migration in lymph node is postulated. The lymphatic endothelial cells, like endothelial cells in any other organ, phagocytose only a small amount of carbon and only after functional overload of the macrophages. — Authors' Summary

Nopajaroonsri, C., Luk, S. C., and Simon, G. T. Ultrastructure of the normal lymph node. American J. Path. **65** (1971) 1-24.

The "normal" lymph node has been studied by electron microscopy. The lymphoid tissue can be divided into three distinct zones. Zone 1 consists of loosely arranged cells surrounding the lymphatic sinuses and blood vessels. This is the only zone in which plasma cells are present. Zone 2 is surrounded by zone 1 and consists of compactly arranged cells in which lymphocytes predominate. Zone 3 (germinal center) appears only after antigenic stimulation. It is characterized by large, ribosome-rich cells and macrophages containing phagocytosed lymphocytes. These zones are arranged with their longest diameters pointing towards the hilus. Zone 1 is the longest and extends across the cortex, paracortex and medulla. Zone 2 spans across cortex and paracortex. Zone 3 usually is confined to the cortex. Our preliminary studies indicate that zone 1 is mainly bursal dependent, zone 2 is mainly thymic dependent and zone 3 is bursal dependent.—Authors' Summary

Epidemiology and Prevention

Smith, J. W. Leprosy, Texas Medicine, (1971) 58-64.

Texas is a leading endemic area for leprosy in the United States. Most of the cases occur in adults and are bacilli-positive. Clinical recognition of the disease is possible, but the diagnosis can be confirmed by biopsy of affected tissue. Treatment with sulfones is efficacious if the disease is diagnosed early. In Texas, surveillance clinics have been set up in an attempt to discover new cases earlier, examine contacts and decrease the incidence of the infection.—Author's Summary

Editorial.—La lèpre: progrès et problèmes. [Progress and problems in leprosy.] Medécine et Hygiéne. No. 970, June 30, 1971.

In the course of the past five years, more than half a million cases of leprosy have been identified and registered in 75 countries. Probably, the total number of cases in 1970 differs little from the estimated 10,786,000 for 1965, at a time when 2097 million persons lived in areas in which the prevalence was 0.5/1,000 or greater. Thus, as a recent World Health Organization committee of experts indicates, leprosy continues to be a serious problem in numerous countries. Current activity in the epidemiology, immunology, prophylaxis, and microbiological investigations are emphasized.

Meade, T. W. Epidemiology and leprosy control. Leprosy Rev. **42** (1971) 14-25

Leprosy "control" must become increasingly concerned with primary prevention (that is, the prevention of disease in those hitherto unaffected). Secondary prevention, or the detection and early treatment of established cases must naturally continue as a service, but is unlikely to contribute much towards the ultimate eradication of leprosy.

Primary prevention depends on being able to predict, more precisely than at present, "high-risk groups", towards which prophylactic measures can be especially directed. The ability to predict will come only through incidence (rather than prevalence) studies, which will be concerned with a much wider range of social, economic, demographic and medical variables than has so far been attempted. Multivariate technics of analysis should be available. There is every reason to believe, from analogies with the epidemiological study of chronic non-communicable disease, that this approach would be fruitful in the leprosy field.

The incidence of leprosy is very low; lepromatous leprosy, in particular, should be regarded (on an incidence basis) as a rare disease. Large study populations (of the order of hundreds of thousands) are ideally needed for epidemiological studies of leprosy; work to date indicates that the obstacles to surveys on this scale are not insuperable.

Three particularly important methodological problems—namely uniformity of case-finding methods, the handling of "suspicious" cases, and the detection of "evanescent" cases-need especial consideration.

"High risk group" studies should be undertaken before the possible widespread introduction of prophylactic measures makes it difficult to carry them out properly.

Useful sudsidiary benefits to clinical, pathological and social studies of leprosy would arise from the epidemiological approach discussed.—Author's Summary

Wheatley, B. Pilot survey of a group of remote villages in Masasi District, Tanzania. Leprosy Rev. **41** (1970) 21-24.

Leprosy is highly endemic in the Masasi district of southern Tanzania, and there exists a well organized dispensary treatment scheme in the region. However, a survey carried out in a group of villages in this district showed that about 40% of persons with leprosy were not coming forward for diagnosis and treatment. The author concludes that the survey has confirmed the need for a case-finding program to be combined with the treatment scheme already in operation.—W. H. Jopling

Other Mycobacterial Diseases

Moulding, T. Chemoprophylaxis of tuberculosis: When is the benefit worth the risk and cost? Ann. Inter. Med. **74** (1971) 761-770.

The number of persons in various risk categories who must be given isoniazid chemoprophylaxis to prevent one case of active tuberculosis has been estimated in order to help decide on indications for chemoprophylaxis. Assuming the protective effect of chemoprophylaxis is limited to 10 years, this number is 14.2 for persons with inactive cases of tuberculosis, 37.5 for

primary tuberculosis in children, 81.3 for household contacts of active cases, 110.3 for tuberculin-positive adolescents with normal chest roentgenograms, and 163.4 for tuberculin-positive adults with normal chest roentgenograms. The cost to prevent one case in each of these categories is $824, $1,612, $813, $4,743 and $7,026, respectively. When weighing this information plus the knowledge of a significant but low frequency of isoniazid toxicity against the cost of treating an active case of tuberculosis and the complications of such treatments, a strong recommendation can be made to give preventive treatment to all cases of primary tuberculosis in children and all inactive cases of tuberculosis. By contrast, the justification for giving isoniazid to all tuberculin-positive adults with normal chest roentgenograms seems weak. In intermediate situations, such as all household contacts to persons with active disease, all tuberculin-positive adolescents with normal chest films, and selected tuberculin-positive adults with normal chest films who have additional conditions that increase the risk of developing active tuberculosis, chemoprophylaxis is probably justified unless isoniazid proves to be more toxic than is now established. — Author's Summary

Although the cost of chemoprophylaxis in leprosy is probably not comparable to that in tuberculosis, the problems of identification of candidates for chemoprophylaxis are much alike. The author of the above manuscript regards chemoprophylaxis as an effective tool to accelerate decline in annual incidence of new cases of tuberculosis in technically advanced nations. Translation of this thought to include all nations in the matter of chemoprophylaxis in leprosy with sulfones is worth a sentence.—(G. L. Fite)