CURRENT LITERATURE

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

Chemotherapy

Ambrose, E. J., Antia, N. H., Birdi, T. J., Mahadevan, P. R., Mester, L., Mistry, N. F., Mukherjee, F. and Shetty, V. The action of deoxyfructose serotonin on intracellular bacilli and on host response in leprosy. Lepr. Rev. **56** (1985) 199–208.

The drug deoxyfructose serotonin has already shown antileprosy activity according to *in vitro* tests on bacillary suspensions, in the mouse foot pad, and in a pilot clinical trial. In a group of further tests in our institute, activity against intracellular bacilli has been obtained both in macrophages from LL patients and bacilli within Schwann cells in organized nerve culture. *In vitro* tests also show enhanced lymphocyte-macrophage interaction promoted by the drug with infected macrophages, suggesting a possible enhancement of cellular immune response. Some protection *in vivo* against sciatic nerve damage by *Mycobacterium leprae* has also been shown in mice.—Authors' Summary

Orege, P. A. and Owili, D. M. Dapsone resistant leprosy, the western Kenya experience. Trop. Geogr. Med. **37** (1985) 139–142.

Forty-one patients out of 804 registered lepromatous (LL) and borderline lepromatous (BL) patients were studied for possible dapsone resistance by a series of biopsy specimens, skin smears and clinical examination. These patients were drawn from a pool of 4384 registered leprosy patients in the west Kenya Leprosy Control Project area.

Six out of 41 cases (14.6%) were confirmed as dapsone resistant by a series of biopsy specimens taken when patients were on supervised dapsone therapy: 11 patients (26.8%) were suspected to be resistant and 24 patients (58.6%) responded well to dapsone therapy. All the confirmed cases were lepromatous leprosy cases. We therefore found that there is dapsone resistance here with a maximal prevalence rate of 7 per 1000 in all lepromatous cases and 14.6% in clinically suspicious cases.—Authors' Abstract

Clinical Sciences

Chavez-Legaspi, M., Gomez-Vazquez, A. and Garcia-De-La Torre, I. Study of rheumatic manifestations and serologic abnormalities in patients with lepromatous leprosy. J. Rheumatol. **12** (1985) 738–741.

We investigated the rheumatic and laboratory features associated with rheumatic syndromes in 32 patients with lepromatous leprosy. Twenty-seven (84%) developed a broad range of rheumatic manifestations, the most common being the presence of arthritis which was symmetric and polyarticular, resembling rheumatoid arthritis. The laboratory abnormalities included an elevated sedimentation rate in 32 cases (100%), a positive rheumatoid factor in 6 (18.7%) and antinuclear antibodies in 1 (3.1%). A careful history and the recognition of rheumatic manifestations will help in the identification of this type of leprosy.—Authors' Abstract

Chiron, J. P., Denis, F., Yvonnet, B., Coursaget, P., Diop Mar, I. and Languillon, J. Lèpre et hépatîte B. [Leprosy and hepatitis B.] Acta Leprol. **3** (1985) 169–199. (in French)

In 1966, B. S. Blumberg, investigating for carriers of the "Australia" antigen which he had discovered 2 years before, found that the percentage was significantly higher in a group of leprosy patients than in controls. In this initial work, done in Cebu, Philippines, he mentions a higher percentage of this antigen carriers among the lepromatous than among the tuberculoid patients. He explains his findings by a genetic hypothesis and by the fact that lepromatous patients are more often hospitalized than tuberculoid ones, thus closer contacts could favor the antigen transmission.

Later, the established relation between Australia antigen and hepatitis B led the authors to disregard the very deceiving genetic hypothesis and to emphasize the most important characteristic of lepromatous leprosy—cell immunity—as opposed to the tuberculoid form where cell immunity is normal.

Investigation for serologic markers of hepatitis B virus in patients with tuberculoid or lepromatous leprosy provides a model for the study on "cell immunity and hepatitis B." The juxtaposition of geographic areas with high prevalence of leprosy patients and of HBs Ag carriers is a supplementary argument for the study of their connection.

Up to now, about 50 works have been published on this subject. Most of them investigate detection of HBs Ag and a few of HBe Ag and HBs Ac. This bibliographical study, including a personal study, reviews markers of hepatitis B virus replication in leprosy patients, incidence of hospitalization and age of these patients, as well as the methodology used.—Authors' English Summary

de Rijk, A. J., Nilsson, T. and Chonde, M. Quality control of skin smear services in leprosy programmes: preliminary experience with inter-observer comparison in routine services. Lepr. Rev. **56** (1985) 177–191.

A description of a systematic approach to periodical re-examination of samples of skin smears for leprosy taken in the routine services is given. Procedures and recordings are described in detail and examples given of test runs in Tanzania and Ethiopia. Scoring of quality control results is done against 3 indicators. The effect of the application of various criteria is shown in the 2 test runs. The exercise was experienced as stimulating and quite revealing.—Authors' Summary

Pareek, S. S. and Tandon, R. C. Epididymal lesion in tuberculoid leprosy. Br. Med. J. **291** (1985) 313.

Epididymal lesions are well recognized in tuberculosis, lepromatous leprosy, genital gonorrhea, and sarcoidosis. They have not, however, been documented in tuberculoid leprosy. We report on a patient with an epididymal lesion who is thought to have had tuberculoid leprosy.

The presence of large giant cells and epithelioid cells in epididymal tissue without central caseation is suggestive of tuberculoid leprosy rather than tuberculosis. This diagnosis was further corroborated by the classical skin lesions with thickened nerves and positive results of a lepromin test. Lepromatous leprosy could be excluded on the basis of the histological examination of epididymal tissue and the absence of *Mycobacterium leprae* in a nasal scraping and on slit smear examinations. Thus this is perhaps the first report describing an epididymal lesion in a patient with tuberculoid leprosy.—(*From* the Case Report)

Reddy, N. B. B., Srinivasan, T., Krishnan, S. A. R. and Bhusnurmath, S. R. Malignancy in chronic ulcers in leprosy: a report of 5 cases from Northern Nigeria. Lepr. Rev. **56** (1985) 249–253.

Five patients, 2 of the usual variety of squamous cell carcinoma and 3 of verrucous carcinoma, are reported. Four patients had BT type of leprosy and 1 had LL type

of leprosy. Interestingly, one of the verrucous carcinomas occurred over the palm which is a rare site.—Authors' Summary

Saha, K., Agarwal, S. K. and Sehgal, V. N. Status of fibrin degradation products in leprosy. J. Dermatol. **11** (1984) 545–549.

Plasma fibrinogen and fibrin degradation products (FDP) were estimated in 45 control subjects and 45 patients with various types of leprosy including 16 patients with erythema nodosum leprosum (ENL). The levels of FDP were quantified by using a suspension of *Staphylococcus aureus* (Newmans D_2C strain). Significantly higher levels of plasma fibrinogen and FDP were observed in patients with lepromatous leprosy, especially with ENL, than in the controls. Only 3 lepromatous patients had plasma fibrinogen levels below the normal range; 2 of them had severe ENL and were suffering from nasal bleeding. Levels of D and E fragments were also estimated in another 20 control subjects and 13 lepromatous patients by hemagglutination inhibition technique and were found to be significantly elevated in the patients. It was inferred that raised FDP levels in such patients indicated an ongoing occult fibrinolysis during lepra reaction. A few lepromatous patients may show hypofibrinogenomia during severe ENL episodes.—Authors' Abstract.

Sarojini, P. A., Humber, D. P., Yemaneberhan, T., Fekete, E., Belehu, A., Mock, B. and Warndorff, J. A. Cutaneous leishmaniasis cases seen in two years at the All Africa Leprosy and Rehabilitation Training Centre Hospital. Ethiop. Med. J. **22** (1984) 7–11.

An analysis of 104 cases of cutaneous leishmaniasis reported at the All Africa Leprosy and Rehabilitation Training Centre, Addis Ababa, Ethiopia, in 2 years showed 98 patients with localized cutaneous leishmaniasis (LCL) and 6 with diffuse cutaneous leishmaniasis (DCL). Of these patients, who included fewer females than males (1:1.6), 62 (59.6%) were between the ages of 10 and 29 years. Single lesions were the most common (74.5%), with the nose being the commonest site of involvement. Of the 104 patients, all with DCL and 63 with LCL were admitted to the hospital and/or treated. Multibacillary leprosy, which is associated with immunological anergy, was diagnosed in 4 of the patients with self-healing LCL, supporting the suggestion that there is a specific rather than a generalized immune defect in multibacillary leprosy.—Authors' Abstract

Shafique, M., Singa, A. K. and Prakash, A. P. S. Relation of herpes zoster with lepromatous leprosy (report of two cases). Indian J. Dermatol. **29** (1984) 31–34.

Heretofore no case of herpes zoster has been found recorded at the site of leprosy or in the same dermatoma. Two such cases are being reported in which lepromatous leprosy has been incriminated as the etiological factor.—Authors' Abstract

Trojan, H. J., Schaller, K. F. and Merschmann, W. [Ocular involvement in leprosy—a study in Togo, West Africa.] Klin. Monatsbl. Augenheilk **185** (1984) 235–242. (in German)

It is well known that ocular changes occur in leprosy, but data on their frequency differ very considerably (0.8–100%). Two groups of leprosy patients in Togo were examined: first, 206 patients who had had the disease for approximately 10 years and a second group (101) patients who had been suffering from it for approximately 24 years and had severe mutilations. It became apparent that sooner or later all leprosy patients suffer from ocular complications. The following symptoms were found: loss of eyebrows in 40.8% (42.6%), loss of eyelashes in 29.6% (34.6%), lagophthalmos caused by involvement of the 7th cranial nerve in 21.4% (31.7%), corneal changes in 34.5% (49.5%), uveitis in 5.8% (19.8%), atrophy of the optic nerve in 12.6% (11.9%), and cataract in 21.8% (12.8%). The duration of the disease, the type of leprosy, and the time when treatment was started are obviously the main factors associated with ocular changes in leprosy.—Authors' English Summary

Immuno-Pathology

Abou-Zeid, C., Harboe, M., Sundsten, B. and Cocito, C. Cross-reactivity of antigens from the cytoplasm and cell walls of some corynebacteria and mycobacteria. J. Infect. Dis. **151** (1985) 170–178.

Leprosy-derived corynebacteria (LDC) are non-acid-fast organisms isolated from leprosy lesions in humans. In this study 20 antigens of native LDC cytoplasm were identified by immunoelectrophoresis, and autoclaving yielded the M_1 component, which strongly crossreacted with antigen 60 of *Mycobacterium bovis* BCG (bacille Calmette-Guérin) and antigen 7 of *M. leprae.* The polysaccharide moiety of M_1 was immunologically related to the LDC cell wall polysaccharide previously characterized as arabinogalactomannan. The latter polysaccharide competitively inhibited the formation of immune complexes by labeled M_1 and antisera to the LDC cell wall; cytoplasm and wall polysaccharides from other bacteria produced lower-level inhibition. In a radioimmunoassay with ^{125}I-labeled antigen 7 of *M. leprae,* sera from patients with leprosy and antisera to the LDC cell wall yielded overlapping curves. Sera from patients with tuberculoid leprosy and those from patients with lepromatous leprosy afforded different levels of inhibition in this radioimmunoassay; this result indicated a difference in antibody specificity in the two forms of leprosy. In conclusion, the cell wall polysaccharide of LDC corresponds to the main thermostable cytoplasmic antigen M_1, which strongly crossreacts with sera from patients with leprosy and, more specifically, with antigen 7 of *M. leprae.*—Authors' Abstract

Bottasso, O. A., Poli, H. O. and Morini, J. C. Influencia del tiempo de exposición al bacilo de Hansen sobre las pruebas cutáneas en convivientes íntimos de lepra. [Influence of length of exposure to Hansen bacillus on skin tests in close contacts of leprosy patients.] Medicina (B. Aires) **44** (1984) 463–466. (in Spanish)

Close contacts of leprosy patients were studied in order to determine whether time of exposure to open, bacilliferous forms of leprosy could be related to changes in the specific cutaneous immune response, both the early skin reaction or Fernandez reaction (FR) and the delayed skin reaction or Mitsuda reaction (MR). A total of 80 healthy close contacts of lepromatous leprosy were challenged intradermally with lepromin and PPD. Time intervals in years were plotted against FR. A high negative correlation coefficient was obtained since FR decreases as time increases ($r = -0.40$, $p < 0.001$). A similar trend was obtained for MR ($r = -0.33$, $p < 0.01$). No relationship between time and PPD was observed, discarding a nonspecific response. This phenomenon could be due to an immunosuppressive mechanism, involving suppressor cells, as a result of a long exposure to the bacillus. In order to prevent the appearance of new cases of leprosy, periodic studies of healthy close contacts are necessary.—Authors' English Summary

Bottasso, O. A., Puig, N. R., Amerio, N. and Morini, J. C. Parámetros inmunológicos *in vivo* e *in vitro* en pacientes con eritema nodoso leprososo. [*In vitro* and *in vivo* immunological parameters in patients with erythema nodosum leprosum.] Inmunologia **4** (1985) 28–33. (in Spanish)

Some *in vivo* and *in vitro* immunological parameters from patients with erythema nodosum leprosum (ENL) in different periods of their evolution have been studied during acute episodes, while the processes

recede and without recent reactional episodes. Delayed-type hypersensitivity (DTH) with dinitrochlorobenzene (DNCB), PPD and lepromin have been done, and in the peripheral blood, the number of lymphocytes, E rosettes, EAC-forming cells, and lymphocytes with Igs+ have been studied. An increment in the number of circulating lymphocytes, E-rosette forming cells, and the positivization of the DNCB test have been verified in lepromatous patients during acute episodes of ENL. This immunological profile was reversed after 2–3 weeks of antireactional treatment with a decrease of circulating lymphocytic populations and the negativization of DNCB test. Furthermore, during the reactional episode (acute or with recent treatment) the skin tests with PPD and lepromin remained negative.

In patients without recent ENL episodes, the enumeration of lymphocytes in the peripheral blood increased a little, without getting to the level of the controls, and only the PPD skin test was positive in 4/6 cases.

We postulate that in the immunopathology of ENL the cell-mediated immunity participates together with immune complexes through a nonspecific activation of helper T cells, and/or with an imbalance of the subpopulation of suppressor T cells.—Authors' English Abstract

Douglas-Jones, A. G. and Watson, J. D. Immunity to leprosy. II. Genetic control of murine T cell proliferative responses to *Mycobacterium leprae*. J. Immunol. **135** (1985) 2824–2829.

T-cell proliferative responses to *Mycobacterium leprae* were measured after immunization of mice at the base of the tail with antigen and challenging lymphocytes from draining lymph nodes in culture with *M. lepare*. This T-cell response to *M. leprae* has been compared in 18 inbred strains of mice. C57BL/10J mice were identified as low responder mice. The congenic strains B10.M and B10.Q were found to be high responders, whereas B10.BR and B10.P were low responders. F_1 (B10.M × C57BL/10J) and F_1 (B10.Q × C57BL/10J) hybrid mice were found to be low responders, similar to the C57BL/10J parent, indicating that the low responsive trait is dominant. Whereas B10.BR mice were shown to be low responders to *M. leprae*, B10.AKM and B10.A(2R) were clearly high responders, indicating that the H-2D region influences the magnitude of the T-cell proliferative response. Gene complementation within the H-2 region was evident. Genes outside the H-2 region were also shown to influence the response to *M. leprae*. C3H/HeN were shown to be high responder mice, whereas other H-2^k strains, BALB.K, CBA/N, and B10.BR, were low responders. Gene loci that influence the T-cell proliferation assay have been discussed and were compared to known background genes which may be important for the growth of intracellular parasites. Because mycobacteria are intracellular parasites for antigen-presenting cells, genes that affect bacterial growth in these cells will also influence subsequent immune responses of the host.—Authors' Abstract

Estrada-García, L., Quesada-Pascual, F., Santos-Argumedo, L., Flores-Romo, L., Estrada-Parra, S. and Buchanan, T. M. The early serodiagnosis of leprosy. I. The use of counterimmunoelectrophoresis and enzyme-linked immunosorbent assay. Rev. Latinoam. Microbiol. **26** (1984) 267–272.

The diagnosis of leprosy is primarily done by clinical, bacteriological and histopathological studies but often the diagnosis is done when the disease is already established and even, in some cases, when nerve injury has occurred. Tests for the early serodiagnosis of leprosy are needed. This is a first report of a long-term study in which the sera of 15 leprosy patients and 80 of their contacts were analyzed; these findings will be correlated with the clinical signs. The ideal serodiagnosis test for leprosy should use a specific antigen for *Mycobacterium leprae*; however, none of the existing antigens are totally accepted. In this work, antibodies against mycobacterial antigens were searched using the counterimmunoelectrophoresis (CEI) technique. The antigens used were whole extracts from BCG, *M. bovis, M. tuberculosis, M. leprae,* and *M. lepraemurium.* We also used an enzyme-linked immunosorbent assay (ELISA) with BCG extract. With the CIE technique, the patients gave 60% positiveness and their contacts, 28%. By the

ELISA, only 5% of the contacts had a positive test.—Authors' Abstract

Gupta, S., Curtis, J. and Turk, J. L. Accessory cell function of cells of the mononuclear phagocyte system isolated from mycobacterial granulomas. Cell. Immunol. **91** (1985) 425–433.

Epithelioid cells from BCG-induced granulomas and macrophages from *Mycobacterium leprae*-induced granulomas were examined for their ability to act as accessory cells for T-cell proliferation to mitogen (ConA) and antigen (PPD). The granuloma cells were separated on a FACS using monoclonal antibody specific to guinea pig macrophages. Epithelioid cells (which are Ia negative) were able to support proliferation to ConA but not to antigen. Cultures containing Ia-positive granuloma macrophages from *M. leprae*-sensitized animals did not show responsiveness to ConA or to PPD. Oil-induced peritoneal exudate macrophages from BCG- or *M. leprae*-immunized animals were able to act as accessory cells for both mitogen and antigen proliferation. The nonresponsiveness of cultures containing epithelioid cells stimulated with PPD or *M. leprae* granuloma macrophages stimulated with ConA was not due to suboptimal or supraoptimal accessory cell : lymphocyte ratios.—Authors' Abstract

Izumi, S., Sugiyama, K., Fujiwara, T., Hunter, S. W. and Brennan, P. J. Isolation of the *Mycobacterium leprae*-specific glycolipid antigen, phenolic glycolipid-I, from Formalin-fixed human lepromatous liver. J. Clin. Microbiol. **22** (1985) 680–682.

A *Mycobacterium leprae*-specific phenolic glycolipid antigen was purified from Formalin-fixed liver preserved from an advanced lepromatous leprosy patient. Its chemical and immunological properties were compared with those of phenolic glycolipid-I (PGL-I) obtained from *M. leprae*-infected armadillo liver. Based on the findings that the glycolipids from the two sources have the same thin-layer chromatographic properties, infrared absorption spectrum, sugar composition, and seroreactivity, we conclude that large quantities of the PGL-I antigen are produced in human lepromatous leprosy lesions and that Formalin-fixed lepromatous livers and spleens from the prechemotherapeutic era are suitable sources of the glycolipid.—Authors' Abstract

Kaplan, G., Weinstein, D. E., Steinman, R. M., Levis, W. R., Elvers, U., Patarroyo, M. E. and Cohn, Z. A. An analysis of *in vitro* T cell responsiveness in lepromatous leprosy. J. Exp. Med. **162** (1985) 917–929.

In lepromatous leprosy, there is extensive replication of *Mycobacterium leprae* within dermal macrophages. This lack of microbial resistance has been attributed to a defective cell-mediated immune response to *M. leprae* antigens. We have examined the *in vitro* response of T cells to *M. leprae* to determine if hyporesponsiveness could be reversed. The study included 40 unselected patients, most with the severe lepromatous form of the disease.

We first noted that lepromatous leprosy patients were of two types: those unable to respond, as assessed by T-cell proliferation and immune (gamma) interferon (IFN-γ) release, and a second group, exhibiting low but detectable responses relative to tuberculoid controls. When the effect of exogenous recombinant interleukin-2 (IL-2) on the response to *M. leprae* antigens was compared in the two groups, many of the low responders, but not the nonresponders, showed enhanced proliferation and IFN-γ release. To evaluate a possible suppressive effect of monocytes, these cells were eliminated with a cell-specific monoclonal antibody and complement. Depletion of monocytes often expanded pre-existing weak responses but did not reverse the anergy of the *M. leprae* nonresponders. The enhancement was not *M. leprae* specific, since it was also observed when bacillus Calmette-Guérin was the antigenic stimulus for proliferation and IFN-γ production. Removal of the suppressor T-cell subset, with OKT8 antibody and complement, also did not restore responses in nonresponder patients. We conclude that a sizable number of lepromatous leprosy patients exhibit a low degree of responsiveness to *M. leprae* and that the responses can be enhanced *in vitro* with IL-2 or with monocyte depletion. Nonresponsiveness, however, cannot be reversed. Since currently available assays

measure the function of previously sensitized T cells, suppressor mechanisms may yet contribute to defective cell-mediated immunity by impairing the initial sensitization to *M. leprae* antigens.—Authors' Summary

Lowe, C., Brett, S. J. and Rees, R. J. W. Adoptive cell transfer of resistance to *Mycobacterium leprae* infections in mice. Clin. Exp. Immunol. **61** (1985) 336–342.

Cells were transferred from mice intradermally vaccinated with killed *Mycobacterium leprae* to sublethally irradiated recipients. Unseparated cells from lymph nodes or spleens of *M. leprae*-vaccinated mice were found to cause significant inhibition of the growth of a subsequent *M. leprae* challenge in mouse foot pads for up to 26 weeks after vaccination. Vaccination with live BCG and cells transferred from BCG-vaccinated mice caused no significant inhibition of *M. leprae* growth in mouse foot pads. Cell separation into fractions containing predominantly B and T lymphocytes showed that the inhibition of growth was due to *M. leprae*-sensitized T lymphocytes. *M. leprae*-vaccinated mice were also skin tested with soluble *M. leprae* antigen and showed maximum delayed hypersensitivity responses 4 weeks after vaccination.—Authors' Summary

Martínez, M. I. and Sánchez, J. L. Treatment of leprosy with weekly intravenous infusion of leukocytes. Int. J. Dermatol. **23** (1984) 341–347.

Two patients with lepromatous leprosy were treated with weekly intravenous infusions of leukocyte concentrates for a period of 12 consecutive weeks. A reversal reaction was induced in one of the patients, and it was possible to control chronic erythema nodosum leprosum in the other subject. Possible pathogenetic mechanisms involved in the induction of these changes include the action of transfer factor, interactions between B and T lymphocytes or the mediation of a lymphokine necessary for the effective function of the cell-mediated immunity. Immunotherapy for chronic infections, such as leprosy, still has not become a reality.—Authors' Abstract

Morris, J. A. and Ivanyi, J. Immunoassays of field isolates of *Mycobacterium bovis* and other mycobacteria by use of monoclonal antibodies. J. Med. Microbiol. **19** (1985) 367–373.

Antigen extracts obtained by sonication of 22 strains of *Mycobacterium bovis* from cattle and badgers together with extracts of strains of *M. tuberculosis, M. paratuberculosis, M. avium, M. africanum. M. kansasi, M. leprae* and BCG were examined with a panel of 10 monoclonal antibodies to *M. tuberculosis* or *M. leprae.* Antigen extracts were coated in aqueous solution (wet coating) and the extracts were also dried on to the polyvinyl plates (dry coating). When dry coating was compared to wet coating, there was a major increase in the binding of monoclonal antibody ML03 to *M. avium* and *M. paratuberculosis,* monoclonal antibody ML02 to *M. paratuberculosis,* and monoclonal antibodies TB71 and TB72 to the majority of *M. bovis* isolates.

The study confirmed that on wet-coated plates, monoclonal antibodies TB71 and TB72 bind poorly or not at all to *M. bovis* and that monoclonal antibodies TB68, TB78, TB77 and TB23 each bind to field strains of *M. bovis* while TB23 binds poorly to BCG in wet-coating conditions. Antibodies TB72 and TB71, originally thought to be specific for *M. tuberculosis,* each reacted with *M. africanum.* Antibody TB78 bound to *M. paratuberculosis* but did not react with *M. avium,* and *M. avium* and *M. paratuberculosis* were distinguished from *M. bovis* and *M. tuberculosis* by the binding of antibody ML03 to dry-coated plates. When wet-coated plates were used, ML03 bound strongly only to *M. leprae.* The panel of monoclonal antibodies did not demonstrate distinct serotype differences between the field isolates of *M. bovis.*—Authors' Summary

Rojas-Espinosa, O., González-Mendoza, A., Estrada-Parra, S., Ortíz, Y., González-Cruz, O., Cornejo, A. L. and Pérez-Suarez, G. Presence of soluble, *Mycobacterium leprae*-derived antigen in the inflammatory exudate of reactional lepromatous leprosy. Lepr. Rev. **56** (1985) 229–238.

By immunofluorescence techniques, immunocomplexes deposition in the wall and periphery of dermal blood vessels have been demonstrated in 8 leprosy-reaction lesions (4 ENL, 4 Lucio's phenomena). Two additional ENL lesions were negative for the presence of immunocomplexes with anti-IgM, IgG, IgA, C3 and C1q antisera. The 10 leprosy reaction lesions, however, were positive for the presence of *Mycobacterium leprae*-derived solube antigen. This antigen, visualized with a potent human anti-*M. leprae* antiserum, was often found in and around the dermal blood vessels showing vasculitis and always in the macrophages (Virchow's cells) present in the leprous granulomas. This finding was independent of the presence of intact or fragmented *M. leprae* in those locations. The role of mycobacteria-derived material in the genesis of type-2 leprosy reactions is discussed.—Authors' Summary

Swinburne, S., Brown, I. N. and Brown, C. A. *Mycobacterium vaccae* and immune responses: implications for leprosy control. Lepr. Rev. **56** (1985) 209–220.

Mycobacterium vaccae, common in some tropical environments, may have a beneficial effect on the incidence of leprosy by acting as a natural vaccine, or have a real or apparent harmful effect by interfering with the protection afforded by BCG vaccination. We are using an animal model to assess these possibilities. The results reported here show that a strain of *M. vaccae* isolated from Ugandan mud can evoke a significant immune response in mice sensitized subcutaneously or orally. Spleen cells from such mice responded equally well *in vitro* to *M. vaccae* and BCG as measured by two independent assays. Good responses were observed for at least 3 months after oral exposure to *M. vaccae* even though no viable organisms could be detected in the organs at this time, showing that persistence of *M. vaccae* is not necessary for expression of sensitization. These experiments support the idea that people who become sensitized to *M. vaccae* or certain other environmental mycobacteria might be expected to show some resistance to leprosy. However, BCG vaccination might appear ineffective in that many individuals would already be sensitized to antigens common to all mycobacteria.—Authors' Summary

Tausk, F. A., Schreiber, R. D. and Gigli, I. CR1 deficiency in patients with Hansen's disease. Trans. Assoc. Am. Physicians **97** (1984) 346–352.

The receptor for the C3b fragment of the human complement system, also known as CR1, has been demonstrated to be an immune adherence receptor. Certain immune complex-mediated human diseases such as systemic lupus erythematosus and rheumatoid arthritis have been reported to be associated with reduced levels of CR1 on the erythrocyte surface. This has led to the hypothesis that CR1 plays a pivotal role in the normal processing of circulating immune complexes and suggests that a CR1 deficiency may be involved in the etiology of these diseases. The present study reports the assessment of CR1 density on the surface of erythrocytes of a normal control population and patients with Hansen's disease. Lepromatous leprosy patients have been shown to present high levels of circulating immune complexes while tuberculoid patients are characterized by an absence of circulating immune complexes. Thirty-one normal volunteers had a mean (±S.D.) of 645 ± 309 CR1 molecules/erythrocyte. In 19 lepromatous leprosy patients and 14 tuberculoid patients the values were 361 ± 156 and 649 ± 279, respectively. The decreased levels of CR1 on erythrocytes of patients with lepromatous leprosy could, in part, result in an impairment to process circulating immune complexes correctly. Long-term studies will provide evidence as to whether or not the levels of CR1 will correlate with the possible shift in clinical and histopathological features toward one of the poles in the disease process.—(*From* the Report)

Thompson, R. A., Sukumaran, K. D. and Rajagopalan, K. Inappropriate responses to *Mycobacterium leprae* infections—C-reactive protein in man and serum amyloid P in mice. Clin. Exp. Immunol. **61** (1985) 329–335.

In a study of C-reactive protein (CRP) levels in the sera of 77 patients with leprosy, it was found that in the majority of newly

diagnosed patients, the level was within the normal range for a healthy Malaysian population. Elevated levels did occur, but were usually found in patients with complications, and were more likely to occur in patients who had been receiving drug treatment for some time. This suggested that *Mycobacterium leprae* infection by itself does not stimulate CRP synthesis and could reflect a failure of synthesis by macrophages of interleukin-1, or related molecules. This was supported by the study of an analogous acute phase protein, serum amyloid P (SAP) in mice bearing *M. leprae* from human sources in their hind foot pads. Such mice showed no significant difference in SAP levels from control mice.—Authors' Summary

Watson, S., Bullock, W., Nelson, K., Schauf, V., Gelber, R. and Jacobson, R. Interleukin 1 production by peripheral blood mononuclear cells from leprosy patients. Infect. Immun. **45** (1984) 787–789.

Peripheral blood mononuclear cells from 21 leprosy patients (19 untreated at the time of assay) were tested for their ability to produce IL-1 in response to LPS stimulation *in vitro*. Whereas cells from the 8 patients with tuberculoid leprosy either released IL-1 spontaneously or after stimulation in amounts comparable to those produced by stimulated cells from 20 normal control people, cells from 5 of the 13 lepromatous cases failed to produce IL-1 even after stimulation.—C. A. Brown (*From* Trop. Dis. Bull.)

Wu, Q., *et al.* [Comparison of the FLA-ABS test employing sera from venous blood and blood from earlobes of 79 cases of leprosy.] Chuno Kuo I Hsueh Ko Hseuh Yuan Hsueh Pao **7** (1985) 69–71. (in Chinese)

With an aim to compare the feasibility of using venous blood, fresh blood and dried blood from earlobes for the FLA-ABS test, a study of 79 cases of leprosy and 26 normal individuals was undertaken. The results of the FLA-ABS tests of the 3 blood samples in leprosy patients were: a) the percentages of positive reaction: sera from venous blood, 65/79 (82.3%); fresh blood from earlobe, 74/79 (93.7%); dried blood from earlobe, 73/79 (92.4%). The results in normal controls were all negative. Chi-squared test indicated that percentages of positive reaction of blood from earlobe were higher than those of sera from venous blood; b) comparisons of the fluorescent intensity of the 3 blood specimens coincided with those from percentages of positive reactions (sera/fresh blood $u = 0.2967$, $p < 0.01$; fresh blood/dried blood $u = 0.5774$, $p < 0.05$). These results indicated that blood from the earlobe can be used instead of venous blood for the FLA-ABS test in the investigation of subclinical leprosy and its relevant epidemiological field study.—Authors' English Abstract

Young, D. B., Fohn, M. J., Khanolkar, S. R. and Buchanan, T. M. A spot test for detection of antibodies to phenolic glycolipid I. Lepr. Rev. **56** (1985) 193–198.

A novel spot test for detection of antibodies to phenolic glycolipid-I of *Mycobacterium leprae* has been developed. This test uses antigen-coated filter strips with a simple non-quantitative visual readout. Results of the spot test were in good agreement with those obtained using a standard microtiter ELISA test for antibodies with the new test being slightly less sensitive than the standard method. The spot test may be useful as a field test for serodiagnosis of leprosy in areas where microtiter plates, spectrophotometers, and multichannel pipettes are not readily available.—Authors' Summary

Young, D. B., Harnisch, J. P., Knight, J. and Buchanan, T. M. Detection of phenolic glycolipid-I in sera from patients with lepromatous leprosy. J. Infect. Dis. **152** (1985) 1078–1080.

Serum samples from 36 patients with leprosy as well as from 6 healthy individuals and 5 patients with tuberculosis were assayed for the presence of phenolic glycolipid-I (PGL-I) and of antibodies to PGL-I.

Control sera from 6 healthy individuals were negative in the antigen- and antibody-detection tests. Similarly, 5 sera from patients with tuberculosis were negative in both tests. Of 14 patients with tuberculoid leprosy, 8 were positive for antibodies, but all

were negative in the antigen assay, including 5 previously untreated patients. Five of 5 patients with borderline leprosy were positive for antibody with 2 also being positive for antigen. All 17 patients with lepromatous leprosy were positive for antibody; whereas in the antigen assay, the 8 patients who had received treatment for one month or less were positive and the remaining 9 were negative.

The ability to detect *Mycobacterium leprae* antigens in biologic samples provides a potentially useful tool in the diagnosis of lepromatous leprosy.

Sensitive serological tests for detection of specific antibodies to *M. leprae* are now available and can be used to give information about exposure to leprosy bacilli. It is likely, however, that positive antibody levels can be generated during a normal immune response to *M. leprae* in the absence of any clinically significant infection. The large amounts of circulating antigen found in sera from lepromatous patients, on the other hand, are not likely to result from casual exposure and are an indication of the presence of very large numbers of bacilli. A combination of antibody- and antigen-detection assays may therefore prove particularly effective in the diagnosis of lepromatous leprosy.

An interesting finding in the present study was the marked reduction in circulating phenolic glycolipid shortly after the initiation of therapy. Although antibody levels in lepromatous patients remain high for many years after the initiation of therapy, the results reported here suggest that levels of circulating antigen decrease dramatically within a few weeks.—(*From* the Article)

Zhu, Y., *et al.* Ultrastructural study on the eccrine glands of leprotic hypopigmented macules with slightly impaired sweating. Chin. J. Dermatol. **18** (1985) 95–96. (in Chinese)

Ultrastructural changes of the eccrine glands in 4 cases of leprotic hypopigmented maculae with slightly impaired sweating function are reported. In the clear cells, electron microscopy showed swollen mitochondria with dissolution of partial cristae and clearing of matrix, increase of glycogen granules in cytoplasm, and muddy appearance of smooth endoplasmic reticula. The relationship between these ultrastructural changes and the slight impairment of sweating function is discussed.—Authors' English Abstract

Microbiology

Kato, L. *In vitro* cultivation of *Mycobacterium X* from *Mycobacterium leprae* infected tissues in propane–tetradecane medium (a preliminary communication). Acta Microbiol. Acad. Sci. Hung. **31** (1984) 373–380.

Host-grown *Mycobacterium leprae* and cultures of *Mycobacterium X,* cultivated from *M. leprae*-infected armadillo and human specimens, were inoculated into propane and propane–tetradecane media. The media contained in one liter distilled water KH_2PO_4, 7g; Na_2HPO_4, 0.5 g; $(NH_4)_2SO_4$, 2 g: $MgSO_4$, 0.1 g; ferric ammonium citrate, 20 mg and yeast extract (Difco), 0.1 g. Twenty ml media, distributed into each of 50 ml screw cap tubes, were inoculated with the bacilli and bubbled aseptically for 10 sec with 99% purity propane gas. Tetradecane–propane media were prepared by adding 0.1 ml tetradecane to each of the tubes containing 20 ml propane medium. When incubated at 32°C a logarithmic growth rate was counted in the propane–tetradecane media following a one to two week latency period. The time of division was estimated at seven days. In the propane tetradecane medium, growth occurred at the interface of the tetradecane oil and water as a thin veil developing into a 1 to 3 mm thick emulsion in two to three months. No growth occurred in the propane medium and growth was extremely slow in the tetradecane medium. When added to the tetradecane medium, propane considerably shortened the

latency period and the generation time, resulting in increased bacterial yield. Bacilli were strongly acid-fast; the culture did not grow on Löwenstein-Jensen or in Dubos media, but produced the localized disease typical of *M. leprae* in the foot pads of mice.—Author's Abstract

Kato, L. Propane and tetradecane as carbon sources for *in vitro* cultivation of *Mycobacterium lepraemurium* in a liquid medium (a preliminary communication). Acta Microbiol. Acad. Sci. Hung. **31** (1984) 381–386

Three strains of host-grown *Mycobacterium lepraemurium* and five strains of *M. lepraemurium,* grown on egg yolk medium, were inoculated into propane–tetradecane media. The media contained in one liter distilled water: KH_2PO_4, 7 g, Na_2HPO_4, 0.5 g, $(NH_4)_2SO_4$, 2 g, $MgSO_4$, 0.1 g, ferric ammonium citrate, 20 mg, and yeast extract (Difco), 0.1 g. Tetradecane 0.1 ml was added to each tube containing 20 ml of the medium. Media were sterilized in the autoclave. Following inoculation with the bacilli, the cultures were bubbled aseptically with 99% purity propane gas for 10 sec. When incubated at 32°C, logarithmic growth rate was counted in the cultures. Bacilli were strongly acid-fast. Growth occurred at the interface of the tetradecane oil and water as a thin veil, developing into a one to three millimeter thick emulsion in two to three months. Cultures were transferred into fresh media at two to three month intervals. Growth pattern in the subcultures were indistinguishable from the growth in the primary cultures. The cultures did not grow on Löwenstein-Jensen or in Dubos media, but produced the characteristic disease of murine leprosy when injected subcutaneously into mice. Bacilli isolated from the subcutaneous lepromas of mice were again cultivable in the propane–tetradecane medium, but not on Löwenstein-Jensen or in Dubos.—Author's Abstract

Experimental Infections

Mor, N., Lutsky, I., Weiss, L., Morecki, S. and Slavin, S. Resistance to mycobacteria in mice treated with fractionated total lymphoid irradiation (TLI) and in mice reconstituted with allogeneic bone marrow cells following radiotherapy. Int. J. Radiat. Oncol. Biol. Phys. **11** (1985) 79–85.

The increased clinical use of total lymphoid irradiation (TLI) as an immunosuppressive adjunct in transplantation suggested the need for determining the effects of TLI on the *in vivo* susceptibility of animals to infections controlled by cell-mediated immunity. TLI-treated, TLI-treated and splenectomized, and chimeric mice prepared with TLI were inoculated in the hind foot pad with *Mycobacterium marinum* or *M. leprae.* Although *M. marinum* organisms multiplied in greater numbers in the TLI mice, ultimately they were destroyed as effectively in TLI mice as in the non-irradiated control mice. *M. leprae* multiplied at the same rate and to the same maximum in TLI mice as in controls. Mice previously challenged with *M. marinum* in one hind foot pad, and challenged subsequently with the same organism in the opposite hind foot pad, showed a solid immunity against this reinfection. It appears that upon recovery from the immediate effects of radiotherapy TLI-treated mice are able to mount an effective immune response to experimental infection with *M. marinum* and *M. leprae.*—Authors' Abstract

Shetty, V. P., Mistry, N. F. and Antia, N. H. Serum demyelinating factors and adjuvant-like activity of *Mycobacterium leprae*: possible causes of early nerve damage in leprosy. Lepr. Rev. **56** (1985) 221–227.

The role of antibody was investigated by a) subcutaneous injection using whole serum obtained from 7 leprosy patients, and b) intraneural injection using immunoglobulins from 8 randomly chosen leprosy pa-

tients in random-bred Swiss white mice. Three out of 15 samples showed positive demyelination.

The adjuvant-like activity of *Mycobacterium leprae* was studied for its role in the causation of primary nerve damage of Swiss white mice. Animals were injected subcutaneously with 20×10^6 live and heat-killed *M. leprae* with and without normal sciatic nerve extract. Biopsies of the sciatic nerves were performed 1 and 3 months after injection. Degenerative changes in the nonmyelinated fibers were observed at the first month in the sciatic nerves of mice injected with live and heat-killed *M. leprae* along with nerve extract.—Authors' Summary

Stach, J. L., Delgado, G., Tchibozo, V., Strobel, M. and Lagrange, P. H. Natural resistance to mycobacteria: antimicrobial activity and reactive oxygen intermediate releasing functions of murine macrophages. Ann. Immunol. (Paris) **135D** (1984) 25–37.

After infection with *Mycobacterium lepraemurium* or with *M. bovis* strain BCG (bacillus Calmette-Guérin), splenic macrophages from mice naturally resistant (NR) to these pathogens (C3H and A/J) spontaneously produced H_2O_2, whereas splenic macrophages from naturally susceptible (NS) mice (C57BL/6 and Swiss) did not. None of them produced superoxide anion O_2^-. In addition, NR macrophages had higher levels of superoxide dismutase (SOD) than did NS macrophages.

In vivo treatments thought to enhance H_2O_2 metabolism (phorbol myristate acetate, SOD, zymosan) decreased *M. lepraemurium* survival; whereas treatment with diethyldithiocarbamate, a potent inhibitor of SOD, had the converse effect. These results favor the hypothesis of a link between natural resistance to BCG (and *M. lepraemurium*) and H_2O_2 metabolism, with higher producers being naturally resistant.—AS/J. Alexander (*From* Trop. Dis. Bull.)

Epidemiology and Prevention

Bottasso, O. A., Poli, H. O., Morini, J. C. and Rabasa, S. L. Estudio genético de la resistencia a la infeccion con el bacilo de Hansen en familias con o sin lepra. [Genetic study of resistance to Hansen bacillus in leprosy and healthy families.] Medicina (B. Aires) **44** (1984) 467–470. (in Spanish)

The genetic influence on resistance to leprosy, measured as the Mitsuda reaction (MR), was investigated in families with leprosy as well as in healthy controls. Figures show the average MR of parents in relation to individual MR in their offspring. Clearly, the trend of MR in offspring with the parents' reactions is upward and roughly linear, that is, positive, and significant correlation coefficients (r) were obtained. The regression coefficients (b) estimated the heritability (h^2) of the character, that is, the parents' contribution with genetic additive component from the whole phenotypic variance of MR. Because of the high h^2 observed in both samples, this result could be explained through a polygenic inheritance of the resistance to leprosy, involving the complex immune response caused by this illness.—Authors' English Summary

Irgens, L. M. and Skjaerven, R. Secular trends in age at onset, sex ratio, and type index in leprosy observed during declining incidence rates. Am. J. Epidemiol. **122** (1985) 695–705.

Epidemiologic surveillance in Norway, the United States, Nigeria, Japan, Venezuela, India, and China, covering periods from 1851 to 1981, demonstrates a consistent decline in incidence rates of leprosy. At the same time, secular trends have been observed which imply an increasing age at onset, an increasing male excess, and an increasing fraction of new cases represented by multibacillary leprosy. Theoretically an increasing age at onset may be caused by two mechanisms, namely, postponement of

infection to a later age and/or an increasing fraction of patients with long incubation periods. Cohort analyses have shown no increase in age at onset in subsequent birth cohorts, but rather have shown a decrease. The latter mechanism, the increasing importance of long incubation periods, is consistent with the shift toward multibacillary cases in which the incubation period is longer than that in paucibacillary cases. Apparently, this mechanism has also been present during the decline of tuberculosis. An increasing fraction of new patients with long incubation periods, resulting in an increasing age at onset, is proposed as a general principle to be expected in any disease in rapid decline which also has a long and varying incubation period. This theory offers a basis for assessment of secular trends.—Authors' Abstract

Keeler, R. and Deen, R. D. Leprosy in children aged 0–14 years: report of an 11-year control programme. Lepr. Rev. **56** (1985) 239–248.

A leprosy control program has been in operation in the entire twin island country of Trinidad and Tobago for 11 years. During the 11 years of the program, the number of new cases of leprosy diagnosed in children aged 0 to 14 years decreased from 65 patients in the third year of the program to 3 in both the 10th and 11th years of operation. The epidemiology of leprosy in Trinidad and Tobago during these 11 years is described.

The success of this program is credited to a) the decisions by the government of Trinidad and Tobago in 1968 to close the leprosarium and to set up a leprosy control program; b) the recruitment and training of qualified personnel; c) active patient identification and aggressive treatment and follow up of infectious patients; and d) the assistance of a vibrant voluntary organization in providing socioeconomic assistance for patients and in educating the public.—Authors' Summary

Neill, M. A., Hightower, A. W. and Broome, C. V. Leprosy in the United States, 1971–1981. J. Infect. Dis. **152** (1985) 1064–1069.

In the period 1971–1981, 1835 cases of leprosy were reported in the United States; only 10% of these cases were indigenous. Since 1977, the number of new cases reported each year has risen because of an increase in imported cases of disease, a situation reflecting the increased number of refugees and immigrants who have entered the United States from areas endemic for leprosy. Forty-five of the 50 states reported cases. In only 25% of the imported cases were the patients known to have had leprosy at the time of immigration; the remaining 75% were diagnosed in this country. The highest rate of disease onset for this latter group occurred within 12 months after entry into the United States, but cases continued to be reported 10 years after entry. Active refugee resettlement programs have widely distributed persons with leprosy, contacts of diseased persons, and persons from endemic areas throughout the 50 states, a situation necessitating the development of expertise by medical professionals and public health officials in the diagnosis, treatment, and long-term follow up of patients with leprosy.—Authors' Abstract

Xu, K., Fei, H., de Vries, R. R. P., van Leeuwen, A., Ma, L., Fan, L., Tao, M., Wang, C., Cheng, R. and Ye, G. [HLA and leprosy. III. Segregation analysis of HLA haplotypes in multicase families of leprosy.] Chung Kuo I Hseuh Ko Hseuh Yuan Hsueh Pao **7** (1985) 25–30. (in Chinese)

HLA-A, -B, -C, and -DR typings were performed on members of 29 families from a leprosy-endemic area in Jiangsu Province, China, containing at least 2 siblings affected with leprosy. The data of 26 families permitted analyses of segregation of parental HLA-haplotypes observed among children in relation to leprosy status. Siblings affected with lepromatous (LL or BL) leprosy shared parental HLA-haplotypes significantly more often than expected ($p < 0.05$) and a highly significant deficit ($p < 0.0005$) of shared HLA-haplotypes was observed among siblings discordant for leprosy type.

Healthy siblings did not share a haplotype more often than expected, and those haplotypes which were shared between all leprosy patients of a sibship did not occur less

frequently than expected among healthy siblings of the same sibship.

An analysis for co-segregation with HLA of the lepromin test observed among healthy siblings showed no evidence for co-segregation.

The main conclusions are: a) predisposition to lepromatous leprosy is controlled by HLA-linked genes; b) HLA-linked genes do no confer susceptibility or resistance to leprosy as a whole; and c) different genetic backgrounds exist in tuberculoid and lepromatous leprosy.—Authors' English Abstract

Rehabilitation

Bourrel, P. [Volar flexion of the fingers as a diagnostic test for palsy of the intrinsic muscles of the fingers, particularly of leprous origin and means of assessment of results of palliative surgery.] Chirurgie **110** (1984) 772–778. (in French)

Active metacarpophalangeal flexion with simultaneous active extension of interphalangeal joints places the fingers in the position in preparation for prehension. This volar flexion of the fingers is due to the action of their intrinsic muscles, and this movement, which is irreplaceable, has been used by the author for the last 20 years as a specific exploratory test of intrinsic finger muscles. It can be investigated as an emergency procedure in cases of ulnar nerve wounds at the elbow or injury to the upper forearm before suture, and clearly demonstrates the presence of an ulnar claw hand. It is a very sensitive test since this position potentiates an ulnar claw hand in its early stage which would have passed unnoticed with finger extended.

This rapid examination is particularly valid during neurologic investigation of the hand in leprosy patients in countries where this disease is endemic, and it forms part of the 10 tests that the author has selected for exploration, within 2 or 3 minutes, in a standing patient, of the facial, ulnar, median, superficial peroneal and posterior tibial nerves.

The test is also the most effective evaluation criterion of palliative surgery for claw hand which, to be considered as successful, must restore volar flexion, as shown by a personal series of over 200 operated hands.—Author's English Summary

Carayon, A. and Languillon, J. [Bone and joint changes in leprosy, 1960–1982.] Acta Leprol. **3** (1985) 133–153. (in French)

Bone changes are frequent in leprosy involving small distal bones of the limbs and, in advanced cases, some cranial bones. The various kinds of osteitis and their radiologic features are described as well as the arthritis to which they can give way. These changes may result directly from the infection by *Mycobacterium leprae,* indirectly through nerve damage, and also by pyogenic infections. The therapeutic tactic is discussed according to this approach of the various types of bones and joint damage.—Authors' English Summary

Kaplan, M. and Gelber, R. H. Evaluation of testing modalities for peripheral neuropathy in lepromatous Hansen's disease. Phys. Ther. **65** (1985) 1662–1665.

To assess methods for detecting peripheral neuropathy, 28 previously untreated patients with lepromatous Hansen's disease underwent upper extremity manual muscle testing, sensory testing by using monofilaments, and electrophysiological nerve conduction studies (motor and sensory) at their initial examination. All but 3 patients demonstrated some abnormality identified by at least one of the testing procedures. Sensory testing with monofilaments located the greatest number of abnormalities found in 24 of the 28 patients. Next, electrophysiological testing demonstrated neuropathy in 21 of the 28 patients tested; 20 of these

patients had sensory abnormalities and 20 had motor irregularities. The least sensitive method was manual muscle testing, which detected abnormalities in only 12 patients. Furthermore, sensory testing with monofilaments revealed peripheral neuropathy in 5 patients whose electrophysiological studies showed normal sensory patterns, and electrophysiological testing detected abnormalities in 1 patient whose sensory monofilament examination was normal. The results of this study support the usefulness of all three testing modalities.—Authors' Abstract

Sankaran, B. Prosthetics and orthotics in developing countries. Int. Rehabil. Med. **6** (1984) 85–101.

Principles of orthoses and prostheses in developing countries are discussed. Appropriate technological adaptations to suit cultural needs in developing countries have been identified and illustrative examples have been given. In view of the importance of the problem of leprosy in many developing countries, a separate description to cover prosthetic and orthotic appliances including footwear has been attempted. The material is a summary of the excellent publication from ALERT in Addis Ababa.—Author's Summary

Other Mycobacterial Diseases and Related Entities

Berginer, V., Baruchin, A., Ben-Yakar, Y. and Mahler, D. Plantar ulcers in hereditary sensory neuropathy. A plea for conservative treatment. Int. J. Dermatol. **23** (1984) 664–668.

Hereditary sensory neuropathy is a rare syndrome characterized by the occurrence, in childhood or early adult life, of perforating ulcers of the feet, lightning pains, and loss of cutaneous sensation and tendon reflexes in the lower extremities. Three patients with hereditary sensory neuropathy were family members. Trophic ulcers may be caused by diseases other than diabetes, syphilis, and leprosy.—Authors' Abstract

Hall, R. M. and Ratledge, C. Mycobactins in the classification and identification of armadillo-derived mycobacteria. FEMS Microbiol. Lett. **28** (1985) 243–247.

Seven strains of armadillo-derived mycobacteria (ADMs) were encouraged to produce the lipid-soluble siderophore mycobactin when grown under conditions of iron limitation. These compounds have recently been shown to be excellent chemotaxonomic markers for the mycobacteria being both species specific and highly conserved. Characterization of the mycobactins was carried out by thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC). Examination of the mycobactins isolated from the ADM strains showed them to be heterogeneous. Four strains synthesized mycobactins closely resembling those of the *Mycobacterium avium-intracellulare-scrofulaceum* (MAIS) complex; whereas the remaining 3 strains formed mycobactins which differed in structure to those of any other mycobacterium previously examined.—Authors' Summary

Heifets, L. B. and Iseman, M. D. Determination of *in vitro* susceptibility of mycobacteria to ansamycin. Am. Rev. Respir. Dis. **132** (1985) 710–711.

The *in vitro* susceptibility of different mycobacterial species to ansamycin (LM427) in concentrations of 2.0, 1.0, 0.5, and 0.2 μg/ml was determined by the agar dilution method. For those strains of *Mycobacterium tuberculosis* and *M. avium* complex tested, susceptibility to ansamycin was compared with susceptibility to rifampin. All *M. tuberculosis* strains susceptible to rifampin were susceptible to ansamycin; the strains that were highly resistant to rifampin also were resistant to ansamycin. The majority of *M. avium* complex strains were "naturally" resistant to rifampin (1.0 μg/ml

and higher), but only approximately 13% of them were resistant to ansamycin in a concentration of 1.0 μg/ml. The crossresistance in *M. avium* strains was made apparent only by comparing patterns of resistance to low concentrations of ansamycin (0.5 μg/ml) with patterns of resistance to higher concentrations of rifampin (5.0 and 10.0 μg/ml).— Authors' Summary

Mitchison, D. A. The action of antituberculosis drugs in short-course chemotherapy. Tubercle **66** (1985) 219–225.

The important point that arises from these considerations is that the three functions of antituberculosis drugs may be and often are entirely unrelated. The ability to prevent the emergence of drug resistance has no bearing on early bactericidal or sterilizing activity. Of even greater importance, early bactericidal activity, by which is meant "bactericidal activity" in conventional terminology, of a drug may well measure how effective a drug is in killing actively growing bacilli but it does not measure the sterilizing activity of the drug. Thus, to say that rifampin and pyrazinamide are good sterilizing drugs because they are highly bactericidal is quite wrong; in fact rifampin is only weakly bactericidal (at least in the dosage usually given) and pyrazinamide has minimal bactericidal activity.

The relative activities of the main antituberculosis drugs in each of the three functions are summarized. Inclusion of drugs which are effective in preventing the emergence of resistance is important in modern chemotherapy regimens because failure in patients with initially resistant organisms will then be less likely. The sterilizing activity of a drug measures its ability to shorten the duration of treatment and is therefore crucial in the design of short-course regimens. The early bactericidal activity of a drug has, however, little bearing on its use in therapy, except perhaps as an indication of the period during which a patient may be considered to be infectious to others.— (*From* the Article)

Pereverzev, N. A. and Levchenko, T. N. [Ultrastructural organization of *Mycobacterium tuberculosis* in cryoultratomy.] Zh. Mikrobiol. Epidemiol. Immunobiol. **8** (1985) 30–33. (in Russian)

The ultrastructural organization of *Mycobacterium tuberculosis* has been studied by the method of cryoultratomy. The cell-wall structures and the connective formations localized in the cytoplasm between parallel intracellular membranes have been revealed. Ethylene glycol and polyvinyl alcohol have been shown to be the most suitable cryoprotecting agents.—Authors' English Abstract