CURRENT LITERATURE

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

General and Historical

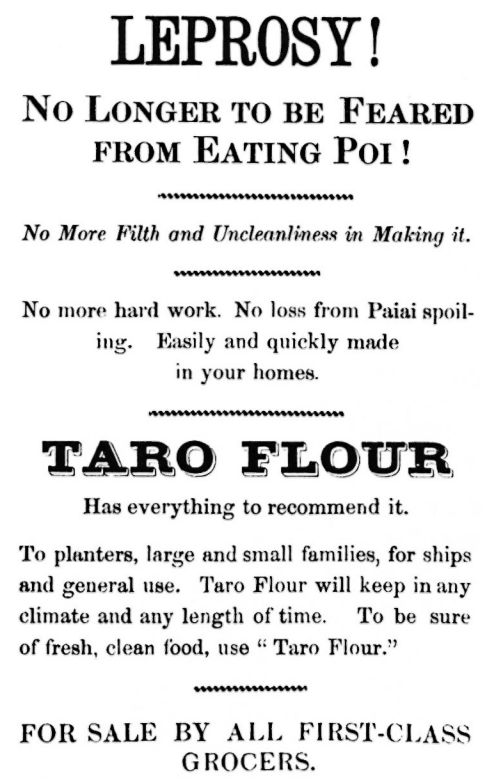
Chapman, R. F. Leprosy in Hawaii: scare advertising at the turn of the century. Hawaiian J. Hist. **13** (1979) 124–125.*

Throughout its long history there has been serious disagreement with respect to the way in which leprosy was transmitted from one person to another. Numerous writers have discussed, for instance, the folk beliefs that the disease was caused by divine wrath or due to sexual intercourse with an infected woman. Worldwide medical beliefs well into the 20th century ran the gamut from cockroaches, flies, mosquitoes, bed-bugs, rats, fish, bananas, sneezing, coughing, dust, and snuff-taking, to tatooing, meteorological conditions, and bare feet as the causative agent, combined with poor nutrition and lack of resistance to the disease.

In Hawaii, where leprosy assumed epidemic proportions, the Kalaupapa leprosarium on Molokai was opened in 1866. It was to this settlement, later made famous by Father Damien, that victims of the disease were forcibly banished, usually for life. As in other parts of the world where leprosy was prevalent, the cause of the disease was unknown. Because Hawaiians were more apt to contract leprosy than were other races, the native food staple, *poi*, was at one time suspected to be the cause.

This flier, distributed with the *Honolulu Evening Bulletin*, ca. 1900, plays on this fear.

Or was this merely an inventive sales technique?



LEPROSY!

NO LONGER TO BE FEARED FROM EATING POI!

No More Filth and Uncleanliness in Making it.

No more hard work. No loss from Paiai spoiling. Easily and quickly made in your homes.

TARO FLOUR

Has everything to recommend it.

To planters, large and small families, for ships and general use. Taro Flour will keep in any climate and any length of time. To be sure of fresh, clean food, use "Taro Flour."

FOR SALE BY ALL FIRST-CLASS GROCERS.

* Editor's Note: Ronald Fettes Chapman, Head Librarian at Honolulu Community College, recently completed his doctoral dissertation on "Leonard Wood and the Culion Leper Colony, 1921–1927." The flier is from his collection.—RCH

Chemotherapy

Bellahsene, A. and Forsgren, A. Effect of rifampin on the immune response in mice. Infect. Immun. **27** (1980) 15–20.

In an investigation of the effect of rifampin on the immune response in mice, the cellular immunity was evaluated with the split-heart allograft technique. The survival time of the heart in animals treated with rifampin at a dose of 20 mg/kg per day from the day of the transplantation until the graft was rejected was longer (33.7 days, $p < 0.001$) than that of animals not treated with antibiotics (14.5 days). When rifampin was given at a dose of 5 mg/kg per day for the same period, the mean survival time of allografts was 19.5 days. The number of demonstrable plaques of hemolysis and the humoral antibodies to sheep erythrocytes were also reduced by a human therapeutic dose (20 mg/kg per day). However, the suppression of the humoral immune response was probably of more limited biological significance, suggesting a differential sensitivity to rifampin. In contrast to rifampin, benzylpenicillin had no noteworthy inhibiting effect on the cellular or humoral immune response.—Authors' Summary

Chapron, D. J., Kramer, P. A. and Mercik, S. A. Kinetic discrimination of three sulfamethazine acetylation phenotypes. Clin. Phamacol. Ther. **27** (1980) 104–113.

The relationship between sulfamethazine disposition kinetics and acetylator phenotype was studied in 19 healthy subjects. Various kinetic parameters for sulfamethazine and its N^4-acetylated metabolite were determined after a dose of a rapidly absorbed oral solution. When plotted on a frequency distribution histogram, the results exhibited a well-defined trimodal pattern for acetylation clearance values and overall elimination or metabolic rate constants. These data were consistent with the well-recognized acetylation polymorphism for sulfamethazine except that they clearly subdivided the previously acknowledged "fast" acetylator mode into intermediate and rapid acetylator groups. The apparent distribution volume and renal clearance for sulfamethazine and acetylsulfamethazine did not differ significantly among the 3 phenotypes. Of special interest was the observation that rapid acetylators initially produce much greater amounts of acetyl metabolite than intermediate acetylators. The potential clinical implications of identifying rapid and intermediate acetylators are discussed in view of evidence showing that acetyl metabolites may be pharmacologically active or function as intermediates in toxic metabolic pathways.—Authors' Summary

Colston, M. J., Hilson, G. R. F. and Lancaster, R. D. Intermittent chemotherapy of experimental leprosy in mice. Am. J. Trop. Med. Hyg. **29** (1980) 103–108.

In this study we assess the degree of prolonged bacteriostasis of *Mycobacterium leprae* after temporary exposure to ethionamide or thiacetazone and relate this to their efficacy when administered intermittently to mice with experimental leprosy infections. The results show that temporary exposure of *M. leprae* to either of these drugs results in a prolonged bacteriostatic effect, but that efficacy is rapidly lost as the interval between doses is increased. Using the mouse foot pad system, growth of *M. leprae* is not inhibited by thiacetazone when the frequency of administration is less than 3 times weekly. When ethionamide is administered once weekly, growth of *M. leprae* is inhibited, but bactericidal activity is lost. When ethionamide is administered in combination with continuous dapsone therapy, either continuously or 3 times weekly, the bactericidal activity of the drug combination is greater than when either drug is administered alone. However, when ethionamide is administered once weekly in combination with continuous dapsone treatment, the bactericidal effect is identical to that when dapsone is give alone: that is, ethionamide makes no contribution to the combination.—Authors' Summary

Fournier, G., Orgiazzi, J., Lenoir, B. and Dechavanne, M. Pseudomembranous co-

litis probably due to rifampicin. Lancet **1** (1980) 101. (Letter to the Editor)

The Letter to the Editor describes a 59 year old woman treated with rifampin and isoniazid for tuberculosis, who developed typical pseudomembranous colitis. After discontinuing anti-tuberculosis therapy and appropriate treatment, the patient made a complete recovery. Isoniazid was resumed with no further problem.

In this case the pseudomembranous colitis was probably due to rifampin. This patient might have been predisposed to this complication because of underlying hepatic disease, leading to higher rifampin serum concentrations. However, the authors propose that rifampin should be added to the list of antibiotics that can induce pseudomembranous colitis.—(*Adapted from* the letter)

Girdhar, B. K. and Desikan, K. V. "Pulsed" rifampicin therapy in leprosy. A clinical study. Lepr. India **51** (1979) 475–480.

A trial of monthly administration of rifampin in 2 doses of 900 mg each on successive days for 3 months along with DDS 100 mg daily has been undertaken. The results have been compared with 2 groups of controls, one which was administered 300 mg rifampin daily for 3 months followed by DDS, and the other which received 100 mg DDS alone. The findings show that the efficacy of this pulsed regimen is almost similar to continuous rifampin administration and better than DDS alone. No significant adverse effects were encountered in the trial. The regimen thus merits large scale trials in the field.—Authors' Summary

Hazra, S. K., Ghosh, S., Kundu, S. K. and Chaudhuri, S. Therapeutic trial of a combination of broxyquinoline and brobenzoxaldine in the treatment of leprosy. Lepr. India **51** (1979) 505–510.

Fourteen previously untreated lepromatous patients were given broxyquinoline (500 mg) and brobenzoxaldine (100 mg) three times daily for periods ranging from 2 months to 2¾ years in the absence of any other chemotherapy. Five patients were treated for less than 1 year; 2 improved clinically, 2 did not improve, and 1 experienced severe reaction (flaring up of the skin lesions). Five patients received treatment for 1–2 years; 2 had moderate clinical improvement, and 3 improved slightly. Of the 4 patients treated for over 2 years, 1 case had moderate clinical improvement, 2 slight improvement, and 1 did not improve. The BI fell 26–47% and MI 33–88% in the treated patients. No adverse reactions were noted in the treatment. The authors conclude that this combination has little antileprotic activity.—(*Adapted from* the article)

Huikeshoven, H., de Wit, M., Soeters, A., Eggelte, T. A., Landheer, J. E. and Leiker, D. L. ELISA inhibition technique for the demonstration of sulphones in body fluids. I. Sulphones specific antibody-enzyme conjugate. Lepr. Rev. **50** (1979) 275–281.

A sulfones specific antibody-enzyme conjugate was developed as a basic tool for an enzyme linked immunosorbent assay (ELISA) for dapsone. The conjugate was found to be specific for sulfones without significant cross-reactions with sulfonamides. The sensitivity for dapsone is in the ng/ml range. The may lead to a simple and sensitive ELISA inhibition technique for the qualitative demonstration of sulfones in body fluids—Authors' Summary

Magna, L. A., Pinto, W., Jr. and Beiguelman, B. Hematócrito e sulfonemia em hansenianos. (Hematocrit and sulfonemia in leprous patients.) Rev. Paul. Med. **93** (1979) 10–12. (in Portuguese)

The level of dapsone (DDS) in the blood was investigated in 105 adult leprosy patients (80 males and 25 females) exhibiting extreme hematocrit values. The concentration of dapsone in the blood after the ingestion of 100 mg of this drug was independent of sex and of the hematocrit being high or low.—Authors' Summary

Min, K. U., Park, S. M. and Hue, S. H. Rifampin-induced tubulo-interstitial nephritis. Tubercul. Res. Dis. **25** (1978) 170–174. (in Korean)

One case of acute renal failure following rifampin administration is presented with a brief review. Acute renal failure developed in a 49-year-old male who had far advanced pulmonary tuberculosis and had taken rifampin accidentally after cessation for several months. The oliguria persisted for 11 days and was followed by prompt recovery with peritoneal dialysis. A renal biopsy showed tubulo-interstitial nephritis.—(*from* Kor. Med. Abstracts)

Moulding, T. The medication monitor for treating tuberculosis in the developing countries. Trop. Doct. **9** (1979) 106–109.

According to the author, the least expensive, reasonably effective treatment for tuberculosis in many developing countries is an 18 months' course of isoniazid and thiacetazone with the addition of streptomycin for the first 2 months. Those in charge of patients are faced with the difficult problem of distinguishing between those who can be trusted to follow the regimen unsupervised and those who cannot. The "indicator monitor" described is claimed to be the best means of doing so.

The tablets of the drug concerned are stacked in a tube with a small uranium source on top and a spring to drive the uranium source and the tablets down. Opposite the radioactive source is a strip of photographic film. As the tablets are removed from the bottom, the radioactive source also moves down, creating a record of dots on the film.

Details of the monitor, the radioactive uranium source, and the film and its development are given. A typical record appears in an illustration which shows that for 4 days the patient removed the tablet regularly. For 3 days no tablet was removed, resulting in a large, excessively dark dot. The patient then removed 4 tablets to catch up, and an area with no dots appeared. The later record on the strip revealed similar irregularity of removal of tablets.

Trials of the monitor were made in the United States and Malawi. In the former, among 122 patients selected as being probably reliable, 31% took less than 70% of their medication. Among 13 unselected patients in Malawi, 6 patients took less than 53% of their medication. A patient could of course remove tablets from the container regularly and produce a faultless film record without swallowing any of them. The author quotes a study involving cross-checking urine specimens for isoniazid with film records which did not demonstrate that this occurs frequently if at all (Moulding, Ann. Int. Med. [1970] **73,** 559).

Details of the advantages of using the monitor by the saving of expensive personnel who would have to be engaged to supervise patients, its cost, operation, and how it may be obtained are given in the paper.—H. G. Calwell (*from* Trop. Dis. Bull.)

Nigam, P., Siddique, M. I. A., Pandey, N. R., Awasthi, K. N. and Sriwastava, R. N. Lepr. India **51** (1979) 521–532.

Irregularity of treatment has proved to be a general problem, and there is scanty information about the reasons for the irregularity. Nineteen-hundred-seventy patients were studied to determine the reasons for irregularity by regularity in attending the clinic as well as by dapsone/creatinine ratio in urine. Fifty-two percent of the patients were regularly attending the clinic and thereby can be said to be regular in treatment whereas dapsone/creatinine ratios in urine showed that only 47.7% were actually regular in taking the drugs. Therefore, regularity of attendance is no guarantee of regularity of dosage. The patients who were irregular in treatment were interviewed to find out the reasons behind their irregularity. It was noticed that most of them (60.6%) attended the clinic for dapsone treatment but could not come regularly for valid reasons, e.g., economic reasons (29.9%), no time to attend clinic (12.5%), ignorance (22.9%), social stigma (1.2%), etc.

Irregularity in treatment can possibly be avoided by providing them extra amounts of drugs when the need arises, having means to contact patients, and creating faith in them about treatment, giving educative talks, and providing jobs in a sheltered workshop until they can be rehabilitated into society.—Authors' Summary

Venkatesan, K., Bharadwaj, V. P. and Girdhar, B. K. Effect of ascorbic acid on

blood levels of DDS. Lepr. India **51** (1979) 511–514.

A study was undertaken to probe the influence of ascorbic acid on the absorption and metabolism of administered DDS in leprosy patients. Vitamin "C" supplementation did not generally exhibit any effect on blood levels of DDS except in cases of BB and LL, where in only 8 hr DDS values showed a statistically significant increase.—Authors' Summary

White, G. de L. Side-effect of thiacetazone. S. Afr. Med. J. **56** (1979) 981. (Letter to the Editor)

This Letter to the Editor describes a 44-year-old Black female, diagnosed as having pulmonary tuberculosis and treated for 3 months with streptomycin, isoniazid, and ethionamide. After 3 months of hospitalization and therapy, she was discharged with instructions to take isoniazid and thiacetazone as an outpatient. At the time of discharge, she appeared to be perfectly well. Five days after beginning isoniazid and thiacetazone, she noticed a few skin bullae, which within 24 hr coalesced and involved the entire body except for the face and the keratinized skin of the hands and feet. The appearance was that of a 90% burn. The lips and oral mucosa were free of lesions. Her temperature was 37.8°C, and she was not in clinical shock or pain on admission. The patient died about two hours after admission.

It was not possible to incriminate anything other than thiacetazone for this illness. The patient did not have features suggestive of Stevens-Johnson syndrome, and the most likely diagnosis was toxic epidermal necrolysis. Another possible diagnosis was acute generalized exfoliative dermatitis. It would appear to be very unusual for thiacetazone to cause such explosive and florid lesions.—(*Adapted from* the letter)

Clinical Sciences

Ahmed, H. A., Belehu, A., Stoner, G., Touw, J. and Atlaw, T. Selection of sites for slit-skin smears. Lepr. Rev. **50** (1979) 283–287.

The results of slit-skin smears from 18 untreated lepromatous leprosy patients showed high bacteriological index (BI) and morphological index (MI) in the ears, fingers, face, buttocks, and toes. Need for standardization of site of smearing is stressed. The ears, fingers, face, and buttocks are suggested as standard sites for slit-skin smearing for diagnosis, follow-up, and assessment of chemotherapy.—Authors' Summary

Barrucand, D., Hermo, J. and Schmidt, C. Syndrome de la queue de cheval et acropathie ulcéro-mutilante. (Cauda equina syndrome and ulceromutilant acropathy.) Ann. Méd. Nancy **16** (1977) 673–686. (in French)

It is now generally accepted that ulceromutilating disease of the extremities (UMDE) may not only be associated with cord lesions, such as compression, trauma, tabes, syringomyelia, but also radiculoneuropathic lesions, as in diabetes, amyloidosis, leprosy, Charcot-Marie-Tooth disease, or teratomatous cysts of the sacral canal. It is in this group, where UMDE is secondary to root lesions, that cases of UMDE accompanying cauda equina lesions may be placed. The latter may be acquired (infective, tumor, trauma) and have been well known since the publication of Barraquer-Ferre and Barraquer-Bordas. However, they may also be due to a malformation. The authors stress this point, little studied up to now, since one of the three cases reported here is special in this respect: firstly, by the role of the dysraphia in the pathogenesis of the collection of multiple malformations existing, and secondly, by the association with peroneal atrophy. From a

descriptive standpoint, this case is junctional, generally referred to as a "paretoamyotrophic form of ulcero-mutilating disease of the extremities."—Authors' Summary

Barton, R. P. E. Radiological changes in the paranasal sinuses in lepromatous leprosy. J. Laryngol. Otol. **93** (1979) 597–600.

At Victoria Hospital, Dichpalli, South India, 16 patients previously untreated and attending for the first time were diagnosed, clinically and bacteriologically, as having lepromatous leprosy. Nasal involvement was confirmed in all patients by anterior rhinoscopy. Microscopy of a stained specimen of the nasal discharge was positive for *M. leprae* in 14/16 patients. Sinus radiographs were taken of all 16 patients in the occipito-mental (OM) and occipito-frontal (OF) projections.

All 16 patients showed radiological abnormalities. The most constant finding was muscosal thickening of the maxillary antra on the OM film. All 16 (100%) showed this at least unilaterally, and 14/16 (87.5%) had bilateral mucosal thickening. In addition to those with mucosal thickening of these sinuses, there appeared to be 2 patients with complete opacity of the frontal sinuses and one patient with bilateral ethmoid opacity. Complete opacity was not seen in the maxillary sinuses, nor was bone erosion noted in this series.

The present study shows that the mucosa of the paranasal sinuses, particularly the maxillary antra, is involved in lepromatous leprosy. That this involvement is lepromatous infiltration and not merely non-specific mucosal thickening due to mechanical obstruction of the sinuses by lepromatous infiltration within the nasal cavity itself was confirmed histologically. Biopsies of maxillary sinus mucosa from 2 patients in the series showed typical lepromatous infiltration and the presence of *M. leprae*.—(*Adapted from* the article)

Barton, R. P. E. and McDougall, A. C. The paranasal sinuses in lepromatous leprosy. Lepr. India **51** (1979) 481–485.

During the course of a larger study of patients with treated lepromatous leprosy attending a hospital in south India, 16 patients with untreated disease presented with symptoms suggesting both intranasal and sinus involvement. Radiological abnormalities of the sinus were recorded in all 16 patients, and the results have been published separately. This paper describes the clinical and bacteriological findings, together with the results of histopathological examination of biopsies of sinus mucosa in two patients, in both of whom there was a histiocytic infiltrate with acid-fast bacilli. In one of these biopsies, bacilli in the lamina propria were numerous; globi were common, and 20% of free-standing organisms were solid-staining.

The significance of these findings is discussed with emphasis on the value of a full ear, nose, and throat examination in all cases of leprosy, especially those with the lepromatous form. In this type of leprosy the upper respiratory tract tissues are clearly of importance for the lodgement of and multiplication of bacilli; it is possible that the paranasal air sinuses, with their large surface area, may contribute to the numbers of bacilli which are disseminated from the nose into the environment.—Authors' Summary

Carrica, A., Fauxpoint, B., Labat, P., Rivaud, C. and Vedy, J. Manifestations ophtalmologiques de la lèpre. (Ocular lesions in leprosy.) Méd. Trop. **39** (1979) 301–306. (in French)

Modern authors estimate from 47% to 78% the frequency of ocular lesions in leprosy. This frequency varies according to the duration and type of the disease.

These lesions may result from a paralysis of the V or VII cranial nerves or from a bacteremia but, more probably, from a spreading of the bacilli from the nasal cavity through the lacrymal ducts. The various lesions of each ocular structure are described with reference to the T or L type of leprosy.—Authors' Summary

Chiron, J.-P., Denis, F., Maupas, Ph., Roux, G. and Languillon, J. Infection par le virus de l'hépatite B chez les hansèniens. II. Titre sérique des antigènes de surface du virus de l'hépatite B et des anticorps homologues. (Infection with hepatitis B virus in persons with leprosy.

II. Serum titers of surface antigens of hepatitis B virus and of homologous antibodies.) Bull. Soc. Méd. Afr. Noire Lang. Fr. **23** (1978) 402–405. (in French)

The quantity of surface antigens (HB_sAg) has been determined in the serum of 143 leprosy patients and the homologous antibodies (anti-HB_s) for 243 leprosy patients having synthesized discernable antibodies. The technique used in both cases was radioimmunoassay. There do not appear to be any statistically significant differences in titers either of HB_sAg or anti-HB_s when analyzed according to the form of leprosy or to the sex of the patients.—(*Adapted from* authors' summary)

Chiron, J.-P., Languillon, J., Roux, G. and Denis, F. Infection par le virus de l'hépatite B chez les hanséniens. III. Relation entre les marqueurs d'enveloppe du virus de l'hépatite B et la transaminasémie. (Infection with hepatitis B virus in persons with leprosy. III. Relation between envelope markers of hepatitis B virus and transaminasemia.) Bull. Soc. Méd. Afr. Noire Lang. Fr. **23** (1978) 406–409. (in French)

Serum glutamic oxaloacetic transaminase and glutamic pyruvic transaminase have been measured in the sera of 445 patients with leprosy and the results analyzed according to the markers of the envelopes of hepatitis B virus (HB_s and anti-HB_s).

It appears that lepromatous patients who are positive for HB_sAg have higher levels of serum glutamic oxaloacetic transaminase and glutamic pyruvic transaminase than lepromatous patients who are HB_sAg negative. Lepromatous patients who are HB_sAg positive also have higher transaminase levels than tuberculoid patients who are HB_sAg positive.—(*Adapted from* authors' summary)

Coudert, J., Dumont, M., Lu, H. T. and Valla, M. C. Lèpre et grossesse. (Leprosy and pregnancy.) Rev. Fr. Gynecol. Obstet. **73** (1978) 103–107. (in French)

It is concluded from a review of the recent literature and from the results of a personal study of 238 families with leprosy kept under medical supervision and treated, that the birthrate among these patients is not negligible: 681 pregnancies, two of them twin pregnancies, with 16 abortions and 4 stillborn children. Twenty children died later from some intercurrent disease; of the survivors, 40 suffered from leprosy and 599 were healthy. The importance of congenital infection is not evident, in spite of the presence of *Mycobacterium leprae* in the cord blood and the placenta. At present the conclusion seems justified that continuation of the specific therapy during pregnancy and BCG at birth are justified, and that the dangers entailed by pregnancy are acceptable.—Authors' Summary

Enna, C. D. Isolated pathological fracture of the capitate bone. A case report. Hand **11** (1979) 329–331.

Isolated fracture of the capitate bone is rare, but an isolated pathological fracture due to leprosy has not been previously reported. Although varying degrees of trauma are implied to be associated with fractures, this case illustrates a pathological fracture of the capitate apparently due solely to a specific disease. Fracture has occurred without a history of trauma, and there has been no displacement of the fragments on x-rays over a period exceeding ten years even though it has been subjected to unrestricted activities by the patient who has clinically inactive disease.—Author's Summary

Gadoth, N., Bechar, M., Kushnir, M., Davidovitz, S. and Sandbank, U. Somatosensory and autonomic neuropathy as the only manifestation of long standing leprosy. J. Neurol. Sci. **43** (1979) 471–477.

The clinical and neuropathological findings in a patient with "neuritic" leprosy are described. In this rare form of leprosy, skin changes are only minimal or absent, and the diagnosis can be established only by nerve biopsy.—Authors' Summary

Harverson, G. and Warren, A. G. Tarsal bone disintegration in leprosy. Clin. Radiol. **30** (1979) 317–322.

Tarsal bone disintegration is characterized by fragmentation and progressive collapse of one or more tarsal bones. It occurs

in 10% of leprosy patients and is responsible for many severe foot deformities associated with this disease. The main cause is micro-traumata, but sensory impairment, sepsis, and osteoporosis are predisposing factors. In this series of 400 consecutive patients, the talus and navicular were involved most frequently (72% of 119 tarsal lesions). Treatment, including prolonged immobilization of the foot, results in dense sclerosis of the affected bone and leaves a functional limb. Initial radiological features include:

1) bone fragmentation
2) calcified fragments in adjacent soft tissues
3) linear fractures
4) progressive compression and deformity of the affected bone
5) flattening of the longitudinal plantar arch

Illustrative case histories are presented and the differential diagnosis discussed.—Authors' Summary

Jiménez, A. M. and Urcuyo, F. G. Carbamazepina en las manifestaciones neurologicas de la lepra. (Carbamazepine in the neurological manifestations of leprosy.) Rev. Fontilles **12** (1979) 147–151. (in Spanish)

The action of carbamazepine (teitegretol) in the symptomatology of neuritis (hyperesthesia, paresthesia, neuralgia, and reactional neuritis) was studied in 20 leprosy patients of whom 11 were lepromatous cases, 8 tuberculoid, and 1 indeterminate. Excellent results were obtained in 65% of the patients, good results in 25%, and no effect was observed in 10% of the patients. Thirty-five percent of the treated patients showed mild somnolence as a side effect.—(*Adapted from* authors' summary)

Jopling, W. H., Rees, R. J. W., Ridley, D. S., Ridley, M. J. and Samuel, N. M. The fingers as sites of leprosy bacilli in pre-relapse patients. Lepr. Rev. **50** (1979) 289–292.

Two dapsone treated patients with apparently quiescent lepromatous leprosy were found to have solid-staining acid-fast bacilli (AFB) in the fingers. The viability of the bacilli from both patients was proved, and dapsone resistance was established in one patient by mouse foot pad inoculation. Subsequently, both patients relapsed bacteriologically, one clinically in addition. Thus solid-staining AFB in the fingers, though there may be none seen in skin lesions, may be the prelude to relapse.

It is suggested that the dorsum of fingers is a favorable site for persister bacilli because it is cool, and nerve bundles are more superficial there than in most other areas.—Authors' Summary

Mehta, J. M., Nimbalkar, S. T. and Thalayan, K. A new approach in the relief of pain of leprous neuritis. Lepr. India **51** (1979) 459–464.

Transcutaneous nerve stimulation (TNS) has been known the last several decades to relieve pain in many conditions. For the first time it was used in the treatment of the severe and agonizing pain caused by leprous neuritis with highly beneficial results without producing any side effects. This study was made on 40 patients, and in the majority of the cases there was total relief of pain with one application of a few hours duration. This encouraging result has led the authors to the conclusion that TNS could be a useful tool in a hospital where leprosy patients are treated.—Authors' Summary

Noussitou, F. Some aspects of tuberculoid leprosy and chemotherapeutic trials. Acta Leprol. **74** (1979) 1–32.

The author describes the progress made in our knowledge of tuberculoid (T) leprosy since the original case of Jadassohn in 1898. The numerical importance of T patients in different parts of the world is reviewed and their role in the transmission of the disease discussed.

An analysis is made of the subgroups into which T leprosy is divided according to the clinical symptoms, bacteriology, histopathology, and immunology in the Madrid classification as well as in the Souza-Lima–Souza Campos and Ridley-Jopling studies. The author concludes that a majority of T patients are immunologically stable and belong to 2 well defined groups, the first called T annular in the Souza-Lima–Souza Campos study and TT in the Ridley-Jopling

classification and the second called T reactional by S.-L.–S.-C. and BT by R. J.

Taking into account the high proportion of T cases in most epidemiological situations, their generally accepted good prognosis under treatment, and the present availability of several drugs of proven efficacy, the author suggests to carry out in T leprosy under controlled conditions a trial of a number of therapeutic regimens of not more than 12 months duration. Follow-up periods will make possible medium and long-term evaluation of results after 3 and 5 years respectively of the initiation of the chemotherapeutic regimens.

The practical implications of effective and well tolerated short-term therapy in T leprosy are stressed. Its widespread use in field programs will represent among other advantages a considerable economy in personnel and drug costs.

The use of a single protocol is recommended. The one worked out by THELEP for therapeutic trials in lepromatous leprosy could be adopted with a few changes made necessary because of the morphological and bacteriological differences between lepromatous and T leprosy.

It is suggested that, if the results of the trial are successful, similar regimens could be tried in indeterminate leprosy.—Author's Summary

Pursley, T. V., Jacobson, R. R. and Apisarnthanarax, P. Lucio's phenomenon. Arch. Dermatol. **116** (1980) 201–204.

A 38-year-old woman had diffuse, nonnodular lepromatous leprosy and Lucio's phenomenon. Most cases of Lucio's phenomenon have been reported to have a leukocytoclastic vasculitis as the underlying pathologic abnormality. In this patient, however, the histologic picture of an early lesion of Lucio's phenomenon showed a mild, mononuclear cell infiltration, endothelial swelling, vascular thrombosis, and ischemic necrosis. Lepra bacilli were abundant around nerves and blood vessels, and many were noted in vascular walls and endothelium. Our findings raise the possibility that some cases of Lucio's phenomenon may be caused by vascular damage due to direct invasion of *Mycobacterium leprae* and not necessarily by leukocytoclastic vasculitis.—Authors' Summary

Ramu, G. and Girdhar, A. Treatment of steroid dependant cases of recurrent lepra reaction with a combination of thalidomide and clofazimine. Lepr. India **51** (1979) 497–504.

Twenty-two adult male lepromatous patients suffering from recurrent lepra reaction have been allotted to either a regimen of combined treatment with clofazimine and thalidomide or thalidomide alone. The initial dosage of either of the drugs was 300 mg daily administered in divided doses of 100 mg 3 times a day. The preliminary assessment of the ongoing study indicates that combined treatment controls the reactional state more rapidly than monotherapy with thalidomide alone. Results of treatment as regards relief of neuritis and arthritis are particularly gratifying. Four months following discontinuation of therapy in the thalidomide group, all the cases relapsed into reactional status from 2 days to 15 days. Five cases on the combined therapy relapsed after from one to three months. Three other cases required six months and three cases 8 months treatment before clofazimine could be withdrawn. It would appear that a maintenance therapy of 6 months with clofazimine would be necessary for maintaining the control of reactional episodes while employing this combined therapy.—Authors' Summary

Sheri, S., El-Sheimy, S., Lasheen, R. and Baddar, M. R. Australia antigen in lepromatous leprosy in Egypt. J. Egypt. Med. Assoc. **60** (1977) 447–455.

The serum from 53 lepromatous leprosy patients and 37 healthy controls was examined for the presence of the Australia antigen, which was reported present in some studies of lepromatous leprosy from different parts of the world. None of our patients or controls carried the antigen. The significance of this total absence both genetically and in relation to the development of lepromatous leprosy is discussed, and the role of environmental factors in the development of this disease is emphasized.—Authors' Summary

Sritharan, V., Venkatesan, K., Bharadwaj, V. P. and Ramu, G. Serum lipid profile in leprosy. Lepr. India **51** (1979) 515–520.

Lipid profiles were determined in sera from 79 leprosy patients and compared to 11 healthy controls. There was a generalized decrease in total lipid concentration in leprosy. Total cholesterol was less than normal in all types of leprosy, and this was most marked with lepromatous leprosy (active) and in lepromatous reaction. Free cholesterol was significantly higher in active lepromatous leprosy and in reactions of lepromatous leprosy. Triglycerides were significantly decreased in all reactive states and also in active lepromatous cases. Significant decreases in phospholipid were noted in all types of reactive states and also in active lepromatous and active borderline-lepromatous cases. B-lipoproteins showed a decrease in all types of leprosy, and the decrease was most marked in lepromatous reactions and in active lepromatous leprosy. Lipase showed significant decreases in lepromatous reactions and also in active lepromatous cases. No significant changes could be observed with serum amylase levels. Serum lipids showed a gradual increase in the order of lepromatous reaction, borderline-tuberculoid reaction, and borderline reation.—(*Adapted from* the article)

Thiagarajan, V., Radhakrishnan, S., Sivarajan, V., Rajasekar, R. and Srinivasan, K. R. Pulmonary candidiasis. Indian J. Tubercul. **24** (1977) 171–174.

As seen in world literature, cases of mucocutaneous candidiasis have been reported in combination with defective cell-mediated immunity. Some of them were also associated with endocrinopathies like hypoparathyroidism, hypothyroidism, hypoadrenalism, and diabetes mellitus. So far to our knowledge no case has been reported of a combination of cell-mediated immunodeficiency with pulmonary candidiasis, lepromatous leprosy, and myxedema. Mediastinal involvement in candidiasis, even though infrequent, is present in our case, which is presented because of its rare combinations.—Authors' Summary

Immuno-Pathology

Campinchi, R., Cottenot, E., Dufier, J. L., Bloch-Michel, E., Dorey, C. and Guyer, J. L. Intraocular production of leprous antibodies. *In: Immunology and Immunopathology of the Eye.* International Symposium on the Immunology and Immunopathology of the Eye. Proceedings of the 2nd Conference, San Francisco, May 8–10, 1978. New York: Masson Publishing, U.S.A., Inc., 1979, 90–92.

Antibody titrations were performed by an immunofluorescence method in 14 cases of leprosy, both in aqueous humor (AH) and in serum (S). Antibody titers were high in AH. In 5 of these cases, correction of the AH/S ratio for the immunoglobulin levels strongly suggested the presence of intraocular antibody formation.

The high level of aqueous antibodies does not seem to depend either on the nature of the disease (lepromatous, tuberculoid, borderline, and others) or on the duration of the disease but only on the presence of enlarged nerves in the cornea.—Authors' Summary

Kado, M., Kitaichi, M., Matsui, Y., Izumi, T., Oshima, S., Asamoto, H. and Ozaki, M. Clinical significance of the PHA skin test in patients with lung cancer, pulmonary tuberculosis and leprosy. Bull. Chest Dis. Res. Inst. Kyoto Univ. **12** (1979) 28–35. (in Japanese)

The clinical significance of a skin test with 5 μg of purified phytohemagglutinin (PHA) was studied by testing 95 subjects, including 45 cases of lung cancer, 27 cases of pulmonary tuberculosis, 14 cases of leprosy, and 9 healthy controls. Forty three of the lung cancer patients were tested simultaneously with 0.05 μg of PPD in order to examine the correlation between the PPD test and the PHA test. The PHA skin reaction was determined 24 hr after intrader-

mal injection of PHA and was judged as positive when the diameter of erythema was 30 mm or more. The mean diameter of erythema was 38.1 ± 3.8 mm (negative rate 0%) in healthy controls, 31.2 ± 8.1 mm (59.3%) in pulmonary tuberculosis, 28.8 ± 8.1 mm (55.6%) in lung cancer, and 13.8 ± 7.2 mm (100%) in leprosy. Lung cancer patients with stage III, IV, or undifferentiated small cell carcinoma showed reduced PHA skin reactivity. In leprosy, the PHA skin reactivity of the lepromatous type was more markedly impaired than the reactivity of the borderline type. A positive correlation between the PPD skin reaction and the PHA skin reaction was observed in 27 (62.8%) of the 43 lung cancer patients tested. It is concluded that the PHA skin test is significant for the evaluation of cellular immunity in patients with various diseases.—Authors' Summary

Kasili, E. G., Wamola, I. A., Pamba, H. O., Shiramba, T. L. and Broekman, J. M. Various pathological manifestations of leprosy: a multidisciplinary study. E. Afr. Med. J. **56** (1979) 59–70.

This paper describes detailed results of a number of pathological investigations on 25 patients under treatment for lepromatous leprosy at Alupe Hospital, Busia District, Kenya, all showing clinical evidence of active lesions. Investigations included full blood counts, sedimentation rates, bone marrow findings, albumin/globulin ratios, liver function tests, urine and stool analyses, skin tests for schistosomiasis, and histochemical reactions for acetyl cholinesterase, alkaline phosphatase, and acid phosphatase. [How many of these results are specifically related to leprosy is not known, for no control tests were made on a comparable group of similar low socioeconomic status drawn from the same locality.]—W. H. Jopling (*from* Trop. Dis. Bull.)

Koranne, R. V., Singh, R. and Iyengar, B. Lymph node involvement in tuberculoid leprosy. Indian J. Dermatol. Venereol. Lepr. **45** (1979) 177–180.

Twenty-two untreated cases of proved tuberculoid leprosy and five healthy persons in the control group were studied histopathologically for involvement of the lymph nodes; 54.54% (12 cases) in the study group showed positive evidence of lymph node involvement. Ten patients (45.45%) showed the presence of granuloma in the lymph nodes. Eight cases (36.36%) had acid-fast bacilli in the lymph nodes; six (75%) of them had granulomas as well, and in two cases (25%) bacilli were present without granulomatous foci. There was no evidence of tuberculosis. In the control group, none showed any pathology in the lymph nodes. The 2 cases, the leprous granuloma and bacilli were seen in lymph nodes which were outside lymphatic drainage area of the cutaneous lesions; 36.84% of cases also showed evidence of leprous pathology in the liver.—Authors' Summary

Moon, K. C., Cinn, Y. W. and Kim, W. S. A study on the prevalence of autoantibodies in Korean patients with leprosy. Kor. J. Dermatol. **16** (1978) 417–421. (in Korean)

It has been increasingly clear that the defense against *M. leprae* appears mainly to depend on the cell-mediated rather than the humoral immune mechanism. Nevertheless, *M. leprae* are not only capable of producing specific humoral antibodies but also of stimulating the formation of a variety of autoantibodies since mycobacteria are known to exert an adjuvant effect.

Although the exact role of the autoantibodies in the pathogenesis of leprosy is not known, it is remarkable that the prevalence of autoantibodies has been reported differently by several investigators, suggesting the possibility of geographical or racial differences.

This study was undertaken to investigate the prevalence of some autoantibodies in Korean patients with leprosy.

Eighty patients with leprosy, registered at the Department of Dermatology, Seoul National University Hospital, entered this study from February 1977 through October 1978. The diagnosis was made by clinical, histological, bacteriological, and immunological assessments, and the patients were classified according to the Ridley-Jopling scale. All patients were under anti-leprosy chemotherapy with DDS (diaminodiphen-

ylsulfone) for various periods at the time of study.

The Venereal Disease Research Laboratory (VDRL) test was performed in 80 patients, and the sera displaying reactive VDRL were subjected to re-examination by *Treponema pallidum* hemagglutinin assay (TPHA). Rheumatoid factor was sought by means of the latex fixation test in 60 patients. Antinuclear antibody (ANA) was detected by means of latex agglutination reaction in 61 patients using polysterene latex complexed with calf thymus deoxyribonucleoprotein. Cryoprotein was detected as described elsewhere.

Four of the 80 patients (5%) showed reactive VDRL while rheumatoid factor and antinuclear antibody were not detectable in all cases. Cryoprotein was detected in 15 patients (27.3%).

Compared with other reports on the prevalence of autoantibodies in Caucasian and African patients, we found a much lower frequency. This result may be explained partly by racial or geographical differences in the pattern of leprosy, as suggested by Turk.—(*from* Kor. Med. Abstracts)

Selezneva, S. P. and Podoplelov, I. I. Content of T and B lymphocytes in the blood of patients with polar types of leprosy. Zh. Mikrobiol. Epidemiol. Immunobiol. (1) (1980) 62–64. (in Russian)

The content of T and B lymphocytes in the peripheral blood of patients with polar types of leprosy and healthy adults was determined. The lepromatous (severe) form of leprosy was found to be accompanied by a sharp decrease in the percentage of T lymphocytes while the percentage of B lymphocytes perceptibly increased. In patients with the tuberculoid type of leprosy, only an insignificant decrease in the percentage of T lymphocytes was observed while the level of B lymphocytes remained normal. These data indicate that in the severe form of leprosy, cellular immunity is deeply suppressed, and the nonspecific stimulation of humoral immunity occurs.—Authors' Summary

Singh, R. and Koranne, R. V. Systemic involvement in tuberculoid leprosy—pathogenesis of leprosy. Lepr. India **51** (1979) 451–458.

The occurrence of leprous pathology/bacilli in the internal organs in cases of polar tuberculoid leprosy supports the systemic nature and hematogenous transmission and spread of the disease process. The pathogenesis of leprosy has been postulated.—Authors' Summary

Microbiology

Mori, T. and Kohsaka, K. Isolation culture of 7 strains of *Mycobacterium lepraemurium* and isonicotinic acid hydrazide or rifampicin resistant Hawaiian strain. Jap. J. Lepr. **47** (1978) 87–91. (in Japanese)

Seven strains of *Mycobacterium lepraemurium* (Douglas, Fukuoka-1, Keishicho, Kumamoto, Kurume-42, Odessa, and Osaka-No. 1 strains) were isolated on 1% Ogawa's yolk medium. These colonies were white yellow, very slow growing, and rough at the time of isolation but gradually changed to smooth colonies on successive cultivation. Kurume-42 and Odessa strains were strongly rough types. The Kurume-42 strain especially did not change to a smooth type until the 17th generation and became extinct on account of failure of cultivation at the 18th generation. The Kurume-42 strain differed from the other 6 strains of murine leprosy bacilli in the characteristic of rough type. All strains secreted coproporphyrin on the medium and colored the surface of the medium red. Many negative tubes were seen every time in the primary isolation culture, and some seeded colonies did not grow in the successive cultivation. All strains were difficult to culture.

INH or rifampin-resistant strains were isolated on 1% Ogawa yolk medium from murine lepromata formed with INH or rifampin-resistant Hawaiian strains. The degree of INH resistance is 16 μg/ml and that of rifampin resistance is 7 μg/ml.

These 7 strains and the INH or rifampin-resistant Hawaiian strains were cultivated successively for several generations; thereafter, these strains were inoculated into mice. These strains produced murine lepromata at the injection site. Many globi were observed on smear preparations of these murine lepromata.—Authors' Summary

Stevens, K. M. Cultivation requirements for *Treponema pallidum, Mycobacterium leprae* and other microbial and mammalian microaerophilic cells. Medical Hypotheses **5** (1979) 1091–1104.

Atmospheric and biological evolution progressed simultaneously and today certain cell types flourish only at oxygen tensions which were ambient 600 million years ago, i.e., at 5 to 10 mm Hg. In man, a continuous oxygen flow at these pressures is supplied in the skin where *Treponema pallidum, Mycobacterium leprae,* and members of the genus *Rickettsia* grow best. *In vitro* studies support the microaerophilic status of these organisms and of certain other microbial and mammalian cells. Vigorous growth in pure culture will await the development of techniques which can maintain these low oxygen tensions at the cell walls of the microbes as they replicate and consume increasing amounts of oxygen. Continuing failure to consistently isolate microbes from active lesions in patients with rheumatoid arthritis or systemic lupus erythematosus may reflect the universal absence of suitable methods for isolation of microaerophilic microbes.—Author's Summary

Experimental Infections

Lagrange, P. H. and Hurtrel, B. The influence of BCG vaccination on murine leprosy in C57BL/6 and C3H mice. Ann. Immunol. (Inst. Pasteur) **130 C** (1979) 687–709.

Cross-reactivity between *Mycobacterium lepraemurium* (MLM) and BCG vaccine was found and evaluated *in vivo* in C57BL/6 mice in terms of delayed-type hypersensitivity, local granulomatous response at the injected site, and limitation of growth of the challenge inoculum in the draining node. Cross-reactive specific protection and local reactivities were transferred in syngeneic normal recipients by means of non-adherent lymphoid cells from immune donors. When BCG vaccine was injected either intravenously or subcutaneously in C57BL/6 and in C3H mice, it was able to induce resistance to local infection with living MLM in both strains, but no alteration of the local granulomatous reaction (equivalent to local specific immune response) was observed in C3H mice as compared to the control. When mice were immunized with one or two injections of heat-killed MLM after the immunomodulating effect of BCG vaccination, better immunization was not achieved. In order to test the presence of strain-related immunosuppressive mechanisms, mice were cyclophosphamide-treated during the immunization process. As expected, higher specific DTH reactions were obtained in both strains but with only a slight increase of the protective mechanism. Protection was always higher in C57BL/6 than in C3H mice.

The specific and non-specific immune responses to BCG vaccine were then evaluated in both strains with different parameters: *in vivo* lymphoproliferative response in the draining node, delayed local granulomatous reaction at the injected site after a subcutaneous injection, increase in spleen index, and kinetics of the immunopotentiation to a thymus-dependent antigen (sheep red blood cells) after a single intravenous injection of BCG. A striking interstrain dif-

ference was observed; C57BL/6 mice were able to mount a more rapid and marked immune response as compared to C3H mice (which only developed a delayed and slight response). Moreover, these differences were associated with the fact that BCG did not seem to multiply properly in C3H mice during the first two weeks after inoculation. Thus, it was concluded that higher natural resistance to pathogens and cross-reactive preimmunization with related microorganisms can interfere with the artificial immunization when living microorganisms are used. Implications for vaccination to mycobacterial infection (tuberculosis and leprosy) are discussed.—Authors' Summary

Nakagawa, K., Sushida, K., Nakano, H. and Iwamoto, K. Serum protein fraction of mice inoculated with the drug resistant murine leprosy bacilli. J. Tokyo Wom. Med. Coll. **47** (1977) 312–319. (in Japanese)

It is well known that drug resistant tuberculous bacilli show decrease in virulence in some experimental animals. Recently, murine leprous bacilli were cultured on Ogawa yolk medium. Therefore, studies were performed to observe whether the virulence of drug resistant murine leprous bacilli grown on yolk media *in vitro* would decrease.

Sushida has already reported that β-globulin (B-G) fraction in serum protein of murine leprosy mice showed marked increase in comparison with normal mice. The purpose of this experiment was based on the change of virulence of drug-resistant murine leprous bacilli in mice by observing the fluctuation of B-G.

Streptomycin (SM)-resistant murine leprous bacilli grown on yolk media *in vitro* were obtained and inoculated in mice. The serum protein fractions of the infected mice were estimated by gel-electrophoresis.

The murine leprous mice in the control group showed marked increase in B-G compared with normal mice. However, the increase of B-G in the SM-resistant murine leprosy was not marked, and some showed almost the same value as that of normal mice. The murine leprosy mice of the control group showed marked increase of B-G with an increase of symptoms after infection, but such a tendency was not seen in the SM-resistant group.—Authors' Summary

Epidemiology and Prevention

Browne, S. G. Organizing a leprosy control programme. Trop. Doct. **9** (1979) 93–96.

The author outlines the fundamentals of leprosy control and the choices available to local officials as to the nature of their control activities based on their available facilities, local population density, prevalence of leprosy, local attitudes towards leprosy, etc. The article outlines the strategies to be employed in leprosy control in order to achieve a limited number of objectives: 1) early diagnosis of leprosy, 2) adequate and regular treatment of the disease, and 3) possible BCG vaccination and eventually a specific vaccine, if and when it becomes available.—RCH

Ekambaram, V. Duration of treatment for "disease arrest" of non-lepromatous cases and relapse rate in these patients. Lepr. Rev. **50** (1979) 297–302.

This is a study of 1879 patients declared disease arrested in the Elep Leprosy Project, Dharmapuri. The study analyzes the duration of treatment needed for rendering a patient disease inactive and disease arrested and the number of relapses occurring among these cases. The relapses have been analyzed with reference to the maintenance and total treatment the patients had before relapse, and the periodicity of relapse after being declared disease arrested with a view to determining the minimum treatment needed for disease arrest, the surveillance needed after discharge from treatment, etc.—Author's Summary

El-Zawahry, M. and El-Zawahry, K. Child

leprosy. J. Egypt. Med. Assoc. **69** (1977) 457–460.

It has been thought that Egyptian records of 1350 B.C. refer to hanseniasis. They appear to be the first records of leprosy in the Nile valley describing leprosy among natives of the Sudan and Darfur. This agrees with what we know of the high incidence of leprosy in central Africa. This is considerable evidence to indicate that leprosy spread from Africa to Egypt, Asia Minor, and Europe.

The age of the patient is an important factor in infection in leprosy. Adults seem to resist infection more than children. The proof of relative unsusceptibility of adults is made clear when we remember that only 5% of married partners acquire leprosy when one of them has the disease. On the other hand, in an endemic area, it has been estimated that 60% of the children acquire the disease, which becomes manifest at some period of their lives. The majority of cases of leprosy declare themselves as manifest cases between 20 and 35 years of age. The first lesion noticed by patients usually begins earlier than that, and if we deduct a latent period of 5 years (it is actually 2 to 7 years and in many cases may be more than that), we can come to the conclusion that most cases of leprosy result from infection before 15 years of age.—(*Adapted from* the article)

Godeau, P., Wechsler, B. and Weisselberg, C. A propos d'un cas de lèpre autochtone. (A case of autochthonous leprosy.) Sem. Hop. Paris **55** (1979) 958–946. (in French)

A case is reported of autochthonous leprosy in a French patient who had never lived in an endemic zone. The disease was of the lepromatous leprosy type, and the liver, spleen, skin, nerves, and muscles were affected. Characteristic findings were Hansen's bacillus in nasal scrapings, a deficiency in cellular immunity, and the presence of cryoglobulins and circulating immune complexes. Autochthonous leprosy, which has not been imported, and without signs of direct contagion, appears to be exceptionally rare. The authors review the clinical forms of leprosy and immunological findings.—Authors' Summary

Kapoor, P. and Yellapurkar, M. V. Strategy of early detection of infectious leprosy patients and the role of medical personnel. Lepr. India **51** (1979) 486–496.

One of the most essential components of effective control of leprosy is the detection of cases of the infectious type in a very early stage. However, this has been found to be difficult to achieve, resulting in the disease remaining unrecognized for at least 3–4 years, thus continuing its spread to the susceptible population.

One important contributory factor for the unsatisfactory state of affairs is non-involvement of the medical personnel to work for leprosy control, particularly in suspecting and diagnosing early lepromatous cases.

Active search operations involve tremendous manpower and huge expenditure apart from their time consuming nature, and yet the achievements in terms of infectious case detection are hardly commensurate with the inputs. The cost per infectious case detected through active search ranges between Rs. 600/- to Rs. 3000/– depending on whether it is the first survey or subsequent surveys.

Although voluntary reporting as a result of health education yields equally satisfactory results in terms of infectious case detection, the desired level of early detection is not attained.

Passive surveillance, which could have been a valuable measure in early infectious detection, has unfortunately proved to be almost ineffective because the medical personnel are not exposed to adequate knowledge about leprosy and simple diagnostic methods and their importance.

If the entire medical fraternity including undergraduate medical students is exposed adequately to training in diagnosis and management of leprosy, doctors would be favorably inclined to participate in the control program actively, helping in early case detection, particularly of infectious cases, and promoting case holding as well and thereby accelerating control of the disease.—Authors' Summary

Kundu, S. K., Ghosh, S., Hazra, S. K. and Chaudhury, S. Nature and familial character of lepromin sensitivity in 27 fami-

lies and their siblings. Lepr. India **51** (1979) 465–474.

A group of 27 families consisting of 176 individuals has been investigated for lepromin sensitivity (with Dharmendra antigen). The families were arranged under group A (9 families) in whom either of the parents or both were suffering from the lepromatous type of leprosy, group B numbering 4 families, of whom either of the parents or both were suffering from the non-lepromatous type of leprosy and group C comprising 14 families where none of the parents was suffering from leprosy but some of each family had the disease in their siblings.

The present study points towards the possible genetic influence on lepromin sensitivity but at times may be influenced by environmental factors. However, the study does not permit one to reach any valid conclusions; further elaborate investigations alone could prove the useful role of genetic influence in the propagation of lepromin sensitivity to the subsequent sibs.—Authors' Summary

Osaka, R. A survey of the social situation of leprosy patients in JALMA Leprosy Centre, Agra, India. I. Survey on the medical aspects of inpatients. Jap. J. Lepr. **47** (1978) 92–98. (in Japanese)

This is a report of a sociological study on 240 inpatients hospitalized at the JALMA Leprosy Centre, India. This survey was carried out from 20 October 1971 to 10 January 1976. Results of the survey on the medical aspects of these patients are summarized as follows:

1. Onset of the disease was most frequently noticed by patients between ages 11 and 15 (39.1%).
2. Seventy-five percent of the patients came to the hospital because of patches on their body surfaces. However, many of them did not know the nature of the disease until the medical staff explained it to them. A considerable number of patients defaulted from regular treatment (46.2%). Their reasons for dropping out were an absence of pain and frustration about retarded improvement of clinical symptoms of leprosy. Many of them changed to other treatment centers in the expectation of better treatment.
3. Forty-five percent of inpatients had leprosy patients in their families or among their relatives. Cases of parents with leprosy were the most frequent (43.1%).
4. Most of the patients more or less changed their food habits after the onset of the disease. A total of 59.7% stopped eating animal foods such as meat, fish, and eggs after they got leprosy.—(*Adapted from* author's summary)

Phillips, M. A. Health education in leprosy: the problem of overcoming fear and misconceptions. Int. J. Health Educ. **21** (1978) 130–136.

Most leprosy patients who receive treatment recover from the disease with no disabilities. Yet those who do become disabled are there for all to see. They may be cured of leprosy yet they live on, often getting slowly more disfigured, for leprosy does not kill. No other disease is associated with so much fear and stigma so that while it is undesirable to single out leprosy as a special disease, its control does present problems which are unique. Without health education, any scheme to control leprosy will be ineffective. Knowledge and attitudes must be studied carefully and slowly changed, using all means available.—Author's Summary

Revankar, C. R., Dewarker, P. R., Mulchand, S. and Ganapati, R. Leprosy in preschool age. Lepr. Rev. **50** (1979) 293–296.

Examination of 4235 preschool age (1–5 years) children from various slums in Bombay revealed 20 active leprosy cases (prevalence rate of 4.7 per 1000). An analysis of pooled figures from clinics showed that preschool children formed 1.3% of the total number of patients attending these clinics: 5% were smear positive; 45% had one or more family members with leprosy (25% of the latter being bacteriologically positive). The high proportion of associated infectious cases (as compared to corresponding data for school age) indicates a strong pos-

sibility of intrafamilial infection in children of preschool age.—Authors' Summary

Serjeantson, S., Wilson, S. R. and Keats, B. J. B. The genetics of leprosy. Ann. Hum. Biol. **6** (1979) 375–393.

Population and family distributions of leprosy in the Bogia Subprovince of Papua New Guinea have been examined for evidence of inherited susceptibility to the disease.

Evidence for multigenic inheritance of leprosy severity is provided by the restriction of pleiotropy with red-cell enzyme 6PGD phenotypes to a single clinical form of leprosy and by the superior fit of pedigree data to a multifactorial, rather than single-gene model, of inheritance.

Discrimination of the multifactorial model as superior to the single-gene model in testing the mode of inheritance of quasi-continuous multiple threshold traits was possible by extending the models to incorporate information on assortative mating for leprosy.

Leprosy epidemiological patterns simulated blood genetic marker gene frequency distributions of 13 polymorphic loci in their dependence on linguistic and distance effects. In an analysis of leprosy prevalence rates in 25 languages, leprosy rates corresponded more closely with linguistic similarity than with geographic proximity, suggesting the importance of ancestral genetic relationships between groups as a determinant of similarity in between-group leprosy susceptibility.—Authors' Summary

Rehabilitation

Beach, R. B. and Thompson, D. E. Selected soft-tissue research: An overview from Carville. Phys. Ther. **59** (1979) 30–33.

Studies are underway on the effect on insensitive feet of repeated, "normal," non-ischemic pressure, such as that caused by walking. Although such stress does not harm normal tissues, it can lead to soft-tissue damage in the insensitive foot. This research is trying to determine such information as the amount of energy input required to damage soft tissue, microscopic and macroscopic changes that occur during early soft-tissue damage, importance of time sequence of energy input, and amount of energy input that causes hypertrophy rather than ulceration. The progress of these studies is reported.—Authors' Summary

Bergtholdt, H. T. Temperature assessment of the insensitive foot. Phys. Ther. **59** (1979) 18–22.

Temperature assessment has proven valuable in detecting areas of inflammation in the insensitive limb. Monitoring the inflammatory response to the stresses of footwear and walking has worked as a "pain substitute." In conjunction with other evaluation methods, the results of temperature assessment can be used to reduce the incidence of injury and ulceration in the insensitive foot. A review of principles and methods, a presentation of a case study, and a discussion will elaborate upon the concepts of temperature assessment.—Author's Summary

Brand, P. W. Management of the insensitive limb. Phys. Ther. **59** (1979) 8–12.

The limb or part of a limb that becomes insensitive often is destroyed or must be amputated. This is largely due not to intrinsic weakness of the limb but to damage from external forces that would normally be avoided by the person experiencing a warning pain. When the lack of pain sensation can be compensated for, the insensitive limb need not become damaged. Techniques for protecting the insensitive foot and hand are presented.—Author's Summary

ffytche, T. J. Cataract surgery in leprosy

patients. J. R. Soc. Med. **72** (1979) 826–830.

Blind patients from 3 leprosy centers in South Korea were examined, and 44 underwent cataract surgery. The ocular findings in these cases are recorded, and the surgical techniques adopted are described. The early visual results demonstrate that the majority of these unfortunate individuals can be benefited by this simple form of cataract surgery, especially as avoidance of the late crippling complications of leprosy depend to a large extent on the patient's own visual surveillance of the anesthetic areas of the body.—Author's Summary

Hampton, G. H. Therapeutic footwear for the insensitive foot. Phys. Ther. **59** (1979) 23–29.

The patient with insensitive feet may be injured by poorly fitted or inappropriate footwear. The risk of soft-tissue injury from friction or pressure can be reduced by careful selection and fitting of footwear and frequent evaluation of both footwear and the patient's feet. Concepts, methods, and materials utilized in treating patients with Hansen's disease can be applied to the prevention and treatment of injuries secondary to sensory deficit caused by other conditions. The microcapsule sock test has been used to assess shear forces and pressures that occur while shoes are worn. Test method and interpretation of test results are described.—Author's Summary

Shipley, D. E. Clinical evaluation and care of the insensitive foot. Phys. Ther. **59** (1979) 13–18.

Until fairly recently, foot deformity was accepted as part of the natural course of a disease with associated sensory loss such as Hansen's disease or diabetes. Now we recognize that most of this deformity is caused by physical forces and that, with proper care, deformity can be prevented. The therapist must perform accurate methods of assessment such as inspecting and palpating the skin, testing for sensory loss, recording footprints, and measuring foot volume and must provide knowledgeable treatment techniques. The patient must be taught how to care for his feet and how to prevent continued trauma with subsequent infection and bony absorption, which ultimately result in deformity that could have been prevented. These evaluation, treatment, and education techniques are discussed in detail.—Author's Summary

Other Mycobacterial Diseases and Related Entities

Aikat, B. K., Pathania, A. G. S., Sehgal, S., Bhattacharya, P. K., Dutta, U., Pasricha, N., Singh, S., Parmar, R. S., Sahaya, S. and Prasad, L. S. N. Immunological responses in Indian kala-azar. Indian J. Med. Res. **70** (1979) 583–591.

The epidemic of kala-azar in Bihar between October 1977 and February 1978 offered an excellent opportunity to investigate, in depth, some of the important immunological parameters in Indian kala-azar. Tuberculin and DNCB skin tests were negative in the majority of cases. There was lowering of T cell population in the untreated cases. There occurred a distinct rise of T cell population after therapy. The MIF also showed a similar trend. In a majority of the group of cases investigated, the percentage inhibition was markedly reduced in untreated cases and showed considerable improvement after therapy. The B cell population was initially raised in a majority of the groups and continued to remain at a high functional level. There was a marked rise of immunoglobulins particularly of the IgG class and a less well marked rise in IgM class. IgM levels tended to come back to normal during therapy. The IgA levels were within normal limits. Apart from demonstration of smooth muscle antibody (anti-SMA) in a significant number of cases, all other tests for autoantibodies against mitochondrial, parietal cells, and nuclear fac-

tors were negative. A majority of the cases gave positive results with latex agglutination.—Authors' Summary

Aluoch, J. A. Practical application of short-course (6 month) regimens of chemotherapy for pulmonary tuberculosis in Kenyan nomads. East Afr. Med. J. **56** (1979) 121–126.

The difficulty of obtaining the cooperation of patients receiving a prolonged course of treatment for tuberculosis is even more pronounced when the patients are nomads such as the Somali people of northern Kenya in whom the success rate with an 18 months' regimen was as low as 33%.

It was therefore decided to carry out an uncontrolled trial of a 6 months' regimen in a temporary treatment camp. All nomads found to have pulmonary tuberculosis were invited to bring their huts to a camp site where they would live under close medical supervision. The conditions of admission were that they should have sputum-positive pulmonary tuberculosis, be aged 15 years or over, and should agree to stay for 6 months.

All were treated with streptomycin, isoniazid, rifampin, and ethambutol for the first 2 months while a sensitivity report was awaited. On the receipt of the reports, patients were allocated to one of two regimens, depending on sensitivity to isoniazid. Those with fully sensitive organisms were given rifampin, isoniazid, and ethambutol for 4 months. Those with isoniazid-resistant organisms were given rifampin, ethambutol, and pyrazinamide for 4 months. The drugs were given daily and under strict visual supervision to make sure that every dose was swallowed.

The total number of patients admitted during 14 months in 1976–77 was 143. All had completed their treatment by April 1978, and all were sputum-negative at 5 months. Eight patients died. Episodes of possible adverse drug reaction numbered 62, but none necessitated the interruption of treatment.

Because of the patients' nomadic life routine, follow-up was not possible. Twenty patients were, however, observed for 6 months during which time none relapsed. The results show that the nomadic Somalis are prepared to cooperate in a short course of treatment in a special camp and "as long as the treatment of tuberculosis remains of such a long duration, this approach provides a partial solution to deal with the problems of organization of treatment of tuberculosis among the Kenyan nomads."—H. G. Calwell (*from* Trop. Dis. Bull.)

Bloom, B. R. Games parasites play: how parasites evade immune surveillance. Nature (London) **279** (1979) 21–26.

There is a great interest in the means by which some parasites can persist chronically in their hosts, evading destruction by the immune system. For example, blood forms of African trypanosomes fluctuate in numbers periodically. Each successive wave of parasites has a different type of surface antigen, and each wave is followed by the appearance of the specific antibody in the blood. This "antigenic variation" is thought to be the main mechanism allowing the parasites to persist. Antigenic variation is seen even in infections started from a single trypanosome and is thought to be the result of either random mutation or the switching-on of successive genes, perhaps by an antibody signal. Now that *Trypanosoma brucei* can be grown *in vitro,* these questions may soon be solved.

Another well known example is concomitant immunity in schistosomes in which adult worms can persist in the host at the same time as schistosomula of new "challenge" infections are killed. The main mechanism here is believed to be acquisition of "camouflaging" host antigens by the worms which develop first. It has been shown that among the host antigens acquired are the blood group substances A, B, and H and major histocompatibility antigens.

Some parasites even manage to survive within cells of the immune system. For example, *Theileria* colonizes lymphocytes, which it transforms to continuously dividing lymphoblasts in the manner of oncogenic viruses. Several other microorganisms parasitize macrophages, such as *Mycobacterium tuberculosis* and *Toxoplasma gondii,* both of which are able to stop fusion of phagosomes and lysosomes and thus survive. *Mycobacterium lepraemurium* and

Leishmania spp. on the other hand, can even survive and multiply after fusion of phagolysosomes, and *Trypanosoma cruzi* escapes from phagolysosomes into the cytoplasm. Another technique of subverting the immune response is used by *Babesia* which actually requires complement activation for penetration of the red blood cell!

Another interesting phenomenon is immunodepression by parasites. For example, African trypanosomes and malaria infections cause a generalized immunodepression of their hosts, and this may prolong their own survival. The mechanisms involved have not yet been fully unravelled but may involve "misdirection" of the immune response by non-specific B-cell mitogens produced by the parasites.—M. G. Taylor (*from* Trop. Dis. Bull.)

Bolivar, R., Satterwhite, T. K. and Floyd, M. Cutaneous lesions due to *Mycobacterium kansasii*. Arch. Dermatol. **116** (1980) 207–208.

A recipient of a renal homograft had cutaneous lesions on the lower extremities that resembled pyogenic abscesses. *Staphylococcus aureus* consistently grew from cultures, and despite appropriate antibiotics the lesions did not completely resolve. When special cultures were done, *Mycobacterium kansasii* were discovered. In immunocompromised patients with infectious cutaneous lesions, skin biopsy using appropriate stains and cultures should be considered early in the course of the illness.—Authors' Summary

Byun, H. W., Palk, S. H. and Kim, D. J. Cellular immunity in pulmonary tuberculosis. Kor. J. Intern. Med. **22** (1977) 18–21. (in Korean)

To evaluate the role of cellular immunity in pulmonary tuberculosis, the transformation of cultured lymphocytes in response to stimulation by phytohemagglutinin (PHA) was studied in 47 patients with active pulmonary tuberculosis and in 17 normal healthy subjects. Phytohemagglutinin induced DNA synthesis in active pulmonary tuberculosis (8.1 ± 9.2) was significantly lower than that shown in healthy subjects (34.9 ± 7.0) ($p < 0.01$).

The PHA stimulation index was 12.9 ± 10.6 in minimal active pulmonary tuberculosis, 10.1 ± 12.2 in moderate advanced pulmonary tuberculosis, 4.9 ± 3.8 in far advanced pulmonary tuberculosis, and 2.3 ± 0.6 in tuberculous pneumonia ($p < 0.01$). The phytohemagglutinin stimulation index of cultured peripheral lymphocytes in active tuberculous pleurisy (2.8 ± 0.6) was significantly lower than that shown in cultured lymphocytes in pleural fluid (143.6 ± 0.5).

These findings suggest that cellular immunity was decreased in active tuberculosis, and it would be helpful to evaluate the activity of pulmonary tuberculosis.—(*from* Kor. Med. Abstracts)

Chagas' disease: potential for immunoprophylaxis. Lancet **1** (1980) 466. (editorial)*

Infection with *Trypanosoma cruzi* (the hemoflagellate responsible for Chagas' disease) elicits a strong immune response, sufficient to control the initial infection (acute stage). The parasites are not completely eliminated but persist as a chronic low level infection (chronic stage) in which parasites can be detected in the peripheral blood only by special techniques. Acute-stage Chagas' disease is seldom fatal; however, years or decades later patients may present with the electrocardiographic abnormalities and digestive disturbances characteristic of chronic Chagas' disease, which have been ascribed to neuronal destruction. Reports of antibody and T lymphocyte autoreactivity to heart, nerve, and vascular structures suggest that the immune response may be responsible for the tissue damage seen in chronic Chagas' disease. More recently, the pathologic findings seen in *T. cruzi* infected rabbits have been reproduced by repeated, long term immunization of normal animals with killed parasites or subcellular fractions. Thus, *T. cruzi* may share antigens with host tissues, and, although immunization may elicit an anti-parasite cell-mediated immune response, the same response may also produce tissue damage. These findings indicate an immunopathogenesis with serious implications for those

* Editor's Note: Is it possible that nonviable, integral *M. leprae* as a vaccine might create problems of this nature?—RCH

groups attempting to produce immunoprophylactic methods: vaccination might eliminate the infection but still produce the disease. It is clear therefore that for a candidate vaccine to be acceptable, it would have to consist of *T. cruzi* components free of antigens that either cross-react with or bind to host cells. On existing evidence, it seems that selective immunization with "protective" *T. cruzi* antigens may be possible without provoking an autoimmune response.—(*Adapted from* the editorial)

Lewis, E. J. and Roberts, J. L. Is autoimmunity a common denominator in immune complex diseases? Lancet **1** (1980) 178–180.

In normal circumstances, antibodies reactive with native DNA appear in the plasma during the course of many clinical conditions associated with inflammation. These antibodies seem to be elaborated in response to the release of exceptional amounts of DNA by nucleated cells. As a result, DNA/anti-DNA complexes can be demonstrated in the cryoprecipitable fraction of plasma from patients with various inflammatory diseases. A significant proportion of these immune complexes contain low-molecular-weight polynucleotide antigens. These polynucleotides are derived from DNA which has been degraded by plasma DNAase. Because of the digestion of DNA in the plasma a spectrum of antigen/antibody complexes forms. While large, relatively insoluble complexes would be expected to be rapidly cleared by the reticuloendothelial system, low-molecular-weight complexes are removed more slowly. It is proposed that the action of plasma DNAase upon both free and immune bound-DNA can lead to a preponderance of small, soluble, polynucleotide/anti-DNA complexes. Under appropriate conditions of vascular permeability, these soluble complexes may be deposited in vessel walls. Hence, regardless of the initiating infectious or inflammatory agent, polynucleotide antigen/anti-DNA antibody complexes form and can result in immune-mediated inflammatory phenomena in diverse disease states.—Authors' Summary

Sauder, D. N., Bailin, P. L., Sundeen, J. and Krakauer, R. S. Suppressor cell function in psoriasis. Arch. Dermatol. **116** (1980) 51–55.

Recent studies suggest that autoimmunity may play a role in the pathogenesis of psoriasis. In view of these findings, it is postulated that the immunologic defect may be associated with regulation of the immune system. A study was undertaken to determine whether a suppressor cell defect was present. Two groups of patients with active psoriasis who were receiving no therapy were selected. Peripheral blood lymphocytes were pulsed with concanavalin A, 40 μg/cc for 48 hr. Their ability to suppress a mixed lymphocyte reaction with both autologous and allogeneic responding cells was assessed. There was a significant decrease in suppressor activity in psoriasis patients compared with normal individuals. Although we have not demonstrated that this mechanism is implicated directly in a causal relationship to psoriasis, it nevertheless gives further support to the possible role of the immune system in the pathogenesis of psoriasis.—Authors' Summary

Shelley, W. B. Bacterial endotoxin (lipopolysaccharide) as a cause of erythema multiforme. JAMA **243** (1980) 58–60.

The classic iris lesions in a patient with erythema multiforme bullosum were reproduced grossly as well as microscopically by the intradermal injection of a variety of heat-killed Gram-negative bacteria as well as their common endotoxin, lipopolysaccharide W. *In vitro* exposure of the patient's blood to these antigens induced specific fibrin microclots characteristic of a hypersensitivity state. It is possible that some cases of erythema multiforme associated with a variety of respiratory, gastrointestinal, or urinary tract infections may represent a single specific delayed sensitivity reaction to the bacterial endotoxin, lipopolysaccharide.—Author's Summary

Singapore Tuberculosis Service/British Medical Research Council. Clinical trial of six-month and four-month regimens of chemotherapy in the treatment of pulmonary

tuberculosis. Am. Rev. Resp. Dis. **119** (1979) 579–585.

In a study in Singapore, Chinese, Malay, and Indian patients with pulmonary tuberculosis received 2 months of daily treatment with streptomycin, isoniazid, rifampin, and pyrazinamide, followed either by daily treatment with isoniazid, rifampin, and pyrazinamide (SHRZ/HRZ regimen) or by daily administration of isoniazid and rifampin (SHRZ/HR regimen) allocated at random. Both regimens were given for either 6 or 4 months by random allocation.

All 330 patients with drug-sensitive tubercle bacilli before treatment had a favorable bacteriologic response during chemotherapy. During the first 6 months after the end of chemotherapy, there was only a single bacteriologic relapse among 84 SHRZ/HRZ and 80 SHRZ/HR patients treated for 6 months, but 8 (10 percent) of 80 SHRZ/HRZ and 4 (5 percent) of 74 SHRZ/HR patients treated for 4 months relapsed. Of a total of 33 patients with bacilli resistant to isoniazid, streptomycin, or both drugs before treatment, only one had an unfavorable response during chemotherapy, and none of 31 patients relapsed during the first 6 months after stopping chemotherapy. The incidence of adverse reactions was low; 11 (3 percent) of 397 patients had hepatitis, but not all episodes were attributable to drug toxicity, and one patient had thrombocytopenic purpura.—Author's Summary (*from* Trop. Dis. Bull.)

Sutherland, I. and Lindgren I. The protective effect of BCG vaccination as indicated by autopsy studies. Tubercle **60** (1979) 225–231.

In a detailed study of the pathology of tuberculous infection made in Finland in 1961, tuberculous foci were found at autopsy in 61 of 67 non-vaccinated subjects and in 35 of 83 BCG-vaccinated subjects, all of whom had died between the ages of 1 and 45 years (with 2 exceptions from causes other than tuberculosis).

In the present note on the same material, national information on tuberculin sensitivity and tuberculosis mortality has been used to calculate the risk of tuberculous infection in Finland at different times and ages during the lifetime of these subjects. From these risks of infection in Finland it was estimated that 63 or 64 of the non-vaccinated subjects had been infected during their lifetime and that between 25 and 31 of the BCG-vaccinated subjects were expected to have been naturally infected (had they not been vaccinated) between the time of vaccination and death.

It is concluded that virtually all tuberculous infections in unvaccinated subjects lead to pulmonary foci, which are demonstrable at autopsy. Further, the same appears to be so in vaccinated subjects; there is no evidence to support the suggestion that in man BCG vaccine can prevent the establishment of infection in an exposed subject. The effects of BCG (as demonstrated in the earlier paper) appear to be confined to limiting the multiplication and dissemination of the bacilli and the development of lesions following infection.—Authors' Summary

Tuberculosis Prevention Trial, Madras. Trial of BCG vaccines in south India for tuberculosis prevention. Indian J. Med. Res. **70** (1979) 349–363.

The protective effect of BCG vaccination is being evaluated in a controlled community trial near Madras in south India. After tuberculin and sensitin testing and radiographic and bacteriological examination, BCG vaccines and placebo were allocated randomly to about 260,000 individuals, of whom 115,000 were definitely tuberculin negative at the time of vaccination. Intensive efforts are being made by means of regular follow-up surveys to identify all new cases of tuberculosis occurring in the community. This report presents findings of the first 7½ years of follow-up. Incidence of infection was high in the study population. However, incidence of bacillary disease was more frequent among initial tuberculin reactors, especially among the older persons, than among nonreactors of whom the majority were in the younger age groups. The distribution of new cases of bacillary tuberculosis among those not infected at intake did not show any evidence of a protective effect of the BCG vaccines.—Author's Summary

Venkataraman, P., Narayana, A. S. L. and Tripathy, S. P. Comparison of plain egg medium with Löwenstein-Jensen medium in the isolation of *M. tuberculosis* from sputum. Indian J. Med. Res. **70** (1979) 875–879.

The isolation of tubercle bacilli from sputum using a plain egg (PE) medium and the conventional Löwenstein-Jensen (L-J) medium has been investigated on 703 specimens. The isolation of positive cultures and the grades of positivity were similar with the two media. There was an indication that the growth on the PE medium was faster than on L-J medium. The incidence of contamination was similar and low (4.0 percent on PE and 3.8 percent on L-J medium). Being cheaper and simpler than L-J medium, the PE medium is ideally suited for the routine culturing of tubercle bacilli.—Authors' Summary

Weiner, M. H. and Coats-Stephen, M. Immunodiagnosis of systemic candidiasis: mannan antigenemia detected by radioimmunoassay in experimental and human infections. J. Infect. Dis. **140** (1979) 989–993.*

A radioimmunoassay (RIA) that detects candida mannan was developed so that immunodiagnosis of systemic candidiasis could be improved. The RIA was evaluated in an animal model of disseminated disease and in a panel of patient sera. Mannan antigenemia was detected with the RIA in 52% of 29 rabbits with systemic candidiasis but not in 60 normal rabbits or 31 rabbits with systemic aspergillosis. In an evaluation of human sera, mannan antigenemia was detected in 5 of 11 patients with systemic candidiasis, 1 of 3 patients with invasive gastrointestinal candidiasis, and 1 patient with a sustained candidemia associated with an infected intravenous catheter. Mannan was not detected in sera from 11 patients with superficial candida infections, 7 patients colonized with *Candida*, 3 patients with chronic mucocutaneous candidiasis, 8 patients with other systemic mycoses, or 22 normal donors. This study demonstrates the utility of this RIA for early, specific immunodiagnosis of invasive candidiasis.—Authors' Summary

Williams, R., Brooksby, J. B., Crofton, J., Griffiths, D. L., Kilgour, J. L. and Kilpatrick, G. S. Research in tuberculosis. A report of a committee set up by the Medical Research Council to study future prospects. Tubercle **60** (1979) 251–258.*

1. Tuberculosis in the developing world is still so frequent that research into its management is a high priority; in the U.K. the disease still justifies priorities in some areas of research.

The following are particular topics identified as calling for research:

2. Characterization of antigens of *M. tuberculosis* to facilitate skin and seriological testing.
3. Search for "virulence" or "attenuation" markers.
4. Search for new phages lysing *M. tuberculosis* and relation of lysogeny or phage sensitivity to virulence and epidemiology.
5. Studies of metabolism of *M. tuberculosis* that might relate to the design of chemotherapeutic studies.
6. Studies of bacterial latency, its significance in relation to treatment, and relapse both in respiratory and non-respiratory disease.
7. Extension of immunological studies (particularly in the U.K.) to further understanding of the disease process and perhaps to aid treatment (especially overseas).
8. Development of new chemotherapeutic agents and the organization of systematic screening of a wide range of drugs.
9. Continuation of field trials of chemotherapy (including the development

* Editor's Note: Is there *M. leprae* antigenemia(s) in addition to bacillemia in lepromatous leprosy?—RCH

* Editor's Note: The similarity of many of the research priorities in tuberculosis and leprosy is striking.—RCH

of slow-release drugs), directed particularly at shorter regimens, with full assessment of cost and effectiveness and of variations in the regimens appropriate to different forms of disease.

10. Identification of the treatment failures, assessment of the reasons, and best methods of retreatment of those in whom the primary course has failed.
11. Studies of the toxicity of various drugs in relation to such factors as race, sex, age, nutrition, and the quality of the drugs themselves.
12. Investigation of the value of "prophylactic" chemotherapy for a few special groups.
13. Investigation of the reason for the excess of non-respiratory tuberculosis in immigrants to U.K.
14. Controlled studies of treatment regimens for non-respiratory tuberculosis, especially meningitis and paraplegia.
15. Development of case finding methods appropriate to developing countries.
16. Study of methods for managing contacts of newly diagnosed cases in U.K.
17. Methods for the best delivery of chemotherapy in the field.
18. Surveillance of tuberculosis in U.K.
19. Studies of ethnic, nutritional, and social characteristics relevant to the continued higher incidence of disease in immigrants to U.K.
20. Standardization of methods for tuberculin skin testing and a further national survey in children.
21. Investigation of the present contribution of the national BCG program in U.K.
22. Study of effectiveness of BCG in infants and immigrants in U.K.
23. Review of current studies on the use of BCG in developing countries and determination of strategy for its use, if considered appropriate.
24. Studies of strategy for case finding and management of therapy in developing countries.
25. Assessment of risk to man from tuberculosis in animals.

— (*Adapted from* the article)