

any special footwear and were not admitted to the hospital, but were trained to clean and dress the ulcers themselves at home. None of the patients was immobilized. Skin biopsies were taken from lesions away from the ulcer (the thigh in 15 cases and the back in ten cases) before and after three months of therapy.

In most of the patients the ulcers became clean and healthy in about two weeks. Healthy granulation tissue and re-epithelialization became obvious in the third week and complete healing took place within 6–12 weeks, depending on the size and depth of the ulcers. No recurrence was seen after up to 12–18 months of follow up. One remarkable observation in the skin biopsies after zinc therapy was neovascularization and endothelial cell proliferation in the der-

mis (The Figure). We have consistently observed this phenomenon of neovascularization in patients who are taking zinc for immunostimulation.

Our observations suggest that zinc sulfate might be helping in the formation of healthy granulation tissue by means of neovascularization and endothelial cell proliferation in addition to wound débridement and epithelialization. Further trials are in progress.

—N. K. Mathur, M.D., F.C.A.I.

*Professor and Head*

—R. A. Bumb, M.B.B.S.

*Senior Resident*

*Department of Dermatology*

*S.M.S. Medical Hospital*

*Jaipur, India*

#### REFERENCES

1. COHEN, C. Zinc in bed sores. *Br. Med. J.* **2** (1968) 567.
2. GOLDEN, M. H. N., GOLDEN, B. E. and JACKSON, A. A. Skin breakdown in kwashiorkor responds to zinc. *Lancet* **1** (1980) 1256.
3. HALLBOOK, T. and LANNER, E. Serum zinc and healing of venous leg ulcers. *Lancet* **2** (1971) 780–782.
4. HALLMANS, G. Healing of experimentally induced burn wounds. *Scand. J. Plast. Reconstr. Surg.* **12** (1978) 105–109.
5. HUSSAIN, S. L. Oral zincsulfate in leg ulcers. *Lancet* **1** (1969) 1069–1071.
6. PORIES, W. J., HENZEL, J. H., ROB, C. G. and STRAIN, W. H. Acceleration of wound healing in men with zinc sulfate given by mouth. *Lancet* **2** (1967) 121–124.
7. SERJEANT, G. R., GALLOWAY, R. E. and GUERI, M. C. Oral zinc sulfate in sickle cell ulcers. *Lancet* **2** (1970) 891–892.
8. SÖDERBERG, T., HALLMANS, G., STENSTRÖM, S., LOBO, D., PINTO, J., MAROOF, S. and VELLUT, C. Treatment of leprosy wounds with adhesive zinc tap. *Lepr. Rev.* **53** (1982) 271–276.

### The “Hansen-nergic Fringe” and Renewed Doubts About Vaccination

TO THE EDITOR:

From extensive observations made during the years 1933–1938 in Sao Paulo, Brazil<sup>(8, 9, 10, 11)</sup>, it was hypothesized that about 20% of the human species is genetically incapable of becoming Mitsuda positive after infection by Hansen’s bacillus. This “Anergic Fringe,” now renamed “Hansen-nergic Fringe” (HAF) in order to stress its specificity<sup>(14)</sup>, was supposedly made up of the “predisposed” persons who, “accessory factors” concurring, would eventually develop the various clinico-pathological aspects of bacillary hanseniasis. On the other

side, the majority who inherited a presumed “natural factor” (“N-factor”) of resistance would react positively to the Mitsuda test after said infection and would either remain healthy (“subclinical infection”) or, with the cooperation of those “accessory factors,” would develop non-bacillary macular or tuberculoid disease. An intermediate range was supposed to be responsible for the “intermediate” (now called “borderline”) aspects of the disease.

This pathogenetical theory diverged from the accepted notions of that time that predisposition depended on general debilita-

tion by malnutrition, alcoholism, various infections and infestations. It diverged also from Mitsuda's own viewpoint<sup>(5)</sup> that Mitsuda negativity was a consequence of advanced bacillary hanseniasis and contradicted the authors who believed that Mitsuda positivity or negativity depended, respectively, on a "general" hyper- or hypoergy of the skin to a variety of test substances.

The "N-factor/HAF" theory was rather skeptically received<sup>(15)</sup>, but soon afterwards favorable editorials<sup>(6, 7, 16)</sup> and numerous articles began to admit its plausibility or validity. The hypothesis is now generally accepted, although most authors have coined a confusing and unnecessary variety of designations for the 46-year-old HAF ("constitutional anergy," "insufficient potential immunity," "monovalent anergy," "genetical incapability to develop resistance," "genetical defect," "inherent incapacity to react to Mitsuda" or "to recognize Hansen's bacilli," "primary cellular defect," etc.) and for the "N-factor" ("unconstitutional immunity," "potential immunity," "unknown constitutional factor," "genetical capability to develop resistance," "host-determined capability of recognizing Hansen's bacilli," "innate cell-mediated immunity," etc.).

Fernandez's observations<sup>(3, 4)</sup> that Mitsuda-negative children were converted to Mitsuda positivity by injections of BCG seemed to most authors to annul the existence of that HAF and to herald the beginning of successful vaccination. However, it was observed<sup>(11)</sup> that the HAF remained Mitsuda negative and could be identified in practically all the articles that followed Fernandez's by a 12.5%–25% fringe of "exceptions to the reversal." This fact has led to the admission of BCG and *Mycobacterium tuberculosis* as stimulants of Mitsuda positivity in the "N-factor" majority, but has also confirmed the existence of "non-reactors" and has cast doubts about its preventive usefulness. This rather pessimistic outlook was confirmed by the practically general failure of the World Health Organization's preventive studies with BCG<sup>(1)</sup>, and by the statement of a WHO Committee<sup>(2)</sup> about the "improbability" of a specific vaccine in the near future.

New vaccines and techniques were recently introduced and are being extensively studied. It is obviously desirable that more optimistic conclusions should be reached. However, before extensive, costly, and time-consuming preventive studies in the field are programmed again, it would be advisable to demonstrate in advance that the various types of vaccines do eliminate or, at least, do significantly reduce, the HAF in comparative studies with BCG. This applies to animal experimentation.

Nevertheless, vaccination with BCG or with any other equivalent or more active material seems to be indicated for the general population of endemic areas, especially for contacts, since it artificially and precociously stimulates the "natural reactors," i.e., the "N-factor" majority. As previously stated<sup>(11)</sup>, it would be better to induce the Mitsuda positivity of that majority and not wait for it to occur naturally after the occasional action of *M. tuberculosis* or, worse yet, of *M. hansenii* itself.

—Abrahão Rotberg, M.D.

Rua Pedroso Alvarenga, 125/74  
04531 São Paulo, Brazil

#### REFERENCES

1. EXPERT COMMITTEE ON LEPROSY. Fourth Report. WHO Tech. Rep. Ser. 459, 1970.
2. EXPERT COMMITTEE ON LEPROSY. Fifth Report. WHO Tech. Rep. Ser. 607, 1977.
3. FERNANDEZ, J. M. M. Estudio comparativo de la reacción de Mitsuda con las reacciones tuberculínicas. *Rev. Argent. Dermatol.* **23** (1939) 425–452.
4. FERNANDEZ, J. M. M. Sensitization to lepromin in presumably non-lepromin individuals. *Int. J. Lepr.* **11** (1943) 15–22.
5. MITSUDA, K. Les lépreux maculo-nerveux, d'une part, les tubéreux d'autre part, se comportent différemment à la suite d'une inoculation d'émulsion de tubercule lépreux. *Proc. III Conf. Intern. de la Lepra*, Strasbourg, 1923, pp. 219–220.
6. MUIR, E. Editorial. *Lepr. Rev.* **10** (1939) 104–106.
7. MUIR, E. The unknown factor in leprosy. *Int. J. Lepr.* **7** (1939) 269–272.
8. ROTBERG, A. Some aspects of immunity in leprosy and their importance in epidemiology, pathogenesis and classification of forms of the disease. *Rev. Bras. Leprol.* **5** (1937) 45–97.
9. ROTBERG, A. The reading of the lepromin test. *Int. J. Lepr.* **7** (1939) 161–166.
10. ROTBERG, A. Modern trends in the study of the

- epidemiology of leprosy. Proc. VI Pacific Science Cong., 5 (1939) 939-945.
11. ROTBERG, A. The influence of allergic factors in the pathogenesis of leprosy. Proc. VI Pacific Science Cong. 5 (1939) 977-982.
  12. ROTBERG, A. "N-factor" of resistance to leprosy and its relationship to reactivity to lepromin and tuberculin. Doubtful value of BCG in anti-leprosy immunization. Rev. Bras. Leprol. 25 (1957) 85-106.
  13. ROTBERG, A. Uma visão panorâmica da leprologia moderna. In: *Medicina Tropical*. Lisbon, 1966.
  14. ROTBERG, A. The specific defect of immunity to hanseniasis ("anergic margin"), a 40-year-old Brazilian theory. (Editorial) Hansen. Int. 2 (1977) 12-14.
  15. The Cairo Congress number; immunology and serology. (Editorial) Int. J. Lepr. 6 (1938) 374.
  16. The lepromin test. (Editorial notes). Lepr. India 12 (1940) 115-116.

## Simultaneous Type I and Type II Reactions

TO THE EDITOR:

Dr. Pfaltzgraff<sup>(1)</sup> raises the question of Type I and Type II reactions occurring together. I believe that this is not too rare a combination in BL patients, and in three cases which readily come to mind, it would appear to have been curative.

The first was a teenage girl seen more than ten years ago with numerous, bewilderingly dissimilar skin lesions, before we had considered the possibility of simultaneous Type I and II reactions.

She had been on low-dose dapsone, and while this was raised she was given high-dose steroids. Within a few months there was not a mark on her, and she took herself off treatment. Despite much encouragement to continue with dapsone, she refused. When she became pregnant, we waited for her to relapse but she passed this penultimate test unscathed, and remains well five years later.

Two men have been seen with a similar clinical picture, both with the addition of severe and widespread paralysis. One man

suffered ulceration of numerous nodules and also of most of the patch on one arm which had been his first (presumably BT) lesion years ago. Both made unusually good recoveries on prolonged steroids and clofazimine and, in the last case, with the addition of thalidomide. Of course, one has scars, but their otherwise normal appearance and neurological status is quite remarkable. They both continue to take dapsone, but I have often wondered whether severe and simultaneous Type I and Type II reactions has cured them, as it apparently did the girl.

—J. K. A. Clezy, F.R.C.S., F.R.A.C.S.

5 Rugby Street  
College Park  
South Australia 5069

### REFERENCE

1. PFALTZGRAFF, R. Short-term, multi-drug chemotherapy of leprosy and Type I reaction. (Letter to the Editor). Int. J. Lepr. 50 (1982) 365-366.

## Risks of Treating Leprosy in a General Hospital

TO THE EDITOR:

The paper of Mathai, Rao and Job, "Risks of Treating Leprosy in a General Hospital,"<sup>(6)</sup> contains very valuable data for persons who must design health care and leprosy control programs in highly endemic areas,

such as India. It would seem to be very desirable that the medical care of leprosy patients should be incorporated into the same system of general medical care available to patients with other diseases. Whereas prolonged isolation of patients with mul-