

the care of diabetic patients with lesions of the feet will welcome any form of treatment which may improve results or shorten the prolonged period of disability.

Surgical debridement has been disappointing unless the lesion is such as to permit total excision and immediate split-thickness graft and this is the rare type of lesion. Chemical or enzymatic dissolution of the necrotic tissue has likewise given unsatisfactory results up to this time. Encouraging results following the use of trypsin are reported by Pote elsewhere in this issue. My limited experience with this agent has been less impressive. The true value of this method will be indicated by the role it plays in the management of these lesions in well-organized diabetes clinics in the years ahead.

Until the efficacy of this or any unproven method of local therapy is definitely established, great care must be exercised by all concerned lest injudicious or unnecessarily prolonged trial of enzymatic treatment may lead to unnecessary expense to the patient, delay in the institution of radical treatment when indicated and even to unnecessary loss of limb or life.

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INSULIN-ZINC SUSPENSIONS

Insulin-zinc suspensions may soon complicate the depot-insulin situation still further. Eighteen years after the development of the first depot preparation, just as clinicians began to feel secure in the possession of an array of different insulins which fit the needs of practically all diabetics under all conditions, new preparations now enter the scene. If they had been discovered twenty years ago, it seems doubtful that any of the protein depot insulins would have emerged at all.

In 1935 D. A. Scott and A. M. Fisher, working in Dr. Best's section of the Connaught Laboratories, showed that the addition of a relatively large amount of zinc (0.01 per cent) to solutions of insulin caused a great prolongation of the action of insulin when injected subcutaneously in rabbits¹.

About two years ago Hallas-Møller and his colleagues at the Novo Terapeutisk Laboratories in Copenhagen, reported the precipitation of insulin in simple combination with zinc in the form of amorphous ("semi-lente") and crystalline ("ultra-lente") suspensions². The amount of zinc required for precipitation in insoluble form is in the range of 0.5 to 2 mg. per 1000 units. Amorphous precipitation then occurs at pH 4.5 to 8 and crystals form at pH 5 to 6. Suspensions of the amorphous material show time-action only slightly more

prolonged than that of insulin in solution, but suspensions of the crystalline preparation act in a true depot-insulin manner, with timing similar to that of protamine zinc insulin. Mixtures of the two types of material in proportions of about 30 per cent amorphous and 70 per cent crystalline material give a suspension, called "insulin lente" by the Novo Laboratories, which has an intermediate type of action similar to that shown by NPH, globin and protamine insulin mixtures in common use.

Clinical confirmation of the timing features of these three new preparations was quick to appear³. It was claimed that some patients with severe diabetes showed better control, chiefly with the "lente" or intermediate form. Local allergic reactions were said to be less common than with insoluble protamine modifications. Experimentation with various extemporaneous mixtures of the amorphous and crystalline forms to suit individual diets and patients has begun, chiefly in Great Britain. Clinical trials in the United States are now under way. The report to appear in a coming issue of *DIABETES* by Peck et al summarizes current data and adds significant new evidence on timing⁴.

A judicial appraisal of the potential practical benefits of these new preparations must await further clinical trials. It seems clear at the present time, however, that any required timing can be produced with only the aid of zinc and control of the pH, and that the protein-precipitated insulins could be replaced with such suspensions, if this were desired. It remains to be determined whether predictability of action can be improved or consistency of response enhanced.

Several words of caution should be expressed to those clinicians who may use these new preparations in comparison with standard insulins. The addition of regular insulin to any of them may yield surprising results. They are suspended in an acetate buffer; this permits the insulin-zinc crystals to remain constant in size and form. Alterations in zinc content may change them and therefore the rate at which they go into solution or release their insulin after injection. Acid solutions of ordinary insulin added to insulin-zinc suspensions may alter the zinc content of the crystals, and therefore their physical form and rate of action. In other words, if the Novo preparations (or any similar products) are used they must not be altered much in pH nor mixed with phosphate buffer, or their time-action will be changed radically. Finally, if the views of this commentator are fairly representative of those of clinicians in the American Diabetes Association, the insulin manufacturers are begged to be cautious, in their zeal to be

first with the newest, about adding other insulins to the present ample market. Hopeless confusion can outweigh minor advantages of new products. Five standard insulins are now available in this country. Most of them are now familiar to practicing physicians and their patients. Those insulins and their combinations can do anything for any diabetic patient that is planned by informed physicians. Few disadvantages are inherent in them. In the various fields in which they are indicated they are fairly consistent, reliable and predictable in action and performance.

Before new preparations are introduced, it should be clearly apparent that they possess decisive advantages over those now available. If that is determined to be a fact, it would be desirable to introduce the new insulins to *substitute for and replace* existing preparations. More need not be added. If those which they replace could be withdrawn from the market, with the simple assurance that the new preparations will do the same job better, and can be substituted directly in the management of individual diabetic patients, the new preparations could simplify rather than confuse the commercial insulin situation.

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THE WORLD MEDICAL JOURNAL

The first number of the World Medical Journal appeared in January 1954. This new Journal has replaced the Bulletin of the World Medical Association as the official publication of that organization. Austin Smith, M.D., Editor of the Journal of the American Medical Association, is the Executive Editor; Louis H. Bauer, M.D., a past President of the American Medical Association and currently Secretary-General of the World Medical Association, is the Business Manager. The Editorial Board consists of Hugh Clegg, M.D., Editor of the British Medical Journal, Paul Cibre, M.D., of France, and Lorenzo Garcia-Tornel, M.D., of Spain. It is expected that the Council of the Association will eventually choose a group of collaborating editors who will give wider representation of the medical world. The text of the Journal appears in three languages—English, French and Spanish. It will be published bimonthly, but it is hoped that it will eventually appear each month. The first number contained original articles concerned with relations between the medical and nonmedical press, medical aspects of social security and the utilization of psychiatry in the daily practice of medicine. It presented a calendar of medical and scientific meetings.

The World Medical Association is a unique organization since its members are national medical societies. It represents no governmental agency. In this respect it is unlike the World Health Organization which represents governments. It has conducted surveys and taken part in discussions and decisions on such issues as standards of medical education, the effect of social security on medical practice, the status and distribution of hospitals and medical manpower. It adopted a Universal International Code of Medical Ethics. In some countries, including the United States, there are special committees of physicians who participate in the support of the World Association because of their interest in the interchange of medical ideas.

Membership dues in the United States Committee are \$10.00, of which \$5.00 is paid as subscription to the World Medical Journal. Correspondence relative to membership in the United States Committee should be addressed to the World Medical Association, 345 East 45th Street, New York 17, N. Y.