

## Observations on the Treatment of Leprosy with Lederkyn, DDS and New Tuberculostatic Substances

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Diagnosis of leprosy is a very difficult area for the physician in a country, such as the Federal Republic of Germany, where this disease has no endemic incidence. All too often patients come to special clinics only by various detours. Under some circumstances, to which Jopling has referred, the disease is often not recognized at all for longer periods of time. Thus one of our patients was initially treated under the diagnosis of universal eczema, and another was treated for Morbus Boeck of the skin, before the real diagnosis, leprosy, was finally reached. A female student from Indonesia, who was hospitalized in a ward for internal medicine as a case of febrile exanthematic tropical disease, was later transferred to us; a Portuguese seaman was admitted with the diagnosis of tuberculosis with erythema nodosum. All these patients were foreigners, some seamen, some foreign students, and some foreign workers, but some were staff members of foreign embassies or consulates. With that composition of our patient group, unfortunately, it is a regrettable fact that, after a certain improvement in their condition, most patients wish to be repatriated, so that there is no follow-up observation. Our experience, therefore, can be little more than partial, based on sporadic observations relating to a very small and random group of patients.

The fact that we have, nevertheless, tried to study various questions, and, perhaps, outline some of the problems resulting from this situation, is the reason why I venture to make this report despite the small number of cases.

The knowledge of Lederkyn as a therapeutic measure for other diseases, in con-

nection with the observations reported by Schneider and Languillon<sup>(9)</sup>, Hirako<sup>(4,5)</sup>, Sakurai<sup>(5,7)</sup>, Rao<sup>(6)</sup>, Saúl<sup>(8)</sup> and Vargas<sup>(8)</sup>, as well as by Hentsch<sup>(3)</sup>, has caused us to use this therapeutic substance also in the treatment of our leprosy patients. My collaborator Asshauer<sup>(1,2)</sup> had reported in 1965 on a first favorable experience with such a method of treatment. Subsequently we have submitted another five patients to such treatment, and can generally say that on the whole the success met by this method was satisfactory.

Sulfa-methoxy-pyridazine, known under the proprietary name of Lederkyn, was applied in this therapy at a dosage of between 0.5 and 1.0 gm. per day. The total dose for four weeks of uninterrupted treatment was between 18 and 21.5 gm. For continued maintenance treatment for longer periods of time we chose a dosage of 0.5 gm., or one tablet, per day. When applying this dosage the following points, appearing particularly striking to us, seem to deserve special mention:

(1) The medicament was found to be fully compatible with the organism of patients, and even after longer application we observed no gastrointestinal side effects in our cases.

(2) It is true that some reactions did occur, but, to the extent that this can be derived at all from so small a number of cases, we have gained the impression that the reactions were not as severe as those seen by us previously when giving Promin and Promizole. In no case was it necessary to discontinue application of the drug. The duration of the treatment in our cases was between two and nearly 16 months.

In our patients under treatment with these medicaments we made a number of observations which were partly reported by Bücken before. In addition to these

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reports I should like to refer to the following points:

(1) We were interested in the behavior relating to the Sabin-Feldman test and the toxoplasmosis complement fixation reaction in leprosy patients. In all of our patients—we investigated a total of six—the test reactions were negative.

(2) We also checked the behavior of the rheumatic serology situation in two of our cases, and found that during the entire period of treatment (6 months) one case had an unchanged high ASL titer of 1:600, an RF-latex titer of 1:40, and a positive CRP reaction. In the second case these test values were only slightly increased.

(3) All cases revealed an increase in gamma globulin, a condition changing little under the treatment.

In conclusion let me refer once again to a case already reported by Bücken, as this observation seems to have a certain significance warranting further attention. Upon the suggestion of Freerksen we treated this patient, suffering from lepromatous leprosy, with Rifampicin and Myambutol. The schedule and dosages applied were as follows: First therapy shock, for 10 days, daily doses: 900 mgm. of Rifampicin and 1200 mgm. of Myambutol, followed by three days of interruption. Second therapy shock: for 7 days, daily doses: 900 mgm. of Rifampicin, and 1200 mgm. of Myambutol.

Fever developed and new skin efflorescences appeared on the last day of the first drug shock. The fever continued during the interruption period and during the second shock therapy, and rose to a very high level toward the end of the second treatment shock. Because of this and the onset of major vomiting, events which could not be checked or influenced by any means whatever, treatment had to be discontinued. The leucocyte count had risen from 11,000 to 21,000. Blood serum globulin was up from 110/122 to 138/144. Of particular significance, however, we regard the following findings: The previously present open skin patches had already begun to close under the treatment. The changes in the laryngeal region, found by Jaffé,

our specialist for ENT diseases, had not yet disappeared, it is true, but had not deteriorated in any way. The general condition of the patient, however, was better after the fever ceased, on the fifth or sixth day following discontinuation of administration of the drug. In the subsequent period the treatment of the patient was continued with Lederkyn, as described above.

Quite obviously this case responded well to the combined treatment. No renewed hepatic and sternal punctures were carried out on this patient. However, it appears to us that the normalization of transaminases, and the continuously improved general condition of the patient, seem to count in favor of the assumption that this treatment has also favorably influenced the hepatic foci. Perhaps, in the future, the occurrence of reactions can be favorably influenced by means of thalidomide, which would seem to open the way for a combined treatment with Rifampicin and Myambutol.

#### SUMMARY

Lederkyn was tested clinically for the first time by Schneider and collaborators in 1958. They found rarer occurrences of reaction episodes and a generally milder course of such reactions. Moreover, the treatment was found to be effective also in cases of resistance against sulfone therapy (Hirako and Sakurai). This therapy seems to be particularly successful in cases of tuberculoid leprosy (Hentsch). But, it produced favorable effects against lepromatous manifestations also (Rao). These advantageous results in lepromatous manifestations were confirmed by findings of Asshauer in 1965. The initial success of treatment led us to try this treatment in five additional cases.

Although leprosy reactions were found to occur even under treatment by Lederkyn, they were not as grave, and did not necessitate any discontinuation of administration of this drug. Another advantage of this treatment was the small dosages required, viz., initially two, later one tablet per day, and to the very good tolerance thereof. Nearly always no gastrointestinal symptoms appeared, even if the drug was administered for longer periods.

Experiments combining Lederkyn and DDS in treatment were also made. If administered in this combination Lederkyn was well tolerated, and appeared to be of favorable effect. It seems recommendable to test the combination in larger series of treatment, as under certain conditions such a combined treatment may permit reduction of dosages of both drugs.

In addition a clinical trial with the combination of Rifampicin and Myambutol is reported. It seems to have a favorable effect, but may result in an intense leprous reaction.

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