

## LIMITED PILOT TRIAL TREATMENT OF LEPROSY BY GRISEOFULVIN

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Because of the interest in Griseofulvin in respect to its fungicidal properties, it was felt that it would be useful to undertake a very limited preliminary trial in order to ascertain whether Griseofulvin has any effect on the *M. leprae*. Early workers, particularly REENSTIERNA, was of the opinion that *M. leprae* was originally a soil fungus and, over the centuries, adapted itself to human tissues. It seems, therefore, to be a reasonable hypothesis that Griseofulvin might have an effect on the *M. leprae*.

The following two cases under a short trial with Griseofulvin are reported:

### CASE NO. 1

**Ladi Bubwa.** Hospital Case No. 6945. Age 9. Body weight 50 lb., dose 0.5 g. daily for one week and 0.75 g. daily in divided daily doses thereafter.

**Classification.** Advanced Nodular Leprosy.

**History.** Both mother and father have leprosy as also have her two brothers. Two sisters are healthy; a half-brother under treatment in the Leprosarium. Onset of disease, 4 years previously (that is 1957). Admission weight: 30 lb., height: 4 ft. 3 in., Hg. index 14 gm. Stools and urine: nothing abnormal discovered. BI highly positive (5+).

*Biopsy No. 1 taken 2.5.62. Lab. No. 4376*

**H.E. Section.** There is a mass of infiltration in the corium occupying 100% of the surface of the corium; the infiltrate does not extend up to the epidermis, but leaves a very clear sub-epidermal zone. The infiltrate consists of closely packed histiocytes with some, but not conspicuous, round celled infiltration. The skin elements are almost completely obliterated by the great mass of infiltration, but there appears to be remnants of a hair follicle around a small focus of lymphocytic cells and a few plasma cells. In this mass of infiltration, individual cells are difficult to recognise. No nerves are seen in the infiltrate and there is some evidence of foamy cell change.

**F.F. Stain.** Large masses of acid-fast bacilli seen in every field. The bacilli show definite morphological change. Nerves are not easy to recognise because they are distorted as a result of proliferation of the connective tissue (perineurium) and the massiveness of the cellular infiltrate tending to obliterate nerve and skin appendages.

**Diagnosis.** An advanced lepromatous case, active, but not in reaction.

*Biopsy No. 2 taken 19.6.61. Lab. No. 4419*

**H.E. Section.** There is an intense and massive infiltration under the epidermis occupying the whole of the dermis leaving a narrow but relatively clear sub-epidermal zone. The infiltration consists almost entirely of a mass of closely packed histiocytes with a great many plasma cells scattered among the histiocytes. An occasional nerve is seen, but the nerves are probably compressed completely owing to the massive histiocytic infiltration. In some areas, the skin appendages are almost entirely obliterated except for an occasional hair follicle cut across and remnants of sweat ducts.

**F.F. Stain.** Very large numbers of acid-fast bacilli showing very marked morphological change.

**Diagnosis.** A very active (? reacting) lepromatous case of moderate severity.

*Biopsy No. 3 taken 5.9.61. Lab. No. 4588*

**H.E. Section.** There is a massive infiltration occupying a hundred per cent (100%) of the corium which does not extend up to the epidermis but leaves a clear sub-epidermal zone. The infiltrate consists almost entirely of histiocytes of the larger macrophage variety; interspersed between the histiocytes is some lymphocytic infiltration, but this is not particularly significant, also here and there, there are collections of plasma cells. In some areas the larger

macrophages have the appearance, but not the setting of epithelioid cells. No nerves are recognisable in the massive infiltration.

**F.F. Stain.** There are numerous numbers of acid-fast bacilli seen, most of which are crammed in the macrophage cells.

**Diagnosis.** This is a very active lepromatous case, not in reaction. The fact that no nerves are discernible in the Trichrome Section may or may not be significant. The diagnosis is an active lepromatous case showing influence of therapy. (It should be noted that while the second biopsy report showed marked morphological change in the bacilli, the third biopsy showed no signs of such changes, and that the number of bacilli, if any, had increase for the note is that 'there are enormous numbers of acid-fast bacilli and most of the macrophages were crammed with bacilli'. In these circumstances it was felt that Griseofulvin was having no effect on the disease and, therefore, the treatment was discontinued.)

#### CASE NO. 2

**Merama.** *Hospital Case No. 6954.* Body weight 120 lb.

**History.** Patient gave history of leprosy for four years. The first lesion started on the left leg, where there is an area of anaesthesia. The patient's husband also has leprosy. She has three children. Two died previously, and now one child, boy aged three months. On admission weight: 120 lb., height: 5 ft. 4 in., Hg: 15 gm. Stools and urine: negative. Bacteriological result: Rt. ear 3+, forehead 2+. The patient clinically shows all the features of a moderately early diffuse lepromatous case and treatment was commenced on 17th May 1961. Dosage given was 0.5 g. daily for 1 week, then 1.0 g. daily thereafter in divided dosage.

*Biopsy No. 1 taken 17.5.61. Lab. No. 4450*

**H.E. Section.** There is a scattered infiltration underneath the epidermis with a relatively clear sub-epidermal zone. In the dermis proper, the infiltration is much more intense, especially in the region of neuro-vascular bundles.

The infiltration generally is lymphocytic and histiocytic; the lymphocytic response, however, is not focalised in any particular pattern. Nerves are most easily recognised because of the intense infiltration, but when they are seen they are not involved.

**F.F. Stain.** Scattered acid-fast bacilli seen in moderately numerous numbers amidst the cellular infiltrate.

**Diagnosis.** A moderately early lepromatous case.

Patient continued treatment from 17/5/61 through to 5/9/61—a period of approximately four months. At the end of this period, that is on 5.9.61, a further biopsy was performed following in the histopathological report.

*Biopsy No. 2 taken 5.9.61. Lab. No. 4587*

**H.E. Section.** There is an infiltration underneath the epidermis extending the whole length of the superficial part of the corium leaving a relatively clear sub-epidermal zone. The infiltrate is moderate to gross in intensity, and consists chiefly of histiocytes and lymphocytes: there is no evidence of foamy cell change, neither is there any evidence of the focal distribution of the lymphocytic response. Because the biopsy is too shallow, nerves cannot be readily seen: I think I can see an occasional nerve twig, which is uninvolved but apart from this I cannot recognise any nerve tissue.

**F.F. Stain.** Moderately large numbers of acid-fast bacilli seen throughout the granulomatous infiltration showing marked morphological change.

**Diagnosis.** The general impression is that this is a moderately early lepromatous case which, because of the granularity of the acid-fast bacilli would indicate that the case is under the influence of therapy.

#### General Conclusion

Although during this period, the *M. leprae* showed considerable morphological change, clinically there was no marked improvement, and further, owing to the fact that when the patient was admitted it was noticed that the *M. leprae* showed morphological change. It was thought that this finding was hardly significant. The morphological change seen in the bacilli in the first biopsy possibly indicated that she had received Sulphone therapy elsewhere, for this is regularly available, or it may simply be that the *M. leprae* showed a significant

change in morphology, because it is known that even when a case is not under therapy *M. leprae* can show morphological change, for in the natural course of the disease, there are periods of quiescence and activity. The conclusion, therefore, was that this patient has shown no significant improvement in the four months she was under Griseofulvin therapy, therefore it was not considered justified to continue her treatment. She was put on standard D.D.S. therapy and has since shown quite marked improvement.

### Summary

Two cases of lepromatous leprosy. One a moderately advanced lepromatous case, the other a moderately early diffuse lepromatous case, were given Griseofulvin therapy, and in neither instance was there sufficient improvement or indication of sufficient improvement to justify the continuation of the remedy, and therefore, it must be concluded that Griseofulvin has little or no action on the *M. leprae*, and therefore, it is not advised as a treatment for the disease.

The Griseofulvin was supplied as Fulvicin by DR. JOSEF KOLENSKI, M.D., of the Clinical Research Division of Schering Corporation, Bloomfield, New Jersey, U.S.A.