voted his whole time (and we could almost say "his whole life") to this purpose. We naturally would not risk opening another workhouse unless we could count on a monitor of his preparation and qualities. Therefore, we have already built a new factory with the same characteristics as the other but with ten times its capacity.

The eradication of leprosy is more difficult in some regions than in others. In our opinion it is an easy task in those countries which are highly developed; here we can mention the Scandinavian countries as a good example. But in order to reach the long wished for eradication of leprosy, as important as the health services are, perhaps even more important is the social problem. To this end we have organized several activities.

In collaboration with the National Health Service, we have organized basic courses in leprology for scholars and people without any previous knowledge of the disease, as well as more advanced courses, given by leprologists and social assistants who work with these people, in order to develop social workers (usually members of the "Amigos de los enfermos de lepra") whom we later send to the endemic provinces in Spain where they make a social and economic study. More specifically, in the first province checked we found 17 new cases in a total of about 400 families interviewed. Also, due to the close relations of our association with several dermatologists there have been some cases of people who come to us fearing that they suffer from leprosy or even from other dangerous skin diseases such as ichthyosis, with the hope that we might help them.

We keep in touch with most of the associations all over the world with similar interests to ours. We are pleased to say that there are a large number of them. We wish these associations all the best and encourage them to surpass us, while we take the opportunity to beg them to share with us their ideas; and we invite them to visit us, wishing to serve, if not as a model, at least as a stimulus.

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Clofazimine Pigmentation

To The Editor:

When Barry first started writing about the successful use of clofazimine he suggested that its extra-ordinary antituberculous effect in mice might be due to the fact that experimental tuberculosis is essentially an intracellular infection and suggested that the drug was phagocytosed into cells containing bacilli. It was this thought, combined with the fact that clofazimine is soluble in lipids that caused the initial work on B663 to be undertaken.

The paper by Sakurai and Skinsnes (IJL **45** [1977] 343-354) shows the presence of a brown pigmentation due to ceroid-like substance in macrophages in a series of three cases of lepromatous leprosy treated with clofazimine. This is indeed interesting but does not explain the blackish-brown pigmentation caused by lesions treated with oral clofazimine because such pigmentation also occurs in the undermined skin of *M. ulcerans* cases treated with clofazimine (Pettit: Br. J. Dermatol. **81** [1969] 794-795). I think it is reasonable to say that lipid-containing macrophages do not seem to be very common in the "buruli ulcer" pathology and so it would be logical to assume that the blackish-brown pigmentation cannot be entirely due to the findings reported by Sakurai and Skinsnes. I hope they will be able to report similar careful studies of hyperpigmented skins from such cases. It is also interesting to note that the successful use of clofazimine in *pyoderma gangrenosum* (Michaelsson *et al:* Arch. Dermatol. **112** [1976] 344-349) was not reported to be associated with any discoloration other than the usual redness. Perhaps studies on other diseases treated by this interesting drug should also be undertaken.

—John H. S. Pettit, M.R.C.P.

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Reply: *It is interesting, as Dr. Pettit notes, that a brown pigmentation also occurs in the undermined skin of* M. ulcerans *lesions treated with clofazimine and that the use of this drug in* pyoderma gangrenosum *is not reported to be associated with any discoloration other than the usually observed redness. We have no experience with this type of material. Dr. Pettit does not indicate whether or not the findings he refers to are based chiefly on routinely stained tissue sections or on extended histochemical studies comparable to those we utilized in studying the pigmentation process in lepromatous tissues.*

Several observations and questions come to mind.

1. *At what location in the skin does the pigment in* M. ulcerans *infection occur—epidermis, upper corium, lower corium, or subcutis? If it is in the epidermis or upper corium it might be melanin.*
2. *Ceroid may be deposited also extracellularly, as is often seen in atherosclerotic lesions. This pigment does not necessarily accumulate intracellularly.*
3. *A later stage brown pigmentation in leprous lesions may follow the destruction of bacillary waxy capsuls with oxidation of lipids. Our findings suggest that the color of the drug itself may not necessarily be the prime factor in the appearance of the lesion pigmentation occurring during its use. Metabolic changes related to the lipid materials from the bacillary capsuls and their oxidation processes, perhaps influenced by the drug, may be significant or even major factors in the development of this pigmentation. Dr. Pettit's observations may support this concept.*
4. *Macrophages ("foam cells") in lepromatous leprosy may have neutral fat in the lipid globules. Such neutral fat may contain carotenoid pigment and also soluble drug and these may play a role in pigment accumulation.*
5. *Melanin and/or hemosiderin may be deposited in skin around ulcerations such as those of* M. ulcerans *infection and need to be differentiated from other pigments.*

It would appear that careful histochemical studies of diseases other than leprosy where clofazimine is used are needed to help determine whether or not the pathogenesis of pigment formation in these instances truly differs from the findings we reported. Though we had a limited series of lesions for our study the findings were consistent.

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