Is It Safe to Treat the Lepromatous Patient at Home?

A Study of Home Exposure to Leprosy in Hong Kong'

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It has been known for several years that Mycobacterium leprae organisms recovered from a lepromatous leprosy patient begin to change their staining characteristics after the patient has been under sulfone-therapy for a few months, giving rise to a higher and higher proportion that do not stain solidly. This has led to the so-called "morphologic index" as a guide to the response of a patient to therapy (⁸). Morphologic changes in the organisms recovered from a patient under therapy can also be observed by electron microscopy (7). Recently Shepard, Fasal, and Levy (9) have shown that after a few months of sulfone therapy the M. leprae organisms recovered from patients fail to grow in the mouse foot pad, even though still plentifully present in the patient. These observations suggest that a lepromatous patient may lose his ability to transmit the disease to others shortly after he begins sulfone therapy. It is the purpose of this study to test this hypothesis in a cohort of children at maximum risk of transmission.

The safety of the generally accepted practice of treating tuberculoid leprosy patients at home has been clearly demonstrated (¹⁴), but the management of lepromatous leprosy is characterized by a wide variability of practices. Some jurisdictions (such as Japan and Hawaii) require that a person with lepromatous leprosy remain isolated from the public until *M. leprae* organisms can no longer be demonstrated by either skin smear or biopsy. This may take as long as five or 10 years with currently used sulfone drugs, resulting in high institutional costs and the creation of permanent psychosocial disruptions in the patient and his family. Other jurisdictions (such as Fiji) (¹) require that the patient remain isolated until sulfone treatment has resulted in a definite change in the morphologic index of the organisms, indicating a response to the drug. This takes a few months in most cases (^{2, 4, 9, 10}).

In most countries where limitations of staff and facilities prevent the long-term hospitalization of lepromatous patients, the hospital is reserved for those requiring surgery or requiring close medical supervision for complications. Meanwhile, many lepromatous patients are allowed to remain at home under sulfone therapy, with supervision from outpatient clinics, supplemented by home visits from public health nurses and social workers as necessary. Hong Kong has followed this practice for many years, with good clinic records and a rather careful system of annual or biennial examinations of household contacts for the past 15 years (11). Because of the low rate of out-migration from Hong Kong, and because of the careful, faithful work of the Medical Department staff, it is possible to test the safety of this practice by observing over a long period of time the development of subsequent leprosy in a large cohort of children who were living at home with at least one lepromatous parent, with no efforts at isolation or segregation within the home.

METHODS

With the kind help of Dr. P. H. Teng, Director of Medical and Health Services, Hong Kong, it was possible to identify, from existing clinic records, all families that met the following criteria:

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1. New admission to Special Skin Clinics during 1954-1960, with histologic and clinical confirmation of lepromatous leprosy.

2. No prior therapy.

3. Sulfone therapy instituted on an outpatient basis (usually DDS in recent years).

4. Patient living at home with his/her children, and exposing them while still bacteriologically positive and while the children were under age 12.

5. Children not receiving chemoprophylaxis, but remaining in residence with a parent and examined regularly at the Special Skin Clinics. A child had to survive to age three to be counted.

Sixty-six such families were identified. Under the very crowded housing conditions of Hong Kong all of these children had varying degrees of bed contact, room contact, or house contact with a lepromatous patient. These children were young enough to be considered at risk of subsequent disease, and also they were descended from at least one parent who had demonstrated a susceptibility to leprosy through developing the lepromatous form of the disease. After identification of this cohort of children at maximum risk, it was possible to separate them into the following three classes: 1. Those already living at the time of onset of the disease in the parent (child exposed prior to the onset of therapy in the parent).

2. Those born into the home *after* the parent had started on sulfone therapy, but while his skin was still bacteriologically positive.

3. Those born into the home after the parent's skin had become bacteriologically negative.

All of the children's records were then categorized as to the age of the child at the time of first exposure, the number of years of *recorded* follow-up at the skin clinic, and the development of subsequent leprosy. No special attempt was made to give these children BCG vaccine, but it is highly probable that a large majority of them received BCG if tuberculin-negative at the time they entered school at age six or seven. Most of these children were born too early to have been included in the present Hong Kong program of BCG vaccination in infancy, which has been very thorough in more recent years.

RESULTS

In two of the 66 families both parents had lepromatous leprosy. Table 1 describes the remaining 64 families (which contained

TABLE 1. Distribution of lepromatous parents^a in 64^b families by sex of infected parent, number of children already in household at the time signs of leprosy began in the parent, and sex of children subsequently developing leprosy (Hong Kong, 1954–1967).

	Sex of infe	cted parent			
	Male	Female	Totals		
Number of parents	37	27	64		
Number of young children in family at time of onset of lepromatous leprosy in					
parent.	69	40	109		
Number of children subsequently devel-	4	2	6 out of 63 boys		
oping leprosy.	2	2	4 out of 46 girls		
	6 out of 69 children	4 out of 40 children			

* Parents identified by 1954–1960 new case admissions to Hong Kong Special Skin Clinics.

^b Two families in which *both* parents were childless lepromatous patients at the time of marriage, have been deleted from the 66 families for the purposes of this distribution.

all 10 of the cases of subsequent leprosy in the children) with regard to the number of young children (109) in these families at the onset of clinical signs in the parent, by the sex of the lepromatous parent, and sex of the child who developed leprosy. One notes an even distribution of risk by sex of parent or sex of child. The slight excess of risk noted in sons of infected fathers is not statistically significant. Among the 64 noninfected spouses, 37 were observed carefully enough over at least a 10 year period to be considered at risk. Of these 37, three (8%)subsequently developed leprosy themselves.

In all 66 families studied a total of 177 children were identified who met the criteria listed above. Table 2 shows the distribution of these children by category of exposure to the parent, length of follow-up in the clinic, and diagnostic outcome of the child at the most recent clinic visit (mostly in 1966 or 1967).

It is evident from Table 2 that children observed less than seven years should not be considered at risk, since follow-up is too brief. It should be noted that the children born after the parents started sulfone treatment have, by now, accumulated a respectable total years-of-experience without developing leprosy. As expected, the small group of children born after their parents became bacteriologically negative have not developed leprosy. In order to look at the effect of the age of the child at the time of first exposure to a parent with clinical signs of lepromatous leprosy, a special distribution was made of the 109 children exposed to the parent before sulfone therapy was started. The children who were followed less than seven years were then excluded from the calculation of risk. The data are shown in Table 3.

On examining the data for each age group in Table 3 one notes a fairly constant risk (allowing for variability due to small numbers) through age six. There is an abrupt drop to zero risk at that point, no subsequent cases of leprosy being observed in those children first exposed during ages 7-11. Two hypotheses to explain this observation are suggested below.

TABLE 2. Distribution of 177^a children in 66 families in which at least one parent with lepromatous leprosy was living at home, by clinical and therapeutic status of the parent and by subsequent leprosy in the child (Hong Kong, 1954-1967).

	Time (yrs.) followed in leprosy clinic ^b	Diag	-		
		Leprosy	Not Leprosy	Total	Person-years of follow-up ^b
Children exposed to	10+	8 (11.6%)	61	69) 95 at	961
parent prior to start of	7-9	2(8.3%)	24	26 risk	$\overline{\mathbf{X}} = 10.1^{\circ}$
sulfones in parent	3–6	0	14	14	
Children born into home	10 +	0	15	15) 30 at	257
after parent started on sulfones, but when skin	7–9	0	15	15 angler sk	$\overline{\mathbf{X}} = 8.6$
was still bacteriologically positive	3-6	0	12	12	
Children born into home	10 +	0	0	0] 5 at	37
after parent's skin became	7-9	0	5	5 rsk	$\bar{X} = 7.4$
bacteriologically negative	3-6	0	21	21	

 ^a Two children who received chemoprophylaxis for one year have been deleted; no other children received any chemoprophylaxis. Children were not counted unless they survived at least 3 years after birth.
 ^b The period of time a child was followed, calculated by subtracting time of first exposure of child to a parent with clinical signs from time of most recent examination in Special Skin Clinic. ^{\circ} $\mathbf{\tilde{X}}$ = person years of follow-up/number of children at risk.

TABLE 3. Distribution of 109 children by age at the time the clinical signs of leprosy first developed in their parent, by duration of clinical observation of the child and development of subsequent leprosy in the child (Hong Kong, 1945-1967).

	Age in years at first exposure												
	0	1	2	3	4	5	6	. 7	8	9	10	11	Total
No. of children Less those not followed at least 7 years ^a	25 1	9 2	9 1	11 2	7 1	12 2	7 1	10 3	9 1	5 0	3 0	2 0	109 14 ^a
Total at risk	24	7	8	9	6	10	6	7	8	5	3	2	95
No. cases of leprosy arising from cohort	1	2	0	2	1	2	2	0	0	0	0	0	10

^a No cases of leprosy have yet appeared in any of these 14 children who have been observed six or fewer years, and therefore they are counted as not being at risk (See Table 2).

The crucial test for this study then becomes the comparison of those 70 children who were exposed prior to age seven to their untreated lepromatous parents (and who were subsequently followed for at least seven years in the clinic) with the 30 children born into these families after therapy was started in the parent and exposed during the first few years of their lives to a parent who still had bacteriologically positive skin (and who were subsequently followed for at least seven years in the clinic). These data are summarized in Table 4.

With Yates' correction for small numbers the difference in risk between these two groups reaches a borderline zone of significance (p = 0.07).

DISCUSSION

The incidence of subsequent leprosy found in this study in the children already in the home at the time the lepromatous parent was diagnosed is in the same general range as that found (11%) in a larger cohort of children living with a lepromatous Hawaiian parent in a study in Hawaii (14). The dramatic drop to zero risk of

TABLE 4. Distribution of children who were age 0-6 when first exposed to a lepromatous parent and who lived at home with him, by therapy of parent during the period of exposure and by development of subsequent leprosy in the child during a 7-22 year period of observation in Hong Kong.

	Diagnos		
	Leprosy	Not leprosy	Total at risk
Children exposed to parent prior to start of sulfone therapy in parent Children bern into home after parent started on	. 10	60	70
sulfone therapy, but when skin was still bacteriologically positive	0	30	30
Total	10	90	100

 $\chi^2 = 4.76$, ldf., p = 0.03. χ^2 with Yates' correction = 3.306, ldf., p = 0.07.

these Hong Kong children first exposed at age seven or older is certainly too sudden to be a part of the generally accepted downward gradient of risk of leprosy as one grows older. The limited data available from the noninfected spouses in this study would indicate that the age gradient is gradual, since the average risk of the young (age 0.6) children (10/70 = 14.3%) is only moderately higher than that of the noninfected parents (3/37 = 8%), who presumably continued in bed-contact with their infected spouses. It is very likely, however, that the sudden drop in risk imong the older children is related to an age-related change in exposure. Under the present housing conditions in Hong Kong, and given the living habits of many of the people, it seems reasonable to advance the hypothesis that the children usually leave their parental bed and have much less physical contact with the parents at about age seven. Cantonese parents fondle and touch their young children very frequently, but this practice ceases almost altogether as a child gets older. An alternative hypothesis would be that upon entering school at age seven the children receive BCG, which lowers the subsequent incidence of leprosy in exposed children (5). An attempt will be made to assess the BCG history of these children. In any case, the data certainly would not fit the pattern one would see with a respiratory route of transmission, since in Hong Kong housing the air is rebreathed intimately with both older and younger children, especially when it gets cold in the winter, and the windows are shut. This observation would also certainly not fit any insect vector hypothesis of transmission.

The epidemiologic evidence presented here is in complete concordance with the morphologic and cultural evidence noted in the first paragraph of this paper and supports the hyothesis that even under conditions of *maximal* risk, sulfone therapy is able to prevent transmission. This hypothesis should be confirmed by other workers who may have access to larger numbers of children similarly exposed and followed. The author intends to follow the children in this study until all have been observed over a period of at least 10 years. If current trends continue, there will be unequivocal statistical reliability at that point.

With our current knowledge, it seems reasonable to suggest the following pattern of management of lepromatous leprosy, a pattern designed to give maximum protection to the physical and social health of a patient *and* his family, while at the same time satisfying all reasonable obligations to protect the health of the general public:

1. The patient with confirmed lepromatous leprosy should be admitted to the hospital for a brief period (probably not over 3 to 4 months) in order to stabilize him on sulfone therapy and to give him intensive education about his disease and his life-long responsibility to cooperate in its management. Necessary social work and vocational rehabilitation activities can be instituted at this time, with full involvement of his family in the entire process.

2. He should then be allowed to return home under continuing therapy to be followed as an outpatient. He should be advised to break bed contact (but not house contact) with his children. This is advisable, but not mandatory.

3. The spouse, children, and all other household contacts should be given BCG for partially effective prophylaxis $(^{3, 4, 12})$.

4. The spouse and all children born prior to the start of therapy of the patient should be placed under sulfone chemoprophylaxis for three years for partially effective prophylaxis (³).

5. All recent household contacts should be examined annually for an indefinite period of time, except for those persons coming into contact *after* the start of sulfone therapy in the patient, who will not need intensive surveillance.

6. The hospital should be available to the patient for temporary readmission to care for medical or surgical complications, or for those who will not or cannot take sulfone drugs, particularly while they are undergoing ENL reactions. If they wish to remain at home during these reactions, it would seem important to continue sulfone coverage (along with the corticosteroids) if it is at all possible. Otherwise they should reenter the hospital temporarily for care during the ENL reactions. This care may be given in either special or general hospitals, depending on the local situation. Antiquated practices, such as fumigation of mail going out of leprosaria, removal of infants from their mothers at birth, etc., should be stopped.

Any program more strict than this would be socially disruptive, unnecessary, and expensive. It might be necessary, however, to run a program less strict than this, because of shortage of funds or trained people, but to do so would allow those people in recent household contact with the lepromatous patient to run a very high risk of developing leprosy. The most difficult part of this suggested program will be to ensure that the patient continues regularly on treatment for an indefinite period. This is a crucial requirement, and may be the most costly element in the program, since someone (who need not be highly trained) may have to visit the patient several times a week to administer the DDS and to make sure that it is, in fact, swallowed.

Relief may soon be in sight, however. A new DDS derivative (DADDS, Parke, Davis & Co.) has the excellent feature of intramuscular administration, requiring only one injection every 75 days to maintain adequate therapeutic levels. Shepard et al. have reported very encouraging clinical trials in 10 patients in the Philippines (10) and extensive mouse foot pad trials (9). This drug is now being given extensive field trials for both therapeutic and chemoprophylactic purposes by Sloan and Worth (12) in Micronesia, where it is demonstrating low toxicity, high patient acceptance, and low cost per person per year.

Those places that shift from a strict hospital isolation program to the program suggested above will continue for a while to face the problem of disposition of patients physically crippled by long-standing disease and/or socially crippled as a result of prolonged institutionalization. A difficult problem will also continue to exist in those few patients who develop sulfone-resistant strains of *M. leprae* (6), and it will become increasingly important to use the mouse

foot pad method as a means of selecting the most appropriate drugs for patients not responding well to sulfones. Since the treatment of lepromatous leprosy by sulfones is so slow and often so discouraging, it is morally imperative to make every possible effort to carry out primary preventive measures to protect those who have been exposed, so that they will never develop this disease.

SUMMARY

In 66 Hong Kong families with at least one lepromatous parent treated at home de novo, there were identified 70 young children who have been examined regularly in skin clinics for a minimum of seven years after the parent first developed the disease. Ten of these children have subsequently developed leprosy. Of the 30 similarly examined children born into these same families after the parent started taking sulfone drugs, but before his skin became bacteriologically negative, none has as yet developed leprosy. This agrees with mouse foot pad and morphologic evidence that sulfone drugs rapidly provided a "chemical isolation" of the lepromatous patient, so that physical isolation of the treated patient is no longer justifiable.

RESUMEN

En 66 familias de la ciudad de Hong Kong que tenían, por lo menos, uno de los padres con lepra lepromatosa tratada de novo en el domicilio, se identificaron 70 niños que se habían examinado regularmente en clínicas para enfermedades de la piel por un período mínimo de siete años luego que el padre desarrolló la enfermedad. Diez de estos niños enfermaron posteriormente de lepra. De 30 niños que fueron igualmente examinados en las mismas familias después que el padre comenzó a tomar sulfonas, peros antes que su piel se hiciera bacteriológicamente negativa, ninguno de ellos ha desarrollado lepra todavía. Esto está en acuerdo con el colchón plantar de los ratonnes y la evidencia morfológica de que las drogas sulfónicas rápidamente establecen un "aislamiento químico" del enfermo lepromatoso, de tal manera que el aislamiento físico de los enfermos tratados no encuentra más justificación.

RÉSUMÉ

Dans 66 familles de Hong-Kong, comprenant au moins un parent lépromateux, traité à domicile et pour la première fois, on a identifié 70 jeunes enfants qui avaient été régulièrement examinés dans des dispensaires pour maladies de la peau, et ceci pour une période de 7 ans au moins après que le parent malade ait développé la maladie. Dix de ces enfants ont ultérieurement développé la lèpre. On a par ailleurs examiné 30 enfants semblables, qui étaient nés dans les mêmes familles après que le parent ait commencé à prendre des médicaments sulfonés, mais avant que les examens bactériologiques cutanés de ce parent soient devenus négatifs; aucun de ces enfants n'a encore développé la lèpre. Ceci est en accord avec les données mises en évidence par les études menées sur la sole plantaire de la souris, ainsi qu'avec les données morphologiques, selon lesquelles les médicaments sulfonés entraînent rapidement un "isolement chimique" du malade lépromateux; il en ressort donc que l'isolement physique du malade traité n'est désormais plus justifiable.

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REFERENCES

 BECKETT, D. W. Personal communication
 BROWNE, S. G. Some observations on the morphological index in lepromatous leprosy. Leprosy Review 37 (1966) 23-25.

- FASAL, P., FASAL, E. and LEVY, L. Leprosy prophylaxis. J. American Med. Assoc. 199 (1967) 905-908.
- GOODWIN, C. S. Histological, bacteriological, and immunological differences between the bacilliferous forms of leprosy in Chinese. Leprosy Review 38 (1967) 171-180.
- KINNEAR BROWN, J. A.; STONE, M. M. and SUTHERLAND, I. BCG vaccination of children against leprosy in Uganda; Results at end of second follow-up. Brit. Med. J. 1 (1968) 24-27.
- PETTIT, J. H. S. and REES, R. J. W. Sulphone resistance in leprosy. An experimental and clinical study. Lancet 2 (1964) 673-674.
- REES, R. J. W. and VALENTINE, R. C. The appearance of dead leprosy bacilli by light and electron microscopy. Internat. J. Leprosy **30** (1962) 1-9.
- REES, R. J. W. and VALENTINE, R. S. 1. Application of quantitative electron microscopy to the study of *M. lepraemurium* and *M. leprae*. In Leprosy in Theory and Practice. Cochrane, R. G. and Davey, T. F., Eds. Bristol, John Wright & Sons, Ltd.; Baltimore, Williams and Wilkins Co., 2nd ed., 1964, pp. 26-35.
- 9. SHEPARD, C. C. Personal communication (manuscript in preparation),
- SHEPARD, C. C., TOLENTINO, J. G. and MCRAE, D. H. The therapeutic effect of 4,4' - diacetyldiaminodiphenylsulfone (DADDS) in leprosy. American J. Trop. Med. & Hyg. 17 (1968) 192-201.
- 11. SKINSNES, O. K. Personal communication (supplemented by personal observations of the author on the scene).
- 12. SLOAN, N. R. and WORTH, R. M. Manuscript in preparation.
- DE SOUZA CAMPOS, N. BCG in the prophylaxis of leprosy. A preliminary report. Internat. J. Leprosy 21 (1953) 307-312.
- WORTH, R. M. and HIRSCHY, I. D. A test of the infectivity of tuberculoid leprosy patients. Hawaii Med. J. 24 (1964) 116-119.