CORRESPONDENCE

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Chemotherapy of Leprosy; "Bubble" or "Calendar" Packs for the Administration of Rifampin, Dapsone, Clofazimine, or Prothionamide/ethionamide

TO THE EDITOR:

The chemotherapy of leprosy for control programs has recently been defined by a WHO study and published in the WHO Technical Report Series as Number 675 ([4]). Combined chemotherapy is recommended for all types of leprosy. Paucibacillary cases will be treated with dapsone and rifampin for a period of only six months and treatment should then be stopped. Multibacillary cases will receive dapsone, rifampin, and clofazimine (or, in some circumstances, ethionamide or prothionamide instead of clofazimine) for a minimum of two years but, whenever possible, until slit-skin smears are negative. Treatment should then be stopped. These regimens—if they are to be successful—call for improved strategies to achieve a high level of patient compliance to both self-administered and supervised medication.

We suggest that one factor of considerable importance may be the way in which drugs are presented to the patient. In the field of contraception, the "bubble" or "calendar" pack has already proved highly successful for the out-patient consumption of pills by millions of women on a daily basis, and it has also been used in tuberculosis. We propose that such packs may be valuable for presentation of rifampin, dapsone, clofazimine, or prothionamide/ethionamide in the treatment of leprosy.

A pack of a standard type which is already available commercially in most parts of the world is shown in Figure 1. It measures 11 × 7.5 cm. The backing is of aluminum foil. The front cover and "bubbles" are of transparent plastic polymer, which is certainly waterproof and not, to our knowledge, easily penetrated by insects. It withstands environmental temperatures of 40°C at least and is difficult to fracture under normal circumstances. Tablets of dapsone vary considerably in size, but a typical example measures approximately 5 mm in diameter and is 2 mm–3 mm thick. It can be accommodated easily in the "bubble" of a standard pack which, in the United Kingdom, is readily available from various packaging companies. The back could carry the words "Dapsone tablets, each 100 mg" and below this could be added "For treatment of leprosy" in those countries where such information is considered a) neither stigmatizing nor otherwise disadvantageous to the patient, and b) of possible value in confining the use of this drug to the treatment of leprosy. The name and number of the patient and clinic or hospital could be added on an adhesive label. Figure 1 illustrates three possibilities for labelling and design: simple figures 1–28, days of the week (×4), and phases of the moon to cover a lunar month. Perhaps because of their somewhat sophisticated appearance, it is often assumed that calendar packs are expensive, or even so expensive as to be discounted in countries where the per capita expenditure per year on health may be extremely low. This is

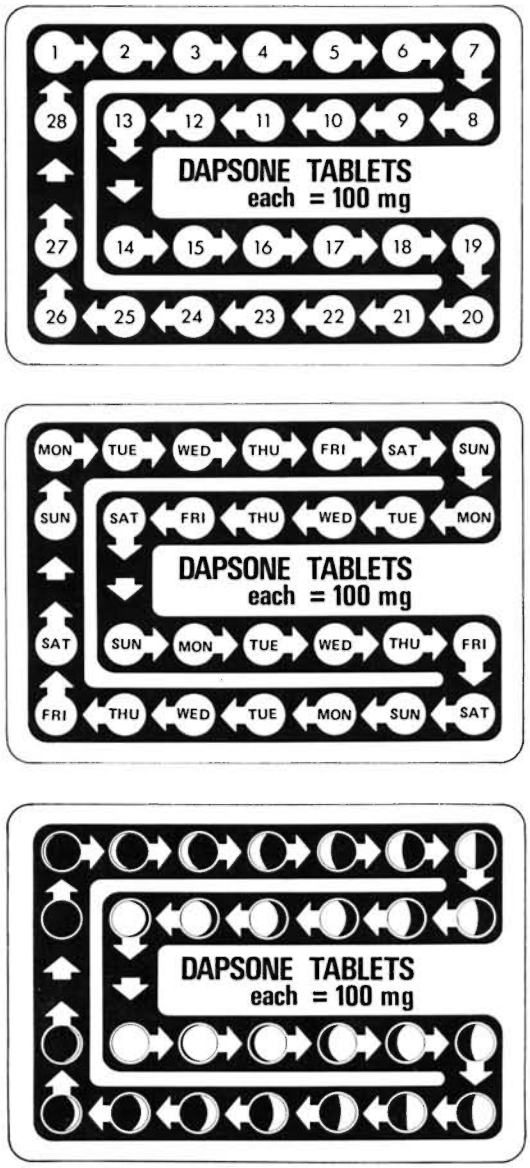

FIG. 1. A simple pack for the daily, unsupervised consumption of dapsone tablets by the patient at home. The back (flat surface) of a pack carrying 28 tablets (i.e., four weeks' supply) is shown, using figures, days of the week, or phases of the moon, over each "bubble." With slight modification, a similar pack could be used for the daily consumption of 50 mg capsules of clofazimine. Dimensions: 11 × 7.5 cm.

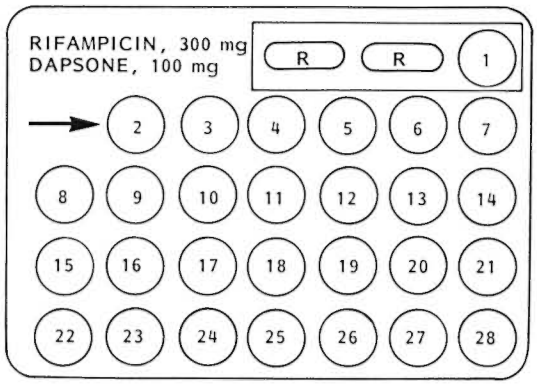

FIG. 2. Combined drugs for the treatment of patients with paucibacillary leprosy. The supervised dose on day 1 consists of 600 mg rifampin (two capsules each of 300 mg), plus one tablet of 100 mg dapsone. Dapsone is then taken in a daily, unsupervised dose of 100 mg by the patient at home. Dimensions: 11 × 7.5 cm.

incorrect. Even in the United Kingdom, where prices may not be competitive, the cost of a simple pack (not the drugs) as illustrated in Figure 1 is not more than £0.11 (US$0.20). Packs for the dapsone component in the six-month treatment of a paucibacillary case would thus only cost £0.66 (US$1.20). No doubt this would be greatly reduced by orders running into many thousands. The production of a special pack to include not only dapsone but also other drugs, as in Figures 2, 3, and 4, would certainly involve appreciable expense at the outset, but this has to be balanced against the intrinsic cost of the drugs, the high cost of leprosy control generally, and the possibility that such a pack may significantly improve patient compliance.

Short of virtually continuous, close, domestic supervision, there is in our view no system which will ensure the ultimate ingestion of medication by a patient: "No method of assessing compliance is completely effective." ([3]) Ingenious mechanical monitoring devices, such as that described by Moulding ([2]), can be used to record the extraction of a tablet from a container, and the testing of urine for dapsone or other drugs by either regular or surprise sampling may reveal valuable information on patient compliance under some circumstances ([1]). Such approaches have, in fact, already indicated that compliance in the sense of regular ingestion of prescribed medication by patients with leprosy and tuberculosis is often very poor. The use of the "bubble" or "calendar" pack described here will cer-

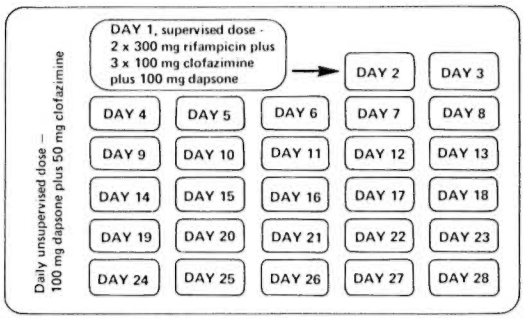

FIG. 3. Combined drugs for the treatment of patients with multibacillary leprosy. The back (flat surface) of a pack is shown for a) the supervised administration of rifampin, clofazimine, and dapsone on day 1, and b) the daily unsupervised consumption of dapsone and clofazimine by the patient at home. The 300 mg dose of supervised clofazimine may be given as 3 × 100 mg capsules (as shown here) or as 6 × 50 mg capsules. The daily dose of clofazimine is 50 mg and the daily dose of dapsone is 100 mg. Dimensions: 14 × 8 cm.

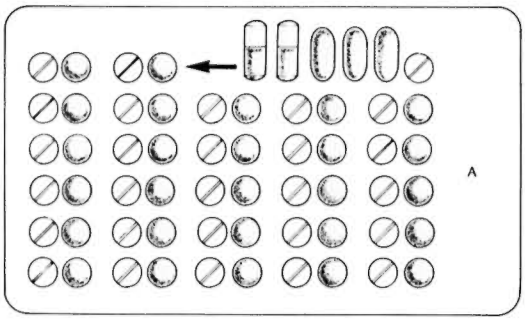

FIG. 4. Diagram of the front or "bubble" surface of the pack in Figure 3 for the administration of supervised and unsupervised drugs to multibacillary patients. The tablets and capsules are pushed through by the supervisor or patient from the "bubble" to the flat side. The space A on the right side is large enough to carry a self-adhesive label bearing the patient's name, number, clinic, and the date. Dimensions: 14 × 8 cm.

tainly not solve the problem of ultimate ingestion of antileprosy drugs, but it is suggested that it may significantly improve matters. The expense, especially if compared with salaries, transportation, and the hospitalization of relapsed or complicated cases, is not high and the appearance of the pack is one which is likely to appeal to many patients, perhaps emphasizing the importance of the drug which is being offered. Once packaged, the drugs will keep as well in these packs (and perhaps much better) than they do in any other form of container in common use. The advantage over the issue of drugs loose, in paper, plastic envelopes, or matchboxes, does not need elaboration. The inclusion of the capsules of the most expensive drug, rifampin, in "bubbles" will certainly not eliminate the possibility of theft and misuse (for other conditions, including tuberculosis and venereal disease), but on common sense grounds it is likely that it will certainly prove more difficult and troublesome to remove a significant number of capsules from these packs than from a stock bottle or other large container. If packs are issued by the manufacturer in hermetically sealed plastic wrapping ("shrink wraps"), this will not only aid preservation of the drugs on the shelf, but also considerably aid stock-checking, since bundles of a standard number of packs can be counted very easily.

Finally, a major advantage, not only to the patient but perhaps more especially to the supervisor or primary health care worker, is that the number of tablets removed at any given time can be checked virtually at a glance. To patients who dislike the feeling of being watched or supervised in their intake of drugs, this check could be made simultaneously with the use of the back of the package as a "calendar" on which to confirm the next date of attendance for supervised drugs.

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