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The Potential Uses of the Medication Monitor in the Treatment of Leprosy[1]

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The inability of many human beings to take medication as directed is a major problem in treating all illnesses. For leprosy, where treatment is very prolonged, it presents a truly formidable obstacle. Human behavior varies markedly from those who take medication very irregularly or not at all to those who take medicines exactly according to instructions. In any reasonable approach to solving the problem, it becomes important to differentiate reliable from unreliable patients so they can be managed differently. The medication monitor, described in this article, is in the author's opinion the most practical way of making this differentiation for most situations.

THE MONITOR

The medication monitor is a specially designed dispenser containing a minute amount of radioactive material and photographic film to record the regularity with which medication is removed ([4]). A model illustrating the principle of the device is shown in Fig. 1.

The dispenser contains individual boxes of medication stacked in sequence and marked with the days of the week when the medicine is to be taken. A window showing the daily markings on the boxes is at the bottom of the dispenser. Each box holds a full daily dose of medication to be taken by the patient. As one box is removed, the box for the next day drops into view.

A small piece of uranium is affixed to the top of the medication stack. A strip of photographic film that is covered to prevent exposure to light runs along one side of the dispenser. As each box is removed, a spring mechanism forces the uranium source downward, exposing different places on the film. These exposures appear as a record of dots after the film is removed from the device and developed.

Filmstrip A (Fig. 2) shows that the medication packets were first removed regularly for 2 days, and the uranium created two equally exposed dots. Then for 3 days no medication was removed; the uranium remained fixed, and a heavy dark dot appeared. At this point the patient removed three packets at one time to catch up, and an area with no dots appeared on the film, clearly revealing irregular drug ingestion.

Filmstrip B (Fig. 2) shows that the medication was initially removed regularly for 4 days, and four equally exposed dots were created. For several weeks no packets were removed; the uranium remained fixed, and an excessively dark dot appeared. On this occasion, the patient did not remove tablets to catch up so no blank spaces appeared on the film. Irregular drug ingestion was still quite evident because of the excessively dark dot and because the number of dots on the film was less than the number of days that the patient had had the device.

Now and then, patients will remove tablets in advance of the time they are to be ingested, usually because they intend to take them while away on a trip. In this circumstance, the blank area on the film precedes the dark dot, and such a record does not necessarily indicate irregular drug ingestion.

EXPERIENCE WITH THE DEVICE

This type of device has been used in the treatment of 122 tuberculosis patients in Denver, Colorado, selected for their apparent reliability in taking chemotherapy ([4]). Thirty-one percent took less than 70% of their medication for one or more months. Among 13 unselected patients taking antituberculosis chemotherapy in Malawi, Africa, six patients took less than 53% of their prescribed medication while seven patients took more than 87% ([5]).

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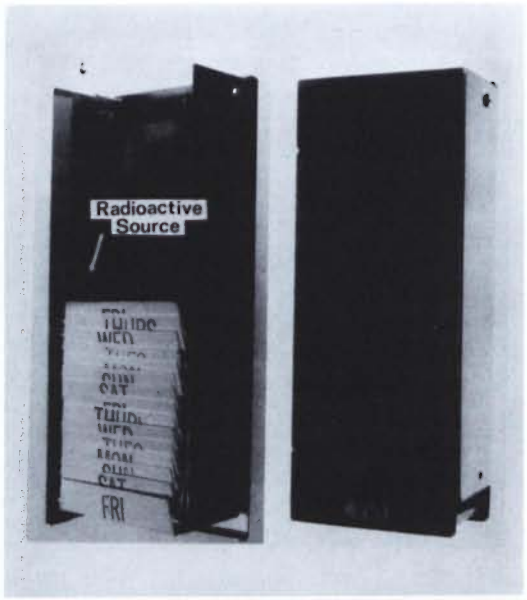

FIG. 1. A model illustrating the principle of the medication monitor.

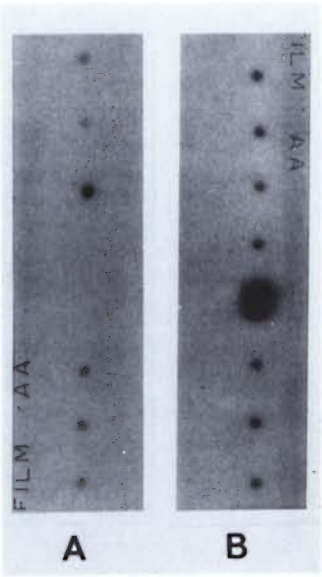

FIG. 2. Filmstrips showing series of dots created by uranium source. Intensity of dots represents interval between removal of boxes.

COST AND CONVENIENCE OF USING THE MONITOR

An inexpensive medication monitor, shown in Fig. 3, has been developed for the tuberculosis regimen of isoniazid (INH) and thiacetazone, which is made up in a combination tablet to be taken once a day. This device has a material cost of about $1.00 and is simple enough to construct so that it can be made in the developing countries. It can easily be filled with a month's supply of medication in two minutes. As long as patients are treated with one flat tablet per day, an equally simple and inexpensive device could be made for leprosy medication. However, if more than one tablet per day were required, such as one tablet of dapsone (DDS) and two capsules of rifampin, a small box similar to that shown in Fig. 1 for each day's dose of three tablets would be required, increasing the cost of the device and increasing the time it requires to fill the dispenser. One solution to this problem might be to make up combination tablets of medication to fit the existing dispenser for isoniazid and thiacetazone. Another solution would be to redesign the dispenser, probably in a circular or spiral form, to fit the desired drug regimen. Such designs would have the advantage of not being as long as the stack type devices shown in Figs. 1 and 3.

In the case of INH and thiacetazone, the medication does not degenerate in moist air so the medication in the monitor does not have to be protected against ambient moisture. In the case of anti-leprosy medications, at least one of them, rifampin, tends to soften in moist air and would need protection if the device were to be used in humid climates. This could be achieved by packaging the day's dose of medication in small moisture resistant boxes or having a moisture tight cap on the monitor that would be lifted to remove medication and would spring back after the medication had been removed.

One problem which has previously inhibited the use of the medication monitor is the lack of a means for immediate development of the filmstrip if developing tanks and darkrooms are not readily available. To solve this problem, we have packaged the film in a water tight envelope or pouch of opaque polyvinyl chloride that is shown in Fig. 4. This envelope prevents the film from being exposed to light and also functions as a developing tank when it is filled with developing solution. The most convenient de-

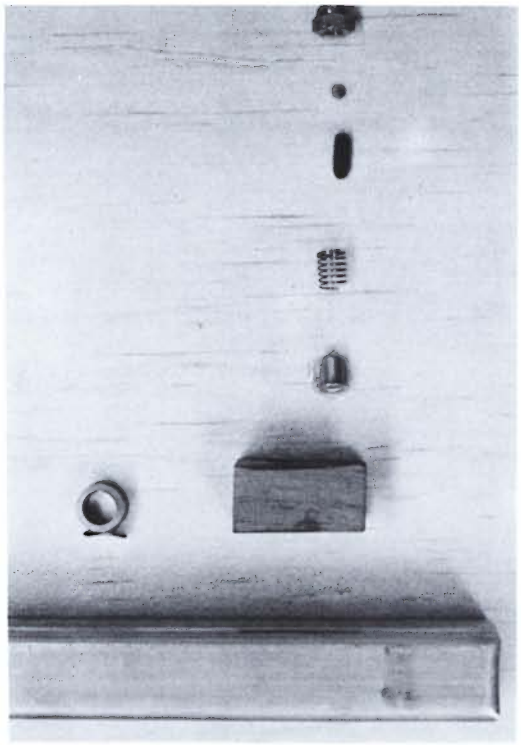

FIG. 3. Component parts of simplified inexpensive medication monitor. From top to bottom: cap nut, radioactive source, screw, compression spring, grommet, block of wood, negator spring, aluminum tube.

FIG. 4. Method of injecting monobath to develop filmstrip, showing plastic envelope with filmstrip.

veloping solution is a monobath which functions as both the developer and fixative. To develop the film, one places the filmstrip in its covering in a vertical position, inserts a 25 gauge needle attached to a 5 cc syringe at the top of the filmstrip, applies a rubber covered clamp across the top of the filmstrip where the needle is located, injects the monobath rapidly, and quickly removes the needle (Fig. 4). After 5 minutes, the filmstrip is removed and examined.

OTHER METHODS FOR DETERMINING REGULARITY OF DRUG INGESTION

Methods of determining how regularly patients take medication are limited. A common way of determining irregular drug ingestion is to keep accurate records of the amount of medication that the patient receives. If the patient picks up an inadequate supply, it usually means that he has not taken the full dose. However, the fact that medication is picked up does not prove it is ingested. More accurate information can be obtained by making surprise visits to the patient's home to count the amount of medication remaining with the patient and correlating this information with the record of how much medication he received. The cost of these home visits, the problem of maintaining records, and the offense to the patient of counting medication in the home make this procedure almost valueless.

Urine tests for the presence of medication or its metabolites are often considered to be the best way of checking outpatient drug ingestion. The DDS/creatinine ratio and the ELISA test have been introduced for studying compliance in leprosy patients ([2,3]). In addition to the cost and technical problems in running the tests, there are practical problems in collecting the specimens. For urine tests to be representative of the patient's usual drug consumption, multiple specimens should be collected by surprise visits to the patient's home or place of work. For routine programs, this is very difficult.

When compared with urine tests where a positive result "proves" that the patient has taken medication, the medication monitor has one potential defect: the patient may remove medication regularly to create a good film record but ingest none of it. In the study of 122 tuberculosis patients, there were only two questionable instances where this occurred, as shown by a negative urine test and good film records [4]. Despite this potential defect, it is obvious from the two trials with tuberculosis patients [4,5] that the medication monitor can detect the vast majority of noncompliance.

Many health workers believe they can distinguish reliable from unreliable patients. In the previously mentioned study with 122 tuberculosis outpatients in Denver [4], the nurse and physician who knew the patient best were asked to predict how regularly the patient would take his medication. Comparison of the physician and nurse predictions with the patient's performance showed a positive correlation between predictions of regular drug ingestion and good film records as measured by the average of the film records, for physicians ($p < 0.005$) and for nurses ($p < 0.01$). However, there was insufficient correlation to consistently predict the performance of individual patients. For example, out of 78 patients that the physician predicted would take 90% or more of their medication, 27% took less than 90% on the average and 27% had one record or more showing less than 70% removal. Conversely, out of 24 patients about whom the physician expressed mild doubts by predicting they would take only 70 to 90% of the medication, 54% took more than 90%, and 42% had no film record showing less than 90% medication removal.

Other authors state there is little or no correlation between staff judgement of patient compliance and actual compliance [1,6]. The relatively high correlation between predictions of compliance and actual compliance in the Denver study may be due to the fact that the staff had an opportunity to observe the patients' behavior on the ward for several months prior to outpatient therapy. Whether staff judgments formed over prolonged periods of time in an outpatient setting, where encounters are only periodic and often brief, would be more or less accurate is something which needs to be determined. The monitor may well be the best way to study the accuracy of staff judgments under these circumstances.

USE OF THE MEDICATON MONITOR IN LEPROSY

Drug resistance to dapsone is unfortunately an established fact. To prevent greater degrees of drug resistance from developing and for treating drug resistant patients, optimal regimens of multiple drugs will have to be developed. These regimens will probably have to be tested on an ambulatory, self-administered basis because of the trend towards keeping leprosy patients in the general community rather than restricting them to leprosy colonies and because of the prolonged period of time needed to treat the disease. Under these circumstances, some patients will not take their medication as prescribed. Therefore, one obvious use of the monitor in the field of leprosy would be to identify noncompliant patients in drug trials and to exclude their response from the overall results.

The monitor could also be used to improve medication consumption in routine programs. Broadly speaking, there are two methods of medication delivery: 1) self-administered medication where the patient is responsible for its ingestion and 2) completely supervised medication where some member of the health team or perhaps a member of the family or village administers each dose. In the treatment of tuberculosis where therapy is required for six to eighteen months, the monitor can be used to select the type of drug administration required by giving all but the most obviously unreliable patient an opportunity to take their medication from the device. If good film records are found, self administration can be continued and the interval between seeing the patient lengthened to two or three months. If poor records are found, the interval between visits can be shortened and the patient given special counseling to improve medication ingestion. If this fails, arrangements can be made to give the medication by direct administration.

In the case of leprosy, where treatment is much more prolonged, the same approach could be used for the initial phase of therapy, but it is difficult to know how long one should continue to use the monitor

for reliable patients. Undoubtedly, some patients who initially take pills faithfully will become less compliant with time. Prolonged use of the medication monitor would detect this type of noncompliance. However, the cost and nuisance of using the monitor for many years might prohibit such a policy. Appropriate studies may find that attendance records or other predictive criteria, together with periodic use of the monitor, are sufficient to identify the vast majority of noncompliant patients.

Finally, there is a great need to study the reasons for noncompliance and to develop intervention strategies to improve compliance. The medication monitor should be an invaluable tool in carrying out such studies.

SUMMARY

A medication monitor has been developed that utilizes radioactive material and photographic film to record the intervals at which patients take medication. In the author's opinion, this equipment represents the most efficient means that has so far become available for determining how regularly outpatients take medication. A monitor for the tuberculosis regimen of isoniazid and thiacetazone has been made at a sufficiently low cost that it is practical to use it in routine treatment programs. An inexpensive system for immediate development of the film that can be used in the most remote locations is also available. Undoubtedly, with appropriate engineering work, a monitor for leprosy regimens could be made. The device has been used with tuberculosis patients and revealed that many patients were grossly irregular in taking their medication. It has been used to oversee medication use by tuberculosis patients and to select those who require either extra attention to improve medication ingestion or completely supervised, directly administered programs. In the treatment of leprosy, it could be used to study new drug regimens, the causes of noncompliance, and for the routine supervision of patients.

RESUMEN

Se ha desarrollado un "monitor de medicación" que utiliza material radioactivo y película fotográfica para registrar los intervalos a los cuales los pacientes toman su medicación. En la opinión del autor, este equipo representa el medio más eficiente que hay hasta la fecha para determinar con que regularidad toman su medicación los pacientes. Se ha producido un monitor para el tratamiento de la tuberculosis con isoniazida y tiacetazona, a un costo lo suficientemente bajo que permite su uso en los programas de tratamiento rutinario. También se ha desarrollado un sistema barato para el revelado inmediato de la película que puede ser usado en los lugares más remotos. No hay duda que, con un apropiado trabajo de ingeniería, se podría fabricar un monitor relacionado con el tratamiento de la lepra. El equipo, usado con los pacientes tuberculosos, ha permitido saber que muchos de ellos son muy irregulares en la toma de su medicación. Su uso, también ha permitido seleccionar aquellos pacientes que requieren atención extra para mejorar su ingestión medicamentosa o una supervisión directa de los organismos que establecen los programas de tratamiento. En el caso de la lepra, podría usarse en el estudio de tratamientos con nuevas drogas, de las causas de la irregularidad en la medicación y en la supervisión rutinaria de los pacientes.

RÉSUMÉ

Un système de contrôle des prises de médicaments a été développé en utilisant du matériel radioactif et des films photographiques pour enregistrer les intervalles auxquels les malades prennent leurs médicaments. Les auteurs considèrent que cet équipement représente la méthode la plus efficace aujourd'hui disponible, pour déterminer dans quelles mesures les malades ambulatoires prennent leurs médicaments de façon régulière. On a pu réaliser un tel système de contrôle pour le traitement de la tuberculose par l'isoniazide et la thiacetazone, à un prix suffisamment faible pour que le système soit pratique à utiliser dans les programmes de traitement de routine. Un système peu coûteux pour le développement immédiat du film, pouvant être utilisé dans les endroits les plus reculés, est également disponible. Sans aucun doute, moyennant un certain travail de mise au point sur le plan technique, un tel système de contrôle pour le traitement de la lèpre pourrait être développé. Le procédé qui a été utilisé chez les malades tuberculeux a révélé que beaucoup de patients étaient fortement irréguliers en ce qui concerne la prise de leurs médicaments. On a utilisé le système pour surveiller la prise du médicament par les malades de la tuberculose et pour choisir ceux qui devraient bénéficier d'une attention particulièrement suivie, afin d'améliorer l'ingestion médicamenteuse ou pour mettre en oeuvre des programmes d'administration supervisés de façon directe. Dans le traitement de la lèpre, on peut utiliser ce système pour étudier de nouveaux traitements médicamenteux, les raisons pour lesquelles les malades ne prennent pas leurs médicaments et également pour la supervision de routine des malades.

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