day; (b) methadone 150 mg (80 mg initially, 70 mg 5½ hours later), rifampicin 150 mg four times a day, isoniazid 100 mg three times a day; (c) methadone 80 mg; and (d) methadone 70 mg. Plasma methadone concentration was measured by high performance liquid chromatography. Blood was collected before the daily dose (methadone was taken by mouth as a single dose except in the second regimen, when the patient split her dose) and at regular intervals for a further 11 to 23 hours.

Figure 1 shows the results of the kinetic studies. The two lower curves were obtained when the patient was receiving antituberculosis treatment; the two upper curves were obtained 11 and 20 months later, when she was taking methadone alone.

The dose and the time since the last dose of methadone will affect the blood concentration of methadone at baseline before the daily dose is taken. These are likely to be reasons for the difference between the values in the third and fourth regimens.⁵ The following pharmacokinetic variables were calculated: oral clearance was 8.97 ml/min/kg for the first regimen, 2.10 ml/min/kg for the third, and 2.12 ml/min/kg for the fourth. We were unable to calculate clearance for the second regimen.

Discussion

So far as we are aware, there are no published reports of an interaction between methadone and isoniazid or pyrazinamide. We assume, therefore, that the lower plasma methadone concentrations during antituberculosis treatment were attributable to the effects of rifampicin. Our methadone measurements agree with those of other clinical reports.¹

This case shows that some patients receiving maintenance treatment with methadone cannot tolerate withdrawal symptoms precipitated by rifampicin and that they may not comply with antituberculosis treatment until their methadone is increased.

1 Kreek MJ, Garfield JN, Gutjah CL, Giusti LM. Rifampicin induced methadone withdrawal. *N Engl J Med* 1976; 294:1104-6.

2 Anonymous. *Drug Ther Bull* 1995;33:28-9.

3 Bhatti N, Law MR, Morris JK, Halliday R, Moore Gillon J. Increasing incidence of tuberculosis in England and Wales: a study of the likely causes. *BMJ* 1995;310:967-9.

4 Haverkos HW. Infectious diseases and drug abuse: prevention and treatment in the drug abuse treatment system. *Journal of Substance Abuse Treatment* 1991;8:269-75.

5 Wolff K, Hay AWM, Raistrick D, Calvert R. Steady-state pharmacokinetics of methadone in opioid addicts. *Eur J Clin Pharmacol* 1993;44:189-94.

Caring for Older People

Aids to compliance with medication

A J Corlett

This is the last in a series of 14 articles edited by Eileen Burns, Neil Penn, and Graham Mulley

Elderly people may need to take several forms of medication, including tablets and capsules, inhalers, insulin, and eye drops. This article describes various aids that are designed to facilitate compliance.

Old people are more likely to suffer from chronic morbidity from multiple diseases—20-30% of older people are taking three or more medications. Several diseases may require concurrent drug treatment; polypharmacy is known to be associated with an increased risk of adverse drug reactions, drug interactions, and poor compliance.

Compliance may be defined as the extent to which a person's behaviour coincides with medical advice. Few patients take their medication as intended by their practitioner; most are partially compliant. Up to 20% of patients do not present their prescription to a pharmacy within one month of issue. Non-compliance is multifactorial and may arise from:

- Not knowing how to take medication (such as orally, twice daily, with food, etc)
- Not understanding the importance of drug treatment in managing disease
- Taking many drugs
- Anticipation or experience of side effects
- Forgetfulness
- Impaired physical function.

Even so, elderly patients with normal cognitive function are more compliant than their younger contemporaries. Simple measures can be taken to improve compliance:

- Educating patients about disease and treatment
- Simplifying drug regimens: minimising the number of drugs and frequency of doses
- Using modified or controlled release preparations to decrease dosage frequency

"Self portrait 1903" by Camille Pissarro (1830-1903)

- Involving carers in management of medication
- Telling patients about common early side effects to which they may develop tolerance
- Using drug diaries, calendars, or medication charts
- Using ordinary bottle tops instead of child resistant containers
- Using large print or jumbo labels on containers
- Using compliance aids, such as dose reminders for tablets and devices to help with administration of inhalers, eye drops, etc.

St James's University Hospital, Leeds LS9 7TF
A J Corlett, senior registrar in medicine for the elderly

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Several types of daily dose reminders are available (see box). Most consist of a box divided into days of the week with several compartments for each day—they are suitable for tablets and capsules only. Effervescent, dispersible, buccal, and sublingual preparations or moisture sensitive medicines (such as Omeprazole) cannot be dispensed in compliance devices. Large solid tablets, or multiple tablets taken at a single time, may not fit into the individual compartments. “As required” (PRN) medication, if placed in a daily dose reminder or monitored dosage system, may be taken unnecessarily on a regular basis.

Some drugs are provided in calendar, “bubble” or “blister” packs. People with impaired manual function may have difficulty in manipulating the packaging.

Recent data have questioned the stability of medicinal products in compliance devices. Medicines should not be kept in sealed monitored dosage systems for more than eight weeks. They should be stored in a cool dry place, protected from light, and kept away from children as most of these devices are not child resistant.

Asthma affects about one in 10 older adults. Inhalers are the first line treatment as direct delivery of a drug to the site of action reduces systemic side effects and enables bronchodilating agents to have an immediate action.

Several drug delivery systems are now available.² Metered dose inhalers, which are the most widely used, have several disadvantages and may eventually be superseded by breath actuated dry powder systems, which seem to increase the percentage of drug deposition in the lungs. The patient should be instructed in the use of whichever inhaler is prescribed; inhaler technique should be monitored regularly.

Metered dose inhalers contain up to 200 doses. Discreet and convenient to use, this type of inhaler is preferred by patients. For patients with hand weakness, a lever attachment, Haleraid, may help. Poor inhaler technique is common and has multiple causes. Even with correct technique, up to 80% of the drug is deposited in the oropharynx; with corticosteroids this may cause oral thrush. Most metered dose inhalers use chlorofluorocarbons (CFCs) as propellants.

Breath actuated metered dose inhalers are similar to standard metered dose inhalers, but more expensive. An automatic spring mechanism is triggered by inspiratory flow rates of 22-36 l/min. Drug delivery is less dependent on inhaler technique.

A 10x10 grid of small, square, light-colored tiles, likely a sample of a material or a decorative pattern. The tiles are arranged in a regular grid, with some tiles showing slight variations in color or texture, possibly due to the manufacturing process or the material's properties. The grid is set against a dark background.

Name: _____

Prescription for:

Medicine			Number of tablets			
Name	Description	Dosage	Morn.	Noon	Even.	Bed

Keep DOSEY® away from children!

- Holds 7 days' medication; marked SUN—SAT (days also marked in Braille)
- Four compartments to each day
- Single daily units are not detachable
- Chart on underside for details of patient's treatment
- Further refinements include a locking device and the Mediset Mini (a pocket sized container with 21 compartments, suitable for small tablets or capsules)
- Though sliding lids on tablet tray have guides, they require considerable dexterity to remove and replace
- Filled weekly by the patient, carer, or pharmacist

[illegible]

- Cassette holds drugs for seven days, with six compartments in each day
- Daily units are not detachable
- Tray is sealed with transparent plastic lid and clear plastic film
- Contains photograph and personal details of patient
- Record of treatment and drug regimen is preprinted on underside of tray
- Filled only under the supervision of a pharmacist

Monitored Dosage System

BOLIVARDA FOR HYPERTENSION
10mg - 1 tablet twice daily
KLM - 1987

MEDICATIONS FOR

TIME:	FILE No:

- Available at Boots and some independent pharmacies
- Medication is heat sealed in large, flat blister packs
- Each pack contains sufficient treatment for 28 days
- Daily units are not detachable
- Packs are colour coded to indicate time of administration—for example, pink indicates morning tablets, white “as required” treatment
- Each pack contains a card with drug dose
- Filled under the supervision of a pharmacist

DRY POWDER INHALERS

The Spincap or Rotacap is a small device which breaks open a capsule containing the drug and the lactate carrier. An inspiratory flow rate >60 l/min is required for effective delivery of the drug, which may be difficult to achieve. Poor technique is common with these inhalers, and they need reloading after each use. The Spincap is less expensive per dose than the equivalent metered dose inhaler; the Rotacap is more expensive.

Examples of some inhaler devices

DISKHALERS AND TURBOHALERS

Diskhalers are larger than metered dose inhaler or dry powder inhalers. A single dose of drug is contained in a blister in an aluminium foil disk; there is a maximum of 8 doses per disk. A dose double that for a metered dose inhaler is usually recommended and an inspiratory flow rate >60 l/min is required. Diskhalers are expensive and complicated to load.

Turbohalers are small, disposable, breath actuated devices containing up to 200 doses. When only 20 doses remain, there is a warning. For people with arthritic hands, an attachment is available to help turn the base for loading. Turbohalers are simple to use but they are more expensive than metered dose inhalers. Because they deliver pure drug, with no lactate carrier, there is no taste; hence there could be uncertainty that the dose was taken.

Insulin

Six per cent of white people over 65 years (and a much higher proportion of older people from the Indian subcontinent) have diabetes mellitus, and 15-20% are using insulin. Treatment regimens vary from a single morning dose of insulin to four daily doses. The type of insulin used (short, intermediate, long acting, or a combination) and the frequency of administration should be tailored to the needs of the individual patients. Most

Insulin pens

B-D pen (Becton Dickinson)

- Used with Humulin cartridges (5 mixes available in packs of 5 × 1.5 ml cartridges)
- Uses B-D Micro-Fine single use needles, available on prescription and from some hospital clinics
- Single unit dose up to 30 units
- Simple "dial-press" operation
- Numbers are easy to read; magnifier can be supplied by hospital clinics
- Day and night tops are available for easy identification of different pens
- Spare cartridge is provided in carrying case

Penmix 30/70 (5 × 3 ml) pens (Novo Nordisk Pharmaceuticals)

- Pre-loaded—300 units of insulin (lasts 1 week on average)
- Holds up to 78 units at one time (in multiples of 2 units)
- Disposable
- Novofine needle—single use

elderly patients treated with insulin have once or twice daily injections of a biphasic insulin.

Patients are encouraged to inject themselves, if necessary with supervision from a relative or district nurse, though poor vision may cause difficulty in inserting the needle into the bottle or seeing that the correct amount of insulin has been drawn up. As well, lack of dexterity in the hands may cause problems in both drawing up and administering the insulin. Several devices are available to encourage independence.

Magnifiers clip onto the syringe, enlarging the scale and making it easier to see. One device contains two channels: a wider one for the insulin bottle and a smaller one for the syringe—sliding the syringe along the smaller channel guides the needle correctly through the rubber cap and into the bottle. One side of the device shows a magnified image of the scale. Magnifiers are not available on prescription but can be obtained through the diabetic liaison nurse at the local hospital.

Preset glass syringes—Two types of preset syringes are available. These can be set or adjusted by the diabetic liaison or district nurse. They allow the plunger to be drawn back to the set level, so patients with visual impairment can draw up their own insulin. Alternatively the nurse can draw up the dose for the next injection in an ordinary insulin syringe.

Insulin pens are designed to give the patient more flexibility. Various combinations of short and intermediate acting insulin cartridges are available; the pens are either reloaded with new cartridges or are disposable. Pens are not available on prescription but are available from hospital diabetic clinics.

Depending on the device, a single dose of insulin varies from 30 to 78 units. Doses are available in multiples of 1, 2, or 4 units.³

Accessories to insulin pens are specific to the make of the pen. All patients should have an extra pen as back up and should be able to use an ordinary syringe and insulin phial in case of pen failure. All pens require considerable dexterity and have single use needles.

Examples of a reloadable and a disposable pen are described in the box.

Eye drops

Glaucoma is the commonest preventable cause of blindness in old age. Unless the patient undergoes surgery management is by long term use of eye drops. An older person may have difficulty using eye drops

Help with eye drops

Autosqueeze (Owen Mumford)

- Clips on to the neck of all bottles; wings are squeezed together to administer the drop
- Popular with patients
- Recommended for patients with arthritis
- Can be used in combination with the Autodrop and Easi-drop

Opticare (Cameron Graham Associates)

- Reusable plastic dispenser fitting most plastic eye drop bottles; fits over the eye and has a finger space for pulling down lower lid
- Squeezing the dispenser requires 25% of the force required to squeeze the bottle
- Difficult to load
- Written instructions provided are poor
- Expensive

Autodrop (Owen Mumford)

- Clips onto most bottles (except Timolol); holds bottle at correct angle for administering drop
- Lip holds lower lid down; cup fits over eye
- Improves aim by preventing blink reflex during administration
- Easi-drop is similar to Autodrop; it fits onto most bottles (including Timolol) and can be left attached to bottle; an open lattice design allows light to enter the eye during use

because of poor eyesight, arthritis, incoordination, tremor, and fear of the bottle touching the eye. The Autosqueeze, Opticare, and Autodrop, shown in the box, may help in squeezing the bottle or positioning the drop.^{4,5} These aids are not available on prescription and have to be purchased; no studies have satisfactorily compared their ease of use and efficacy.

- 1 Royal Pharmaceutical Society of Great Britain. *Medicines, ethics and practice; a guide for pharmacists*. London: RPSGB, 1994;12,9-13,96.
- 2 Delivery systems for inhaled drugs in asthma. *Drugs and Therapeutics Bulletin* 1989;27(17):66-8.
- 3 Pen injections for insulin. *Drugs and Therapeutics Bulletin* 1992;30(1):3-4.
- 4 Walker R. Aids for eye drop administration. *Pharmaceutical Journal* 1992;249:608.
- 5 Morrison J. Eye drop aids and counselling sessions for glaucoma patients. *Hospital Pharmacy Practice* 1993;3:413-8.

Passive smoking and health: should we believe Philip Morris's "experts"?

George Davey Smith, Andrew N Phillips

See p 907

A series of adverts has recently appeared in newspapers across Europe comparing the risk of lung cancer from passive smoking with a variety of other apparent risks from everyday activities (see fig 1). The implication is that the increased risk of lung cancer among those exposed to other people's tobacco smoke, of around 20%, is minuscule in comparison with the apparent 500% increased risk of lung cancer associated with a diet high in saturated fat, the 180% increase with frequent cooking with rape seed oil, the 60% increase with drinking 1-2 glasses of whole milk per day, or the 70% reduction in risk associated with high fruit diet. The advert, entitled "What risks do you take?" is cleverly tailored to the public's scepticism about the apparent health risks of everyday activities.¹ A few weeks after the adverts appeared the main headline in a major British Sunday newspaper was "Beef-burgers linked to cancer."² The frequent appearance of such news stories, which are then often contradicted or reversed by subsequent reports, leads to distrust in pronouncements from experts—what may be called the "now they're saying" syndrome.

The central message of the advert is that passive smoking is not "really a meaningful health risk to people who have chosen not to smoke." Readers were asked to write for a copy of a report "Environmental tobacco smoke and lung cancer: an evaluation of the risk," from a team of authors referred to as "The European Working Group on Environmental Tobacco Smoke and Lung Cancer."³ The report focused only on the risk of lung cancer, while the adverts referred to an absence of risks of health problems in general with passive smoking. The title of the working group has the ring of authority to it, although unsurprisingly it turns out to be an industry funded enterprise.

Passive smoking and lung cancer: the European working group report

The review of the evidence linking passive smoking to lung cancer risk produced by the tobacco industry sponsored working group is of limited use as a scientific document. It is, however, interesting as a demonstration of the rhetorical mode adopted to dismiss the possibility of a link between passive smoking and lung cancer. The core of the report relates to a summary and meta-analysis of observational epidemiological studies regarding the risk of lung cancer in people who have never smoked but who are exposed to environmental tobacco smoke. These investigations have looked at never-smoking spouses (or cohabitantes) of smoking partners, never-smoking people whose parents smoked, and never-smokers exposed to smoke at their workplaces. As with other meta-analyses of this issue,^{4,5} an increased risk of about 20% was seen in the spousal studies. The working group considers only studies with female never-smokers with male smoking spouses, on

the grounds that there are only nine studies with male never-smokers. This is odd as later the group goes on to carry out subgroup meta-analyses of as few as four individual studies. The suspicion is aroused that the male studies are ignored because they show larger increased risks on average than the female studies.

Having found a significantly increased risk in its meta-analysis of spousal studies, the working group goes on to attempt to discredit this finding. This could be seen as a welcome antidote to the usual practice of scientists attempting to shore up their embattled hypotheses against challenges from newly accruing empirical data. More plausibly, however, it could be seen as a way of getting the accumulated data to fit with the already agreed conclusion. A series of possible biases are considered, which will here be dealt with in turn.

University of Bristol,
Department of Social
Medicine, Bristol
BS8 2PR
George Davey Smith,
professor of clinical
epidemiology

University Department of
Primary Care and
Population Sciences,
Royal Free Hospital
School of Medicine,
London NW3 2PF
Andrew N Phillips, reader in
epidemiology and biostatistics

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SECOND-HAND TOBACCO SMOKE IN PERSPECTIVE

Is everything bad for us? Or are we getting things out of proportion?

Almost every day, it seems that one thing or another has been discovered to be some kind of health risk.

In one scientific study, even the ordinary amount you drink to heart disease.

But so common sense suggests that scientists confirmed that everything described essentially as a risk is a meaningful risk.

For example, lots of people have been persuaded that second-hand tobacco smoke is harmful.

But for pricing, perhaps.

After all, we recognise that smoking itself is a risk factor for certain human diseases and that some people find second-hand tobacco smoke unappealing and unpleasant.

But what about second-hand tobacco smoke? Is it really a meaningful health risk to people who've chosen not to smoke?

Not, we think, if you look at the evidence.

The United States Environmental Protection Agency recently conducted a major review of studies on the risks of second-hand tobacco smoke to non-smokers. These studies typically involve non-smokers living with smokers over a long period, such as 10 years.

And this review put the risk of lung cancer from second-hand tobacco smoke at a level well below the risk reported by other studies for many everyday home and outdoor.

And below, in fact, the risk to health that one other study reported for taking one breath a day.

As the table below shows, many everyday activities have been statistically associated at one time or another with apparent risks to health.

But reputable scientists say that weak associations aren't necessarily meaningful.

So there's no big campaign to persuade you to give up your daily breath.

But is there any sound justification for a campaign against second-hand tobacco smoke?

If you'd like to decide for yourself, please write to us at Philip Morris Europe S.A., c/o P.O. Box 107, 1000 AC Amsterdam, The Netherlands or fax us on 00 31 20 671 00 00.

We'll send you the evidence about second-hand smoke.

We believe you'll find the case convincing.

Activity	Relative Risk	Study
Second-hand tobacco smoke	1.20	British Journal of Cancer, 1994, 70, 1000-1005
Drinking 1-2 glasses of whole milk per day	1.60	British Journal of Cancer, 1994, 70, 1000-1005
Drinking 1-2 glasses of whole milk per day	1.60	British Journal of Cancer, 1994, 70, 1000-1005
Drinking 1-2 glasses of whole milk per day	1.60	British Journal of Cancer, 1994, 70, 1000-1005
Drinking 1-2 glasses of whole milk per day	1.60	British Journal of Cancer, 1994, 70, 1000-1005
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Drinking 1-2 glasses of whole milk per day	1.60	British Journal of Cancer, 1994, 70, 1000-1005
Drinking 1-2 glasses of whole milk per day	1.60	British Journal of Cancer, 1994, 70, 1000-1005
Drinking 1-2 glasses of whole milk per day	1.60	British Journal of Cancer, 1994, 70, 1000-1005

Philip Morris Europe S.A.

Second-hand tobacco smoke. Let's keep a sense of perspective.

Fig 1—One of the Philip Morris advertisements