Drug Treatment of Disease**COUGH MIXTURES**

BY

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Cough mixtures retain an honourable place in therapeutics. They still comprise some 10–15% of doctors' prescriptions, and most chemists are able to offer a choice of forty to fifty remedies which are designed to relieve cough by one means or another. A generation ago a considerable range of expectorants was prescribed, some of which were reputed to act directly upon the bronchi and others reflexly by irritating the stomach. The range has gradually narrowed over the years, as successive editions of the *British National Formulary* show, and of those that remain the ammonia salts, the iodides, and ipecacuanha are now the most popular. Combinations of these drugs are frequently prescribed—for example, ammonia and ipecacuanha mixture (*B.P.C.*), and potassium iodide and ammonia mixture (*B.P.C.*). They are often referred to as stimulant expectorants, to distinguish them from depressant or sedative expectorants containing a sedative, usually an opium derivative, in addition.

The distinction between stimulant and depressant expectorants has become progressively blurred in recent years by the introduction of new ingredients which, in addition to their specific actions upon the respiratory tract, often have central stimulant or depressant properties. Unfortunately, no suitable term exists which covers the full range of antitussive agents. "Expectorants" are peripherally acting drugs. "Cough mixtures" are aqueous solutions, usually with a standard dosage of $\frac{1}{2}$ oz. (14 ml.). "Cough remedies," which include mixtures, linctuses, tablets, lozenges, and inhalations, covers best the scope of this article but is not a term which is likely to find much favour.

Undoubtedly the greatest recent advance in the treatment of cough is the discovery of antibiotics, and many proprietary cough mixtures contain one or more of them. They are not further discussed here. Concurrently, the active ingredients have undergone a change. Table I shows a comparison between fifteen

and "decongestants" which aim to relieve coughing by enlarging the air passages rather than by reducing the viscosity of the sputum.

Opium Derivatives

Perhaps opium derivatives should be considered first for historical reasons. For centuries they have been the most potent antitussive drugs. Of the various alkaloids in opium, morphine and codeine are particularly valuable in depressing the cough reflex. They must be used with circumspection and are indicated when exhausting paroxysms of ineffective coughing are caused by irritation or pain in the throat. By diminishing the stimulus to cough, their general narcotic effect is enhanced. In conditions such as bronchitis and bronchiectasis, in which expectoration is desirable, they eliminate much unnecessary coughing by raising the threshold of stimulus, but they should be avoided when early expectoration is essential—for example, in post-operative pulmonary collapse.

In computing the dosage of morphine in cough mixtures, a balance must be struck between the sensitivity of the cough centre and the risks of addiction. Most of the common preparations contain very little. For instance, $\frac{1}{2}$ oz. (14 ml.) of camphorated opium compound mixture (*B.N.F.*) has 1/150 gr. (0.4 mg.) and 60 minims (3.5 ml.) of squill opiate linctus (*B.P.C.*) (Gee's linctus) 1/100 gr. (0.65 mg.) of anhydrous morphine. Probably, a dose of less than about 1/30 gr. (2 mg.) of morphine has little effect on the cough centre, but at least addiction rarely if ever occurs with these smaller amounts. Perhaps the undoubted benefits of these ancient remedies are due in part to their many other ingredients. Camphorated tincture of opium (*B.P.*) (*tinct. camph. co.*, paregoric) contains benzoic acid, a gastric irritant to cause reflex expectoration, camphor, an irritant and carminative, and oil of aniseed, a carminative and mild expectorant. For its expectorant effect, camphorated opium compound mixture relies greatly upon ammonia salts. Squill opiate linctus (equal parts of camphorated tincture of opium, syrup of tolu, and oxymel of squill) has syrup and honey to enable it to form a coating over the upper air passages, tolu as an irritant and antiseptic and squill as another irritant. The very complexity of these mixtures, soothing as they are in many instances, is militating against their popularity. The modern trend is towards simplification, while morphine, for all its advantages in times of crisis, is yielding to codeine as a safer sedative in cough mixtures.

Of all the opium derivatives, codeine is the simplest and safest. It is a mild hypnotic and analgesic, does not depress the respiratory centre so much as morphine, and is less constipating. Addiction is rare, mainly because it is only mildly euphoric, and overdosage is apt to cause nausea and vomiting. The commoner preparations of codeine include syrup of codeine phosphate (*B.P.C.*) and codeine linctus (*B.P.C.*). Pholcodine

TABLE I.—Comparison Between the Active Ingredients of 15 Cough Mixtures in the *British National Formulary* (1957) and a Similar Number of Proprietary Mixtures Advertised in Current Medical Journals

Ingredients	<i>B.N.F.</i>	Adverts.
Ammonia salts	7	1
Opium derivatives	6	2
Tolu	2	0
Sodium bicarbonate	2	0
Iodides	2	3
Ipecacuanha	3	2
Ephedrine	1	10
Antihistamines	0	6
Aminophylline	0	4
Barbiturates	0	3

cough mixtures in the *B.N.F.* (1957) and a similar number of proprietary preparations, listing the ingredients which occur at least twice. The trend is away from opium derivatives and the old-fashioned expectorants towards antispasmodics, antihistamines,

has recently appeared in many cough mixtures. It is less toxic than codeine, has fewer side-effects, can be given in smaller dosage, and is no more likely to cause addiction; it probably represents a real advance in therapy. Pholcodine linctus (*B.P.C.*) is now in the *B.N.F.* Dihydrocodeinone bitartrate, prescribing of which is restricted by the Dangerous Drugs Act (*D.D.A.*), is altogether more powerful than codeine weight for weight, but should be used sparingly if addiction is to be avoided.

Methadone ("physeptone"), while not an opium derivative, deserves special mention as a cough suppressant. It may be prescribed as methadone linctus (*D.D.A.*, *B.N.F.*).

Antispasmodics and Antihistamines

Of the antispasmodics, stramonium, which relies for its effect upon hyoscyamine and atropine, is falling into disfavour. Ephedrine is still very much to the fore, and many modifications such as desoxy- and phenyl-ephedrine HCl and ephedrine combined with resins are being introduced. It is certainly an efficient antispasmodic, but may cause thumping of the heart, faintness, and sleeplessness. Theophylline and theophylline ethylene diamine (aminophylline) are steadily gaining in popularity. Until recently, they have really been effective only when injected intravenously or inserted as a suppository, but oxytriphylline, or choline theophyllinate ("choledyl"), seems to be almost as good when taken by mouth. The limiting factor in dosage is gastric irritation, but 200 mg. of choline theophyllinate thrice daily is usually tolerated for long periods and twice the dose for a few days.

These drugs are rarely given singly for the relief of cough, though they are often prescribed in cough mixtures, tablets, and sprays. A recently advertised spray contains ephedrine, hydrocortisone, an antihistamine, neomycin (to combat Gram-positive bacteria), and polymyxin B (to combat Gram-negative bacteria), and a tablet contains a barbiturate, ipecacuanha, ephedrine, caffeine, and aminophylline, with a view to producing mental sedation, decongestion, expectoration, and bronchodilatation. Such polypharmacy may be deplored, but at least most of the ingredients are known to have beneficial effects when properly used. They may alleviate cough among other symptoms in minor acute respiratory infections, which are by nature of short duration.

Inhalations

Perhaps the most desirable property of steam inhalations is that they should have a pleasant smell, for their main virtue is the expectorant effect of hot, moist air. Fortunately a large range of substances is available; most of them are extracts of trees and plants and have mild irritant and antiseptic properties. Amongst the best known are menthol, eucalyptus, thymol, benzoin, and creosote. For occasional use, inhalation from a jug with a towel over the head is recommended, but is not suitable for young children. A better, but more elaborate, method is to place a screen around the top of the bed with sheets draped over it and then direct the steam from a bronchitis kettle towards the head of the bed. This produces a thorough penetration of the respiratory tract without causing a feeling of suffocation, and is applicable to the young and very ill. By clipping the sheets to the screen, soiling can be kept to a minimum.

Local Anaesthetics

Phenol has anaesthetic and antiseptic properties. In the form of phenol lozenges (containing phenol $\frac{1}{2}$ gr. (32 mg.)) a temporary local effect may be obtained. It has the reputation for allaying the anxieties of opera singers with ticklish throats. Benzocaine compound lozenges (*B.P.C.*) may also be used for this purpose. When pain rather than irritation is the cause of coughing, a powder containing equal parts of orthocaine and benzocaine may be sucked through a glass tube, particularly before meals. In the last resort an amethocaine lozenge, which has ten times the activity of cocaine, may be tried.

Conclusion

So long as people cough—and the causes range from excessive smoking to carcinoma of the larynx—cough mixtures will be demanded. Medical practitioners rely to a great extent upon proved remedies which have survived successive axes in the *British National Formulary*. These include simple liquorice lozenges, hot-water mixtures, inhalations, expectorants, antispasmodics, antihistamines, and sedatives of varying strength. At present many unrelated drugs which have, among other properties, a bronchodilator effect are being tried; preparations of theophylline which can usefully be taken by mouth are being synthesized; anaesthetics both local and central are being tested; the effect of ion-exchange resins upon the rate of release of drugs is being explored; and some newer sedatives such as pholcodine and methadone are proving their worth. In the meantime the public is waiting for the day when we can "with some sweet oblivious antidote cleanse the stuff'd bosom of that perilous stuff which weighs upon the heart."

WHY ADMIT TO A MENTAL HOSPITAL?*

BY

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Those of us who have worked in mental hospitals for many years can remember a time when we had to use all our persuasive powers in order to get patients to admit themselves for treatment on a voluntary basis. But as every aspect of mental hospital life has been steadily upgraded—improved food, clothing, and furniture; considerably reduced restrictions (for example, very few locked doors), modern specialized treatments, better facilities for occupation and recreation, and so forth—many of us have found our admission rates growing like the proverbial snowball. At first we were gratified, for we were given the opportunity of treating mental illness in its earlier stages, when prospects of recovery are better; and the ever-increasing readiness of patients to be admitted was proof of the improvements in every aspect of mental hospital life for which we had striven. But latterly many of us have begun to wonder whether the journey

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