CORRESPONDENCE

APPEARENTLY EMPTY OXYGEN CYLINDERS

Sir,—We report the discovery of an apparently full oxygen cylinder from which oxygen could not be obtained. One of a batch of four size D oxygen cylinders supplied by the British Oxygen Company Limited (B.O.C.) was connected to a new portable anaesthetic apparatus (Penlon Longworth Limited) supplied for use with an obstetric flying squad. The intact red plastic seal around the spindle was removed immediately before attaching the cylinder to the apparatus. When the spindle valve was opened the customary hiss of escaping gas was not heard and no pressure registered on the gauge. The cylinder was thought to be empty and was replaced by another.

Subsequent investigation by B.O.C. revealed that part of the soft nylon seat of the spindle had been extruded, forming a "pip" which effectively blocked the passage of gas. This cylinder was, in fact, full.

It is the practice of many anaesthetists to test that a cylinder is full immediately before use by connecting it to a pressure gauge and opening the spindle valve.

However, the valve may remain loosened and continue to leak oxygen slowly until the cylinder is empty. When cylinders are taken from store and not used at once it is natural to assume that the presence of an intact seal around the spindle guarantees not only that the cylinder is full, but that oxygen can be delivered. However, our experience demonstrates that this may be false assumption. Fortunately this type of fault is said by B.O.C. to be not very common (approximately 1 or 2 per month), but the consequences may be serious if only one cylinder is available.

C. E. BLOGG
M. P. COLVIN
London

HYPERSENSITIVITY TO INTRAVENOUS ANAESTHETIC AGENTS

Sir,—The Editorial by J. W. Dundee (Editorial, 1976) on hypersensitivity to intravenous anaesthetic agents is timely.

In the Wellington Hospital group, such hypersensitivity reactions were unknown before 1972. In the period 1972-75 there were 13, with two fatalities. This is an incidence of 1 in 5000 general anaesthetics.

The reactions were produced by:
- Althesin (4)
- Suxamethonium (4)
- Thiopentone (1)
- Gallamine (1)
- d-Tubocurarine (1)
- No cause determined (fatal) (2)

These reactions have been described in detail elsewhere (Brown, 1975; Fisher, 1975; 1976a, b).

The two fatal cases were the only two fatalities in association with anaesthesia in fit patients during that period and this increases our concern about such reactions.

Professor Dundee noted the high incidence of previous exposure in reactions to induction agents and in our five patients previous exposure had occurred. Interestingly, the converse applied to muscle relaxants, and in all instances in Wellington, and in every case we have found in the literature with one exception (Watt, 1973), the reactions occurred following a first exposure. This would seem to suggest a different mechanism from true IgE cytotoxic antibody-induced anaphylaxis, but when Prausnitz-Kustner testing was performed, two women who suffered severe reactions to suxamethonium on first exposure showed positive Prausnitz-Kustner tests to suxamethonium. A similar phenomenon has been described by Jerums, Whittingham and Wilson (1967). This suggests that the patients who had never received suxamethonium had antibodies to the drug before the reaction. Thus cross-sensitivity may be important in the increasing incidence of such reactions, and this may explain the higher incidence of females exhibiting such reactions.

Our incidence of reactions to Althesin was 1 in 900, which is similar to that recorded by Watt (1975) and significantly different from that of Clarke and others (1975), and the possible explanations for this have been discussed (Fisher, 1976a). The possibility of variation in batches of drugs prepared by manufacturers has been demonstrated elegantly by Lorenz and others (1976) as significant in reactions to Haemaccel and similar variations may occur with Althesin.

Another interesting epidemiological finding was that seven patients had high plasma concentrations of IgG. In the light of demonstrations of complement consumption in hypersensitivity reactions (Watkins, Appleyard and Ward, 1975) this suggests that IgG antibodies (which do not require a latent period of sensitization and may involve the complement pathway) may be important in such reactions.

M. FISHER
Adelaide

REFERENCES

PHARMACOKINETIC MODELS: SIMPLE OR COMPLEX?

Sir,—Beneken Kolmer and his colleagues (1975) reported in this Journal an interesting study of the uptake and elimination of halothane in dogs. They claimed that their results could be described adequately by equations involving only two exponentials and, therefore, in terms of a two-compartment system. They went on to expound the advantages of a two-compartment system over a multi-compartment system as that originally propounded by Kety (1951).

However, the choice between a simple and a complex model depends upon the object of the study. If the object is only to provide an empirical description of experimental results then a simple equation may well be adequate—at least if the constants in the equation are chosen on the basis of what will fit the data best. Since Beneken Kolmer’s equations have four or five constants it is not surprising that, by choosing different values of the constants for each animal and for each sampling site, they get a good fit of the calculated curves to the measured tensions in restricted circumstances, that is during $1\frac{1}{2}$ h of elimination. Indeed, Lowe (1972) has gone even further and claimed good fits for a range of anaesthetic agents given at constant alveolar concentration with an equation of the form $at^{-0.8}$ (where $t$ is time). This equation includes only one arbitrary constant, $a$.

Empirical equations are valid only for the circumstances in which they were derived. For an equation to be applicable over a wide range of circumstances it must be based on sound theory; then it can be used to predict uptake and elimination from a knowledge of the physiological properties of the body and the physical properties of the anaesthetic.

For predictions of this kind to agree with experiment, multi-compartment models are necessary (Mapleson, 1962; Eger, 1963; Cowles, Borgstedt and Gillies, 1972); and it now appears that even these may be inadequate if they allow communication between compartments only by perfusion; direct diffusion between compartments may need to be taken into account (Allott, Steward and Mapleson, 1976).

A further advantage of a theoretical model is that it can be used to make predictions of the effects of changes of circumstances; but how could the effect of obesity, for instance, be deduced from Beneken Kolmer’s equation?

Thus, the complexity of the equation required depends upon the use to be made of it: by all means use a simple equation where this is adequate but, because a simple equation fits in some circumstances, do not think that it will fit in all circumstances.

Finally, it is a little quixotic that, at the same time that Beneken Kolmer and his colleagues are drawing attention to the merits of simple empirical models, non-anaesthetic pharmacokineticists, who have traditionally used such models, are beginning to appreciate the merits of theoretical models (Benowitz et al., 1974).

W. W. MAPLESON
Cardiff

REFERENCES


