THE SAFETY OF VINYL ETHER

BY

C. J. MASSEY DAWKINS, M.D., F.F.A.R.C.S.
D.A.

*Consultant Anaesthetist and Lecturer in Anaesthesia,
University College Hospital, London*

In the absence of any information about the number of times any particular anaesthetic is administered it is impossible to evaluate its mortality rate in conjunction with the tables of deaths occurring under anaesthesia issued annually by the Registrar-General of England and Wales and of Scotland. In any given operation there are many variable factors present which may influence the ultimate result: the skill of the surgeon, anaesthetist, and nursing staff; the physical condition of the patient; and the risk carried by the particular operation performed. If a fatality occurs it is extremely difficult, in the absence of any gross error, to apportion the blame. Also, it is usual for the anaesthetist to give several different anaesthetic drugs to each case. When the Ministry of Health carried out its survey of explosion risk in 1954, a table was published showing the frequency of use of each anaesthetic drug, and it was found that on the average 2.4 different drugs were used for each operation performed. But this survey covered only the hospitals of England and did not include anaesthetics given in clinics, in nursing-homes, and in general practice. From this table can be drawn some interesting comparisons of the various anaesthetics given in different types of hospital, but that is all.

Examination of the tables of mortality issued by the Registrars-General also shows that many combinations of anaesthetic drugs are used in major surgery; but in minor surgery it is quite usual to employ only one drug to provide the short period of anaesthesia required. In a short operation, too, the skill of the surgeon and that of the nursing staff are not of such paramount importance as they are in major surgery; while the patient is usually an out-patient well enough to be able to attend hospital. All this makes the responsibility of the anaesthetist even greater, and it behoves him to use the safest possible anaesthetic for the operation. The anaesthetic drugs in common use for minor surgery are nitrous oxide, thiopentone, hexobarbitone, trichlorethylene, ethyl chloride, and vinyl ether. The number of times these anaesthetics are given singly is unknown, with the exception of vinyl ether. Thanks to the courtesy of the sole manufacturers of vinyl ether ("vinesthene") the number of ampoules issued for single-dose anaesthesia each year is known.

During the last ten years 521,800 ampoules of 3 ml. and 5 ml. were issued, and during the same ten years there has been only one death where vinyl ether was the sole anaesthetic. It may be argued that occasionally more than one ampoule is used for a single case. But against this may be set the fact that vinyl ether is also issued in 25-ml. bottles and it is possible to give several short inductions from one bottle. The number of times this occurs it is impossible to estimate, but it is likely to make up for the number of cases which ought to be subtracted from the total number because more than one ampoule has been used.

Side-effects

Vinyl ether was introduced as an anaesthetic by Gelfand Bell in 1933. The preliminary favourable reports were somewhat modified by the occurrence of five cases of acute yellow atrophy of the liver. In each case more than

300 ml. had been given and the operation had lasted for more than one and a half hours. Since 1941 no other case has been reported, but in most textbooks the reservation has been made that the drug should not be given for longer than half an hour. In my experience it has been given on many occasions for over three hours without untoward sequelae, but the total amount used has never exceeded 200 ml. Convulsions occurring under vinyl ether were encountered (Dawkins, 1940). These convulsions were of two distinct types. One variety took place under deep anaesthesia with soda-lime absorption, the incidence being about 1 in 40. The other type made its appearance during the recovery period following a single dose of vinyl ether for dental extraction. This has an incidence of about 1 in 400, but as there has never been a report of a fatal case the aetiology of these complications must remain obscure. No other side-effects of vinyl ether anaesthesia are known.

Comparison with Ethyl Chloride

It is surprising that an anaesthetic with such a high degree of safety is not more widely used. It may be objected that it is extremely volatile and so difficult to give; that it decomposes rapidly when exposed to air, and so must be used within 24 hours of opening the container; that it is rather expensive; and that the garlic-like smell is unpleasant. But the safety of the drug should outweigh these disadvantages. The drug most often used for short anaesthetics in young children is ethyl chloride, but the phrase coined about ethyl chloride, "dead easy—easy dead," is all too apt. This anaesthetic has many serious disadvantages. It is so toxic that only one dose may be given. If an overdose is given the respiratory centre and the cardiac centre are likely to fail together; there is no safety margin as there is in all other anaesthetics except chloroform. With an impending overdose, spasm of the masseter is common, so that it is very difficult to open the mouth to pull the tongue forward. Involuntary micturition during anaesthesia is also common.

None of these complications is encountered with vinyl ether. Ethyl chloride is, of course, widely used in this country by anaesthetists who are trained to overcome its dangers, but it is best avoided by the occasional anaesthetist. It is perhaps significant that in one hospital in the U.S.A. the use of ethyl chloride by a resident results in instant dismissal; while in others a form accepting all responsibility in the event of a fatality has to be signed before its use.

It has been shown (Jarman, 1939) that deaths from anaesthetics could be classified into three groups according to the experience of the administrator. If anaesthetists in training, whose skill is difficult to assess, are excluded, in 80% of deaths the administrator was a newly qualified houseman, in 12% a general practitioner, and in 8% a consultant anaesthetist. But, although striking, these figures are not very much use in the absence of information about the numbers of anaesthetics given by each class. In recent years, with the increased number of anaesthetists, trained or in training, available, it has become more rare for newly qualified housemen to be asked to give an anaesthetic. And if they do give one they may, as a recent case has shown, find themselves in court accused of negligence. Therefore, if a houseman has to give an anaesthetic for a minor operation, he should use that which is safest. The mortality from ethyl chloride is unknown, as it is impossible to ascertain the number of times it is given, but the Ministry of Health tables show that it was given six and a half times more often than vinyl ether. During the last ten years there have been 69 deaths under anaesthesia where ethyl chloride was the sole anaesthetic—and one with vinyl ether.

Deaths under Various Anaesthetics

For the sake of comparison with the other anaesthetics used in minor surgery, the numbers of deaths under each

anaesthetic in England, Wales, and Scotland during 1947-56 are shown. They were:

Nitrous oxide	350	Trichlorethylene	15
Thiopentone	792	Ethyl chloride	69
Hexobarbitone	13	Vinyl ether	1

Where the anaesthesia was prolonged by the addition of nitrous oxide and oxygen the figures were:

Nitrous oxide and trichlorethylene	118
" " thiopentone	407
" " hexobarbitone	3
" " ethyl chloride	57
" " vinyl ether	0

In the absence of information on how often each anaesthetic was given it is unwise to draw any conclusion, but in the case of vinyl ether it has been shown that the mortality is less than 1 in 500,000.

REFERENCES

- Dawkins, C. J. M. (1940). *Brit. med. J.*, 1, 163.
Jarman, R. (1939). *Brit. J. Anaesth.*, 16, 100.
Ministry of Health (1954). *Public Health Report*, 2, 247.

VACCINES AGAINST POLIOMYELITIS STATEMENT BY MEDICAL RESEARCH COUNCIL ON THE CURRENT POSITION, APRIL 29, 1958

This statement was issued by the Medical Research Council immediately after the Minister of Health's speech in the debate in the House of Commons on May 1 on supplies of poliomyelitis vaccine (see p. 1128).

1. The Medical Research Council have been asked by the Government to advise whether, in view of the present shortage of poliomyelitis vaccine, American or Canadian Salk vaccine which has satisfactorily passed safety tests and been licensed for issue in the country of origin should be made available for use in this country without first being subjected to the safety tests of the Medical Research Council.

2. The Council have made a full review of the current situation in the light of their responsibilities for safety testing poliomyelitis vaccine in this country. They have given careful consideration to all the available evidence on the risks attending the use of the various poliomyelitis vaccines now being produced; on the risks in different circumstances of leaving a large number of children and others in special need of protection unvaccinated during the late spring and early summer months of this year; and to information on the amount of vaccine likely, under present arrangements, to become available for use in the next few months.

Vaccines Available

3. Three vaccines against poliomyelitis are available for consideration: the British vaccine; imported American or Canadian vaccine that has passed British safety tests; and imported vaccine from the American or Canadian sources that has not been subjected to British safety tests. The two former are now in use in this country: the latter, at present, is not, although vaccine of this type has been used extensively elsewhere.

4. All poliomyelitis vaccine at present in use is made from three types of virus, types I, II, and III. In both the British and the American or Canadian vaccines, similar strains of the type II and type III viruses are used. On the other hand, two different strains of type I virus are used. The American and Canadian vaccines include the relatively virulent type I strain, known as Mahoney; the British vaccine, the much less virulent type I strain, known as Brunenders. If, therefore, some of the virus failed to be inactivated in the course of manufacture, the British vaccine would be less likely to produce poliomyelitis on injection than would vaccines made from the Mahoney strain.

It is the use of a type I strain of low virulence that makes the British vaccine the safest yet produced.

5. All vaccines are submitted to a series of safety tests at several stages before issue, both during and after manufacture, with the object of detecting any virus that has survived the process of inactivation. Of necessity only samples

of each batch of vaccine can be tested, and the possibility inevitably remains that in the untested part of the batch a few particles of live virus may still be present. It follows, therefore, that the greater the size and number of the samples tested, the smaller is the chance of any surviving virus remaining undetected and the greater the assurance that can be given regarding the safety of the vaccine.

6. If vaccine is submitted to an adequate number of safety tests of the full range now in use, there is little chance of contamination with live virus escaping detection. If a few particles of live virus do escape, the effect on the safety of the vaccine will depend upon their virulence. With the Brunenders strain of relatively low virulence used in the British vaccine, it is most improbable that any ill effects would follow inoculation; with the Mahoney strain, used in the American and Canadian vaccines, such a possibility could not be excluded with the same assurance.

7. It was because the more virulent Mahoney strain is used in the preparation of American and Canadian vaccine that the Medical Research Council, when recommending that vaccine should be imported from these countries to meet the shortage of poliomyelitis vaccine in the summer of 1957, linked that recommendation with the proviso that such vaccine should be submitted to further safety testing in this country in order to increase the safeguards against any particle of live virus of the virulent strain being present in the vaccine when issued.

Order of Safety

8. Taking all these factors into account, the Medical Research Council believe that the three vaccines under consideration can be placed in the following order of safety:

(a) Vaccine made according to the British formula that has successfully passed British safety tests.

(b) Imported vaccine from America and Canada that has successfully passed safety tests in the country of origin and also British safety tests.

(c) Imported vaccine from the same sources that has successfully passed safety tests and been licensed for issue in the country of origin.

9. After carefully weighing all the available evidence bearing on this complex problem, the Council are satisfied that the risk of producing paralytic poliomyelitis by injecting any one of these three vaccines is very slight and that a person inoculated with any one of them is substantially less likely to contract paralytic poliomyelitis than if he is left un inoculated. Nevertheless, no vaccine can be guaranteed to be wholly free from risk, and the preference should always be for the safest known vaccine.

10. The Council reaffirm their view that British-type vaccine which has successfully passed British safety tests is the safest poliomyelitis vaccine known; that the only justifiable permanent policy is to use every endeavour to produce this in such quantities as to meet all the needs of this country; and that any policy which has recourse to less safe vaccines should, however slight the risk, only be regarded as temporary.

Next in order of preference is imported vaccine that has passed successfully British safety tests as well as tests in the country of origin.

Third is imported vaccine which, although it has successfully passed safety tests in the country of origin, has not been submitted to the further British tests carried out by the Medical Research Council in this country.

Recommendations

11. The present problem arises because supplies of British vaccine and imported vaccine that have passed British safety tests are together insufficient to meet requirements, and cannot become sufficient in time to prevent a substantial deficit during the summer months when the incidence of poliomyelitis may be expected to increase.

12. After carefully examining the present situation the Medical Research Council have concluded that, as it would