often they have failed to appoint independent observers even of behaviour, and less still have they made thorough investigations into the psychological state of their patients. Our experience, we think, emphasizes the importance of design in a trial of this kind and draws attention to the paucity of evidence on which claims are made about drugs alleged to allay apprehension.

So far as overt conduct is concerned, we are of the opinion, from our present findings, that for children 6 years of age and over preliminary sedation before dental extractions undertaken with a general anaesthetic is usually unnecessary. Below this age any method of improving behaviour would be an advantage. Methylpentynol, butobarbitone, and chlorpromazine scarcely provide the answer, at least in the doses we used, and there is the risk that with higher doses side-effects might be manifest. Moreover, many "elixirs" are unpalatable, and often their administration may itself contribute to loss of confidence.

Summary

The case for the pre-operative sedation of children before general anaesthesia for dental operations as out-patients is examined.

The problem of assessing the effect of a pre-operative sedative drug is considered. A method of solving it by using a behaviour-grading process was evolved and tested.

Methylpentynol, butobarbitone, and chlorpromazine were selected as potentially useful premedicant drugs.

Using the "double blind" technique and our method of assessment, a pilot trial and a major trial of these three drugs were carried out within the framework of the routine dental gas session in Guy's Hospital.

A very marked difference was shown between the patterns of behaviour of the older and the younger children.

None of the three drugs could be distinguished from a placebo by their effect on the behaviour of the children about to be anaesthetized.

Possible explanations of this negative result are discussed.

We thank Mr. R. E. Rix and Mr. K. E. Pringle and their assistants for their courtesy in allowing this investigation to be undertaken at their dental extraction sessions, and also the sisters and nursing staff concerned for the help afforded to us. We are indebted to Dr. W. S. McConnell, the anaesthetist in charge of one session, for his ever-willing and experienced advice, to Dr. A. Cashmore and Miss Putzel for their help as assessors in the pilot trial, and to Miss Treadgold and Miss Waldron for their assistance in the presentation of the results. We are obliged to Mr. Moore, the chief dispenser, for his co-operation with the preparation of the premedications, and to Miss Grossman for her help with the records. Finally, we thank Messrs. May and Baker for supplies of chlorpromazine and butobarbitone and Messrs. British Schering for methylpentynol.

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CARDIAC ARREST DURING TRICHLORETHYLENE ANAESTHESIA

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In this country trichlorethylene is widely used as an anaesthetic or analgesic agent. Many regard it as suitable for almost all types of surgery (Ostlere, 1953). Its value lies in providing a non-inflammable supplement to nitrous oxide and oxygen, enabling light anaesthesia to be produced without restriction of oxygen. Although bearing some resemblance to chloroform, it appears to lack the dangers of this drug. In particular, despite its widespread use, primary cardiac failure during trichlorethylene anaesthesia has seldom been reported.

Such a mishap, however, occurred recently in this hospital. Discussion of this case has brought to light several similar unpublished episodes which we feel will be of interest to all who have occasion to use this drug.

Survey of Literature

Twenty cases of cardiac arrest during trichlorethylene anaesthesia have been reviewed by Ostlere (1953). In only three of these is he prepared to incriminate trichlorethylene—namely the cases originally reported by Haworth and Duff (1943), de Soldenhoff (1949), and Rait Smith (personal communication to Ostlere).

Details of the second case illustrate the characteristic features. The patient was a healthy young girl undergoing tonsil dissection. The premedication was morphine $\frac{1}{4}$ gr. (11 mg.), and atropine 1/100 gr. (0.65 mg.). Anaesthesia was maintained by endotracheal nitrous oxide, oxygen, and trichlorethylene. Anoxia and respiratory obstruction were absent. In the course of the operation the pulse was noted to be mildly irregular, and almost immediately after this cardiac and respiratory arrest occurred. Resuscitative measures, including cardiac massage, were of no avail.

Another five cases of Ostlere's series are sufficiently similar to the above to merit further consideration.

1. Hewer and Hadfield (1941) reported the death of a young adult operated on for drainage of empyema under nitrous oxide, oxygen, and trichlorethylene anaesthesia. Cardiac arrest occurred during skin closure. As this was the first fatality of its kind reported during trichlorethylene anaesthesia it is not surprising that Hewer should look elsewhere for the cause of death. The suggested alternative of air embolism seems hardly justified in view of the post-mortem findings. Now, fifteen years later, this would appear to be a case of primary cardiac failure similar to that described above.

2. Stout (1951) reported a case of forequarter amputation in a 37-year-old man under thiopentone and endotracheal nitrous oxide, oxygen, and trichlorethylene anaesthesia. Cardiac and respiratory arrest occurred suddenly after 15 minutes of surgery. Ostlere describes this as a case of "forequarter amputation without transfusion" and states that "shock and haemorrhage seem the more likely causes [of death]": this in spite of the fact that Stout in his report states, "Progressive onset of shock was absent. One pint of

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blood was given during operation and nearly compensated for the loss during surgery. The collapse was sudden and dramatic." It would appear more reasonable to include this as a case of cardiac arrest where trichlorethylene is at least suspect.

3. De Soldenhoff (1949), in addition to the case accepted by Ostlere, reported a case of sudden death under trichlorethylene analgesia administered from a Hayward-Butt inhaler. Necropsy revealed no cause of death. This is yet another unexplained collapse, and there would appear to be no good reason for excluding trichlorethylene as a possible cause of death.

The fourth and fifth cases were originally reported by Cope (1949), but are dismissed by Ostlere from his series because "details of them cannot be found." However, in a personal communication Dr. Cope has supplied us with the following information.

4. A healthy young primipara was delivered under nitrous oxide, oxygen, and trichlorethylene without incident. Blood loss was within normal limits and the patient was fully conscious at the end of the third stage. Anaesthesia was then induced with nitrous oxide, oxygen, and minimal trichlorethylene to permit repair of the perineum. Induction was stormy, with cyanosis and spasm, and cyanosis was still present when the obstetrician inserted his first deep stitch. Instantly respiration ceased, the colour changed to grey-white, and on rapid examination there was no sign of a heart-beat. Resuscitative measures, including cardiac massage, were of no avail.

5. A woman of 48 was undergoing dental clearance in the dental chair under nasal nitrous oxide and oxygen from a Walton machine. After eight teeth had been extracted anaesthesia was deemed inadequate and the extractions were suspended until a satisfactory depth of anaesthesia had been achieved by the addition of trichlorethylene to the gases. On extraction of the ninth tooth respiratory and cardiac arrest occurred. Resuscitation again failed.

Dr. Cope comes to the justifiable conclusion that trichlorethylene played some part in the deaths of these two women.

The report of the Committee upon Deaths Associated with Anaesthesia of the Association of Anaesthetists of Great Britain and Ireland (1952) includes four fatalities due to sudden circulatory failure under trichlorethylene anaesthesia. It is significant that the only other agent producing this type of collapse was chloroform (five cases).

Bernstine (1954) reports a case of cardiac arrest occurring in a healthy young man after five minutes of trichlorethylene analgesia from a "cyprane" inhaler administered for wound dressing. The heart, found to be in asystole, responded after 45 minutes of cardiac massage, but a year later the patient still showed signs of impaired cerebral function.

In a recent review of anaesthetic hazards in obstetrics, Lock and Greiss (1955) report three deaths under trichlorethylene. At least one of these would appear to be of significance. Trichlorethylene was used for delivery of a 29-year-old 1-para at term. She suddenly became cyanotic and pulseless and died during delivery. "The autopsy findings were non-contributory."

As can be seen from this survey few reports of cardiac arrest under trichlorethylene anaesthesia have appeared in print. This may well be explained by a natural reluctance to publicize misadventures in face of the prevailing enthusiasm for trichlorethylene in this country. While we have not attempted any extensive investigation and the cases which we now report occurred, with one exception, in the West of Scotland, discussions with anaesthetists in other parts of Britain would lead us to believe that similar incidents occur elsewhere.

Case 1

A healthy young man aged 22 presented for exploration of palm of hand after attempted removal of a foreign body

under local analgesia (without adrenaline) had failed. The premedication was atropine 1/100 gr. (0.65 mg.). Anaesthesia was induced with nitrous oxide, oxygen, and trichlorethylene. Within two minutes of adding trichlorethylene sudden collapse occurred with pallor, apnoea, and apparent cardiac arrest. Recovery followed manual inflation of the lungs, using 100% oxygen with the patient in the Trendelenburg position. When normal respiration and cardiac action had been restored, anaesthesia was inadequate for the operation to be started. Minimal trichlorethylene was again added and the cycle of events was repeated. As it now appeared that the collapse was related to the administration of trichlorethylene the operation was performed under nitrous oxide, oxygen, and ether without further incident, and the patient made an uneventful recovery.

The cause of arrest in this case seems obvious. The myocardium may have been sensitized by a high level of endogenous adrenaline due to the preliminary exploration under local analgesia. Although the heart was not exposed the condition of the patient on collapse left little room for doubt that cardiac arrest had occurred. This case is similar to one of Johnstone's (1955) series, where under almost identical circumstances an electrocardiographic tracing showed asystole. In both cases spontaneous respiration and heart-beat returned after artificial ventilation. This was presumably due to rhythmic compression of the heart by the expanding lungs.

Case 2

A healthy woman aged 38 was admitted to hospital for tonsil dissection. Premedication was by atropine, 1/100 gr. (0.65 mg.). Anaesthesia was induced with thiopentone and suxamethonium and maintained with endotracheal nitrous oxide, oxygen, and trichlorethylene. After removal of the first tonsil respiration suddenly ceased and simultaneously the surgeon reported the absence of bleeding from the tonsil bed. Resuscitative measures, including cardiac massage, were of no avail. This case is identical to that reported by de Soldenhoff (1949) and accepted by Ostlere (1953) as a case of primary cardiac failure caused by trichlorethylene.

Case 3

A child aged 9 was submitted for appendicectomy. Premedication was by morphine, $\frac{1}{4}$ gr. (8 mg.), and atropine, 1/100 gr. (0.65 mg.). Anaesthesia was induced with nitrous oxide, oxygen, and trichlorethylene. Almost immediately after the addition of trichlorethylene respiration suddenly ceased. Rapid examination at this stage revealed pallor and absence of the heart-beat. Manual inflation of the lungs with 100% oxygen in the Trendelenburg position resulted in the resumption of normal respiration and cardiac action. Appendicectomy was performed under nitrous oxide, oxygen, and ether without incident.

Case 4

A child aged 2 years presented for incision of a superficial abscess of buttock. Premedication was by atropine, 1/100 gr. (0.65 mg.). Anaesthesia was induced with nitrous oxide, oxygen, and trichlorethylene. After a few breaths of trichlorethylene collapse occurred suddenly, with pallor and cessation of respiration. Active measures similar to those described in Case 3 again resulted in the resumption of respiration and heart-beat.

Case 5

An elderly man presented for removal of stitches and suprapubic tube under trichlorethylene analgesia from a cyprane inhaler. A prostatectomy had been performed without incident the previous week. Cardiac arrest occurred before surgical intervention had begun. Resuscitation was of no avail. Although this patient was not in good physical condition, suffering from hypertension and chronic bronchitis, it is significant that death should have occurred

during a trivial procedure when he had successfully withstood a suprapubic prostatectomy so recently. This patient was premedicated with atropine 1/100 gr. (0.65 mg.). The cyprane inhaler was at no time set beyond the third mark.

Case 6

A healthy man aged 40 was admitted to hospital for block dissection of glands of the right side of the neck. He was premedicated with papaveretum, $\frac{1}{2}$ gr. (22 mg.), and scopolamine, 1/150 gr. (0.43 mg.). Anaesthesia was induced with thiopentone and suxamethonium. The throat was sprayed with lignocaine 4%, a No. 9 plain endotracheal tube passed, and a throat pack inserted. Anaesthesia was maintained with nitrous oxide, oxygen, and trichlorethylene. Following the adoption of a 15–20-degree foot-down tilt and intermittent doses of hexamethonium bromide to a total of 100 mg., the blood systolic pressure was stabilized at a level of 85 mm. Hg. While the dissection proceeded round the subclavian vein a small puncture was made in the vessel, but this was rapidly sealed without entry of air. When dissection had proceeded to the level of the hyoid bone respiration suddenly and dramatically ceased. Carotid pulsation was no longer visible and the apex beat was absent. Immediate artificial ventilation with 100% oxygen in the head-down position was performed and cardiac massage was instituted within 1½ minutes of arrest. The heart was restarted within 30 seconds, and respiration began within a further minute, with restoration of systolic blood pressure to the previous level. The operation was completed under nitrous oxide, oxygen, and intravenous pethidine without further incident. The patient was conscious and rational on termination of the anaesthesia.

The hypotension in this case was never marked and in fact the blood pressure remained at a stable level for 45 minutes, never falling below 80 mm. Hg systolic. The dramatic nature of the collapse is in marked distinction to the usual manner in which death occurs during hypotension (Committee upon Deaths Associated with Anaesthesia 1953). Coronary thrombosis, whether due to the hypotension or occurring as a primary condition, can presumably be excluded by the rapid response of the heart to cardiac massage and the subsequent uneventful recovery. Air embolism is not consistent with the suddenness of the collapse and the equally rapid and complete recovery.

Case 7

A healthy young primigravida aged 30 was admitted to hospital for lower uterine segment caesarean section for contracted pelvis and foetal distress. Premedication was by atropine, 1/100 gr. (0.65 mg.). Anaesthesia was induced with thiopentone and maintained with nitrous oxide, oxygen, and trichlorethylene. After delivery of a live infant the uterus was well retracted and the blood loss was within normal limits. As the abdomen was being closed cardiac arrest occurred. Resuscitation restored a feeble pulse and spontaneous respiration but the patient failed to regain consciousness and died two hours later. Necropsy revealed no cause of death.

Haemorrhage in this case was by no means excessive and up to the time of arrest the patient gave no cause for concern to either surgeon or anaesthetist.

Comment

Cardiac arrest occurring during trichlorethylene anaesthesia is not necessarily cardiac arrest due to trichlorethylene. Before the drug is incriminated certain conditions must be fulfilled. (1) The pattern of arrest must be essentially similar in all cases. (2) Other possible causes of arrest must be absent. (3) The technique of administration of the drug must be beyond reproach, avoiding both anoxia and overdosage.

In each of the cases reported above the clinical picture has been essentially the same, displaying the features originally described by Snow when he first reported primary

cardiac failure under chloroform anaesthesia. Recovery without cardiac massage does not preclude the diagnosis of cardiac arrest in those cases exhibiting the classical features—namely, pallor, apnoea, and absence of pulse and heart sounds. This has recently been demonstrated conclusively by Johnstone (1955) who also showed that resuscitative measures short of cardiac massage may suffice under certain circumstances.

In four of our cases arrest occurred during induction and before surgery had been started. In the remainder the picture is more complicated, but for the reasons given with each report we feel that trichlorethylene was responsible for the arrest which occurred.

In one case trichlorethylene was administered from a cyprane inhaler, a method commonly used both in this country and abroad. In the other cases administration was from the chloroform bottle of the standard Boyle machine, the oxygen varying between 25 and 30% and the minute flow being 7 to 8 litres. Only minimal quantities of trichlorethylene were added, the lever being never more than half-way open and the plunger fully elevated. Enderby (1944) has condemned the use of the chloroform bottle on the Boyle machine for the administration of trichlorethylene. He maintains that even in the minimal position the concentration of trichlorethylene administered is excessive for maintenance of anaesthesia, while anything approaching the maximum concentration is in excess of that required to anaesthetize any patient. Within these limitations, however, the Boyle bottle is still commonly used, and without it the use of trichlorethylene for anaesthesia would virtually cease in this country.

Reassessment of the Place of Trichlorethylene in Modern Anaesthetic Practice

Trichlorethylene, being a powerful analgesic, neither irritant nor explosive, has been widely used in the following circumstances: (1) As a supplement to nitrous oxide and oxygen in the production of light anaesthesia without anoxia. Since after-effects are minimal its popularity became rapidly established in dental, casualty and obstetric practice. (2) To produce the analgesia of Gray's triad (Gray and Rees, 1952) in conjunction with thiopentone, nitrous oxide, and a muscle relaxant. In this respect it is used in lower abdominal surgery and in such operations as herniorrhaphy and haemorrhoidectomy, where some relaxation is desirable but assisted rather than controlled respiration is indicated. (3) As a suitable agent for maintenance of anaesthesia when the explosion hazard is present. (4) As an analgesic vaporized by air.

Hunter (1944) has suggested that the use of trichlorethylene as a routine supplement to nitrous oxide and oxygen should cease. To facilitate the introduction of ether, vinyl ether anaesthetic mixture is just as effective and much safer to the cardiac rhythm. For maintenance of light anaesthesia trichlorethylene may well be replaced by minimal ether, the increased incidence of post-operative vomiting which may ensue being a small price to pay for the increased safety of the agent used. Since the introduction into anaesthetic practice in this country of intravenous pethidine (Mushin and Rendell-Baker, 1949) this drug has largely supplanted the more toxic volatile anaesthetics, and it may well be that alphaprodine hydrochloride ("nisentil"), at present under investigation, will prove even more satisfactory in this respect.

For dental and casualty anaesthesia Bourne has recently advocated the use of cyclopropane and oxygen; where the explosion hazard is present the oxygen is diluted with nitrous oxide. While this technique has still to stand the test of time the results so far are encouraging. Another suitable alternative for this type of anaesthesia is vinyl ether anaesthetic mixture. In obstetrical anaesthesia the skilful use of ether dispenses with the need for trichlorethylene, and indeed in a recent report Lock and Greiss (1955) condemn its use as an anaesthetic in obstetrics under any circumstances. Similar

considerations apply when reviewing the choice of analgesic agent for use with a relaxant in lower abdominal surgery.

The use of diathermy precludes the employment of any inflammable agent, but once again the introduction of pethidine has reduced the indications for trichlorethylene in this sphere.

The use of trichlorethylene as an analgesic vaporized by air in the apparatus commonly used to date is obviously not without risk. Whether these dangers have been completely overcome by the introduction of thermostatically controlled vaporizers remains to be seen.

Conclusions

Pharmacologically, trichlorethylene bears a strong resemblance to chloroform, and while it is not suggested that the incidence of cardiac arrest is at all comparable it may well be that the occurrence is not so rare. Reported cases are indeed few, but it is possible that this is due to a natural reluctance to publicize mishaps. When cardiac arrest occurs during anaesthesia many possible factors may be implicated. As this is an infrequent occurrence in the clinical experience of any one anaesthetist, and as trichlorethylene is reputedly a safe anaesthetic, it is not surprising that the blame in these cases is apportioned elsewhere and the incident passes unrecorded. This is well seen in Case 6 of our series, where if death had occurred the exclusion of air embolism or coronary thrombosis would have been virtually impossible.

We feel that the place of trichlorethylene in modern anaesthesia is very limited, and in the absence of strong indications for its use other, and safer, agents should be employed. When it is used, however, the possibility of cardiac arrest should be borne in mind and the risk balanced against the advantages to be gained. There is still a place for a safe non-inflammable volatile anaesthetic agent should such be discovered.

Summary

A critical survey of the literature pertaining to cardiac arrest during trichlorethylene anaesthesia is presented. Seven previously unpublished cases are reported. The aetiology of the cardiac arrest in these cases is discussed and the possible role of trichlorethylene is emphasized. The scope of trichlorethylene in modern anaesthetic practice is reassessed and the employment of alternative agents whenever possible is recommended.

We are indebted to Dr. R. W. Cope for making available to us further details of the cases already reported by him. We are grateful to our colleagues whose cases are included in this report, and no less to those whose cases have for various reasons been omitted. Finally, we thank Dr. A. C. Forrester and Dr. D. M. Armstrong for their encouragement in the preparation of this paper.

ADDENDUM.—Since this paper was prepared the Committee upon Deaths Associated with Anaesthesia has produced a further report (*Anaesthesia*, 1956, **11**, 194). In this report nine cases of primary cardiac failure are mentioned and a typical case history is given. This type of death accounts for 1.5% of the cases where the anaesthetic is considered to have been responsible for the fatality.

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AN OBSCURE CASE OF RUPTURED DIAPHRAGM

BY

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The following case of herniation of the stomach into the left pleural space may be considered rare enough to be placed on record.

Case Report

A man aged 54 was admitted to hospital as an emergency case on April 26, 1956. He was too distressed to give a history; he was gasping for breath, cold sweat was running down his face, and his extremities were blue and cold. It was noted that the heart pulsations were over to the right of the sternum, the trachea was also displaced to the right, the left chest was moving poorly and air entry could not be heard.

The history relevant to this episode is that he had been admitted to hospital as an acute abdominal emergency on September 9, 1954, and a diagnosis of perforation of a diverticulum of the pelvic colon was made. At operation the peritoneum was found to be full of foul-smelling fluid and a large, immovable inflammatory mass was felt in the pelvic region. Left iliac colostomy was performed and the abdomen drained. After a stormy convalescence, complicated by bilateral bronchopneumonia, he left hospital a month later.

On September 5, 1955, he was again admitted and a diagnosis of right-sided subphrenic abscess was made. At operation, after resecting the 12th right rib, foul-smelling pus was evacuated from the anterior superior space beneath the diaphragm and the space was drained for 15 days. He was discharged 21 days after his operation, and he remained at home, reporting to hospital occasionally, until the catastrophe here reported.

Immediately after the present admission a skiagram of his chest showed almost complete collapse of the left lung, with displacement of the mediastinum to the right, apparently due to an extensive hydropneumothorax (Fig. 1). On viewing the skiagram, the Senior Medical Registrar (Dr. D. C. Watson) passed a needle into the chest posteriorly,

FIG. 1.—Extensive hydropneumothorax with collapse of the lung.