tion, and we are of opinion that our figures are significant enough to justify the adoption of a similar scheme in this country.

Conclusions

Of 1,869 recruits referred to the Welsh National Memorial Association's tuberculosis officers by the medical boards and then seen for the first time, 112 (6%) were found to be suffering from active tuberculosis, as compared with 23.8% of male new cases in the same age group examined in 1940 in the ordinary course of work, and with 1.4% of the men called up and examined as a routine measure, and not because they were referred by medical boards, by Dr. Robert E. Plunkett.

Of the 112 recruits found tuberculous, 108 (or 5.7% of all those referred) had pulmonary tuberculosis, and 4 (0.3%) non-pulmonary tuberculosis.

An additional 30 cases (1.6%) required further observation.

The percentage figures of cases found tuberculous analysed under the four main headings set out in Table II show that the indications for the reference of cases by medical boards to tuberculosis officers should be comprehensive, and even then cases of active or latent tuberculosis may be missed. It is better that the total cases referred should be large, and the percentage found tuberculous low, than that only a few cases should be referred, with a high percentage found tuberculous.

The finding of a substantial number of tuberculous recruits in Wales strongly supports the view held by most tuberculosis workers that all recruits should be subjected to a radiological examination. It is regrettable that the Horder Committee has advised that this "was impracticable at the present time." The difficulties are appreciated, but with the modern developments of miniature radiological technique (Cranch, 1940) we feel it would have been a task not impossible of accomplishment, and at a reasonable cost.

It is unfortunate that the Public Health (Tuberculosis) Regulations, 1940, were not in force when the first age groups were called up, as these regulations apply only to men aged 33 and upwards and the "new 20's."

The percentage of cases (6.6) found tuberculous who were referred by medical boards to tuberculosis officers solely on account of an intimate contact history emphasizes the importance of the contact examination of young adults, and it would be well if all recruits with a family history of tuberculosis were referred to the Tuberculosis Service by the medical boards.

Our thanks are due to Prof. Picken, Mansel Talbot Professor of Preventive Medicine, University of Wales, for his very valuable advice and assistance. The tuberculosis officers of the Welsh National Memorial Association readily put all their records at our disposal and gave every help. To Dr. D. A. Powell, principal medical officer of the Memorial Association, we are particularly indebted for making this investigation possible and for his guidance throughout.

ADDENDUM

Since writing the above, an exhaustive report on pulmonary tuberculosis in recruits has been published by Major Douglas Galbraith (1941), Deputy Assistant Director-General of Medical Services, Australian Army Medical Corps, together with the report on the bacteriological examinations by Reginald Webster (1941), Honorary Major, Australian Army Medical Corps Reserve.

More than 100,000 recruits of the Australian Imperial Forces have been subjected to routine chest x-ray examination by the method of miniature radiography, and of that number 0.56% presented radiological evidence of active pulmonary tuberculosis; 1.04% gave radiological evidence of active or latent tuberculosis of the reinfection type; and 0.25% and 0.12% showed radiological evidence of non-tuberculous pulmonary pathology and of cardiac or vascular lesions, respectively.

The importance of radiological examination of all recruits is stressed by Major Galbraith, who gives three main reasons as follows:

"Disregarding the humanitarian aspect and examining the problem strictly from the Army standpoint, the most important factors which operate when a soldier develops active tuberculosis are: (1) the loss of his services and of the work hours spent in giving him his military training; (2) the danger of his infecting others in the close proximity entailed in hutments and tents; (3) the financial loss to the taxpayer represented by the cost of treatment and by pension."

His figures are, of course, not comparable with our figures any more than are those of Dr. Plunkett.

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TRICHLORETHYLENE AS AN INHALATION ANAESTHETIC

BY

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WITH A PREFATORY NOTE

BY

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Prefatory Note

Some months ago, in my capacity as honorary secretary of the Anaesthetics Committee, I received a letter from Mr. C. Chalmers of Muswell Hill asking for information about the anaesthetic properties of trichlorethylene. I had at the time no information on the subject, but, from the references that I could find (and these were very few, as I was working at a distance from all medical libraries) and from the very pregnant facts supplied by Mr. Chalmers himself, it seemed obvious that the anaesthetic properties of this drug merited an investigation by my committee. After some correspondence with my friend, and colleague on the committee, Mr. C. Langton Hewer, I was glad to know that he was in entire agreement with me and, further, was himself willing, even anxious, to undertake the investigation. Needless to say, it could not have been placed in more competent hands, and this paper, although only an interim report, certainly suggests that the research was completely justified.

My purpose in writing this prefatory note is not only to record the facts stated above but also to secure adequate recognition of the unusual part taken by my correspondent. Mr. Chalmers is not himself a medical man, though he appears to be a proficient chemist and to possess an uncommon knowledge of medical matters. At the time the investigation began we were all unaware that trichlorethylene was obtainable in this country in a form pure enough for inhalation, and in consequence Mr. Chalmers himself prepared and provided at his own cost the supplies of the drug that were first employed. It was only some time later, when this supply had been used up, and Mr. Chalmers, owing to war conditions, found himself unable

to prepare any more, that he suggested application to Imperial Chemical Industries. We then found that this firm was already manufacturing, under the trade name of "trilene," a purified form of the substance specially prepared for medical purposes, though with no reference to inhalation or general anaesthesia. Trilene is, in fact, nothing but specially purified trichlorethylene to which a small proportion of a stabilizing agent has been added.

Even before communicating with me Mr. Chalmers had made experiments to test the anaesthetic qualities of trichlorethylene. He explained to me that, not being a medical man, the only subject upon whom he could experiment was himself. Accordingly, using very makeshift apparatus, he actually anaesthetized himself and carefully noted, so far as was possible, his sensations and the resulting after-effects. In general his report tallied very closely, so far as it went, with Mr. Hewer's later findings, but he specially stressed the absence of nausea and vomiting. He did, however, mention one sequel which is not referred to in the present paper. It may have been accidental, but it is worth recording as a subject for further observation. He noticed, about one day following administration, a slight distension of the intestines accompanied by some pain in the region of the descending colon. This he thought might be due to a decomposition of the inhaled anaesthetic, possibly into carbonyl chloride.

More could be written about the active part taken by Mr. Chalmers in instituting and assisting this investigation, but it seems unnecessary to stress further the credit due to him.

For the information of any who may be interested in the properties of this almost new and apparently useful anaesthetic agent it may be added that although trilene is manufactured by Imperial Chemical Industries it is actually marketed for them by Messrs. Macarthy's, Ltd., wholesale chemists, Market Place, Romford, Essex, from whom no doubt adequate supplies are obtainable.

C. F. H.

Physical Properties and Uses of Trichlorethylene

Trichlorethylene has the chemical formula $\text{CCl}_2:\text{CHCl}$ and is a colourless heavy liquid with a fruity smell which somewhat resembles, but is quite distinguishable from, that of chloroform. The specific gravity of the liquid is 1.47 at 15°C ., and its boiling-point is the high one of 87°C . It is not inflammable under any circumstances, nor will its vapour explode when mixed in any proportion with air, oxygen, or nitrous oxide. Pure trichlorethylene tends to decompose in strong sunlight and should therefore be stored in amber-coloured bottles. The addition of 0.01% thymol greatly retards decomposition. The drug has high solvent power for fats, but is practically insoluble in water. It was first described in 1864.

Commercial Uses.—Trichlorethylene is chiefly used for the dry-cleaning of clothes, the de-greasing of metals, and the de-waxing of lubricating oils. For these purposes the fluid is sold under a variety of trade names, such as trethylene, gemalgene, chlorylene, and triklone. These preparations are not pure enough to be used for inhalation.

External Application.—A few years ago the use of trichlorethylene was recommended as a skin cleanser and to clean up dirty wounds and burns (Trumper and others, 1936). For these purposes Imperial Chemical Industries, Ltd., produced a specially purified liquid known under the name "trilene." This product has been generously supplied by the company for inhalation purposes in the work about to be described.

Therapeutic Inhalation.—The drug has been in use for some years for the relief of pain in trigeminal neuralgia.

For this purpose the vapour is inhaled from broken capsules as in the case of amyl nitrite. The origin of this procedure is curious. It was reported by two separate observers that patients suffering from chronic trichlorethylene poisoning showed complete bilateral paralysis of all divisions of the trigeminal nerve (Plessner, 1916; Gerbis, 1928). It was supposed that the drug had some specific action on this nerve, and its administration for trigeminal neuralgia was suggested (Oljenick, 1928) and shown to be effective (Glaser, 1931). It appears to me that it is much more probable that the pain is relieved because a state of general analgesia is induced. This condition has been demonstrated several times before consciousness was lost.

Industrial Poisoning.—Several European writers have recorded cases of poisoning in workers in factories when trichlorethylene was employed. Various symptoms have been described, including giddiness, vomiting, optic neuritis, and various palsies (Plessner, 1916; Gerbis, 1928). Some cases have proved fatal (Stüber, 1931). So far as can be ascertained, all the affected patients had been exposed to the vapour of commercial trichlorethylene, which may contain a great variety of impurities.

Animal Experiments

In 1921 Joachimoglu found that pure trichlorethylene vapour was not irritating to the respiratory tract, did not haemolyse the blood, and did not cause fatty degeneration of the liver. In 1934 Herzberg reported that the liver, spleen, kidney, diaphragm, pancreas, heart muscle, lung, adrenal, and pectoral muscle taken from three dogs killed by overdosage of trichlorethylene after having been deeply anaesthetized for periods of two and a half to three and a half hours showed no gross or microscopical pathological changes. In 1935 Krantz and others anaesthetized the same rats repeatedly (up to thirty times) with trichlorethylene. The animals were then killed and the various organs examined. Although some pathological changes were found they were in the main slight and inconclusive. In rabbits slight hyperglycaemia was noted. The same workers found that anaesthesia could not be obtained by rectal administration of the drug and that nerve conduction was not affected by local application of trichlorethylene. In 1939 Lande and others anaesthetized rabbits, guinea-pigs, rats, and mice with trichlorethylene daily for two and a half months, the duration being from fifteen minutes to one, and a quarter hours a day. After being killed some inflammatory changes in the liver and kidneys were noted.

It may reasonably be concluded from these extremely severe tests that in animals trichlorethylene is only slightly toxic—certainly much less so than chloroform.

Previous Work in Human Anaesthesia

The only published work which can be traced is that on a series of 300 patients anaesthetized with trichlorethylene by Striker and others in America in 1935. These were all short administrations for minor operations, and in some cases analgesia only was produced. Eight patients became violent in the second stage, and the third stage of anaesthesia could not be reached. One patient stopped breathing from an overdose but recovered under artificial respiration. After-effects were slight, and on the whole the drug was regarded as a satisfactory anaesthetic.

In the following year (1936) the Council of Pharmacy and Chemistry of the American Medical Association considered the evidence for usefulness of trichlorethylene and concluded that "the case had not been completely made out."

After careful consideration of the data summarized above it was thought justifiable to pursue the investigation of trichlorethylene as an anaesthetic in the human subject.

Details of Present Investigation

The number of administrations was 127 and, although this is admittedly a small series, an effort was made to choose representative cases. Most of the commoner major operations were performed under trichlorethylene anaesthesia, their duration varying from seven minutes to three hours ten minutes, the average being about forty-five minutes. The patients were either (a) air-raid casualties, (b) soldiers—most of whom were wounded evacuated from Dunkirk—and (c) ordinary hospital civilian patients. Their ages varied from 14 months to 81 years.

Methods of Administration and Cost

It soon became evident that an open-mask administration was not practicable owing to the low volatility of trichlorethylene. In America a special apparatus has been devised to vaporize the drug, incorporating an air compressor driven by an electromotor (Jackson, 1934). It was felt, however, that if the anaesthetic was to be of any use under Service or overseas conditions, standard apparatus should be employed. In most administrations, therefore, trichlorethylene was put in the chloroform bottle of a continuous-flow apparatus and used as an adjuvant to nitrous-oxide-oxygen. When used with partial rebreathing this method was quite satisfactory. In most cases a face-piece was employed, but, when indicated, a nasal or oral endotracheal tube was passed.

With the CO₂-absorption technique it is essential to have the vaporizer in the patient's respiratory circuit. Insufficient concentration of trichlorethylene is obtained if the basal oxygen feed only is used to vaporize the drug as in the single-phase Waters system or in the two-phase apparatus supplied as standard to the E.M.S.

If the drug had been purchased at hospital price it was calculated that the cost per case would have averaged about 4½d.

Stages and Signs of Anaesthesia

In most respects trichlorethylene resembles chloroform rather than ether, and the signs of the various stages of anaesthesia are similar to those encountered with nitrous-oxide-oxygen with chloroform as an adjuvant. Some degree of general analgesia appears to be present in the first stage, and this was proved to be due to trichlorethylene and not to the nitrous oxide by occurring when pure oxygen was used to vaporize the drug. The second stage was not usually marked, but in one or two patients violent excitement did occur. This can, of course, be avoided by starting with an intravenous barbiturate, but it was not done lest it should confuse the issue. The third stage was characterized by quiet automatic breathing and a variable degree of muscular relaxation. This was sufficient for the operative procedures except in three patients. The first was a muscular young man who was having a partial gastrectomy for ulcer; the second was a patient from whom a large malignant ovarian cyst was removed; and the third was a soldier who underwent manipulation of the spine. In each instance the addition of diethyl ether vapour for a short time secured the necessary relaxation.

One opportunity occurred for observing the effect of trichlorethylene upon the uterine musculature. An abdominal hysterotomy was performed to terminate pregnancy because of active phthisis. The surgeon remarked upon the exceptionally good retraction of the uterus following extraction of the foetus.

After an average of twenty minutes' administration it was found that the vapour concentration of trichlorethylene could be greatly reduced without prejudice to muscular relaxation. On one occasion an overdose was inadver-

tently given. Respiratory arrest occurred, but no difficulty was encountered in restoring natural breathing. The pulse remained steady throughout.

Effects on Respiratory System

The odour of trichlorethylene is not pungent, nor does its vapour appear to have any irritant effect upon the respiratory passages. It follows that the vapour concentration can be increased quickly, leading to the rapid induction of anaesthesia. No excessive salivation or secretion of mucus was noticed even if premedication had been inadequate or badly timed. Nineteen major thoracic operations were included in the series, as were six abdominal sections on patients suffering from severe chronic bronchitis or active phthisis. In no case was there any noticeable exacerbation of the pulmonary disease.

The depth of respiration was not appreciably altered, but in about 30% of patients some increase in the rate occurred. This usually subsided after fifteen to twenty minutes, but in a few cases it persisted. The respiratory rate was particularly high in some patients during operations involving an open pleura, and this constituted a definite disadvantage in thoracic surgery.

Effects on Cardiovascular System

The blood pressures remained within normal limits except for some rise if the second stage of anaesthesia was marked by much excitement. No case of pronounced shock occurred in the series. The pulse rate was usually slightly higher than normal, as is the case with most inhalation anaesthetics.

Particular attention was paid to the heart rhythm, as trichlorethylene contains three chlorine atoms in its molecule, and at least two other compounds with this characteristic can cause grave cardiac irregularities and even primary cardiac failure. (These drugs are chloroform and trichlorethanol.) (Wood, 1938; Hewer and Belfrage, 1938.) No cardiac irregularities could be detected clinically except sinus arrhythmia in a few young patients, which disappeared when full anaesthesia was reached. Several patients with extrasystoles before operation showed a regular rhythm after anaesthesia had been induced with trichlorethylene. This is, of course, common with most inhalation anaesthetics.

Dr. K. D. Keele kindly took electrocardiograms with the Cossor-Robertson cardiograph during the induction of anaesthesia in 15 cases. Continuous visual direct observation was made in all the cases included. This was started previous to the induction of anaesthesia, when a short photographic record of Lead II was taken; direct observation was then continued until the patient was well into the third stage of anaesthesia, when a second record was made. Of the 15 cases so observed, in 14 there was no alteration in the tracing, apart from a slight decrease in the sinus tachycardia as the third stage of anaesthesia was reached. In one instance regular auricular extrasystoles alternating with normal systoles occurred over a period of some three minutes and then ceased. In two other cases occasional ventricular extrasystoles were seen during the second stage. These disappeared as the third stage was reached. In no case were multiple ventricular extrasystoles seen. These were particularly looked for in view of their comparatively frequent occurrence during chloroform anaesthesia. This limited number of observations thus suggests that there is no evidence of any particular cardiac danger from trichlorethylene.

It seems only fair to mention a fatality which occurred after the conclusion of this series, following the administration of trichlorethylene by a colleague.

The patient was a woman, aged 32, who was to have an empyema drained. Anaesthesia was induced uneventfully with nitrous-oxide-oxygen and trichlorethylene. After a rib resection a large exploring needle was passed in several directions to locate the pus, but without result. At this point temporary apnoea occurred, but natural breathing was soon re-established, and the remainder of the operation was completed under pure nitrous-oxide-oxygen. Just as the wound was being closed the respiration and circulation ceased, apparently simultaneously, and all efforts at resuscitation failed.

The relevant findings at the necropsy were: (1) a localized empyema higher than the exploring needle had reached; (2) free blood in the pleural and peritoneal cavities; and (3) degeneration of the heart muscle. Some air was present in the cerebral arteries, but the diagnosis of air embolism could not be definitely established as the vessels were unfortunately not ligated before the brain was lifted out of the skull.

It is my opinion that trichlorethylene was not responsible for this patient's death, and I have knowledge of an almost exactly parallel case in which local analgesia only was employed. It might be noticed that, since no trichlorethylene had been used for five minutes before circulatory failure occurred, the concentration of the drug in the air passages (with a partial rebreathing circuit) must have been negligible.

Effects on Sugar Metabolism

Dr. A. Jordan kindly made some blood-sugar estimations before, during, and after anaesthesia with trichlorethylene. In no case was there much disturbance, and on taking an average it could be said that there was no significant change. This contrasts with the rise which constantly occurs with chloroform and ether (Hewer, 1939).

Chart showing range of change in blood-sugar level during trichlorethylene anaesthesia.

One diabetic patient was included in the series. An abdominal operation lasting 1 hour 15 minutes was performed under nitrous-oxide-oxygen-trichlorethylene. The sugar tolerance was tested one week after operation, and was found to be unchanged.

Effects on Blood Urea

Blood-urea estimations were made by Dr. Jordan upon 5 patients before, during, and after anaesthesia. The changes were so slight as to be within the range of experimental error. Here again the contrast with ether and chloroform is marked.

After-effects

Of the series of patients 61% had no nausea or vomiting, 26% had nausea or slight vomiting, and 13% had severe vomiting; 5% complained of headache. Those who had had experience of diethyl ether commented favourably on the absence of an unpleasant taste or smell.

In most cases the urine was tested as a routine on the day after operation. In one instance only was the presence of albumin found but acetone was always absent. This is in marked contrast with other anaesthetics. For example, albuminuria has been found almost constantly after the prolonged administration of ether and in about 20% of patients anaesthetized with chloroform (Stephen, 1929). Acetonuria has been demonstrated in 67% of patients operated upon under all forms of general anaesthesia and in 85% under local analgesia (Schulze, 1924).

No pulmonary complications were observed, and, as already mentioned, existing lesions did not appear to be affected.

Summary and Conclusions

This article must be regarded as an interim report, and it is not suggested that our present knowledge of trichlorethylene warrants its recommendation as an inhalation anaesthetic. At the same time the drug appears to have enough good qualities to render a more exhaustive investigation profitable.

It appears that trichlorethylene generally resembles chloroform but is less potent and less toxic.

It is desired to express thanks for much help from Mr. B. Rait-Smith, who made nineteen administrations; also to Dr. Keele for his electrocardiographic work and to Dr. Jordan for his biochemical investigations. C. L. H.

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USE OF SULPHAPYRIDINE IN SUBACUTE BACTERIAL ENDOCARDITIS

WITH REPORT OF A CASE

BY

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In the treatment of subacute bacterial endocarditis attention has recently been focused on the use of sulphapyridine combined with heparin. The rationale of this treatment is that the latter drug is thought to prevent the deposition of further thrombus on the affected valves. As a result the bacteria are exposed to the sterilizing action of the sulphapyridine, and the check in the growth of the vegetation gives the processes of repair an opportunity to gain the ascendancy. The results of published cases treated along these lines are noted in Table I.

TABLE I.—Cases treated with Sulphapyridine and Heparin

No.	Author	Result
1	Kelson and White (1939)	Death from pulmonary infarct 2 weeks after treatment stopped
2	"	Bedridden with congestive heart failure, but "no evidence of bacterial endocarditis" 19 weeks after treatment stopped
3	"	Symptom-free and negative blood cultures 18 weeks after treatment stopped. Returned to work
4	"	Death during treatment from subdural haemorrhages following emboli
5	"	Death during treatment following a reaction due to faulty heparin
6	"	Little change
7	"	Free from evidence of disease 4 weeks after treatment stopped
8	Friedman, Hamburger, and Katz (1939)	Death during treatment from cerebral haemorrhage. No sulphapyridine used in this case
9	Dockeray and Kawerau (1940)	Death 3 months after treatment stopped
10	Witts (1940)	Death during treatment from subarachnoid haemorrhage
11	Fletcher (1940)	Remained well for 6 months "
12	Petch (1940)	Death from intracranial haemorrhage
13	"	"
14	"	"
15	"	Death from toxic "aundice "

These results are not encouraging. Death from haemorrhage, particularly cerebral haemorrhage, is a very real danger.

Maegraith and Vollum (1938) claim that sulphapyridine is the drug with the most definite inhibitory action on the