BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 4 1944

CRANIAL-NERVE PALSIES WITH HERPES FOLLOWING GENERAL ANAESTHESIA

A REPORT FROM THE CENTRAL MIDDLESEX COUNTY HOSPITAL

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During a period of four months 13 cases of cranial-nerve palsies following general anaesthesia have occurred at this hospital. The cases occurred in three small groups, with free intervals of four and nine weeks between. Two of the affected persons died, while the remainder are at various stages of recovery. The degree of severity varied from subjective trigeminal anaesthesia only to a complete picture of encephalitis, but the main features were remarkably constant and readily recognized. Twenty-four to forty-eight hours after use of a general anaesthetic the patient complained of a sense of coldness, numbness, or tightness round the lips, which in most cases during the course of the next two or three days had spread to involve the whole distribution of the fifth nerve on both sides. This subjective anaesthesia was usually associated with analgesia and anaesthesia over the same area, and in nearly every case there was difficulty in swallowing solid food owing to its "getting lost in the mouth." Three of the cases also showed motor fifth-nerve weakness. About the third post-operative day, in the majority, there appeared circumoral herpes of the febrile type. At this time, in those persons showing further involvement, affection of other cranial nerves became apparent—e.g., diplopia, facial weakness, palatal weakness, and tremor or deviation of the tongue. In those cases which showed improvement this began on the fifth to the tenth day, and the milder cases recovered rapidly (almost completely in a fortnight), whereas the severer cases still had residual subjective changes after five months. The herpes had disappeared by the end of ten days. On no occasion did we observe affection of the first, second (including rough testing of the visual fields), ninth, or eleventh nerve, but all the other cranial nerves were involved in one or more cases. Taste over the posterior one-third of the tongue was not tested, and the ninth nerve may have been involved. Only one patient had an extensor plantar response, and that was unilateral. None ran unduly high temperatures during the post-operative period. Six vomited more severely than we normally expect after operation, and five were noticeably depressed, listless, or confused for two or three days. Three only complained of severe headache. A typical history is that of Case 4.

A Typical Case (No. 4)

A woman aged 25 was subjected to appendicectomy for acute appendicitis on July 30, 1943. Premedication was by morphine gr. 1/6 and hyoscine gr. 1/150. The anaesthetic employed was a combination of intravenous pentothal with cyclopropane and a little ether, given by closed circle with CO₂ absorption. The operation was a short one and the anaesthesia was without incident.

On Aug. 1 she complained that she had had a feeling of coldness of the face with double vision for 24 hours. At the same time there was some difficulty in opening and closing the mouth. On examination the left pupil was larger than the right. The reactions to light and accommodation were normal. There was double vision in all directions. The position of the false image indicated that the

diplopia was of third-nerve origin. There was no nystagmus and the fundi were normal. Hypo-algesia and hypo-aesthesia affected all the trigeminal field of each side. The corneal reflexes were diminished and the jaw-jerk was depressed. No muscular weakness affecting the fifth nerve could be detected. Subjectively the lips felt cold and the face numb and swollen. Food placed in the patient's mouth felt cold. There was bilateral facial weakness affecting the upper and lower face. No other abnormality could be detected in the cranial nerves. There was no neck rigidity or retraction.

The symptoms and signs remained unchanged until Aug. 2, when herpetic vesicles were found on the buccal mucous membrane on the left side of the mouth. These continued for three or four days. On Aug. 4 she complained of difficulty in swallowing. A lumbar puncture performed on the 6th yielded a clear fluid under normal pressure; no white cells were found. There was a gradual diminution in the cranial-nerve palsies; by Aug. 11 the difficulty in swallowing had disappeared, and by the 18th the diplopia had cleared. The scalp still felt abnormal. The skin over the forehead and the cheeks felt "swollen and stretched," and she complained of a peculiar tingling sensation around the nose. The tongue and the teeth still felt cold and numb. The pupils were equal in size and the external ocular movements were full. Hypo-algesia and hypo-aesthesia were present over the whole distribution of the fifth nerve, but around the nose stimulation with a pin produced an exaggerated reaction. There was still left facial weakness. She was transferred for convalescence on Aug. 27.

The patient was seen again on Oct. 7. She stated that she had had transient diplopia, when tired, up to a week before her visit. The upper lip still felt "twice its size" and the eyelids and the forehead seemed heavy. Since her discharge on Aug. 27 she had noticed involuntary twitchings of both sides of the face, of very short duration. There was a slight degree of diminution of sensation to pin-prick on the right side of the face, affecting all divisions, with a slight left facial weakness. No other abnormality was found in the central nervous system.

Table I summarizes the clinical aspect of the cases. In it are included only those which showed definite cranial nerve involvement; but it should be mentioned that in association with them we encountered three cases of unexplained herpes developing about the third post-operative day, without complications other than severe headache or transient tingling of the lips. The clinical features require no further comment, except that involvement was usually (but not always) bilateral, and that in some the subjective fifth-nerve changes were accompanied by very definite changes in sensation to pin-prick and light touch.

History of Two Fatal Cases

Necropsies were performed upon the two fatal cases. Since Case 8 differed from all the others, a brief history is given.

Case 8

This patient was a woman aged 56. On Aug. 4, 1943, a cholecystectomy was performed, the anaesthesia lasting about one hour. She received premedication with morphine gr. 1/6 and atropine gr. 1/100, and anaesthesia (pentothal, nitrous oxide, oxygen, and ether) was maintained through a naso-tracheal tube by a closed-circle technique. The operation and anaesthesia were smooth and without incident. Post-operatively she was somewhat slow in returning to consciousness, and vomited rather more than is usual. Next

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day she was apathetic, and in the evening she became delirious, with twitching round the mouth during the night.

On the following day she was ill and confused. Her left pupil was larger than the right, and was fixed and inactive to light. There was bilateral fifth-nerve analgesia with absent corneal and conjunctival reflexes. She had a gross tremor of the tongue, and marked incoordination of the arms, which was worse on the right than on the left. Her condition gradually deteriorated, and bilateral facial

enlarged prostate, bronchopneumonia, and some general oedema of the brain.

Histology.—Occasional small capillary haemorrhages were seen in sections through the pons and midbrain, together with small perivascular collections of lymphocytes in the substantia nigra. In addition to the lymphocytic cuffing, macrophages containing haemosiderin were found in sections through the cerebellum. The upper part of the medulla oblongata contained occasional collections of

TABLE I.—*Clinical Summary of Cases*

No.	Sex	Age	Operation Date	Nature of Operation	Anaesthetic	Duration of Anaesthesia	Post-op. Vomiting	Herpes	Cranial Nerves Involved	Comment
1	M	53	28/6/43	Bone graft	Pent., cyclo., O ₂ , induction—→trilene maintenance	1½ hours	—	—	Subjective V	Not discovered until 4½ months later
2	F	21	28/6/43	Appendectomy	Pent., cyclo., O ₂ , + a little ether	½ hour	+	+	V (all divs.) and motor XII	
3	F	19	28/6/43	"	" "	"	+	+	V (all divs.) and motor	Followed Case 2 on table
4	F	25	30/7/43	"	" "	"	—	+	III, V (all divs.), VII, X	
5	F	62	30/7/43	Cholecystectomy	Pent., cyclo., O ₂ , + a little gas-O ₂ -ether	1½ hours	±	+	III, V (all divs.), mainly subjective, X, XII	Followed Case 4 on table
6	M	41	2/8/43	Appendectomy	Gas, O ₂ , ether, "to-and-fro" (on circle machine)	½ hour	+	+	Subjective right V (all divs.)	
7	F	45	3/8/43	Laparotomy	Pent., cyclo., O ₂	½ "	+	—	Subjective bilateral V (1 and 2 divs.) R. VII	
8	F	56	4/8/43	Cholecystectomy	Pent., gas, O ₂ , ether	1 "	—	—	III, V, VII, X, XII	Died in coma on 2nd post-operative day
9	F	46	17/8/43	Removal of cystadenoma of breast	Pent., trilene + O ₂ induction—→cyclo. maintenance	½ "	+	+	V (all divs.), R. VII	
10	F	39	21/10/43	Hysterectomy	Cyclo., O ₂ , + a little ether	1½ hours	±	+	III, V, VI, VII, VIII	Very severe headache. R. extensor plantar response
11	M	74	27/10/43	Cystoscopy and suprapubic cystostomy	Cyclo. + O ₂	½ hour	±	—	V (+ motor), L. VI, VII	Died on 16th post-operative day
12	F	18	27/10/43	Appendectomy	"	35 mins.	—	+	V, R. VII	Under treatment for myasthenia gravis
13	F	35	27/10/43	Evacuation of uterus; severe blood loss	"	5 "	—	+	L. V, transient L. VII	Followed Case 12 on table

Pent.=pentothal. Cyclo.=cyclopropane. Gas=nitrous oxide. O₂=oxygen. Trilene=trichloroethylene.

weakness became apparent. During the afternoon she became stuporous, with jerking movements of the legs and arms. Lumbar puncture yielded 3 c.cm. of clear faintly yellow fluid under normal pressure: protein, 1.70 g. per 100 c.cm.; 14 polymorphs per c.mm. She died in coma at 10 p.m. on Aug. 6.

Necropsy was performed by Dr. W. Pagel 12 hours later: "The operation wound was sound. There was no gross abnormality of any organ except the brain, which showed marked oedema. Cultures of c.s.f. were sterile, and there was no meningitis."

Histology (Dr. Pagel).—There was no evidence of fat embolism anywhere in the parts examined. In all sections through the mid-brain and the floor of the fourth ventricle there was marked deposition of thready material in the perivascular lymph spaces (oedema). There were seen in addition a few vessels surrounded by a single row of lymphocytes, and a few capillary haemorrhages into the perivascular lymph spaces, together with collections of microglia in the neighbourhood of vessels. The ganglion cells in the central grey matter and the medulla oblongata were free from appreciable changes.

Summary of Case.—Marked oedema in the midbrain, pons, and medulla oblongata. Small capillary haemorrhages and beginning slight cuffing around the vessels. No changes in the ganglion cells. Portions of brain from the region of the affected nuclei were removed for animal inoculation.

Case 11

This patient, a man aged 74, was suffering from retention of urine due to an enlarged prostate (blood urea, 168 mg. per 100 c.cm.) and from chronic bronchitis with emphysema. He had auricular fibrillation, which was controlled by digitalis. A cystoscopic examination was made and suprapubic cystostomy performed under cyclopropane-and-oxygen anaesthesia, after premedication with morphine gr. 1/6 and atropine gr. 1/100. The anaesthesia lasted about three-quarters of an hour. Post-operative cranial-nerve involvement was extensive but not severe, and included the fifth nerve: subjective numbness in all divisions, with hypo-algesia and pins-and-needles sensation over the nose. His jaw deviated to the left. The palatal reflex was absent, although palate movement was normal. The sixth nerve showed slight left external rectus weakness, and the seventh nerve slight bilateral lower facial weakness. His chief difficulty lay in an inability to swallow solids, though he had no nasal regurgitation. Although suprapubic drainage was adequate he went progressively downhill. He was quite unable to swallow fluids towards the end, and died on the sixteenth post-operative day. At the necropsy, performed by Dr. Pagel, the only findings of significance were an

microglia in star formations. Oedema was also present, but was much less intense than in Case 8. The small haemorrhages might be due to terminal respiratory embarrassment. In photomicrographs taken of sections from the two brains the most noticeable feature in each case was probably the oedema of brain and brain-stem, although there was no clear histological evidence of the cause of the condition.

Other Pathological Findings.—Lumbar puncture was performed upon nine of the patients during the first week. The pressure was never raised and in all cases the cerebrospinal fluid was bacteriologically sterile. In only two cases was there a small increase of polymorphs (10 and 14 per c.mm.). In four the protein content was 0.04% or less, while the remainder contained 0.055%, 0.07%, 0.085%, 0.09%, and 1.7%.

Animal Inoculation.—We were fortunate in obtaining the help of Dr. C. H. Andrewes, of the National Institute for Medical Research, who performed many of the inoculations. Cerebrospinal fluid from five cases and portions of brain removed at necropsy from two cases (some glycerinated, some filtered through a 0.7 µ membrane and held at -70° C.) were injected intracerebrally or intratesticularly into a total of 44 mice, 12 rabbits, and 1 rhesus monkey. No evidence of transfer of a virus infection was obtained.

Theories of Aetiology

The cases described were operated upon by four different surgeons and anaesthetized by three different anaesthetists. None of them showed signs of anoxaemia or other complication upon the table. There was no evidence to incriminate any definite ward, but it was notable that all the anaesthetics were given in one theatre and all on the same type of machine. It seemed to us that the damage must have been directly due to the anaesthetic or to the lighting up of some latent virus infection, or both. The mode of anaesthesia and certain serological findings are presented with these possibilities in mind.

Anaesthetics

It will be observed from Table I that the anaesthetics were variable and that no one drug was common to all cases. The major surgery of the hospital is done in two operating theatres. The anaesthetic machine used in 12 of the 13 cases is one with which either a simple semi-open "to-and-fro" method may be used or else a closed-circle technique, with a soda-lime

canister incorporated to absorb the carbon dioxide. There is only one bottle on the machine. It contains a gauze wick. This wick retains a little of whatever anaesthetic drug has been in the bottle previously, and thereby contaminates the drug next used—e.g., ether following trichloroethylene, or vice versa (see accompanying diagram).

Although a number of tests had shown the bag and corrugated rubber tubing of the machine to be free of viable bacteria when swabbed immediately after use, this machine was sent to be sterilized in August. While it was away the same type of circle absorber was attached to a Boyle apparatus, and on this one case of palsy occurred (No. 9). In the other theatre a simple Boyle apparatus without soda-lime absorber is used, and on this there were no cases.

The anaesthetics administered were varied, but all except two were well-tried mixtures—namely, Cases 1 and 9, which received pentothal followed by cyclopropane and trichloroethylene, using the closed-circle technique. Ether, pentothal, and cyclopropane are drugs which have been used very extensively and have withstood the tests of time and experience. Trichloroethylene has been more recently introduced into anaesthetic practice, and has only been widely used in England since Hewer's report of 400 administrations and review of experimental work on animals (Hewer, 1942), although, in America, Striker and his colleagues were using it in 1935. Two reports of fifth-nerve palsy following the administration of trichloroethylene anaesthetics appeared during the past year (Hewer, 1943; McAuley, 1943). In the cases reported by Hewer impurities in the drug were considered to be the cause. Earlier reports in the German literature record cases of trigeminal palsy developing in industrial workers using trichloroethylene, toxic contaminants being regarded as a possible cause (Stüber, 1931; Jackson, 1934). Therefore, although this drug was used upon only two of our cases it was naturally suspect.

During the four months July to October 1940 inhalation anaesthetics were administered in the two theatres, of which 600 were given in Theatre I (where all the cases occurred) and 340 in Theatre II. Each main drug, associated with others, was used in the following proportion of cases: ether 35%, cyclopropane 24%, trichloroethylene 16%, and pentothal 25%. Nitrous oxide was used in many and oxygen in all. On the circle machine in Theatre I there were 80 administrations of trichloroethylene, and on the Boyle apparatus in Theatre II there were 65.

These figures appear to give very little clue to the problem, but the occurrence of all the cases on the circle machine led us to suspect that a possible toxic agent might result from the interaction of traces of trichloroethylene with soda-lime or the other drugs used. It has been pointed out (Morton, 1943; Stüber, 1931) that chemical reactions may occur between trichloroethylene and alkalis, particularly when heated. Owing to its low volatility trichloroethylene is not regularly used on a closed circuit, but during the period under review this was done on several occasions (including Cases 1 and 9). It is also conceivable that in our anaesthetic machine (described above) trichloroethylene used by the "to-and-fro" technique might linger in the machine or in the gauze wick, and thus be carried over into the soda-lime when a subsequent anaesthetic was given by closed circuit. In either case there would be definite possibilities of chemical reactions occurring, especially since we have noted temperatures of the order of

70° C. in the soda-lime canister. Our suspicion was strengthened by the presence of an unusual sweetish penetrating odour frequently noted about the machine during this period. (The odour was subsequently reproduced by incubating trichloroethylene with soda-lime.)

Dr. H. E. Cox, D.Sc., F.I.C., undertook to analyse the drugs used, paying particular attention to possible chemical reactions or impurities. A summary of his report is as follows:

(1) The cyclopropane, ether, and trichloroethylene fulfilled the prescribed conditions of purity. (2) There is no evidence of any change, under the conditions of administration, in (a) cyclopropane or (b) ether which would cause injury. (3) There is evidence of reaction between trichloroethylene and soda-lime, and (4) this reaction produces dichloroacetylene. This substance readily combines with oxygen to form phosgene, carbon monoxide, and carbon dioxide, but does not further oxidize in the presence of sufficient excess of trichloroethylene. (5) The reaction is greatly stimulated by rise of temperature in the soda-lime; it proceeds markedly even at blood heat. (6) There is no evidence of direct formation of oxidation products in the trichloroethylene without soda-lime. (7) The effects of dichloroacetylene in trichloroethylene are not known, but should be ascertained. (Dichloroacetylene is a substance explosive in the presence of limited oxygen.)

Experiments are at present being undertaken to find out the physiological effects of the reaction products of trichloroethylene and soda-lime. Dr. Cox's observations have been confirmed by the Department for Research in Industrial Medicine of the Medical Research Council, which is meanwhile making investigations of the toxicity of these substances to rats. We ourselves have obtained some striking preliminary results with rabbits. The animals were subjected to anaesthetic mixtures consisting of trichloroethylene plus 0.5–1.0% dichloroacetylene or of ether plus trichloroethylene plus 0.5–1.0% dichloroacetylene given in the same way, and on the same anaesthetic machine as was used for the cases under review. Each animal received the mixture under test for three periods of about 20 minutes at five-day intervals. Anaesthesia was light, and difficult to maintain when ether was not used, and the rabbits appeared to recover quickly and to show no untoward symptoms. After the third anaesthesia one rabbit was killed by an overdose of anaesthetic, and the other was killed seven days later by stunning. Histology of both was very similar, and showed little change in any organ except the brain and the liver, in which there was slight necrosis. In the brain there was extremely marked perivascular cuffing and glial proliferation throughout, with numerous foci of necrosis. There was even a marked meningeal reaction, and the picture at first sight was one of encephalitis. We have never met such a histological picture in any other of our rabbit stock, and, although further work is necessary, have no hesitation in attributing it to the anaesthetic. On the strength of this preliminary evidence it would appear advisable not to use trichloroethylene in the presence of soda-lime.

Temperature

It is well known that when artificial hyperthermia is induced in normal persons a high proportion (about 70%) develop labial herpes 2 to 3 days later (Keddie, Rees, and Epstein, 1941). A combination of anaesthesia with overheating of the patient by heat generated in the soda-lime might have provided a possible explanation for the herpes, the palsies, and the peculiar incidence. In a number of cases the temperature in the rubber tubing leading to the patient was recorded, the maximum reached being only a few degrees above room temperature. The axillary temperatures of the patients rarely varied more than $\pm 1^\circ$ F. during operation. Although none of these patients developed symptoms there was no evidence to support this idea as a possible explanation.

Virus Infection

The occurrence of herpes on the third day in nine out of the twelve patients who survived this period was particularly striking in view of the fact that none of them had colds or any other condition commonly associated with herpes, and that half of them after careful questioning denied ever having previously had this condition. Among other operation cases the incidence at that time, in the absence of colds, was very low.

The lesions were characteristic of herpes febrilis, consisting of numerous discrete vesicles upon the muco-cutaneous junction of the lips, the chin, and occasionally the buccal mucous

membrane and soft palate. In four cases successful transfer to rabbits was obtained by intracorneal inoculation of vesicle fluid, and the strains behaved typically. One strain (Case 10) was studied particularly by Dr. C. H. Andrewes and ourselves, and was adapted to rabbit testicle and skin, to guinea-pig pads, and to mouse brain. None of the strains was particularly neurotropic in rabbits or guinea-pigs, although direct intracerebral inoculation in a rabbit produced death from encephalitis after some weeks.

Herpetic encephalitis in man has never been authenticated, although during the epidemic of encephalitis lethargica in Europe after the last war numerous attempts were made to incriminate the virus, and its isolation was claimed from the brains of the affected and of normal persons (Doerr and Berger, 1922; Flexner and Amoss, 1925). Studies by Andrewes and Carmichael (1930) and by Brain (1932) showed that 70 to 75% of hospital patients have antibodies to herpes in their blood. In the majority of such persons overt lesions can be produced by artificial hyperthermia, intravenous T.A.B. vaccine, lobar pneumonia, meningococcal meningitis, the common cold, etc. Herpes occurs occasionally after injection of the Gasserian ganglion (Harris, 1937).

All the cases showed a definite incubation period between operation and the first appearance of symptoms, ranging from 24 hours to three days. This is very short, by accepted standards, for a virus infection. The post-mortem findings, on the other hand, were not inconsistent with an encephalitis, and were comparable with descriptions of some of the findings in the encephalitis lethargica epidemic. In the absence of a completely satisfactory "toxic" explanation, it was considered worth while to investigate the sera of these patients for antibodies against the herpes strain from Case 10 and another strain isolated at the National Institute for Medical Research by Dr. Andrewes. The viruses were adapted to the rabbit's skin, and each serum was tested for its power to inhibit the production of lesions by 5 to 10 infective doses of virus injected intracutaneously. The results are given in Table II.

TABLE II.—Results of Tests for Antibodies against Herpes

Case No.	Herpes	Herpetic History	Time of taking Serum after Operation	Neutralizing Antibodies	
				Strain 10	M.R.C. Strain
1	—	—	13 weeks	+	+
2	—	—	19 "	+	+
3	+	—	6 "	+	+
4	+	—	4 days	+	+
5	+	—	3 "	+	+
6	+	+	Not done		
7	—	—	7 days	+	+
8	—	?	2 "	+	+
9	+	—	11 "	+	+
10	+	+	6 weeks	+	+
11	—	—	4 days	+	+
12	+	+	1 day	+	+
13	+	+	1 "	+	+

It is evident that every serum contains antibodies against both strains. The most significant samples are the early ones from patients without herpetic histories, since in these cases the formation of antibodies would have been too rapid to be due to the herpes occurring at that time, quite apart from the fact that some never developed the condition. Herpes antibodies are commonly found in persons with latent infection, and the implication is that all these patients had latent herpes.

We were not able to demonstrate any immunological difference between the two strains by cross-protection tests, and cannot claim unusual virulence for the strain 10 studied. If herpes or any other virus infection is involved it must have been "lit up" by the anaesthetic. There is some experimental evidence for this possibility in the observation of Fiala (1943) that subdural or intravenous injection of vaccinia virus in rabbits is not normally followed by encephalitis, but is so if the rabbits are under urethane anaesthesia; or the work of Silberstein and Hoff (1925), who showed that a normally latent encephalitis virus could be activated in dogs with an Eck fistula by feeding with a diet of meat only. Argument by analogy is dangerous, however, and in the absence of positive findings from the inoculation of post-mortem material into susceptible animals we are unwilling to do more than suggest the possibility that herpes virus played a part.

Discussion

The clinical evidence favours two possible theories, or a combination of both, but the experimental results are strongly in favour of a toxic theory. If the latter is adopted there must have been great susceptibility, since one anaesthesia (Case 13) was of five minutes' duration and the patient developed well-marked palsy.

The only drug which could be incriminated is trichloroethylene plus soda-lime, and this only on the assumption that it could have persisted in the machine or in the soda-lime between the anaesthesias in which it was used. On two occasions as long as three days elapsed between the use of trichloroethylene and the anaesthetic which was followed by palsies, and during the intervals there had been given nine and twelve closed-circuit cyclopropane or ether anaesthesias respectively on the same machine without any ill effects. On another occasion trichloroethylene was followed on three succeeding days by varied anaesthetics which developed palsies. Four closed circuits, but no further trichloroethylene, had meanwhile been administered. Seven only of the cases were associated with the use of trichloroethylene on the same day, and of these two actually received the drug in closed circuit. It should be mentioned that the soda-lime was periodically "rested" for any time up to two or three days, and the use of contaminated soda-lime at a later date might explain the intervals between trichloroethylene administration and the anaesthesias which were followed by palsies. We consider it to have been a definite possibility that the majority of the patients who were anaesthetized on the circle machine were subjected to this risk. The fact that only a small proportion showed symptoms would mean that there must be great variation in susceptibility. Such variations are well known in toxicology.

The first case of the series was missed until 4½ months later, when a chance remark of the patient's drew attention to his lesion. It seems to us possible that mild cases may have occurred elsewhere, and the facts recorded above have been published in the hope that the observations of others may help to shed light upon the problem.

It is now over three months since we ceased using trichloroethylene in association with soda-lime, and although many trichloroethylene anaesthesias, some lasting up to three hours, have been given, no further palsies have occurred.

Summary

Thirteen cases of cranial-nerve palsy following general anaesthesia are reported. The nerves involved were mainly the fifth and seventh, but the third, fourth, sixth, tenth, and twelfth were involved in some cases. The condition was associated with labial herpes in 9 cases.

No anaesthetic drug was common to all cases, but all were administered on a circle absorber anaesthetic machine.

Evidence is given for chemical reactions between soda-lime and trichloroethylene in the system, with the production of dichloroacetylene.

Preliminary results show that this substance is toxic to rabbits.

Antibodies against herpes were found in the sera of all cases.

The aetiology of the condition is discussed. It is concluded that until further investigations have been made trichloroethylene should not be used where there is any possibility of its coming into contact with soda-lime.

Our thanks are due to Dr. C. H. Andrewes, Dr. Donald Hunter, Dr. C. L. Hewer, Dr. J. G. Greenfield, and Dr. H. E. Cox for much help and advice.

REFERENCES

- Andrewes, C. H., and Carmichael, E. A. (1930). *Lancet*, **1**, 857.
 Brain, R. T. (1932). *Brit. J. exp. Path.*, **13**, 166.
 Doerr, R., and Berger, W. (1922). *Schweiz. med. Wschr.*, **52**, 862.
 Fiala, S. (1943). *Zbl. Bakt.*, **150**, 260.
 Flexner, S., and Amoss, H. L. (1925). *J. exp. Med.*, **41**, 218.
 Harris, W. (1937). *The Facial Neuralgias*, London.
 Hewer, C. L. (1942). *Proc. roy. Soc. Med.*, **35**, 463.
 — (1943). *Ibid.*, **36**, 463.
 Jackson, D. E. (1934). *Anesth. & Analges.*, **13**, 201.
 Keddie, F. M., Rees, R. B., and Epstein, N. N. (1941). *J. Amer. med. Ass.*, **117**, 16.
 McAuley, J. (1943). *British Medical Journal*, **2**, 713.
 Morton, H. J. V. (1943). *Ibid.*, **2**, 828.
 Silberstein, F., and Hoff, H. (1925). *Z. ges. exp. Med.*, **44**, 257.
 Striker, C., et al. (1935). *Anesth. & Analges.*, **14**, 68.
 Stüber, K. (1931). *Arch. Gewerbepath.*, **2**, 398.