EVALUATION OF RECOVERY AND "STREET FITNESS" BY E.E.G. AND PSYCHODIAGNOSTIC TESTS AFTER ANAESTHESIA*

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RECOVERY AFTER ANAESTHESIA is usually judged from the behaviour of patients and the findings in their diseased state. Patients, however, in the course of their disease and the postoperative stress situations, are subject to varied detrimental influences the sequelae of which cannot be separated from the effects of the anaesthetic. Therefore, it seemed desirable to measure the depth and duration of anaesthesia and the time needed for recovery on healthy volunteers. This enables some factors to be eliminated which are difficult to control. However, healthy people react differently from sick people with a disturbed metabolism, and the results obtained in health cannot be directly applied to diseased states. Examinations of healthy persons with fairly comparable initial behaviour and exactly definable functions allow better information to be obtained of the differences in activity between individual anaesthetics and their combinations. Only under such comparable conditions is it also possible to assess the additional effect of alcohol after anaesthetics. The opportunity to determine anaesthetic sequelae more precisely in order to obtain practical information for patient anaesthesia justified our anaesthetizing healthy volunteers.

METHOD

Anaesthesia on healthy volunteers was carried out in the morning; most volunteers received two or three anaesthetics at intervals of not less than four weeks. The same safety measures were observed as with patient anaesthesia. For evaluation of the depth of anaesthesia and tendencies to sleep, the E.E.G. was recorded from the time of anaesthesia for 12 to 24 hours; street fitness was examined by psychodiagnostic tests at definite intervals, independent of the electro-encephalographic examination on other volunteers, or at different times on the same persons.

In some tests, volunteers were also given alcoholic beverages one, two, and six hours after anaesthesia to evaluate the combined effect of alcohol and the agent under study (120 ml. of 38% liquor was given to produce an alcohol level in the blood of .8 per mille).

E.E.G. recordings were made with 12-channel Hellige and Schwarzer apparatus, with a paper speed of 7.5 mm./sec. While the E.E.G. was written on 8 channels, we used the other channels to record the oculogram at the same time (by gluing electrodes to both temporal palpebral corners), an electrocardiogram (lead I), respiration (with a mechanoreceptor under a belt around the chest) and the mass

*Presented at a panel discussion of anaesthesia for out patients during the Second European Congress of Anaesthesiology, Copenhagen, August, 1966. This work has been supported by the Deutsche Forschungsgemeinschaft.

movements of the body (with a sensitive Philips system mechanograph). The blood pressure was measured initially every minute, later at intervals of 15 to 30 minutes.

Depth of anaesthesia and tendency to sleep were assessed by visual evaluation of the E.E.G. curves. For each 40-second period the depth of sleep was estimated according to a modification of Loomis's[7] classification (Table I). The values therefore represent the averages of every 40 seconds (shorter variations of sleep depth are neglected). They were continually recorded in an ordinate system and constructed as a graph.

We designated the prenarcotic transitional states of irregular tracings as A-states, the onset of narcosis with fast activity as B-states, and the analgesic state with an increasing content of low and high voltage-waves as C and D states. Deep anaesthesia which shows patterns of slow δ-waves was denominated as E-state, and coma showing periods of silence in the E.E.G. as F-state.

The psychodiagnostic tests used to evaluate street fitness after anaesthesia are

TABLE I

CLASSIFICATION OF DEPTHS OF SLEEP

Gibbs	Dement/K	Loomis	Description
Mental relaxation	I		A_0: Distribution of α-rhythm as seen in normal E.E.G.-tracing
Very slight sleep	I	A	A_1: Diffusion of α-rhythm. Diminution of α-frequency (in some E.E.G.'s after a preceding increase of the amplitude).
			A_2: α-waves become smaller and scarcer, "on-off-effect" still existing.
		B	B_0: Flat ϑ-waves. Sensory stimuli may remain ineffective.
			B_1: Diffuse ϑ-waves of increasing amplitude, small and fast activity in the central regions.
			B_2: Appearance of small vertex-waves; after arousal stimuli, reactivation of α-waves (return to stage A).
Light sleep	II	C	C_0: Diffuse ϑ-activity, random δ-waves. Spindles of fast waves in the precentral regions (σ-rhythms) and K-complexes after sensory stimuli.
			C_1: σ-rhythms of increasing amplitude ("sleep-spindles") and K-complexes.
			C_2: Temporal transition to δ-waves, stretched K-complexes; after arousal stimuli return to B or A.
Moderately deep sleep	III	D	D_0: δ-series up to 30% of time, slowing σ-rhythms, irregular K-complexes.
			D_1: High δ-waves during 50% of time.
			D_2: Predominating slow δ-waves during 80% of time. After intensive arousal stimuli return to stage C.
Deep sleep	IV	E	E: Continual high δ-activity, no isolated K-complexes or σ-rhythms; after arousal stimuli, synchronous, slow waves or lack of reaction.
Paradoxical sleep	REM		Period of eye-movements. Flat and fast activity.

TABLE II

PSYCHODIAGNOSTIC TESTS USED TO EVALUATE "STREET FITNESS" AFTER ANAESTHESIA

Sequence of tests	Test (apparatus)	Psychodiagnostic investigation	Time needed (min.)
1	Track-Tracer	Fine motor skilfulness, senso-motor co-ordination	2
2	Labyrinth (Chapuis)	Logical thinking, ability to co-ordinate, combination	10
3	Counting test—count down 1000 to 975	Judgment, concentration	5
4	Reaction apparatus (Mierke). Kieler determination apparatus	Ability to react	2
5	Reaction apparatus (Beck) modified with physioscript (Schwarzer)	Reaction speed	2
6	Düker KLT counting test	Ability to concentrate and perform	30

listed in Table II. They comprised: (*a*) The number test[6]—counting down from 1000, as many numbers as possible must be inscribed into a field five squares by five squares. Evaluation is by points based on the total number of squares used and the general form. This is a test of concentration and continuous mental activity. (*b*) Chapuis' labyrinth test[1]—finding the right path out of a labyrinth as quickly as possible. Three squares of increasing complexity make one test, scored for time and errors. This test demands grasp of a situation, logical thought, combination, and quick reaction. (*c*) Reaction time—Beck's original apparatus consists of a buzzer and flashing red and green signals that have to be answered by pushing the appropriate buttons. Our apparatus has two different consoles with five buttons for color and one for sound. The results were inscribed on a 6-channel recorder. (*d*) Track-tracing—this consists of tracing a curving pathway as fast as possible with an electric stylet. The apparatus automatically records every error in the track. It tests sensory-motor co-ordination. (*e*) Düker's[4] concentration test, which consists of the repetition of calculations. It quantifies reaction rate, ability to concentrate, resistance to disturbing factors, and general productivity. This test battery requires a minimum of 30 minutes and therefore could only be applied before and 8 hours after anaesthesia. Independent of this series of examinations, an investigation of certain cardiac and circulatory functions was carried out in the form of continuous registration.

Two hundred and ninety-four anaesthetics were administered (Table III). In 205 of these the E.E.G. could be continually observed for 24 hours. Psychodiagnostic tests were additionally taken, independent of E.E.G. examinations, by 64 volunteers, and 17 were examined only in this way, without E.E.G. The total number of psychologically tested volunteers is thus 81.

Of the 294 anaesthetics, 64 were with thiobarbiturates, 63 with methohexitone and 143 with Epontol. Epontol was used for induction of 61 anaesthetics which were continued with halothane, ether, or nitrous oxide. In a still continuing study methoxyfluorane replaces halothane, and thiopenthal and methoxyfluorane are included in the comparisons.

TABLE III

CLASSIFICATION OF SUBJECTS TESTED (TOTAL 294)

Anaesthetic	Dosage (mg./kg.)	E.E.G. + psychodiagnostic test + blood level studies (64 subjects)	E.E.G. alone (135 subjects)			E.E.G. + blood level studies (20 subjects)		Psychodiagnostic tests (75 subjects)		Subtotals	Total each group
			anaesthetic alone	alcohol added	circuit	5 injections	10 injections	no alcohol	alcohol added		
Thiopenthal	7 3·5	29								29	
Thiopenthal + halothane 10 min., 1 vol. %	7	12								12	
Thiobutabarbitone	7 3·5	23								23	64
Methohexitone	2		10	14	12			15	12	63	63
Epontol	7		19	14	14	10	10	15		82	
Epontol + halothane 10 min., 1 vol. %	7		12		7				7	26	
Epontol + N_2O-O_2	7				7				7	14	
Epontol + ether + O_2	7				7				7	14	
Epontol + N_2O-O_2 + halothane	7				7					7	143
CI 581	2				12				12	24	24

Results

Single Anaesthetics and Their Comparison

The postanaesthetic effect of thiobutabarbitone will be shown in an E.E.G. example. Postanaesthetic sleep tendency relates to the serum concentration, but not the night sleep.

The data on this volunteer show that plasma thiobutabarbitone may rise to

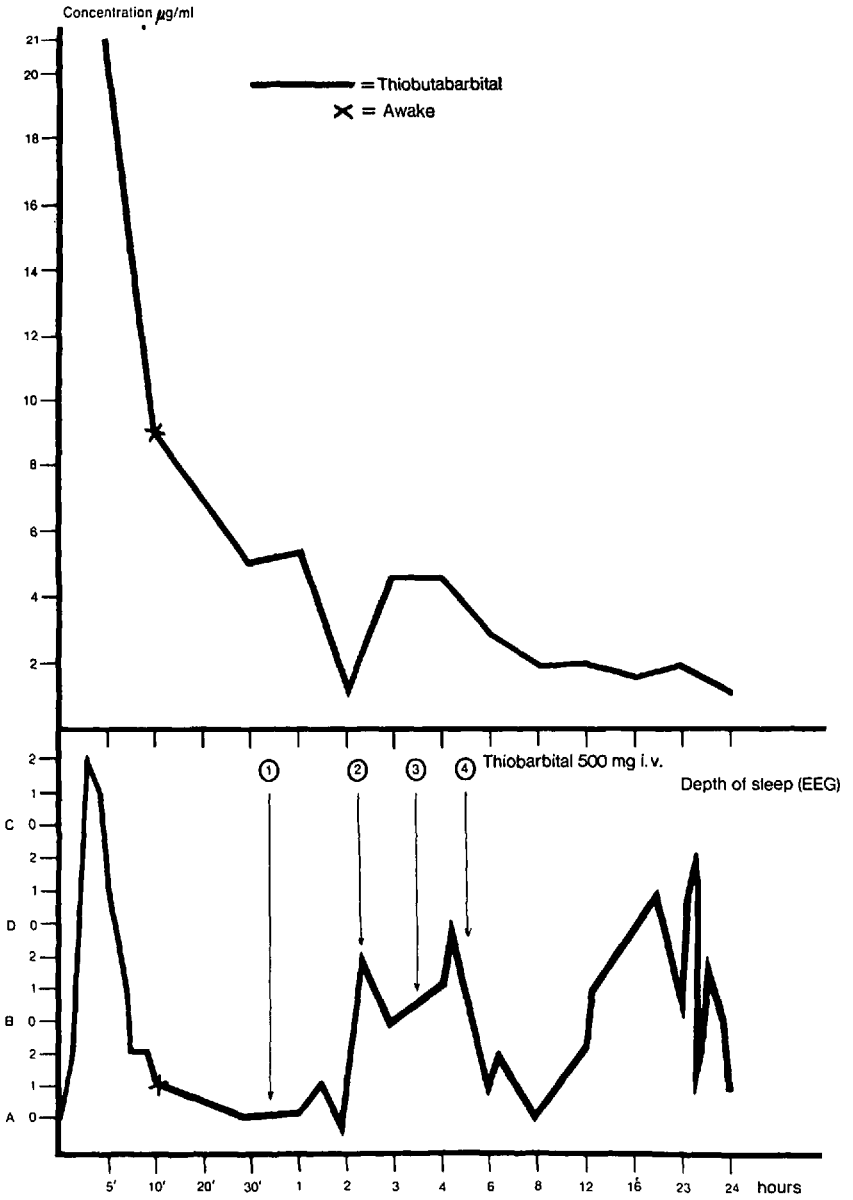

FIGURE 1. Thiobarbiturate concentration in serum after 500 mg. i.v. (subject 7).

5 mg./ml. or even higher three to four hours after the anaesthetic, and the sleep curve is seen deepening to a light sleep stage (Fig. 1). The corresponding E.E.G. record reveals changes in depth of sleep: after the administration of 500 mg. thiobutabarbitone, values returned to normal within 30 minutes; two and a half to three and a half hours later (samples 2 and 3) there is drowsiness which after four and a half hours turns to a sleeping stage. Vertex waves are seen (Fig. 2).

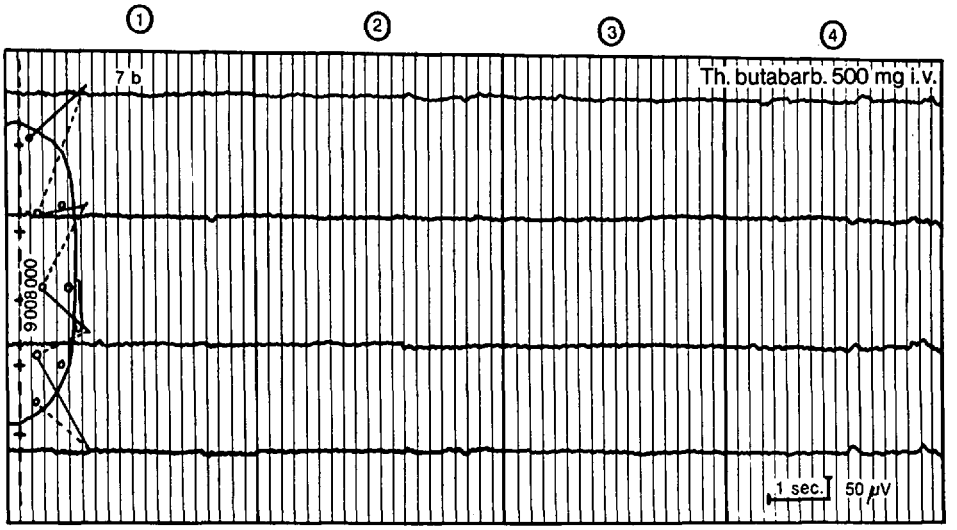

FIGURE 2. Characteristic E.E.G. tracings.

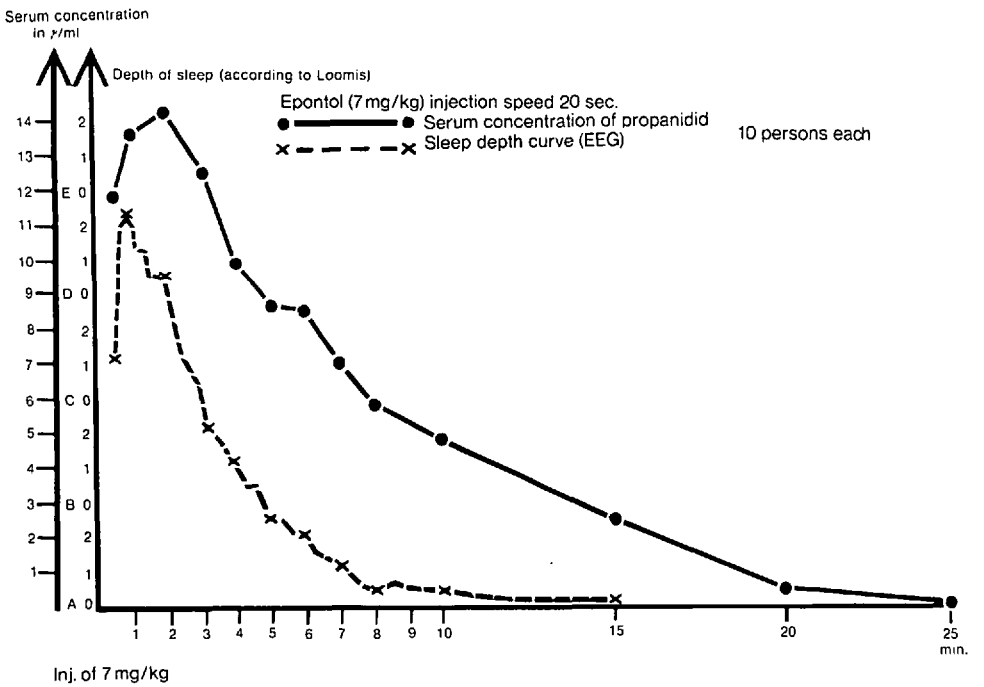

FIGURE 3. E.E.G. recordings compared with propanidid concentration.

*Propanidid** is rapidly broken down, but its determination in the serum was achieved. Epontol injected within about 20 seconds could be measured in the serum for the next 25 minutes. The method of estimating the propanidid serum concentration will be published in the near future.[3] With the disappearance of a measurable propanidid serum concentration there was a return to the initial E.E.G. tracing. The E.E.G. recordings shown in Figure 3 do not contain any sign of drowsiness. We compared methohexital, reported to have a very short-lasting effect, and Epontol in cross-over. For two to twelve hours after anaesthesia induced with 150 mg. of methohexital the E.E.G. of a volunteer revealed drowsiness and sleeping. No such phenomenon appeared after Epontol (Figs. 4 and 5).

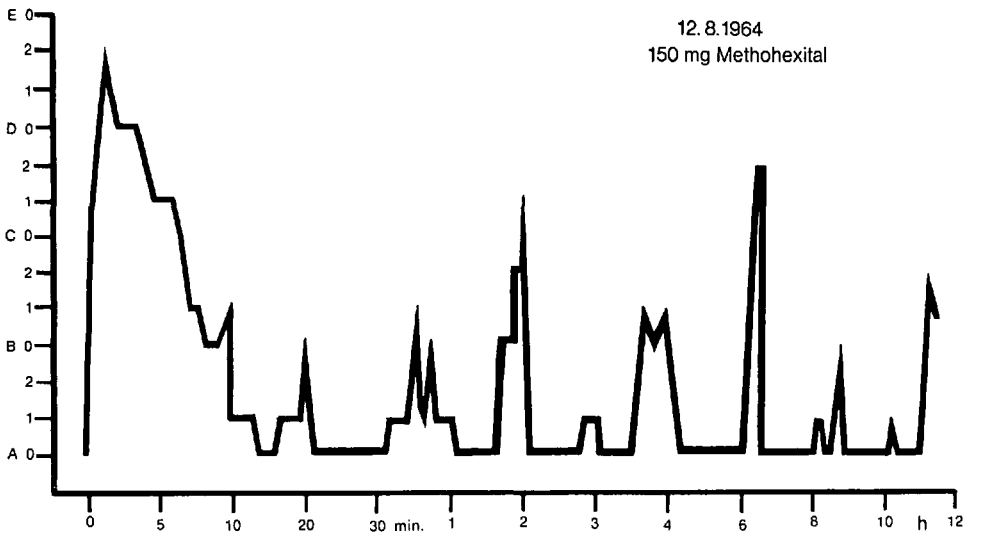

FIGURE 4. Sleep depth curve during and after methohexital anaesthesia. Frequent short episodes of tiredness and sleep occur throughout the day.

It is not possible to compare directly the effects of the new anaesthetic agent CI-581 with methohexital. CI-581 produces peculiar electrical changes: a continuous bilateral 6–9 per second activity, predominantly in precentral regions, persists for 20 to 60 minutes. This continuous pattern does not fit into the well-known stages of sleep or anaesthesia, with typical variations in the course of time and correlated with the vanishing effect of the barbiturates (Fig. 6). Psychodiagnostic tests revealed a prolonged decrease of performance ability, until the fourth hour. Pulse rate and blood pressure rose to maximal value of 150 in four minutes.

Combination of Narcotics

The volunteers in these studies disliked induction by inhalation. Therefore, anaesthesia was induced with an intravenous drug and continued with an inhalation agent. In our experience, Epontol was liked best by the volunteers, particularly because its effect wears off within a few minutes. The rapid disappearance

*The injectable anaesthetic Epontol® consists of Cremophor EL, the solubilizing agent, and the active substance propanidid.

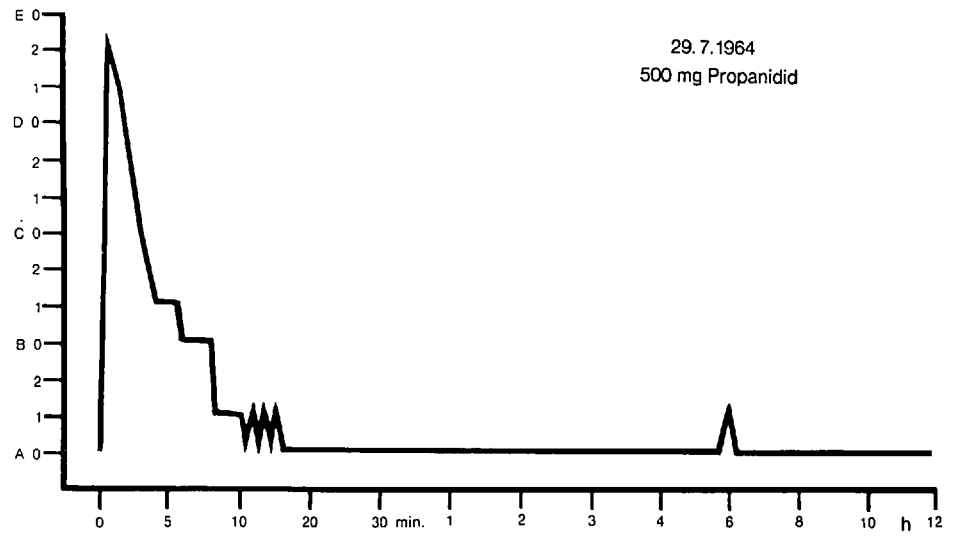

FIGURE 5. Sleep depth curve during and after propanidid anaesthesia. There are no episodes of tiredness and sleep.

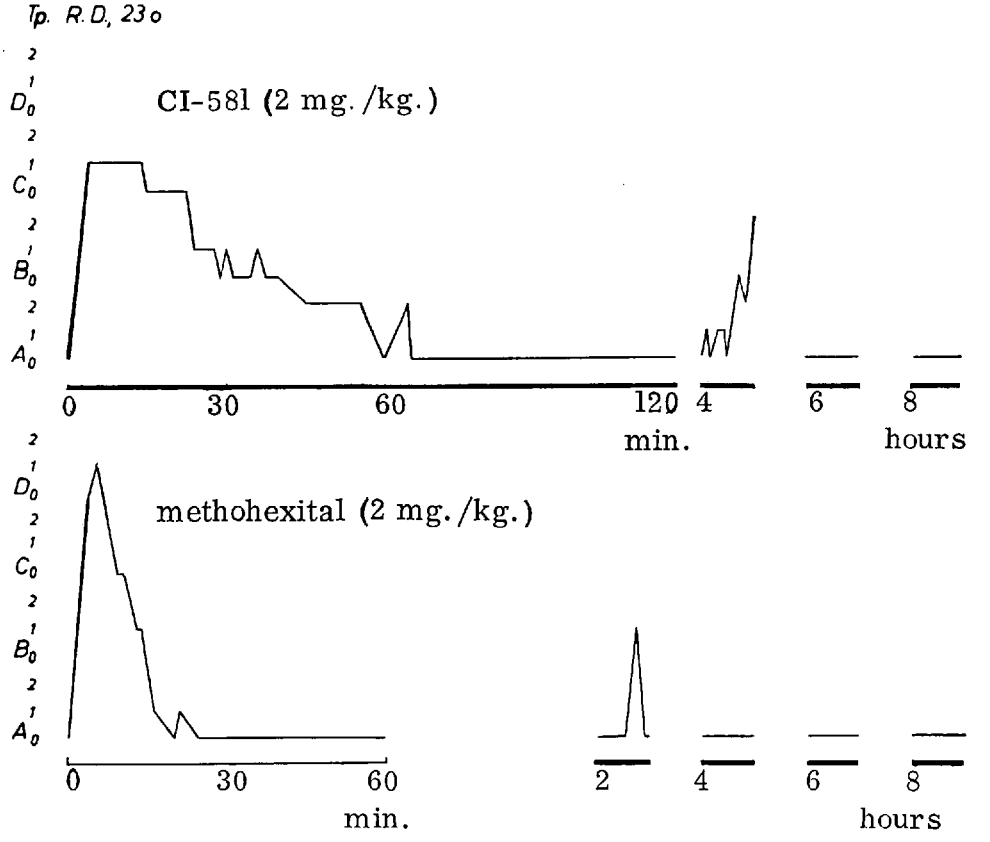

FIGURE 6. Sleep depth curve after induction with CI-581 and methohexital.

of Epontol from the serum ensured that seven to eight minutes after its administration only halothane or nitrous oxide would be anaesthetically still effective.

When halothane is used after Epontol the course of anaesthesia, with fast E.E.G.-activity, is prolonged for some minutes. Two minutes after the halothane

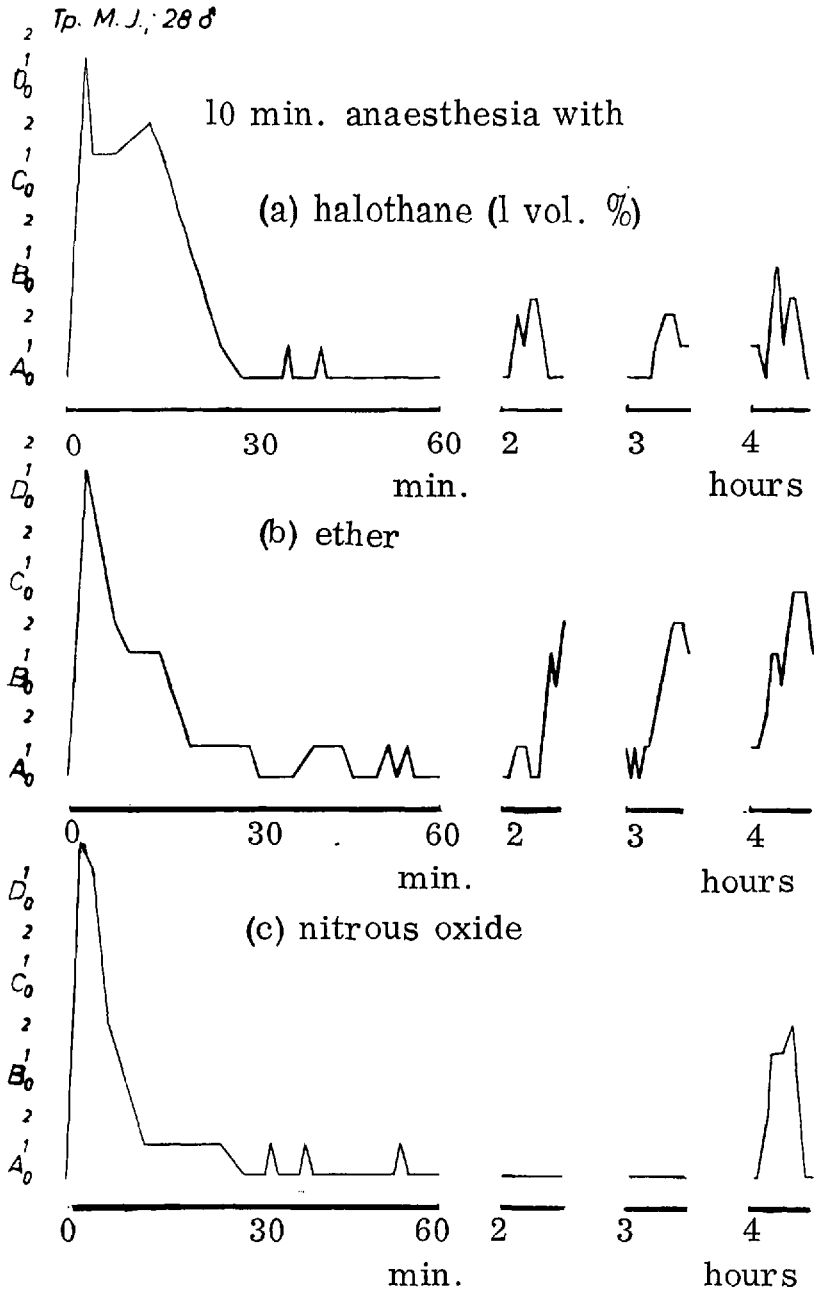

FIGURE 7. Sleep depth curve during and after induction with propanidid (7 mg./kg.).

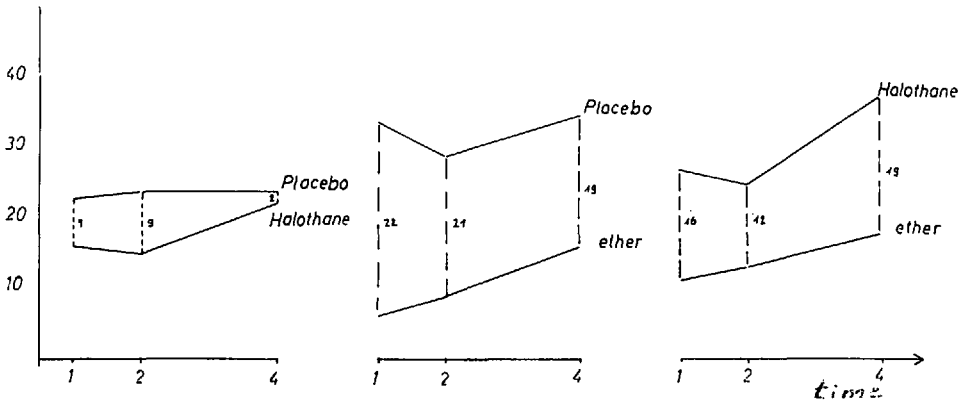

FIGURE 8. Course of the different results of psychodiagnostic test methods after halothane, diethylether, and a placebo in time intervals of one, two, and four hours after anaesthesia.

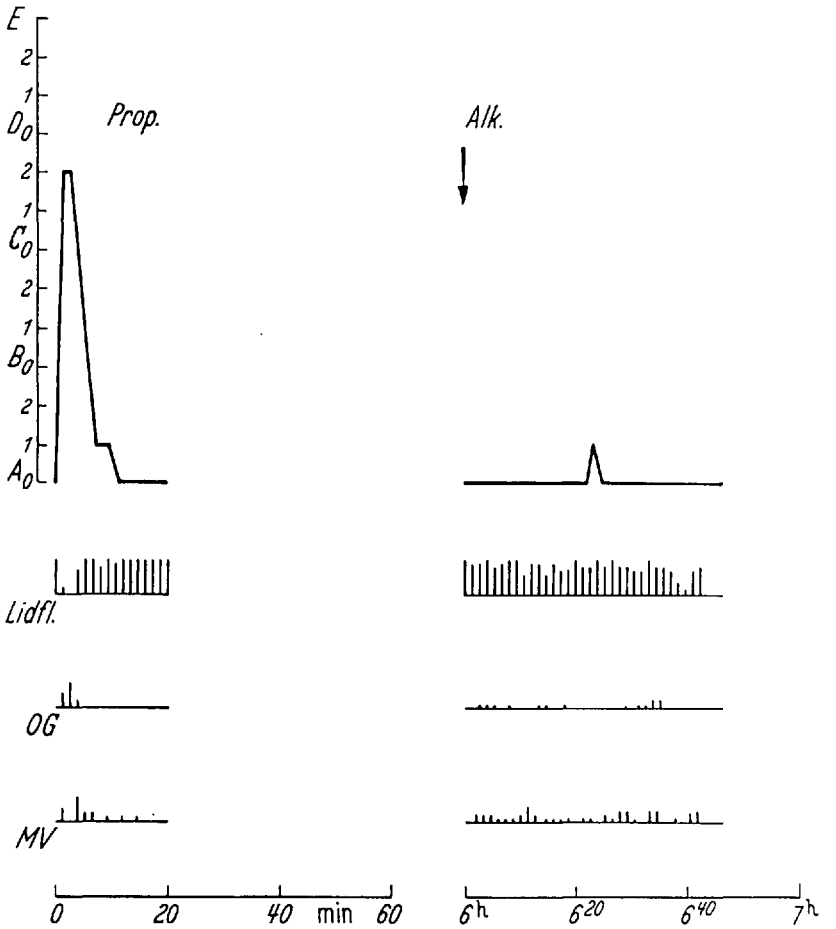

FIGURE 9. Course of depth of anaesthesia and sleep in a 21-year-old female weighing 55 kg., six hours after propanidid (7 mg./kg.), 38 per cent alcohol (0.8 × 0.7 × 3 × kg. body weight, in ml.). Ordinate—depth of sleep. Lidfl.—eyelid flickering. OG—oculogram. MV—movement.

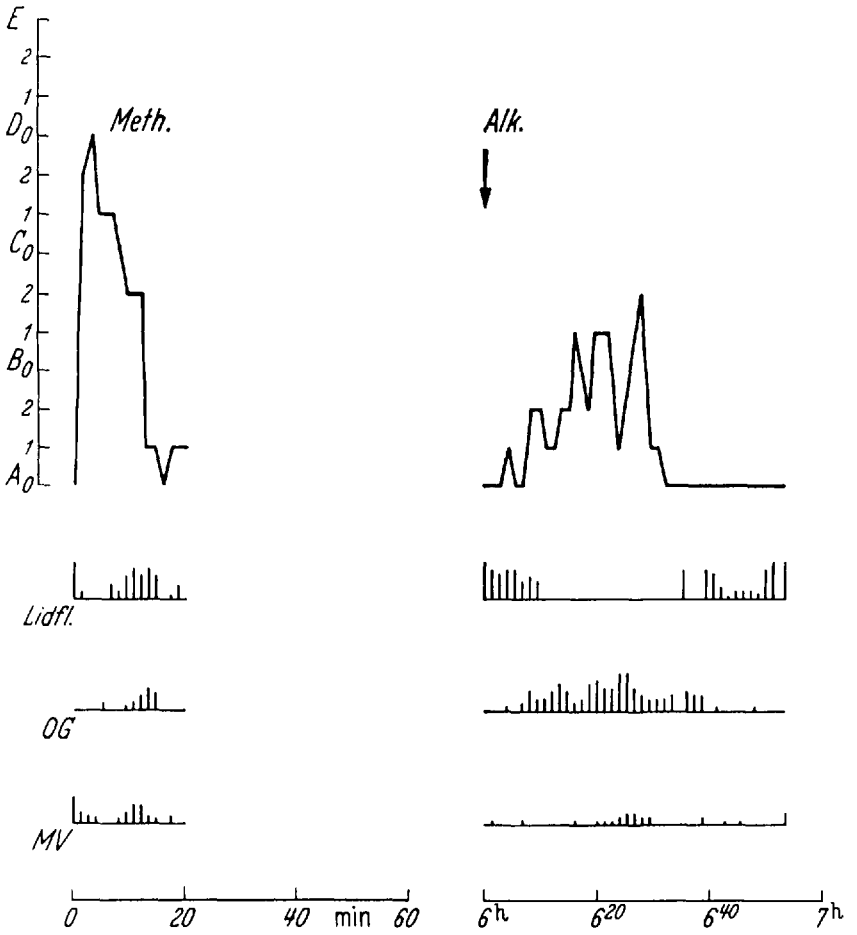

FIGURE 9. Course of depth of anaesthesia and sleep in a 21-year-old female weighing 55 kg., six hours after methohexitone (Brietal 2 mg./kg.), 38 per cent alcohol (0.8 × 0.7 × 3 × kg. body weight, in ml.). Ordinate—depth of sleep. Abbreviations as in Figure 9.

administration is stopped (15 minutes after its start), there is a return of α-waves in the E.E.G., and 20 minutes later return to pre-injection E.E.G. patterns. Moreover, in this case there is only a short drowsiness, but no sleep stage occurs during the following hours (Fig. 7).

Shifting from Epontol to ether was difficult because excitation usually occurred within the second minute. However, from the sixth minute on, anaesthesia was established, as manifested by δ-waves in the electroencephalogram. After the cessation of ether, return to preanaesthetic levels was slow. Even three or four hours later deeper sleep stages, with vertex-waves, were found than following halothane (Fig. 7).

With nitrous oxide alone it was difficult to produce a sufficient depth of anaesthesia. However, after induction with Epontol no difficulties were encountered with subsequent nitrous oxide. Six to seven minutes after the administration of

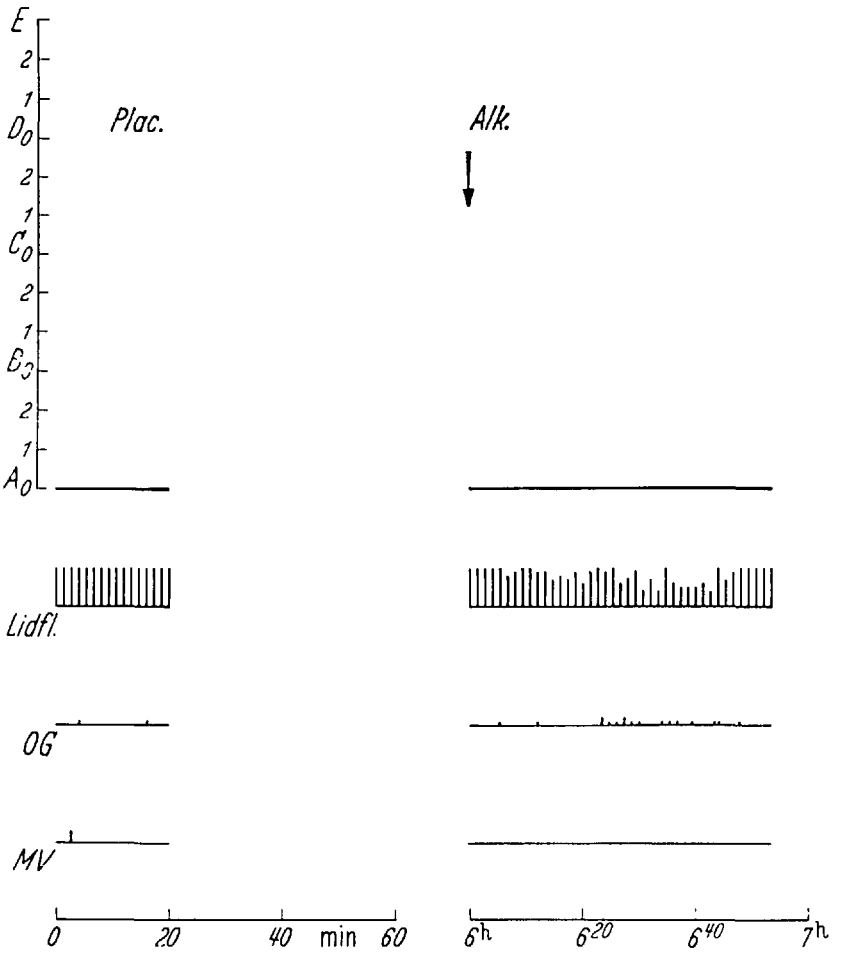

FIGURE 11. Course of depth of anaesthesia and sleep in a 21-year-old female weighing 55 kg., six hours after placebo (10 ml. NaCl. i.v.), 38 per cent alcohol (0.8× 0.7 × 3 × kg. body weight, in ml.). Ordinate—depth of sleep. Abbreviations as in Figure 9.

nitrous oxide, the planes of anaesthesia did not deepen any more, despite 75 per cent of nitrous oxide in the mixture. The E.E.G. returned to the resting pattern half an hour after anaesthesia (Fig. 7).

The results of psychodiagnostic tests with placebo, ether, nitrous oxide, and halothane, as well as the E.E.G. recordings, showed halothane to be significantly superior to ether (Fig. 8).

Combination with Alcohol

Certain anaesthetic drugs, particularly barbiturates, are potentiated by alcohol. This led us to undertake an alcohol test after anaesthesia with Epontol and methohexital. The results were compared with those after injection of isotonic sodium chloride combined with alcohol. Students drank the liquor one or two

hours after starting the tests. The assay of alcohol was by Widmark's method. We paid particular attention to not exceeding blood alcohol levels of .8 per mille to prevent dangerous side-effects. Figs. 9, 10, and 11 show the E.E.G. results on one volunteer. Thirty, 45, and 60 minutes after alcohol intake, the blood level was determined. The alcohol was ingested within 15 minutes. Concern about keeping the alcohol blood level under .8 per mille proved to be necessary. One volunteer (Fig. 12, #9) exhibited drunkenness 20 minutes after the drink and 80 minutes after methohexital anaesthesia. He remained drunk for several hours, even when the blood level fell to less than .6 per mille. The same volunteer did not show such symptoms after Epontol plus alcohol. Four students fell asleep during the day after methohexital and alcohol whereas they could perform their studies during the afternoon after receiving Epontol and alcohol.

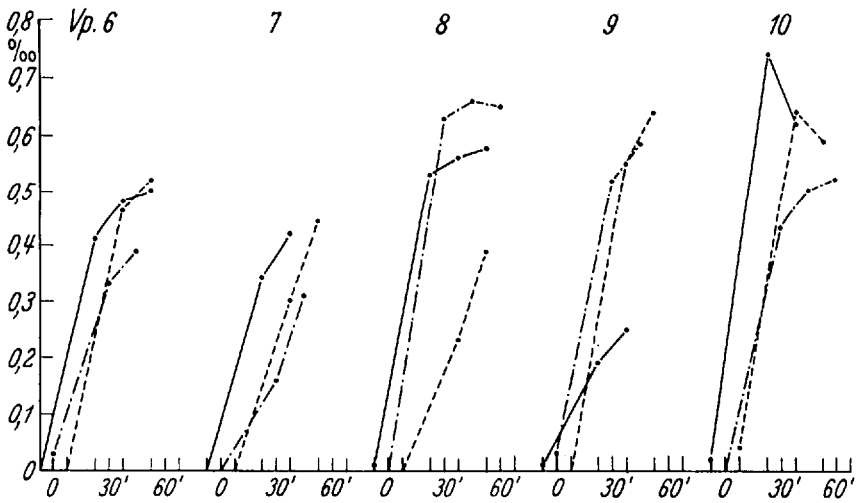

FIGURE 12. Ordinate—alcohol blood level (ADH method). Abscissa—time. Solid line—placebo, alternating dots and dashes—propanidid (7 mg./kg.), dashed line—methohexitone (2 mg./kg.). Two hours after start of test, 38 per cent alcohol was consumed (0.8 × 0.7 × 3 × kg. body weight, in ml.).

Performance on the labyrinth test, the count-down test, and the Düker concentration test[4] show the greatest changes (Fig. 13). It is important that these express disturbances at higher integration levels of the brain, while track tracer and Mierke reaction test depend on fine motor skilfulness and sensomotor co-ordination and need only a relatively short effort which can be maintained even with a disturbed higher brain function.

DISCUSSION

The criteria often used to differentiate orthodox and so-called paradoxical sleep stages in the electroencephalographic description of sleep did not prove useful in our anaesthetic controls because the rapid eye movements in stages of anaesthesia are different.

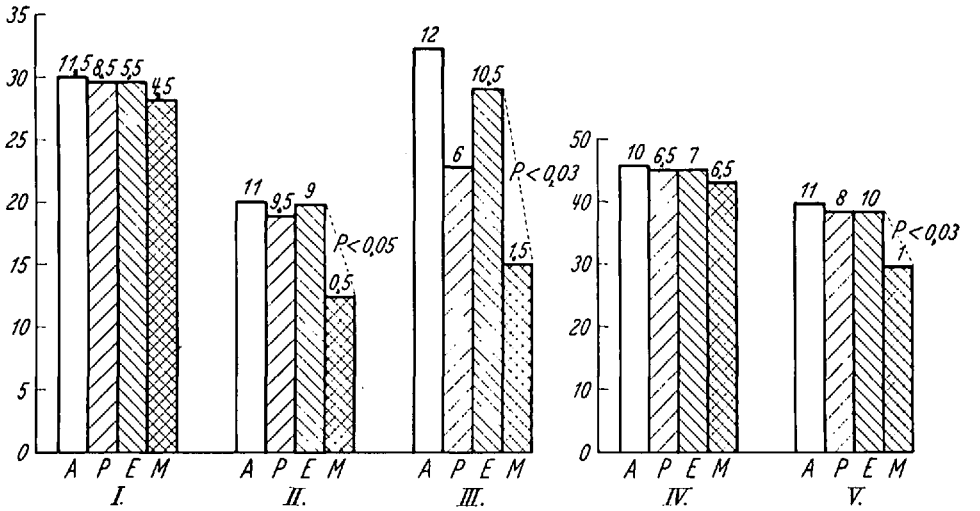

FIGURE 13. I—track tracer, II—labyrinth, III—counting test, IV—Mierke, V—Dücker CPT. Comparison of average values of psychodiagnostic tests on five healthy volunteers. Performance of test 2½ hours after start of the experiment. Intake of alcohol, 38 per cent (0.8 × 0.7 × 3 × kg. body weight, in ml.), half an hour before beginning test. The figures above the columns state the sum of the individual scores of the five volunteers (order scoring). Significance calculation by H. Rost, Institute of Mathematics, University of Munich. Ordinate—error and time scored by points. Abscissa—A: initial value without alcohol, P: placebo (10 ml. physiol. NaCl) plus alcohol, E: propanidid (7 mg./kg.) plus alcohol, M: methohexitone (2 mg./kg.) plus alcohol.

Concerning automatic analysis of E.E.G. curves the studies carried out since 1957 with different types of frequency analysers and amplitude integrations[8] have shown that the essential gain is obtained with methods using time-condensing demonstrations. The practical informational value does not differ much in this respect between frequency histograms, filtered amplitude integrations, and interval analyses. No analytic method is able to replace or even facilitate visual evaluation of the E.E.G. curves[7] but can merely give additional information at extra expense.

Individual differences in starting condition are sometimes the reason for abnormal reactions even in healthy people. In the case of our volunteer 9, who after a barbiturate anaesthetic was completely drunk with a .8 per mille blood alcohol level, the E.E.G. curves had shown marked functional lability on several control examinations. The question arises whether special irregularities in the E.E.G. permit predicting stronger reactions.

The observed delayed barbiturate effects throw some doubt on the interpretation of neuro-physiological experiments on animals shortly after a barbiturate anaesthetic for trepanation of the skull. Findings in such experiments often neglect the prolonged postanaesthetic influence of the drug.

Our studies on healthy human volunteers revealed definite postanaesthetic effects. Results of examinations of healthy people cannot without reservation be applied to patients. The assumption suggests itself that most patients with metabolic damage excrete anaesthetics rather more slowly and that even more

pronounced postanaesthetic effects have to be anticipated. These postanaesthetic effects were not appropriately judged in the past; on hospitalized patients they cannot usually be distinguished from the sequelae of operation, and in out-patient surgery they are not carefully observed for a sufficiently long time.

Comparing the inhalational anaesthetics halothane and ether (Fig. 7) showed that ether has a more prolonged hang-over, in accordance with its physicochemical properties. In an investigational series that has not yet been concluded results similar to those after ether have been recorded after methoxyfluorane.

One and two hours after anaesthesia with methohexitone, alcohol produced considerably stronger subjective disturbances, and more marked fluctuations of alertness were recorded in the E.E.G., than after Epontol. From this finding it follows that the impairment of street fitness after methohexitone should not be ascribed to the alcohol alone. As also indicated by disturbances in psychodiagnostic tests, such impairment may more readily be explained by the combination of alcohol with the barbiturate (Fig. 14).

Correlation of the serum barbiturate concentration with the sleep pattern after the ingestion of alcohol and the sleep pattern after lunch (Fig. 1) confirms the pharmacologically determined fact that the lipid soluble barbiturates are stored in adipose depots. After the intake of fluid or food they can be remobilized; their concentration in the brain temporarily rises and sleepiness increases.

We have previously considered the after-effects of thiobarbiturate anaesthesia with regard to street fitness.[2] The experiments lead to a practical conclusion for the anaesthetist: in *every* case of out-patient anaesthesia with barbiturate (methohexitone included) the patient should be cautioned against occupations in which

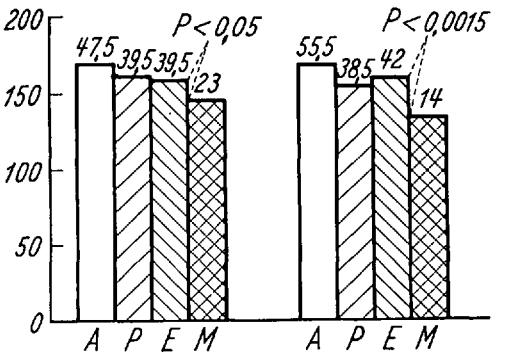

FIGURE 14. Summary of the psychodiagnostic tests 1½ hours (left) and 2½ hours (right) after the start of the experiment. Intake of alcohol, 38 per cent (0.8 × 0.7 × 3 × kg. body weight, in ml.) one-half hour before beginning test. Average values of the points with order scoring. Significance calculation by H. Rost, Institute of Mathematics, University of Munich. Ordinate—error and time scored by points. Abscissa—A: initial value without alcohol, P: placebo (10 ml. physiol. NaCl) plus alcohol, E: propanidid (7 mg./kg.) plus alcohol, M: methohexitone 2 mg./kg. plus alcohol.

a decrease of concentration power may be a hazard. In view of the legal risk it is advisable that the patient confirm in writing that he has been told this.

Nunn and Payne (1962)[9] reported on the postoperative respiratory insufficiency after inhalational anaesthetics induced with barbiturates. Postoperative hypoxia after halothane anaesthesia and neuroleptanalgesia were compared by Gemperle (1965)[5] on the basis of blood-gas analyses. The blood-gas values are better after neuroleptanalgesia than after halothane anaesthesia. Our observations indicate as the reason for this difference that the halothane is not given alone but in combination with a barbiturate. This was not considered in Gemperle's studies. The hypnotic and sedative effect of barbiturates continues for hours after the operation and is one cause of postanaesthetic hypoxia. The short-lived action of Epontol, with less burden in combination with halothane, may lead to new methods in anaesthetic practice.

During the past two years we have preferred (except for small children) induction with Epontol and continuation with N_2O/O_2, 3:1, and approximately 0.7 vol. per cent halothane for all anaesthetics.

Summary

After barbiturates or ether anaesthesia, drowsiness lasting 12 hours was observed but was not recorded with Epontol and halothane. Psychodiagnostic tests and E.E.G. records showed reduced fitness for as long as eight hours after barbiturates and ether anaesthesia. With Epontol such symptoms did not last longer than half an hour.

Epontol appears to be the only truly short-acting anaesthetic at present. Taking into account the stress associated with minor surgery, in our opinion, it takes two hours after Epontol anaesthetic for the patient to regain street fitness, unless there are other reasons for a longer delay. As a result of our knowledge of Epontol we have induced all our out-patient anaesthetics with this drug for the last year. We combined halothane with Epontol in about 8,000 cases without any complications and consider this the method of choice over the formerly employed barbiturate-halothane combination. We believe this to be also true for in-patients.

Résumé

Après l'anesthésie à l'éther et aux barbituriques, nous avons observé que le malade demeurait étourdi durant 12 heures, ce qui n'existe pas avec l'épontol et l'halothane. Après l'anesthésie à l'éther at aux barbituriques, des tests psychodiagnostiques et des tracés électroencéphalographiques ont montré chez le malade des aptitudes diminuées durant aussi longtemps que 8 heures. Avec l'épontol ces signes n'ont pas persisté plus d'une demi heure. Actuellement, l'épontol semble être le seul vrai agent anesthésique à action courte. D'après notre opinion, tenant compte de la tension accompagnant la chirurgie mineure, il faut deux heures, après une anesthésie à l'épontol, pour qu'un malade puisse prendre la rue, à moins que d'autres raisons justifient un plus long délai.

Comme résultat de notre connaissance de l'épontol, au cours de la dernière

année, nous avons fait toutes les inductions de nos anesthésies à la clinique externe avec ce produit. Nous avons associé l'épontol et l'halothane chez 8,000 malades sans aucune complication et nous estimons que cette façon de procéder est supérieure à l'association barbiturique-halothane employée antérieurement. La chose est également vraie pour les malades hospitalisés.

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