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THE ACTIONS AND USES OF PENTAL.

BY

DAVID CERNA, M.D., PH. D.,

Demonstrator of Physiology in the Medical Department of the University of Texas; formerly Demonstrator of and Lecturer on Experimental Therapeutics in the University of Pennsylvania, etc., etc.

REPRINT FROM

American Medico-Surgical Bulletin,

October, 1893.

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Address:—P. O. Box, 2535,
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Editor American Medico-Surgical Bulletin.

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ERRATUM.

The diagrams, Fig. 2 and Fig. 3, were transposed by the printer's error. Properly the plot marked "Fig. 3, PLOT OF EXPERIMENT VI," should be "Fig. 2, PLOT OF EXPERIMENT V," and *vice versa*.

THE ACTIONS AND USES OF PENTAL.*

By DAVID CERNA, M.D., Ph. D.,

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PENTAL is a product obtained from amylene hydrate when this latter substance is heated with acids. The new anæsthetic is also termed *Trimethylethylene* and *Beta-iso-amylene*, the chemical composition of which is represented by the formula, $(CH_3)_2$:C:CH (CH_3); or C_5H_{10}.

Pental is a colorless, highly inflammable liquid, burning with an illuminating flame. It has a specific gravity of 0.678, and a boiling point of 100 4° F (38° C). Although exceedingly volatile, it does not decompose on exposure to light or to the atmosphere. Pental is soluble in alcohol, ether, and chloroform, but is insoluble in water.

The interest which the new drug has awakened as a general anæsthetic in surgical practice, necessitates that its physiological action be studied carefully. More or less extended researches in the clinical wards have been made, especially in Eu-

* Read before the Texas State Medical Association, at Galveston, May, 1893

rope, regarding the effects of pental in the animal economy ; but no elaborate studies as to *how* such effects are brought-about have been made.

The alleged chief action of the agent as an anæsthetic, leads to the importance of a knowledge of the behavior of the new drug, particularly on the circulation and the respiration. To these two ~~symptoms~~ symptoms I have confined for the present my experimental studies.

In a paper entitled "Chloride of Ethyl and Pental," published by Prof. H. C. Wood and the writer (*), a note is appended in regard to the actions of pental ; but this latter study, only preliminary and superficial, cannot be considered by any means as conclusive. From the details, however, of one of the experiments performed, it was observed that the production of anæsthesia with pental in dogs was each time accompanied with a marked fall of the arterial pressure. The rate of the respiration was increased, although the extent of the respiratory movements, most of the time, was not distinctly above the normal. The accompanying tracing in the paper referred-to, shows the depressing effect of pental upon the heart ; this organ being affected much more severely than the respiratory centers, since the respiratory movements continued after the cardiac viscus had ceased to beat.

* *Dental Cosmos*, July, 1892 ; also, *Transactions of the Philadelphia County Medical Society*, 1892.

Wood and the writer concluded, then, from such evidence, that pental would probably prove to be a dangerous anæsthetic; and that, if extensively used, it would produce death by cardiac paralysis; and further, that, even in non-fatal cases, the after-effects, in the human being, would be disagreeable from the fact that in the dog a peculiar wild excitement was noticed directly after the anæsthesia from the drug had gone off.

In continuing my own studies with pental, I have instituted a special series of experiments, begun at the laboratories of the University of Pennsylvania, and finished at the physiological laboratory of the University of Texas, at Galveston. My experimentation may not be an elaborate one, perhaps, but it is sufficient, I believe, to show the range of action of the drug in question upon the circulation and the respiration.

I divided my experiments into three series, as follows: 1, those performed upon normal animals; 2, those made in animals whose vagi had been previously cut; and 3, those performed upon animals in which the spinal cord and vagi had been previously severed. The animals used were exclusively dogs.

The dog was first etherized in order to perform the various operations for the preparation of the animal. After the connection with the recording kymograph was made,—of the respiratory apparatus by means of a

tracheal tube and the corresponding Marey's tambour, and of the circulatory apparatus by the usual methods,—the animal was allowed to recover completely from the effects of the ether, in order to avoid, as far as possible, vitiated results.

The pental was administered by inhalation or intravenously. As objection might be taken to this latter method of administration, I may here repeat what Wood and the writer (*) have already remarked: that "it is plain that whether a drug be injected directly into the jugular vein, or whether it enter the system by absorption into the pulmonary capillaries, it must first reach the heart before being diffused throughout the general circulation. In the one case the drug passes first into the right side of the heart, while in the other case it goes into the left side of the heart."

Various experiments, in tabular form, and also by means of plots, are presented herewith.

The most superficial analysis of these experiments will reveal the fact that pental is capable of producing anæsthetic effects, but that these effects are generally accompanied with disturbances of respiration and, particularly, of the circulatory system.

Thus, in Experiment I, the first inhalation of ten grammes of the drug was followed by

* *Loc. citat.*

EXPERIMENT No. I. DOG-WEIGHT, 11.5 KILOS.

TIME. M. S.	DOSE.	PRESSURE. MM.	PULSE. PER MIN.	RESP. PER MIN.	REMARKS. NORMAL.
					Pental by inhalation.
0.		160	134	24	
8.00		162	132	24	Inhalation begun, of one bottle (10 grammes), poured into an ordinary inhaler.
8.30		140	102	38	
8.40		138	102	46	
9.00		130	92	50	Palpebral reflexes weak; inhalation ended.
9.20		150	96	58	
9.40		158	98	52	Reflexes normal again; animal much excited; salivates and urinates.
11.30		164	136	60	Inhalation of second bottle begun.
11.50		128	98		Respiration irregular and shallow.
12.00	*See "Remarks."*	98	68	102	Anæsthesia apparently complete; but conjunctival reflexes not entirely lost.
12.50		98	152	102	Pulse small; respiration exceedingly shallow; removed inhaler.
13.10		142	146	96	
13.40		150	134	82	
14.20		158	132	52	Reflexes normal again; dog very restless and whines.
17.30		162	136	40	Dog continues very restless.
18.40		162	134	40	Inhalation of third bottle begun.
19.50		60	76	78	Inhalation ended; respiration shallow, with a tendency to the Cheyne-Stokes type; reflexes weak, but animal apparently narcotized.
20.20		132	142	62	
20.50		166	168	52	
21.30		162	162	42	Animal has regained consciousness, whines, and is very much excited.
24.00		160	168	48	Dog continues excited; pants as if much fatigued. Was afterward killed.

a decline of both the blood-pressure and the

EXPERIMENT No. II. DOG-WEIGHT, 12 KILOS.

TIME. M. S.	DOSE. GME.	PRESSURE. MM.	PULSE PER MIN.	RESP. PER MIN.	REMARKS. NORMAL.
					Pental intravenously.
0.		170	148	18	
10.00	0.2	176	152	18	Injection begun.
10.20		158	136	24	Injection ended
10.40		146	120	36	Pulse irregular; palpebral reflexes weak; pupils dilated.
11.00		148	120	38	
12.50		152	142	32	
13.30		168	148	36	Apparently conscious again, but restless.
14.00	0.3	168	148	36	Injection begun.
14.20		130	116	42	Injection ended.
14.40		120	98	56	
15.00		102	128	66	Narcotized, but eye reflexes not entirely gone; pupils widely dilated: respiration shallow.
15.30	0.5	110	136	68	Injection begun.
16.00		92	166	70	Injection ended.
16.30		80	178	76	Continues narcotized: pulse small.
18.30	1.00	96	180	68	Injection begun.
19.00		62	172	68	Injection ended.
19.20		40	186	52	Anæsthesia complete, but eye reflexes can still be elicited mechanically.
25.00		158	196	60	Consciousness has returned; animal very much excited, whining; pupils continue dilated.
28.00	2.00	162	186	62	Injection begun.
28.30		56	164	64	Injection ended.
29.00		32	146	60	
29.30		28	126	48	
30.00		16	96	36	Pulse very weak. Spasm.
30.30		....	....	6	Heart ceased.
31.00		....	....	4	
31.30		....	....	2	Two minutes afterward the needle registered two or three respiratory movements.

pulse-rate, even before the production of anæsthesia. The pressure from its normal height, 162 mm., fell to 140 mm. in the course of half a minute after the beginning of the inhalation, and to 130 mm. in half a minute longer, when the eye-reflexes became weak and the animal was apparently narcotized. The pulse was also reduced in rate, while the respirations were increased in number, though no change was observed in the depth of the movements. Forty seconds after the removal of the inhaler the conjunctival reflexes became normal, and the animal exhibited a condition of great excitement, accompanied with marked salivation and apparently involuntary urination.

The second inhalation was followed by similar phenomena as regards blood-pressure, pulse, and respiration. At a time, however, when the anæsthesia was complete, although the pressure remained at the height of 98 mm., there was a sudden rise in the number of pulsations even above the normal, although the character of the pulse indicated weakness. In the course of nearly two minutes after the occurrence of this phenomenon, but pulse and pressure returned to their normal standard, *pari passu* with the disappearance of the anæsthesia; yet, the respiration continued above the normal, and the animal gave evidence of marked excitement.

After an interval of about five minutes, the

third inhalation was administered. The same results were produced : reduced arte-

EXPERIMENT No. III. DOG-WEIGHT, 18.5 KILOS.

TIME. M. S.	DOSE. GME.	PRESSURE. MM.	PULSE PER MIN.	RESP. PER. MIN.	REMARKS. NORMAL.
					Pental injected intravenously. One vagus prepared.
0.		172	182	21	
10.00		170	182	21	Tested irritability of vagus with a medium current of electricity. Applied to central end, heart-beat ceased in 15 seconds ; to peripheral end heart-beat arrested in 8 seconds.
15.00	0.5	176	178	24	Injection begun.
15.20		160	156	36	
15.40		142	138	48	Injection ended.
16.00		108	128	58	
16.20		98	112	68	The same electrical current applied to either end of vagus, is followed by an almost instantaneous arrest of the heart.
22.00		168	162	38	
22.20	0.5	168	162	38	Injection begun.
22.40		146	148	68	
23.00		126	126	78	Injection ended.
23.30		92	108	82	Dog narcotized ; pupils widely dilated.
24.00		82	102	78	Same effect as before, on application of electrical current to cut ends of vagus.
24.30	0.5	106	112	64	Injection begun.
25.00		92	126	60	Injection ended.
26.00		42	204	62	
27.00		40	214	62	
27.30		36	224	68	Complete anæsthesia ; same electrical current applied to vagus had now *no* effect on cardiac action. Animal died eventually.

rial pressure and pulse-rate, and an increase

of the respiratory movements. And now the breathing, essentially shallow, showed a tendency to the Cheyne-Stokes type, at the very time, indeed, when the dog ap-

EXPERIMENT No. IV. DOG-WEIGHT, 12.8 KILOS.

TIME. M. S.	DOSE. GME.	PRESSURE. MM.	PULSE PER MIN.	RESP. PER MIN.	REMARKS. NORMAL.
					Pental intravenously; ischiatic nerve prepared.
0.		142	168	26	
15.00		144	166	24	
16.00	0.5	144	166	24	Injection begun.
16.30		126	148	38	Injection ended.
17.00		118	120	42	Pulse-waves large.
17.40		116	126	48	
19.30	0.5	120	136	48	Injection begun.
20.00		102	116	52	Injection ended.
20.30		98	112	52	
21.00		98	110	58	Pulse-waves large; animal narcotized; faradization of ischiatic nerve for 15 seconds.
21.30		120	124	42	
21.45		128	130	48	
22.30	0.5	130	142	48	Injection begun.
23.00		112	120	56	Injection ended.
23.40		80	116	56	
25.00	1.00	116	120	52	Injection begun.
25.40		98	102	52	Injection ended; pulse-waves large. Spasm of tetanic nature
26.00		102	148	50	
26.40		100	182	48	
27.40		108	196	48	
28.00		102	198	42	
29.00		...	...	..	Heart ceased suddenly to act; animal continued to gasp for some time afterward.

peared to be completely under the influence of the anæsthetic. About three minutes af-

terward, however, the animal had regained consciousness, and the signs of excitement were again manifest. The pressure went back to normal, and the pulse even beyond its original rate.

In the second experiment, the drug was given intravenously. The results obtained, similar in almost every respect to those of the preceding instance, are sufficiently clear when observed in the tabular form given. There was produced the same depressant action upon the heart and the rate of the cardiac beat, and the same stimulating action on the respiration. As will be noticed, the fall in the number of pulsations was later followed by a decided increase of the same above the normal. The last injection of two grammes proved fatal to the animal, death taking place through cardiac paralysis.

The explanation of the results obtained in Experiment III (these being practically the same as those of the other experiments) will be given later; that is, when I shall enter into the discussion of how the circulatory phenomena are brought-about. I may here state that many other normal experiments gave almost invariably the same results.

It is seen, then, from the foregoing experiments that pental is capable of producing anæsthesia; but that this is, although rapidly established, rather too fugacious for practical purposes, and that it is usually ac-

companied by a depressing effect upon the circulation ; that the action on the respiration, though apparently stimulating, is unimportant, and that sometimes the latter function is dangerously interfered-with also ; lastly, that the after-effects are those of excitement, which, in all probability, are of a disagreeable nature.

EXPERIMENT No. V. DOG-WEIGHT, 10.5 KILOS.

TIME. M. S.	DOSE. GME.	PRESSURE. MM.	PULSE PER MIN.	RESP. PER MIN.	REMARKS. VAGI CUT.
					Tube in trachea ; pental intravenously.
0.		180	210	8	
10.00		180	212	8	
10.30	0.5	180	212	6	Injection begun.
11.00		168	182	8	Injection ended.
12.00		162	176	16	
13.30	0.5	164	174	22	Injection begun.
14.00		156	166	38	Injection ended.
15.00		160	150	42	Animal narcotized.
16.30		162	158	48	
17.00	0.5	162	158	46	Injection begun.
17.30		142	140	56	Injection ended.
18.00	1.00	128	132	50	Injection begun.
18.30		106	120	32	Injection ended.
19.30		82	80	10	
21.00		40	32	10	
22.30		22	18	8	
23.00		...	...	4	Heart stopped.
24.00		...	...	2	
26.00		...	...	..	Animal dead.

These general results appear to sustain those previously obtained by Wood and myself. Again, my own experience with

the drug agrees more or less with that of CALAB (*) and that of WEBER (†). Calab, as a result of considerable clinical experience and of a series of experiments on dogs, has concluded that anæsthesia as produced by pental is superficial; that the time necessary to obtain sufficient anæsthesia for ordinary

EXPERIMENT No. VI. DOG-WEIGHT, 10.3 KILOS.

TIME. M. S.	DOSE. GME.	PRESSURE. MM.	PULSE PER MIN.	RESP. PER MIN.	REMARKS. Vagi and Cord severed; cord cut in cervical region (‡)
					Pental intravenously.
0.		68	124		
1.30	0.5	68	122		Injection begun.
2.00		52	102		Injection ended.
2.30		42	98		
3.00		44	98		
4 30	0.5	46	98		Injection begun.
5.00		32	80		Injection ended.
5 4		28	46		
6.00		22	30		
7.00		18	22		Killed eventually.

surgical operations is much longer than with chloroform; that pental has a depressant effect on the circulation, and, when given in sufficient quantity to produce complete anæsthesia, may cause grave results; and that, finally, the local anæsthesia produced by pental is inferior to that caused by ether.

* *Clinica;* Bucharest, January, 1892.

† *Deutsche Medicin. Wochenschr.;* Leipzig, Feb. 16, 1892; and *Münchener Medic. Wochenschr.;* No. 2, 1892.

‡ Post-mortem examination showed that the cord had been completely severed.

FIG. 1.—PLOT OF EXPERIMENT II. (Normal.)

Heavy line—*Blood-pressure*. *Broken* line—*Pulse*. *Dotted line* (with numerals to the extreme left)—*Respiration*.

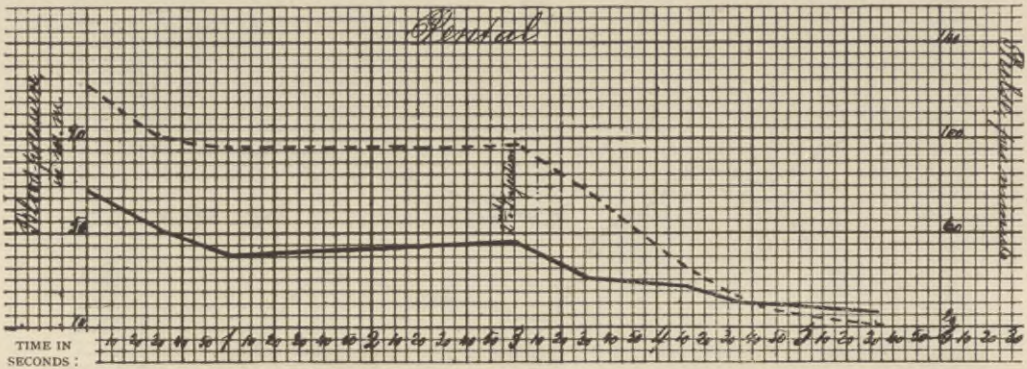

FIG. 2.—PLOT OF EXPERIMENT V. (Vagi cut.)

Heavy line—*Blood-pressure*. *Broken* line—*Pulse*. *Dotted line* (with numerals to the extreme left)—*Respiration*.

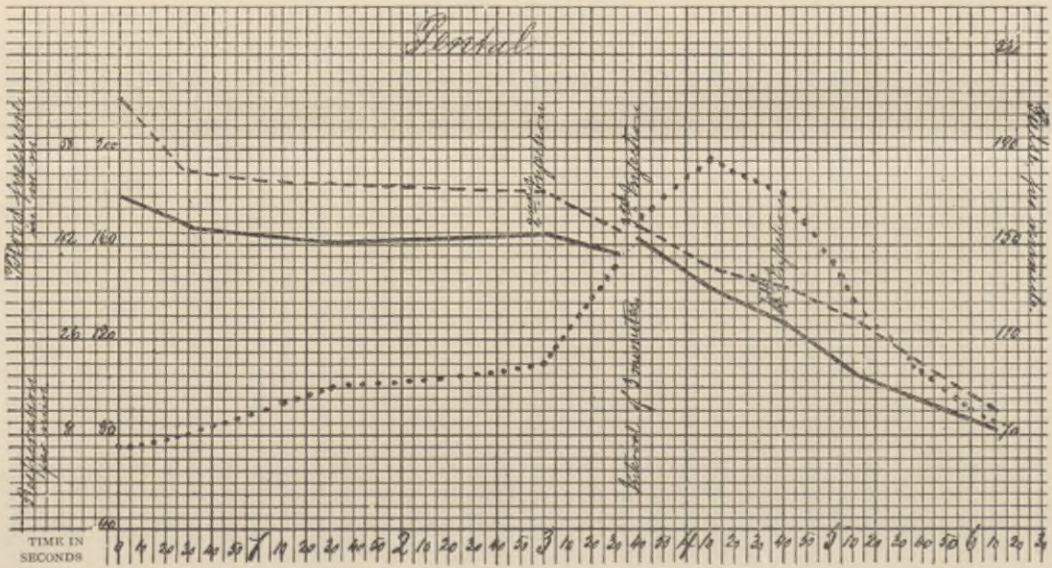

FIG. 3.—PLOT OF EXPERIMENT VI. (Vagi and Cord cut.)
Heavy line—*Blood-pressure*. *Broken* line—*Pulse*.

Weber noticed excitement in some human beings, and in a few other instances slight tetanic spasms in the arms and legs. In the case of an alcoholic, the excitement was very marked.

Let us examine into how the various phenomena above described are brought-about.

Anæsthesia.—When pental is administered by inhalation, the anæsthesia occurs, as is shown by Experiment I, in from 1 minute to 1 minute and 20 seconds, and lasts for a period varying from 20 seconds to 1½ minutes after the removal of the inhaler, although this must depend largely upon the quantity of the drug inhaled. No doubt a longer period of anæsthesia than the one I have referred-to could be induced by a persistent administration of the drug.

The same may be said in regard to the administration of the agent intravenously. I found that I could keep the animal narcotized as long as the repeated introduction of small quantities of pental was maintained. When the drug is given intravenously there is a tendency for the anæsthetic effects to occur sooner and last longer than when the drug is administered by inhalation; probably from the fact that a larger amount of the medicament is acting at once in the former instance; and that in the latter the drug is rapidly eliminated by the lungs, owing to the volatile nature of pental. Yet,

even when not taken directly into the circulation, the drug produces quick anæsthetic effects, it is true; but these disappear also in a comparatively rapid manner.

The anæsthesia caused by pental is chiefly of central origin, as shown by the fact that even when the loss of consciousness was complete, the conjunctival or palpebral reflexes were not entirely destroyed, since they could be elicited by mechanical stimuli. Undoubtedly, the local anæsthetic action of pental, if it has any, is very weak.

EFFECTS ON THE CIRCULATION.

On blood-pressure.—The blood-pressure in the normal animal is usually depressed by pental, as an examination of the preceding experiments reveals.

A careful study of these experiments will show also that for a certain period of time the rate of the pulse varied *pari passu* with the changes of the pressure; the former being slowed, or increased in rapidity, according as there occurred a diminution or an increase in the height of the latter. So that two curves, for instance,—one representing the rate of the cardiac beat, and the other the changes of the arterial pressure—taken from a tracing of an animal under the influence of pental, would undoubtedly show a more or less parallel course. This, in itself, is a very significant fact, and appears to point to an action of the drug exercised on the heart itself or upon the innervation

of the organ. An opposite course of the curves would indicate a vaso-motor spasm.

An irritation of a sensitive nerve by a sufficiently strong current of electricity, as is seen in Experiment IV, caused an almost immediate rise of the column of mercury in the manometer, this showing evidently that the vaso-motor system was intact. But, this is not all. The same phenomenon of blood-pressure reduction occurs after previous section of the pneumogastrics, and similarly after division of both vagi and the spinal cord. It would, therefore, be inferred that pental causes a lowering of the arterial pressure mainly by an action upon the heart.

The fall of pressure is not, however, so marked after previous section of the vagi, and it would seem as if peripheral irritation or stimulation of the pneumogastrics was another factor in causing the decided diminution observed in normal animals. As will be noticed in Experiment II, the pulse, after a poisonous dose of pental, became suddenly rapid,—due, no doubt, to a peripheral paralysis of the vagi (a phenomenon clearly shown toward the latter part of Experiment III); but there was noticed (in No. II) at the same time a corresponding rise of the arterial pressure,—this being subsequently depressed by another dose of the drug.

There is no doubt, then, that two factors must be taken into consideration to explain

the fall of the arterial pressure: a direct cardiac action, and a stimulation of the cardio-inhibitory centers peripherally.

The pulse.—In Experiment I, the first inhalation of 10 grammes brought down the pulse-rate, in a few seconds, from 132 to 102, and by the end of the inhalation, when the palpebral reflexes showed evidence of weakness, to 92. About two minutes afterward, the cardiac pulsations returned to the normal standard, to be again reduced by a second administration of the drug. When anæsthesia became complete, apparently, the pulse-rate marked 68, and in a few seconds it jumped to 152,—that is, about twenty (20) beats above the normal rapidity. The effects of the drug were allowed to pass off. A third inhalation was followed by the same phenomenon: a reduction at first, and a marked increase shortly afterward,—that is, as high as 168, this increase continuing even after the anæsthesia had disappeared.

The same results were observed when pental was administered intravenously, as is shown in Experiments II and III.

Pental, then, causes a slowing of the pulse, followed by a return to the normal, or by an increase above this point if the dose has been sufficiently large.

In studying the causes of these changes, it is ascertained that the drug produces the same effects on the pulse-rate, after previous

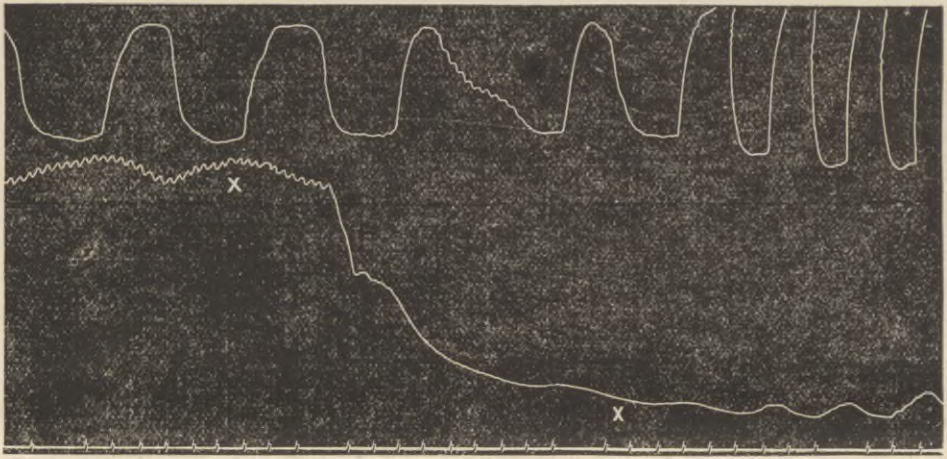

FIG. A.

TRACING.—Dog weighing 8.2 kilos. Injected intravenously, between x-x marks, one gramme of Pental. Upper line represents the respiratory movements; middle line, the arterial pressure and pulse-rate; lower line, abscissa.

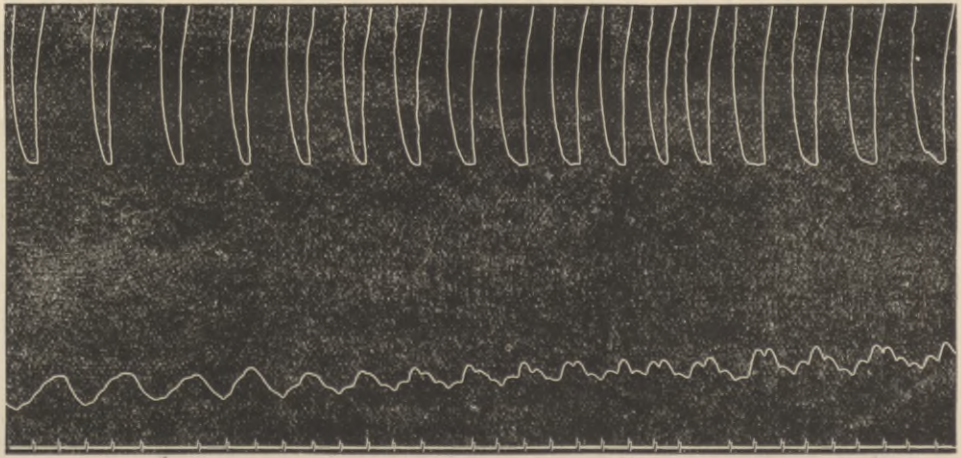

FIG. A (continued.)—The same, half-a-minute afterwards.

section of the vagi, and similarly after all nervous connection with the heart has been destroyed by previous division of the pneumogastrics and of the spinal cord. Is the action of pental, then, confined to the heart itself in causing the phenomenon of pulse-rate reduction?

It has been demonstrated that the drug exercises a stimulating action on the cardio-inhibitory centers peripherally, this being one of the factors to be taken into consideration in explaining the fall of the blood-pressure. Now, then, an examination of Experiment III shows that faradization of a vagus in an animal under the full influence of pental, produces arrest of the heart more rapidly than in normal conditions. These results are sufficiently clear. Again, when the pulse has become markedly increased above the normal point, as is also observed in the same Experiment III, electrical stimulation fails to arrest cardiac movements, a result similarly self-explanatory.

There is, therefore, under the action of pental, a primary stimulation, followed, especially when the drug has been absorbed in large doses, by a paralysis of the cardio-inhibitory centers, peripherally; this alone explaining the changes in the pulse-rate observed.

When the vagi have been previously divided, the drug causes a reduction of pulse-rate; but though in some instances the cardiac pulsations, under such circumstances,

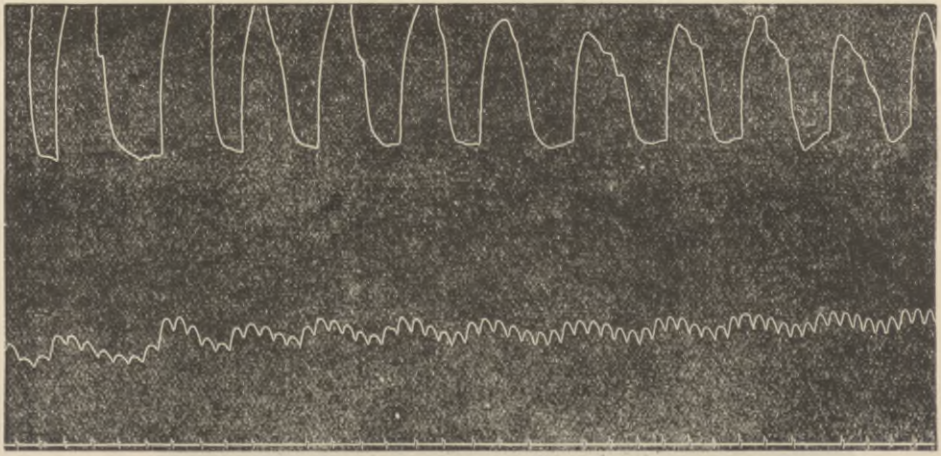

FIG. A (continued.)—The same, one minute afterwards.

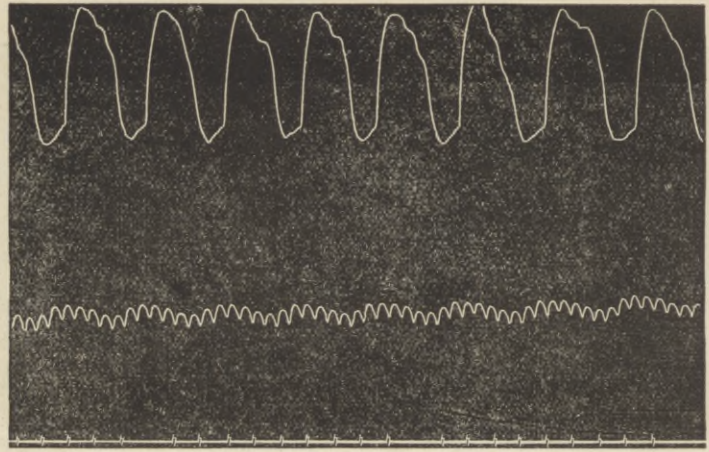

FIG. A (concluded).—The same, one minute and a-half afterwards, at which time anæsthesia was apparently completely established.

may return to the starting-point, I have never seen them go beyond this. If the dose of pental is sufficiently poisonous, the fall of the pulse-rate, in such cases, is generally progressive, with slight changes, till the occurrence of death. Just before a fatal issue takes place, the pulse is apt to become small and rapid, but these are evidences of weakness of the cardiac viscus.

It is evident, then, that the primary reduction of the pulse-rate caused by pental is due to a direct cardiac action, and to a stimulating influence exercised on the peripheral cardio-inhibitory centers ; the secondary increase above the normal mainly to paralysis of the latter ; and the final fall to an action upon the heart itself.

I made a few experiments on the heart of frogs, but the results, though apparently similar to those obtained in dogs, were not very satisfactory.

The mammalian heart is decidedly affected by pental, and I found that in many instances the organ, after death of the animal, failed to respond to mechanical or electrical stimulation. Usually death was caused by pental through cardiac paralysis, although sometimes the respiration and the heart stopped simultaneously.

The Blood. — At no time were there noticed any marked changes produced upon the blood itself, as the result of an action of pental.

Fental, whether administered by inhalation or intravenously, usually causes a marked increase in the rate of the respiratory movements, as well as in their depth, although the latter phenomenon was not always well marked in my experiments. The increased respiratory rate occurs similarly after previous section of the vagi, showing that the action of the agent is directly on the respiratory centers in the medulla oblongata. But pental, so far as my observations go, cannot be considered as a respiratory stimulant in the true sense of the term.

Large quantities of the drug produce, ultimately, a depression of the respiration, and sometimes pental causes death through failure of this function. The disturbances of respiration before the occurrence of a fatal issue are sometimes manifested in the production of the Cheyne-Stokes type of movements,—this phenomenon, when it does occur, being almost surely the precursor of death. Though not entirely in accord with my own observations, RIETH-TIEBINGER (*), in a recent study, states that the respiration is more affected by pental than the cardiac action ; but the author adds that the respiration is stopped at first, it then becomes stormy and rapid, becomes gradually quiet and slow, and more superficial.

—I may state, in passing, that among

* *Beit. zur. Klin. Chir.*, Band X, Heft I., 1893.

other noticeable effects produced by pental, there was observed a marked dilatation of the pupil, and sometimes a tendency to tetanic spasms.

Clinical Uses of Pental.

The clinical uses of pental are few and far between ; in fact, the drug has been employed so far as a general anæsthetic only, as a substitute for the other well-known agents possessing such powers. The literature of the subject is meagre, and yet the evidence brought forward by several clinicians is somewhat contradictory.

Let me again refer to the experience of Weber (*). This investigator used the drug as an anæsthetic in the Halle Clinic in over two hundred (200) cases. In a few of the chlorotic or hysterical patients there was a moderate stage of excitation. The excitement was great, however, in the case of a chronic alcoholic drinker. In a few instances there were noticed slight tetanic spasms in arms and legs. No untoward after-effects, such as headache, vomiting, or even malaise, were noted, nor were there observed any changes in the pulse or respiration. The corneal reflexes disappeared late, and in some cases the pupils were widely dilated. There was no salivation, and laughing occasionally occurred. In some cases the

* *Loc. citat.*

anæsthesia continued for a short period of time after the patient had regained consciousness, and enough to allow the author to remove another stump of a tooth without causing pain. Usually five to ten grammes were sufficient to produce anæsthesia in from two to three minutes. The pental was used in minor operations, such as the extracting of teeth, opening of buboes, abscesses, whitlows, etc. In the case of fixed joints, however, the narcosis was not deep enough to relax the muscles involved.

According to BREUER and LINDNER (*), the chief action of the drug is that of an anæsthetic, and it may be administered in the ordinary way from a mask, or even from a pocket-handkerchief. The after-effects are said to be slight in most instances, though in some cases dizziness and trembling of the extremities may occur. In two of the cases observed by the authors, the patients cried after the operation, but could not give any reason for so doing. Narcosis was generally established in from 1 to 1½ minutes, and in children sooner than in adults. In the cases reported by the authors, the shortest time for the production of anæsthesia was 40 seconds, and the longest 31 minutes. Alarming symptoms were noticed in one case. In two, erythema was produced. The pulse was not affected in an unfavorable manner. For slight narcosis, 75 to 150

* *Wiener Klin. Wochenschrift*, June 22, 1892.

grains (4.38 to 8.75 gme.) of the anæsthetic were used; for the deepest narcosis about 1 ounce (27.9 gme.).

Although no unpleasant effects were produced, the writers believe that, as with chloroform, great caution should be taken in administering it. They conclude, from their clinical observations, that pental, while it will not bring-about such deep narcosis as does chloroform, will produce it sufficiently to permit of major, as well as minor, operations being performed; and further, that the narcosis occurs rapidly, disappears quickly, and is not followed by ill after-effects. And yet KRAMER (*) affirms that—out of the 101 cases of pental anæsthesia, occurring in the experience of Breuer—in one, artificial means had to be resorted-to in order to bring the patient back to consciousness!

HOLLÄNDER (†) believes that for short operations, especially for the extraction of teeth, pental is much superior to bromoform, ether, or chloroform, and that it is exceedingly safe. The author emphasizes the entire lack of all disagreeable feelings on awakening from pental anæsthesia.

According to PASCHKIS (‡), pental can be administered in the same way as ether. The first effect is that of excitation, then contraction of the various muscles, and even

* *Centralblatt f. Chirurg.*, No. 27, 1892.

† *Therapeutische Monatshefte*, an., 1892.

‡ *Centralblatt f. d. g. Therap.*, Feb., 1892.

opisthotonos may be produced in some cases. The corneal reflexes disappear late, but a stage of analgesia occurs early, which can be made-use-of for minor operations. Narcosis comes in from 1 to 1½ minutes, and lasts only so long as the administration of the drug is continued. The recovery of the patient is pleasant and prompt; and yet the author further remarks that a staring countenance, difficulty of speech, and a stumbling gait, lasting for a few minutes, are observed. Sometimes a slight redness of the face is seen during the narcosis. The same writer refers to two cases of death produced by pental.

C. G. VELEZ (*) employed this anæsthetic in 108 cases of minor operations, especially of a dental nature, with apparent good results. In cases where it was necessary to keep the patient under the influence of pental for a considerable time, consciousness was allowed to return and then the drug was again administered. After this procedure, ½ minute only was required to induce a complete narcosis. It is stated that in one case pental was thus given three times in 30 minutes; and two hours afterward the patient, a man, 28 years of age, was able to walk home by himself. The only disagreeable after-effect noticed was a feeling of intense drowsiness during the remainder of

* *Revista de Medicina y Cirugia Prácticas*, Feb. 7, 1893; *Brit. Medical Journ.*, March 18, 1893.

the day. The author affirms that 15 centigrammes (about 2.3 grs.) given on a mask filled with coarse wool will produce narcosis in one minute ; and that instead of losing its effect, the drug seems to act better on the same individual at each successive application. In some cases, insensibility is absolute, but generally, however, consciousness is not entirely lost. The pulse is at first accelerated, but soon recovers its normal condition. Velez adds that patients will take pental repeatedly without the slightest repugnance. Being inflammable, the drug should not be used at night.

According to Rieth-Tiebinger (*), patients awaken quickly from pental narcosis ; it lasts, at most, five minutes, even when deep. The patients, shortly after awakening, are in a state of intoxication ; they are confused, although unaware of what has happened during the narcosis. Their speech is stammering, their gait staggering. Some patients are excited ; a few complain of headache, others of weakness in the legs,—but all this for a short time only. The odor of pental is unpleasant both for the patient and the anæsthetizers. The author advises caution in pental narcosis,—its dangerous effect consisting in the cessation of respiration shortly after the appearance of anæsthesia, followed by a secondary cessation

* *Loc. citat.*

of cardiac activity. He concludes from his experiments that pental is, for short operations requiring no complete muscular relaxation, an available, but by no means harmless, narcotic.

This experimental and clinical evidence, incomplete as it may be, shows that pental is not entirely free from danger, and that the careless use of the drug may bring about fatal results. Further investigations are wanting in order either to place pental on the list of good and comparatively safe anæsthetics, or to discard it entirely as a worthless and dangerous agent. I, myself, shall not, for the present, at least, recommend pental as a safe or an efficient general anæsthetic, and until further and sufficient clinical evidence of its usefulness is brought forward, I shall continue to regard it more as a chemical curiosity than as a valuable therapeutic agent.

The conclusions which I have been able to draw from the preceding study, may be summarized as follows:

1) Pental possesses general anæsthetic properties.

2) The local anæsthetic effects produced by the drug are feeble.

3) Pental anæsthesia is rapidly established, but it also quickly disappears. It is chiefly of centric origin.

4) Pental depresses the circulation to a dangerous degree, causing a fall of the arte-

rial pressure and of the rate of the pulse, the latter phenomenon being followed by an increase even above the normal standard.

5) The lowering of the pressure is due to an action upon the heart and to a stimulation of the peripheral cardio-inhibitory centers. The vaso-motor system is apparently not affected by the drug.

6) Under pental the pulse-rate is decreased at first, due, similarly to a direct cardiac influence and to excitation of the cardio-inhibitory centers peripherally; the secondary increase to paralysis of the latter; and the final diminution to an action upon the heart.

7) The respiratory rate is increased through a direct action of the agent upon the respiratory centers. The respiration is afterwards depressed by an influence exercised upon the same. The drug sometimes causes the Cheyne-Stokes type of respiratory movements.

8) Pental produces death mainly by cardiac paralysis. Sometimes, however, the heart and the respiration stop simultaneously; at others, a fatal issue is the result of respiratory failure.

9) The drug, in poisonous amounts, diminishes to a certain extent the irritability of the cardiac muscle.

10) Pental dilates the pupil,—this phenomenon being probably of centric origin.

11) The narcosis of pental is not unattended by unpleasant after-effects, the na-

ture of these being principally that of excitement.

12) Pental cannot be considered as a safe or even as an efficient general anæsthetic, and is certainly inferior to ether and chloroform.

GALVESTON, Texas; 1320 Avenue E.

Issued Monthly. $2.00 per year.

American Medico-Surgical Bulletin

A JOURNAL OF PRACTICE AND SCIENCE.

THE BULLETIN PUBLISHING COMPANY, 73 William St., New York.

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