HEDONAL AS AN ANÆSTHETIC.

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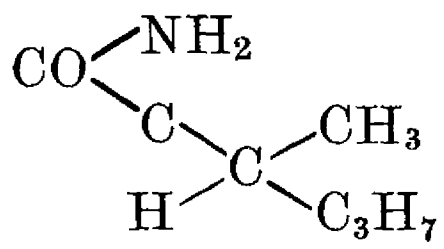
When experimentation is being vigorously pursued in any branch of practical science it may be assumed that the investigators are not content with what is known and practised. In recent years several new drugs and new methods of application have been used for the production of analgesia and anæsthesia, and, although they have met with varying success, no one will deny that their introduction is due to a healthy and honest dissatisfaction with the routine use of chloroform and ether by inhalation.

In 1910 Federoff, of St. Petersburg, first employed hedonal as an intravenous anæsthetic. Its success on the Continent led to its adoption in England last Easter, since when it has been used extensively in London and Leeds.

Encouraged by the report of Mr. Page last May in the *Lancet*, and by what I saw in Leeds this summer, I have used this anæsthetic in thirty cases during the last four weeks, and obtained full surgical anæsthesia in all.

Before, however, going into details regarding them, the characteristics of hedonal may be considered. Hedonal, or methyl-propyl-carbinol urethane is an organic compound, the molecule of which contains a urethane nucleus

joined to a methane group, as the structural formula shows :—



It follows that in the hedonal molecule there is only one atom of nitrogen, or 14 grammes of nitrogen in 119 grammes of hedonal. As, however, the maximum dose of hedonal is 15 grammes intravenously, the extra work thrown on the excretory organs is the elimination of 1.76 grammes of N_2. If this is excreted as urea, as is stated, a full dose of hedonal is equivalent to only 3.75 grammes of urea. The carbon and hydrogen are oxidised to CO_2 and H_2O. This explains the tolerance shown by nephritic cases towards the drug. Four estimations of the urea excreted were made in my series, but the results, owing to the small amount involved, were entirely conclusive. As a one per cent. solution of hedonal is saturated at 100° F. it is used at a strength of 0.75 per cent. in normal saline. The solution of the drug is effected by using saline at about 140° F. and the preparation finished by filtering and boiling the fluid. Although, owing to its volatility, a little hedonal is lost in boiling, none is decomposed. When cool the hedonal crystallises out in fine needles.

The *technique* of administration is simply that of continuous venous infusion, bearing in mind that the flow must be carefully regulated. The apparatus I have used is that made by Thackray, of Leeds, and consists of a container, with thermometer and level gauge, a dropper, to indicate the rate of flow, and a fine cannula. The container is filled with solution at 119° F., and the cannula is introduced under local anæsthesia into a suitable vein,

usually the cephalic. If the operation is on the upper part of the body the internal saphenous vein in front of the internal malleolus is most convenient. In ten of my cases it was chosen. In one instance no adequate vein was found. This patient was an emaciated girl, fourteen years of age, and as the operation was amputation of the leg it was considered advisable after failing to get a vein in the arm to resort to ether.

During induction the fluid is run in at a rate of 50 to 150 cc. a minute. While less is needed, the more rapid the flow, I have found it advisable in the case of feeble patients to slow the infusion to 40 or even 20 cc. a minute, to avoid marked depression of the respiratory centre. In two or three minutes the patient becomes drowsy and yawns with subjective sensations of warmth and well-being. This drowsiness emerges rapidly into deep sleep, the conjunctival reflex goes, and a little later the corneal reflex is lost. A minute later the operation may be started. Usually the induction is unaccompanied by any struggling whatever, only one of my patients proving troublesome. This patient was sent up from the country for emergency operation of amputation of a crushed hand. He arrived at hospital prepared for operation as in the pre-anæsthetic days.

As has been mentioned, the danger during induction is marked respiratory depression, which causes cyanosis. This is immediately checked by slowing the infusion. Normally, the breathing becomes quiet, so that special pains should be taken to keep the tongue forward.

In two of these cases slight cyanosis, due to an overdose of anæsthetic, developed, but was immediately relieved by diminishing the drug. A little oxygen was also given as it was ready, but I do not think it was necessary. Both of

these patients were carcinomatous, one being a woman of fifty and the other a man of seventy-eight.

The time of induction has varied from six to fifteen minutes, and the amount of solution from 250 cc. to 1,250 cc. The latter dose was necessary in a strongly-built man of thirty, though given at a rate of 130 cc. per minute, while the former was sufficient for a man of seventy-eight, though given at a rate of only 20 cc. per minute. Once the skin incision is made the flow is cut down so as to keep up anæsthesia with as little fluid as possible. The patient is well asleep when the corneal reflex is gone; the pupil is one to two mm. in size and reacts to light. On relaxing the anæsthesia the pupil enlarges and the corneal reflex returns. The oxygenation of the face and ears should always be good.

On beginning the infusion the pulse-rate increases to about 120 per minute, and then falls in a few minutes to about 80. The subsequent regularity of the pulse is remarkable, and is due, I think, to the constant infusion. For example, at the commencement of an amputation of the breast for cancer in a woman of forty-five the pulse was 80, while on leaving the table sixty-five minutes later it was 72. In only four cases was the pulse-rate more than 100 after operation, and in all these the hæmorrhage had been exceptionally severe.

A few minutes before the end of the operation the anæsthetic is stopped, and, as a rule, the corneal reflex has returned before removal of the patient from the theatre. The period of sleep afterwards varied from half an hour to, in one case, eighteen hours. In about twenty-four cases the patient spoke within two hours, and soon fell asleep again to wake occasionally throughout the night. That is to say, in no case suitable for the anæsthetic was

there anything like prolonged unconsciousness. Drowsiness, however, persists for twenty-four hours.

For five patients of the series morphia was required; of these, three had undergone bone operations. Only three patients vomited after operation, one of whom had stones removed from the common bile-duct, while the other two were suffering from intestinal obstruction. Finally, one patient had slight headache for twenty-four hours, but did not volunteer the information herself.

Retention of urine occurred after hernia operations, as with ether anæsthesia, but was never prolonged. In no case was there suppression of urine, glycosuria, or albuminuria.

On leaving a catheter in the bladder during operation it was found that in the third stage of anæsthesia no urine was secreted—a phenomenon which also occurs during the administration of ether and chloroform.

The blood-pressure records of this series are, unfortunately, very incomplete, but, so far as they go, bear out Mr. Page's results. A fall in pressure of about 20 mm. of mercury occurs at first, after which the pressure remains constant.

The total amount of the drug given must vary greatly according to the age and condition of the patient and the nature of the operation. An arbitrary maximum is 2,000 cc., or about 66 oz., but it is only under exceptional circumstances that so much should be given. My fourth case received 2,020 cc., but, as the operation was the removal of a large epithelioma of the scalp and grafting of the exposed area, this great amount of fluid had no deleterious effect whatever. In fact, it no more than compensated for the hæmorrhage. On the other hand, the introduction of a large quantity of fluid into the circulation of a patient who does not need it, is a dangerous procedure, and is

responsible for most of the complications which have recently been classified by Dr. Veale, of Leeds, under the headings—cutaneous, pulmonary, and venous, complications. Under the first head are mentioned—patches of œdema in the gluteal region, blisters on the heels, and bedsores. None of these have occurred in my series, but they should be guarded against by giving instructions to the nurse in charge to change the position of the patient while asleep. With regard to pulmonary trouble, it must be stated that this anæsthetic is distinctly contra-indicated in the case of young robust people, who are undergoing operations of moderate severity unaccompanied by serious loss of blood. Such patients invariably require up to, and over, 1,200 cc. for an operation lasting half an hour, and are, therefore, peculiarly liable to develop œdema of the lungs. On the 10th of this month I anæsthetised J. F., a boy of seventeen, for the cure of an inguinal hernia. The anæsthetic was taken well, but had to be infused rapidly. In all, 1,250 cc. were used. On return to bed at 12 noon his corneal reflex was very sluggish, and he was still unconscious. An hour later he was not completely anæsthetic. Towards five o'clock his breathing quickened, his temperature rose, and he became slightly cyanotic. I saw him at six, when the respirations were 40, the pulse 144, and the temperature 101.4° F. His face was flushed and wet with perspiration. The corneal reflex was gone, but he still moved slightly when stimulated. A catheter was passed and 20 oz. of urine withdrawn. He was propped up in bed, the tongue was drawn forward and some frothy mucous removed from the mouth. One bag of oxygen was administered, and in fifteen minutes his breathing had slowed to 30, and his pulse to 108, while the corneal reflex had returned, and he

moved briskly when stimulated. During the night he remained in the same condition, and mucus was sucked out of the larynx at 1 a.m. Towards morning he steadily improved, and awoke at 6 a.m., eighteen hours after the operation. He made an uneventful recovery. In such cases the indication is to open a vein and withdraw about 10 oz. of blood, if the symptoms do not improve on clearing the air passages.

Bronchitis is the second lung complication that may occur. In this series two patients developed a cough that lasted about twenty-four hours. As one of them had only 550 cc. infused, it was probably in this case due to a chill rather than the anæsthetic. In a third case—a woman of thirty-five, suffering from gall-stones—a small patch of broncho-pneumonia developed in the right apex. She recovered from this, however, in a few days. As she was in feeble health, and only required 750 cc. of solution, I do not think it is likely that the anæsthetic was at fault. Nevertheless, pneumonia is a definite, though very infrequent complication, and has been responsible for three reported deaths.

Of the occurrence of infarct from a dislodged thrombus I have no experience. It could hardly happen unless the vein were infected, and only one case is reported in which it probably occurred. Thrombosis of the femoral vein has not been found in any of my cases, and in the five cases reported by Dr. Veale it has not been proved that the method of anæsthesia used was responsible. We have had no case of cerebral thrombosis, and one alone has been reported.

In concluding a discussion of the possible complications of this anæsthetic it is desirable to mention the more severe operations performed with its assistance.

The series includes excision of the lower jaw for cancer, excision of epithelioma of the scalp, excision of carcinomatous glands in the neck, amputation of the breast for cancer, gastro-enterostomy for advanced pyloric cancer, two colostomies for rectal cancer, laparotomy for obstruction, two appendicectomies, cholecystotomy, choledochotomy, two amputations, cerebellar decompression and cranioplasty. The ages of the patients vary from seventeen to seventy-eight years, and the duration of anæsthesia from ten minutes to one hour fifty-three minutes.

Already some of the disadvantages of this method have been mentioned. First is the occasional difficulty in finding a suitable vein. In the case of one patient the cannula was introduced into a vein so small that the infusion was delayed, and consequently anæsthesia was not obtained until twenty minutes had elapsed. Secondly, the absolute necessity for asepsis renders the method unsuitable outside the hospital theatre; while, thirdly, it is unnecessarily complicated for short operations. On the other hand, in operations on the head and neck the surgeon is not hampered by the anæsthetist in the least degree; oozing from the skull and dura mater is remarkably slight, and in abdominal operations muscular rigidity is entirely absent. Neither of these points has, I think, been sufficiently emphasised. With any other anæsthetic the greatest danger in brain work is hæmorrhage; in abdominal work the operation is often delayed, and correct *technique* rendered impossible through rigidity of the muscles. With hedonal both of these undesirable factors are practically eliminated. Moreover, in cases of hæmorrhage and collapse the constant infusion of saline is useful, while if more saline be needed the tube can be removed from the container and a further infusion of ordinary

saline given. This was done in two of these cases with distinct benefit.

From the occurrence of œdema in a youthful patient, which I have described, and from exactly similar accounts mentioned in the journals, it may be fairly argued that the anæsthetic is contra-indicated in the young and vigorous, who are to undergo slight operations. On account of the possibility of such a complication, I would endeavour in all such patients, if the anæsthetic were desirable for other reasons, to lessen the amount of infusion necessary by administering, two hours before operation, two to four grammes of hedonal by the mouth, as recommended by Mr. Page.

With regard to the contra-indications, it is impossible to speak authoritatively, except to mention that as the laryngeal reflex is abolished very early and completely, a tracheotomy must be performed, and the pharynx plugged before an operation on the mouth, nose, or neighbouring air sinuses is attempted. This precaution was observed in the removal of the lower jaw and part of the tongue, mentioned already, and the results were excellent. Slight cyanosis occurred on introduction of the tube, but was due to blood clot in the tube and was immediately relieved on removal of the clot.

In cases of uncompensated heart disease the infused liquid might throw a dangerous strain on the right ventricle, but I have no definite information on this question. On the other hand, nephritic patients prove good subjects, and so far no cases of suppression are recorded. This is due to the distinct diuretic effect of the saline infused. In six severe cases the average amount of urine passed in the twenty-four hours after operation was 900 cc. Also, as has been shown, the amount of nitrogen to be excreted is

extremely small, so that the absence of kidney complication which obtains is only what might be expected. In this series no death occurred which can be attributed to the anæsthetic. Three patients died while in hospital, the first of whom was suffering from left-sided hemiplegia. She was almost comatose before operation, being only able to move the right arm and leg feebly when stimulated. In the whole course of the operation, which lasted one hour and three-quarters, only 300 cc. were injected, and on leaving the table the patient was no more comatose than before. Death occurred eighteen hours later, and it was found on examination that she was suffering from vegetations on the aortic valves, long-standing infarcts in the kidneys, spleen and liver, and finally a relatively large aneurysm in the right internal capsule, which caused the hemiplegia.

The second death occurred in a boy of eighteen years, who came to hospital with a history of three weeks of severe vomiting and partial obstruction. He was operated on at once, and laparotomy confirmed the diagnosis of pelvic sarcoma. His recovery from the anæsthetic took place within an hour, but he died the following evening. The *post-mortem* examination showed a huge sarcoma infiltrating the pelvic wall and pressing severely on the rectum.

The third patient was a man of seventy-one, who came to hospital suffering from prostatic retention. He had been tapped six times suprapubically during the previous week, and was in a very feeble condition. The urine was very foul. A suprapubic cystotomy was done to drain the bladder and the prostate was removed. The operation lasted six minutes, and the amount of hedonal used was 500 cc., but he died two days later. *Post-mortem* the only

cause of death found was pelvic peritonitis, a condition, it may be assumed, due to infection when the bladder was being tapped.

In conclusion, my thanks are due to those surgeons who allowed me to anæsthetise their patients, and, more especially, to Sir Thomas Myles, whose cases constitute the majority of this series.

THE PRESIDENT thanked Mr. Crawford for his paper, which very fairly set forth the advantages and disadvantages to be derived from the use of hedonal as an anæsthetic. All who were concerned with abdominal operations well knew the advantage of having the abdominal muscles in a relaxed state.

MR. W. I. DE C. WHEELER considered the paper of the greatest interest, as he thought the question of anæsthesia was not in a satisfactory state at present. As to hedonal, he considered that its administration could not be praised or condemned until we had more experience of it. In his opinion there was sometimes a difficulty in giving the anæsthetic, as patients very often object more to the giving of an intravenous injection than to the operation. How chloroform had been given so long in cases where it is contra-indicated he found hard to understand. He mentioned that he had been using omnopon in simple operations, and so far had found it satisfactory. When given before the administration of ether, patients when anæsthetised would remain so for hours. There was a complete absence in every case of anything in the nature of cyanosis. The procedure is very simple, and the contra-indications are practically nil.

DR. KIRKPATRICK had not seen the method tried, but it seemed to him, from the theoretical point of view, that it was attended with great advantages and some considerable disadvantages. It was, he said, admitted that the present method of anæsthetising patients are not altogether satisfactory. Whether it was the fault of the methods or the

patients, it was exceedingly hard to get satisfactory relaxation of the muscles, especially in pelvic operations, and the surgeon may be very considerably hampered in his work on this account; consequently, any method that would improve this state of things would be of very great value. He had seen so many methods of using different drugs as anæsthetics introduced that it made him doubtful, as over and over again, notwithstanding new methods put forward as panaceas, return had to be made to ether. He, therefore, thought that no one had yet sufficient experience to be able to pronounce definitely on hedonal. Regarding the point that the anæsthetist could administer hedonal in a way that he could be out of the way of the operator, it should not be lost sight of that, no matter how the anæsthetic is given, the anæsthetist must have access to the patient's head.

Dr. Smith said that so far all forms of anæsthetics administered by inhalation, excluding morphine, belonged to the marsh gas series. Local anæsthetics belonged to the aromatic group. He was not in a position to speak of hedonal in practice, but was inclined to think that the older methods were more satisfactory.

Mr. Crawford, in replying to the remarks, said his experience was that patients would sooner have the small operation necessary to administer hedonal than to have the mask placed over their face. He considered that it was much more under control than omnopon. He agreed with Dr. Kirkpatrick that the outlook for a new method is not hopeful, but this method has now been taken up in England after having been used for some time on the Continent, which speaks well for it. With regard to the danger of cyanosis if the anæsthetist is at the patient's feet instead of at the head, he found it necessary to stay at the patient's head, and to signal when the tap was to be turned off. He considered the anæsthetic as safe as any other in practice.