10. The actual condition of the child at birth.
11. The health of the child some time after birth, say at three months.

In the foregoing I have set out the best methods of ante-natal supervision as they appear to me in the present state of knowledge. As these are not in general use, and as no standard method has been laid down or applied, it is practically impossible to assess the value of ante-natal care from the gross results which are available. If, however, the different authorities and practising physicians could be persuaded to keep records such as I have indicated, we should shortly have the necessary information to enable us to arrive at such a valuation, and to decide how best we can achieve satisfactory ante-natal supervision.

The history of medicine shows that obstetrics in the limited sense has always been regarded as a special art. The present discussion raises a wider problem than the art of obstetrics, because the nation to-day is interested in the rearing of a healthy race. The care of the mother and the child is therefore all-important. Indeed, it seems to me that this should be a division of medicine for special study and practice. A new kind of specialist is required: one whose functions would be first, ante-natal care in its wide sense, having regard to both the mother and the unborn child; secondly, the confinement of the mother; and, thirdly, the care of the mother and child for a period after the birth. A wider specialism on these lines would, I believe, secure better results in the rearing of healthy children than specialisms limited, as at present, to the much narrower fields of obstetrics and gynaecology on the one hand and paediatrics on the other.

PHARMACOLOGY AND THERAPEUTICS OF SODIUM EVIPAN

WITH SPECIAL REFERENCE TO ABNORMALITIES
UNDER EVIPAN ANAESTHESIA

BY

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Sodium evipan has now definitely established itself as an anaesthetic both in medical and in dental practice, and the purpose of this article is to give a short account of its pharmacology, and the pathology of such cases as have come under the authors' notice.

Sodium evipan is the soluble salt of a new barbituric acid derivative: *n*-methyl-C-C-cyclo-hexanyl-methyl barbituric acid. It is not a volatile anaesthetic, but is rapidly detoxicated by the liver. Detoxication depends upon its decomposition within the liver, and it is stated that a rabbit can disintegrate half the narcotic dose within thirteen minutes.¹ Kennedy has also shown that detoxication of sodium evipan in mammals is very rapid.² Another characteristic of this drug is its high therapeutic quotient. In a cat this is represented by the figure 4, since 25 mg. generally gives full anaesthesia, while 100-110 mg. is the lethal dose.³ In the dog the quotient is 3.3. It may fairly be inferred, therefore, that only 20 to 30 per cent. of the lethal dose is used to produce clinical anaesthesia, and this factor must be noted when criticism of the unreversibility of evipan is made. Traces of the unchanged substance are found in the urine, but it is mostly eliminated in the form of urea.

During narcosis the blood pressure may fall by not more than 20 mm. Hg, and respirations are depressed both in rate and in amplitude.⁴ Overdose causes the cessation of respiration, the heart continuing to beat until secondary heart failure occurs, due to anoxaemia. Kennedy and Narayana have shown that the depressant action of sodium evipan on the frog's heart is very rapidly removed by washing, and is antagonized by adrenaline. They obtained complete recovery in a few seconds. The ventricle, apparently, is affected before the auricle; when the beats had completely ceased excitability still remained.⁵ Even while suffering from overdose, some animals have been kept alive by artificial respiration until enough of the drug had been excreted to allow the respiratory centre to resume normal function.

Technique of Administration

The technique of administration is well known, and consists of the intravenous injection of a 10 per cent. solution in sterile distilled water. This solution is made up immediately prior to injection, and is run in at rates which vary with different operators. An average figure would be about 1 c.cm. in ten seconds, although we, personally, deliver the first 2 c.cm. with greater rapidity. A common indication of the dose is to instruct the patient to count aloud, to note the volume given before unconsciousness supervenes, and to give the same volume again, or more, according to the duration of anaesthesia required. The symptoms produced by the injection are dramatic. While the first 2 c.cm. are entering the circulation the patient counts aloud with great confidence, but during the administration of the third c.cm. he usually begins to hesitate; a surprised look comes over his face, rapidly followed by a vacant stare, the counting becomes disordered and whispered, and finally with a deep sigh or yawn he drifts into anaesthesia. Unconsciousness usually occurs about the time of "hesitation," and is immediately preceded first by a feeling of intoxication and then by intense drowsiness. Respiratory and circulatory changes have been mentioned above, and the problem of "twitchings" will be dealt with later.

Duration of Anaesthesia

It is sometimes difficult to estimate the time during which anaesthesia occurs, since with identical doses different patients have remained anaesthetic for as little as five minutes and as long as an hour, but in most cases fifteen to twenty minutes can be promised with certainty. For recovery, four hours or longer is the general rule, varying according to the dose and the constitution of the patient. In neurotic people the recovery period is frequently accompanied by emotional crises, but people of stable temperament usually recover quite quietly. The patient generally remembers nothing either of anaesthetic or recovery period, except the fact that he has slept well.

Abel and Jarman rightly point out that with "minimal doses" (that is, injecting 2 c.cm., waiting thirty seconds, and giving the third c.cm. cautiously until unconsciousness occurs, and then discontinuing) the anaesthesia lasts from five to fifteen minutes; the patient then wakes, is quite rational, and after half an hour's rest, or sleep, is often able to walk home.⁶ It must be stressed that until recovery is complete the usual tests for sobriety are not satisfied, and the patient should be allowed to rest in quiet until feeling fit. We only know of one case of nausea or vomiting after recovery; this was in a man who was sent home on a tram, having previously had a large draught of black coffee. In a few cases headaches have been recorded (always after large doses), and these are usually likened to the aftermath of alcoholic excess.

In order to lengthen, deepen, and stabilize evipan anaesthesia some workers, Abel and Jarman,⁷ have recommended injection of an ampoule of omnopon 2/3 grain and scopolamine 1/150 grain one hour before operation. On the other hand, the Anaesthetic Committee of the Medical Research Council⁸ decided that it was inadvisable to give any sedative. In our practice we have found that the combination of sedative premedication and evipan has never given the slightest anxiety in adults of moderate health.

Difficulties under Anaesthesia

The first difficulty that occurs is at the onset of anaesthesia, when the muscles attached to the jaw become relaxed and the patency of the airway is imperilled. To prevent this, an assistant should be at hand to turn the head to one side and lift the jaw if necessary. If neither of these manoeuvres is successful it is better to insert a Hewitt's airway.

Muscular twitchings are another nuisance, both to anaesthetist and to the surgeon, for they may either jerk the needle out of the vein or hinder the operative procedure. These movements are independent of stimuli, although they are accentuated and become vaguely purposive during skin incisions. Sedative premedication diminishes this trouble, however, and a further injection of a few centimetres of evipan completely abolishes the movements.⁹

We have had one case where 10 c.cm. of evipan produced amnesia but no signs of anaesthesia. The patient, however, was also in attendance at a mental hospital near by. This man took the usual four hours to recover, in a delirious manner. We have also first-hand knowledge of another case (also that of a mental patient), who showed merely drunkenness after 20 c.cm. was injected into a large vein. One of us (G. S.) has had two cases, both in men, in which the full dose of 10 c.cm. of the 1 per cent. solution was given without any kind of anaesthesia being produced nor any apparent change, either physically or mentally. Witnesses of all these inductions were fully satisfied that the injection was intravenous.

In our experience one difficulty has been that of respiratory spasm, which sometimes involves the glottis and occurs early in anaesthesia. The patient goes a blue colour, has sighing respirations, and the condition may become an alarming one; it clears up readily, however, with the passage of an intratracheal catheter. We have also had patients who stopped breathing for a time, but who, fortunately, started with artificial respiration or intubation. One or other of us has had experience with the following cases.

CASE I

A woman, aged 65, attempted suicide by cutting her throat. The larynx was exposed and opened, and evipan 3 c.cm. was injected for the purpose of induction. Unconsciousness was immediately followed by inhibition of respiration; the pulse was normal in rate and volume. Breathing recommenced on the introduction of an intratracheal catheter, and an inhalation anaesthetic was continued through it. The patient recovered consciousness about an hour after the operation ceased. The repair was successful, but the patient died five days later. Post-mortem examination revealed that bronchopneumonia was the cause of death.

CASE II

A man, aged 62, was admitted after two days' unsuccessful treatment for severe epistaxis. He had a large aortic aneurysm, and was chronically bronchitic; his weight was about 15 st. Nine c.cm. of evipan was administered for the thorough packing off of the nose. Respiration ceased; the pulse was good but the colour bad. On the introduction of an intratracheal tube respiration recommenced, and about half a pint of gastric contents containing altered blood was regurgitated. The packing was completed and the patient recovered consciousness. Two days later 10 c.cm. evipan was administered

for repacking without any untoward effect. Three days after the second operation the man died, and post-mortem examination revealed the existence of diffuse meningitis.

CASE III

In this case, that of a man aged 70, an operation for the insertion of radon into an extensive lingual carcinoma was performed. The patient was toxic, and was suffering from chronic bronchitis. Omnopon 1/3 grain and scopolamine 1/150 grain were injected an hour before operation, when 8.5 c.cm. of evipan was given intravenously. Breathing became progressively more shallow, and ceased about ten seconds after the completion of the injection. The face was cyanosed and the pulse became imperceptible. The insertion of an intratracheal catheter was followed by a sigh, and artificial respiration, which had been commenced before intubation, was discontinued. Breathing was irregular at first, but became rhythmic by the time carbon dioxide and oxygen were insufflated through the tube. Owing to the return of the cough reflex the tube was soon withdrawn, without any ill effect.

At the end of the operation the corneal reflex was brisk, and an hour later the pharyngeal reflex was also active. Six hours later the pulse became poor in volume, and the patient's colour unsatisfactory. Intravenous coramine 2 c.cm. produced a temporary improvement, which was maintained for a short while with carbogen inhalation. The pulse and respiration rates steadily rose, however, to 40 and 140 respectively (even after temporary discontinuation of carbogen) and the temperature to 101°. Breathing was bubbly, and some oedema at the lung bases was detected. Atropine 1/100 grain and digitaline 1/100 grain were injected intravenously, but the condition steadily declined. The patient died sixteen hours after operation, never having recovered consciousness. At post-mortem examination the chief pathological changes were: (a) carcinoma of the tongue; (b) fatty myocarditis; and (c) oedema and congestion of the left lung. Microscopical section showed (a) congestion of the spleen, (b) cloudy swelling of kidney and of heart muscle, and (c) a few necrotic areas in the lung.

CASE IV

A man, aged 56, of plethoric type, who had sustained several injuries through riding, was admitted complaining of sciatica. An epidural injection of novocain and manipulation was contemplated. The injection of evipan to secure anaesthesia was started in the usual way, and after 5 c.cm. the patient went an intense plum-blue colour, and after two or three sighing respirations ceased breathing. The injection was stopped immediately, the tongue was pulled forward, and some frothy mucus, which had collected in the mouth, was removed. Artificial respiration was begun, and in about half a minute the spasm of the glottis passed off and a normal evipan anaesthesia supervened. The patient was unconscious during the time of the cyanosis, and remained so for a period of about ten minutes.

CASE V

A woman of slight build, aged about 40, also suffering from sciatica, as in Case IV, was admitted to hospital for similar treatment. She also ceased breathing after about 5 c.cm. had been administered, and went a deep blue colour. An intratracheal catheter was not available, as the operation was being performed in the ward. The airway was cleared and artificial respiration started, and after a period of three or four minutes the spasm passed and she again breathed normally. Pituitrin and adrenaline were administered immediately without any obvious result. During the spasm the pulse was perceptible but very feeble. It is clear that the condition was one of glottic spasm and failure of the respiratory centre without involvement of the cardiac centre.

The following complication is recorded by Drs. Landau and Wooley¹⁰ in a patient of 23, who was admitted for a minor operation. The patient complained of headache following the operation, which became severe on the third day, when the heart rate dropped to 40 and drowsiness supervened. No other abnormality was detected. The urine was normal. The patient was treated with atropine, adrenaline, and hypertonic intravenous glucose, which

caused the attack to become less severe. The pulse gradually rose to normal, and he made an uninterrupted recovery.

In two of the preceding cases direct laryngoscopy revealed that the vocal cords were in abduction, while in Case I a Magill's tube (passed transnasally) entered the larynx with the greatest facility, and could be seen *in situ* during operation. Artificial respiration demonstrated the patency of the airway in Cases I, II, and III, as the recommencement of respiration was immediately consequent upon laryngeal intubation and occurred before the catheter could be connected to the gas-oxygen machine. Cases IV and V, although not viewed by a laryngoscope, appeared to be conditions of glottic spasm which eventually yielded after prolonged artificial respiration. The fact that the cough reflex returned so rapidly once breathing recommenced seems to suggest that a temporary inhibition of the respiratory centre occurred rather than any undue depression. Furthermore, stimulation of the vocal cords seems to have overcome this inhibition, and so enabled normal respiration to reappear in a perfectly satisfactory manner. In Case III death was partly due to respiratory failure, but several other factors contributed to this besides the previous administration of evipan.

Fatalities under Anaesthesia

A number of cases are on record of death following evipan anaesthesia, and for details of some of these we are indebted to Dr. G. H. Morrison.

CASE I

A man, aged 67, with extensive disease of the kidneys, myocardial degeneration, and bronchitis, was given 7 c.cm. of evipan for the excision of a growth of the knee. He died under the anaesthetic, and the verdict at the inquest was that "Death was due to chronic heart and kidney disease, accelerated by evipan anaesthesia."

CASE II

This was a case of a young woman, aged 27, who was in hospital for appendicectomy. She was given 10 c.cm. of evipan, but died during the operation. The post-mortem examination showed a persistent thymus, and the verdict was "Death by misadventure."

CASE III

A man, aged 64, had chronic myocarditis, circulatory failure, oedema, and hydrothorax. Because of the toxæmia derived from his mouth, he was given 10 c.cm. of evipan for the extraction of eight teeth. The operation was decided upon in the faint hope that the extraction might keep the patient alive for a few more weeks. He died shortly after the teeth were taken out, and the verdict at the inquest was "Death by misadventure due to syncope while under anaesthetic, to wit, sodium evipan."

CASE IV

A woman, aged 50, received the anaesthetic prior to an operation on the jaw for removal of some septic teeth. Respiratory and heart failure, which followed the injection, was obviously due to a far advanced pathological condition of the heart. The verdict was "Death by misadventure."

CASE V

A woman, aged 60, had very severe rheumatoid arthritis. She was given 5 c.cm. of evipan before she fell asleep, whereupon a further 1 c.cm. was given in order to extract three very septic and painful teeth. She died at the conclusion of the operation, and a post-mortem examination showed extensive myocardial degeneration and a very advanced state of rheumatoid arthritis. The coroner's verdict was "Death by misadventure due to syncope while under evipan anaesthesia."

We are indebted to the Westminster Hospital for the report of the following case:

CASE VI

A woman, aged 42, with four years' history of bronchitis and asthma, was admitted to hospital three weeks before death with cardiac failure, which was secondary to her lung condition. Her physical signs on admission were dyspnoea, oedema of the ankles, liver enlargement, and dilated right heart. She improved considerably under treatment, and was due to be discharged on the day following her death. She had gross dental sepsis, and the physician in charge of her case decided that a clearance was necessary. Previous local injection of cocaine had prompted an alarming attack of asthma, so the anaesthetist decided to give her evipan, as there was now no palpable enlargement of the liver.

Three c.cm. of evipan was administered into one of the antecubital veins, the patient being in bed in the ward. She gave a typical yawn and then immediately showed signs of obstruction, with rapid and marked cyanosis. The injection was stopped, her airway cleared, and when her head was hung over the edge of the bed another breath was taken. By this time, however, she was pulseless, and in spite of carbon dioxide and oxygen, artificial respiration, intracardiac adrenaline and cardiac massage, she did not recover. Dr. John Taylor, at the post-mortem examination, found marked bronchitis, right-sided enlargement of the heart, and a nutmeg liver. A piece of tartar the size of a tooth had got lodged in the glottis, and in his opinion the inhalation of the tartar, presumably during the evipan yawn, had caused the spasm, and the effort at inspiration had proved too much for the already diseased heart. The condition here does not seem to have been caused primarily by evipan in view of the small dose and the direct incitation to glottic spasm by the presence of a foreign body.

Cutaneous Idiosyncrasies

Although some papers state that a cutaneous wheal in animals has caused no irritation, in one case in our experience, where evipan was administered to a fat patient (and some must have escaped from the vein during injection), the arm became swollen and a local abscess developed not unlike that which one experiences after leakages during the use of N.A.B. We have had experience of another case of the same sort where actual suppuration did not occur, but the arm was tender and swollen for four or five days. The pain was readily relieved by antiphlogistine poultices and aspirin. These have been the only two instances in a large series, and it is interesting to note that in a batch of asthmatics, who were anaesthetized for the purpose of dental extractions, we have had no difficulty of this kind.

Dr. G. A. Grant Peterkin¹¹ reported the case of an anaesthetist who came to him with an intermittent rash on his hands and fingers. It took the form of a papulo-vesicular eruption. From the history this was thought to be a contact dermatitis, and, after several cutaneous tests, was found to be due to contact with sodium evipan solution. The anaesthetist remembered cutting himself while making up the solution from the glass ampoules. So far as we know this is the only case of the sort that has occurred.

Miscellaneous Uses

We have used evipan therapeutically in cases of chorea, and one of us has reported an instance in the *Lancet*.¹² The patient is usually a child, and the doses are given daily up to 5 c.cm. We have had no untoward experience with this condition; 1/2 c.cm. produces drowsiness but not sleepiness in a child of 8, while 1 c.cm. usually effects temporary anaesthesia.

Evipan was also used by one of the authors (G. S.) under the following circumstances.

A patient, about 45, who suffered from a severe head wound contracted during the war, was constantly liable to attacks of Jacksonian epilepsy. He was well known to the ambulance men of the hospital, and these attacks frequently lasted for

over an hour, and were associated with great emotional disturbance, shouting, and other evidence of cerebral irritability. On one occasion, while we were doing out-patients, this man was brought into hospital in a typical state of epilepsy; four attendants were necessary to hold him down, and he was very violent and twitching all over. He was given 10 c.cm. of evipan intravenously and his condition quieted at once into normal evipan sleep; on recovery, about an hour later, he was far less excited and almost normal.

This is the only case so far in which opportunity has occurred of using this drug in this way, but it would seem to indicate further possibilities for exploration. Doses of 5 to 10 c.cm. have also been used with success in cases of renal and gall-stone colic.

Conclusions

Sodium evipan in the majority of cases can be considered a safe anaesthetic. It should not, however, be administered single-handed, in view of the possibility of respiratory spasm, or of obstruction of the airway, which may occur while the doctor's attention is engaged elsewhere. Evipan can be repeated on several occasions without ill results; it is not advisable to follow the injection with chloroform; gas and oxygen being the ideal or, where thought necessary, ether.

Premedication with omnopon and scopolamine is a useful adjunct to anaesthesia, and, owing to the high therapeutic quotient of the evipan, and its rapid detoxication, does not carry with it the usual dangers so popularly ascribed to the clandestine association of morphine with the other barbiturates. As Moncrieff¹³ points out, however, the double depression produced by the combination of morphine and drugs of this type may cause respiratory failure, and we strongly deprecate preliminary sedation in patients who are bad anaesthetic risks. It would appear that the most valuable treatment in cases where respiratory depression has supervened would be the inhalation of a mixture containing oxygen and 7 per cent. carbon dioxide,¹³ though in a case above described this proved of no avail. Artificial respiration of itself is unlikely to be useful because carbon dioxide is washed out of the lungs; in combination with the above-mentioned inhalation, however, this difficulty is remedied. Although we have as yet had no experience with alpha-lobeline, we have not been impressed with the efficacy of stimulants. In those cases where we used coramine, it produced at most a temporary improvement, although given by the intravenous route. It is significant to note that, in the fatalities reported, the patients have been extremely ill, and most of them have died of respiratory failure.

Four practical points that seem to be evolved are as follows:

1. To avoid using the drug in cases of severe liver embarrassment, because detoxication cannot occur efficiently.

2. Where there is any question of depression of the respiratory centre—for example, in operations for cerebral tumour, or severe lung conditions—evipan would seem to be contraindicated.

3. In cases where evipan is contraindicated, but after careful weighing of risks it is thought to be the safest method of anaesthesia, it should be given alone without reinforcement by other drugs; the dosage should be cautious, and a preliminary injection of atropine should be administered with a view to counteracting the tendency to oedema of the lung.

4. Facilities should be at hand to administer oxygen and carbon dioxide mixtures ("carbogen") containing a minimal proportion of 7 per cent. CO₂ either by mask or, where necessary, via an intratracheal catheter in cases which are considered to be bad anaesthetic risks.

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INJECTION TREATMENT OF COMPLETE RECTAL PROLAPSE

WITH REPORT OF TWO CASES

BY

ARTHUR S. MORLEY, F.R.C.S.

The treatment of ordinary haemorrhoids by submucous injection of carbolic acid in almond oil has become a well-recognized and ordinary procedure, and since I introduced this particular technique into England in 1928¹ it has been very extensively adopted. I notice, however, that many writers upon the subject still emphasize the importance of a very careful selection of cases, and many of them have said that cases of haemorrhoids with marked prolapse requiring digital reposition are unsuitable for any treatment short of operation, except as a palliative. I have always dissented from this view, and have treated a very large number of such cases by submucous injection with gratifying success.

I describe below some cases of *complete prolapse of the whole rectal wall* which I have treated by means of injection, and I urge that a conscientious trial of this method should be made by other rectal surgeons before submitting patients to one of the ordinary operations for rectal prolapse. All operations for rectal prolapse are severe, and all are very liable to failure. It follows, therefore, that if there is a less dangerous and less drastic method of treating patients suffering from this distressing condition it is worthy of trial, even if the relief it gives is only temporary. One of the greatest advantages of treatment by injection is that it is an *ambulatory* method—that is, it does not necessitate any confinement to bed.

Of operations for rectal prolapse one of the most generally employed is that of Lockhart-Mummery. In describing his operation² Lockhart-Mummery writes:

"*Treatment After Operation.*—The wound is dressed twice daily and fresh dressings applied, but the packing is not removed for a week. At the end of this time an anaesthetic is given and the packing removed, and a fresh lot of gauze introduced. . . . The wound should not be allowed to heal under three weeks; in fact, the more slowly it heals the better the result. The bowels are kept confined until the seventh day after operation, when they are relieved by an enema before the removal of the packing; after this they are opened daily with an enema, a slipper bed-pan being used. The patient is not allowed out of bed for six weeks, and not allowed to sit up for an action of the bowels for two months at least. It is most important, in view of the large area of cellular tissue opened up, that there should be no sepsis at the time of the operation, but sepsis later is almost certain to occur after the removal of the packing, and is of no consequence" [sic]. "The slower the wound heals, and the more fibrous tissue involved, the better the result. Out of a total of thirty-two cases there have been only five failures" [that is, a recurrence rate of over 15 per cent.], "and two of these were permanently cured by repeating the operation."