and suffocation. I decided as a last resource to give him 5 grains of quinine sulphate every four hours to steady his temperature, and in the hope that the resulting leucocytosis might be helpful. After continuing this for five days he said he felt better, his temperature became normal, and he felt less exhausted. I then reduced the quinine to 10 grains in twenty-four hours, and he gradually improved, until at the end of three weeks he got up and felt very much better. The quinine was then stopped, and his temperature did not go up again. The liver extracts were continued. He has maintained his progress since, but is still on liver treatment. The following represent the results of the later blood films.

October 20th, 1932.—R.B.C. 2,960,000 per c.mm. W.B.C. normal; differential count: neutrophils 31 per cent., eosinophils 55.5 per cent., lymphocytes 12.5 per cent., monocytes 1 per cent. Haemoglobin 50 per cent. Colour index 0.8. *Remarks:* R.B.C. vary in size, but regular for such low count.

November 14th, 1932.—W.B.C. normal; differential count: neutrophils 33 per cent., eosinophils 55 per cent., lymphocytes 12 per cent.

December 23rd, 1932.—R.B.C. 3,000,000. W.B.C. 12,600; differential count: neutrophils 16 per cent., eosinophils 55 per cent., lymphocytes 27 per cent., monocytes 2 per cent. Haemoglobin 60 per cent. Colour index 1.

February 8th, 1933.—R.B.C. 3,490,000. W.B.C. 17,500; differential count: neutrophils 10 per cent., eosinophils 78 per cent., lymphocytes 11 per cent., basophils 1 per cent. Haemoglobin 80 per cent. Colour index 1.1. *Remarks:* R.B.C. show anisocytosis. Numerous cells 8 to 10 microns. No nucleated R.B.C. No polychromasia. Reticulocytes numerous.

March 1st, 1933.—R.B.C. 3,300,000. W.B.C. 20,000; differential count: neutrophils 12 per cent., eosinophils 76 per cent., lymphocytes 12 per cent. Haemoglobin 65 per cent. Colour index 1. *Remarks:* Reticulocytes numerous. R.B.C. as above.

May 8th, 1933.—R.B.C. 3,390,000. W.B.C. 12,000; differential count: neutrophils 9 per cent., eosinophils 73 per cent., basophils 1 per cent., lymphocytes 13 per cent., monocytes 4 per cent. Haemoglobin 70 per cent. Colour index 1. *Remarks:* The red cells vary in size from 6 to 10 microns. They are regular in shape. No myelocytes found.

DIAGNOSIS

With the definite absence of tapeworm the diagnosis of this case presents a very difficult problem. There is no history of eating raw pork, and there are certainly no signs of trichinosis. Although there was nothing in the history to suggest ankylostomiasis he was given 30 grains of thymol in three successive doses, with negative results. There are no symptoms of filarial infection. There is no localized tumour. No hydatid thrill can be elicited in the liver, and a negative complement-fixation test for echinococcus eliminated the possibility of a hydatid cyst being deeply embedded in the liver substance. Cancer of the liver can be ruled out in view of the patient's improved condition, the absence of jaundice and of any cachectic signs, and the smoothness of the liver surface. Syphilis was thought of, but the Wassermann test was negative. There is no history of gonorrhoea. He never suffered from asthma, any skin disease, or pediculosis.

Recently a few cases of inherited eosinophilia have been reported, but his excellent family history does away with this possibility. Blood cultures were negative. Examination for malarial parasites was negative. The various agglutination reactions for enteric and Brucella groups were negative. The one definite thing about his present condition is his tendency to go down the hill when he is not taking liver in some form. One might therefore reasonably assume that if this were discontinued he would most probably develop pernicious anaemia, considering that even with active liver treatment his red blood count is only about 3,400,000 per c.mm. It is unlikely that the condition is one of the so-called eosinophil-leukaemias, as the total leucocyte count is relatively low. I consider this an unusually interesting case, and am forced to regard it as one of pernicious anaemia with an extraordinarily high eosinophil count.

In conclusion, I wish to thank Dr. W. J. O'Donovan of the pathological department, University College, Cork, for so kindly placing his services at my disposal in gratuitously carrying out many blood examinations and other tests in this case.

ORAL ADMINISTRATION OF NEMBUTAL AS A PRE-ANAESTHETIC MEDICATION

BY

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In embarking upon the pre-anaesthetic administration of nembutal I did so somewhat prejudiced against the drug, as I considered all forms of pre-medication, excluding the use of atropine, to present more difficulties than advantages. It is true that some patients are easily anaesthetized, show no ill effects afterwards, and present no difficulties during anaesthesia when they have previously had a dose of hyoscine or morphine or both. On the other hand, one is often embarrassed by a patient with extremely shallow breathing—even to the point of suspended respiration—when administering ether after hyoscine, and, less frequently, after morphine. The continuous use of CO₂ in such cases may be necessary, but it is none the less undesirable.

There is, of course, no doubt that McGill, who introduced nembutal to this country, gets good results by its intravenous use, but many of us prefer a drug which is not administered in this way, provided that an accurate dosage is possible. In the belief that intravenous medication is only introducing one more danger and complication into the field of anaesthesia, I have set out to explore the uses of the oral administration of nembutal. The results of a 100 consecutive cases are given below, and these include the first few cases, which were deliberately underdosed. There is no harm in giving an underdose of this drug provided that the patient has not been told to expect an amnesia for the time of operation. A small dose calms the patient's fears considerably, and is of definite use.

One of my earliest experiences with nembutal was with a retired Army major, who had been previously primed with regard to the wonders of this drug. At his request I consented to administer it, and he awoke twenty minutes after the operation, spending the remainder of the day ringing his bell for a nurse merely to say, "I'm not asleep, and I ought to be!"

INDICATIONS AND TECHNIQUE

In the first place I consider it essential that the anaesthetist should see the patient previously and himself assess the dose. To be shown a sleeping patient to whom nembutal has already been administered and to be asked to anaesthetize him without awakening or examining him is not only embarrassing, but definitely unfair to both anaesthetist and patient, although one would undertake it in the case of a straightforward surgical procedure in a healthy patient who lives at a long distance after a telephone conversation with his physician.

The nembutal should be given by mouth in cachets, with a small drink of water* one hour before operation. At the same time the patient should have a subcutaneous injection of atropine, and, if not to be anaesthetized in bed, be placed on a stretcher or trolley. The dose varies from 3 to 6 grains—occasionally 1½ grains is sufficient to answer a purpose. It is often advisable to allow the patient 1½ grains on the night before operation. If this last course is adopted it must be reckoned with in prescribing the dose for the next morning.

In assessing the dose one must consider: (1) Sex. (2) Age. (3) Body weight. (4) Physical fitness (being wary with toxic patients, particularly if they have septicaemia).

* Even after a patient has had his stomach washed out for a gastrectomy there is no harm in doing this. It is effective, and is a great comfort to him.

(5) Temperament. (6) The particular disease from which the patient is suffering.

Taking these considerations seriatim:

1. The sex seems to matter little in the smaller doses, but in the larger doses makes more difference. The type of man who requires a very large dose will probably need 6 grains, whereas the woman who requires a large dose will do with $4\frac{1}{2}$ grains, particularly if she has had $1\frac{1}{2}$ grains on the previous night.

2. Children hardly come within the scope of this paper, but very large doses are never necessary in the average patient up to the age of 25 years. A possible exception to this statement will be found in Case 86 in the cases reviewed. It is wise to consider reducing an estimated large dose to a normal one if the patient is over the age of 65—for example, Case 7.

3 and 5. The body weight is a factor to be considered as in the administration of all other drugs, but temperament plays such a remarkable part in the patient's reaction to nembutal that the former becomes somewhat insignificant. A fat woman weighing 12 to 14 stone will snore loudly and not awaken after a dose of 3 grains, which is often insufficient for a thin nervous woman of 8 stone.

4. The toxic patient has a reduced power of elimination, and a smaller dose should be given. If it is considered that 3 grains would be just insufficient, it is better to give $1\frac{1}{2}$ grains the night before and 3 grains the morning of operation, than to give a single dose of $4\frac{1}{2}$ grains.

6. The peculiarities of the actual disease must be considered. For example, a patient suffering from Graves's disease requires a greater dosage than even the nervousness would lead one to expect (see Case 31).

The correct dosage depends upon assessing the relative significance of the above factors, taking into account any psychological factor which is known. As an instance of the latter, a patient who has been terrified by a previous anaesthetic, largely comprising asphyxia, must be classed, although apparently placid and normal, with the very nervous. A little regular practice makes this apparently difficult and inaccurate method an easy task; for, after all, is not the experienced physician's dose of any drug more accurate than a rule-of-thumb method which attempts to be general and fool-proof?

To those who wish to use this drug for the first time I would suggest the following procedure. Choose ordinary healthy adult patients for simple surgical procedures—such as cases of interval appendicectomy—and administer $1\frac{1}{2}$ grains of nembutal at night and 3 grains in the morning without telling the patient what to expect. Induction should be done with pure ether, whether they are awake or not. About 30 per cent. of these cases will be underdosed, but no possible harm can be done, and it will very soon be apparent to the anaesthetist which type should be given $4\frac{1}{2}$ grains and which should have the overnight dose in addition. The consideration of the special points mentioned will help in dealing with abnormal cases later.

CASE RECORDS AND RESULTS IN 100 CASES

A few cases of particular interest are described below:

Case 11.—Major; for tonsil dissection. Given $1\frac{1}{2}$ grains at night and $4\frac{1}{2}$ grains one hour before operation. Spoke and resisted induction of anaesthesia. Anaesthetic far from easy and patient awoke within twenty minutes of being put back to bed. This was a definite underdose, and I regard the case as an absolute failure.

Case 86.—Married woman, aged 24. Extremely frightened, about 11 stone in weight. Operation for interval appendicectomy. Dose: $4\frac{1}{2}$ grains one hour before operation. Awakened by nurse after being taken to the anaesthetic room, but was very placid. Spoke to anaesthetist, addressing him by name. Amnesia complete. No nausea. Conscious of surroundings about four hours later.

Case 7.—Man, aged 83. Operation: epithelioma of lip for insertion of radium under local anaesthetic, general condition very poor. Dose: 3 grains forty-five minutes before operation. Slept through the operation.

Case 31.—Girl, aged 21. Very serious Graves's disease. Admitted with pulse rate of about 140. Exophthalmos + +, tremors + + +, von Graefe's sign +. Breathlessness and palpitation always present, and at times distressing. Three weeks in hospital brought the pulse rate down to between 88 and 100, but it rose rapidly again, and at the time of operation was 96 to 128. Basal metabolism figure was plus 60 per cent. The dosage and the results were as follows: Saturday night, $1\frac{1}{2}$ grains. Sunday, 10 a.m., 3 grains. Neck prepared for operation and patient placed on a stretcher. The drug had apparently no effect. The patient was reading a newspaper and spoke normally at noon. Monday, 9 a.m., 6 grains. Patient prepared as before. Did not stir on being touched at 9.45 a.m. Awoke and became restless on removal to theatre. Easy induction with pure ether, and anaesthesia maintained intratracheally on very little ether and no other anaesthetic. Restless on recovery. Morph. sulph. $1\frac{1}{4}$ grain at 1.45 p.m. and morph. $1\frac{1}{6}$ grain at 5 p.m. The patient had an amnesia from noon Sunday to noon Tuesday! She went home in a fortnight with a pulse of 70 to 88, and has had no trouble since (seventeen months).

Case 72.—Man, aged 63; suffering from pyloric stenosis due to carcinoma. Admitted to hospital as urgent; was very exhausted, with dry skin; described as "completely dehydrated." He was kept on a continuous intravenous drip saline for two days and then, although still very ill, it was decided that his condition was unlikely to improve further. He was given 3 grains of nembutal by mouth after a stomach wash-out one hour before operation, and this rendered him unconscious and slightly restless. Operation was performed at 2.15 p.m.—easy induction, and anaesthesia and condition little altered after Polya gastrectomy. The patient died at 3 a.m. without regaining consciousness.

The following table gives an idea of the results obtained with various doses as accurately as they can be tabulated, and takes into account all cases, whether purposely underdosed or not, with the exception that ten cases have been omitted because, either by administration of some other drug or by alteration of the procedure described—for example, a change in the time of administration—they cannot be classified under any of the headings used. Unfortunately, I cannot give reliable figures with regard to post-operative restlessness, but roughly speaking my experience of it tallies with McGill's figure of 10 per cent. It tended to occur in women rather than men, and after large doses rather than small—although a large dose suggests a nervous patient, which somewhat discounts this last observation.

Dose	Number anaesthetized without movement or awakening	Apparently awake but amnesia complete	Cases having merely a faint memory of seeing the anaesthetist	Nervous patients rendered calm and placid, not asleep and no amnesia.	Dose not effective	Total (90)
$1\frac{1}{2}$ grains at night, and 3 grains one hour before operation	6	nil	4	2	1	13
$1\frac{1}{2}$ grains at night, and $4\frac{1}{2}$ grains one hour before operation	6	3	1	nil	1	11
$1\frac{1}{2}$ grains one hour before operation	nil	nil	nil	3	nil	3
3 grains one hour before operation	15	5	3	17	5	45
$4\frac{1}{2}$ grains one hour before operation	7	4	5	nil	2	18

The 100 cases include three patients who died at various times after the operation. The only one to which the anaesthesia or nembutal might have in any way contributed is Case 72.

I am obliged to all the surgeons at Northampton for a completely free hand in dealing with these cases. Their comments have been fair and helpful, and I have had every opportunity to see my patients beforehand and to follow them up afterwards.