has been able to follow up a considerable number of these children, and he reports that all those he has been able to examine have remained in good health.

In conclusion, let me repeat that in all probability the earliest sign of disease is distension and increased permeability of the walls of the capillaries; that this may be recognized clinically by lack of translucency of the ophthalmoscopic picture; that what can be seen in the eye is an index of what is occurring in other parts of the body where the phenomena are hidden from view; and that by means of the ophthalmoscope it is sometimes possible to recognize disease in its earliest stages—that is, at a time when in all likelihood it is easily curable.

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AVERTIN NARCOSIS IN OPERATIONS FOR TOXIC GOITRE

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The operation of partial, or "subtotal," thyroidectomy for toxic goitre is potentially a highly dangerous procedure, and the reasons for this element of danger are plain to see. Many of the patients submitted to operation are acutely ill, and removal of part of the thyroid gland is sometimes undertaken as an emergency or life-saving measure. Even when the patient is not so ill as this, she is often existing on the edge of a precipice, and any disturbance, even of moderate severity, may be enough to push her over, either by the production of "thyroid crisis" or by putting just too much strain on an already overburdened and damaged heart. The degree of strain produced by the operation is bound to be considerable if it is completed in one stage, since it entails a wide dissection of the neck and "dislocation" of the thyroid gland, a sinister-sounding term, which seems to imply some violence. But although the potential danger of the operation is great, the actual danger seems to have been reduced in some hands to an almost negligible amount if figures of operative mortality are to be taken as a reliable indication. It is the purpose of this article to examine briefly the factors responsible for this remarkable change brought about in what was formerly regarded as an exceedingly dangerous procedure, and to support my own belief that the choice of anaesthetic has great importance. It will be illustrated from a consecutive series of 243 operations performed during the last four years on 220 patients.

FACTORS DIMINISHING OPERATIVE RISK

It would be platitudinous at the present time to enlarge upon the improvement wrought in recent years by the use of iodine in preoperative medication. It is well known that a large part of the reduction of the operative mortality has been due to this, and that iodine has its chief value in the preoperative stage, the initial improvement not being maintained if the use of iodine be prolonged. It would be difficult, also, to exaggerate the importance of improvement in the technical skill and in

the judgement of the operator. Thyroidectomy is technically one of the most exacting of operations, and one in which any failure in detail may cost the patient's life. Gentleness and precision, control of haemorrhage, and avoidance of unnecessary delay are all of importance to the patient's safety. It is notorious that the larger the number of thyroid operations in any one clinic the safer are the patients, since frequent practice makes for the establishment of an efficient routine on the part of the team and for the necessary familiarity with operative details on the part of the surgeon. This applies, in some degree, to the performance of all operations, but it is of superlative importance in the performance of partial thyroidectomy for toxic goitre.

Of great importance also is the judgement of the collaborating physician and surgeon as to when the right moment for operation has arrived, and which patients are actually so ill that any operation means certain death—nowadays a vanishing proportion of the whole. Important also is the judgement of the surgeon as to which patients should be treated by operation in two or more stages. Here, again, experience is an important factor, for which there can be no substitute.

It is clearly difficult to disentangle the relative importance of these different factors in the clinical and operative complex. One more remains, however, which I wish to consider in detail, and that is the choice of anaesthetic. A great variety of anaesthetic methods have been used, from the "thyroid-stealing" method of Crile under hypnotic suggestion to the somewhat complicated method presently to be described. Ten years ago ordinary ether anaesthesia was regarded as satisfactory for operations on toxic goitre, though it was found that the inevitable disturbance to the patient from post-anaesthetic coughing and vomiting was distressing, if not directly prejudicial to her prospects; and it may be taken as a rule in dealing with toxic goitre that all disturbance reacts unfavourably on the patient, and is therefore indirectly prejudicial. An effort was accordingly made to eliminate ether anaesthesia, and a phase followed in some clinics of using local analgesia aided only by a preliminary injection of morphine and hyoscine. It was thought necessary to reinforce the effect of the narcotics by elaborate precautions directed towards the removal of external stimuli, such as noise and light—and very difficult it was to do this effectively in a busy hospital ward. The efficacy of morphine and hyoscine, too, is very variable; sometimes these drugs fail to produce adequate narcosis, and occasionally the patient becomes actually excited, the drugs having only produced loss of control without depressing the main centres of consciousness. The use of local analgesia was found to give improved results compared with ether anaesthesia, and its use was continued for some years. The injection technique which I employed was that learnt from Sir Thomas Dunhill, and consisted of local infiltration of the field of operation with 0.5 per cent. novocain solution in normal saline with 1 in 500,000 adrenaline hypochloride. Usually only about 150 c.cm. were used, so that the total amount of novocain injected amounted to 0.75 gram. A field-block of the cervical nerves was added for a short series of patients, but the analgesia appeared to be equally good without it, and it was soon abandoned as superfluous. Considering that the toxic goitre patient would seem, by the nature of her disease, to be pre-eminently unsuited for any operation under local analgesia, the results were remarkably good. Many patients, however, left the operating table with high pulse rates, and the operation entailed a great strain on both patient and surgeon. Any thyroid operation is already sufficiently exacting for the surgeon without the necessity for watching closely the patient's mental reaction throughout the procedure, and for the

patient it could only be described as an ordeal. The elimination of these objectionable features had already been attempted by various operators with the use of a rectal anaesthetic or narcotic such as ether or paraldehyde. I had myself used the former, but rejected it as being unsafe and as upsetting the patient almost as much as an inhalation ether administration. I therefore welcomed the introduction of rectal avertin when I found that it was regarded by the anaesthetists, represented by my colleagues Dr. C. L. Hewer and Dr. Frankis Evans, as a safe and reliable form of narcotic for patients with toxic goitre.

EXPERIENCE WITH RECTAL AVERTIN

Our first experience of the use of avertin in toxic goitre was gained in treating a patient who was one of the most seriously ill that I have seen.

A boy aged 17 was under treatment by Dr. Langdon Brown in St. Bartholomew's Hospital. His physical and mental development were those of a boy of 12, and there were no signs of puberty. Exophthalmos was extreme, and all the other signs of toxic goitre were fully developed, with enlargement of the heart, frequent attacks of vomiting, and great nervous irritability. His metabolic rate was estimated to be only +34 per cent., but he was nevertheless obviously extremely ill, with a pulse rate of 100 to 130 in bed, rising occasionally to 160 or 170. After he had been under treatment for nearly four weeks his condition was worse rather than better. His general pulse level had risen to 130 to 150, and it was clear that he would soon die if nothing further were done. An operation was therefore undertaken on December 31st, 1929, for ligature of the superior thyroid arteries, the anaesthetic being local infiltration with 0.5 per cent. novocain followed by gas and oxygen. The patient was exceedingly apprehensive, and reacted violently to this interference. His pulse rate rose to 200 and remained in the neighbourhood of that figure for thirty-six hours, and he was restless and noisy. He barely survived, but his condition eventually returned to much the same level as before the operation. It could not be said that he was really any better than this when a second operation was undertaken three weeks after the first. On this occasion, however, he was given rectal avertin to the amount of 0.1 gram per kilo of body weight, and was soundly asleep when put on the operating table. After the neck had been infiltrated with novocain the right lobe of the thyroid was removed, no further anaesthetic being required. His pulse rate at the beginning of the operation was 172, and at the end 140. His pulse rate did not rise after this time above 160, and there was no further reaction. He steadily improved, and a month later the greater part of the second lobe was removed, again under avertin, though on this occasion narcosis was not so deep, and gas and oxygen had to be given in addition. The patient has since made a complete recovery, with rapid mental and physical development, though I received the impression that without the help of avertin he would not have survived the second operation.

We accordingly resolved to employ rectal avertin systematically for patients with toxic goitre, and this communication is based on experience of its use in patients operated upon since January 1st, 1930, at St. Bartholomew's Hospital, at the L.C.C. Thyroid Clinic, New End, or in nursing homes. We agreed from the start that no attempt should be made to obtain full anaesthesia with rectal avertin, but that it should be regarded only as a basal narcotic, and should be supplemented as a routine by a local infiltration of the neck with novocain and, whenever necessary, with gas-and-oxygen inhalation. It was also agreed that no risk of respiratory depression should be introduced by excessive premedication, though a small dose of morphine should precede the avertin as a general rule. We hoped by these means to achieve the blissful state of having the best of both worlds—that is to say, of totally eliminating mental disturbance in the patient while giving the surgeon the advantage of having an unconscious patient whose welfare was not

being endangered by the absorption of any drug in sufficient quantity to produce toxic effects.

Each patient has accordingly received morphine 1/8 grain two hours before operation and 1/12 grain one hour before, or, more frequently, a single injection of 1/8 grain one hour before operation. The danger of producing respiratory depression by giving larger doses than this has unfortunately been demonstrated more than once, in spite of warnings by Sir Francis Shipway and others. In our series no patient has ever given anxiety from this cause, so that morphine 1/8 grain appears to be a safe dose, though probably it is not *essential* to give any morphine at all.

Forty-five minutes before operation the patient is given avertin solution per rectum to the amount of 0.09 or 0.1 gram per kilo of body weight. In four patients of the present series the amount was increased to 0.11 gram, but in others, if the patient was heavy, less than the calculated amount was administered. The larger total is given to the more acutely toxic patients and the smaller to those that are less ill, for it is noticeable that individuals with a metabolic rate that is much above normal are less deeply narcotized by a given dose than are those with a lower metabolic rate. This constitutes an additional safeguard in using avertin for toxic goitre, and it seems to be clear that an upper limit of 0.1 gram per kilogram constitutes a safe dose, since no patient in our series has been unduly narcotized. All the patients have been unconscious when brought on to the operating table except one, who was suffering from diarrhoea and was unable to retain more than a fraction of the dose. On this occasion the operation was not performed, but was done on another day with the help of omnopon and hyoscine instead of avertin.

When the patient has been placed on the operating table the mask for gas-and-oxygen administration is fixed in position on the face, but as a rule no gas is given at this stage. The skin is cleaned, towels are put in position, and the operation area is then infiltrated with 0.5 per cent. novocain solution in normal saline containing 1 in 500,000 adrenaline hydrochloride. It is quite unnecessary to use a solution of greater concentration than this. With the help of a Dunn's self-filling syringe the infiltration is rapidly effected, and as the volume of solution used is usually in the neighbourhood of 100 c.cm. to 150 c.cm. the total amount of novocain given is about 0.5 gram to 0.75 gram, and no patient, so far as I know, has ever suffered any deleterious effect from it.

For some of the more mildly toxic patients this combination of basal narcosis and local infiltration with novocain is all that is needed, but in fewer than 10 per cent. is the operation completed without any gas and oxygen being given. Some of the more acutely toxic patients are disturbed by their removal from the trolley to the operating table; others are roused by the first prick of the local anaesthetic needle; and yet others remain quiescent until half-way through the operation. Once the patient has been roused she is, although still unconscious in the ordinary sense, always uncontrollably restless, so that gas and oxygen is begun at once whenever this occurs; but an expert administrator can, with this combination of drugs, maintain perfect anaesthesia with a minimal amount of gas, and can entirely avoid cyanosis. It is particularly important that the patient should not be allowed to become cyanosed, experience having taught me that there is no factor more potent in producing a rising pulse rate in a toxic patient.

When the patient is back in bed, after the completion of the operation, she usually remains quiescent for two or more hours, so that mental disturbance is eliminated at this stage as effectually as before, and this constitutes another important advantage in the use of avertin.

In the days of ether anaesthesia and of conscious patients with a novocain infiltration, I was accustomed to seeing the patients leave the operating table with a somewhat high pulse rate, which was an indication of an unfavourable reaction to the procedure. Under avertin narcosis the pulse rate may rise a little with the initial disturbance and the induction with gas and oxygen, but not infrequently the pulse rate is actually lower at the conclusion of the operation than at the beginning, which is a truly remarkable reversal of the usually accepted effect of operative intervention. Very seldom is there any alarming rise of pulse rate during the operation, and the post-operative reaction is correspondingly mild and transient. This appears to me to be one of the greatest of the benefits conferred by the use of avertin, since there is seldom any anxiety period for patient, nurse, or surgeon. In a few patients unusual events were noticed, and it is of interest to describe these in detail as perhaps throwing light on the question as to whether avertin in moderate dosage is ever really deleterious to toxic patients.

A patient, aged 25, with a resting pulse rate of 100 to 130, was given the usual dose of avertin (0.1 gram per kilo). She was restless from the start, and before the operation had begun the pulse rate had risen to 140. The operation was therefore limited to ligature of the right superior thyroid artery. The pulse fell to 80 to 90 within forty-eight hours, and seven days after the first operation the right lobe of the thyroid was removed, the pulse rate on this occasion rising to 130. Improvement again followed. A fortnight later avertin was again given, and on this occasion the pulse rate immediately rose to 160. Again, therefore, no more was done than to ligature the left superior thyroid artery. Ten days later avertin was given for the fourth time, and the operation was completed without causing the pulse rate to rise above 120.

At the third operation it might have been concluded that the extreme rise in pulse rate was due to the avertin, but that this conclusion would be erroneous seems to be shown by the following:

A patient, aged 22, with a severe degree of toxic goitre and a resting pulse rate of 100 to 140 was treated medically in hospital for over three weeks without any improvement at all. Her pulse remained exceedingly irritable, and her average pulse rate was higher after three weeks than when she was admitted. It was therefore decided to operate in stages without further delay. She was given the usual dose of avertin, and the right superior thyroid artery was ligatured under local anaesthesia and gas and oxygen. The pulse rose to 160, and remained for three days at 150 to 160, after which it fell to the same level as before. A week later the left superior thyroid artery was tied as before, the pulse rate on this occasion remaining for three days at 130 to 150, after which there was considerable improvement. A fortnight later the patient was given avertin for the third time, and the right lobe of the thyroid was removed. The reaction was relatively mild, the pulse not rising above 140. After another fortnight's interval avertin was given for the fourth time, and on this occasion the pulse rose to 180 before the operation had been begun, and the patient was immediately returned to the ward. This extreme rise in pulse rate was difficult to explain, but it was suggested that it might be in some way due to the repeated doses of avertin. It was therefore decided to perform the last stage of the operation without avertin, and to give only morphine $1/4$ grain and scopolamine $1/100$ grain, local anaesthesia and gas and oxygen being given on the operating table. The rise in pulse rate, however, was much as before, and for three days remained at 130 to 160. Within ten days after the operation had been completed the pulse rate was normal, and the patient has been virtually cured since that time.

It appears, therefore, that this patient had an unusually irritable heart, and that its rapid rate was to be attributed to its being sensitive to minor disturbances rather than to any specific effect of the avertin. It would appear, indeed, from the following case that if any specific effect

on the heart is produced by avertin it will be a sedative rather than an irritative effect.

A patient, aged 16, who was under treatment at the L.C.C. Thyroid Clinic at New End, had already had all four thyroid arteries tied by Sir Thomas Dunhill. In spite of this she remained in a state of severe mental derangement, and showed a resting pulse rate for week after week of 140 to 180. No improvement was being obtained, and I therefore decided, in Sir Thomas Dunhill's absence, to operate in spite of the rapid pulse rate. She was given avertin, and immediately the rate fell to 120. It remained at about that level throughout the operation for removal of the right lobe of the thyroid, and rose again to 140 when she regained consciousness. Twelve weeks later she was again given avertin for the final stage of the operation, and again her pulse rate fell to a much lower level during the operation. Her later history was one of steady recovery, and she was discharged from hospital quite sane and with a pulse of 110.

The sedative effect of the avertin narcosis in this patient was most striking and reassuring.

SUMMARY AND CONCLUSIONS

The primary object of using the somewhat complicated anaesthesia technique that I have described was, of course, the reduction of operative mortality to as near zero as possible. That this object has been achieved is suggested by the fact that of the 220 patients who have been operated on under avertin narcosis only three have died soon afterwards. One of these was a woman of 24, who was clearly acutely ill and rapidly losing ground, so that operation was undertaken lest worse befall. The operation under avertin was successfully performed without any undue disturbances. On the day following, however, the pulse rate rose to 170, and remained about this level for over forty-eight hours. She then rapidly improved, and by the sixth day after operation all danger seemed to be over. On the seventh day, however, vomiting started, and the patient died twenty-four hours later in a condition resembling acute dilatation of the stomach. A critical review of the case afterwards suggested that the real cause of death was probably digitalis poisoning, the resident medical officer having given nine injections of digitalin $1/240$ grain in the course of five days.

Of the other two patients who died one had gross auricular fibrillation and died from heart failure a few hours after the operation. The other was so ill that she developed an acute thyroid crisis a few hours after the ligature of one superior thyroid artery, and quickly died.

The immediate operative mortality among these patients has therefore been less than 1 per cent., and it can be claimed that this low figure has not been obtained by any selection of patients. Some of them have been mildly toxic, but a large proportion have been seriously ill, and operation has never been refused when asked for by a medical colleague, even when the reason for operation was the patient's desperate condition. In nineteen cases the patient was so ill that the operation was performed in two or more stages. Twenty-four patients were suffering from gross auricular fibrillation. Judged by ordinary standards the "operative risk" in most cases was considerable, and I cannot avoid the conclusion that the low mortality is to be attributed, to some extent, to the systematic use of rectal avertin.

My patients, therefore, owe a very great debt of gratitude to the skill of the nursing staff who have attended them and to the anaesthetists with whom I have collaborated. The majority of the anaesthetics were supervised or administered by Dr. C. Langton Hewer, Dr. Frankis Evans, and Mr. Brian Rait-Smith. The anaesthetics at New End were given by Dr. E. A. Seymour.