

hemolytic streptococci. In all instances the throat cultures became negative for this micro-organism during penicillin therapy. Seven patients were subsequently followed by serial throat cultures. In 1, the throat culture again became positive before penicillin therapy was terminated, in 1 case two days after termination and in the remaining 5 four weeks after termination. The hemolytic streptococci recovered at this time in the latter group of 5 patients were found to belong to different types than were found at the initial examination.

COMPLICATIONS

Urticaria appeared in 4 cases, lasting an average of three and three fourths days and appearing an average of fourteen days after penicillin therapy was started. Three of these episodes of urticaria were followed by increased joint pains and elevation of the pulse rate and temperature.

INITIAL ONSET OF ACUTE RHEUMATIC FEVER DURING PENICILLIN THERAPY

In addition to the cases described in which the therapeutic effect of penicillin in rheumatic fever was studied, 2 patients were observed who developed characteristic manifestations of acute rheumatic fever during the course of penicillin therapy for severe group A

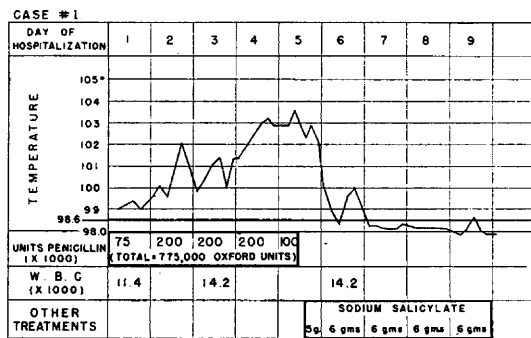


Chart 2.—Acute rheumatic fever progression of clinical disease during period of penicillin therapy, with prompt remission following a substitution of sodium salicylate.

hemolytic streptococcal infections. In these cases the joint manifestations developed two and four days respectively after the initiation of penicillin therapy and thus contrast to the allergic joint manifestations described. It therefore appears evident that penicillin exerts no beneficial influence in rheumatic fever when given after the establishment of the hemolytic streptococcal infection that apparently induces that disease.

CONCLUSIONS

1. A study of the value of penicillin therapy in 38 cases of acute rheumatic fever disclosed no evidence of benefit.
2. In some cases it appeared clinically that the course of the disease was aggravated.

Special Diabetic Food.—Special foods for the diabetic patient are seldom necessary. On the contrary, the effort today is to permit the patient as far as possible to eat the ordinary foods which come to the table, which, with the more liberal carbohydrate diets now in use and with the aid of insulin, is not difficult. There are the further objections that, while specially prepared diabetic foods are sometimes attractive, they are often unpalatable and they vary greatly in percentage composition. The claims made for them are sometimes misleading, and as a rule they are expensive.—McLester, James S.: Nutrition and Diet in Health and Disease, Philadelphia, W. B. Saunders Company, 1943.

PENTOTHAL SODIUM INTRAVENOUS ANESTHESIA IN PEACE AND WAR

THE FIRST TEN YEARS OF PENTOTHAL SODIUM INTRAVENOUS ANESTHESIA, JUNE 1934 TO JUNE 1944

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It usually takes several years to establish a new method in any field of medicine. This has been especially true of the introduction of new anesthetic agents and methods and of intravenous anesthesia in particular. The attitudes of different members of the medical profession to the introduction of new methods of anesthesia have often been diametrically opposite; the skepticism of some has been overbalanced by the unbounded enthusiasm of others. These widely divergent attitudes have not always worked to the best interest of the new method or agent. The history of the evolution of intravenous anesthetic agents amply bears this out.¹

In the case of intravenous anesthesia the skepticism on the part of many surgeons and anesthetists was not entirely without justification. For fifty years anesthetic agents had been introduced for intravenous administration, and only a few of them had produced uniformly safe and desirable anesthesia. Therefore, when pentothal sodium was introduced as another intravenous anesthetic agent it is understandable that many surgeons and anesthetists looked askance at the possibilities of its being of unusual clinical significance.

Pentothal sodium was introduced to clinical practice by Lundy in June 1934, so that this month marks the end of the first decade of its clinical use. While some of the ideas with regard to the use of the agent and method have changed, the original conception of its usefulness has been justified many times over, a fact which has been most gratifying to those of us who have had the opportunity to take a part in its development. Intravenous pentothal sodium anesthesia now stands on its own merits as an established method and has passed well beyond the experimental stages of its development.

However, each one of these ten years has brought about changes in our attitude toward the use of the method, its scope, administration and so forth. There are still many things that one should like to know about the pharmacologic action of pentothal sodium. The most important of these are its site of detoxication and the factors which influence its rapidity of detoxication in various persons. We are not at all sure that it is detoxicated by the liver, like its oxygen analogue pentobarbital sodium.

We are now convinced that pentothal sodium does not appreciably interfere with the function of the normal or damaged liver or kidneys and that it does not untowardly affect the metabolic processes of the body in general, provided it is administered with due regard to the patient's physical state.

In spite of the present day pharmacologic and clinical conceptions that have been generally accepted for pento-

From the Section on Anesthesiology, Mayo Clinic.
Read before the Section on Anesthesiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Adams, R. C.: Intravenous Anesthesia: Evolution of the Method; Application in Clinical and Military Practice, and Consideration of the Use of the Barbiturates and Analeptics, New York, Paul B. Hoeber, Inc., 1944.

thal sodium intravenous anesthesia, the opinions of those who have employed the method extensively are still widely divergent, particularly in relation to the types of surgical cases for which it is suitable. Some feel that it is applicable for almost any type of surgical operation. Others are of the opinion that certain limitations must be recognized unless it is used as an adjunct to some other method of anesthesia—particularly for major surgical cases.

Despite the diversity of opinion on the subject, it is possible to make a few general statements regarding the changes that have been made during the past ten years of its use in civilian surgical practice.

When the use of pentothal sodium was introduced, it was felt that its field should be limited to short and minor operations, requiring little or no muscular relaxation, the duration of which would be approximately fifteen to twenty minutes. Used in this manner as the sole anesthetic agent, its field of usefulness was comparatively narrow. Maximal doses were set between 0.5 and 1 Gm.

As physicians became more familiar with the action of pentothal sodium on patients with varying physical states and for different types of operations, many features of its application were clarified. It was found that the solution of pentothal sodium might be used with safety after it had been made up for periods as long as forty-eight hours. My associates and I have reduced the concentration of the solution from the original 10 per cent to 5 per cent and then to 2.5 per cent. This, we feel, has increased the margin of safety of the method and has reduced the incidence of intravenous or extravascular irritation from the solution to practically nil. Furthermore, it became apparent that comparatively long operations which did not necessitate much muscular relaxation could be performed safely and that many patients would tolerate total doses exceeding 1 Gm. if administered over longer periods.

At the same time, it was recognized that debilitated and toxemic patients had a lowered tolerance to pentothal sodium and took comparatively small doses to produce surgical anesthesia and that the administration to such patients must be carried out slowly and cautiously. The postoperative sleeping time was found to be more or less in direct proportion to the total amount of the drug administered, the amount of preliminary medicaments used and the capacity of the patient to detoxicate the drug. Additional observations revealed the fact that it was not a satisfactory method of anesthesia for most abdominal operations or for operations in regions where the reflexes were particularly hyperactive, such as those of the nose, throat, larynx and the anal region. Some anesthetists are of the opinion that pentothal sodium anesthesia is satisfactory for such operations and provides sufficient relaxation. We continue to feel that its use for major abdominal operations, unaccompanied, does not carry the margin of safety that may be attained by the use of some methods of inhalation or spinal anesthesia. In other words, the advantages that one hopes to derive are often outweighed by the disadvantages, if the operation is long and complicated and requires profound relaxation.

As a result of these findings the value of intravenous anesthesia in combination with other methods began to become apparent. The principle of such combinations was to take advantage of the desirable features

of pentothal sodium anesthesia without depressing respiration unduly and producing a prolonged postoperative sleep.

One of the important advances was the administration of oxygen during intravenous anesthesia. This served to decrease respiratory depression and to prevent anoxemia and seemed to favor better muscular relaxation and anesthesia using smaller doses of the drug than otherwise would be necessary. The oxygen may be administered by the ordinary face mask, B. L. B. mask, nasal catheter, nasopharyngeal tube or intratracheal tube.

The next step forward was the administration of 50 per cent nitrous oxide with the oxygen or if necessary as high as 70 per cent nitrous oxide. This serves to reduce further the amount of pentothal sodium required and increases the degree of anesthesia and relaxation. This combination of intravenous anesthesia with inhalation anesthesia has broadened the field of intravenous anesthesia and has increased its safety. The administration of oxygen or of nitrous oxide and oxygen is now routine at the Mayo Clinic during pentothal sodium anesthesia.

Combinations of other methods with intravenous anesthesia have been increasing during the last two or three years. This has been chiefly evidenced in its use with local or regional anesthesia. Among the purposes for which intravenous anesthesia may be combined with local or regional anesthesia are the following: (1) to render local infiltration and block anesthesia painless, such as during a block for bunionectomy; (2) during the course of an operation under local anesthesia if the patient is nervous; (3) to supplement local anesthesia that is wearing off or that is not quite adequate; (4) combined with block of the abdominal wall or intercostal block for abdominal operations in certain cases. These combinations result in adequate abdominal relaxation without one's having to employ large and depressing doses of pentothal sodium.

Similarly, intravenous anesthesia has been useful with spinal anesthesia for nervous patients who prefer to be asleep. Comparatively small doses will control nausea and prevent straining during the course of spinal anesthesia or to supplement spinal anesthesia that is wearing off.

Other combinations may be mentioned, such as the use of intravenous anesthesia as an induction to an inhalation or an ether anesthetic and its combination with topical anesthesia for certain operations about the throat, larynx and upper part of the respiratory tract. For certain operations about the head and neck its combination with nitrous oxide and oxygen administered intratracheally has been particularly useful. With an intratracheal tube inserted, a free airway is established and since none of the agents in this combination are flammable or explosive, a cautery may be used freely and without hazard.

As a result of all these things, the frequency of intravenous anesthesia has been gradually increasing in civilian surgical practice over these first ten years of its use. Owing to the combinations mentioned heretofore, pentothal sodium may now be used safely for many operations in which formerly we would have considered it contraindicated.

We continue to recognize certain contraindications. We do not consider intravenous anesthesia to be as

safe for young children as it is for adults. It should not be used for patients who have degenerative diseases of the myocardium, particularly if dyspnea is present. It is not as safe for operations in which the integrity of the airway cannot be assured as for other operations. One should always remember that intravenous anesthesia is another form of general anesthesia and that many of the complications that are associated with the latter can occur under intravenous anesthesia. We still feel that the method is safest when employed in institutional practice, although its use in the office or home is permissible provided the anesthetist has available equipment for establishing the airway and administering oxygen.

Having observed the progress that intravenous anesthesia has made in civilian practice over this ten year period, we have been extremely interested in what its value would be in army and navy medical practice in time of war. At the beginning of World War II we could only assume that it would play an important role for anesthesia in the armed forces. The simplicity of the equipment, the ease of transportation and its fire proof qualities were obviously in its favor, but we could not be sure how adequate it would be for robust soldiers and sailors or for patients in shock.

Doubts as to the safety of intravenous anesthesia for patients in shock were engendered in the minds of many at the very beginning of the war, when reports began to leak through from Pearl Harbor that its use had proved dangerous and even fatal in a number of such cases. At the same time, experience in civilian practice had convinced us that it could be used safely for many types of operations in such cases provided certain precautions were observed. Subsequent experience on the various battle fronts has corroborated the truth of this statement, the details of which may be summarized as follows:

1. A patient in shock, with or without loss of blood, is much more intolerant to pentothal sodium and requires much smaller doses to produce anesthesia than does the same man without shock. As a result, the effective dose of the drug is materially reduced—sometimes to as little as a fourth or a sixth of the usual dose. If this decreased tolerance as a result of shock is taken into consideration throughout the administration, satisfactory anesthesia may be obtained without producing severe respiratory depression or otherwise endangering the life of the patient.

2. Shock should be controlled, at least partially, before the anesthesia is begun. This maxim applies equally to other methods of anesthesia.

3. Previous administration of morphine should be known as to time of administration and size of dose, in order that a cumulative effect of two depressant drugs may not be superimposed.

4. Airways and oxygen equipment are as essential adjuncts to intravenous anesthesia as they are to inhalation anesthesia. Whenever possible, they should be available when the method is used.

The use of intravenous anesthesia for military surgery not only varies from its present use in civilian practice but also varies in the different types of surgical units within the services. In army or navy base or general hospitals its use parallels that in a civilian hospital. When it must be used in setups close to the combat area such as dressing stations, casualty clearing stations and

on the beaches, some of the standard criteria for, and contraindications to, its use must necessarily be subordinated to the urgency of the need for prompt treatment. Perhaps equipment is not readily available or the wounded man may have food in his stomach. In other words, through necessity, certain chances may have to be taken when the method is used under such circumstances.

However, the important consideration here is that the anesthetist has been sufficiently trained in the use of the method and effects of the drug so that he may judge how far he may safely go. The army and navy training programs in various departments of anesthesia throughout the country have been an important factor toward improving anesthesia in the armed forces. We have had letters from all over the world from physicians whom we have trained in our institution and from these reports I should like to draw some conclusions regarding the present status of intravenous anesthesia in military surgery at home and abroad.²

Before the United States entered the war we had obtained some information regarding the use of intravenous anesthesia in the surgical services of the British army and navy and for victims of bombing during the battle of Britain. From these reports it was learned that the method had been useful for preliminary débridement of bomb-burn victims and persons who had sustained minor war injuries. When shock was minimal, intravenous anesthesia did not appear to aggravate the shock further and some went so far as to say that its use appeared to protect somewhat against the increase of this state. Early reports from England bore out experimental work showing that pentothal sodium is not contraindicated when patients are undergoing treatment with the sulfonamide compounds. This is contrary to the former supposition.

Reports of the use of pentothal sodium from anesthetists in the armed forces throughout the world vary somewhat according to the type of hospital in which it is used. Most of the reports, however, tell the same general story: that pentothal sodium is of outstanding value. Statements such as "It's been a godsend," "We couldn't do without it" and "If I had to choose a single anesthetic agent, it would be pentothal sodium" are read from the letters of medical officers abroad every day. One officer who had spent eighteen months in the New Hebrides stated that "pentothal sodium has been a life-saver, used as the sole anesthetic in some cases or in combination with other anesthetics." Most of these reports come from physicians who are trained in anesthesia and who recognize its disadvantages and dangers as well as its advantages. These men recognize the fact that there are many types of injuries and operations in which the method may be hazardous and do not use it under such circumstances. While some comparatively recent reports have come through to the effect that the mortality rate under pentothal sodium anesthesia is higher than it should be, the men who are administering it on the battlefronts say that in most instances the fault lies in improper methods of administration and dosage and improper selection of cases.

I should like to sum up some of this information from the personal experiences of anesthetists in the

2. Information quoted from the communications of army and navy medical officers is understood to represent the personal opinion of these officers and does not necessarily reflect the attitude of the army and navy medical services in general.

armed forces at home and abroad. A 2.5 per cent solution is generally employed, but where syringes are scarce 5 per cent solutions or 3.3 per cent solutions are sometimes used. When made up in quantity and kept from exposure to light and air, solutions up to seven and even to ten days old have been employed.

The percentage of cases in which pentothal sodium is used as the sole anesthetic agent or in combination varies. The average appears to be between 25 and 50 per cent. One officer in charge of anesthesia in an outfit immediately behind the front lines stated that, of 500 patients, 95 per cent received pentothal sodium anesthesia. Another, under similar conditions, said that in 78 per cent of operations, excepting those that were intra-abdominal, intravenous anesthesia was used. The distribution of 1,730 anesthetics administered in a base hospital in England over a six months period is shown in the accompanying table.

While the dangers of administering pentothal sodium to a shocked patient who has received a large dose of morphine must be kept in mind, intravenous anesthesia produces better results in robust soldiers or sailors if full doses of barbiturates, morphine and atropine are administered as preliminary medicaments, provided no shock exists. Satisfactory results have been reported by one officer for certain intra-abdominal operations when other methods were not available. In

Distribution of Type of Anesthesia

Type of Anesthesia	Percentage
Intravenous.....	41.6
Spinal.....	31.4
Regional.....	16.9
Inhalation.....	5.3
Combined.....	4.8

these cases thorough premedication and slow induction with pentothal sodium were used.

Total doses vary widely, but a possible average may be estimated to be between 1,000 and 2,000 mg. In 1 case 5.9 Gm. was used over a period of eight hours. This demonstrates a fact often repeated, that the total dose of pentothal sodium and its administration over several hours need not be a reason to discontinue its use if the patient's condition remains satisfactory throughout. Some very prolonged and extensive operative procedures are possible, provided a good airway can be maintained and if profound muscular relaxation is not essential. This is evidenced by the following report of a case of multiple fractures resulting from an airplane crash:

While the patient was under pentothal sodium anesthesia the following procedures were performed: open reduction of a compound fracture of the right humerus; suture of the ulnar nerve in the region of this fracture; open reduction of a compound fracture of the right olecranon and application of a cast; reduction of a fracture of the left radius and ulna with cast; reduction of fracture of right tibia and cast. These were done sixteen hours after the injury, shock was treated prior to the operation and 1,000 cc. of blood was administered during the operation.

The types of operations in which intravenous anesthesia has found most favor are too numerous to set down in detail. Most reports state that it is used in almost 100 per cent of orthopedic operations. It is used extensively for the débridement of burns, for skin

grafting, in most operations on the skin, in operations on the eyes and for most operations that do not involve the cranial, thoracic or abdominal cavity or the upper part of the respiratory passages.

Army and navy anesthetists seem to be fully aware of the advantages to be gained by intravenous anesthesia in combination with other methods. As in civilian practice, reports of its use with oxygen, with 50 per cent oxygen and 50 per cent nitrous oxide, and with local, block and spinal anesthesia are becoming routine. In those cases in which it is used for intra-abdominal operations it is supplemented by intracostal or abdominal wall block in most instances. It appears to be becoming more frequently used as an induction to general anesthesia, since it decreases the stage of excitation in some of these patients and also lessens the formation of mucus and secretion.

The fireproof qualities of pentothal sodium and its nonflammable supplementary agents are reported to be of decided advantage in the forward areas, on battle-ships, during bombings or when operations must be performed with emergency lighting equipment which might ignite a flammable anesthetic agent.

While administration of pentothal sodium is by trained medical personnel or under their supervision, it has often been found necessary to utilize the services of nurses or corpsmen, one medical officer supervising the administration of several intravenous anesthetics. Medical officers inform us that many of these corpsmen and nurses have been doing an excellent job, under the proper supervision, and have fulfilled a very useful purpose. The principles of safe administration of pentothal sodium are quickly learned by intelligent nonmedical personnel. The instruction in venipuncture, in this connection, has been of benefit to those who help the medical staff with the administration of plasma and intravenous fluids.

SUMMARY AND CONCLUSIONS

Pentothal sodium intravenous anesthesia has traversed the first ten years since its introduction. During each of these ten years its use has increased generally throughout the country. Knowing that it is an agent of unusual anesthetic value, many of us have purposely overemphasized certain precautionary measures relative to its method of administration, dosage and selection of cases for its use. This attitude, we believe, is justified in teaching the use of a new anesthetic agent, the administration of which is so simple, the effects of which are so rapid and the results so satisfactory in most cases. The trouble has been that in the past many of the potential dangers incident to its use for certain patients and for certain operations have been overlooked or have been outweighed by its desirable effects. It is under these circumstances that untoward effects have occurred which at times have resulted in justifiable criticism of its safety. Pentothal sodium intravenous anesthesia carries as wide a margin of safety as any established method of anesthesia if it is correctly administered and correctly applied. Those who have had a wide experience with the method have naturally found it a suitable method in more complicated surgical interventions than are generally considered to be within its scope. The most important advance has been the recognition of its potentialities when combined with other methods of anesthesia. These

combinations have increased both the scope and the safety of the method.

The value of the method in military surgery up to the present phase of World War II is more than gratifying. In the final analysis, the application of the method in military surgery does not differ materially from its use in civilian practice. The same principles apply to the two, with the exception that the anesthetist must take into consideration those additional factors inherent in war surgery—shock, loss of blood and often the lack of skilled help and equipment. The anesthetist must weigh these additional factors if he would apply the method to the best advantage. The use of intravenous anesthesia up to the present stage of World War II has even yet been too limited to permit one to draw definite conclusions. Its use in military surgery should provide much additional information for those who will use it in future years.

There is still much to learn about intravenous anesthesia, and no doubt our present attitudes will continue to be modified from time to time. Perhaps new and structurally different agents will be evolved which will completely alter our present opinions of the method. Until such changes do occur, one has in pentothal sodium an intravenous anesthetic agent of undisputed usefulness, which has probably resulted in the most significant advance in anesthesiology throughout the last decade.

ABSTRACT OF DISCUSSION

DR. ALICE McNEAL, Chicago: In the earlier work in Germany anesthetists determined the dose by the patient's weight. Dr. Lundy has changed it from a haphazard method to something that is as controllable as inhalation anesthesia. We are grateful to Dr. Adams for bringing up the subject of untoward effects. I have seen statements that there are no warnings and therefore no possibility to anticipate difficulties. I have had Dr. Adams's experience with the prolonged use of the anesthetic producing a depressing effect after the patient has been returned to the room. We have been using the drug for most vaginal operations. In the early period we were being called down a couple of times a week to see patients who were depressed. Now I have found how useful is Dr. Lundy's method of a combination of nitrous oxide with the drug, and I have reduced the amount of pentothal sodium toward the end of the operation and have had no further calls for resuscitation. I should like to ask Dr. Adams about the use of the anesthetic for operations on the head and neck. The more I see of it the less enthusiastic I am. I have discovered that no surgeon is to be trusted to watch the airway properly or to do something about it if he does interfere with it. So far I haven't attempted to use the drug for abdominal surgery when complete relaxation is needed.

DR. ROBERT A. HINGSON, U. S. P. H. S.: I wish to report 10,000 pentothal sodium administrations. They have been administered in a somewhat unorthodox fashion. Because of the shortage of help in our larger marine hospitals we have solicited the aid of nurse anesthetists and medically trained pharmacists' mates. In the latter series of 5,000 cases, administered chiefly by nurses and trained pharmacists' mates, there has been only one anesthetic death, whereas in the first 5,000 cases administered wholly by physicians there were two deaths. Individuals with the background of a nurse anesthetist or pharmacist's mate can be trained to use this technic. We have trained 36 pharmacists' mates who have gone to Coast Guard cutters throughout the North Atlantic, and on occasion these Coast Guard pharmacists' mates have performed magnificently where there was only one physician on a cutter of 150 to 200

men and an anesthetic was needed. We believe that pentothal sodium in their hands is one of the safest forms of anesthesia. We would like to substantiate all of the warnings that Dr. Adams has given. The group at the Mayo Clinic, in introducing this new agent, has always been fair in calling attention to the dangers as well as to the good points. I would urge individuals who report difficulty with this type of anesthetic to go to a clinic where it is being properly used. Only by such dissemination of information can we make final progress. Stimulation of the patient who has been overdosed can be accomplished by administration of 25 mg. of ephedrine in the vein just as promptly as with metrazol.

DR. S. A. SWENSON, Rushville, Neb.: In the hands of an expert there is little danger, although I think one death in 5,000 is rather high. That is about as high as with chloroform. We men out in the country using these methods of experts should use them with due care and with considerable awareness of the danger.

DR. HUGH A. CUNNINGHAM, Milwaukee: I have administered intravenous pentothal sodium 212 times over a period of twenty-six months to a woman aged 27. In the light of the early work on pentothal, this would be strictly contraindicated. This patient has at varying times received all of the sulfonamides. Her lesions were caused by *Bacillus necrophorus*, an anaerobe that travels by way of the lymphatics, leaving a necrotized area or a large abscess. Pentothal, as it was first introduced by Dr. Rovenstine, should not be administered more than every third to fifth day and should then be carefully watched. This patient frequently has had pentothal as often as twice a day, over an extended period of time. Since the thirty-third administration, periodic liver and kidney function tests have been taken. Over the last forty administrations she has demonstrated from time to time from 4 to 12 per cent dye retention in her liver function tests, but on a short rest she replaces this. She still has the disease; we are still using pentothal, so I would like to ask how often it can be repeated, what changes we should expect, and to how young a patient Dr. Adams has ever given pentothal.

DR. ARTHUR C. McCARTY, Louisville, Ky.: The Surgeon General of the Army has directed the medical officers to use greater care in the administration of pentothal sodium to avoid untoward results. A directive has been issued saying that pentothal must be limited to minor cases, shall not be used for operations around the head and neck, particularly when there is danger of hemorrhage into the respiratory passages when there is infection in that neighborhood, and in brain operations, prolonged operations, it shall be used rarely or with great caution. This is no news to experienced anesthetists, but obviously difficulties have arisen as the result of the use of pentothal in these circumstances. I am situated in a general hospital which is a neurosurgical center. We have found pentothal useful. One of the discussers mentioned the difficulty of controlling the airway in operations about the head. I have found it useful to pass an intratracheal tube, with the patient under pentothal anesthesia, cocaineizing the throat sometimes. At other times I use a local anesthetic in the lubricating solution; sometimes I use no supplementary anesthesia. I have found that the use of an intratracheal tube is of great assistance in controlling respiration in head operations, and it makes these much simpler and cuts down many of the complications that might otherwise arise from respiratory obstruction and from hemorrhage of the respiratory passages.

DR. HERMAN LENOWITZ, Maywood, Ill.: At a government hospital we have given 5,000 pentothal anesthetics with one death attributable to the drug. The man was in partial congestive failure before the anesthetic was given. We have used pentothal extensively for lesions about the head and neck and for genitourinary work as well as for orthopedic surgery. We do not hesitate to use pentothal in extensive prolonged operative procedures over a long period of time. We have

used as little as a few cubic centimeters of a 2.5 per cent solution and as much as 4.5 Gm. We frequently have occasion to work about the larynx. These are our troublesome problems, because the bleeding has to be controlled in some way, and we have found that by introducing an intratracheal tube and giving oxygen with a catheter the patient does very well. This is particularly true in total glossectomies and in lesions of the nasopharynx. We have discarded the use of the 2.5 per cent sodium pentothal solution. We find a weaker solution is just as effective and that it gives the same type of anesthesia. The control is better, the toxicity is less and the reactions of the patient are very few. We have modified this solution to 1:250, 1:500 or 1:1,000, depending on the purpose for which it is being used. We have used it in conjunction with a spinal anesthetic for an apprehensive patient who wants to be asleep, although we find that spinal anesthesia is the procedure of choice in this particular case. We use it extensively in amputations, in genitourinary work and in thoracic surgery. We do not use it in pneumonectomies or lobectomies, but in thoracoplasties we find it to be a desirable agent.

DR. STUART C. CULLEN, Iowa City: I want to ask Dr. Adams if he concurs in the opinion, expressed by a previous discussor, that the administration of pentothal (which includes a knowledge of the care of the airway, judgment as to its use in certain situations and an ability to remedy untoward reactions promptly and efficiently) is so simple that this agent and technic can be turned over to nonmedically trained persons for unsupervised use.

DR. R. CHARLES ADAMS, Rochester, Minn.: Dr. McNeal's question about the use of pentothal for surgery about the head and neck has been answered by Dr. McCarty. I agree with what he had to say. For extensive operations about the head and neck intratracheal anesthesia carries a wider margin of safety and control, particularly in regard to the airway, than does intravenous anesthesia. When it is necessary to maintain fireproof conditions, an intratracheal tube may usually be inserted under intravenous anesthesia without undue difficulty. This is facilitated by spraying the pharynx and glottic region with a local anesthetic solution. I have no argument with those who wish to use pentothal sodium as a sole anesthetic in abdominal surgery. I have not been able to provide most surgeons with the relaxation they prefer without using excessive doses of pentothal sodium and causing undue respiratory depression in most cases. Under these circumstances I feel that the advantages of intravenous anesthesia are outweighed by the disadvantages. However, by supplementing intravenous anesthesia with an abdominal wall or intercostal block, satisfactory anesthesia can be obtained without undue depression of respiration and without using a large dose of pentothal. In regard to the use of intravenous anesthesia for children, I feel that we have much better and more controllable anesthetics for children under 10 years of age than pentothal sodium. Dr. Cullen's question as to how long it takes to attain judgment in selecting suitable cases for pentothal anesthesia and when you can and when you cannot control the airway is apropos. I believe that its intelligent application requires considerable skill and experience not only with intravenous anesthesia but with other types of anesthesia for the many and varied types of operations. It would be hazardous to entrust the administration of pentothal sodium under these circumstances to nonmedically trained persons, particularly if they were not carefully supervised. To illustrate this point I will cite the case of a boy of 15 years with a little fibroma in his postnasal region for implantation of five or six radon seeds. Pentothal sodium was used, and after the operation had been completed the boy became cyanotic and stopped breathing. I visualized his glottis with a laryngoscope and pulled a large clot of blood out of the trachea, which had resulted in a complete respiratory obstruction and which would have caused his death if I had not had the equipment to remove it promptly.

CLINICAL OBSERVATIONS IN TYPHUS FEVER

WITH SPECIAL REFERENCE TO THE
CARDIOVASCULAR SYSTEM

MAJOR THEODORE E. WOODWARD

IN COLLABORATION WITH

MAJOR EDWARD F. BLAND

MEDICAL CORPS, ARMY OF THE UNITED STATES

This study was undertaken principally to observe the various physiologic changes occurring in typhus fever with special attention directed to the status of the general circulation. Previous descriptions of the disease frequently refer to cardiac collapse, cardiac failure or cardiac weakness and in areas where typhus is prevalent it is almost a routine procedure to administer cardiac stimulants in the form of digitalis, ouabain or perhaps some other substitute. Likewise, in certain sections cardiac drugs are given because of the extremely weak and toxic appearance of the patient with the thought in mind that these cardiac tonics will improve the circulation. The latter is not in accord with the actual physiologic effect of digitalis, and Luten¹ has shown that the only clinical indication for digitalis and drugs with digitalis-like action is "evidence of cardiac failure" and in certain arrhythmias. In our study there was no clear indication for cardiac stimulants and hence they were not employed. Actually there was evidence to suggest that a possible harmful effect might ensue from their use.

On the other hand little mention has been given to "peripheral circulatory weakness" with minimal stress directed toward its explanation or to this factor playing the major role, exclusive of the heart per se, as the real cause for this very apparent circulatory deficiency. Wolbach, Todd and Palfrey² mention 4 fatal cases showing irregular pulse which until death demonstrated no evidence of cardiac insufficiency. The very pathology of typhus suggests an overwhelming generalized involvement. The rickettsias invade the entire circulatory tree, causing swelling of the endothelial cells with actual thrombosis of the smaller and occasionally larger vessels. More commonly the changes are in the smaller vessels, causing multiple minute foci of necrosis (figs. 1 and 2). The typhus lesion has been especially well demonstrated in the skin, liver, kidney, cardiac and voluntary muscle and brain but also in every organ of the body.

Recent progress in handling the various forms of surgical shock³ indicates an increase of capillary permeability which alters the electrolytic composition of the blood, lowers the osmotic pressure by escape of plasma proteins into the tissues (lowering blood volume) and finally, when circulatory failure is established, creates a vicious cycle with resulting tissue anoxia accentuating the capillary damage. In typhus one does not have to

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Capt. Daniel S. Ellis, M. C., of the 6th General Hospital, assisted in much of the clinical study. Major Eugene R. Sullivan, M. C., and Capt. Sedwick Meade, M. C., of the 6th General Hospital Laboratory, aided to a considerable extent in the technical investigation.

1. Luten, D.: *Clinical Use of Digitalis*, Springfield, Ill., and Baltimore, Charles C. Thomas, Publisher, 1936.

2. Wolbach, S. B.; Todd, J. L., and Palfrey, F. W.: *Etiology and Pathology of Typhus*, Cambridge, Mass., Harvard University Press, 1922.

3. Moon, V. H.: *Shock: Dynamics, Occurrence and Management*, Philadelphia, Lea & Febiger, 1942. Blalock, A.: *Principles of Surgical Care, Shock and Other Problems*, St. Louis, C. V. Mosby Company, 1940.