THE ROLE OF PICROTOXIN IN THE TREATMENT OF ACUTE BARBITURATE POISONING *

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Ten years have elapsed since the interest in picrotoxin was revived by the fundamental experiments of Maloney, Fitch and Tatum (1, 2) who demonstrated the life-saving action of this drug against barbiturate poisoning in rabbits. The first reports of its favorable clinical action in barbiturate poisoning in humans, reported by Arnett (3) and Koppanyi and collaborators (4), stimulated further experimental and clinical work, removing picrotoxin from the shelf of pharmacological oddities and placing it on the active list of therapeutic measures.

The work of the first years of experimental and clinical research has been reviewed repeatedly as, for instance, by Kline, Bigg and Whitney (5), Dille (6), and Maloney (7). For this reason we believe it unnecessary to refer again to all of the publications already quoted in these review papers. The Council on Pharmacy and Chemistry of the American Medical Association has twice taken position regarding the usefulness of picrotoxin in the treatment of barbiturate intoxications in humans (8). In both of these reports the Council preserves its commendable conservative attitude against new procedures involving highly potent drugs. In their compilation of clinical cases they contrast the favorable results with the use of picrotoxin which had appeared in the literature with the outcome of other barbiturate poisonings not treated with picrotoxin. The severity of symptoms, speed of recovery and the mortality rate, particularly in relation to the dose taken, were used as a yardstick to compare the results. The Council was aware of the difficulty of an accurate evaluation of the data, particularly in the face of the limited number of cases and the great variation in the response of the individuals to barbiturates. In the final conclusion a stimulating action of picrotoxin in human cases of severe barbiturate poisoning is conceded, but the results are apparently not considered convincing. The cautious use of picrotoxin was recorded as being "justifiable." The Council ends its last report with a statement that "much must be learned regarding the behavior of picrotoxin before it can be used with assurance of safety in the liberal doses that appear to be necessary."

In spite of this rather discouraging report, a study of the literature and personal contacts have made it clear that the use of picrotoxin

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is constantly expanding. Without claim for completeness, we have collected from the literature 25 cases of barbiturate poisoning treated with picrotoxin and reported after the last review of the Council. The majority of the reports appeared in the American literature, some in the English, and one in the Dutch: Smyth (9) (Recovery after 112 grains of nembutal), Hoekstra (10), Cardle and Hagen (11), Stephens and Anderson (12), Reifenstein and collaborators (13), Eisele and Brosin (14), Reifenstein (15), Gillman (16), Slot (17), and Anderson (18). Furthermore, reference to the use of picrotoxin without reports of self-observed cases was made in the South American literature (19) and in the French literature (Pagniez, 20).

We are reporting here 11 more cases, 10 of which were seen by us, and for permission to list the 11th case (table 1), we are indebted to Dr. Schwartz who will report this remarkable observation separately in greater detail in another place. Both the amount of the nembutal taken (105 grains) and the 1,944 mg. of picrotoxin which he used seem to represent a record, especially considering that the case ended in recovery. Not included in this report are two cases of Anderson (18) and one of ours which in the judgment of the attending physicians did not receive adequate picrotoxin treatment.* There were 4 deaths among the 25 cases of the literature and 5 out of 11 cases given in the table. Detailed descriptions of the clinical course of barbiturate poisonings have been given frequently enough, and so, in order to be brief, we have condensed our 11 cases in the form of a table which gives the most important data. With one exception (case 3) all of them presented the picture of a severe or very severe poisoning. This classification was based upon the impression of the attending staff and of the consultant (R. K. R.), who has seen a considerable number of cases of barbiturate poisoning. One must consider that most of these cases were hopeless when observing the high mortality even with picrotoxin therapy.

Maloney (7), in a meritorious effort to collect unpublished cases, has obtained by questionnaire records of 54 barbiturate poisonings treated with picrotoxin with 9 deaths. In a postscript to this paper Maloney states that he collected 48 additional cases with 8 deaths. However, since it is not clear how many of these are taken from the literature, we are not including them in this statistic. Thus, we can summarize the result of a total of 90 cases (25 of the literature, 11 of our table, and 54 from Maloney's collection) with a total of 18 deaths, a fatality rate of 20 per cent.

Leschke (21) found an average mortality of almost 25 per cent in barbital poisoning and about 7.6 per cent in phenobarbital poisoning. Hambourger (22) collected 643 cases of acute barbiturate poisoning from different hospitals in the United States. Of the barbital cases

* Also omitted is one case reported by Lovibond and Steel [Lancet 2: 561 (Sept. 2) 1939] which received very large amounts of coramine in addition to picrotoxin. This patient recovered.

8.6 per cent were fatal; of the phenobarbital, 6.6 per cent, and of the amytal cases, 5.2 per cent, an average fatality of 7.3 per cent for barbiturate poisoning. This checks rather closely with a mortality of 6.5 per cent which we found in collecting 184 cases of poisonings with barbituric acid derivatives from the records of two consecutive years (1938 and 1939) in the Cook County Hospital.

A study of the published reports in which picrotoxin was used reveals that without exception the authors have attributed to the use of

TABLE 1

Case No.	Age and sex	Drug and dose	Clinical condition	Total dose picrotoxin	Course and outcome
1	58—Male	Phenobarbital and amytal—Unknown amt.	Deep coma; all reflexes, including corneal reflex, negative. Considered very serious.	1,380 mg. in 5 days.	Good response, one attack of convulsions (2 min.). Active movements 2nd day. Recovered. Committed suicide 3 mo. later. Autopsy: pleurisy and fatty changes in liver.
2	28—Female	?	Complete loss of reflexes, including pupils. Deepest cyanosis. Considered very serious.	2,296.5 mg. in 5 days.	Pupillary reflexes + after 45 mg. Twitching. Coma lightened, died of pneumonia 5th day. Autopsy: pneumonia, fatty liver.
3	53—Male	Nembutal 18 gr.	Pain reflex absent, corneal reflex +; rather deep coma, considered of moderate severity.	33 mg. in 2.5 hr.	Recovered.
4	44—Female	Barbital, more than 75 gr.	Found 24 hr. later; deepest coma; complete loss of reflexes; pulmonary edema. Considered very serious.	400 mg. in 24 hr.	Return of corneal reflexes was only response. Died after 24 hours.
5	39—Female	Amytal, more than 36 gr.	Found 36 hr. later in deep coma with negative reflexes and dilated pupils. Considered serious.	180 mg. in 2 days.	Good response; recovered.
6	44—Female	Phenobarbital 60 gr.	Found 72 hr. later; deepest coma, advanced bilateral pneumonia. Considered very serious.	405 mg. in 3 days.	Only slight stimulation resulted; died 6th day of bronchial pneumonia.
7	48—Female	Barbital 250 gr. in ½ pint whisky.	Found 12 hr. later; deepest coma, complete loss of reflexes; considered very serious.	1,079 mg. in 5 days.	Corneal reflexes + after 50 mg.; slight muscular twitching 3rd day. Complete consciousness restored with metrazol. Recovered.
8	24—Female	Barbital unknown amount.	Found 24 hr. later; deepest coma; complete loss of reflexes; very poor circulation. Considered very serious.	879 mg. in 3 days.	Came out of coma after 2 days, but died 12 days later of multiple, pulmonary abscesses.
9	Middle-aged Male	Barbital 100 gr. + Phenobarbital 50 gr.	Deep coma; complete loss of reflexes, including pupils. Considered very serious.	219 mg. in 2 days.	Pain reflexes restored after 48 mg.; restless and active after 180 mg. sulfathiazole against pneumonia; recovered.
10	65—Male	Phenobarbital 80 gr.	Found 24 hr. later; most reflexes absent; deep coma, edema of left arm, injuries on left shoulder. Bronchial pneumonia. Cerebral edema. Considered very serious.	2,154 mg. in 7 days.	Little response to treatment. Sulfapyridine against pneumonia. Died of pneumonia and circulatory failure on 8th day.
11	32—Male	Nembutal 105 gr.	Found after 1.5 hr.; deep coma; considered very serious.	1,944 mg. in 5 days.	Two attacks of pulmonary edema; regained consciousness after 4.5 days; recovered. Treated and observed by Dr. Schwartz in Cincinnati. Received sulfathiazole for pneumonia.

Remarks.—All of the cases listed received the usual form of supportive treatment. Other stimulants were not used, or only in an amount negligible with reference to the seriousness of the case. Almost all of them showed a more or less pronounced degree of lung involvement during the course.

the drug an important, frequently life-saving role in the cases in which recovery occurred. Furthermore, the review of these cases in which picrotoxin was used proves that the majority of them was of a serious nature, while the statistics made up from hospital records, including ours from the Cook County hospital, comprise all cases, even those in which only a light stupor followed the ingestion of moderate or small doses of the drug. This is also evident from the above quoted publication of Hambourger. This is undoubtedly an important point which makes the comparison of mortality rates from barbiturate poisoning with and without picrotoxin therapy impossible on a general statistical basis.

Another factor to be considered is the amount of the drug taken. The variation of the individual response to the action of the drug appears to be particularly great with the barbiturates. Even in well controlled laboratory experiments in which all possible factors are standardized there is a tremendous variation in the m.l.d.

In our experiments (23) the fatal dose for individual rabbits was not infrequently only 50 per cent or less of the statistical average. Similarly, other rabbits survived doses of 50 per cent more than the average lethal amount. One can obviously expect much greater variation among an unselected group of humans with all conditions varying and uncontrolled. A particularly complicating factor is the frequently performed stomach lavage which will, depending upon the time it is performed, remove a significant amount of the drug. Thus, the total dose taken, if it can be ascertained at all, assumes only limited importance in many cases.

Most of the statistical analyses do not consider the general condition of the patient before he took the drug. It is our impression that greater age, in general, makes a prognosis more grave, other circumstances being equal. This holds true, of course, even more if any important pathology, as lung involvement, circulatory diseases, or impairment of liver or kidney function is present. It has rightly been stated that the prognosis of every serious barbiturate poisoning is doubtful and recoveries may occur even without any specific treatment in cases presenting at first a grave clinical picture, but this is undoubtedly more the exception than the rule. We do not hesitate to state that in our experience the clinical picture has been one of the most important guides for the prognostic evaluation of the case, and we have found the picrotoxin therapy to be of additional help in this connection. If a patient did not show any response to a vigorous treatment with picrotoxin supported by the other measures, and continued for several hours, as will be outlined later, the outcome was invariably fatal. This does not hold for the opposite in as much as death due to complications may follow even after a response with picrotoxin has been elicited.

In several of our cases that underwent energetic treatment with picrotoxin we made a careful check of the blood status and blood chemistry, as creatinin, NPN, and blood sugar in order to see if there was any detrimental effect of the therapy. However, no damage could be noticed. Also, cases which came to autopsy did not present findings different from those common in barbiturate poisonings. However, one possible picrotoxin side action needs some consideration. There are disconcerting reports in the literature regarding a secondary depression following the stimulating action of picrotoxin. Dille and Hazleton (24) found some depressive action of metrazol and picrotoxin in rats and rabbits, as evidenced by the loss of placement reactions. With picrotoxin this was the case also in sub-convulsive doses. Maloney (25) is not convinced of the conclusions drawn by these authors. Barlow (26) found a depressive effect of picrotoxin in barbitalized rabbits only after the use of excessive amounts of this stimulant, and Werner and Tatum (27) found no significant depression after the use of picrotoxin in rabbits under nembutal anesthesia if no convulsions occurred. We have mentioned in a previous publication (28) how, clinically, a picrotoxin convulsion leads to a period of increased depression, and this is one reason to avoid an overdosage. We do not believe that the present experimental and clinical information permits an accurate statement whether or not complete recovery of all cerebral functions is delayed by the use of large, but sub-convulsive, doses of picrotoxin. But what clinician would not be willing to accept some slight delay in complete restoration of normal cerebral activities, which the picrotoxin might bring about, if he can promptly remove the more serious danger in which a patient will remain as long as the sub-cortical and medullary centers are deeply depressed by the barbiturate? This brings up the principal question of the usefulness of stimulation.

Acute death due to respiratory failure in barbiturate poisoning in which the drug has been taken orally is extremely rare; in fact, the majority of the patients die two to five days after the ingestion of the drug. The deaths are either due to the general depression, cerebral edema, or pulmonary complications. The treatment is obviously directed against the symptoms which directly or indirectly follow from these effects as well as against the cause. One of the most disheartening outcomes is the case in which the patient shows a progressive lightening of the depression and dies later of bronchial pneumonia or lung abscess. The mechanism of these pulmonary complications is composed of several factors: the poor ventilation due to depression of the respiratory center, the secondary depression of the circulation, the possible direct effect of the barbiturates upon the capillaries (those of the lungs in particular), and the constant danger of aspiration due to the abolition of the swallowing reflex. A number of measures can be employed to obviate or mitigate these factors, such as, oxygen insufflation with or without carbon dioxide, artificial respiration (if necessary), proper position of the

patient, etc. However, one must consider it logical to try to stimulate those centers which are depressed below their normal activity and thus to remove the underlying cause for these dangerous symptoms. Experimental and clinical efforts leave no room to question that picrotoxin possesses an extremely potent stimulating action upon these centers. Schriver and Perschmann (29) have brought forward experimental evidence that picrotoxin acts not only on the medulla, but also on certain centers in the mesencephalon ("Bahnungs centers") which facilitates the transmission of stimuli to the medulla and down to the spinal cord. Thus, theoretically, and practically, an effective dose of picrotoxin will improve respiration and restore other vegetative reflexes as, for instance, the swallowing reflexes. If, in addition to this, the dose is slowly raised just to the degree where the patient becomes restless and moves his limbs involuntarily, the dangerous stasis of the circulation is removed. In fact, if picrotoxin did not do anything else but this, it would justify its use in the treatment of severe barbiturate poisoning. To attain this aim should be the primary objective of a rational picrotoxin treatment. Naturally, there is a limit even for the most powerful stimulant, and if the dose of the barbiturate has been too great, or if the patient has been permitted to suffer already irreparable brain damage due to prolonged deep coma and anoxia, no stimulation will result. We have seen this in a few cases in which even heroic doses of picrotoxin resulted in no response. A cerebral edema which not infrequently complicates severe barbiturate poisoning may likewise cause resistance against picrotoxin therapy.

If one agrees, principally, that stimulation is a useful procedure in cases of profound barbiturate depression, one will, necessarily, have to answer the question of how picrotoxin compares in this respect with other stimulants. It appears useless at this time to review again the vast literature on this subject. We are satisfied with a short consideration of the comparative properties of picrotoxin and metrazol which appear experimentally and clinically to be the most useful stimulants in this indication.

In regard to sheer potency of action, experimental evidence indicates the superiority of picrotoxin. This has been stated definitely by Werner and Tatum (27) who found that this drug, if given in a single dose, can save rabbits which were anesthetized with doses in excess of 110 mg. per Kg. of nembutal intraperitoneally. This is not the case with metrazol. Also, Barlow (30) ranks picrotoxin first based upon his experimental studies of different analeptics. Clinically, Burstein and Rovenstine (31) seem to give preference to picrotoxin for the treatment of acute barbiturate poisoning. In a well controlled clinical study, Bleckwenn, Hodgson, and Herwick (32) compared the analeptic properties of picrotoxin, metrazol, and coriamyrtin. This latter substance has a number of properties similar to picrotoxin and acts faster. Patients were anesthetized by intravenous barbiturate injections which

were followed by the administration of one of the three stimulants. The authors found that from the viewpoint of potency coriamyrtin was the most powerful, followed by picrotoxin and metrazol. However, since the first named drug led very easily to convulsions, they rate the stimulants in the order of picrotoxin, metrazol, and coriamyrtin as far as clinical effectiveness and safety are concerned. The question of the comparative duration of action of picrotoxin and metrazol is not yet quite settled. According to Werner and Tatum (27) both drugs are inactivated in the body at approximately the same rate. Barlow (26) stresses the longer action of picrotoxin as an advantage of this drug. Clinically, we have always had the impression that this is the case, and we believe this is substantiated by the experiences of some of the investigators using picrotoxin as a convulsant in the treatment of schizophrenia, similar to metrazol. Low and collaborators (33) noticed that after a minimal convulsive dose of metrazol only one convulsion occurred, while a corresponding dose of picrotoxin frequently resulted in repeated attacks.

Metrazol is preferable in two indications. First, its immediate analeptic action together with a marked respiratory stimulation makes it more suitable in cases of acute depression, as after intravenous administration of the barbiturates, a subject which we are not discussing here. Secondly, its stimulating action seems more effective on the higher centers than picrotoxin. This is substantiated by the statements of Burstein and Rovenstine (31), and by our own clinical experience. However, it appears to us that in cases of deep depression, the medullary and sub-cortical centers should be denarcotized first, and this can be done best with picrotoxin. If the patient remains in a state of stupor, particularly following a poisoning with the long-acting group of barbiturates, further high doses of picrotoxin administered at this stage may overstimulate the medullary centers and lead to convulsions. Metrazol is useful at this point for stimulation of the higher centers. We have observed this very instructively in case 7 of table 1. The patient was brought out from a very deep coma by the administration of about 1000 mg. of picrotoxin within four days, but remained stuporous. Further administration of small doses of picrotoxin resulted in slight muscular twitching without producing complete denarcotization. For this reason, a total of 10 cc. of metrazol in three divided doses was given at about five minute intervals. This led to considerable improvement. The patient responded to the calling of her name and even began to talk. After that it was easy to prevent relapse by small intramuscular doses of picrotoxin.

Even the physician convinced of the beneficial action of picrotoxin in barbiturate poisoning should recognize that it is not a panacea and its administration means neither the solution of the problem nor that other forms of treatment are superfluous. It is just one important part of our armamentarium. The clinical reports mentioned are uniform in stressing its usefulness.

We do not feel in need of repeating here in detail the well-known procedures which have proved useful in the management of barbiturate poisoning. We believe that the essentials can be summarized as follows: Evacuate the stomach and leave a saline laxative, sodium phosphate or sodium sulfate, in the stomach; administer oxygen by nasal tube as long as signs of anoxia are present, and insure a free airway. If the swallowing reflexes are absent, elevate slightly the foot end of the bed in order to obviate the disastrous aspiration of mucus. Clean the mouth frequently by suction or careful removal of the mucus with cotton plugs. Bronchoscopy may become necessary. Promote diuresis by judicious intravenous fluid administration, best a mixture of dextrose and saline. Also, a diuretic of the mercury or purine type can be administered. Beware of too much fluid, particularly in cases with impending pulmonary or cerebral edema.

It is important to distinguish between a true pulmonary edema and the rales which are produced by the accumulation of mucus in the trachea and bronchi. The rales disappear under proper nursing care, and with the methods just outlined, the mucous secretion can be greatly diminished by injection of 1/100 grain of atropine once or twice daily. True pulmonary edema is a very serious complication. It calls for restriction of the administration of fluid and energetic support of the circulation. Frequently, in not too serious cases the low blood pressure which accompanies barbiturate poisoning improves with the general treatment, but in very severe cases, and particularly in older persons or in those with impending pulmonary edema, direct measures should be taken. We have found the injection of 0.25 mg.–0.5 mg. strophanthin K intravenously to be helpful. This can be followed by 1 or 2 cc. of obstetrical pituitary solution subcutaneously. This has been found useful experimentally and clinically in tightening the capillaries. Ephedrine, 3/8 grain subcutaneously, two or three times daily, serves also to support the circulation. Barlow (26) has given experimental evidence for the rationality of combining ephedrine with analeptic procedures. Cerebral edema, one of the worst complications, should be treated according to the rules for this condition. Intravenous injection of 50 per cent sucrose or sorbitol solution is helpful in dehydration of the brain. Symptoms of increased intracranial pressure are an indication for spinal puncture. The patient should be kept warm by appropriate measures, but extreme care should be taken not to produce burns. Oral feeding by means of a Levine tube can be instituted, as soon as the swallowing reflex is restored. We always administer a good dose of vitamin C with it, particularly in patients running a high temperature, which accompanies almost all cases of severe barbiturate poisoning.

The technic of the picrotoxin administration has also been described repeatedly by various authors, and we have detailed our method in previous publications (28, 34). There are two somewhat different procedures, the one, the injection of picrotoxin at the rate of 1 mg. per

minute until signs of stimulation occur, and the other, the fractionated administration at intervals. We prefer the latter method. Generally, we believe that picrotoxin should be reserved for serious cases in which the patient shows no or only little response to pain stimuli. If diagnosis of severe barbiturate poisoning has been made, it appears safe to inject an initial dose of 2–3 cc. of the 0.3 per cent solution (6–9 mg.) intravenously and wait for about ten minutes for a response. This response consists of improvement of respiration and reoccurrence of reflexes previously absent. If there is no such effect, another dose of 3 cc. or more should be given ten to fifteen minutes after the first one. We have injected up to 6 cc. in one single dose, but it is advisable to make the increase from dose to dose not too large. This therapy should be continued until the patient starts movements or shows slight muscular twitching of the face or extremities. This is the sign to be careful, since an attempt to enforce awakening will readily lead to convulsions. At this stage one should reduce the dose and may resort to intramuscular instead of intravenous administration. The latter can be used again if the patient becomes more depressed. The longer-acting barbiturates are more difficult to antagonize than the short-acting group. The use of metrazol in removing the stupor after picrotoxin has restored the subcortical activities to a satisfactory degree has been explained above. Overdosage of picrotoxin, if not too heavy, may lead to a short attack of convulsions which, if not more than one or two minutes in length, and not reoccurring, do not require particular treatment. However, if convulsions should become more severe and more frequent, they may be stopped best by intravenous administration of a small dose of a soluble barbiturate, such as nembutal, amytal, or pentothal. The injection should be made very slowly and only as much should be given as is necessary to control the convulsions. We have made it a strict rule for ourselves, despite considerable experience with picrotoxin, not to start a treatment with picrotoxin without having an injectable barbiturate immediately on hand. So far, no limit regarding the total dose of picrotoxin can be given. It can only be stated safely that if a patient really needs picrotoxin, he usually needs large amounts of it. Therefore, it appears advisable that a hospital has a sufficient supply of this material on hand, particularly since it has been shown by us (35) and by Crittenden (36) that the solution is stable for more than two years if kept at ordinary room temperature. In recent experiments we have shown (37) that intracisternal administration of picrotoxin in rabbits produces convulsions without, or with a very short, latent period. It was also possible to antagonize the effect of nembutal by the administration of very small doses of picrotoxin intracisternally. The effect of the stimulation is of an almost purely medullary type in that it produces respiratory stimulation and twitching, but no lightening of the cortical depression. We have not yet had a chance to apply this method clinically, but we

would do so in desperate cases where intravenous administration shows no response.

Only two other complications of barbiturate poisoning should be mentioned; one is the dreaded pneumonia. It appears only natural that attempts have been made to administer sulfapyridine or sulfathiazole to these patients. Adriani (38) published an experimental study in which he showed that rats subjected to large doses of sulfanilamide become more susceptible to the depressive action of the barbiturates. However, we have shown (39) that this is the case only with unphysiologically high concentrations of the sulfonamides as they are never reached under clinical conditions, and even if extremely high concentrations were produced experimentally, the increased depression produced by barbiturates could readily be combated by picrotoxin. Lorhan and collaborators (40) have essentially corroborated our findings. Butler and collaborators (41) found an equally slight decrease of the minimal and the minimal lethal dose of pentobarbital in mice treated with sulfanilamide. No undesirable effects from the administration of the two classes of drugs have been reported (King and Moersch, 42; Smith, 43). We have not seen a deepening of the depression in our cases of barbiturate poisoning following the treatment with sulfapyridine. Not a frequent, but quite a disturbing, complication of barbiturate poisoning is a prolonged peripheral neuritis, afflicting mostly both arms or legs, or hands. One of our patients (case 7) developed a symmetrical radial paralysis and recovered within a few days from this under the administration of thiamine by subcutaneous injection. While we are, of course, not sure how far this treatment contributed to the rapid restoration, it appears reasonable to give it a trial in such cases. Anderson (18) has also employed this type of treatment in a similar case.

Summary

The use of picrotoxin in the treatment of acute barbiturate poisoning is constantly expanding. All reports in the literature are uniform in stressing the usefulness of this therapy. Neither these reports nor our own observations have, so far, revealed organic damage, even after administration of very high doses of picrotoxin, provided it is done with the necessary care. The difficulty of a statistical evaluation of the results has been outlined, and a clinical study of the technic and the limits of picrotoxin therapy presented.

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For the information of anesthesiologists who are contemplating application for certification by the American Board of Anesthesiology, Inc., or who are training physicians for the specialty, the following questions have been employed for Part I (written) examination in the past in *Anatomy:*

1. Describe the anatomy of, or make anatomical drawing of, the nose and pharynx, having particular regard to the parts involved in passing tubes into the pharynx and trachea.
2. What landmarks are used and how is the plexus approached in performing a brachial plexus block by the supraclavicular route?
3. Describe a method for producing block anesthesia for a surgical procedure involving a bunion.
4. State *a.* the distance from the incisor teeth to the bifurcation of the trachea in the average adult male; *b.* the distance from the incisor teeth to the vocal cords in the average adult male.
5. What is the extent of anesthesia of the arm after satisfactory brachial plexus block? What landmarks are used to induce the block?
6. If the veins at the elbows are not accessible, what locations, arranged in the order of their most likely usefulness, would you examine to select a site for transfusion?
7. Give the innervation of the diaphragm and name the important structures passing through its orifices.
8. Name and illustrate by diagrams the nerve supply of the rectus abdominis.