forming for several days unrecognized. The clinical picture was that of sudden heart failure from such a cause. I have made autopsies in two cases in which death occurred under very similar circumstances; antemortem clots were present in both.

Examination of the pus obtained from the brain showed a profusion of rod organisms with the usual microscopic characteristics of pus. No other organisms were found. On careful cultural experiments the organisms showed all the characteristics of the Eberth bacillus, and bacteriologically could not be labeled anything else. No history of typhoid fever could be obtained, but it is well known that many cases of typhoid fever are very mild, and it is more than probable that the patient had been the victim of such an attack which passed under some other name. The typhoid fever organism is well known to be pyogenic in character and has been known in a number of instances to remain latent in the organisms for years and later become virulent with the production of local suppurative or other morbid processes.

The possible relation of the injury on the left side of the nose three years before the examination is a point worth considering. From the history given, the injury appeared to be exclusively to the left of the median line. It does not seem probable that there

Diagram of right lateral surface. Large heavily shaded area indicates locations of abscess cavity. Small heavily shaded spot, a point at which pus was found in small quantities. Dotted line, area of brain uncovered by surgeon—about 1 by 2 inches.

could have been any actual brain injury excepting by transmitted force. If the infection had been a streptococcus or some of the other more common pyogenic organisms, the possibility of the local infection traveling from the side of the injury to the brain would be more plausible. But it would certainly seem as though the infection must almost necessarily reach the corresponding side of the brain, rather than the opposite one if such a relation existed. The presence of the typhoid bacillus, furthermore, seems to exclude a local infection of this character. That there may have been some contusion of the brain from the injury which lowered the resistance of the brain tissue and made it a prey to the pyogenic processes of the organism which in some manner found its way there is quite possible. Unless such a latent injury can be assumed, and the history at the time of and following the injury does not give the slightest indication of such an injury, the case must be looked on as strictly one of the so-called idiopathic type developing from a latent typhoid infection of unknown date and origin, the latter being in either event sufficient cause for the abscess.

OPERATION AND REMARKS BY DR. PORTER.

Mr. A. T. was operated on at the request of Dr. G. W. McCaskey, on Sept. 27, 1902, at St. Joseph's Hospital.

The scalp was prepared in the usual way. Dr. E. V. Sweringer anesthetized the patient, using ether. A horseshoe-shaped flap was turned down and a section of bone one by two inches removed by the use of the trephine, Gigli saw and De Vilbiss' instrument. A crucial incision in the dura was made and the flaps reflected. Nothing abnormal could be discovered by sight or touch. A small trocar and canula inserted in various directions discovered nothing until a thrust was made in a downward and backward direction at the posterior extremity of the opening in the bone, when the point of the instrument appeared to have entered a cavity, whereupon the trocar was withdrawn and a few drops of pus flowed from the canula. Using the canula as a guide the opening was enlarged and a small soft rubber drain introduced. Thinking the amount of pus removed insufficient to account for all the trouble other areas were explored and we were finally rewarded by discovering a cavity not larger than a pea located at the anterior internal aspect of the uncovered area. This was drained by a strip of gauze. The posterior cavity was about an inch beneath the surface and the anterior one about one half or three-fourths of an inch beneath. All told I do not think the quantity of pus from both cavities would reach 2 drams. The bone was not replaced, the flap was turned back and sutured, leaving only enough opening for the drain. The operation was not followed by shock or any untoward symptom save a slight increase in paralysis such as was expected.

The unhappy ending of the case was, in my opinion, in no wise the result of the operation. This is not the first case in which the exact location of a subcortical lesion was first made known to me by exploratory puncture. A sudden change in the resistance offered to the progress of the instrument, even though slight, is easily appreciated. Had I been using a probe or a needle in this case I would have felt perfectly justified in enlarging the openings, for the sudden lack of resistance offered to the trocar was what first made me aware of the location of the cavities.

On another occasion¹ a subcortical tumor was located because of the increased impediment offered to the progress of the exploring needle by the capsule of the tumor. Exploration by this means is, if carefully done, almost without danger. One's anatomic knowledge should keep him from puncturing large vessels or the floor of the fourth ventricle. Vessels of lesser size may be avoided if, when the needle is arrested by their coats, it is slightly withdrawn and its direction slightly changed. It is to be regretted that no autopsy was allowed.

SHOCK PRODUCED BY GENERAL ANESTHESIA,

WITH RELATION TO DISTURBANCES OF THE BLOOD AND GASTROINTESTINAL TRACT.*

FENTON B. TURCK, M.D.

CHICAGO.

Shock as a result of simple anesthesia in the absence of trauma, hemorrhage or fright has not been carefully worked out. The term "shock" is unscientific. It is the clinical expression for a group of symptoms, the result of failure of important functions of the body, as those of circulation, respiration, excretion and secretion, and general metabolism. A lowered bodily temperature is a more or less constant phenomenon. Shock is intimately connected with the nervous mechanism.

1. THE JOURNAL A. M. A., Jan. 25, 1902.

* Read before the Chicago Academy of Medicine, January, 1902, and Chicago Medical Society, March 4, 1903.

In studying shock from anesthesia it is not only essential to consider the specific toxin of the anesthetic used, but the resulting toxic bodies generated through the immediate or more remote influence of general anesthesia. Shock can not, therefore, be expressed in a single definition. The phenomena of shock are so complex that in experimental work on animals it is necessary to study each condition separately, and compile the associated facts obtained and compare them with clinical experience.

The present paper deals with (1) the consideration of the anesthetic as a cellular poison; (2) the disturbances of function as a result of the anesthesia; (3) the toxins that are evolved either from the direct effect of the anesthetic or the disturbances of certain functions of the body.

In experiments on dogs with chloroform and ether, we have not determined the direct toxic effect on cells, as this has been done by numerous observers. Sabaarth,¹ in 1866, reported 119 cases of death from chloroform anesthesia, only 48 of which were due to the toxic effects of chloroform. This led Nothnagel² to study the pathologic effects of chloroform and ether on the various cells of the body. Rabbits were chiefly used, and the anesthetics were employed by inhalation, by subcutaneous and intraperitoneal injections, and by direct introduction into the stomach. Doses of different size and at varying intervals were employed. The pathologic findings showed overwhelming evidence of the specific toxic effects of chloroform and ether on cells, whether the animal died from anesthesia or not. Waller's³ research on isolated nerves showed that their electrical reaction is suspended, or ceases permanently, according to the percentage of chloroform used, and the time of exposure.

In experiments on animals I have frequently noticed that some animals would show evidences of shock more readily than others of the same species, and that even with the most trivial manipulations under anesthesia the animals would die during the same night, the following day or the second day after. They would show all the evidences of shock, as a fall in blood pressure, respiratory failure, lowered temperature, loss of sensation to a greater or less degree, and failure of the excretory organs. This led to the investigation of the question of shock from anesthesia without surgical operation.

METHODS OF OBSERVATION.

Dogs were selected, as they appear more resistant to the after-effects of anesthesia than rabbits and guinea-pigs. Chloroform and ether were used; sometimes they were combined or used alternately. The animal's temperature, pulse and respiration were observed before, during and after the anesthesia, and they were observed sometimes at intervals for forty-eight hours thereafter. The maximum blood pressure was determined, comparisons made, and changes in the blood serum were noted. The condition of the motility of the stomach and intestines was observed. A study of excretion and secretion was made. Where death occurred, a postmortem examination was made. Where shock was evident, the abdomen of some of the animals was opened under local anesthesia. The condition of the splanchnic circulation was determined by direct inspection before external factors brought about any changes, such as might be produced by air, room temperature and manipulations. The serum was secured in some immediately, and in other cases twenty-four hours after anesthesia, by the usual method of bleeding the animal in order to observe any changed condition and its toxic properties. The mucous

membrane of the stomach and intestines was dissected out, and both mucosa and muscularis were chopped up separately, to determine the presence of the anesthetic used, by distillation and appropriate tests. The length of time of the anesthesia ranged from one to six hours. A distinction was noted between the immediate or primary effects and those that were remote or secondary.

The conclusions that can be drawn from the details of the experiments made on animals under chloroform or ether are that where shock is produced it does not materially differ from the shock that results from trauma. The most constant pathologic factor is failure of circulation, and this is especially expressed in splanchnic congestion. The failure of temperature and respiration has been considered to be the result of vascular failure, with the corresponding fall of blood pressure.

It will be seen, however, by referring to the Protocols 13 and 15 that the temperature fell several degrees after the injection of the serum, while the blood pressure did not always show a corresponding fall.

Wilson⁴ holds that death following chloroform and ether anesthesia is always due to a failure of circulation, and this failure renders the nutrition of vital centers impossible. This would seem to imply that we are dealing with a question of time and degree of circulatory disturbance. White⁵ echoes the universal clinical observation that anesthesia always adds to shock. But it is not always recognized that shock itself is often produced by the general effects of anesthesia without trauma, hemorrhage or other etiologic factor.

Kirk⁶ has shown experimentally that irregularity of the heart and syncope occur in animals after the last drop of chloroform has left the blood; and it is well known that chloroform and ether may be found in the urine as long as a week after the anesthesia. Horsley⁷ demonstrated that death arose from shock to the medullary centers, and that the question of dosage was more of time than amount. The evidences of vomiting, long-continued after anesthesia, are associated with severe circulatory depression, and not infrequently syncope. Ceccherelli⁸ experimented on animals with chloroform to determine changes in body temperature, and Angel-esco⁹ carried out similar experiments with chloroform and ether. They found the fall in temperature was in direct relation to the disturbance of the circulation; that where blood pressure fell rapidly the temperature might fall from three to four degrees F. On the other hand, improved respiration and circulation caused an improvement in the temperature. Duplay and Hallion¹⁰ demonstrated by experiments on dogs, with chloroform and ether, that there was always a fall of pressure under chloroform, also with ether, where the medullary centers were deeply narcotized. From the animals experimented on they concluded that if the failure of the circulation was the direct result of the respiratory failure, as a result of anesthesia, then we ought to expect prompt recovery from the syncope under artificial respiration. But this was not borne out in these experiments. Hill¹¹ concludes that chloroform paralyzes the splanchnic vasomotor tone, and, at the same time, diminishes the respiratory pump, and shock or fear, he claims, acts like chloroform by its tendency to abolish the compensatory mechanism for the hydrostatic effect of gravity. Hare¹² holds that in overdoses the heart and respiratory centers are paralyzed, and that in the usual proper doses chloroform produces death in the same manner as hemorrhage does, that is, by failure of the respiratory center, because it is deprived of blood, and a pulse failure because the heart has no blood to pump with.

Bland,¹³ in comparing the effects of ether and chloroform, shows that chloroform invariably causes a fall in blood pressure, while ether does not except at the end of anesthesia and after narcosis. Hewett¹⁴ claims that surgical shock will occur more readily under ether than chloroform.

The explanations that are usually given for the complex symptoms found in shock from anesthesia can not be explained by the simple failure of blood pressure and respiration, but there appear to be some direct toxic bodies formed that are found in the blood serum. The injection of the serum from animals that have shown evidences of shock produces many of the symptoms manifested in shock, which include loss of sensation, general malaise, marked fall in blood pressure, stertorous respiration and, what is generally more significant, rapid fall in blood pressure. (See protocols.)

Kast and Mester¹⁵ are of the opinion that the blood contains the products of disturbed metabolism, for they found that after prolonged narcosis in healthy individuals a continued disturbance in metabolism of albuminous substances occurred, similar to that in phosphorous poisoning. Becker¹⁶ of Bonn states that there is found in the majority of healthy persons acetoneuria of varying duration after narcosis. Boyer¹⁷ found cases of acetoneuria with coma and death in from twenty-four to forty-eight hours after operation.

These observations would seem to prove that there are poisonous substances or toxins produced in the serum. The question, however, becomes more complicated when it is remembered that there is a deficiency in elimination, and therefore a retention of toxins. This may be inferred from the experiments of Galeazzi¹⁸ and Grillo with methylene blue. They conclude that the anesthetic lessens the elimination of toxic substances, just as it lessens the elimination of methylene blue. Kemp¹⁹ found that ether causes a rise in blood pressure in the carotid artery, followed by a fall, the urine becoming scant and containing albumin soon after the commencement of the fall in pressure. A similar phenomenon was observed after chloroform; the fall was more gradual, and secretion from the kidneys lessened as the circulation was depressed. Eisendrath²⁰ found cylindroids and other evidences of damage to the kidneys after anesthesia.

It is clearly evident that the toxicity of the blood may be increased through toxins elaborated by the direct effect of anesthesia, and by the retention of poisonous toxins which are normally excreted.

It is now well recognized that the blood serum normally has the power to neutralize to a greater or less degree toxins that circulate in the blood. One of the important properties of normal serum is its antiferment action, which is shown by the work of Firmi,²¹ Roden²¹ and Morganroth.²¹ Landsteiner²¹ shows that the normal blood weakens the fermentive action of pepsin, and Simniczki²² follows up this work and demonstrates that blood serum has an antiferment action on papayotin; and also, that alcohol weakened or destroyed entirely this antiferment action of the blood.

The writer found that mixing chloroform and ether with normal blood serum lessened the antiferment action of the serum on trypsin in egg albumin. This was demonstrated by the following method: Blood serum was mixed with chloroform and ether and kept in an incubator, after which the narcotic was driven off from the serum, and the serum then mixed with one to two grains of pancreatin and a disk of egg albumin, which it digested completely, while the normal blood serum unmixed with chloroform and ether only softened the disk.

We must conclude that not only the chloroform or ether may possess this property, but an alteration in metabolism may generate a substance that counteracts the antiferment action of the blood.

OBSERVATIONS ON THE BLOOD SERUM.

We next consider the antiferment action of normal serum as compared with serum from animals that have shown symptoms of shock after anesthesia. In the following observations of the relative antiferment action of the sera, the Mett method was used. This consists of simply aspirating egg albumin into a capillary glass tube, 1 to 2 mm. in diameter, and allowing the albumin to coagulate in the tube at a temperature of 95 C. The tube is divided into short lengths and dropped into 2 to 5 cm. of the sera under investigation, with the addition of pancreatin or carica papaya. This is placed in an incubator at 37 C. After a period of twelve hours the tubes are taken out and the length of the undigested column of egg white is measured off by placing on a small glass millimeter scale under a low-power microscope. The difference between the length of the column of undigested white of egg and the length of the tube gives the degree of digestive power of the fluid. The sera into which the lengths of tubes with their albumin contents were dropped were prepared by taking from 2 to 10 c.c. of blood serum from dogs that had been anesthetized and mixing it with 15 decigrams of pancreatin or carica papaya, and this was controlled with normal sera prepared in the same way, the Mett method being then put into practice, as described above.

The following tables show the relative degree of inhibition of the sera to the action of the ferments of normal dog serum, as compared with the sera from animals that have been under chloroform or ether anesthesia.

In order to show the direct effects of chloroform and ether on normal blood serum, the following tables show the findings in a number of experiments performed. The anesthetic was mixed with normal serum and allowed to remain two to three hours, after which the anesthetic was driven off by heat at a temperature of 45 C., aided with a vacuum.

AFTER TREATING WITH CHLOROFORM.			
Serum and Pancreatin Mixture.		Digested 10 Hours. Serum and Carica Papaya Mixture.	
5 c.c.	6.1 mm.	5 c.c.	4.1 mm.
2 c.c.	8.2 mm.	2 c.c.	7.2 mm.
3 c.c.	7.1 mm.	3 c.c.	4.3 mm.
AFTER TREATING WITH ETHER.			
Serum and Pancreatin Mixture.		Digested 10 Hours. Serum and Carica Papaya Mixture.	
5 c.c.	5.1 mm.	5 c.c.	4.4 mm.
3 c.c.	3.1 mm.	3 c.c.	5.6 mm.
4 c.c.	6.1 mm.	4 c.c.	5.8 mm.
NORMAL SERA.			
5 c.c.	3.2 mm.	5 c.c.	2.4 mm.
2 c.c.	2.1 mm.	5 c.c.	1.5 mm.
4 c.c.	2.2 mm.		
PANCREATIN, FIFTEEN DECIGRAMS.			
Time Animal Was Under Anesthetic.		Time Animal Was Under Anesthetic.	
6 hours	9.0 mm.	1 hour	3.4 mm.
6 hours	8.4 mm.	1 hour	4.3 mm.
4 hours	7.4 mm.		
CARICA PAPAYA, FIFTEEN DECIGRAMS.			
Time Animal Was Under Anesthetic.		Time Animal Was Under Anesthetic.	
6 hours	8.8 mm.	1 hour	4.7 mm.
6 hours	8.6 mm.	1 hour	4.1 mm.
4 hours	8.7 mm.		

The blood serum of these animals experimented on also showed a marked hemolytic effect. After shock was evident from anesthesia and the animal was bled, the blood frequently showed a tendency to lake, and this was also noticed where a considerable amount of serum was

injected into an animal, the blood showing the same tendency. The following observations show this more definitely:

The serum from an animal that had been five hours under anesthesia, in shock, showed 15 per cent. hemoglobin. When fresh blood was added and centrifuged, the serum showed 50 per cent. hemoglobin.

Blood serum taken from a dog that had been six hours under anesthesia; hemolysis shown in the serum after standing eight hours; 4 c.c. of this serum added to 5 c.c. of fresh blood produced laking immediately in the test tube; .015 of blood in 4 c.c. of serum also produced laking. Hemoglobin in serum, 10 per cent.; after adding fresh blood and centrifuging, it was raised to 15 or 20 per cent.

Microscopic slide irrigated with shock serum and one drop of normal blood; placed in incubator; shadow corpuscles formed.

Agglutination.—Serum from an animal that had been under anesthesia for three hours; one drop of blood under slide irrigated with serum showed immediate clumping. When blood from an animal six hours under anesthesia was used, the same condition was observed after the fourth and fifth dilutions.

Precipitins.—Immediate coagulations of blood have been frequently noted after prolonged anesthesia when the blood was withdrawn. One drop of normal blood added to 5 c.c. of sera showed coagulation within two minutes after having been placed in incubator. Equal parts of shock serum with normal blood showed immediate clotting of the whole mass.

The following condensed table represents the effect of serum taken from dogs which had been under the influence of chloroform or ether from one to six hours:

SERUM FROM CHLOROFORM.			
	Hemolysis.	Agglutination.	Precipitins.
6 hours.....	Positive.	Positive.	Positive.
5 hours.....	Positive.	Positive.	Positive.
4 hours.....	Positive.	Positive.	Negative.
2 hours.....	Slight.	Plus minus.	Negative.
1 hour.....	Slight.	Negative.	Negative.
ETHER.			
	Hemolysis.	Agglutination.	Precipitins.
6 hours.....	Positive.	Positive.	Positive.
5 hours.....	Positive.	Positive.	Positive.
4 hours.....	Positive.	Positive.	Positive.
2 hours.....	Slight.	Negative.	Negative.
1 hour.....	Not constant.	Negative.	Negative.

These experiments suggest the explanation of the cause of death in animals that have been in shock from the after-infection with saprophytic germs, which, without the shock, would have proven negative. Experiments made by the writer,²³ which have been previously published, show that the *Staphylococcus albus*, *Staphylococcus pyogenes aureus*, and the colon bacillus were equally prompt and positive in their toxic effects when injected after shock. The *Staphylococcus albus* and colon bacillus, when injected into normal animals used as controls in these experiments, gave negative results.

EFFECTS OF CHLOROFORM AND ETHER ON THE STOMACH AND INTESTINES.

We have still to consider another source of toxemia and irritation that follow the use of anesthetics when administered only for a short period. I refer to the disturbances that arise from the gastrointestinal tract following narcosis. That anesthesia from chloroform or ether interferes with the functions of the stomach and intestines is, I think, admitted by all clinicians, but just what disturbances occur is not always made clear. These disturbances include those of motility and secretion, as the direct result of the anesthesia and the splanchnic congestion.

The local effect of the anesthesia is shown in the following experiment:

The animal's esophagus was plugged to prevent the swallowing of chloroform or ether, and this was found to be quite as effective as tracheotomy for the purpose of administering the anesthetic through the tracheal opening. On examining the stomach through a fistula, previously produced and after gastric lavage, there was found an initial increase in the flow of hydrochloric acid, followed later by a diminished production of hydrochloric acid and ferments and the formation of a large quantity of mucus, which is always the product of irritation. Chloroform and ether were found in the wash water, they being recovered by distillation and the usual tests.

The fact that local irritation causes an initial rise in the formation of hydrochloric acid was first noted and published by the writer in 1894.²⁴ It was subsequently demonstrated by him in 1895²⁵ and in 1896,²⁶ and can be found by referring to the literature of his experiments with nitrate of silver, tannic acid, mustard and many other substances used in experimental acute and chronic gastritis. This initial rise in the formation of hydrochloric acid and pepsin was invariably followed by a decrease in their formation, and a corresponding increase in the formation of mucus, until subsequently no hydrochloric acid or ferments were secreted. It is, therefore, surprising to find that Pawlow²⁷ of St. Petersburg, in his recently published work, claims that these phenomena were first observed in his laboratory, and were the result of the observations of Sawrieu,²⁸ in 1900, which is six years after my observations, published both in this country and Europe.

It seemed desirable to determine whether the mucous membrane of the stomach and intestines contained ether or chloroform after anesthesia. To demonstrate this point, mucous membranes and muscle walls were examined separately. The stomach was washed out after a narcosis of two or three hours' duration, and the mucous membrane dissected from the muscle walls of both stomach and intestines. These were placed in separate receptacles and finely chopped. After thorough maceration, the products were distilled, and it was found that both muscle walls and mucous membranes contained a considerable amount of the anesthetics used. (The chloroform test is benzoisonitrile, C_7H_5N .) Ether was detected after distillation by the odor.

With both chloroform and ether, even after one hour's anesthesia, there was a distinct reaction for both found in distillation, but after two hours it was much more marked and distinct, and where six hours' anesthesia was used, the reaction was very much increased. In some of the experiments the mucous membrane was removed several hours after the effects of the anesthesia passed off, and still the anesthetic could be detected in the mucous membrane. The irritating effects of these would seem to account for the large amount of mucus produced, which is referred to above.

The writer has also found that constant irritation of the mucous membrane with substances, such as ether and mustard, if continued for any length of time, or if large enough in quantity, produced marked disturbances of the circulation. This was demonstrated in the experiments reported in my paper,²⁹ read before the American Gastro-Enterological Association, at Washington, D. C., in 1900. This is in conformity with the observations of irritations of mucous membrane that may affect the heart and circulation reflexly. Kionka³⁰ found that ether ex-

exercises an irritating action on all mucous membranes, even on those with which it has not been brought in direct contact. Guinard,³¹ by experimental research in narcotics, found that any irritation of the intestines caused by reflex action arrested respiration and circulation. Guirni³² observed that irritation, which may arise from mucous membranes affecting the pneumogastric and other nerve filaments, is more strikingly observed when the nasal mucous membrane is irritated, and may cause an inhibition of the heart's action. Rosenberg³³ suggested the application of 10 per cent. solution of cocain to prevent this irritation. It was suggested to the writer to use applications of cocain over the area of the stomach and intestines, with a view to blocking the irritation that might arise from the anesthetics.

Meyer and Prebrium,³⁴ in 1873, showed the reflex effect of gastric irritation on the heart, causing inhibition.

When it is remembered that vomiting and disturbance of the circulation are usually associated with anesthesia, and that the removal of the ether from the stomach by lavage will check the vomiting and frequently stimulate the depressed circulation, it is evident from both scientific and clinical observations that this reflex irritation is a very potent factor in the production of the symptoms of shock following anesthesia. This is strengthened by the observations of Brunton,³⁵ who found that chloroform taken internally produces vomiting, and that even though coma and death be averted, the irritations of the stomach and intestines continue and produce the evidences of circulatory depression analogous to shock.

It is therefore evident that the atony which is noticed clinically may have some relation to the degree or quantity of anesthetic that is found in the walls of the stomach. The anesthetic used and the resulting toxic condition may act similarly to the toxic effect of fatigue stuff. This, with the effect of the anesthetic on the nerve centers, producing splanchnic congestion, may account for the lack of motion in the stomach and intestines. This atony results in the accumulation of gases in the stomach, and gases that are found normally in the stomach will distend it when the tone of the muscle wall is diminished or lost. Experimentally, through a gastric fistula, with the pylorus and cardia tied off, I have found that after the stomach has been emptied of its gases, the formation of gas in the stomach continues, which could not have been the result of fermentation, but must have been due to the gases from the blood. The great distension that is sometimes noted soon after prolonged anesthesia produces considerable effect on the splanchnic circulation.

Meyer and Prebrium³⁵ observed that distension of the stomach caused a rise in blood pressure. The writer's observations, previously published, were that the initial rise was followed by a fall in blood pressure, especially if the distension was chronic or prolonged. The disturbance of the circulation, as the result of atony and distension, must constitute a very important factor in anesthesia, and as long as there is a disturbance of the splanchnic circulation we must expect a disturbance of the motor power of the stomach and intestines.

It must also be remembered that where there is a lack of motor power with retention the excretion of chloroform and ether into the stomach seems to increase the toxicity of the stomach contents. From this we would deduce the observation that chloroform and ether either form a new compound or have the power of dissolving out the toxic principles that are readily absorbed. The injection of the normal stomach contents does not produce such toxic effects up to 40 c.c.; whereas in atony

of the stomach, especially after chloroform or ether anesthesia, the toxicity of the stomach contents is markedly increased. The increased bacterial growth and the formation of toxins in gastric atony have been repeatedly shown in the author's literature of the past eight or nine years.

SUMMARY.

The complex clinical picture of the after-effects of chloroform or ether anesthesia is made more clear by experimental research, from which we may deduce the following facts:

1. The circulatory disturbance is a direct result of the chloroform or ether acting on the vasomotor centers.
2. The prolonged effect of chloroform and ether on the splanchnic circulation results in congestion associated with fall in temperature. Temperature may fall without fall in blood pressure.
3. The direct effect of the toxins of chloroform and ether acting on cells, with disturbance of metabolism, may produce toxic products.
4. The resulting elaboration of toxins produces symptoms of "auto-intoxication," associated with the formation of hemolytic and agglutinating bodies, and precipitins.
5. Indirect toxic effects result from retention of toxic products through disturbances of elimination.
6. There is lessened resistance of the blood serum to normal excreted toxins.
7. There is lessened resistance of the blood serum to bacterial toxins.
8. There is diminished resistance to the development of saprophytic and pathogenic micro-organisms.
9. This may be partly explained by the changes observed in the sera, such as diminished antiferment properties, hemolysis, agglutination, precipitins, etc.
10. That reflex effects result, such as reflex irritation set up by the excretion of the anesthetic into the stomach and intestines.
11. As the result of atony there is the formation of toxins in the stomach and intestines through bacterial growth.
12. Atony of the stomach and intestines results in the accumulation of gases and interference with the circulation.
13. There is increased toxicity of the stomach contents in the presence of chloroform and ether.

PROTOCOLS.

EXPERIMENT 1.—Dog; fox terrier, mongrel; weight, 11 kilograms. Ether anesthesia, by inhalation. Rectal temperature, 39 C. Time, six hours. Maximum blood pressure obtained by the modification of a Riva-Rocci "tonometer," 130-140 mm. At the end of three hours temperature 36.1 C. Blood pressure, 90-95. At the end of four hours the rectal temperature was 35 and the blood pressure 70. At the end of five hours blood pressure is 65-70. The rectal temperature 35. Six hours, 60-70; rectal temperature, 34.8.

Anesthesia removed. Twenty-four hours after: Blood pressure, 110; rectal temperature 36.5. Animal bled from carotid; coagulation prompt.

EXPERIMENT 2.—Dog; curly, black mongrel; weight, 20 kilograms. Rectal temperature, 39 C. Ether anesthesia, by inhalation. Time, six hours. Ether removed at intervals, and as soon as dog showed evidence of recovery, the anesthetic was again administered. After four hours, the animal showed marked depression. Rectal temperature, 36 C. Respirations weak. Anesthetic removed. After four hours and thirty minutes, slight movements, but no return of consciousness. Reflexes returned. After four hours and forty-five minutes, animal awoke. No activity. Rectal temperature, 35.8 C. After five hours and ten minutes, anesthetic administered. Rectal temperature 35.5

C. Shallow respiration. Five hours and twenty minutes, anesthetic removed. Marked depression. Five hours and fifty minutes, anesthetic administered until sixth hour. Rectal temperature, 35.2 C. Respirations shallow; blanched surface; gums pale; rapid, weak pulse.

Animal put in warm place; twelve hours after the removal of anesthetic, rectal temperature was 36.5 C.

Clinical symptoms of "shock." Refuses to eat; will drink; very listless; extremities cold; weak, with occasional trembling. Again placed under ether. Carotid opened, and secured 850 c.c. of blood, which shows rapid coagulation.

EXPERIMENT 3.—Dog; curly, black; weight, 16.2 kilograms. Anesthesia, chloroform. Five hours. Temperature at the beginning was 38.3 C., by rectum. Blood pressure, 120. In one hour, temperature, 37.2. At the end of four hours temperature was 35. Anesthesia removed. Animal shows no sign of awakening. Four hours and thirty minutes after, temperature, 37. Chloroform was then used. Five hours, temperature 36. The animal was placed in a warm location. Twenty-four hours afterward temperature was 36.5. Refused to eat; marked depression; blood pressure, 90. The animal was bled; recovered 550 c.c. of blood. Coagulation prompt.

EXPERIMENT 4.—Dog; mongrel bull terrier. Ether. Weight, 18.5 kilograms. Blood pressure, 150. Temperature, 38.6, rectum. At the end of two hours, the blood pressure was 95 to 105. Temperature, 37. Four hours, blood pressure, 78; temperature, 36.1. Animal placed in warm place. Twelve hours after rectal temperature, 36.5; blood pressure, 90-95. Animal bled; recovered 380 c.c. Coagulation prompt.

EXPERIMENT 5.—Dog; black and white, mongrel; weight, 18 kilograms. Blood pressure, 140; temperature, 38.3. Chloroform. At the end of three hours, anesthetic removed; temperature 35.6; blood pressure, 90-100. Twelve hours afterward, temperature 37.5. Blood drawn, 500 c.c.

EXPERIMENT 6.—Dog, mongrel; weight, 17 kilograms. Blood pressure, 130. Temperature, 38. Ether anesthesia. At the end of two hours changed from ether to chloroform. Pressure, 100. Three hours, pressure, 80. Anesthetic removed. Twelve hours afterward, removed 600 c.c.

EXPERIMENT 7.—Dog. Chloroform anesthesia, two hours. Blood removed at once after the anesthesia. Recovered 650 c.c. Coagulation prompt.

EXPERIMENT 8.—Dog, mongrel pointer; weight, 12.5 kilograms. Blood pressure, 130-140. Temperature, 38.5. At the end of four hours, blood pressure, 60-70. Anesthetic removed. Twenty-four hours, blood pressure 100-110; temperature, 37.2. Animal bled; 550 c.c. Coagulation prompt.

EXPERIMENT 9.—Dog, black setter; weight, 15 kilograms. Anesthesia, chloroform; two hours. Temperature, 38.5; at the end of two hours, 36. Removal of anesthesia one hour afterward; animal bled; 600 c.c. Coagulation.

EXPERIMENT 10.—Dog, white and black mongrel; weight, 9.5 kilograms. Temperature, 38. Animal under anesthesia three hours. Temperature, at the end of this time, 36.1. Twenty-four hours afterward temperature 37.2; 600 cubic centimeters.

EXPERIMENT 11.—Dog. Anesthesia, chloroform; two hours. Temperature, 38.4. At the end of four hours, temperature 35.5. Blood removed the following day. Coagulation.

EXPERIMENT 12.—Dog, black and tan; weight, 6.8 kilograms. Ether, one hour. Temperature at the beginning, 39, and at the end of one hour, 37.7. Removed blood five hours afterwards. Coagulation not prompt.

EXPERIMENT 13.—Dog; weight, 15 kilograms; temperature, 38. Normal blood pressure taken at 11:20. Injection of blood serum from animal that had been five hours under anesthesia. Blood was removed one hour after the end of anesthesia: Injected into jugular vein, 11:20, 25 c.c. serum; 11:30, 15 c.c. serum; 11:35, 20 c.c. serum; 11:45, 25 c.c. serum. At 12 o'clock the temperature was 36.1; 12:20, 35. No marked fall in blood pressure; 12:30, 33.4; tongue pale; surface cold; marked twitching; 1:15, temperature inside the tissues, 33.2. Blood withdrawn, 700 c.c. Coagulated at once.

EXPERIMENT 14.—Dog, mongrel pointer; weight, 17 kilograms; 4 p. m., blood pressure, 140-145. Kymographic tracings.

Anesthesia, chloroform. Injected serum from dog, removed twenty-four hours after anesthesia, which had been continued for six hours. Twenty minutes after this injected 25 c.c. of serum. 4:30 p. m., 50 c.c. of serum injected. Blood pressure, 110; 25 c.c. injected; blood pressure, 80. At 6:05 p. m., 30 c.c. injected; pressure, 57-60. Chloroform anesthesia changed to ether; blood pressure rose 20 mm. Again dropped to 50. Anesthetic was withdrawn, aseptic dressings applied, and dog put in a warm place. Result, death in six hours.

EXPERIMENT 15.—Dog, black and white mongrel; weight, 17 kilograms. One grain of morphine injected at 10 a. m.; 10:45, ether anesthesia. Normal record. Injected into jugular serum taken from a dog twelve hours after anesthesia which had lasted four hours. Rectal temperature, 39; 11 a. m., injected 10 c.c. of serum; 11:10, 20 c.c.; 11:20, 15 c.c.; 11:25, 10 c.c.; 11:30, 30 c.c.; 11:35, 30 c.c. Total amount of serum, 105 c.c. Temperature, 35.2. No marked fall in blood pressure. Changed anesthesia to chloroform, with a marked fall in blood pressure.

EXPERIMENT 16.—Mongrel, placed under ether anesthesia; pressure, 140; kymographic tracings. Ether. Temperature, 41. Injected 90 c.c. serum from dog which had been under anesthesia for five hours. The serum had been removed the following day. Blood pressure fell 80 to 70; forty-five minutes, temperature 36 C. Coagulation marked, interfering with further blood pressure records. Anesthesia removed; animal placed in warm location; temperature following day, 37 C. After three days, animal still showed symptoms of shock. Died on the third day. Post-mortem revealed no evidence of infection. Cultures negative.

EXPERIMENT 17.—Small black and tan under chloroform. Blood pressure, 130. Serum used from a dog which had been under anesthesia five hours, and bled the following day; 25 c.c. of serum injected. Fifteen minutes, pressure fell to 115; twenty minutes, 110; thirty minutes, 95; in one hour, 25 c.c. serum injected. Blood pressure, 15 minutes, following the last injection, 65-70. Wide excursion. Anesthesia removed. Animal died the following day.

EXPERIMENT 18.—Mongrel bull. Ether anesthesia. Blood pressure, 150. Serum from an animal that had been under ether for four hours. The animal had been bled immediately after removal of anesthetic. Injections of 22 c.c., followed by another injection of 22 c.c. No effect on blood pressure, 20 c.c.; no effect on blood pressure, 20 c.c.; pressure, 100. In one hour, pressure 85. Anesthetic withdrawn, and animal recovered.

EXPERIMENT 19.—Dog, mongrel; weight, 15 kilograms; blood pressure, 130; temperature, 29 C. Serum used, removed the following day from an animal that had been three hours under anesthesia. 80 c.c. injected. After a period of fifteen minutes, pressure 90-100. One hour and fifteen minutes, pressure ranged from 90 to 100. Temperature, 38. Animal recovered. The following day the temperature, 39.4.

EXPERIMENT 20.—Dog, mongrel. Serum taken five hours after ether anesthesia, which had continued for two hours. Blood pressure, 135; after injection of 90 c.c., blood pressure, 100. Anesthesia changed to chloroform. Blood pressure, 90. Ether again administered, pressure 110. Ninety minutes, pressure 90-95. The following day the animal bled; removal of blood, 550 c.c.

EXPERIMENT 21.—Fox terrier; female. Temperature, 39.4. Injection of serum taken from dog twelve hours after two hours' anesthesia; 16 c.c. injected, with a fall of blood pressure, followed by a chill as soon as the anesthetic was removed. At the end of one hour temperature was 37.3; one and three-quarter hours after, 37.2. Animal placed near a warm room, and continued in a condition of shock, and died six hours afterwards.

EXPERIMENT 22.—Dog, yellow; temperature, 38.8. Injected serum from an animal six hours under anesthesia. Temperature, 38.3. Amount injected, 25 c.c. and 20 c.c. Temperature went down to 37.2. The following day rectal temperature 38.3. Animal listless; can not be aroused, and lips appear pale; marked loss of sensation. Second day, temperature 39.5. Animal depressed; marked loss of appetite. Fourth day, animal bled; shows rapid coagulation and laking.

THE HEMOLYTIC EFFECT, AGGLUTINATION AND PRECIPITINS OF BLOOD SERUM FROM ANIMALS AFTER PROLONGED ANESTHESIA.

EXPERIMENT 23.—Dog. After five hours' anesthesia blood was taken from the carotid; shock evident from low blood pressure; temperature 97; shallow respiration; collapse imminent fifteen minutes after the removal of anesthesia. Blood shows a tendency to lake, with almost immediate coagulation. Blood placed in refrigerator for twelve hours, obtained 110 c.c. of serum; hemoglobin (Fleischl), 10 per cent. One measure of Fleischl (7.65) added to fresh blood centrifuged showed twenty to thirty per cent. hemoglobin. The addition of 5 c.c. to 1 c.c. of fresh blood hemolysis within five minutes well marked, with "ghosts" floating in the serum. One-half c.c. of fresh blood, with 5 c.c. of serum, diluted two volumes with normal salt, hemolysis shown within five minutes. Four c.c. of serum added to 5 c.c. of blood showed immediate laking.

EXPERIMENT 24.—Dog, female pointer; weight 18 kilograms. Five hours under chloroform. Anesthesia removed, and animal allowed to recover from the anesthesia. Five hours later blood removed, 160 c.c. of serum obtained after standing eleven hours. Serum tinged, showing 8 to 10 per cent. hemoglobin. By adding fresh blood serum, 20 to 30 per cent. hemoglobin after centrifuging. One c.c. of fresh blood, 5 c.c. of blood serum, immediate laking; incubator five hours, marked hemolysis; hemoglobin (Fleischl) 100 per cent.

Microscopic slide with serum taken from dog under anesthesia, one drop of normal blood, showed shadow corpuscles.

EXPERIMENT 25.—Bull pup, female; weight 20 kilograms. Blood pressure taken with kynograph; injected 90 c.c. of blood serum taken from an animal that had been under anesthesia for five hours. This animal was placed under anesthesia for one hour only, and injected; no marked fall in blood pressure. At the end of one hour blood was withdrawn and obtained 80 c.c. of serum. One drop of normal blood with 5 c.c. of serum, showed hemolysis within five minutes. Equal quantities of blood and serum showed marked laking. One drop of normal blood irrigated under slide with serum placed in incubator showed shadow corpuscles. Blood serum, to which is added fresh blood (7.65 c.c.), increased the hemoglobin from 15 to 20 per cent. after centrifuge.

EXPERIMENT 26.—Dog. Under anesthesia two hours. Withdrew serum and blood, and after twelve hours serum clear. Adding one drop of normal blood does not produce any marked discoloration after centrifuging, only slight discoloration. Equal parts of normal blood serum produced slight laking. Irrigating one drop under microscope; after thirty minutes in incubator clumping is observed; no marked ghost or shadow corpuscle.

Serum taken from a dog that had been under chloroform for three hours; one drop of normal blood mixed with serum from an animal that had been under chloroform showed immediate clumping. Coagulation took place within five minutes, with 1 c.c. of blood added to 5 c.c. of serum.

Animal six hours under anesthesia; ether used; serum obtained the following day. Added normal blood to such serum produced immediate coagulation. Adding one drop of normal blood produces immediate clumping. Fourth dilution with normal salt solution, 10 c.c.; added 1 c.c. of normal blood, coagulation with laking.

One drop of normal blood added to 5 c.c. of serum after four hours' anesthesia. Equal parts of blood with serum obtained during profound narcosis after four hours.

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ANTITOXIN AND THE PHARMACOPEIA.

PLEA FOR THE ADOPTION OF A TEST WHICH IN THE AUTHOR'S EXPERIENCE PRESENTS THE LEAST DIFFICULTIES.

WILLIAM R. HUBBERT, B.S., M.D.

DETROIT.

The proposed admission into the Pharmacopeia of antitoxin for diphtheria in accordance with the resolutions of the committee appointed to confer on the subject, means, if finally admitted, the necessary adoption of a suitable standard for testing which shall be at once comprehensive, and yet so simple, to use the trite expression with reference to the introduction of tests into that most important work, one "that any intelligent pharmacist may be able to apply." While I am much in favor of the recognition by the Pharmacopeia which this most important biologic product rightly deserves, I am in favor of the adoption of the simplest test which shall show not only the number of units present in any bulb of serum, but one which can be performed within the shortest possible time in any pharmacy in the land and by a person not necessarily experienced in biological work.

There is so little known on this subject of testing antitoxin, outside of a few laboratories in the land, that it is necessary to describe in detail the methods used in testing before one can take up the consideration of the simplest method. Down to a comparatively recent time it was supposed that if a definite amount of serum had neutralized a hundred least fatal doses of toxin, which least fatal dose had been determined by injecting varying amounts of the filtered toxic solution in which the diphtheria germs had been grown, into 250 gram guinea-pigs, it was supposed that a like amount of the same antitoxin would always neutralize 100 least fatal doses of toxin from whatever source the toxin was obtained. Accordingly, Ehrlich defined a unit of antitoxin to be the least amount of antitoxin which would neutralize a hundred minimal fatal doses of diphtheria toxin. This definition remained the accepted one for some little time and either 10 or 100 m.f.d. were used in testing antitoxin the world over; but Ehrlich found by testing a number of different toxins obtained from different sources, either grown from the same or from different cultures, or using old toxins in comparison with new ones, that there was a vast discrepancy in the re-