ACETONURIA

ITS RELATION TO POSTOPERATIVE VOMITING IN SEVEN
HUNDRED CASES OF ETHER ANESTHESIA *

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In 1907, a patient on whom I had operated for acute appendicitis with abscess, eighteen hours after operation developed great restlessness, vomiting, convulsions and coma. She was treated by injection of normal salt solution by rectum and intravenously, hot packs and stimulation; and fortunately she recovered. Although not recognized at the time, the condition was later thought to be due to acid intoxication, but no examination of the urine for acetone or diacetic acid was made. About a year later two other cases of this kind occurred among Dr. F. F. Simpson's patients, and in these acetone was present after operation. Both of these patients recovered under similar treatment except that sodium bicarbonate was given by bowel. Ether was the anesthetic used in all three cases.

These cases led Dr. Simpson to have the urine examined for acetone and diacetic acid both before and after operation. Since this routine examination has been made no further serious cases of acid intoxication have occurred in Dr. Simpson's service at the Allegheny General Hospital. Much has been written on this subject since that time, and there seems to be some difference of opinion in regard to the significance of postoperative acetonuria. For example:

Rice¹ in 1908 found acetone in the urine of 90 per cent. of 202 cases reported, but in only 10 per cent. of these were there any symptoms attributable to it, and at about the same time Wallace and Gillespie² reported a very marked decrease in the secondary vomiting when the percentage of acetone cases was diminished.

In order to ascertain whether in our experience at the Allegheny General Hospital there is any connection between the ordinary postoperative vomiting and acetonuria this series of cases has been collected. It includes about an average of abdominal operations, pelvic operations of all kinds, appendix, gall-bladder, kidney cases and a few plastic and rectal cases. Only those cases having a complete record both before and after operation were included. This practically limited the cases to abdominal sections as only in these was there an accurate record of the postoperative vomiting. Each patient had a special nurse day and night for forty-eight hours after operation.

Any patient who vomited at any time during the forty-eight hours was included in the postoperative vomiting class. In practically all cases, the ether was given by the open drop method, by Dr. W. C. Maxwell, an expert.

The urine was tested usually the day before operation, and after the operation a specimen of the first urine voided was tested and later the complete twenty-four hour specimen. In no case was diacetic acid found without acetone and, although not tested for in about 25 per cent. of cases, it was thought safe to consider those without acetone negative for diacetic acid also. This agrees with the experience of Rice and others.

LEGAL'S QUALITATIVE TEST FOR ACETONE

Take 1½ inches of urine in a tube with about 1/15 as much acetic acid. Then add about 8 or 10 drops of freshly prepared sodium nitroprussid solution, shake well and add ammonium hydroxid. A purple color indicates acetone.

QUANTITATIVE TEST FOR ACETONE

Distil 100 c.c. of urine for about fifteen minutes, allowing the distillate to pass through a cooling box over into a flask containing distilled water. Be sure to have end of tube, running from flask of urine through cooling box to flask containing distilled water, immersed. Then take the flask of distilled water and distillate and add iodine solution (iodine sol. n/10 12.085 c.c., KI 25.37 gm., aqua dest. q.s. 1,000 c.c.) 10, 15 or even up to 50 c.c.; be guided in amount by the color reaction in qualitative test. Then add concentrated sodium hydroxid solution (U. S. P.) until color disappears, followed by concentrated hydrochloric acid until color reappears; then add a few drops of boiled starch as an indicator. Then titrate with sodium thiosulphate solution (sodium thiosulphate sol. n/10 24.8 c.c., aqua dest. q.s. 1,000 c.c.); take reading when blue color disappears, after which multiply the reading by 0.0967 to give amount of acetone in 1,000 c.c. of urine.

GERHARDT'S DIACETIC ACID TEST

Take 1½ inches of urine plus 10 drops of tincture ferric chlorid, shake and if a reddish brown color is obtained, take another specimen of urine and boil, then again add 10 drops of tincture ferric chlorid and if a yellowish-brown color still appears, diacetic acid is positive; if a yellowish-brown color, diacetic is negative.

VOMITING

In Table 1 is shown the average vomiting in all cases and the influence of acetone, and acetone and diacetic acid both before and after operation.

TABLE 1.—SHOWING THE VOMITING IN ALL CASES AND
THE RELATION TO VOMITING OF ACETONE AND
DIACETIC ACID BEFORE AND AFTER
OPERATION

	Numbers	Per Cent.	No Vomiting		Vomited.		Number of Times Vomiting Occurred	Onset of Vomiting After Anesthesia in Hours	Duration of Vomiting from Anesthesia in Hours
			Number	Per Cent.	Number	Per Cent.			
Av. for all cases..	700		105	15.00	595	85.00	6.44	6.02	27.03
BEFORE OPERATION									
No acetone	588	84.00	90	18.85	498	84.69	6.27	4.85	25.90
Acetone present ..	100	14.29	15	15.00	85	85.00	6.9	11.1	31.74
Acetone and diacetic acid present	12	1.71	0	0	12	100.00	7.2	4.5	28.5
AFTER OPERATION									
No acetone	151	21.55	32	21.19	119	78.81	5.14	5.01	20.32
Acetone present ..	332	56.00	51	13.3	341	86.7	6.70	6.05	30.9
Acetone and diacetic acid present	157	22.45	22	14.00	135	86.00	6.7	6.02	25.88

It was found that 85 per cent. of all patients vomited at least once, some time during the first forty-eight hours; the average number of times vomiting occurred was 6.44, the onset 6.02 hours, and the duration 27.63 hours after operation.

BEFORE OPERATION

In those without acetone the proportion vomiting was practically the same as the average, and the severity but slightly less.

Those with acetone present were slightly above the average in all respects but the difference is again not marked. Only twelve of the 700 patients had both acetone and diacetic acid. These all vomited after anesthesia, slightly more than the average but the duration was not so great as those with acetone alone. These are too few in number to enable us to draw any conclusions.

AFTER OPERATION

Acetone or both acetone and diacetic acid were found in 549, or 86.45 per cent, of all cases. This practically agrees with the findings of Rice,¹ previously quoted.

* Read in the Section on Obstetrics and Gynecology of the American Medical Association, at its Sixty-Third Annual Session, held at Atlantic City, June, 1912.

1. Rice: Boston Med. and Surg. Jour., clix, No. 2, p. 48.

2. Wallace and Gillespie: Lancet, London, 1908, ii, 1665.

In the 21.5 per cent. without acetone the vomiting was less frequent than the average, practically 79 per cent. as compared with 85 per cent. On referring to Table 1 it is seen that the vomiting was less frequent and less severe in those without acetone than in those with acetone or with both acetone and diacetic acid.

TABLE 2.—SHOWING THE PERCENTAGE OF POSTOPERATIVE ACETONURIA IN THE NON-VOMITING AND VOMITING CASES

	Total Cases		No Acetone or Diacetic Acid		Acetone		Acetone and Diacetic Acid	
	Number	Per Cent.	Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
No vomiting	700	100	151	21.55	392	56.00	157	22.45
Vomited	105	15	32	30.48	51	48.57	22	20.95
	595	85	119	20.00	341	57.31	135	22.60

Table 2 shows the proportion of acetone and diacetic acid after operation among those who did not vomit and those who did. Among the former 30 per cent. were free from acetone and in the latter, or those who did vomit only 20 per cent were free from acetone. This would seem to show that the presence of acetone or of acetone and diacetic acid either before or after operation increased to some extent not only the liability to post-operative vomiting, but also the duration and severity.

We were not able to determine any relation between the amount of acetone present and the severity of the vomiting. Not all the patients had a quantitative test made. One patient with 0.899 gm. acetone per 1,000 c.c. of urine, the greatest amount found, and diacetic acid, also, did not vomit at all.

As I have already stated, there were no cases of acid intoxication among those patients. In order to determine whether there was any connection between the more severe cases of vomiting and the presence of acetonuria, I collected the cases in which the vomiting lasted more than twenty-four hours after operation. This is shown in Table 3. In a total of 285 cases the

TABLE 3.—SHOWING THE RELATION BETWEEN DURATION OF VOMITING, IN PROTRACTED CASES, AND ACETONURIA, AND ALSO THE RELATION WHEN THE ONSET OF VOMITING IS LATE

	Number	No Acetone or Diacetic Acid		Acetone		Acetone and Diacetic Acid	
		Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
Total	700	151	21.55	392	56.00	157	22.45
Vomiting lasting more than twenty-four hours	285	41	14.38	183	64.21	61	21.41
Onset of vomiting more than twelve hours after operation	79	22	27.85	40	50.63	17	21.52

proportion of those free from acetone is below the average. On the other hand in those patients in whom the vomiting began late, in 79, more than twelve hours after operation, those free from acetone were in greater proportion than the average. This would seem to indicate that when vomiting does occur it is liable to be more prolonged when acetone is found in the urine.

CAUSES OF POSTOPERATIVE ACETONURIA

In order to determine whether there was any relation between the length of anesthesia, or the amount of ether, and the acetonuria, I divided these cases into half hour periods (Table 4). In a general way, there was a gradual

TABLE 4.—DURATION OF ANESTHESIA IN RELATION TO ACETONE AND DIACETIC ACID *

	Total	No Acetone or Diacetic Acid		Acetone		Diacetic Acid and Acetone	
		Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
All cases	700	151	21.57	392	56.00	157	22.43
30 min. or less; average 24.5 min.; 3.4 oz.	67	7	10.45	41	61.19	19	28.36
31 to 60 min.; average 48.4 min.; 5.57 oz.	326	57	17.48	195	59.81	74	22.7
61 to 90 min.; average 73.5; 7.85 oz.	189	48	25.39	107	56.61	34	18.5
Over 90 min.; average 98.6; 9.12 oz.	36	7	19.44	10	44.44	13	36.11

* Record of anesthesia incomplete in eighty-two cases.

increase in the number of cases free from acetone as the length of anesthesia and the amount of ether increased.

We are forced, therefore, to look for some cause for acetonuria outside of the anesthetic itself. Ewing³ in 1908 showed that acetone compounds are "derived mainly from the fat tissues and to a less extent from the food," and "that the complete combustion of fats requires the simultaneous katabolism of carbohydrates, in the absence of which there is a defective and possibly abnormal course of fat combustion lodging in the acetone compounds." Frew⁴ has more recently emphasized the importance of carbohydrate starvation.

In the preparation of patients for operation, it is our custom in Dr. Simpson's service at the Allegheny General Hospital to put them on liquid diet for the entire day before operation and this includes practically no carbohydrates, the diet consisting of broths and milk entirely. They are also given a purge of castor oil or more recently compound cathartic pills. It would seem that possibly this starvation, particularly of carbohydrates, caused a disturbance of the metabolism of the fats with the production of acetonuria.

Waugh⁵ in the discussion of Frew's paper says that he has abandoned the pre-anesthetic purge and restriction of diet. He reports over 2,000 chloroform anesthetics in children without a single case of acid intoxication.

In order to overcome this carbohydrate starvation, for a time glucose was given before operation but no decided difference was noticed in the post-operative vomiting. The majority of the patients objected strongly to the glucose when given by mouth and it was impossible to give it by rectum on account of the purge, so that this was abandoned.

DURATION OF ANESTHESIA IN RELATION TO VOMITING

This is shown in Table 5. There is a gradual increase in the percentage of those who vomited as the duration of anesthesia increases. This difference is not great but is definite and uniform and would seem to show that the longer the anesthesia the greater the liability that vomiting will follow it.

3. Ewing: Arch. Int. Med., 1908, II, 330, 448.

4. Frew: Proc. Royal Soc. Med., 1912, v, No. 5, p. 60.

5. Waugh: Proc. Royal Soc. Med., 1912, v, No. 5, p. 73.

TABLE 5.—DURATION OF ANESTHESIA IN RELATION TO VOMITING

	Total	No Vomiting		Vomited	
		Number	Per Cent.	Number	Per Cent.
30 minutes or less.....	700	105	15.00	595	85.00
31 to 60 minutes.....	67	13	19.4	54	80.6
61 to 90 minutes.....	326	47	14.42	279	85.58
Over 90 minutes.....	189	22	11.65	167	88.35
	36	4	11.11	32	88.89

TREATMENT

As acetoneuria seems to be due to carbohydrate starvation it would seem that patients should have this form of food before operation. Glucose was not satisfactory and the other forms of carbohydrates have not been tried on account of the liability of forming gas in the intestine. In a large proportion of abdominal cases it is necessary to pack off the field of operation and this is impossible unless the intestine is empty.

For the acetoneuria itself large doses of alkalis, sodium bicarbonate, by bowel, by mouth if possible, or lavage with sodium bicarbonate solution, seems to be rational and in this series of cases has been of undoubted value in many cases.

CONCLUSIONS

1. Vomiting occurs in a large percentage of cases after anesthesia.
2. The liability to vomiting is increased when acetone is found in the urine.
3. Protracted vomiting is best treated by sodium bicarbonate by bowel and by lavage. These patients need careful watching on account of the liability of acid intoxication.
4. Acetoneuria is due to faulty metabolism and increased by carbohydrate starvation.
5. Acetoneuria has no relation to the length of anesthesia.
6. The duration of anesthesia has only a slight influence on vomiting.

I want to express to Dr. F. F. Simpson my appreciation of his kindness in permitting me to review these cases, the great majority of which were his, only a few of them being my own, the laboratory work was done under his direction.

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ABSTRACT OF DISCUSSION

DR. JOHN M. SWAN, Rochester, N. Y.: The conclusions reached by Dr. Chalfant seem to me to point to disturbed metabolism as the cause of the acetoneuria after anesthesia. It would be interesting if Dr. Chalfant could tell us whether the patients who had acetoneuria after operation were the same ones who showed an increase in acetone before operation. I am inclined to think that such a study would show that the patients with excess of acetone before operation would have an excess afterward, and that the vomiting would be more troublesome in such cases than in patients with no acetoneuria before operation and little afterward. The method by which Dr. Sutter determined the amount of acetone in the urine of the patients just referred to is as follows: The twenty-four-hour specimen was measured, and 250 c.c. were distilled until the distillate amounted to 50 or 70 c.c., which would represent all the acetone in that urine. The distillate was put into a graduated cylinder and treated with Lugol's solution three times the ordinary strength. The iodoform produced by the action of Lugol's solution on the acetone in the distillate was dissolved with ether. The total amount of ethereal extract was measured and 10 c.c. of that extract were evaporated to

dryness in a weighed glass dish. From the weight of the iodoform in the 10 c.c. of ethereal extract the amount in the entire ethereal extract was calculated, and this was expressed as acetone.

DR. S. A. CHALFANT, Pittsburgh: Of the patients who had acetoneuria before operation, the proportion not vomiting is shown to be 15 per cent., which is the same as the 15 per cent. of all cases, so that the influence of acetone before operation did not seem to be very important.

TREATMENT OF TUBAL PREGNANCY

WITH SPECIAL REFERENCE TO IMMEDIATE OPERATION
FOR RUPTURE, BASED ON A STUDY OF
TWO HUNDRED OPERATIONS * †

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Gynecologists are agreed as to the necessity of immediate operation in unruptured tubal pregnancy; it is in the ruptured variety that opinions differ with regard to the indication for immediate operation.

While I have always maintained that tubal pregnancy is a surgical disease, requiring surgical intervention as soon as possible, I have never insisted, and do not now, that an unruptured tubal pregnancy must be rushed to operation; on the contrary, there is no particular danger or risk to the patient if, for some good reason, the operation is postponed for a short time, provided, however, that the patient is kept under close observation and is so situated that an operation can be performed at once in the event of rupture. On the other hand, it is in ruptured tubal pregnancy, especially when it is accompanied by shock and collapse, that I advocate and urge the immediate operation.

My object in presenting this paper is to offer an earnest plea for the general recognition by abdominal surgeons of the dictum that hemorrhage into the peritoneal cavity must be sought for and checked as soon as diagnosed; and that opening the abdomen of a patient profoundly shocked and anemic from abortion or rupture of a tubal pregnancy does not *per se* offer any graver risk than opening the abdomen for any other intra-abdominal condition; and, furthermore, that delay in operating, no matter how slight, means increased risk, greater danger and probably death to the patient. This plea is based on a study of 200 operative cases.†

That patients do die of hemorrhage, the result of ruptured tubal pregnancy or abortion, will be seen from the following case, which is reported in detail:

CASE 1.—*Patient*.—B. F., aged 28, called at my office with Dr. M. J. Katz, July 8, 1911. Patient had been married seven years and had three children; the last child was 9 months old; she was still nursing. She did not menstruate for four months subsequent to her delivery, and, after menstruating twice, had amenorrhea for two months. Then for six weeks she had irregular uterine bleeding and pain in lower abdomen.

Examination.—She was examined at a clinic on the previous day and a diagnosis of "tumor" was made. The patient was well nourished and in good physical condition. Her pulse was normal and strong. On vaginal examination I felt a large,

* Read in the Section on Obstetrics and Gynecology of the American Medical Association, at its Sixty-Third Annual Session, held at Atlantic City, June, 1912.

† Because of lack of space this article is abbreviated by the omission of the table of cases. The complete article appears in the Transactions of the Section and in the author's reprints.