ACETONURIA AND ITS RELATION TO DIABETIC COMA.

BY

SAMUEL WEST, M.D.

Received October 16th—Read November 27th, 1888.

THE discovery by Gerhardt of a body in diabetic urine, giving a peculiar reaction with perchloride of iron, which was at first regarded as ethyl diacetate but later as diacetic acid, and the detection of acetone subsequently by Petters in the urine, blood, and breath of diabetic patients, when taken together with the ease with which acetone may be derived from diacetic acid or ethyl diacetate, led to the ready adoption of the belief that the symptoms of diabetic coma were due to poisoning by acetone, and the name acetonæmia passed almost at once into common use. But more than a grave doubt now exists whether both these bodies are not rather the accidental concomitants than the essential causes of the comatose condition.

The relation of acetonæmia and acetonuria to diabetic coma has been investigated on the one hand by experimental intoxication with acetone, and on the other by clinical observations. This paper is a contribution to the clinical side of the problem. I desire to acknowledge the valuable assistance I received from Dr. Mary Goodman at the Royal Free Hospital, without whose co-operation so

extended a series of observations would not have been carried out.

The results of experiment go very far to disprove the theory, and though, as would be expected in so difficult an inquiry, the conclusions of different observers do not agree in all particulars, still the balance of evidence inclines strongly against it.

Petters and Rufstein, by the injection of acetone, produced in dogs symptoms which they regarded as similar to those of diabetic coma, but Fleischer, Kussmaul, Reinecke, and others showed that to produce these symptoms more acetone was required in the blood than had ever been found in diabetes, and they were also of opinion that the symptoms obtained differed materially from those of diabetic coma.

Frerichs and Le Nobel failed entirely to produce the toxic effects required with acetone, diacetic ether, or diacetic acid.

Albertoni¹ conducted a most elaborate series of experiments, and found that in dogs it was necessary to administer eight grammes per kilogramme of body weight to produce a fatal result, while four grammes per kilogramme produced only a kind of drunkenness and a delirium similar to that resulting from alcoholic intoxication. Such quantities as these are far in excess of the amounts possible in diabetes. He therefore concludes against acetone as the cause of diabetic coma.

Acetone has been administered also to man, in full doses, as a remedy in phthisis, without any unpleasant symptoms. Frerichs² gave to a man ten to twenty grammes daily, and larger amounts to dogs, without producing any symptoms at all, and Albertoni gave fifteen to twenty grammes with no other symptom than a little drowsiness.

Against these results the objection has been urged that though acetone may fail to produce the required symptoms.

¹ 'Jahresb. d. Ges. Med.,' 1884, p. 243; 'Arch. f. Exper. Path. u. Pharm.,' xviii, 218.

² 'Zeitsch. f. klin. Medic.,' vi, 1.

in *healthy, i. e. non-diabetic* men, it does not necessarily follow that it would fail in diabetics. The experiment has, however, been made, I believe, upon diabetics, and without untoward results.

Frerichs further found that acetone administered to rabbits and dogs was found in the urine, so that it was not destroyed or rendered inert, and as the result of his experimental observations he also concludes against the theory that acetone can be the cause of diabetic coma.

Le Nobel performed similar experiments, though not on so extensive a scale, and arrived at a similar conclusion.

It has also been shown by v. Jaksch¹ that acetone cannot be derived from sugar by alcoholic fermentation, though it may be by lactic acid fermentation. This form of fermentation, it was thought, might take place in the intestines by the action of some special ferment, but experiment with the contents of the intestines in diabetic patients upon the fermentation of sugar showed that *alcohol* was produced, but no acetone.

The different lines of experiment lead to the same conclusion, and are directly opposed to the theory that acetone is the cause of diabetic coma.

The investigation of the question from the clinical side was for a long time rendered difficult by the want of delicate and at the same time reliable tests suitable for bedside use. The most valuable work on this subject has been performed by v. Jaksch,² who in a recent paper has investigated the various reactions and recorded his own clinical observations. It is upon this paper that my own observations have been based.

The tests which he gives are six. They follow in order of delicacy.

1. *Lieber's iodoform test*.—To some cubic centimetres of the destillate of the urine are added a few drops of strong caustic soda and several drops of a solution of

¹ Loc. cit.

² v. Jaksch, 'Ueber Acetonurie u. Diaceturie,' Berlin, 1885.

iodine in iodide of potassium. If acetone be present a precipitate falls, either in the crystalline or the amorphous form. The iodoform can be recognised on drying by the odour and by Vitali's test, *i. e.* a violet colour with a little solid caustic soda and a drop of thymol, the colour on the addition of an acid passing into scarlet.

This is an extremely delicate test, and will detect easily 0.01 milligramme of acetone, or even much less than this, it is stated as little as 0.0001 milligramme.

The objection to it is that other substances also give the reaction, such as alcohol and aldehyde, but of these alcohol alone is likely to be found in the urine. With alcohol, however, the test is not nearly so delicate, and the amount of alcohol in the urine is stated to be small.

2. *Gunning's iodoform test*.—This test consists in the use of ammonia instead of soda or potash and of an alcoholic tincture of iodine instead of the solution of iodine in iodide of potassium.

2 *a.* Le Nobel further modified this by using iodine dissolved in iodide of ammonium. A dark precipitate is obtained of iodide of nitrogen, which when acetone is present is slowly decomposed to form iodoform, the time required depending upon the amount of acetone present.

The disadvantage of the test lies in the black precipitate which forms, but the advantage is that alcohol does not give the reaction, nor, it is stated, does aldehyde. Its delicacy is, however, much less than that of Lieben's test.

3. *Reynolds's test*.—This depends upon the property which acetone has of dissolving freshly precipitated oxide of mercury.

To a strong solution of mercuric chloride is added some of the solution to be tested, and then an excess of caustic soda solution.¹ The yellow mercuric hydrate first precipitated by the alkali redissolves, and an alkaline liquid is obtained which is rich in mercury. If the filtrate be now

¹ v. Jaksch uses an alcoholic solution of caustic soda, as mercuric hydrate is slightly soluble in water, but not at all in alcohol.

rendered acid, mercury can be demonstrated in it by means of sulphide of ammonium.

This reaction will detect 0.01 milligramme of acetone, but acet-aldehyde, v. Jaksch states, will also dissolve mercuric oxide.

If to the acetone-mercuric solution previously obtained some acetic acid be added, until the liquid be faintly acid, a white precipitate is obtained which coagulates on heating like a solution of albumin or white of egg = $(\text{CH}_3\text{COCH}_3)_3\text{HgO}$.¹

If aldehyde be present instead of acetone, the precipitate of mercuric oxide does not redissolve, but on heating it gradually becomes greyish white.

4. *Legal's test*.—If to the urine containing acetone a solution of nitro-prusside of potassium and a little caustic soda be added, a ruby-red colour is obtained, which on the addition of a few drops of acetic acid passes into dark purple. This will detect about 0.5 milligramme of acetone.

5. *Le Nobel's test*.—The same as the preceding, except that ammonia or carbonate of ammonia is used instead of caustic potash. This also gives a violet red colour, which develops more quickly if a little acetic acid be added, provided that the solution still remains alkaline. After about ten minutes the colour fades to yellow. The yellow colour without the previous violet may develop without the presence of acetone.

6. *Penzold's test*.—If to a solution containing acetone some solution of ortho-nitro-benz-aldehyde be added, with some caustic soda, till the reaction be alkaline, the colour becomes at first yellow, and then green, and in about ten minutes indigo blue separates.

This is the least delicate test of them all, for by it only 1.6 milligrammes of acetone can be detected.

As the nitro-prusside test gave such a well-marked colour, I thought some characteristic spectrum might be obtained, but I failed entirely either with acetone solution or

¹ Reynolds's 'Experimental Chemistry—Organic,' p. 106.

with urine containing acetone, with and without the addition of acetic acid.

The two tests which seemed most convenient were the nitro-prusside test in the urine direct, and the iodoform test in the destillate. Although it is stated that the iodoform test may be applied to the urine direct, I have only twice succeeded in obtaining the reaction, and then imperfectly.

The iodoform test is readily given by alcohol and by aldehyde. Alcohol may occur in the urine, but only, it is said, in small amount, and the reaction is much less delicate.

It appeared to me that if in the urine direct the nitro-prusside test was given, and in the destillate the nitro-prusside test and also the iodoform reaction, the conclusion might be safely drawn that acetone was present. It is upon these two tests that I have relied in the following observations.

I did not at the time fully appreciate the delicacy of Reynolds's reaction, or I should have also used this test to confirm the results obtained by the other methods.

Though the special object of my inquiry was to ascertain the relation which existed, if any, between acetonuria and diabetic coma, I at the same time applied the perchloride of iron test, which had also, it was formerly supposed, some relation to the same condition.

Before applying the tests in diabetes, I examined with the same tests the urine of thirty non-diabetic patients taken at random, convalescent from various diseases. In none of them was any iron reaction obtained. With the nitro-prusside test out of the same thirty cases, ten gave no colour reaction at all, fifteen gave a colour but not that characteristic of acetone; it was unaffected by acetic acid in nine, and discharged by it in six. Out of these thirty, three gave an imperfect nitro-prusside reaction; one was a case of cirrhosis of the liver, one a case of chronic rheumatism with slight albuminuria, and the third a case of Jacksonian epilepsy; in this last case the reaction was obtained only on one occasion.

The urine of the cirrhosis case was distilled. In the distillate neither the nitro-prusside nor the iodoform test was successful, but the nitro-prusside reaction was given by the residue in the retort. I have observed the same thing in a few other cases, so that there must be some non-volatile substance capable of giving the reaction, but it is not often met with.

In another series of similar cases taken at random from the wards of St. Bartholomew's Hospital, the iron reaction was absent in all, as was also the true nitro-prusside colour. In twenty-five a reddish-brown colour was obtained with nitro-prusside, but it either became lighter on the addition of acetic acid or faded altogether.

It was clear that acetone was not often found in the urine of healthy persons. Still further investigations showed that acetonuria was not infrequent among non-diabetic patients, while suffering from actual disease.

In non-diabetic patients the reactions indicating the presence of acetone were obtained in the following cases:

	Reaction with perchloride of iron.
In four cases of pneumonia, 12, 12 b, 14, 15	. Present in all four.
In two cases of typhoid fever, 16, 17	. . None.
In one case of gastric ulcer, 24	. . . "
„ cirrhosis hepatis, 25	. . Present.
„ spinal affection in a child, 28	. . . "
„ cerebral hæmorrhage from injury, the patient dying comatose, 11	. . . "
„ delirium tremens, 26	. . . "
And in four cases of rheumatic fever	. . None.

Besides these there were reactions which indicated the possible presence of acetone, but which did not seem to me quite conclusive; in a case of bronchitis (22), in a case of cancer of the liver (26), in a case of pyæmia (27), and in a case of abdominal section (32). In all of these cases except the first, that of bronchitis, the iron reaction was also present.

These cases were all taken more or less at random, and they are sufficient to show that acetonuria is a fairly

common phenomenon of disease in non-diabetic patients, and as only one of them was in a comatose state, it is clear that acetonuria is not necessarily associated with coma. Moreover, it is clear that, in many of them, the acetonuria depended upon the illness for which the patients were under treatment, for on recovery the acetone reactions were no longer obtained (14, 16, 25, 26); but in many of the cases referred to this point was not specially investigated, the observations terminating when the existence of acetonuria had been established.

Another point of interest is the variation in the intensity of the reactions on different days (12 b, 19), variations which stood in no evident relation to any change recognised in the condition of the patient. The iron reaction, though not always present with acetonuria, was still sufficiently often associated with it (eight out of sixteen) to suggest some other than a merely accidental connection between them.

These observations confirm the statements made by other writers. V. Jaksch, who has especially investigated this question, has shown that acetonuria is common in all diseases accompanied with high continuous fever, and he names this febrile acetonuria; and further, that it is also frequent in some forms of cancer, in inanition, and in some of the psychoses. Acetonuria therefore is not peculiar to diabetics, and is not necessarily associated with coma.

Diabetic Cases.

Fourteen cases of diabetes were examined, and two cases of temporary glycosuria, the one in a case of alcoholism, and the other in a case of cirrhosis of the liver. Of these four died comatose (5, 6, 13, 14), and one died of septicæmia; in two of the coma cases (5 and 6) both the iron and the nitro-prusside reactions were well marked in the urine direct, and the nitro-prusside and the iodoform reaction in the destillate. In the third (14) these reactions

were all absent, and in the fourth (13), in which only one determination could be made, neither the iron nor the nitro-prusside reactions were obtained in the urine direct.

In the septicæmic case, the patient dying of *asthenia* and not of coma, all the reactions were well marked.

In the remaining nine cases the acetone reactions were well marked in six, and absent in the three others ; but in two of these only one determination could be made.

Thus acetonuria may be absent in diabetic *coma* and present in diabetics who are *not* comatose.

These general statements, made as the result of comparing these cases broadly with one another, are amply confirmed by daily observation of individual cases. Take, for example, Case 1 (diabetes, doing well). The reactions were at first fair, and gradually increased until they became unusually well marked, the patient being, so far as could be seen, in her usual health. They then became less and less, and after being faint for a day or two again returned to their previous intensity.

The urine in this case was examined on thirty different days almost consecutively. The patient left the hospital much improved in health, and since leaving has been frequently seen, and the urine has presented the same reactions.

In Case 7 similar variations occur. The patient improved greatly under treatment, and towards the end of the time in the hospital the reactions diminished in intensity.

In Case 8 the variations were very well marked. The patient died, but not comatose, and as she grew worse the reactions diminished in intensity.

In Case 13 a woman whom I only saw once as she was dying with panting dyspnoea but not comatose, the urine contained, if any, only the merest trace of acetone, though the room in which she lay, and indeed the whole house, reeked with the odour usually ascribed to acetone.

Case 14 again was under observation for some time, and died comatose, but never had acetonuria at any time.

The facts which the foregoing observations establish are these :

1. Acetonuria is common in diabetics without coma.
2. It is not constantly present in cases of diabetic coma.
3. It varies greatly in the same case from time to time without any evident cause.
4. It stands in no relation to the amount of sugar, but varies independently of variations in the sugar, specific gravity, &c.
5. It may even disappear when coma develops.

The conclusion to be drawn is clear, viz. *that acetonuria does not stand in any definite relation to diabetic coma.*

The Iron Reaction (? Diaceturia).

If the iron reaction and the acetone reaction be compared in the Tables given it will be seen :

1. That the iron reaction is rare except in cases of diabetes.
2. That it may be present when acetone is absent.
3. That it may be absent when acetone is present.
4. That they may be both present or both absent at the same time.
5. That one may be well marked when the other is ill developed.
6. That neither stands in any definite relation to coma.

While the facts just stated make it clear that there can be no necessary or essential relation between the two substances, still they are often enough associated to suggest some indirect connection between them.

Although it is clear that acetonuria is not associated constantly with diabetic coma, still, it might be objected, it is not a safe conclusion to draw that therefore acetone may not be the cause of the coma, for alcohol produces very serious and marked symptoms, and yet but little appears as such in the urine. This objection is answered by the results of experimental intoxication with acetone,

for, as already stated, the symptoms produced are not those of diabetic coma, and also by the fact that acetone administered by the mouth is eliminated as such, *i. e.* unaltered in the urine.

Is then the presence of acetone in the urine of no clinical importance? I do not think so; on the contrary, it seems to me that the presence of *acetone*, and still more of the iron reaction, is a hint that the patient is in a worse condition than when either or both are absent. It may be that the symptoms of poisoning depend upon some defective chemistry in the body, by which a poisonous substance of a nature at present unknown is produced, and that one or other or perhaps both of these substances may be developed as by-products, so that their presence in the urine may be useful as giving a hint of danger, though not as indicating the actual poisonous bodies upon which the symptoms depend. This seems to be especially the case with the iron reaction. Its appearance can be brought about almost at will in any diabetic patient by excitement, worry or fatigue, and how important these conditions are in determining the occurrence of coma is well recognised.

The observations here recorded were made some months ago, but I hesitated to publish them, feeling that the ground had already been covered so much more completely by v. Jaksch and others working in Germany. I hope, however, they may have their use, as they support by clinical observation the more elaborate results obtained in the laboratory, and as they confirm the conclusions at which v. Jaksch had already arrived, that *acetonæmia* or *acetonuria* is a misleading and erroneous term, if used as synonymous with diabetic coma.

CASE 1.—Diabetes, doing well.

Date.	Quantity of urine in ounces.	Sp. gr.	In urine direct.		In distillate.		
			Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Nov. 11	...	...	Good	Good			
12	156	1040	"	"	Good	Good	
13	177	1040	"	"	"	"	
15	226	1036	"	"	"	"	
16	241	1038	"	"	"	"	
17	224	1040	"	"	"	"	A slight trace of albumen.
18	196	1040	Fainter	Fainter	"	"	No albumen.
19	196	1040	Strong	Strong	"	"	
20	184	1040	"	"	Very pronounced		
22	180	1042	Fainter	Fainter	Poor	Poor	No residue when all acetone had been distilled over. No
23	180	1046	Good	Good	Good	Good	reaction was obtained with FeCl ₃ , and
24	...	1024	"	"	"	"	but with N.P., and
25	...	1040	"	"	"	"	excess of strong
26	...	...	"	"	"	"	KHO, a dirty violet was obtained.
27	...	...	Stronger	Stronger	Stronger	Stronger	
28	...	...	Good	Good	Good	Good	
29	...	...	"	"	"	"	
30	...	...	"	"	"	"	
Dec. 1	...	...	Strong	Very strong	Very strong	Very good	
2	...	...	Good	Good	Good	"	
3	...	...	"	Very good	Very good	"	
4	...	...	Fair	Good	Good	Good	
6	...	...	Very good	"	"	"	
7	...	...	Good	"	"	"	Iodoform obtained in urine direct.
8	...	...	Fair	"	"	"	
9	...	...	Good	"	"	"	
10	...	...	Fair	Fair	Fair	Fair	
11	...	...	"	"	"	"	
13	...	...	"	"	"	"	
14	...	...	Poor	"	Good	Good	
15	...	...	"	"	"	"	
23	...	1050	Good	Very good	Very good	Very good	Patient left hospital, but was seen on three occasions subsequently.
Jan. 13	...	1052	Fair	"	"	"	
Mar. 18	...	...	Poor	Fair	"	"	

CASE 2.—Diabetes, with cataract, doing well.

Date.	Quantity of urine in ounces.	Sp. gr.	In urine direct.		In destillate.		
			Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Jan. 20	...	...	Fair	Fair	Good	Good	Urine alkaline.
21	...	...	"	Poor	Fair	Fair	
22	...	...	"	"			
23	...	...	Very good	"	Very poor	Very poor	
24	...	...	Slight	Very poor	Poor	Fair	
25	...	...	Fair	"	Very poor	Very poor	

CASE 3.—Diabetes, doing well.

Date.	In urine direct.		In destillate.		
	Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Feb. 8	0	Poor	0	0	The quantity of water varied from 40-70 oz. Sugar varied from 12-17 grains per oz. Patient had had diabetes once before, and said she was "cured." On her discharge there was only a faint trace of sugar. Her chief complaint was pruritus.
11	0	Fair	Poor	Poor	
12	0	"	Fair	Fair	
15	?	"	?	0	
16	0	"	?	0	
17	0	"	0	0	
18	0	"	Not distilled		
23	0	0	"		
24	0	0	"		
25	0	0	"		
28	?	Fair	"		

CASE 4.—Patient suffering from Cirrhosis of Liver with temporary glycosuria.

Feb. 8	0	Good	?	0	Left hospital with urine free from sugar.
10	...	"	Poor	0	
11	...	Poor	0	0	
15	...	Good			
22	...	Fair	?	Fair	
23	...	Poor	?	?	
Mar. 1	...	Very poor	Very poor	Very poor	
3	...	...	...	...	

CASE 5.—Diabetes, doing well for some time, but dying comatose.

Date.	In urine direct.		In distillate.		
	Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Feb.					
11	Very good	Very good	...	Very good	
12	Fair	Good	...	Good	
14	"	Very good	...	Very good	
15	Good	Very strong	...	"	
16	"	Good	...	"	
17	"	Very good	...	"	
18	Very good	"	...	"	
21	Fair	Good	...	Good	
22	Poor	"	...	Poor	
23	Better	Poor	...	"	
24	Fair	Very good	...	Good	
25	Good	Good	...	"	
28	"	Very good	...	Very good	
Mar.					
1	Very good	Good	...	"	
2	"	Very good	...	"	
3	Good	"	...	"	
4	Fair	Poor	...	"	
5	"	"			
7	"	Good	...	Good	
8	"	Very good	...	"	
10	"	Poor	Poor	Very good	Fits of drowsiness came on, and the patient eventually died comatose.
11	"	Very poor			
14	"	Good			
15	Good	Very good			
16	"	Good	Fair	Very good	
18	Poor	Very good			
20	Good	Good			
28	Fair	Fair			
29	"	"	Very good	Good	

CASE 6.—Diabetic coma; death.

May				
10	Very good	Very good	Very good	Good
11	"	"	"	Very good

CASE 7.—Diabetic coma; child admitted moribund.

	0			
--	---	--	--	--

CASE 8.—Diabetes, gained flesh.

Date.	In urine direct.		In distillate.		
	Iron reaction.	N. P.	N. P.	Iodoform reaction.	
May 11	Very poor	Fair	Good	Very good	Not distilled.
12	"	Good	"	"	
13	"	"	"	"	
14	Poor	"	"	"	
15	"	Fair	"	"	
16	"	Good	Very good	Very good	
17	"	Fair	Poor	Slight	
18	"	Very poor	?	?	
20	"	Good	Very poor	Poor	
21	"	"			
22	Very poor	Fair			
23	Very good	Good			
24	0	Poor			
25	0	Very poor			
26	0	"			
27	Very poor	"			
28	Poor	Poor			
29	"	Very poor			
30	"	"			
June 1	"	"			
3	"	Poor			
5	Very poor	Very poor			
7	0	0			
Feb. 29, 1888	0	0	...	...	

CASE 9.—Septicæmia in coma of Diabetes; death.

May 7	0	0	0	0	
9	Very poor	?	0	0	
10	Poor	Very poor	0	0	
16	0	Fair			
18	0	Poor			
20	Poor	Good	Poor	Poor	
21	Fair	"			
25	Good	Very good			
26	Fair	Good			
27	Poor	Very good	Very good	Good	
28	Fair	Good			
29	"	"			
31	Poor	Poor			
June 2	"	"			
5	"	"			
7	Very poor	Very poor			

CASE 10.—Diabetes, doing well.

Date.	In urine direct.		In distillate.	
	Iron reaction.	N. P.	N. P.	Iodoform reaction.
Nov. 29	0	Good	0	0
30	0	Very good	Fair	Fair
Dec. 10	0	Good	"	"
14	0	"	Faint	"
Feb. 8	0	Very good	Poor	?
10	Good	"	Good	Good

CASE 11.—Dying comatose from Fractured Skull.

Dec. 4	Fair	Good	Fair	Good
6	"	"	"	"
7	"	"	"	"
8	"	"	"	"
9	Slight	"	Good	"
11	Poor	"	Very good	"
13	"	"	"	"
15	Good	Very good	"	"
16	Poor	Fair	Poor	Poor
17	Fair	Good	Good	Good
20	?	Poor	Poor	Very poor
22	?	Fair	Very poor	"
23	...	...	0	0
24	...	Fair	0	0

CASE 12.—Broncho-pneumonia.

Jan. 13	Very good	Very good	Very good	Very good	Urea 1.6 %. Urea 2.0 % Sp. gr. 1025.
14	"	"	"	"	
15	Fair	"	"	"	
17	Good	"	Fair	"	
18	"	Fair	Good	"	
19	Fair	Very good	Very good	"	
20	"	Good	"	"	
21	"	Fair	Fair	Fair	
22	"	Good	"	"	
24	Slight	Fair	Poor	Poor	
25	?	Poor	?	0	
26	0	"	0	0	

CASE 12 b.—Child with Broncho-pneumonia and Measles.

Date.	In urine direct.		In distillate.		
	Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Feb. 15	Very good	Very good	Very good	Very good	
17	"	"	"	Fair	
18	"	"	"	"	
21	"	"	"	"	
22	Fair	Good	"	"	
23	"	Poor	0	0	
25	Very good	?			
Mar. 2	"	0			

CASE 13.—Pneumonia; death.

Apr. 19	Slight	Good	0	Good	
20	"	"	0	Fair	

CASE 14.—Pneumonia.

Feb. 24	Poor	Good	Very good	Good	
25	"	"	Fair	Very good	
28	"	Fair	"	Poor	
Mar. 1	Fair	Good	Poor	Fair	
2	Poor	Fair	"	Poor	
3	"	Poor	"	"	
4	...	...	...	...	Temp. normal; urine alkaline.
5	Poor	Poor	0	0	
12	0	0			
25	Poor	?			

CASE 15.—Traumatic Pneumonia.

Mar. 4	Fair	Very good	Good	Fair	High temp.; recovery.
--------	------	-----------	------	------	-----------------------

CASE 16.—Typhoid Fever in child of 14.

Jan. 11	0	Good	Faint	Very good	Urea 4 %
12	?	Very good	Good	"	" 4.4
13	Slight	Good	Fair	Good	" 3.3
14	"	Very good	"	Very good	" 3.5
15	"	Good	"	Fair	" 3.0
18	"	Poor	Poor	"	" 3.8
19	"	Good	"	"	" 4.0
24	0	Poor	?	?	" 4.0

Urine scanty, 13—
16 oz. in 24 hours.
Sp.gr. 1025—1030.

CASE 17.—Typhoid.

Date.	In urine direct.		In destillate.		
	Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Apr. 25	Poor	Good	Very good	Very good	Temp. 101°.

CASE 18.—Acute Rheumatism.

Mar. 2	Good	Very good	Poor	Poor	Temp. 101°.
3	Sod. Salicyl.	Good	Good	"	Temp. normal.
8	Poor	Fair	Fair	0	

CASE 19.—Acute Rheumatism.

Mar. 4	Poor	Good	Fair	Poor	Temp. 102°.
5	Sod. salicyl.	Fair	Good	Good	
7	"	"	Fair	Fair	
8	"	"	Very poor	0	
10	Good	Very good	Poor	Poor	Temp. normal.
11	0	Good	...	...	
14	0	Fair			
25	Good	Good			
Apr. 24	0	?			

CASE 20.—Acute Rheumatism.

Mar. 18	Sod. salicyl.	Very good	Poor	Slight	Temp. 103°.
22	"	Good			Temp. 101°.
25	"	Very good	...	...	

CASE 21.—Acute Rheumatism.

Mar. 17	Sod. salicyl.	Good	Good	Very good	Temp. 101°.
18	"	Very good	"	"	
19	"	"	0	0	
22	"	"			
26	"	Good	0	0	

CASE 22.—Bronchitis.

Apr. 25	Poor	Good	?	Fair	Temp. 100°.
---------	------	------	---	------	-------------

CASE 23.—Carcinoma of Liver.

Mar. 29	Fair	Good	?	Good	Temp. 99°.
---------	------	------	---	------	------------

CASE 24.—Gastric Ulcer.

Date.	In urine direct.		In destillate.		
	Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Jan. 24	?	Good	Fair	Fair	
25	0	Poor	0	0	
Feb. 7	0	0			

CASE 25.—Cirrhosis of the Liver; Paracentesis.

Feb. 10	Slight	Good	Fair	Slight	Temp. 98.4°.
11	Very good	Very good	Very good	Very good	
12	Good	"	Fair	Poor	
14	Very poor	Good	Poor	"	
15	"	Fair	?	0	
Mar. 3	Slight	"	0	0	

CASE 26.—Alcoholism, with temporary glycosuria.

May 14	Very good	Very good	Very good	Very good	Sugar 4 %.
16	Good	Good	Fair	Fair	
17	Fair	Fair	Poor	Poor	
18	"	Poor	0	0	No sugar on leaving.
20	"	Fair	0	...	
21	"	Very poor	0		
23	Poor	?	Poor		

CASE 27.

Apr. 27	Fair	Fair	Poor	Poor	
Mar. 5	Poor	"	"	"	

CASE 28.—Spinal affection in a child.

Mar. 10	Good	Very good			
11	"	"	Good	Fair	
14	Fair	?			
28	"	Poor	0	"	

CASE 29.—Diabetes, improving. F., 65.

Oct. 11	Poor	Poor			
25	0	0			

110 ACETONURIA AND ITS RELATION TO DIABETIC COMA.

CASE 30.—Diabetes, improving. F., 49.

Date.	In urine direct.		In distillate.		
	Iron reaction.	N. P.	N. P.	Iodoform reaction.	
Oct. 13	0	0			
27	0	0			

CASE 31.—Diabetes. F., 58.

Oct. 17	0	0			
---------	---	---	--	--	--

CASE 32.—Abdominal Section for Tumour; death.

For several days after operation there was a strong iron and N. P. reaction; but before the operation none.

CASE 33.—Diabetes; patient dying with Dyspnœa, but not comatose.

—	Very good	Poor	0		
---	-----------	------	---	--	--

CASE 34.—Diabetes, severe case; dying comatose.

Dec.	Good	0	...	...	Urine examined many times, but no acetone found. Comatose; still no acetone.
Mar. 3	„	0	...	...	

CASE 35.—Diabetes; not comatose.

May 10	Strong	Good	Good	Good	
11	0	Fair	„	Very good	

(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. i, p. 28.)