

CONCLUSIONS

In conditions in which a prolonged reaction is desired, as in conferring immunity, the nonsensitized vaccines seem preferable.

In conditions in which no general reaction is wanted and a quick response of the protective powers desired, as in active typhoid fever, a sensitized vaccine would seem preferable.

607-612 Griffith McKenzie Building.

THE ACETONE BODIES IN DIABETES
MELLITUSINFLUENCE OF LOW AND HIGH PROTEIN INTAKE ON THE
EXCRETION OF ACETONE, DIACETIC ACID AND
BETA-OXYBUTYRIC ACID

JACOB ROSENBLOOM, PH.D., M.D.

PITTSBURGH

INTRODUCTION AND REVIEW OF LITERATURE

I have frequently noted that the administration of increased amounts of protein to diabetics often increases the amounts of acetone, diacetic acid and beta-oxybutyric acid excreted in the urine. Magnus-

Levy¹ has had a similar experience, and asserts that the increased excretion of the acetone bodies does not mean that they have been formed from the protein but on account of the high protein content of the diet, which makes an extra tax on the oxidizing powers of the body and diverts these from the combustion of the acetone bodies.

It is now firmly settled that the acetone bodies are mostly derived from the fats and especially from the fats composed of the lower fatty-acids.² Knoop,³ Ringer⁴ and others have shown that in the catabolism of fatty acids the carbon chains are broken down by the oxidation of the third carbon atom from the end, that is, in the beta position, and the two end carbon atoms are then split off. It follows that two carbon atoms are separated at a time, and therefore every fatty acid which contains an even number of carbon atoms can be converted into beta-oxybutyric acid.

1. Magnus-Levy: Bull. Johns Hopkins Hosp., 1911, xxii, 46.

2. Excellent reviews of acidosis are given by Ewing, James: Acidosis and Associated Conditions, Arch. Int. Med., November, 1908, p. 330; Lusk, Graham: Metabolism in Diabetes, *ibid.*, February, 1909, p. 1; Magnus-Levy: *Ergebn. d. inn. Med. u. Kinderh.*, 1908, i, 374; Gigon: *Ibid.*, 1912, ix, 285, and Rosenbloom: New York Med. Jour., 1915, cii, 294.

3. Knoop, quoted by Porges: *Ergebn. d. Physiol.*, 1910, x, 6.

4. Ringer: Jour. Biol. Chem., 1913, xiv, 43, 525.

TABLE 1.—RESULTS OF TESTS *

Case Number	Day	Urine				Intake		
		Glucose, gm.	Acetone, gm.	Diacetic Acid, gm.	Beta- Oxybutyric Acid, gm.	Protein, gm.	Fat, gm.	Carbohydrate, gm.
1.....	1	1.6	0	0	0	135	220	45
1.....	2	1.8	0.58	0.42	0	135	220	45
1.....	3	0	1.22	1.06	3.0	175	220	45
1.....	4	12	1.34	1.28	2.6	175	220	75
1.....	5	8	0.52	0.31	+	90	220	75
1.....	6	0	±	±	0	90	220	45
2.....	1	80	±	±	...	135	220	10
2.....	2	78	1.62	0.92	1.3	135	220	10
2.....	3	74	1.48	1.92	0.9	135	220	10
2.....	4	77	1.72	1.03	0.8	135	220	10
2.....	5	77	1.65	0.94	1.2	135	220	10
2.....	6	83	1.24	0.87	1.1	135	220	10
2.....	7	67	1.11	0.76	0.7	135	220	10
2.....	8	82	1.38	0.92	0.9	135	220	10
2.....	9	70	3.20	2.60	2.3	185	220	10
2.....	10	82	3.09	2.07	1.9	185	220	10
2.....	11	70	3.17	1.99	2.4	185	220	10
2.....	12	60	3.45	3.65	2.9	185	220	10
2.....	13	70	4.18	2.17	3.4	185	220	10
2.....	14	46	3.27	2.18	2.7	185	220	10
2.....	15	80	4.20	5.15	2.9	185	220	10
2.....	16	68	3.18	2.16	2.3	185	220	10
2.....	17	65	3.40	2.92	2.1	185	220	10
2.....	18	49	3.18	2.72	1.5	185	220	10
3.....	1	40	1.49	1.82	1.0	135	220	45
3.....	2	25	1.17	0.92	0.7	135	220	45
3.....	3	20	1.15	0.74	0.5	135	220	20
3.....	4	20	1.02	0.17	0.7	135	220	15
3.....	5	9	1.04	0.62	0.8	135	220	15
3.....	6	0	2.17	2.29	1.7	180	220	15
3.....	7	0	3.26	4.32	2.7	180	220	15
3.....	8	0	4.22	4.29	3.2	180	220	30
3.....	9	0	4.18	3.96	3.7	180	220	30
3.....	10	0	1.08	0.82	0.9	135	220	30
4.....	1	18	0	0	0	135	220	10
4.....	2	9.3	0	0	0	135	220	10
4.....	3	0	0.72	0.54	±	135	220	15
4.....	4	0	0.91	0.53	±	135	220	15
4.....	5	0	0.64	0.32	±	135	220	15
4.....	6	0	0.82	0.95	±	135	220	15
4.....	7	0	1.43	1.37	0.9	135	220	15
4.....	8	0	2.94	2.82	1.2	180	220	15
4.....	9	0	4.42	3.30	1.9	180	220	15
4.....	10	0	4.70	3.94	3.0	180	220	15
5.....	1	50	0	0	0	135	220	45
5.....	2	8.2	0	0	0	135	220	45
5.....	3	5.4	±	±	±	135	220	45
5.....	4	4.3	0.72	0.33	±	135	220	15
5.....	5	0	0.64	0.42	±	135	220	15
5.....	6	0	0.85	0.36	±	135	220	15
5.....	7	0	1.74	1.82	0.7	150	220	15
5.....	8	0	3.34	3.47	2.7	190	220	45
5.....	9	0	4.32	2.70	3.5	190	220	45
5.....	10	0	5.68	3.12	4.2	190	220	75
5.....	11	0	1.74	1.62	0.9	150	220	75
5.....	12	0	0.72	0.14	±	135	220	75

* A trace is indicated by +, and a faint trace by ±.

Normal fatty acids which contain an odd number of carbon atoms cannot yield beta-oxybutyric acid.

The acetone bodies might readily be formed from proteins, by separation of the NH_2 group from the amino-acids.⁵ It was formerly thought that they could be formed from carbohydrates, as is the closely related lactic acid, but we now know that this is not true.⁶ It is to be remembered, therefore, that theoretically the acetone bodies may be formed at the expense of proteins or fats, but that usually they are formed from

diabetics has a ketogenic influence which in time may be of serious import. Moorhouse, Patterson and Stephanson¹⁷ have recently shown that in experimental diabetes in dogs the course of the acetone excretion bears a close relation to the protein metabolism, and they think that the acetone excretion depends on the character of the proteins fed, as they found that when feeding erepton, the acetone excretion was high. On feeding caseinogen, the amount of acetone excreted fell, and on feeding gelatin the acetone was markedly diminished.

TABLE 2.—COMPOSITION OF OX MEAT

	Per Cent.
Glycocoll	2.06
Alanin	3.72
Valin	0.81
Leucin	11.65
Prolin	5.82
Phenylalanin	3.15
Aspartic acid	4.51
Glutamic acid	15.49
Serin	?
Tyrosin	2.20
Arginin	7.47
Histidin	1.76
Lysin	7.59
Ammonia	1.07
Tryptophan	Present

the fats and in severe diabetes from the fatty acids produced by the deaminization of amino-acids.⁷

It has been asserted by several observers⁸ that sugar produced from protein can inhibit the formation of acetone bodies just as well as carbohydrate can. This statement is based on the fact that with an increase of protein catabolism the acetonuria is lessened, if at the same time the protein given does not drive up the glucosuria and thus do away with the inhibitive action that the protein sugar would exert.⁹ In health the catabolism of large quantities of protein can dissipate acidosis on account of its partial conversion into sugar, but in diabetes protein does not act so, as the sugar is not burned up.

Borchardt¹⁰ found that protamin, histon, egg albumin, pancreas and casein, which contain monamino-acids, increasing in the order named, when given to healthy subjects, showing acidosis from carbohydrate starvation, produced different effects on the amount of the acetone bodies excreted. Protamin increased the acidosis, while casein reduced it. Rosenthal¹¹ found that when meat, casein, egg albumin or thymus were added to a high protein diet they all increased the acetonuria. He thought the higher the glycogen-producing quantity of the protein and its content of monamino-acids, the less is its ability to produce acetone. Lüthje¹² asserted that calf thymus reduced diabetic acidosis, while casein increased it. Labbé,¹³ Cammidge,¹⁴ von Noorden,¹⁵ and Hugounenq and Morel¹⁶ have all shown that a high protein feeding to

METHODS

The standard strict diets of von Noorden¹⁸ were used in this work. The increased amount of protein added to the diet was always given as meat. The glucose was estimated by Benedict's¹⁹ method, the acetone and diacetic acid by Folin's²⁰ method, and the beta-oxybutyric acid by Shaffer's²¹ method.

EXPERIMENTAL

Table 1 presents the results obtained in this study. All of the five cases studied show a marked increase in the amounts of the acetone bodies excreted in the urine when the protein intake was increased; and when the protein intake was lowered, the amount of the acetone bodies excreted was lessened.

TABLE 3.—COMPOSITION OF GELATIN

	Per Cent.
Glycocoll	16.5
Alanin	0.8
Valin	1.0
Leucin	2.1
Isoleucin	—
Phenylalanin	0.4
Tyrosin	0
Serin	0.4
Cystin	7.7
Prolin	3.0
Oxyprolin	0.6
Aspartic acid	0.9
Glutamic acid	0
Tryptophan	7.6
Arginin	2.8
Lysin	0.4
Histidin	0.4
Ammonia	0.4

These results may also explain partially the remarkable effects of the so-called green days and oatmeal days in lessening the amount of acetone bodies excreted in the urine. As both of these diets contain very little protein (typical green days 30 gm., and typical oatmeal days 51 gm.), it may be that part of the lessened excretion of acetone bodies is due to the lowering of the protein intake.

It is most likely that the increased excretion of the acetone bodies produced by increasing the protein intake is due to the fact that some of the amino-acids present in the protein act as ketogenic substances. In Table 2 is given the most complete analysis of ox meat.²²

It is well known that of these constituents the *leucin*, *tyrosin* and *phenylalanin* are ketogenic, and it may be that the increased excretion of the acetone bodies is due to the presence of these amino-acids in the increased amount of meat protein ingested.

5. Fittipaldi: Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechs., 1901, v, 161. Emden and Engel: Beitr. z. chem. Phys. u. Path., 1907, xi, 323.

6. Satta: Beitr. z. chem. Phys. u. Path., 1905, vi, 1, 388. Waldvogel: Die azetone Körper, 1903. Schwarz: Deutsch. Arch. f. klin. Med., 1903, lxxvi, 233.

7. Blumenthal and Neuberg: Beitr. z. chem. Phys. u. Path., 1902, ii, 238. Orgler: Beitr. z. chem. Phys. u. Path., 1900, i, 583. Emden, Salomon and Schmidt: Beitr. z. chem. Phys. u. Path., 1906, viii, 129.

8. Talma: Therap. d. Gegenw., 1901, p. 385. Hirschfeld: Ztschr. f. klin. Med., 1895, xxviii, 176. Waldvogel: Ibid., 1899, xxxviii, 506. Rosenfeld: Zentralbl. f. inn. Med., 1895, No. 51.

9. Von Noorden: Metabolism and Practical Medicine, 1907, iii, 590.

10. Borchardt: Arch. f. exper. Path. u. Pharmacol., 1905, liii, 388.

11. Rosenthal: Zentralbl. f. inn. Med., 1908, 185.

12. Lüthje: Ztschr. f. klin. Med., 1900, xxxix, 397.

13. Labbé: Semaine méd., 1911, p. 506.

14. Cammidge: Lancet, London, 1913, ii, 1319.

15. Von Noorden: Med. Klin., 1913, ix, 612.

16. Hugounenq and Morel: Semaine méd., 1911, p. 505.

17. Moorhouse, Patterson and Stephanson: Biochem. Jour., 1915, ix, 171.

18. Von Noorden: Die Zuckerkrankheit und ihre Behandlung, Berlin, 1912.

19. Benedict: Jour. Biol. Chem., 1911, ix, 57.

20. Folin: Jour. Biol. Chem., 1907, iii, 177.

21. Shaffer: Jour. Biol. Chem., 1908, v, 211. Shaffer and Marriott: Ibid., 1913, xvi, 265. Pritbram: Ztschr. f. exper. Path. u. Therap., 1912, x, 279, 284. Cook and Gorslin: Jour. Biol. Chem., 1911, x, 291.

22. Osborne and Jones: Am. Jour. Physiol., 1909, xxiv, 438.

Another reason to suspect that this is the case may be found in the results obtained by Moorhouse, Patterson and Stephanson. They found that, of the various proteins studied in regard to their effect on the excretion of acetone in dogs rendered diabetic, gelatin produced a marked diminution in the excretion of these bodies. I think the explanation of this result is due to the fact that gelatin contains very small amounts of *leucin*, *tyrosin* and *phenylalanin*, as may be seen from the analysis²³ given in Table 3.

The importance of restricting the amount of protein in the diet in diabetes has long been well known in regard to the sugar excretion.²⁴ I present in this paper data showing the importance of restricting the protein intake in diabetes in relation to lessening the amount of excretion of the acetone bodies in the urine. It is possible that by selecting proteins free from those amino-acids that are ketogenic we may be better able to control the formation of the acetone bodies in this disease.

5737 Forbes Street.

THE PREVENTION AND TREATMENT OF RINGWORM AND FAVUS OF THE SCALP

J. E. LANE, M.D.

NEW HAVEN, CONN.

In a recent case report of "Two Favus Families,"¹ I illustrated some of the results of neglecting to attend properly to every case of favus of the scalp as soon as it is discovered.

Ringworm and favus of the scalp are not common diseases in many of our smaller cities and towns. The importance, therefore, of properly caring for the early cases, in order to prevent their spread, is often insufficiently appreciated by the health authorities and physicians of such localities.

In addition to this, the profusion of drugs recommended for these diseases, as well as the lack of detailed information of the method of carrying out the treatment and of what is expected from it, leave the physician, who is unfamiliar with these diseases, uncertain what to do.

As ringworm and favus are closely related, and as their treatment is similar, they may well be considered together. Both are children's diseases and preeminently diseases of the school age. Ringworm of the scalp heals spontaneously at the approach of puberty, and is almost never found in an adult. Favus almost always begins in childhood, but unlike ringworm, does not usually heal spontaneously until it has destroyed all the hair of the scalp, which frequently is not until late in life.

These diseases do not affect the general health, and their importance consists chiefly in the loss of education to the individuals affected, as the children are usually excluded from school. In the case of favus this exclusion generally includes the whole school life of the child, if he is not properly treated.

The objects to be sought in the management of these diseases are the prevention of their spreading to others and the cure of the affected individuals.

In order to prevent their spread:

1. All cases should be reported to the health authorities, who should have the power of supervising them. Diseases which are excluded from this country by the federal government are not too unimportant to be noticed when they are found here.

2. Whenever a case is discovered in a school, all the children in the room should be examined. This is more necessary in the case of ringworm than in that of favus, as it is much more contagious than the latter, which is usually contracted only by members of the immediate family.

3. Whenever a case is found, it should be ascertained whether there are other children in the family or house, and if there are, all these children should be examined, for it is the exception for only one child of a family to be affected in the case of ringworm, and in the case of favus more than one are frequently affected. This is easily understood, as both diseases are especially found in unhygienic and crowded quarters.

4. Houses in which cases have been found should be thoroughly disinfected after the disease is cured or when they are vacated.

Other precautions for the prevention of the spread of the diseases naturally come under the head of treatment and will be considered there.

The modern and only satisfactory rapid method of curing these diseases is by the use of the Roentgen ray, but as it can be employed only by a skilled roentgenologist who has had an opportunity of previously seeing its application, and as it is not practicable in localities in which there are only a few cases to be treated, it will be simply mentioned in this place.

Strickler² of Philadelphia recently reported good results in ringworm with a vaccine treatment, which will be of great value if further use confirms his results.

Before considering the treatment in detail, it will be well to consider some of the difficulties to be contended with. In the first place the fungi are extremely tenacious of life when removed from the scalp. Ringworm can ordinarily be produced from crusts which have been preserved for from three to six months, and instances of successful inoculation have been known to take place after eighteen months, though the spores are always dead after two years. The life of the fungus in the hair is longer, and spores in removed hairs will usually grow after fifteen or eighteen months. Favus spores have been found living in scutula after two years.

In locations in which they can be reached by antiseptics, the fungi are easily destroyed, but in both diseases a large number of the fungi are buried deeply in the hair follicles and in the interior of the hairs. When we consider the fact that in the case of ringworm "soaking the hair in absolute alcohol for as long as twelve hours will not inhibit the growth of the fungus," we are not surprised that "the resistance of the parasite in the hair follicle has up to the present time remained almost absolute to all chemical agents." This statement may be extended to include the Roentgen ray, which does not kill the parasites.

23. Fischer, Leyene and Aders: *Ztschr. f. physiol. Chem.*, 1902, xxxv, 70. Kossel and Kutscher: *Ibid.*, 1901, xxxi, 165. Fischer and Boehner: *Ibid.*, 1910, lxxv, 118.

24. Kossel: *Deutsch. med. Wchnschr.*, 1898, p. 58. Müller and Seeman: *Ibid.*, 1899, p. 209. Stiles and Lusk: *Am. Jour. Physiol.*, 1903, ix, 380.

1. Lane, J. E.: Two Favus Families, *THE JOURNAL A. M. A.*, Oct. 16, 1915, p. 1362.

2. Strickler, Albert: The Vaccine Treatment of Ringworm of the Scalp, *THE JOURNAL A. M. A.*, July 17, 1915, p. 224.