A NEW INTERPRETATION OF HYPERGLYCEMIA IN OBESE MIDDLE-AGED PERSONS

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The term diabetes mellitus has in the past implied a single cause. Ever since the days of von Mering and Minkowski this disease has been attributed to a pancreatic abnormality. However, within the last few years the work of a number of investigators has made it clear that this conception is far too restricted. Houssay,[1] for example, has shown that the rapidly fatal diabetes produced by pancreatectomy in animals may be strikingly ameliorated by subsequent hypophysectomy. In the same sense Mann [2] has produced fatal hypoglycemia in depancreatized dogs by hepatectomy. A number of workers have produced hyperglycemia and glycosuria by injection of pituitary extracts, and Young [3] reported that he obtained permanent "diabetes" in dogs solely as the result of prolonged injection of anterior pituitary extracts.

It is therefore clear that clinical investigators must now attempt to discover the specific cause of the hyperglycemia in all patients who present the classic signs and symptoms of the abnormality to which the clinical term diabetes mellitus is attached. In this paper we are endeavoring to show that we have isolated etiologically one group of persons characterized by obesity and spontaneous glycosuria.

Joslin [4] has emphasized the frequency of obesity in the patients who come to him for the treatment of diabetes mellitus. He reported on a group of 3,094 patients, 20 or more years of age, whose weight at the onset of the disease was known. Of the males 63 per cent and of the females 67 per cent were obese. Our investigation concerns only those patients who were obese and middle aged when they came to us for the treatment of spontaneous glycosuria.

Table 1 shows how many patients were obese when they were first accepted at the University Hospital during the year 1936 for the control of diabetes mellitus. It will be seen that close to two thirds of the patients who were from 30 to 65 years of age were overweight when treatment for diabetes was first begun. Since this middle-aged group accounted for 72 per cent of the patients, 44 per cent of all the patients treated for diabetes were obese and middle aged when they were first accepted for treatment.

These patients had been obese for many years. Glycosuria was often discovered in a routine examination of the urine. Generalized pruritus, pruritus vulvae, mild polyuria and polydipsia or visual disturbances often caused the patient to seek the physician. Glycosuria may have been discovered several years earlier and been ignored without the development of any marked symptoms. On the other hand, some of the patients had been receiving treatment for diabetes for many years. The physical examination revealed no constant abnormality other than obesity. Hypertension was present in 40 per cent of the cases. Moderate hepatic enlargement was noted in 12 per cent. Cataracts were not uncommon.

METHOD OF INVESTIGATION

We chose for study only those patients who were obese, middle aged and spontaneously glycosuric on an unrestricted diet. Each subject satisfying these conditions was fed a standard normal diet (300 Gm. of carbohydrate, 80 Gm. of protein and approximately the maintenance number of calories) for at least three days prior to a standard dextrose tolerance test. The amount of dextrose ingested (1.75 Gm. per kilogram) was calculated on the basis of ideal weight.[5] If under these conditions the response was such that it would be generally accepted as indicative of diabetes mellitus, the patient was included in the group.

A number of the patients who conformed to the standard diagnostic criteria for diabetes mellitus described were studied with regard to their ability to oxidize dextrose. The data were obtained by means of a respiration chamber employing the principle of continuous indirect calorimetry by the open circuit method.[6] The patients ate a standard preparatory diet for at least three days before the respiratory data were obtained. These data were compared with those obtained from normal control subjects under identical conditions.

TABLE 1.—*New Cases in Which a Diagnosis of Diabetes Mellitus Was Made During 1936 at University Hospital*

Age Groups, Years	Number in Each Group	Percentage of Total Number	Number Obese	Percentage of Group Obese	Percentage of Total Number Obese
0-29	54	14.6	2	3.7	0.5
30-65	266	71.9	162	61.3	43.8
Over	50	13.5	19	38.0	5.0
Totals	370	100.0	183	....	49.0

Having secured these preliminary data while the subjects were both obese and glycosuric, we then placed them on reduction diets. No other treatment was instituted. The carbohydrate of the diet was reduced only to the degree made necessary by the restriction of calories. Dextrose tolerance tests were repeated during the period of weight reduction. These tests were done after the standard dietary preparation used for the original ones. Some of the patients were unwilling to adhere to the diet long enough for us to obtain any information. Only those who continued to reduce their weight by adherence to the diet were studied further. We are at present reporting the results obtained with thirty-five such patients.

The blood sugar was determined by the Benedict method [7] and the urinary nitrogen by the Kjeldahl

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1. Houssay, B. A., and Biosotti, A.: Pankreasdiabetes und Hypophyse beim Hund, Arch. f. d. ges. Physiol. **227**: 664-684, 1931.

2. Mann, F. C., and Magath, T. B.: Studies on the Psysiology of the Liver: Effect of Total Removal of Liver after Pancreatectomy on Blood Sugar Level, Arch. Int. Med. **31**: 797-806 (June) 1923.

3. Young, F. G.: Permanent Experimental Diabetes Produced by Pituitary (Anterior Lobe) Injections, Lancet **2**: 372-374 (Aug. 14) 1937.

4. Joslin, E. P.; Dublin, L. I., and Marks, H. H.: Studies in Diabetes Mellitus: IV. Etiology, Am. J. M. Sc. **192**: 9 (July) 1936.

5. We have chosen as the "ideal weight" for all people over 35 years of age that weight which, according to the standard weight for height tables, is average for people between 30 and 35. Since at this weight life expectancy is greatest for middle-aged people, we have termed it ideal weight.

6. Newburgh, L. H.; Johnston, M. W.; Wiley, F. H.; Sheldon, J. M., and Murrill, W. A.: A Respiration Chamber for Use with Human Subjects, J. Nutrition **13**: 193 (Feb.) 1937.

7. Benedict, S. R.: The Analysis of Whole Blood: II. The Determination of Sugar and of Saccharoids (Nonfermentable Copper Reducing Substances), J. Biol. Chem. **92**: 141 (June) 1931.

method. Frequent alcohol checks on the respiration chamber demonstrated that the method was capable of determining over 99 per cent of the gaseous exchange.

RESULTS

That the disturbance in the utilization of carbohydrate from which such patients suffer is intimately related to their obesity is shown in table 2. The ability to dispose of dextrose normally has returned after reduction of weight. Chart 1 shows the composite dextrose tolerance curves of twenty-one patients before and after weight reduction. Thus far only one patient

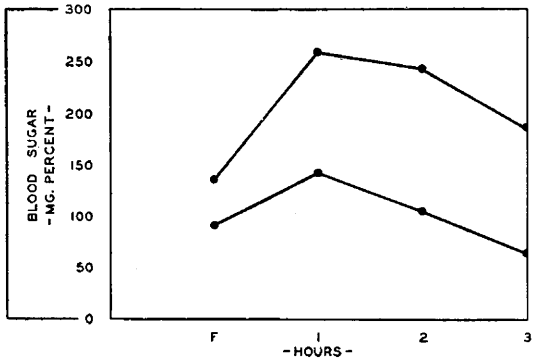

Chart 1.—Composite dextrose tolerance curves for twenty-one patients before and after reduction of weight.

whose weight has been reduced to normal has failed to show a completely normal dextrose tolerance curve (table 2, last patient). The reduction of weight did, however, cause marked improvement in the utilization of dextrose by this patient. Several patients who after

TABLE 2.—*Effect of Reduction of Weight on Disposal of Dextrose*

	When Obese				After Reduction of Weight			
	Fasting	1 Hr.	2 Hr.	3 Hr.	Fasting	1 Hr.	2 Hr.	3 Hr.
	105	236	256	152	78	126	107	52
	127	303	244	174	93	146	115	59
	168	290	370	302	104	113	90	74
	166	300	344	264	106	153	136	69
	99	212	216	164	82	156	105	70
	162	202	210	240	71	146	129	50
	124	294	125	99	86	154	93	60
	161	300	202	178	91	166	87	51
	148	234	282	176	93	156	136	113
	113	212	200	115	78	178	100	77
	73	188	200	97	93	147	110	94
	115	200	196	196	76	121	109	76
	133	300	236	164	112	149	50	68
	148	314	270	146	89	170	93	57
	113	234	200	164	98	109	88	59
	119	230	185	102	85	135	107	66
	121	172	192	107	89	117	96	96
	141	230	202	156	97	139	84	62
	106	270	252	222	83	154	119	63
	117	238	242	192	92	192	129	58
	300	504	508	428	111	192	76	59
Averages	136	260	244	183	91	149	104	68
	*124	278	266	111	87	200	188	88

* Only patient showing incomplete recovery after reduction of weight.

reduction of weight had lost all demonstrable evidence of disturbed utilization of carbohydrate gained weight against our advice. Table 3 demonstrates the close relationship between change in weight and dextrose tolerance in one of these patients. The excess weight was again lost, with a second return of normal metabolism of carbohydrate. Table 4 and chart 2 show the striking improvement following partial weight loss in the remaining thirteen patients, who are still in the process of weight reduction.

Some of the patients have attained normal dextrose tolerance before all the excess weight has been lost. The two patients showing the earliest return of a normal response had lost 46 per cent and 52 per cent, respectively, of the calculated amount of excess weight. This represented a loss of 35 pounds (16 Kg.) in the former and 38 pounds (17 Kg.) in the latter. In contrast to these, others who had lost as much as 80 per cent of the excess weight, the highest loss amounting to 50 pounds (23 Kg.), continued to show some delay in the disposal of ingested dextrose. After the loss of the remaining

TABLE 3.—*Effect of Recurrent Obesity on Dextrose Tolerance Curve*

Overweight, Percentage	Fasting	1 Hr.	2 Hr.	3 Hr.
45	128	314	322	202
0	91	140	72	61
25	119	230	185	102
0	87	135	107	66

20 per cent of the excess weight, however, the response became normal. Tables 5 and 6 present the data obtained by means of the respiration chamber. It is evident that the obese hyperglycemic patients are able to oxidize dextrose as well as the normal controls.

COMMENT

In a preliminary note [8] we reported that the delayed utilization of dextrose in obese middle-aged patients could be completely corrected by reduction of weight. This observation is extended and amplified in this paper. The same favorable response to reduction of weight has been obtained recently by John [9] and by Fetter, Durkin and Duncan.[10] There should be no doubt then that the hyperglycemia and delayed disposal of ingested dextrose so prevelant in obese middle-aged people can, with few exceptions, be abolished by reduction of weight. When the normal weight was established, these

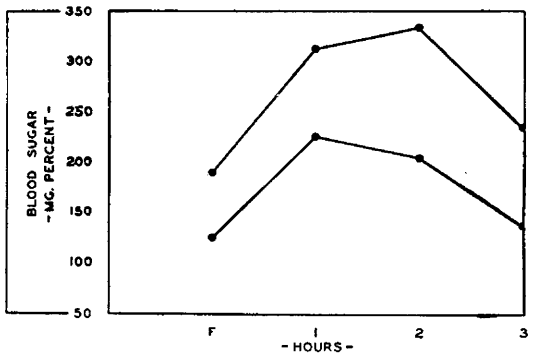

Chart 2.—Composite dextrose tolerance curves for fourteen patients before and after partial reduction of weight.

patients maintained normal blood sugar values and remained aglycosuric on unrestricted diets. They were urged to avoid gain in weight. We have been able to show that glycosuria and delayed utilization of dextrose

8. Conn, J. W., and Newburgh, L. H.: Hyperglycemia Due to Impaired Hepatic Glycogenesis, Proc. Soc. Exper. Biol. & Med. **36**: 236 (March) 1937.

9. John, Henry J.: Some Interesting and Obscure Problems in the Diagnosis and Treatment of Diabetes Mellitus, Ohio State M. J. **33**: 741 (July) 1937.

10. Fetter, Ferdinand; Durkin, J. K., and Duncan, G. G.: Dietary Versus Insulin Treatment of the Obese Diabetic Patient, Am. J. M. Sc. **195**: 781 (June) 1938.

recur when weight is subsequently gained. This abnormality in utilization of carbohydrate again disappears when the excess weight is lost a second time.

What is the meaning of this diagrammatic relationship between overweight and faulty metabolism of carbohydrate? Up to the present, all authors have taken it for granted that obese glycosuric patients were diabetic in the ordinary sense of the word. It was believed that they were suffering from an incurable weakness or injury of the mechanism that deals with the utilization of carbohydrate and that the underlying disease was merely accentuated by the burden of adiposity.

If this conception is a true explanation of the facts, one would predict that obesity would cause hyperglycemia only in an occasional adult. Just the opposite is the case.

Kisch [11] found that about 50 per cent of all markedly obese people were glycosuric. Paullin and Sauls,[12] studying the dextrose tolerance curves of twenty-six obese patients without glycosuria and between the ages of 16 and 71, found that 58 per cent had abnormally high curves. In the group between 30 and 50, 75 per cent had curves indicative of impaired dextrose tolerance. John [13] did dextrose tolerance tests on 182 aglycosuric, obese adults who had come to the clinic with various complaints. He found that 65 per cent were unable to clear the blood of dextrose in the normal length of time. Thus a majority of all obese persons show a delayed utilization of ingested dextrose. The work of Ogilvie [14] seems to answer the question of why the other 30 to 40 per cent of obese people exhibit a normal response. In a study of sixty-five obese women without glycosuria he found that impaired carbohydrate tolerance was related to the duration and not to the degree of obesity. Tolerance appeared to be unimpaired until the obesity had existed for more than eleven years. Thereafter tolerance began to diminish. After eighteen years of obesity, every woman in the series showed a diminution in the tolerance for carbohydrate. This finding explains why the incidence of the obesity-glycosuria syndrome is so rare in people under the age of 30 and increases rapidly from 35 to 55, when it reaches its peak.

TABLE 4.—*Effect of Partial Reduction of Weight on Disposal of Dextrose*

	When Obese				After Partial Reduction of Weight			
	Fasting	1 Hr.	2 Hr.	3 Hr.	Fasting	1 Hr.	2 Hr.	3 Hr.
	174	306	262	152	130	226	166	98
	116	236	260	170	120	184	130	55
	112	202	254	240	96	168	172	145
	278	374	416	468	242	340	410	364
	242	460	404	308	115	192	234	117
	240	356	410	364	196	364	356	244
	186	344	352	324	112	272	244	107
	150	205	200	266	100	186	166	135
	134	280	284	210	91	216	176	124
	258	352	500	340	124	228	147	88
	296	446	500	440	122	184	226	222
	152	278	300	278	85	228	167	90
	178	303	287	222	111	167	141	76
Averages	196	318	341	291	126	227	210	151

11. Kisch, E. H.: Diabetes in the Elderly, J. A. M. A. **64**: 1038 (March 20) 1915.
12. Paullin, J. E., and Sauls, H. C.: A Study of the Glucose Tolerance Test in the Obese, South. M. J. **15**: 249 (April) 1922.
13. John, H. J.: A Summary of the Findings in 1,100 Glucose Tolerance Estimations, Endocrinology **13**: 388 (July-Aug.) 1929.
14. Ogilvie, R. F.: Sugar Tolerance in Obese Subjects: Review of Sixty-Five Cases, Quart. J. Med. **28**: 345 (Oct.) 1935.

The work cited clearly shows that prolonged obesity usually results in a delay in the utilization of carbohydrate. If this response to adiposity means that a hidden diabetes has been brought to light, then one is forced to the conclusion that most adult human beings have latent diabetes. Such an assumption is unacceptable. We offer a more reasonable explanation of the facts.

TABLE 5.—*Oxidation of Dextrose, Four Hours*
Preparation: 200 Gm. of carbohydrate, 3 days
Test: 100 Gm. of dextrose

Sex	Age, Years	Weight, Kg.	Percentage Over-weight	Carbohydrate Oxidized: Gm.	Carbohydrate Oxidized: Percentage of Total Calories
			Controls		
♂	22	75	0	49	48
♂	25	65	−10	54 (48)	68 (55)
♂	55	64	0	42	48
			Middle-Aged Glycosuric Patients		
♂	65	104	55	59	59
♀	50	90	68	49 (50)	58 (54)
♂	51	81	24	50	63
♂	53	111	61	40	35

The demonstration that the majority of persons in any large group respond in a specific manner to a specific insult has always been taken to mean that the type response of the healthy or normal stock has been discovered. The majority of adult human beings eventually respond to obesity by becoming hyperglycemic.

TABLE 6.—*Oxidation of Dextrose, Four Hours*
Preparation: 300 Gm. of carbohydrate, 3 days
Test: 60 Gm. of dextrose

Sex	Age, Years	Weight, Kg.	Percentage Over-weight	Carbohydrate Oxidized: Gm.	Carbohydrate Oxidized: Percentage of Total Calories
			Controls		
♂	25	80	14	38	35
♂	55	64	9	50	64
♂	39	75	12	41 (43)	42 (48)
♂	50	76	10	48	54
♀	48	60	0	36	47
			Middle-Aged Glycosuric Patients		
♀	63	64	10	38	49
♂	58	96	40	50 (44)	57 (49)
♂	55	83	26	53	59
♂	54	119	61	36	32

This is the type reaction to the irritant. It is the normal human reaction to prolonged obesity. When the irritant, namely obesity, no longer exists, the hyperglycemia disappears.

What then is the mechanism of hyperglycemia and glycosuria in obese glycosuric persons whose capacity to oxidize a normal quantity of dextrose is retained? Since in the normal person two major functions, namely oxidation of dextrose and deposition of dextrose as glycogen, account for the rapid removal of dextrose from the blood stream, there appears in the obese

glycosuric patient to be a deficiency in the mechanism by which glycogen is deposited rapidly in the liver. It seems evident therefore that the glycogenic mechanism is disturbed by the adiposity.

As far as is known there are two ways in which hepatic deposition of dextrose as glycogen may be impaired. First, a disturbance in the functional capacity of the liver cells themselves to lay down glycogen has been produced by the use of hepatotoxic chemicals and demonstrated in association with diseases of the liver.[15] Second, lack of insulin leads to an inability to deposit normal quantities of glycogen in the liver as well as to decreased oxidation of dextrose. If one wished to develop the latter hypothesis further with regard to the cases under consideration, he would be forced to conclude that a mild insulin insufficiency may reduce hepatic glycogen retention without at the same time affecting the oxidation of dextrose. If this is true, then this is the first demonstration in human beings that lack of insulin may adversely affect glycogen storage and yet not reduce the ability of the organism to oxidize dextrose. There are no facts available, however, that lead to the belief that insulin production is reduced by obesity. Nor is there evidence that removal of obesity increases insulin secretion.

On the other hand, we[15] have shown that hepatic glycogenesis, impaired in the presence of normal oxidation of dextrose in patients suffering from low grade infections of the biliary tract, becomes normal when the cause of the hepatitis is removed. It therefore seems more likely that in the type of patients discussed in this paper the abnormal accumulation of fat in the liver interferes with its capacity to lay down glycogen at the normally rapid rate.

CONCLUSIONS

1. A statistical analysis of spontaneous glycosuria associated with delayed disposal of ingested dextrose indicates that approximately half of the patients are obese. These obese glycosuric patients are, with few exceptions, more than 30 years of age.

2. After the weight of these patients has been reduced to normal by simple underfeeding, they remain aglycosuric, do not become hyperglycemic when they are placed on maintenance diets containing 300 Gm. of carbohydrate and exhibit normal dextrose tolerance curves.

3. There is an occasional exception to this rule, but more than 90 per cent of the patients respond in this manner.

4. Recurrence of the obesity is capable of reproducing the hyperglycemia and the delayed utilization of dextrose. Subsequent reduction of weight again corrects the disturbance in the metabolism of carbohydrate.

5. It has been demonstrated that the majority of persons who have been obese for many years show delayed utilization of carbohydrate. Since the majority respond in this way to adiposity and again dispose of carbohydrate normally when the excessive weight has been removed, this phenomenon must be regarded as being the type response of the previously normal mechanism carbohydrate metabolism to the overload of obesity.

6. It is suggested that the occurrence of the hyperglycemia and glycosuria in such persons depends on the excessive accumulation of fat in the liver, with a resulting impairment in its capacity to lay down glycogen at the normally rapid rate.

7. The studies described establish a clinical entity in which obesity is the principal abnormality and hyperglycemia is a secondary phenomenon.

15. Conn, J. W.; Newburgh, L. H.; Johnston, Margaret W., and Sheldon, J. M.: A Study of Deranged Carbohydrate Metabolism in Chronic Infectious Hepatitis, Arch. Int. Med. **62**: 765 (Nov.) 1938.

ABSTRACT OF DISCUSSION

DR. BERTNARD SMITH, Los Angeles: Clinically, it is well to keep in mind that this obese group, even with the mild degree of diabetes, continue to show poor diabetic control with large doses of insulin so long as they remain obese. They can tolerate large doses of insulin without the usual sharp hypoglycemic reactions. A report of studies on a small group of these patients has recently been given by Duncan and his associates of Philadelphia. In this group of patients the severity of the diabetes cannot be measured by the units of insulin taken so long as excess body weight is present. The respiratory studies in this report are of particular interest and are in agreement with studies on the respiratory quotient in similar groups of patients in indicating that the obese middle-aged person with diabetes of mild degree can oxidize dextrose. The diabetic condition must be due to a difficulty in glycogen formation and storage. Whether this difficulty concerns only hepatic glycogen remains a problem. Not all obese persons of middle age are diabetic, and not all show dextrose tolerance curves indicative of even potential diabetes. The group of patients included in this report have been shown to be definitely diabetic while obese. They become aglycosuric, with a normal amount of sugar in the blood so long as they follow such dietary restrictions as maintain an ideal weight. When these restrictions are not followed, loss of diabetic control results. The use of the word "cure" may subject the authors to some criticism, since the diabetic condition would appear to be present even with the perfect control of weight. This group of obese diabetic persons of middle age does not include all patients with diabetes of the insulin-resistant type. During my early studies with protamine insulin, sixty-two juvenile diabetic persons were under observation, and twenty-five of these were definitely of the insulin-resistant group. Also, among middle-aged patients with insulin-resistant diabetes will be found some who do not come under full diabetic control with reduction of body weight. These patients, in whom the diabetes appears to be more severe, will still require the help of insulin after weight has been reduced. However, the insulin requirement after reduction of weight may be small, and the diabetes may show more even control than before. It is possible that the persons with more severe insulin-resistant diabetes may have some defect in oxidation of dextrose as well as the decreased ability to store glycogen.

DR. J. W. SHERRILL, La Jolla, Calif.: The members are indebted to Drs. Newburgh and Conn for calling attention to this classification which they have made in diabetes. They have described relief from diabetic symptoms in this type which might be classified as the potential or prediabetic type. This work helps to explain the mildness of this condition which was recognized formerly as the prediabetic type. This differs remarkably from the true diabetic as well as the juvenile type, in that the patients preserve the ability to oxidize dextrose. If the definition of diabetes, that it is a condition in which there is failure to utilize dextrose, is to be adhered to carefully, then it cannot be said that this type would be classified as diabetes. Studies with the respiration chamber show a normal ability to oxidize dextrose. The group differ from normal persons only in that they are unable to clear their blood in normal time. Drs. Newburgh and Conn have demonstrated in graphic form the well known factor in diabetic treatment, namely, that reduction of body weight or body mass increases ability to burn dextrose and carbohydrate tolerance. Certainly they have shown that the reduction of obesity is the mechanism whereby they obtain normal tolerance curves and the ability to metabolize a normal diet. Nevertheless, physicians must still be cautious, as these persons probably have an impairment of insulogenic function. It is well known that the standard carbohydrate tolerance tests of a group of obese persons in the

normal population reveal impaired curves in direct relation to the duration of obesity. Therefore, before the word "cure" can be used in this instance these patients would have to be studied several years hence, say ten years, because possibly it is not the obesity itself which has produced this decrease in carbohydrate tolerance but a deficiency in pancreatic function. One can hardly get away from this factor because by permitting these persons to become obese again impairment in their carbohydrate tolerance can still be demonstrated. It would be well to keep in mind that the duration in years may bring about diabetes of a more specific character in this group. This contribution will be helpful particularly from the insurance angle for the group of persons who have been denied insurance in the past. It may permit them to obtain insurance to which they are entitled.

DR. FRANK N. ALLAN, Boston: Every one will agree with the facts presented by Drs. Newburgh and Conn and will feel pleased to see these results. Yet I share the opinion that their conclusions cannot be accepted without challenge. Can one say that diabetes has been cured simply because tests for blood sugar made after treatment give negative results? One would not say that heart disease is cured when signs of decompensation disappear. I think the authors should be asked to report the fate of these same persons twenty years from now, or even five years from now. It is not uncommon to find that diabetes which has become latent will cause trouble later on as a result not only of neglect but of the strain of infection or other misfortune. Can one say that these patients do not have real diabetes simply because of inability to demonstrate any change in oxidation in the body? The difference may be only a matter of degree. Diabetes of only the slightest degree now may become so severe as to endanger life later on, particularly if the condition is aggravated by infection. Let this report be accepted as confirming the favorable prognosis which may be expected in diabetes associated with obesity. That gives hope and encouragement. But the diagnosis of diabetes should not be abandoned; this will surely lead to neglect and eventually to disastrous results.

DR. J. W. CONN, Ann Arbor, Mich.: We were unable in the time allotted to discuss some of the points brought up. The question that Dr. Smith raised is this: Do all obese middle-aged persons have some degree of this disturbance in the metabolism of carbohydrate? If this disturbance is due to obesity, it should be found in all middle-aged obese persons. A large number of dextrose tolerance tests done by Kisch, Paullin and Sauls and by John indicate that from 60 to 70 per cent of all of these apparently normal people without glycosuria have lessened dextrose tolerance. The work of Ogilvie seems to answer the question of why the other 30 to 40 per cent of obese people gave a normal response. He found that impaired tolerance was related to duration rather than to degree of obesity. Thus, after eighteen years of obesity every patient in his series showed diminished dextrose tolerance. I should like to answer Dr. Sherrill's question regarding the prediabetic state. One considers the so-called prediabetic state that in which the patient shows a diabetic type or a tendency toward a diabetic type of dextrose tolerance curve but does not have sufficient rise in the sugar content of the blood to cause spontaneous glycosuria. When a patient has spontaneous glycosuria and a diabetic type of curve, he is called diabetic. The obese patients with glycosuria that we have described do not fall into the group considered by some to be prediabetic. Our group comes to the clinic with heavy glycosuria, a blood sugar value during fasting as high as 350 mg. per hundred cubic centimeters and a dextrose tolerance curve rising as high as 550; and after reduction of weight the dextrose tolerance test is normal. After the weight becomes normal these patients are not given diets. They are told to eat whatever they care to eat, candy, ice cream, potatoes and bread. They are simply instructed that they must not gain weight. Under this kind of a regimen, these patients have remained aglycosuric and have shown normal dextrose tolerance for two years thus far. Regardless of all theoretical considerations, the fact remains that obese middle-aged persons with glycosuria hitherto diagnosed and treated as true diabetes mellitus can regain and retain the normal metabolism of carbohydrate by simple reduction of weight to normal.

SPREADING PERITONITIS COMPLICATING ACUTE PERFORATIVE APPENDICITIS

ROUTINE OPERATIONS VERSUS SCIENTIFIC MANAGEMENT

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Routine defined means any regular course of action or procedure adhered to through force of habit.

Fifty-three years ago Fitz described acute appendicitis, and since then opinions and procedures of surgeons adhered to through force of habit have been responsible for the major part of the management of patients suffering with this disease and its complications. No more striking illustration of this fact can be found than what is called the mortality of acute appendicitis. During these five decades, thousands of articles have been written about it; eminent men who are relied on for accurate statements regarding the mortality of the disease have used the term, but there is practically no mortality from acute appendicitis. One in 183 dies. Patients die of peritonitis, not appendicitis.

Likewise because of force of habit, surgeons have not discussed with physicians the problem of spreading peritonitis complicating acute appendicitis. Physicians know that the mortality of acute appendicitis as reported throughout the United States is anything from zero to 5 per cent. Do they know that the gross mortality of spreading peritonitis is from 27 to 50 per cent? According to Hoffman, the average mortality rate of appendicitis per hundred thousand in Philadelphia was 13.4 from 1928 to 1933. During the same period in the United States it was 17.1. The average mortality of spreading peritonitis in Philadelphia was 26.97 per cent. According to this ratio it must have been at least 33 per cent throughout the United States.

TABLE 1.—*Mortality of Appendicitis and Appendical Peritonitis*

	No. of Cases	Deaths
Acute appendicitis	12,259	67 — 1 in 183 died
Acute appendicitis with local peritonitis	3,855	88 — 1 in 44 died
Acute appendicitis with spreading peritonitis	2,573	694 — 1 in 4 died
Total	18,687	849 — 1 in 22 died

Have surgeons told physicians that the surest method of reducing the mortality of spreading peritonitis is to send to hospitals patients whose appendixes have not ruptured?

In Philadelphia, the third largest city in the United States, with a population of over two million, a prophylactic campaign has resulted in a reduction in the number of patients with perforated appendixes admitted to twenty-eight hospitals, with a corresponding reduction in the mortality for appendicitis of from 5.97 to 3.54 per cent. Three hundred and sixty-five surgeons have managed a gradually diminished number of patients with spreading peritonitis, but in the last four years the mortality has not been materially reduced.

Are surgeons and not physicians responsible for this situation? Is it significant that during the past fifty years the number of articles on acute appendicitis published in reputable medical and surgical journals in

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