DIABETES MELLITUS AND OBESITY

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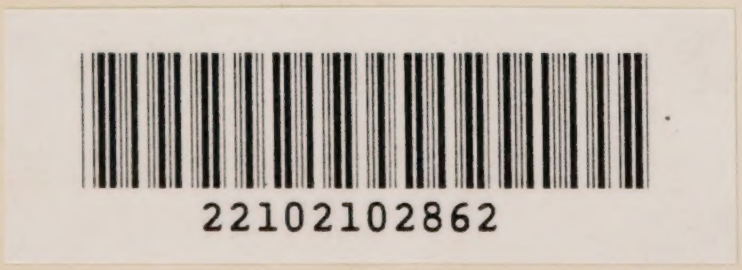

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PREFACE.

THE practical aspects of diabetes mellitus and obesity have received first consideration in this publication. I offer no apology for the omission of much purely scientific, theoretical and controversial matter. My motive has been to present a treatise, the study of which, I hope, will give the general practitioner and the medical student a good working knowledge of these disorders and their complications.

In regard to diabetes, no other disease involves exactly the same responsibility for the physician. On him depends not only the immediate control of the disorder, but the ultimate course and outcome of the patient's life and the influence which it may have upon others. If we merely make a severe diabetes appear mild, if we disregard moderate degrees of glycosuria, and accept, because it is easier, a plan of treatment which permits hyperglycemia, we are responsible for the economic failure of the diabetic, for his subnormal health and his early death.

On the other hand, a proper understanding, treatment and instruction combine to afford these people normal health, splendid opportunities, longevity, and give to the physician great satisfaction.

I have made no attempt to present a complete bibliography, but have included references to works which, in my estimation, are the most comprehensive.

The section on Obesity is included because of its relationship to diabetes; because its correction and prevention will

mean that there will be less diabetes; and because the treatment of obesity is quite similar to that of mild diabetes.

My thanks are due Professor Thomas McCrae for his many kindnesses and suggestions; and to Dr. Frederick M. Allen, to whom I owe much of my training in diseases of metabolism. I am exceedingly grateful to the late Dr. Elmer H. Funk, whose interest, advice and encouragement were ever an incentive.

I am indebted, also, to Mrs. Marjorie Wyant, Miss Ruth Evans, and particularly Miss Martha Alderman for assistance with the section on Diet.

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INTRODUCTION.

THE problem of diabetes mellitus is steadily becoming more important. The number of deaths from it is increasing and it seems altogether probable that they will continue to increase. Thus far it has not become a public health problem, except as regards the supply of insulin for indigent patients, but one which has been a matter of individual management by the physician for each patient. It is a disease which the members of the profession who treat patients with it should know thoroughly in all its aspects. Insufficient knowledge may be disastrous to the patient. The emergency of a patient desperately ill with diabetic coma or insulin reaction may come to any of us without warning. To know what to do may mean life or death to the patient. The knowledge must be with us; there is not likely to be time to consult books. Hence the value of clear cut, perhaps rather dogmatic, directions.

There are many books dealing with diabetes but there is always room for another good book. For the recent graduate and the students of today there is perhaps not the same difficulty in understanding modern treatment as for the practitioner who has been longer in practice. We have gone far in the management of diabetes as compared with fifty years ago. I well remember the case of an elderly relative of my own who had the disease in a mild form. At one time a large barrel of some spring water came for him, which was supposed to have wonderful curative qualities.

Again I recollect going for a special prescription which was expected to be of great benefit. This was not a quack remedy but was prescribed by the leading authority on the disease in Ontario at that time. The patient had to acknowledge that neither did him any good.

With the influence of heredity playing a definite part we have to endeavor to aid in the prevention of the disease in the members of diabetic families. This will be no easy matter but is a part of the problem which is of great importance.

There has been so much new work and so many side issues, if they may be so termed, that it is not surprising that some men have found it difficult to keep up with the newer developments and understand them thoroughly. Then the different methods of treatment and the changing fashions in therapy are confusing to many who have difficulty in knowing which it is best to use. One may hold that it is not necessary to follow all the work on insulin in the endeavor to explain its action, for example, to be able to use it intelligently, and this is perfectly true. The theoretical considerations concerned with insulin and its action are exceedingly complicated and puzzling.

The discovery of insulin altered over night the outlook for the diabetic but added enormously to the difficulty of management. We have to recognize the fact that while insulin is powerful for good under certain circumstances it has possibilities of harm. To learn when and how to use insulin is an important part of the treatment of diabetes and requires considerable knowledge on the part of the physician. No one in a book can lay down rules that will apply to any particular patient, but certain principles can be stated. With a knowledge of these the practitioner is in a position

to solve satisfactorily most of the problems that come to him, but let no one think for a moment that the use of insulin does not require knowledge, skill and care. When one learns of the haphazard way in which it is sometimes given, the wonder is that disasters are not more frequent.

In this book the author has kept before him the need for simplicity and clarity, so that there should be no confusion regarding what it is intended to convey. I can bear testimony to the ability of the author in managing patients with diabetes mellitus. With reference to the question of clarity sometimes a man is so full of his subject that in writing a monograph he is unable to put matters in such form that they are easily understood by others who have not his knowledge of the problems. There are some striking examples of this. I feel that Dr. Duncan has avoided this difficulty.

The problem of obesity is closely related to that of diabetes mellitus. Good hard sense and the ability to understand human nature are essentials in the management of both. I feel confident that this book will prove helpful in the management of patients with these diseases.

THOMAS MCCRAE.

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DIABETES MELLITUS AND OBESITY.

PART I.

DIABETES MELLITUS.

CHAPTER I.

GENERAL CONSIDERATIONS.

Diabetes mellitus is a disease of metabolism characterized by a deficiency of the internal secretion of the islands of Langerhans of the pancreas, *insulin*. In consequence, the total food metabolism is disturbed. The interference with the metabolism and storing of sugar is predominant. Hyperglycemia results and glycosuria follows as the blood sugar exceeds the renal threshold.

HISTORY OF DIABETES MELLITUS.[1]

"In Papyrus Ebers, a copy of an Egyptian medical compilation, already old in the time of Moses, there is mention of a disease, one of the symptoms of which was the frequent passing of large quantities of urine" (Saundby). This may have been diabetes. The symptom mentioned is common to other disorders, however.

Aretaeus of Cappadocia (30–90 A.D.) is the first known to

[1] Much of the early history of diabetes mellitus has been taken from the writings of Allen, Stillman and Fitz, appearing in Monographs of The Rockefeller Institute for Medical Research, 1919.

have called it by the name διαβαίνειν (to run through); διαβήτης (a siphon). He described it as "the flesh and bones running together into urine." It was Celsus (30 B.C.–50 A.D.) who gave a more distinctive description, but not until 1675 was it suggested that sugar might be lost in the urine. Willis, an Englishman, at that time spoke of the urine as being "wonderfully sweet as if imbued with honey." Matthew Dobson, in 1775, proved the presence of sugar in diabetic urine and observed that the blood serum was sweet. In 1778, Thomas Cawley gave the first description we have of a fatal case of diabetes with abnormal changes in the pancreas.

Diabetes mellitus was considered a "disease of digestion" by John Rollo, who, in 1796, began treatment by diet, using almost exclusively animal food and low value green vegetables. Von Mering and Minkowski, in 1889, proved the relationship between the pancreas and diabetes by removing the pancreas of a dog and thus producing severe diabetes. The beneficial effect of exercise in decreasing the amount of urinary sugar was recognized by Bouchardat (1806–1886). It was Cantani (born 1839) who introduced a new standard of strictness in treatment. His patients were isolated and were allowed a diet of meats and fats only. If sugar did not disappear from the urine, fast days were imposed.

Von Mering and O. Minkowski's[1] discovery that removal of the pancreas was followed by a rapidly fatal diabetes, opened avenues of research and therapy leading to the present-day management of this disease.

Opie[2] (1901) further crystallized the subject by proving the real seat of the disease to be in the islands of Langerhans.

Individually planned diets, based on the number of calories needed, were first advocated by Kulz (1845–1895) while the undernutrition régime was put on a thorough and

[1] v. Mering, J., and Minkowski, O.: Zentralbl. f. klin. Med., p. 393, 1889; Arch. f. exper. Path. u. Pharmakol., **26**, 371, 1889–1890.

[2] Opie, A.: Bull. Johns Hopkins Hosp., **12**, 263, 1901.

accurate working basis by Dr. Frederick M. Allen in 1914. This proved to be a great advance. The principles established by Allen still govern the dietetic control of diabetes. To reduce functional overstrain on the damaged pancreas, the total food value of the diet, hitherto very high, was reduced. The body weight fell and the tolerance for carbohydrate was increased. Many patients, who formerly would have died, survived on this program. Then in 1921 insulin was discovered.

For the epochal discovery of insulin we are indebted to two Canadians, Drs. Frederick Banting and Charles Best,[1] of Toronto. In 1902, Ssobolew had observed that if the duct, which carried the digestive juice from the pancreas to the intestine, was tied off, all the glands (acinar tissue) of the pancreas with the exception of the islands of Langerhans quickly degenerated and died. It was Banting who, in 1921, conceived the correct idea of making an active extract of the islands of Langerhans thus isolated. Hitherto the whole pancreas had been used for experimental work. Now we know that the failure to obtain an effective extract was due to the mixing of the two types of glands and their products. Insulin is rendered inert by contact with the digestive juice secreted by the pancreas. We owe tribute to these investigators and to Dr. Collip and Prof. Macleod, who, in the latter's laboratory at the University of Toronto, helped to make insulin safe for general use.

ETIOLOGY OF DIABETES MELLITUS.

Loss of pancreatic island tissue is considered responsible for the sequence of subjective and objective disturbances which characterize diabetes mellitus. We are in ignorance as to why the islands of Langerhans should be reduced in certain individuals or why, in others, an apparently sufficient number of islands do not produce a normal supply of insulin.

[1] Banting, F., and Best, C.: Jour. Lab. and Clin. Med., **7**, 251, 1922.

1. **Primary or Determining Causes.**—The direct cause or causes of diabetes are unknown. Experimentally, diabetes can be produced by removal of upwards of nine-tenths of the pancreas. No one questions that, if the human pancreas is reduced to a similar vestige in any manner whatsoever, diabetes results. Therefore, damage to the pancreas, a reduction in the number of islands of Langerhans, deserves first consideration. Allen attributes the primary pancreatic injury to infection—a pancreatitis. There is a growing tendency against this belief, but as yet with no plausible substitute. Injury short of causing diabetes may leave the pancreas a *locus minoris resistentiæ*, subject to further damage by overeating, obesity, or repeated minor infections, any of which may reveal the underlying condition months or years after the initial infection has subsided. It is not surprising then that the exciting or precipitating causes of diabetes have been placed in a position of seemingly greater significance than some infection which has been obscured by time.

We are obliged to consider a disturbed relationship between the various endocrine glands, more especially the thyroid, the suprarenal and the pituitary glands as a possible, though doubtless uncommon, cause of diabetes.

Thyroid secretion is known to inhibit insulin action; hyperthyroidism aggravates the diabetes, while amelioration of the signs of diabetes follows thyroidectomy.

Epinephrine also tends to neutralize the effect of insulin; cortical tumors of the suprarenal gland are known to cause diabetes (Achard-Thiers syndrome) and removal of one suprarenal gland alleviates moderately an experimental diabetes.[1]

Alkaline extracts of the anterior pituitary gland given to animals over a period of months have caused genuine dia-

[1] Barnes, B. O., Scott, V. B., Ferrill, H. W., and Rogoff, J. M.: Proc. Soc. Exper. Biol. and Med., **31**, 524–525, 1934.

betes;[1] basophilic adenomata[2] of the anterior pituitary has a similar effect while hypophysectomized animals are unusually sensitive to insulin. Combined disturbances of at least two of these glands is the rule when the altered function is such as to cause diabetes. This is especially true of tumors of the anterior pituitary and of the adrenal cortex.

The lack of a hypothetical insulin activator deserves mention as a possible cause of diabetes. Secretin activates the pancreas to liberate the external secretion. It is not beyond the realm of possibility that either in the stomach or in the duodenum a pre-insulin hormone is formed, the absence of which might explain the paradoxical presence of diabetes and ample pancreatic islands.

By way of summary we might expect to find in the diabetic a reduction of the functional elements of the pancreas normally present for the elaboration of insulin or a pancreas containing a number of islands of Langerhans too far in excess to be consistent with the experimental production of diabetes. Whether this is accounted for by inhibitory influences or lack of activation is not known.

2. **Predisposing Causes.**—Experience accumulated in statistics teaches that certain abnormalities precede the development of diabetes mellitus in a high percentage of cases. It is unknown how these predisposing influences operate, except that in some way they injure the islands of Langerhans and cause diabetes. The same influences in other individuals may damage the kidneys, causing Bright's disease; or the circulatory system, causing high blood-pressure or chronic heart disease. The selection seems to be best explained by an inherited vulnerability of certain organs. It still remains true that many, in fact the majority, have vital organs which are not sensitive to these influences and thus escape complications. The predisposing causes of diabetes will be dealt

[1] Evans, H. M., *et al.:* Proc. Soc. Exper. Biol. and Med., **29**, 857–858, 1932.

[2] Cushing, H.: Bull. Johns Hopkins Hosp., **50**, 137–195, 1932.

with in order of their apparent importance. Any combination of these influences multiplies the likelihood of bringing out of obscurity a latent diabetes mellitus.

Obesity.—The frequency with which overweight antedates the onset of diabetes in patients over forty years of age is remarkable—between 75 and 90 per cent. The influence of change in weight on the tolerance of the diabetes—*a gain in weight causes loss of tolerance and a loss of weight due to diet restriction a gain in tolerance*—makes it obvious that obesity increases the functional burden of the pancreas. A normal pancreas is adequate for the occasion and this no doubt explains why some obese persons escape having diabetes. An injured pancreas, on the other hand, is subjected to functional overstrain and frank diabetes results. Poor musculature, a characteristic of the obese, deprives the patient of much of the sugar burning properties of normal muscular exercise. The pancreas must carry the added burden.

The total metabolism in obesity exceeds normal. A man whose normal weight is 70 kilograms may weigh 100 kilograms. Instead of requiring about 2000 Calories, as he would if his weight were normal, he needs approximately 3000 Calories to maintain his weight. There can be no doubt that this needless increase in the total metabolism—a waste of enough food to maintain a child weighing 25 kilograms—eventually fatigues an injured pancreas, transforming the condition from a latent to an active diabetes.

Fat people who wisely reduce will rarely develop diabetes. *Members of the adult—not the child—diabetic regiment are, for the most part, conscripted from the fat candidates.*

Heredity.—It has long been known that a predisposition to diabetes is inheritable. Between 10 and 20 per cent of the diabetics give a family history of the disease. Living standards conducive to obesity are also inherited. The two combined make avoidance of diabetes less likely, while if overweight and infections are prevented, the inherited tendency may never assert itself.

Sympathy is certainly due the individual who falls heir to the tendency to diabetes through no fault of his own. Note that he falls heir *to the tendency, not to the diabetes.* Diabetes is not inherited. In compiling statistics, one is apt to forget the large number of ancestors, any one of whom may stamp the patient as a hereditary case (Joslin). Let us bear this in mind lest we exaggerate the importance of heredity as a predisposing cause of diabetes. On the other hand, the importance which heredity plays should not be minimized. Of Joslin's diabetic children, 44 of every 100 who have had diabetes for ten years have diabetic relatives. Doubtless, the number having diabetic relatives will increase in proportion to their longevity now that diabetics may live out a normal life expectancy. In one family of 12, reported by Joslin, all had diabetes. Landis has reported a diabetic family in which the disease developed in 5 blonde, but not in 4 brunette children of a diabetic mother. Such marked evidences of familial diabetes are rare, while instances of three generations punctuated here and there with diabetes are common. Relatives of diabetics are justified and are to be commended for submitting themselves to appropriate examinations to rule out diabetes mellitus or any tendency to this disease. Frequently these investigations permit early recognition of actual or potential diabetes, and open the way for preventive treatment.

Marriage.—It has been my custom, in answer to the question whether or not a diabetic should marry, to advise marriage if the other contracting party is free from and has no family history of diabetes. Two diabetics should not marry. It is unwise for two non-diabetics, each with a strong family history of diabetes mellitus, to marry. A sporadic diabetic, one with no history of diabetes in the family, marrying into a family free from this disorder is not likely to transmit a hereditary tendency.

Infection.—Allen states that infection is the primary cause of diabetes. It may also be the exciting cause. The recog-

nition of diabetes during or shortly after acute infections is common. Diabetes in the much larger group, in whom the onset is gradual, may be influenced by chronic infections such as sinusitis, infection about the teeth, tonsillitis, bronchitis, gall-bladder disease, appendicitis, prostatitis, etc. Infections may be local, as those mentioned above, or general, as pneumonia, typhoid fever, influenza, etc. An acute infection may have left the pancreas as a *locus minoris resistentiæ* for subsequent infections and intoxications. The bacteria or their toxins having gained entrance to the blood stream set up an irritation in the impaired organs and gradually increase the damage in them. Infection impairs the carbohydrate tolerance of the diabetic and improvement follows its eradication. It can be assumed that infection increases the demand on the slightly damaged pancreas as well as the truly diabetic. Infection with a predilection to injure the islands of Langerhans coëxisting with another pancreatic burden, obesity, doubtless produces diabetes. The combination of obesity, gall-bladder infection and diabetes in an individual between forty and sixty years of age is too frequent to be accidental.

Injury.—Body injury is occasionally mentioned as a cause of diabetes. The infrequency of diabetes among the soldiers in the World War is conclusive evidence against this belief. On the other hand, Case No. 2566 of the Physiatric series, a man, aged fifty-four years, was pronounced free from diabetes by the various tests, yet before six months of good health had elapsed, a moderately severe diabetes developed immediately following a serious automobile accident. Such an occurrence is rare. There was, in all probability, direct damage to the pancreas. This case should in no way influence the decision that physical injury plays little part in causing diabetes.

Miscellaneous.—Injury to the pancreas by tumors may produce diabetes. The tumor may involve the pancreas or adjacent structures. A stone blocking the pancreatic duct

has been known to precipitate diabetes. Arteriosclerosis may prevent normal absorption of insulin from apparently healthy islands of Langerhans and may account for a mild diabetes. Pregnancy imposes a functional burden on the pancreatic islands. It may suffice to bring to light a so-called potential or border-line diabetes.

INCIDENCE OF DIABETES MELLITUS.

Joslin, Dublin and Marks[1] estimate that there are between 300,000 and 400,000 diabetics in the United States and that, according to mortality statistics, 2,500,000 persons now living (2.08 per cent of the present population) may be expected to succumb ultimately to diabetes. This knowledge gives an added impetus to research in this field of pathology.

When all discounting factors—better and earlier diagnoses, more frequent health and insurance examinations and more reliable statistics—are considered, there is still a remarkable increase in the incidence of diabetes and diabetic mortality throughout the civilized world. The increase is greatest in the United States, moderate in Europe and least in Japan. It is greater in urban than in rural sections and greater in the higher strata of society than in the poorer classes.

It is notable that in all statistical reviews the increased death-rate is in the older age group—over forty years of age. The death-rate of young diabetics has been greatly reduced since the use of insulin has become universal. In effect the average age at death is becoming steadily greater.

Racial.—Jews are prone to become diabetic after middle life. This may be due to the tendency of the adult Jew to become overweight and to neglect physical exercise. Restriction of the diet and at the same time increasing outdoor exercise will accomplish much in attenuating the effect of what is undoubtedly a racial predisposition.

[1] Joslin, E. P., Dublin, L. I., and Marks, H. H.: Am. Jour. Med. Sci., **187**, 433–457, 1934.

Age.—Diabetes has been known to develop at any time from birth to old age. There is, however, a well known diabetic zone in which diabetes usually appears, namely, in the fourth, fifth and sixth decades. Diabetes in children is becoming more prevalent. This increase is more apparent than real. Diabetic children live now, while prior to 1922 their span of life was short. The actual number of children with diabetes mellitus will steadily increase during the first generation subsequent to the discovery of insulin.

Sex.—Diabetes mellitus, in recent years, is more prevalent among females than males. In the seventh decade of life there are nearly twice as many female as male diabetics. The difference decreases gradually until at, and below, forty years of age there is little difference in the frequency of diabetes in the two sexes.

PATHOLOGY OF DIABETES MELLITUS.

Removal of all the pancreatic tissue of an animal causes a severe and rapidly fatal diabetes, yet, in routine autopsies on cases of diabetes, obvious pathological changes in the islands of Langerhans are frequently lacking; and, furthermore, quite often no alterations in the pancreas can be detected by any of our laboratory methods. This does not necessarily mean that there are no changes in the cells of the pancreas. On the other hand, extensive changes have been found in both the acinar and island tissues in persons who were not diabetic before death.

The changes which are seen in the island tissues in patients who have died of diabetes, or in animals made diabetic by operation, are no doubt of great significance. Nine-tenths of a dog's pancreas is removed to produce experimental diabetes. The enormous reserve of the normal pancreas is thus drawn forcibly to one's attention. By subjecting the remaining fragment to functional overstrain by overfeeding and by giving an abundance of quickly absorbable carbo-

hydrate foods—hydropic degeneration of the islands of Langerhans can be produced.[1] The *beta* cells of the islands show signs of exhaustion. They become swollen and the specific granules, the pre-insulin state, disappear. Vacuoles appear in the cells from two to four weeks. Finally the cells rupture and disappear.

Prior to the discovery of insulin, Allen considered it probable that the hydropically degenerated cells could be restored to normal if the cell membrane and nucleus were still intact. Copp and Barclay[2] were successful in proving that hydropic degeneration is reversible with control of experimental diabetes. This may explain the gain in tolerance which ensues with successful treatment. When relief from functional overstrain was greatly delayed the *beta* cells were "practically completely lost." Figure 1 is a photograph of a typical island showing hydropic degeneration. Loss of the cells involved would greatly reduce the total island tissue. Figure 2 shows a typical island after fifteen days of symptomatic control by insulin. The amount of island tissue is not visibly reduced.

"If degeneration is not accompanied by regeneration, the islands will disappear or will manifest the atrophy described by Weichselbaum.[3] Or the degenerated islands may undergo hyaline transformation secondary to pancreatitis as described by Opie[4] or may become fibrosed." We may say, therefore, that in examining a pancreas for evidence of diabetes we must look for: (1) Hydropic degeneration—a state of fatigue due to abnormal demands for which the diabetes is accountable; (2) diminution in the number of islands; (3) the atrophy of Weichselbaum; (4) hyalinization; (5) fibrosis (Boyd).[5]

[1] Allen, F. M.: Jour. Metab. Res., **1**, 1–41, 1922.

[2] Copp, E. F., and Barclay, A. J.: Jour. Metab. Res., **4**, 445, 1923.

[3] Weichselbaum, A.: Sitzungsber. d. kais. Akad. d. Wissensch., Math.-Nat. Klasse, **119**, 73, 1910.

[4] Opie, W. L.: Special Cytology, edited by E. V. Cowdry, New York, Paul B. Hoeber, **1**, 393, 1932

[5] Boyd, W.: The Pathology of Internal Diseases, Philadelphia, Lea & Febiger, p. 387, 1931.

The first and more acute changes, often associated with lymphocytic infiltration of the islands, are in general more frequent in the young, and the more chronic in those past middle life.

Other organs may show important secondary changes. The glycogen of the liver is greatly reduced or absent—if

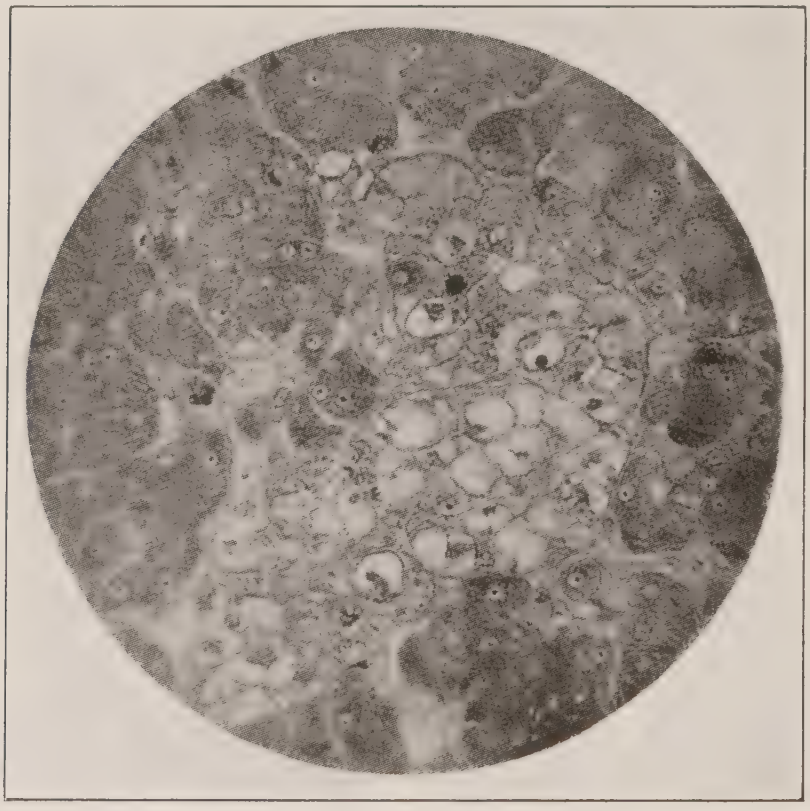

FIG. 1.—A photograph of a typical Island of Langerhans undergoing hydropic degeneration. The pancreatic tissue was taken from a diabetic dog before insulin treatment. (Copp and Barclay, J. Metab. Research.)

the diabetes has been unchecked. The glycogen in the muscles, the myocardium excepted, is depleted. This is true, too, of the skin, normally a reservoir for glycogen.

The liver cell nuclei are engorged with glycogen. Striking, also, is the presence of glycogen in the renal tubules. This constitutes the most definite pathological finding in the

postmortem diagnosis of diabetes (Boyd). The glycogen disappears from the tubules if insulin is used to best advantage.

The pancreas should be examined very promptly after death in order to observe the acute lesions which have been described. Blocks of tissue should be placed in proper

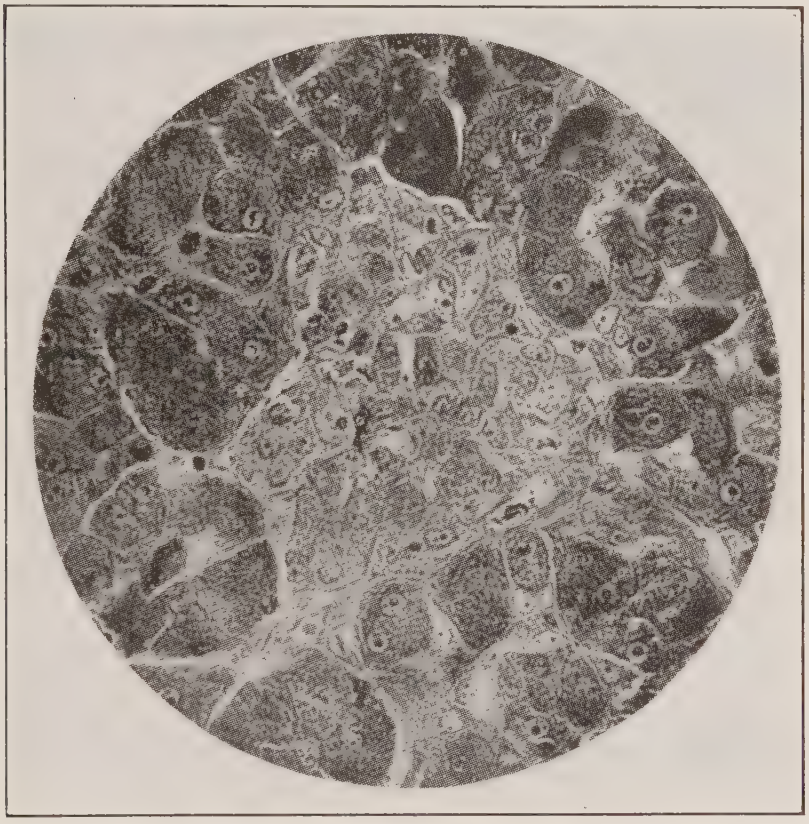

FIG. 2.—A typical Island of Langerhans after fifteen days of symptomatic control of the diabetes with insulin. Note the absence of hydropic degeneration and vacuolization. (Copp and Barclay, J. Metab. Research.)

fixatives[1] within two hours. Likewise, glycogen disappears from the tissues so rapidly that unless thin pieces of tissue are placed in absolute alcohol within an hour or two, this complex carbohydrate will be lost.

[1] A satisfactory fixative is chromic sublimate solution, *i. e.*, Zenker's fluid without acetic acid.

Arteriosclerosis may be generalized or local in the older patient. The arteries of the feet and legs are particularly affected by atheromatous changes. Coronary artery disease is common. I have no doubt the hyperglycemia, as well as hypercholesterolemia, contributes to the development of these degenerative changes.

The reader is referred to the excellent work of Warren[1] for a comprehensive presentation of the pathology of diabetes.

[1] Warren, S.: The Pathology of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1930.

CHAPTER II.

FOOD.

Food has been defined as a palatable mixture of foodstuffs. "A foodstuff is a material capable of being added to the body substance, or which when absorbed into the blood stream will prevent or reduce the wasting of a necessary constituent of the organism" (Lusk). It satisfies the energy and tissue requirements of the body. It is fuel, the source of body heat. Food makes possible normal growth, the repair of worn-out tissues, as well as the liberation of energy. A fasting man or animal burns his own tissues for these purposes. Loss of weight ensues. Food stores—fat and reserve glycogen—are first depleted. The vital organs are spared until the last. The preservation of life depends on food.

The organic foodstuffs which contain the stored energy are carbohydrate, protein and fat. The proportionate selection and adjusting of these food factors to meet the individual need of each patient comprises an important chapter in the successful treatment of diabetes.

Food for the maintenance of normal health must contain adequate quantities of certain non-heat forming and non-energy producing constituents. These are vitamins, mineral salts and water. They may appear to play a secondary part in the treatment of diabetes. The truth is that the foods chosen to control this disorder are generally rich in vitamins and contain ample mineral salts. All foods, in their metabolism, yield water. Liquid, in addition to that carried by the food, is necessary to satisfy thirst. In accomplishing this, the water needs of the body are usually satisfied. A general knowledge of the food, its origin, qualities and fate is desirable for wise selection of a dietary.

PROTEIN FOODS.

Protein is the basis of all cellular life and growth. Growing children require more in proportion to their weight than adults. Protein is the only food material containing nitrogen and sulphur that can replace tissue waste and build up new cells. Substitutes are possible for other foods, but not for protein. The chief protein foods are *meat, fish, eggs, milk, wheat gluten, cottage cheese, gelatin, peas, beans* and *nuts.* Egg-white is a pure form of protein free from carbohydrate and any appreciable amount of fat. Meat, eggs and milk contain the amino acids—tryptophane, lysine, tyrosine and histidine—which are essential for maintenance of normal health and growth.

FAT FOODS.

Fat is the big heat producer. It carries more than twice the number of calories per gram than do protein or carbohydrate. Fat cannot build or repair tissues, but when present in ample amounts it spares the protein.

Fat has an important bearing on diabetes. The glycerin of the fat, comprising 10 per cent by weight, is converted into sugar; and excess fat, leading to obesity, has a depressing influence on the insulin-producing islands of Langerhans and restricted fat has the opposite effect.

Fat is derived chiefly from *butter, cream, cheese, fat meat, salad oil, olive oil, corn oil* (Mazola), *cottonseed oil* (Wesson), *lard, nuts, chocolate, egg-yolks* and *certain fruits* (olives and alligator pears). Note: vaseline, mineral oil, paraffin and other petroleum products have no food value.

CARBOHYDRATE FOODS.

Carbohydrate or starchy and sweet foods are the chief sugar-containing constituents of a diet. Starch is in reality a complex sugar, whether we consider the starch of the grains,

corn starch, potatoes, or other vegetables and fruits. All carbohydrate before it can be absorbed through the intestinal wall into the blood must be reduced to simple sugars.

Glucose is the most readily absorbed form of carbohydrate, hence the efficacy of orange juice as an antidote for an insulin reaction. Orange juice contains glucose. One drop of orange juice boiled in the usual amount (5 cc.) of Benedict's solution for testing urine specimens gives a mild reaction for sugar; 3 drops a moderate and 9 drops a heavy reaction. Cane sugar, being a complex sugar, does not give a reaction for sugar when boiled with Benedict's solution.

The reduction or splitting-up of the starches takes place gradually. This is important in diabetes. The more complicated the sugars are (cereals and vegetables) the more slowly they are changed into simple sugars; the more slowly they are absorbed; the more slowly they affect the level of the blood sugar and the slower is the demand on the insulin-producing portion of the pancreas. Honey, candy and syrups are undesirable because they are not supplied gradually; they are absorbed rapidly; they affect the blood sugar quickly; they demand a sudden big supply of insulin; they are concentrated and so do not provide the satisfying and filling effects of a bulky meal with the same or less sugar value. Soldiers who have had to make forced marches know well the rapid, fatigue-relieving and energy-giving properties of candies.

Broadly speaking, carbohydrate supplies two-thirds of the energy of animal life. Being of simple chemical structure in comparison with fat and protein, it is the most readily available for energy demands. In excess the sugars are normally converted into fat and are stored as such throughout the body. Knowledge of this effect is made use of by the farmer in fattening stock and poultry. Unlike protein and fat, carbohydrate food is not utilized, except when in excess, even in part as other food factors but entirely (100 per cent) as sugar.

The chief carbohydrate foods desirable for the diabetic diet are *vegetables*, *cereals* and *fruit*. Oranges and grapefruit are pure carbohydrate foods, being free from fat and protein. Their low food value makes them desirable for the diabetic diet. The carbohydrate foods which are undesirable for the diabetic, and yet are excellent antidotes for insulin reactions (hypoglycemia), are cane sugar, candy, honey and syrups.

SELECTION OF FOODS.

Fruits.—Fruits are of value in the diabetic diet because of their relatively low food value and laxative properties. Furthermore, they are appetizing; they contain vitamins and their ash tends to neutralize excess acidity. Fruits may be preserved without sugar and kept indefinitely. When equal quantities of the juice and fruit are used, the food value is the same as the corresponding fresh fruit; but when the fruit alone is used, the food value is reckoned as one-half that of the fresh fruit.

Cereals.—A word of caution must be sounded in regard to these foodstuffs. Sweetening agents are frequently added. This is true particularly of bran preparations. Washed bran may be used if necessary with a portion of the allowed cream. One cannot go far astray by using only oatmeal, rolled oats, Shredded Wheat, Wheatena, Farina, Puffed Wheat and Mead's cereal. Cereals which require cooking are more easily digested if cooked from two and a half to three hours.

Bread.—Bread has been described as the staff of life. In preparing the diabetic diet there is no choice but to fill the carbohydrate allowance largely with bulkier foods—fruits and vegetables. They become the "staff of life" for the diabetic. Bread made with Lister's flour, and muffins with soy bean flour, serve admirably as substitutes for bread. They are low in carbohydrate and yet provide a pleasant vehicle for butter. The uncertainty of the food value of the

various "diabetic breads" renders their use inadvisable. Included in this group is gluten bread which closely approximates and, in some instances, equals the carbohydrate value of white bread.

Meat, Eggs and Fish.—All fresh meats and fish of known food value and in proper amounts are permissible in the diabetic diet. Liver and kidneys should be included. Meat provides protein of the best quality. Meat is unjustifiedly blamed for a multitude of disorders. Except in certain conditions of ill health, especially renal and advanced liver disease, it is not necessary to stint the meat intake. Sugar is frequently added in the process of canning meat, which excludes this form of meat from the diabetic diet. Sausages, on account of great discrepancies in food value, are best omitted. Freezing or smoking meat does not detract from or add to its nutritive properties. Such meats can be used in suitable amounts without fear. Meat extracts and clear broths are practically free from food value. Their satisfying effect is doubtless due to their palatability, and to the stimulating effect they have in increasing digestive juices.

Eggs have an important place in special diets. They are high in food value and rich in vitamins. They contain protein of the best quality. The average egg weighs about 60 grams (2 ounces). Eggs are easily digested if soft or well cooked.

Vegetables.—Vegetables cooked and raw lend bulk to the diet. They supplement meat nicely in satisfying the appetite. Their numbers allow frequent substitutions and in this way prevent monotony. Vegetables contain carbohydrate, protein, vitamins and minerals. Peas and beans are particularly rich in protein. "Thrice cooking" vegetables is an excellent method of retaining bulk, while decreasing the food value, but one which is no longer necessary. Vegetables lose their vitamins when heated if not properly covered. Canned vegetables should be heated before the can is opened.

Fresh green vegetables such as cabbage, peas, spinach, beans, asparagus and carrots should be boiled in as little

water as possible and cooked until just tender. Strong flavored vegetables should be cooked in plenty of water.

Dairy Products.—Milk is a splendid food and essential for very young children. Older diabetics prefer eating to drinking their food allowance. It is a good plan to substitute cream on cereals and in other ways when possible. The quantity used will be small in comparison with milk and much of the carbohydrate will be spared, permitting more fruit and vegetables. The top 4 ounces of a quart of milk which has been undisturbed for twenty-four hours contains approximately 20 per cent fat. Whipping cream is 40 per cent of fat. Butter contains the fat of milk. It is the most easily digested form of fat and has high fuel value. Eaten with carbohydrate foods it tends to improve digestion by delaying their egress from the stomach. Unsalted butter contains a slightly higher percentage of fat than salted butter.

Cheese is rich in fat, protein and mineral elements, as well as vitamin A. Its high food value gives it a place in the concentrated diet. Thoroughly masticated and eaten with other foods it is readily digested.

Miscellaneous.—*Beverages.*—Weak tea and coffee may be included in the diabetic diet. Kaffee Hag makes an agreeable substitute. Patients are glad to have these beverages to which they can add some of the cream. Saccharin (no food value) may be used as a sweetening agent, though successful reëducation of taste will not call for sweet flavoring. An infusion of cocoa shells is a tasty and useful drink which for practical purposes has no food value. Patients on low diets find it particularly satisfying between meals.

Agar.—This is useful as a thickening agent. It may be used in making bran bread or jellies. It may be flavored with saccharin and the various extracts. It has a great advantage over bran in correcting constipation when intestinal irritation is to be prevented.

Flavoring Agents.—Vanilla, lemon and other extracts have negligible food values and can be used for flavoring purposes,

as can peppermint, anise seed, curry, ginger, paprika, celery salt, mustard and onion extract. Vinegar may also be employed if carbohydrate-free (distilled). Small quantities of horse-radish may be used without reckoning its food value. Caraway seeds may be added to bran biscuits before baking.

Mineral oil (no food value) used in mayonnaise serves as a good substitute for salad oil, which is a pure fat. It may be used for greasing pans. In simple reducing diets and in low-calorie diabetic diet, mineral oil may be used in preparing mayonnaise, pie crust, griddle cakes and Cellu-bran cookies.

CHAPTER III.

FOOD METABOLISM.

Introduction.—A clearer conception of diabetes mellitus and of obesity is obtained and a better understanding of the rationale of their respective treatments is gained, if one is familiar with the common methods of approach to the study of food metabolism.

Metabolism may be defined as the sum total of physical and chemical changes which have to do with the utilization and ultimate disposal of food in the maintenance of body tissue and their functions. Using McLester's words—"The activity of the various organs, the maintenance, of body temperature, the performance of work and the development of electrical currents all express the transformation of potential energy into an active equivalent." Heat, measurable in a calorimeter, is evolved as these transformations take place. The gaseous exchange between the living organism and the surrounding atmosphere may be observed simultaneously. The total heat, expressed in calories, liberated in the metabolism of food can thus be calculated.

The minimum rate of energy exchange during fasting (twelve to eighteen hours without food), and while the body is at complete physical and mental rest is the *basal metabolism*. It follows that the amount of food which exactly provides the calories to cover this need is the *basal diet*.

The basal metabolism increases and decreases with the surface area of the body. DuBois[1] has prepared a chart, Fig. 3, which simplifies the calculation of the surface area when the height and weight are known. The Benedict and

[1] DuBois, E. F.: Basal Metabolism, 2d ed., Philadelphia, Lea & Febiger, 1927.

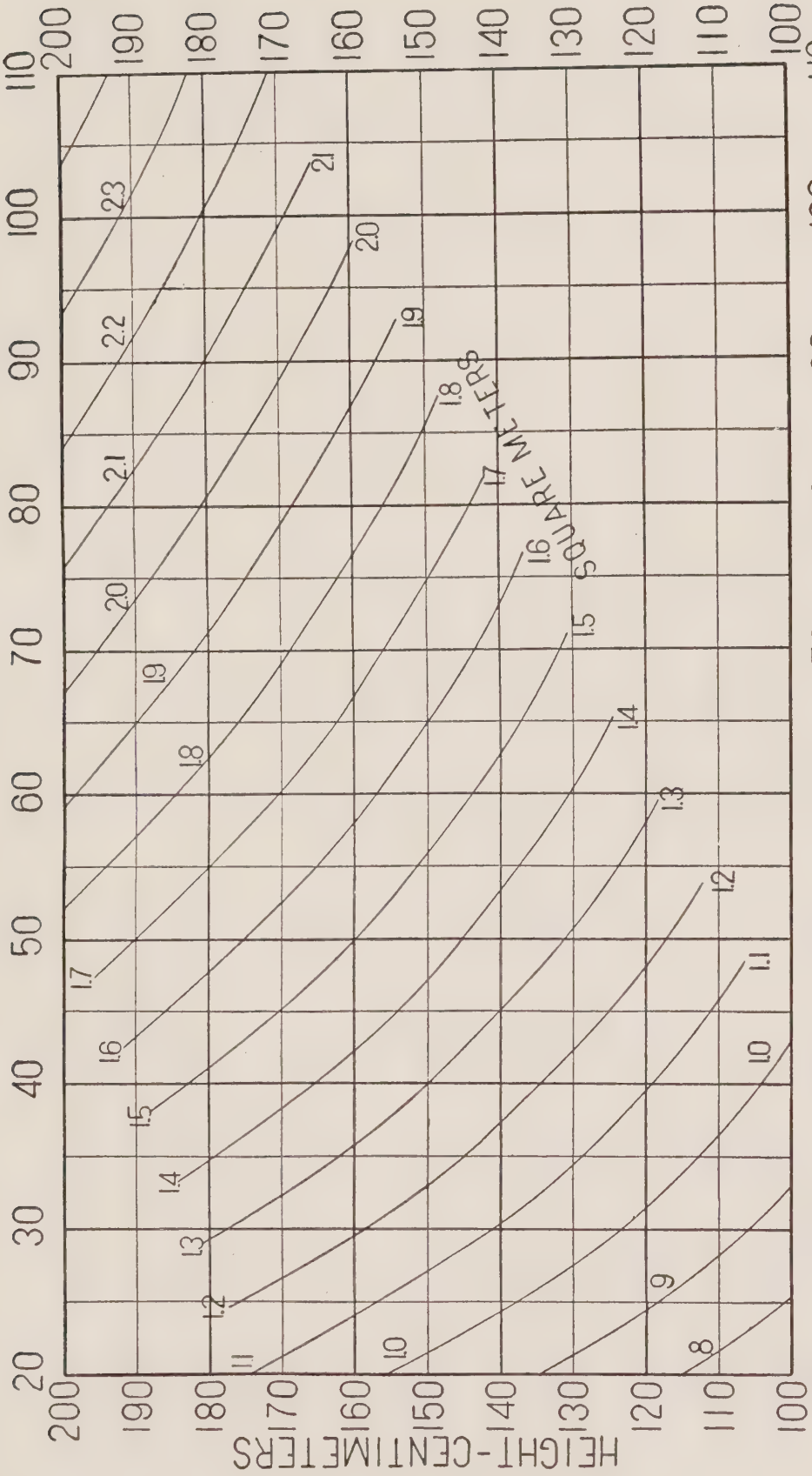

FIG. 3.—Chart for determining surface area of man in square meters from weight in kilograms (Wt.) and height in centimeters (Ht.) according to the formula: Area (sq. cm.) = $Wt.^{0.425} \times Ht.^{0.725} \times 71.84$. (DuBois.)

Talbot[1] table, Table 1, is used for estimating the surface area of children.

TABLE 1.—ESTIMATED BODY-SURFACES FOR BODY-WEIGHTS FROM 3 TO 40 KILOGRAMS (BENEDICT AND TALBOT).

Body-weight (without clothing).	Surface* estimated for boys.	Surface* estimated for girls.	Body-weight (without clothing).	Surface* estimated for boys.	Surface* estimated for girls.	Body-weight (without clothing).	Surface* estimated for boys.	Surface* estimated for girls.
kilos.	*sq. m.*	*sq. m.*	*kilos.*	*sq. m.*	*sq. m.*	*kilos.*	*sq. m.*	*sq. m.*
3	0.208	0.210	16	0.711	0.686	29	1.086	1.048
4	.252	.255	17	.740	.714	30	1.110	1.072
5	.292	.295	18	.769	.742	31	1.134	1.095
6	.330	.333	19	.797	.769	32	1.159	1.119
7	.388	.388	20	.825	.796	33	1.183	1.142
8	.424	.424	21	.853	.845	34	1.207	1.164
9	.459	.459	22	.879	.872	35	1.230	1.188
10	.492	.492	23	.906	.898	36	1.254	1.210
11	.524	.534	24	.932	.924	37	1.277	1.233
12	.556	.566	25	.958	.949	38	1.300	1.255
13	.586	.597	26	1.009	.974	39	1.323	1.277
14	.616	.627	27	1.035	.999	40	1.345	1.298
15	.645	.657	28	1.060	1.024			

* Surfaces estimated, using formula $K\sqrt[3]{w^2}$, for values of K at the different weight-ranges.

The basal metabolic rate is subject to certain influences. For instance, when diabetics were severely undernourished, it was reduced from 5 to 20 per cent. This is true, also, of a normal person who submits to prolonged undernutrition. Age and sex influence the basal metabolism also; children have a higher rate per square meter than adults, and males a higher rate than females. These differences are illustrated after Aub and DuBois[2] in Table 2.

Fever and certain drugs, particularly thyroid preparations, alpha-dinitrophenol, dinitro-ortho-cresol and epinephrin increase the basal metabolic rate. This behavior stands out

[1] Benedict, F. G., and Talbot, F. B.: Carnegie Inst. of Washington, Pub. No. 302, 1921.

[2] Aub, J. C., and DuBois, E. F.: Arch. Int. Med., **19**, 824, 1917.

in the diabetic in whom it causes a decrease of food tolerance and in consequence an increased insulin requirement. It is noteworthy, also, that when metabolism is increased by muscular exercise, as is always the case, the opposite effect holds; *i. e.*, the food tolerance is increased and the need for insulin becomes less.

TABLE 2.—CALORIES PER SQUARE METER OF BODY SURFACE PER HOUR (HEIGHT-WEIGHT FORMULA). (AUB AND DUBOIS.)

Age, years.	Males.	Females.
14–16	46.0	43.0
16–18	43.0	40.0
18–20	41.0	38.0
20–30	39.5	37.0
30–40	39.5	36.5
40–50	38.5	36.0
50–60	37.5	35.0
60–70	36.5	34.0
70–80	35.5	33.0

The metabolism of food itself stimulates the metabolic rate. This influence is more pronounced with protein than with fat or carbohydrate. In treating diabetes stimulation of metabolism other than by exercise is not desirable. Great excesses of protein are therefore avoided.

Certain diseases, notably Graves' disease, leukemia and, less noticeably, pernicious anemia, increase the metabolic rate.

Total Metabolism.—The total metabolism is the sum of the basal metabolism and the increment over and above the basal need for the performance of work, assimilation of food and response to fever, etc. For purpose of illustration, assume that a patient with a normal weight of 154 pounds (70 kilograms) has a basal requirement of 1750 Calories (25 Calories per kilogram) and that 600 additional Calories are required for the accomplishment of light work. The total metabolism is then 2350 Calories. If this patient is allowed to gain in weight to 220 pounds (100 kilograms) the basal requirement increases to approximately 2500 Calories (25 Calories per

kilogram). This increase is in proportion to the increase in weight and surface area. The calories in excess of the basal need may or may not remain unchanged though the obese person may conserve energy and in reality may accomplish the same ends as formerly with less energy output. Nevertheless, the total metabolism is greater when he is obese than it was formerly, even though the basal metabolic-rate per square meter remains normal.

It would seem that the extra functional demand on the vital organs due to the increase in the total metabolism could account for many of the complications of obesity to which we attribute the shortened longevity. It is not unusual to have the total metabolism of an obese patient as high as 25 per cent above the metabolism calculated according to his ideal weight.

Is this the explanation of the early decrease of functional reserve of the various organs which leaves the obese person with diabetes, gout, disease of the circulatory system or kidneys, as the case may be?

RESPIRATORY QUOTIENT.

The respiratory quotient is the ratio of the volume of carbon dioxide expired to the volume of oxygen inspired during the same interval of time. The quantity of oxygen required in metabolism depends on the kind of material oxidized in the organism; and the relation between the amount of oxygen absorbed and the carbon dioxide eliminated depends on the same factor (Lusk).[1]

As metabolism of food proceeds, oxygen is consumed; carbon dioxide is given off and energy is liberated.

Lavoisier found that there was more oxygen inspired than CO_2 expired. Knowing that any volume of oxygen uniting with carbon produced a like volume of carbon dioxide

[1] Lusk, G.: The Science of Nutrition, Philadelphia, W. B. Saunders Company, p. 57, 1923.

(Avogadro's law), he concluded that some of the inspired oxygen must have been used to oxidize hydrogen in the production of water. When the volume of carbon dioxide eliminated is less than the oxygen inspired, in other words, when the respiratory quotient, $\frac{\text{Volume } CO_2}{\text{Volume O}}$, is less than unity, some of the oxygen has been used to oxidize hydrogen to form water.

Carbohydrate molecules carry adequate oxygen to unite with the hydrogen content to form water. It is obvious then, when carbohydrate alone is burned, the R.Q. is unity; or above unity if carbohydrate is converted into fat, a poor container of oxygen.

The fat molecules lack sufficient oxygen to bring about complete reduction to carbon dioxide and water. The reduction of the R.Q. below unity is in direct proportion to the volume of inspired oxygen utilized for this purpose. It is known that R.Q. of fat alone is 0.71; while that of protein is 0.8. The average R.Q. on a mixed diet is about 0.83.

The impaired utilization of carbohydrate in diabetes tends to decrease the R.Q. It may be as low as 0.7, but with control of the diabetes a prompt increase follows.

Respiratory quotient studies aid in determining the value of new remedies for treating diabetes. With other factors constant a rising R.Q. indicates improved utilization of the carbohydrate, while no change may indicate the worthlessness of the preparation which is being evaluated.

The relative amounts of carbohydrate, protein and fat metabolized may be calculated when the R.Q. and the nitrogen excretion are known. Each gram of urine nitrogen represents, in the absence of renal disease, metabolism of 6.25 grams of protein, the oxidation of which requires 8.45 grams oxygen and sets free 9.35 grams of carbon dioxide. The oxygen and carbon dioxide that have to do with the protein metabolism is thus calculated and deducted from the total respiratory exchange. The non-protein R.Q. rep-

TABLE 3.—ANALYSIS OF THE OXIDATION OF MIXTURES OF CARBOHYDRATE AND FAT. (LUSK.)

R.Q.	Percentage of total oxygen consumed by: Carbohydrate (1)	Fat (2)	Percentage of total heat produced by: Carbohydrate (3)	Fat (4)	Calories per liter O_2. Number (5)	Logarithm (6)
0.707	0.0	100.0	0.0	100.0	4.686	0.67080
0.71	1.02	99.0	1.10	98.9	4.690	0.67114
0.72	4.44	95.6	4.76	95.2	4.702	0.67228
0.73	7.85	92.2	8.40	91.6	4.714	0.67342
0.74	11.3	88.7	12.0	88.0	4.727	0.67456
0.75	14.7	85.3	15.6	84.4	4.739	0.67569
0.76	18.1	81.9	19.2	80.8	4.751	0.67682
0.77	21.5	78.5	22.8	77.2	4.764	0.67794
0.78	24.9	75.1	26.3	73.7	4.776	0.67906
0.79	28.3	71.7	29.9	70.1	4.788	0.68018
0.80	31.7	68.3	33.4	66.6	4.801	0.68129
0.81	35.2	64.8	36.9	63.1	4.813	0.68241
0.82	38.6	61.4	40.3	59.7	4.825	0.68352
0.83	42.0	58.0	43.8	56.2	4.838	0.68463
0.84	45.4	54.6	47.2	52.8	4.850	0.68573
0.85	48.8	51.2	50.7	49.3	4.862	0.68683
0.86	52.2	47.8	54.1	45.9	4.875	0.68793
0.87	55.6	44.4	57.5	42.5	4.887	0.68903
0.88	59.0	41.0	60.8	39.2	4.899	0.69012
0.89	62.5	37.5	64.2	35.8	4.911	0.69121
0.90	65.9	34.1	67.5	32.5	4.924	0.69230
0.91	69.3	30.7	70.8	29.2	4.936	0.69339
0.92	72.7	27.3	74.1	25.9	4.948	0.69447
0.93	76.1	23.9	77.4	22.6	4.961	0.69555
0.94	79.5	20.5	80.7	19.3	4.973	0.69770
0.95	82.9	17.1	84.0	16.0	4.985	0.69770
0.96	86.3	13.7	87.2	12.8	4.998	0.69877
0.97	89.8	10.2	90.4	9.58	5.010	0.69984
0.98	93.2	6.83	93.6	6.37	5.022	0.70091
0.99	96.6	3.41	96.8	3.18	5.035	0.70197
1.00	100.0	0.0	100.0	0.0	5.047	0.70303

Formula for column (R.Q. = R)

$$(1)\ \% = \frac{100\,R - 0.707}{0.203} \qquad (3)\ \% = \frac{505.7\,(R - 0.707)}{5.047\,(R - 0.707 + 4.686)\,(1.00 - R)}$$

$$(2)\ \% = \frac{100\,1.00 - R}{0.293} \qquad (4)\ \% = \frac{468.6\,(1.00 - R)}{5.047\,(R - 0.707) + 4.686\,(1.00 - R)}$$

$$(5)\ \text{Calories} = \frac{4.686 + R - 0.707 \times 0.361}{0.293}$$

(6) Logarithm = log. of Column 5

resenting the fat and carbohydrate remains. Lusk's[1] modification of Zuntz and Schumburg's table, Table 3, makes it a simple matter to determine the relative quantities of carbohydrate and fat metabolized.

A knowledge of the R.Q. is not necessary for the successful treatment of diabetes. In fact this study remains only of scientific interest. It is an instrument of precision for the research worker.

A calorimeter which permits the simultaneous measurement of the heat produced by the organism (direct method) and the gaseous exchange or a Tissot or a Douglas bag apparatus which allow measurement of the gaseous exchange are satisfactory for estimating the R.Q.

FOOD METABOLISM IN THE NORMAL AND IN THE DIABETIC.

Normal food metabolism depends on many factors, but in dealing with diabetes we are particularly concerned with those features, the disturbance of which characterizes this disease.

Food—protein, fat and carbohydrate—received by the digestive tract is of complex molecular structure the disintegration of which is one of the first steps in digestion. Mastication and gastric peristalsis allow intimate contact with salivary and stomach digestive juices.

The food or chyme reaches the first part of the small intestine in liquid form. Here it is subjected to further reduction by the action of the various secretions, the most important being the one supplied by the pancreas. This secretion reaches the duodenum by way of the pancreatic duct (Wirsung's duct). It is secreted by the acinar portions of the pancreas. It is quite distinct from the internal secre-

[1] Lusk, G.: The Science of Nutrition, Philadelphia, W. B. Saunders Company, p. 61, 1923.

tion, insulin, which is absorbed directly into the blood stream when freed from the islands of Langerhans.

It will simplify matters to deal separately with the assimilation of the different food factors from their entrance to the digestive tract to their ultimate disposal.

Carbohydrate.—Carbohydrate digestion begins in the mouth. Ptyalin of the saliva starts the reduction of the starches (polysaccharides) to simple sugars. Its activity continues in the stomach until arrested by increasing quantities of hydrochloric acid. The acid hydrolyzes cane sugar to some extent.

In the intestine, amylase of the pancreas quickly reduces starches to maltose while invertase of the succus entericus reduces cane sugar to glucose and levulose; maltase reduces maltose to glucose and lactase reduces lactose to glucose and galactose. By far the most important of these monosaccharides is glucose. Glucose is absorbed from the small intestine and is carried by the portal vein to the liver, where it is largely stored as glycogen. Small quantities may go directly to the muscles. Glycogen is normally found in practically all organs of the body, but particularly in the liver, muscles and skin. It is used in the expenditure of energy. The supply is renewed by withdrawals from the glycogen storehouse—the liver. The glycogen is changed to sugar and is carried in this form to the muscles where it is again converted to glycogen. The fact that energy is being expended continuously accounts for the presence of the sugar normally found in the blood. It is refueling all parts of the body. Sugar in excess of that needed for energy and adequate glycogen storage is deposited throughout the body as fat. The quantity of sugar in the blood, the storage of glycogen and the utilization of sugar by the tissues are under the control of insulin. Insulin, by virtue of this influence over the oxidation of sugar, is indirectly responsible for the complete combustion of the fats.

The end-products of carbohydrate metabolism are carbon

dioxide and water. Elimination is by way of the kidneys, lungs and skin.

Carbohydrate is a source of energy, 4 Calories per gram, and it is the largest antiketogenic factor in a diet.

In unchecked diabetes, with the lack of insulin, there follows an arborizing effect on the entire field of food metabolism. The immediate and striking disturbance is in the utilization of sugar. The reduction in the sugar metabolized is proportionate to the diminution of the insulin supply, and only traces of glycogen may be found in the liver. There is, however, no interference with the absorption of sugar from the intestine; nor is the production of the normal quota of sugar from the fat and protein diminished. Considering these facts along with the inability of the organism to use or store sugar, the resulting hyperglycemia and glycosuria are not surprising.

Coinciding with the reduction of sugar metabolism the respiratory quotient decreases from the normal (0.83) to as low as 0.7.

Protein.—Protein digestion begins in the stomach where pepsin and hydrochloric acid convert the protein to peptone, rennin converts caseinogen to soluble casein and the nucleo-proteids are reduced to nuclein. In the duodenum, trypsin in an alkaline medium, facilitated by the bile salts, carries the reduction process to the polypeptid stage and nuclein is hydrolyzed, liberating nucleic acid.

Erepsin in the small intestine completes the transformation of the protein to amino-acids. Nucleic acid under the action of a series of ferments is reduced to adenine and guanine.

The protein is absorbed through the intestinal wall and reaches the portal circulation as amino-acids. They are conveyed to the liver. Some pass on into the general circulation for the building and repair of tissues, while the balance undergoes a process of deamination in the liver. A non-nitrogenous residue remains while ammonia is liberated.

The ammonia is converted by the liver into urea, which is eliminated in the urine. Part of the non-nitrogenous residue is converted into glucose and part gives rise to ketone bodies. The intermediary metabolism of protein—from the amino acid to the excretory stage—is complex. There are gaps in our knowledge of the process. It will suffice here to state that the nitrogenous end-products are urea, creatinine, uric acid, ammonia, inorganic sulphates, etc., and that they are excreted chiefly by the kidneys and to an unimportant extent in the feces and perspiration. Nitrogen in the urine is an exact index of protein metabolism (under normal conditions each gram of urinary nitrogen represents the metabolism of 6.25 grams of protein). Nitrogen is always excreted in normal urine whether food is taken or not; protein is always being used. When the intake is inadequate the protein (endogenous) of the less important body structures is sacrificed to maintain the proper repair and regeneration of the tissues of the more important organs. The nitrogen excretion is then high in proportion to the intake; in other words, a negative nitrogen balance exists. Nitrogen equilibrium is one of the requisites of a properly balanced diet. This is accomplished when the nitrogen excreted equals exactly that taken in the food. High-carbohydrate and, to a much less extent, liberal fat diets spare protein metabolism. Diets deficient in carbohydrate and fat increase protein metabolism.

The amount of protein converted into glucose to furnish energy is variable. Less is used for this purpose if the protein intake is low and more if the intake is high.

Protein metabolism is also affected by diabetes and should be considered. In the first place, protein is a source of sugar. Therefore, incomplete use of protein, so far as the sugar content is concerned, accompanies diabetes. In the starving diabetic who has lost all his available carbohydrate stores, the amount of sugar excreted is in constant relation to the nitrogen output. This suggests that the sugar is derived from tissue protein. When the dextrose-nitrogen

(D-N) ratio is 3.6, protein is the source of the entire amount of sugar, as 1 gram of urinary nitrogen represents the metabolism of 6.25 grams of protein, of which 58 per cent (3.6 grams) becomes sugar. Secondly, protein has definite ketogenic properties, 46 per cent. In normal metabolism these influences are amply balanced by its own antiketogenic properties. The advantages offered by the latter may be greatly reduced in severe diabetes. They may, in fact, be so slight, along with the general depression of carbohydrate metabolism, as to allow the ketogenic influence to contribute to the development of ketosis. Thirdly, protein has a stimulating effect on metabolism—an undesirable action in diabetes. Experimentally, this effect is quite evident. Clinically, I believe its importance is overemphasized, particularly where excess total calories are avoided. Fourthly, protein is a source of calories, a property of major importance in the calculation of a diet for the diabetic.

Fat.—The digestion of fat by a lipase commences in a small way in the stomach while in the small intestine the pancreatic lipase and the succus entericus assisted by bile actively hydrolyzes the fat, liberating fatty acids. The alkaline pancreatic juice, the intestinal juices and the bile convert the fatty acids into soap. This soap aids in forming an emulsion, allowing the lipase greater freedom and effectiveness of activity. Finally, the soap, glycerine and fatty acids, assisted by the presence of bile, are taken up by the epithelium of the small intestine. Fat is reformed in the cells of the intestinal villi; it is carried by lymphocytes to the lacteals where it is liberated, thence to the thoracic duct and the systemic circulation.

Fat is found in the blood as neutral fat (chiefly), lecithin, free cholesterol and cholesterol combined with fatty acid. The blood fats are increased in diabetes, pregnancy and also in nephritis, anemia and slightly during starvation.

Accumulations of fat throughout the body are derived

largely from the fat of the food though carbohydrate, and to a much less extent protein also contributes.

Fat may be directly utilized by the tissues. Macleod[1] believes it is transformed to carbohydrate before it can be used by the muscles. During the process of utilization of fat certain fatty acids (ketogenic factors) are formed, the complete oxidation of which depends upon the simultaneous combustion of sugar (antiketogenic factor). More will be said of this later. The glycerol content of fat (10 per cent) is utilized as sugar and as such exerts an antiketogenic influence. Normally the ultimate fate of fat is complete reduction to CO_2 and water.

Fat is the chief source of the acids which cause ketosis. These are aceto-acetic acid, β-hydroxybutyric acid and acetone. These acids are partly oxidized fats. Without the kindling effect of adequate carbohydrate combustion the fats remain in this highly toxic and soluble stage. They are in part excreted in the urine and acetone is expelled also by way of the lungs. The air hunger of ketosis is a compensatory effort to eliminate these acids.

Ninety per cent of the fat and approximately 46 per cent of the protein are used as fatty acids. Together they represent the total ketogenic properties of a diet. The need for an important antiketogenic influence is obvious. This is best filled by sugar, the combined sources of which are: carbohydrate, 100 per cent; protein, 58 per cent, and fat, 10 per cent.

Shaffer[2] observed that when the combustion of antiketogenic molecules equalled the ketogenic molecules, there was no significant increase in ketonuria. Woodyatt[3] worked out the ketogenic-antiketogenic ratio based on the molecular

[1] Macleod, J. J. R.: The Fuel of Life, Princeton University Press, p. 2, 1928.

[2] Shaffer, P. A.: Jour. Biol. Chem., **47**, 433 and 449, 1921; **54**, 399, 1922; **61**, 585, 1924.

[3] Woodyatt, R. T.: Arch. Int. Med., **28**, 125, 1921.

weight of glucose (180) and fatty acid (270). The ratio being:

$$\frac{\text{Ketogenic}}{\text{Antiketogenic}} = \frac{\text{K}}{\text{AK}} = \frac{.9\ \text{F} + .46\ \text{P} \quad \text{(molecular wt. 270)}}{\text{C} + .58\ \text{P} + .10\ \text{F} \quad \text{(molecular wt. 180)}} = 1.5$$

(F = fat; C = carbohydrate; P = protein.)

This ratio has been based on the fairly definite relationship which exists between the metabolism of fatty acids and glucose. It is considered that, under ordinary circumstances, the combustion of 1 gram of glucose will serve for the complete oxidation of 1.5 grams of fatty acid.

In general, when this ratio is adhered to, an adequate diet will not in itself be a cause of ketosis. It allows a maximum caloric intake without danger of ketosis.

Recently, with the trend to the use of more liberal carbohydrate allowances, the margin by which the glucose equivalent exceeds the fatty acid content largely eliminates the necessity of calculating the $\frac{\text{K}}{\text{AK}}$ ratio.

CHAPTER IV.

THE SYMPTOMS AND DIAGNOSIS OF DIABETES MELLITUS.

THE SYMPTOMS OF DIABETES MELLITUS.

While consideration is given to the varied symptomatology of diabetes—loss of weight, general weakness, polyphagia, polydipsia, polyuria, backache and skin symptoms—it is well to remember that many diabetics have no symptoms and that the disease is often recognized accidentally. This group is not immune to symptoms, nor is their diabetes innocent; but the actively progressive stages have not been reached.

The physician who recognizes diabetes during this early phase renders his patient a great service. The disorder is easily controlled without exacting treatment and insulin is rarely needed. Many of these patients owe much to chance examinations for other disorders, to regular check-up and to insurance examinations.

Loss of Weight.—A rapid loss of weight in the afebrile patient suggests diabetes. The weight loss is due to food loss. Sugar is lost in the urine; ketone bodies, also a potential food (acetone 4 Calories and β-oxybutyric acid 7.5 Calories per gram) are excreted in varying quantities; and the water loss is especially significant as the ketosis becomes more intense. It is difficult to attach too much importance to the question of weight because the untreated diabetic who is losing weight is at the same time losing his pancreatic reserve. Once he becomes thin, the necessity of using insulin for an indefinite period may be inescapable. Compare him with the patient whose diabetes is recognized and treated while he is still overweight, whose pancreas is put at rest

by reduced food intake—not starvation by any means—the glycosuria ceases, water loss stops, pancreatic efficiency is increased by virtue of a release from functional overstrain. In this case, also, a gradual loss of weight will ensue, but this reduction is due to a limited intake, not an abnormal output which represents that which the pancreas, when worked to capacity, is unable to utilize.

Risking monotony by repetition, I reiterate: a loss of weight, a decrease in total metabolism by restriction of the total diet, decreases food loss, gives the pancreas functional rest, and affords a remarkable improvement in tolerance. A loss of weight due to the activity of the diabetes destroys tolerance; the diabetes becomes more severe, and the need for insulin increases.

Polydipsia, Polyuria and Other Symptoms.—Increased thirst and polyuria are the outstanding symptoms which suggest diabetes to the laity. They are not always present; but the thirst is often distressing and many quarts of liquid daily may fail to quench it. The onset of these symptoms may be gradual, or it may occur with dramatic suddenness.

Bachache receives little attention as a symptom in the literature. Most diabetics who suffer from severe polyuria have some backache. It is probably due to distention of the kidney capsule. Normal persons can produce this symptom by taking large quantities of water.

The other symptoms scarcely require comment. The polyphagia is a compensatory effort to replace lost nourishment. The general weakness is attributable to the loss of food in the form of sugar and ketone bodies. It is a form of starvation peculiar to diabetics. The skin symptoms—furuncles, carbuncles, intertrigo, pruritus and eczema—may be the first evidences of diabetes. These disorders, as well as symptoms referable to the extremities, are complications of diabetes and will be dealt with as such in their respective chapters.

PHYSICAL EXAMINATION OF THE DIABETIC.

Many diabetics have no physical evidences of the chronic disorder from which they suffer. It must be said, however, that the more careful the search, the more often it will be rewarded. From the obviously robust diabetic to the other extreme, that of fatal intoxication, all shades of health are observed.

Unusual distress from an upper respiratory tract infection, a boil, eczema, etc., may cause the patient to present himself for treatment. Certain complications may at once suggest diabetes. A series of staphylococcic skin infections are especially suggestive. Xanthochromia, xanthomata and xanthoma diabeticorum (rare) may be observed on inspection. Evidence of weight loss and dehydration may be apparent.

The routine examination of the diabetic may uncover: diabetic cataract, diabetic retinitis, decreased intra-ocular tension (in coma), dry skin, dryness of mouth and pharynx, poor teeth, gingivitis and arterial disease, especially in the extremities, accounting for disturbed nutrition of tissues.

Furthermore, infections to which the untreated diabetic is specially susceptible may be recognized. The most common in addition to those already mentioned are tuberculosis, septicemia (staphylococcic and streptococcic), pneumonia, pruritus, especially due to hyphomycetes about the genitalia while glycosuria persists, carbuncles, furuncles and trichophyton infections.

The signs of ketosis and circulatory diseases so common with diabetes are omitted here as they will be dealt with in some detail later. This also applies to the other important complications.

THE DIAGNOSIS OF DIABETES MELLITUS.

Laboratory Studies.—Glycosuria is the most common lead to the diagnosis of diabetes. Hyperglycemia after a fast

exceeding four hours is more conclusive. In the usual case the foregoing findings establish the true nature of the disorder.

Any evidence suggestive of diabetes should instigate an investigation, the result of which should clearly confirm or exclude the suspicion. A verdict of "a tendency to diabetes" is indecisive.

The blood and urine may be normal under the usual circumstances, yet under additional strain—test meal, excessive sweets, overfeeding, or during an infection, etc.—hyperglycemia and glycosuria may appear. The term "potential diabetes," which rightly implies the need of continued caution, has been applied to this group. We must not hide behind a diagnosis of "alimentary glycosuria" without first determining its certainty. Observation and study, clinical and laboratory, are essential to establish the diagnosis and to deduce the approximate severity of the diabetes. The treatment will depend upon the "degree of diabetes."

The Urine.—*Glycosuria.*—Great dependence is placed on the routine urinalysis. It has proved to be the most important, though not the most delicate, test in recognizing diabetes. Glycosuria may vary from a single trace appearing in only one specimen per day to heavy reactions, 2 to 15 per cent, appearing in all voidings. The specific gravity is proportionately higher with increasing sugar. Pale urine with a specific gravity above 1.030 suggests glycosuria. The volume of urine is usually increased, amounting from a quart and a half to several gallons in twenty-four hours. Large amounts of water are necessary to eliminate large quantities of sugar without renal damage.

Examination of twenty-four-hour collections of urine enables quantititative estimation of the amount of sugar excreted. One should remember that sugar excreted for only a short period in the entire day may be diluted beyond detection in a twenty-four-hour accumulation. Of the single specimens, the one most likely to contain sugar is the one voided from three to five hours after the biggest meal of the

day; not in the morning after a night's fast. Ordinarily, glycosuria occurs when the blood sugar exceeds 0.15 per cent. This is the renal threshold—the level at which the kidneys can no longer hold back sugar. The renal threshold has a normal fluctuation from 0.15 to 0.17 per cent. Young diabetics have renal thresholds within this range, but the older diabetic and the patient with diabetes of long standing tend to have higher threshold values, from 0.18 per cent to the high but uncommon level of 0.28 per cent.

The blood sugar concentration may exceed the threshold levels for short periods without glycosuria, but when this degree of hyperglycemia is protracted, sugar appears in the urine. I have noted many times that the renal threshold appears to be elevated for a short period after insulin treatment is begun.

Glucose reduces Benedict's and Fehling's solutions; it is fermentable and rotates the plane of polarized light to the right (dextro-rotatory). Glycosuria is not always indicative of diabetes, nor does its absence exclude it. Renal glycosuria, due to faulty absorption of sugar by the tubules of the kidneys, may account for the finding in a non-diabetic. Furthermore, lactose, levulose, pentose, glycuronic acid and alkaptonuria will give misleading reactions for sugar when the usual tests are employed. There are minute quantities of sugar in normal urine, less than 0.01 per cent.

Glycosuria is influenced by several factors. A low-calorie diet is second only to insulin in decreasing the urine sugar. Restriction of the carbohydrate, and of less importance, the protein intake have a similar influence. The substitution of polysaccharides for the more rapidly absorbed simple sugars decreases glycosuria; hence the value of fruits and vegetables which have the added advantage of having a low carbohydrate and caloric value. Increased physical activity, eradication of infection and the rapid emaciation attending malignant disease all tend to decrease glycosuria, as do certain unusual cases of fulminating tuberculosis.

It follows that overfeeding especially with high-carbohydrate, high-calorie diets and simple sugars (monosaccharides); decreased exercise, infections, gain in weight, as well as too rapid reduction of insulin, increase glycosuria.

Ketonuria.—Ketonuria is common in the diabetic. Increasing amounts of acetone, aceto-acetic acid, and later β-oxybutyric acid in the urine are easily detected signs of impending ketosis and coma. Prompt remedial measures are called for. Small quantities of ketone bodies may be excreted indefinitely without harm. This was a common occurrence when high-fat and low-carbohydrate diets were employed. Ketonuria is also attributable to undernutrition and to complications which tend to cause ketosis. It is corrected by increasing the carbohydrate or decreasing the fat of the diet, or both. Any influence which tends to increase carbohydrate combustion tends to overcome ketonuria.

Renal Glycosuria.—Renal glycosuria is an innocent condition, the peculiarities of which are: constant loss of sugar (glucose) in the urine without hyperglycemia. This occurs chiefly in young patients contrary to the general behavior of diabetes mellitus with which it is confused at times. It causes no symptoms or inconvenience to the patient. It is not affected by diet or insulin, nor is it, in my estimation, a forerunner of diabetes. Cases have been reported in which it is believed that diabetes followed renal glycosuria.

Experimental renal glycosuria may be provoked by the administration of phlorizin. Temporary renal glycosuria, attributable to a transitory depression of the renal threshold, occurs in pregnancy, hyperthyroidism and pituitary disease.

Importance attaches itself to this form of glycosuria because of the danger of mistaking it for diabetes. It is obvious that the safety of the patient may lie in the correct diagnosis.

I have under observation a diabetic: a girl, aged twenty-two years, who has had diabetes for eight years and who developed a coincident renal glycosuria approximately three years after the onset of the diabetes. In this instance the

glycosuria is affected by insulin and diet, but never to the point of aglycosuria. Her treatment in recent years has of necessity been guided by blood analyses chiefly.

Renal glycosuria is probable if, when the diet is restricted, or when insulin is given, there is no decline in the urine sugar. Parallel examinations of blood and urine (see Table 4), revealing constant glycosuria with no hyperglycemia establishes the diagnosis.

TABLE 4.—THE FINDINGS IN THE PRESENCE OF RENAL GLYCOSURIA.

1 P.M.	1.30 P.M.	2 P.M.	2.30 P.M.	3 P.M.
Blood sugar	Urine sugar	Blood sugar	Urine sugar	Blood sugar
0.092 per cent	0.2 per cent	0.1 per cent	1.9 per cent	0.096 per cent

It may be necessary to exclude a coëxisting latent or potential diabetes by further tests, after test meals or glucose.

Lactosuria.—Lactose may be found in the urine during the last days of pregnancy and during the nursing period. The blood sugar remains normal. Lactose reduces Benedict's and Fehling's solutions; but unlike glucose, it does not ferment. Rubner's test may be used to detect lactose.

Levulosuria.—Levulose (fructose) rarely appears in the urine without glucose. When this does occur in the non-diabetic, it is due to an individual intolerance for this sugar. It reduces copper and ferments as does glucose. It differs from the latter, however, in possessing the power of rotating the plane of polarized light to the left (levo-rotatory).

Pentosuria.—The chronic form of pentosuria (essential pentosuria) bears no relation to diabetes. The pentose excreted is arabinose, a reducing sugar the source of which is not known. It does not rotate the plane of polarized light.

Alimentary pentosuria results, in certain persons, from ingestion of large quantities of pentose-rich fruits—prunes, cherries, plums, grapes, fruit juices, etc. The pentoses appear only temporarily in the urine.

Glycuronic Acid.—The output of the conjugate glycuronates is greatly increased as the result of the administration of acetyl-salicylic acid, antipyrin, borneol, camphor, chloral hydrate, menthol, morphine, naphthol, pyramidon, turpentine, etc. As a group, the glycuronates reduce Benedict's solution, but are non-fermentable.

Alkaptonuria.—Homogentisic acid, which is present in the urine of alkaptonuric patients, reduces Benedict's and Fehling's solutions. It does not, however, react to Nylander's reagent. The urine turns dark on standing, due to the alkalinizing effect of the ammonia. Prompt dark discoloration of urine occurs when sodium hydroxide or ammonia are added. Homogentisic acid does not ferment or rotate the plane of polarized light.

The Blood.— *Normal Blood Sugar.*—Different methods of determining the blood sugar account for some variation of normal values. With the new Benedict[1] technique, which is probably the most accurate and most generally used, the normal blood sugar, principally glucose, ranges between 0.07 and 0.1 per cent. This method is used at the Jefferson and Pennsylvania Hospitals, Philadelphia, and unless otherwise stipulated, the values used in this book are according to this method. The other procedures in common use are shown in Table 5.

TABLE 5.—THE NORMAL BLOOD SUGAR (WHOLE BLOOD) DETERMINED BY DIFFERENT METHODS.

	Per cent.
1. Benedict[1]	0.07–0.10
2. Folin's modification[2]	0.08–0.11
3. Folin-Wu[3]	0.09–0.10
4. Hagedorn and Jensen, also Bang method	0.09–0.11

Micro methods, by which the sugar content in a minute quantity of blood is determined, are passing out of vogue. The methods themselves are satisfactory, but the possibility

[1] Benedict, S. R.: Jour. Biol. Chem., **92**, 141, 1931.
[2] Folin, O.: Jour. Biol. Chem., **77**, 421, 1928.
[3] Folin, O., and Wu, H.: Jour. Biol. Chem., **41**, 367, 1920.

of error is unnecessarily increased. Furthermore, the hope that less pain would attend the taking of the blood sample for micro study was unfounded. If skilfully taken, larger quantities of blood can be drawn from one of the superficial veins with least discomfort.

The sugar content of the plasma is higher than that of the corpuscles, but for clinical purposes no distinction need be made. Normal arterial blood contains a higher concentration of sugar than venous blood. In severe untreated diabetics this difference partially or completely disappears. Following treatment the ability of the tissues to extract sugar from the blood returns, in consequence of which there is again a lower sugar concentration in the venous than in the arterial blood.

Blood Sugar in Diabetes.—Hyperglycemia is the most decisive sign of diabetes. Without it the diagnosis cannot be made, yet there is no elevation of the blood sugar in the controlled and potential diabetic. A fasting blood sugar above 0.11 per cent is usually due to diabetes. The fact that mild diabetics frequently have a normal fasting blood sugar should be remembered, and on no account should this be a basis upon which diabetes is excluded.

Example (Case No. 8643): P. B., male, aged sixty years, was treated in January, 1929, for an acute pharyngitis and myocardial disease. A trace of urine sugar was found on one occasion. A normal fasting blood sugar served, but falsely, to exclude diabetes. The patient was admitted to the Pennsylvania Hospital in June of the same year in diabetic coma with a blood sugar of 1.28 per cent (Folin-Wu method).

The mild diabetic has the lowest blood sugar in the morning before breakfast, at the end of the longest period without food. Generally speaking, the highest values are found between two or three hours after the biggest meal of the day.

The severe untreated diabetic also has the lowest, but not normal, blood sugar before breakfast and the highest

about three hours after the evening meal—since the three meals in close succession give the pancreas no opportunity to catch up. The severe diabetic receiving three doses of insulin is likely to have the highest blood sugar before breakfast, at the end of the longest period in the day without insulin.

Note that the mild diabetic has adequate endogenous insulin, after the three meals are taken care of, to bring the morning blood sugar to the lowest point of the day. In other words, the pancreatic islands are gaining ground during fasting metabolism. This is not so in the severe insulin-treated diabetic. The functional integrity of the insulin-producing mechanism is such that the fasting metabolism gains on it after the effect of the evening dose of insulin has worn off. When this occurs a steadily increasing blood sugar is the rule. The wisdom of giving insulin early in the morning is apparent.

It is an obvious mistake in the case of a patient who ordinarily takes insulin and has breakfast between 6 and 7 A.M. to delay breakfast and insulin until 9 A.M. to have a blood sample taken. If the specimen of blood cannot be taken before the usual time of insulin administration, it should be taken after. Otherwise a misleading hyperglycemia may be obtained at 9 A.M. on the day of the test, while at this same time other days normal values may exist (see Table 6).

TABLE 6.—ILLUSTRATION OF A MISLEADING HYPERGLYCEMIA CREATED BY DISTURBING THE ROUTINE OF A SEVERE INSULIN-TREATED DIABETIC.

Date.		Blood sugar, per cent.	
		6.30 A.M.	9 A.M.
January 4	Insulin, 6.45 A.M.; breakfast, 7.15 A.M.	0.108	0.120
January 6	Insulin and breakfast delayed for 9 A.M. test. Insulin, 9 A.M.; breakfast, 9.15 A.M.	0.108	0.200
January 8	Insulin, 6.45 A.M.; breakfast, 7.15 A.M.	0.110	0.116

The blood sugar alone is not an accurate index of the severity of the diabetes. Mild diabetics may have blood sugars between 0.3 and 0.4 per cent and a severe diabetic

a blood sugar of 0.2 per cent. A knowledge of the blood sugar and of the body weight is of special significance in summing up the "degree of diabetes." Almost without exception a persistent hyperglycemia (fasting), in an underweight person, is indicative of a severe diabetes; while a fat person who has never taken insulin is always a mild diabetic. A reduction in weight in the latter case is feasible and desirable and will result in a prompt control of the diabetes without insulin. The thin hyperglycemic diabetic cannot afford to lose weight, nor is it desirable. In fact, a gain in weight and an increase in the total metabolism may be essential to good health. To accomplish this end, and at the same time to control the diabetes, insulin will be needed.

The blood sugar in diabetes varies from normal to many times this amount. The average for the first visit will be between 0.2 and 0.25 per cent. In diabetic coma it is higher—from 0.3 to 0.8 per cent. One of Dr. Allen's patients, seen in 1924, had a blood sugar exceeding 1.4 per cent (Benedict). That patient, then aged seventeen years, has since graduated from college and is now married. Argy[1] reported a blood sugar value of 1.71 per cent and Lawrence[2] a value of 2.06 per cent in cases of coma.

In contrast to the normal person whose blood sugar rises promptly and returns to normal within two hours of taking sweets, the sugar concentration in the blood of the diabetic increases slowly and is maintained longer—three or more hours.

Insulin given subcutaneously, or intravenously, lowers the blood sugar of the normal as well as of the diabetic. This effect begins promptly and the extent depends on the size of the dose; yet, oddly enough, the sugar lowering effect is not in direct proportion to the dosage. A dose of 40 units does not lower the blood sugar twice as much as one of 20 units.

[1] Argy, W. P.: Boston Med. and Surg. Jour., **193**, 1236, 1925.
[2] Lawrence, R. D.: Brit. Med. Jour., **3817**, 377, 1934.

It is well known that the smaller the dose of insulin given the greater is the effectiveness per unit.

The blood sugar, in severe diabetes, begins to increase from six to eight hours after insulin. In the mild diabetic the apparent effect of insulin is more protracted—even to eighteen hours.

TABLE 7.—COMPOSITION OF HUMAN BLOOD.*

Constituent.	Normal range, mg. per 100 cc.†	In diabetes.
Hæmoglobin per cent (Haden)	15.6	Increased in ketosis
Urea N.	10–15	Increased in ketosis
Glucose	70–100	Increased
Total fatty acids	290–420	Increased
Cholesterol	150–190	Increased
Lipoid phosphorus (lecithin)	12–14	Increased
Total acetone bodies (as acetone)	1.3–2.6	Increased
Acetone aceto-acetic acid (as acetone)	0.3–2.0	Increased
β-hydroxybutyric acid (as acetone)	0.5–3.0	Increased
CO_2 capacity (plasma) vol. per cent	55–75‡	Decreased in ketosis
CO_2 content (arterial blood) vol. per cent	45–55‡	Decreased in ketosis
CO_2 content (venous blood) vol. per cent	50–60‡	Decreased in ketosis
Chlorides as NaCl	450–500	Decreased in ketosis
Sodium (serum)	330	Decreased in ketosis

* Extracted from Hawk and Bergeim's Practical Physiological Chemistry, by courtesy of P. Blakiston's Son & Co.

† Figures express concentration in milligrams per 100 cc. of whole blood unless otherwise indicated in first column.

‡ Figures represent weighted averages of the observations of several investigators.

Overdosage of insulin causes abnormally low blood sugar values. The typical hypoglycemic, or insulin reaction, usually occurs when the blood sugar falls below 0.05 per cent. Lower percentages—down to 0.03 per cent—are not uncommon while complete disappearance of sugar from the blood, on one occasion, was reported by Smith.[1] The clinical features of hypoglycemia will be dealt with in detail later.

Brain injury, from hemorrhage, tumors, and degenerative changes, may cause hyperglycemia and glycosuria in the non-diabetic. Recently I have seen 3 patients, comatose as a result of cerebral hemorrhages, who had not diabetes, yet

[1] Smith: Boston Med. and Surg. Jour., **195**, 663, 1926.

the blood sugars were in the neighborhood of 0.2 per cent and there was glycosuria. Hyperglycemia also occurs in renal disease, febrile disturbances, Grave's disease, diseases of the liver, and of the circulatory system, especially arterial hypertension.

Blood Lipids.—Great interest surrounds the subject of blood lipids and their behavior in the diabetic. Gray[1] considers blood fat a reliable prognostic indicator; its elevation affecting the prognosis adversely. Rabinowitz[2] selects one of the lipids, cholesterol, to be of special value in prognosis. Joslin[3] has left no doubt that he believes high blood lipids are contributory to the development of arteriosclerosis and gangrene in the diabetic. He reports, furthermore, that patients with a very low blood cholesterol—below 90 milligrams per 100 cc.—die early while those with a very high cholesterol content in the blood—above 400 milligrams per 100 cc.—are especially prone to complications, *i. e.*, arteriosclerosis, lipemia retinalis and cataract. The bearing which increased cholesterol has upon the development of arteriosclerosis has been discussed by Bowen and Koenig.[4]

The four fatty substances: cholesterol, lecithin, glycerin esters, and cholesterol esters, present in normal blood, are increased in the untreated diabetic and especially so in cases of ketosis.

For clinical purposes, cholesterol estimations are valuable guides as to the blood lipids as a whole. The normal blood cholesterol varies from 0.13 to 0.19 per cent while in the diabetic the concentration not infrequently exceeds 0.3 per cent.

This abnormal lipid accumulation, hypercholesterolemia, is overcome by maintaining a normal blood sugar; if the diet

[1] Gray, H.: Treatment of Diabetes Mellitus, by Joslin, Philadelphia, Lea & Febiger, p. 239, 1928.

[2] Rabinowitz, I. M.: Canadian Med. Assn. Jour., **17**, 171, 1927.

[3] Joslin, E. P.: Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, p. 252, 1928.

[4] Bowen, B. D., and Koenig, E. C.: Buffalo Gen. Hosp. Bull., **51**, 3, 1927.

contains adequate carbohydrate, and if the patient is not overnourished, or severely undernourished.

Hypercholesterolemia is, in short, an indication of poorly controlled diabetes. It is not surprising, therefore, that diabetics with excessive blood cholesterol have a less favorable prognosis and are prone to the chronic degenerative disorders which too frequently complicate diabetes.

Further blood studies will be dealt with in the chapter on Ketosis.

Special Tests.—When the blood and urine are normal, further tests than those already alluded to are needed to establish the diagnosis. The value of such investigations is emphasized when one recalls seeing a patient who has been needlessly and ineffectively dieting to correct renal glycosuria. On the other hand, a beneficial restraint may be laid on the person with a true but latent diabetes. Any one of several tests may serve to identify diabetes, but as proof that no impairment in the carbohydrate tolerance exists, greatest reliance is placed, and properly so, on a normal response to the glucose tolerance test.

Assuming that the fasting blood sugar and urinalyses are normal, the examinations mentioned below may be carried out in sequence. The need of each successive step arises when the preceding one is found to be normal.

1. *Blood Sugar Estimation and Urinalysis.*—(*a*) Fasting; (*b*) two hours after an ordinary meal; (*c*) two hours after a high carbohydrate meal, see Table 8.

Table 8.—Test Meal Containing 100 Grams Carbohydrate.

		P.	F.	C.
Banana . . .	155 grams (1 medium)	1.5	....	34.1
Shredded Wheat .	30 grams (1 biscuit)	3.3	0.3	22.5
Milk	240 grams (1 cup)	7.2	9.6	12.0
Bread (white) .	60 grams (2 slices)	5.4	0.6	31.8
Butter	10 grams (2 teaspoonsful)	....	8.5	
Total calories, 642		17.4	19.0	100.4

2. *Glucose Tolerance Test.*—The details of this test are as follows:

7.55 A.M.—The bladder is emptied and the specimen examined for sugar. Blood for sugar estimation is taken at this time, the patient having had no food since the previous evening.

8.00 A.M.—One hundred grams of pure glucose dissolved in 200 cc. of water are given by mouth, the juice of a lemon or a few crystals of citric acid being added to make it more palatable and to prevent nausea.[1]

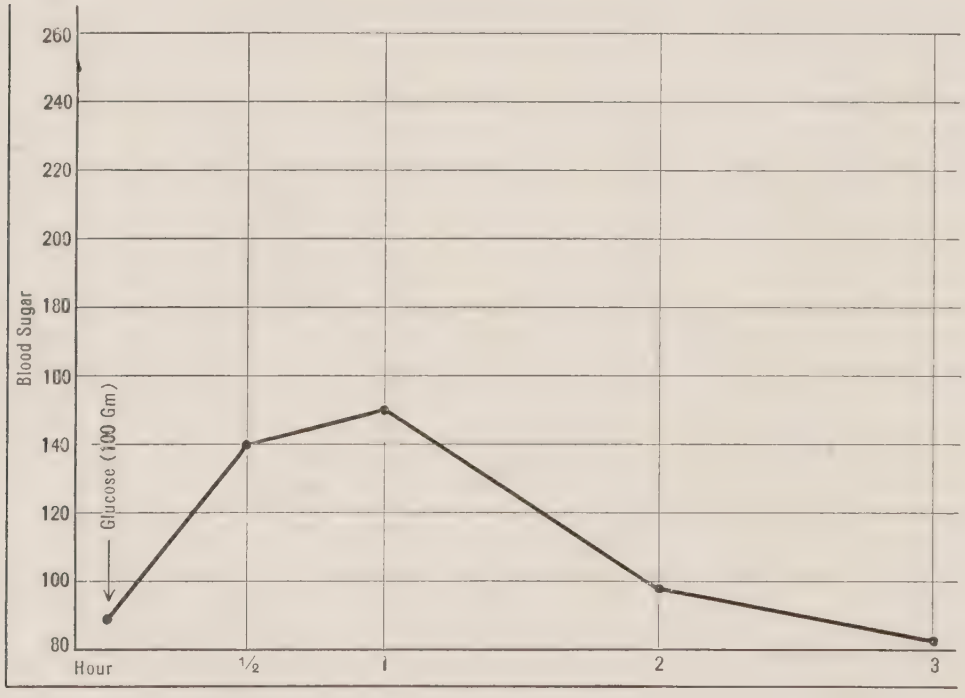

FIG. 4.—Normal glucose tolerance curve.

8.30 A.M.—One-half hour later; blood and urine samples are taken, and also at 9, 10 and 11 A.M.

The test reveals the fasting blood sugar and the levels to which the sugar rises, and how rapidly it falls during the three-hour period. Information regarding the kidney thresh-

[1] The quantity of glucose used is usually 100 grams for the adult. Less may be employed for children. The author uses 50 grams for young children, and 75 grams from about ten to fifteen years of age.

old is gained by noting at what point sugar is first found in the urine. Glycosuria does not occur, as a rule, in the absence of diabetes.

Diabetes can be excluded with certainty if the blood sugar does not exceed 0.16 per cent and has returned to normal (below 0.1) in two hours.

Diabetes is present beyond doubt if the blood sugar is in excess of 0.18 per cent and has not returned to normal in three hours. Between these two groups are the questionable cases.

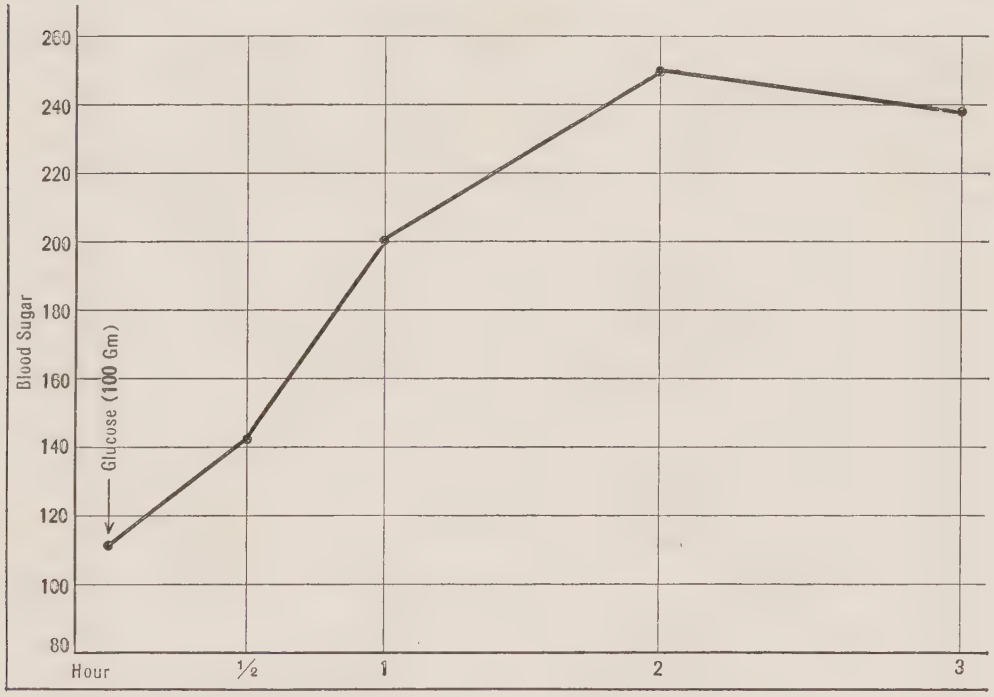

FIG. 5.—Glucose tolerance curve of a diabetic.

While probably not actually diabetic, they may become so if exposed to definite predisposing influences.

Glucose makes experimental diabetes more severe, while starch carrying the identical glucose equivalent may not. Normal tests after a high carbohydrate meal are valuable antecedents to the glucose tolerance test. I have made it a practice to obtain this proof of pancreatic efficiency before subjecting patients to the more severe test. It would be well if insurance companies would return to this procedure in

preference to the indiscriminate resort to the glucose tolerance test, when evidence, slight or gross, of diabetes presents itself in applicants for insurance.

Hamman and Hirschmann[1] have shown that one dose of glucose given by mouth will lessen the hyperglycemia resulting from a second dose. This is believed to be due to a sensitization of the insulin secreting mechanism by the first dose. Ellis[2] succeeded in reducing the insulin requirement of diabetics by frequent administration of glucose. Part of this result was undoubtedly due to the increased effectiveness per unit of insulin brought about by small and frequent in place of larger and less frequent doses of insulin.

Staub[3] and Traugott[4] have incorporated the above principle in a test for diabetes. In this test the greater is the increase and the more prolonged is the elevation of the blood sugar after the second dose of 20 grams of glucose, given ninety minutes after the first dose, the more severe is the diabetes.

[1] Hamman, L., and Hirschmann, I. I.: Bull. Johns Hopkins Hospital, **30**, 306, 1919.

[2] Ellis, A.: Quart. Jour. of Med., **3**, 137, 1934.

[3] Staub, H.: Biochem. Ztschr., **118**, 93, 1921; Ztschr. für klin. Med., **43**, 98, 1922.

[4] Traugott, K.: Klin. Wchnschr., **1**, 892, 1922.

CHAPTER V.

DIABETES MELLITUS IN CHILDREN AND IN THE ELDERLY.

DIABETES MELLITUS IN CHILDREN.[1]

It is well known that diabetes is usually severe in children. Insulin is needed in addition to accurate dietetic management in most cases to assure normal growth. Unlike adult diabetics, the majority of children do not give a history of overweight prior to the onset of diabetes, but they tend to be taller than normal.

The diabetic child does splendidly under accurate treatment. He grows, plays and achieves equally with the normal child. If permitted, these children will often neglect exercise and relaxation in order to attain a high mark at school. The mature desire for distinction appears early, and may result from the fact that in dealing with diabetes they have had to contend with problems advanced for their years. Diabetes afflicts children of the better class with greater frequency than those in poorer stations of life. The latter may be less pampered and have more wholesome foods with less sweets. They may get more outdoor exercise; and at an early age necessity demands that they earn a livelihood by physical rather than mental effort. I have never seen a newsboy who had diabetes.

The child with advanced diabetes is blessed with the advantages of insulin. While the urine and blood tests are satisfactory, he enjoys perfect health, but he is close to a precipice at all times. A misstep may end fatally within two or three days if the parents are not adequately informed.

[1] A comprehensive presentation of this subject is given by Dr. P. White: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932.

Children with diabetes are in greater immediate potential danger than adults. The danger is from ketosis. This dangerous complication is usually the result of carelessness. Parents may become neglectful of the tests after many months of uneventful progress. At first a few, later many tests are omitted. Would it not be a good plan to allow well meaning, but careless, parents to see the next child admitted to the hospital in diabetic coma? The struggle for life is pathetic. If health is restored, the diabetes is found to be more severe than formerly. It is more difficult to control, and larger doses of insulin are necessary.

Parents must be alert to these possibilities, and to their prevention. The well informed need have no fears. They see that the tests are made regularly and that the diet is accurately prepared; that the child gets enough exercise; and that the physician is notified at once if sugar appears in the urine, if vomiting occurs, or if there is evidence of infection.

My earnest exhortation to parents is, "Trust no one with your child's health until he is prepared to relieve you of this responsibility." Education is important. Let diabetes be his first course. His knowledge of this subject will mean more to him than anything else. It is a means of life. With it achieved he can reach out in other directions.

The child makes an excellent patient. He is more frank than the adult. Neither parents nor physicians should reveal any suspicion or distrust to the child. He will learn to live up to the standard which your attitude sets for him. The child's confidence is the physician's first goal. The novelty of the new régime of diets, charts, and tests may be made sufficiently interesting to be readily accepted by the well-disciplined child.

Record of a Child Diabetic.—L. C., male, aged four years, was seen on April 4, 1928. The chief complaints were: excessive thirst; failure to gain weight and frequent urination, 20 times daily, and frequent bedwetting. Sugar

had been found in the urine in March when his family physician was consulted for treatment of a laryngitis and bronchitis.

The family history is negative except that one brother, aged fifteen years, weighs 68 kilograms (150 pounds).

The past illnesses consisted of measles at two years of age, two attacks of tonsillitis, one attack of bronchitis and laryngitis in March, 1928.

Present Illness.—The symptoms already mentioned were troublesome for one month and the bedwetting was a common occurrence since infancy.

The positive findings on physical examination were: height, 42½ inches; weight, 16 kilograms (36 pounds); appeared underweight, face thin, dark rings under eyes, posterior cervical glands enlarged, tonsils diseased, chest rachitic, abdomen moderately distended. The other findings were irrelevant.

The urine contained 0.5 per cent sugar and the blood sugar was 0.13 per cent. A restricted diet had been observed for four weeks prior to these tests. In consequence the glycosuria was reduced.

NOTES.—By referring to Table 9 it will be seen that an initial diet of 50 grams of protein (3 grams per kilogram of body weight), 75 grams fat, 80 grams carbohydrate and 1200 Calories (75 Calories per kilogram of body weight) was prescribed. Increases were made from time to time until in June, 1934, a diet of 65 grams protein (1.8 grams per kilogram), 157 grams fat, 180 grams carbohydrate and 2400 Calories (67 Calories per kilogram) was reached. I have not been able to determine why this boy requires such a high caloric intake while other children have accomplished a satisfactory gain in weight with 800 Calories less.

In the space of six years the blood sugar was found elevated 3 times though glycosuria occurred more frequently. Enuresis proved an accurate indication of glycosuria. The

TABLE 9.—CASE L. C., ILLUSTRATES THE SATISFACTORY PROGRESS OF A CHILD WITH MILD DIABETES. NOTE THE INCREASING WEIGHT AND HEIGHT AND THE FINAL ELIMINATION OF THE INSULIN—THE REWARD OF CONTINUED CONTROL OF THE DIABETES.

Date.	Diet.				Insulin.	Blood sugar, mg.	Glycosuria, per cent.	Weight, kg.	Height, inches.
	P.	F.	C.	Cals.					
1928:									
April 20	50	75	80	1200	3–2	130	0.5	16.0	42.5
April 21	..	...	...	....	3–2	...	0		
April 22	..	...	...	....	3–2	...	0		
April 23	50	71	90	1200	3–2	...	0		
April 25	..	...	...	....	5–4	...	0	16.5	
April 28	..	...	...	....	6–5	...	0	17.0	
May 5	..	...	...	....	6–5	...	0		
May 12	55	131	100	1800	3–0	...	0		
May 18	..	...	...	....	3–0	102	0		
May 29	..	...	...	....	3–0	...	0	17.5	
June 23	..	...	...	....	3–0	98	0		
October 2	..	...	...	....	3–0	118	0	18.0	
October 25	..	...	...	....	2–2	...	0		
December 28	..	...	...	....	5–5	140	0.6	19.0	44.5
1929:									
January 26	45	124	125	1800	8–7	...	0		
February 22	..	...	...	....	8–7	100	0	20.0	
May 25	..	...	...	....	9–8	...	0	21.5	
September 28	55	140	130	2000	12–11	100	0	24.0	
December 4	..	...	...	....	11–10	110	0		
1930:									
June 10	..	...	...	....	5–5	140	0.5		
1931:									
January 31	55	151	180	2300	6–5	110	0	27.0	
June 10	..	...	...	....	7–6	...	0	29.0	
November 14	55	153	150	2200	6–5	80	0	30.0	
1932:									
October 10	65	171	150	2400	7–6	...	0	....	55.0
1933:									
March 28	60	173	150	2400	5–4	98	0	36.0	
September 30	..	...	...	....	5–4	...	0	....	56.0
November 21	..	...	...	....	5–0	...	0	36.0	
1934:									
January 13	..	...	...	....	2–0	...	0	37.0	
February 24	..	...	...	....	0–0	92	0		
March 27	..	...	...	....	0–0	88	0	37.0	
May 5	65	157	180	2400	0–0	...	0		
June 11	..	...	...	....	0–0	90	0	36.0	56.5

insulin requirement increased from 5 units daily in 1928 to 23 units daily in 1929. Subsequent to 1929, despite normal growth in height and weight, the insulin was slowly reduced until stopped in February, 1934. The urine and blood tests have continued to be satisfactory.

The patient's physical activities, school work, body growth and development have been normal. The only reminder of the diabetes is the need of an accurate diet.

DIABETES MELLITUS IN THE ELDERLY.

Diabetes developing in the patient past middle life is usually mild in contrast to the diabetes in children. It progresses slowly in comparison. Overweight, present or past, is common. The elderly diabetic also responds well to treatment. The majority do not need insulin, but management by diet is essential. Exercise may need more emphasis than is the case with children. Treatment may be accurate and effective without being exacting. There is not the need of rapid control of the disorder. In fact a slow decrease in the blood sugar is preferable. Reduction in weight may be difficult and is often inadvisable if the patient is over sixty years of age. I aim to keep the urine free from sugar, and the blood sugar below 130 mg. in old patients, believing that by so doing the chronic, degenerative complications are largely prevented.

The danger which neglect carries for the middle-aged or elderly patient is usually insidious in its onset. Months and years of fairly good health may be enjoyed in spite of the fact that sugar is excreted daily in the urine. Nevertheless—"Sure signs precede sure events" (Cicero). If no complicating infection intervenes to make the danger an immediate one, this patient will come face to face with the error of his ways after irreparable damage has been done. Degenerative changes, due to a chronic high blood sugar, have been grad-

ually developing. The arteries may be thickened, causing gangrene. The heart may be affected, and failing vision be a prominent symptom.

Gangrene with secondary infection changes the entire aspect of the diabetes. The hitherto mild, slowly progressing disorder bursts into flame and is replaced by an apparently severe diabetes requiring urgent treatment. Insulin is then always necessary. When eradication of the infection and clearing of the gangrenous area have been accomplished, either by successful local and general treatment or by amputation of the affected limb, the need for insulin decreases. The diabetes is no longer severe, though the tolerance may be reduced.

CHAPTER VI.

THE PREVENTION AND TREATMENT OF DIABETES MELLITUS.

THE PREVENTION OF DIABETES MELLITUS.

The prevention of diabetes should concern everyone. It is of utmost importance to members of a family in which diabetes is prevalent. We have no control over our inherited constitution, but we can avoid some of the predisposing causes of diabetes: overeating, obesity and infection.

Food in moderation, wholesome food and regular habits of eating are conducive to good health and thus to the prevention of diabetes. Sugar and candies do not cause diabetes, but contribute to the burden on the pancreas and so should be used sparingly. Sweets are usually taken in addition to a diet sufficient to maintain a satisfactory weight and are then excess food and promote obesity. Furthermore, sugars are promptly absorbed into the blood stream, calling for a sudden supply of insulin. The pancreas should be spared this rush order. Carbohydrates are best taken in starchy forms: fruits, vegetables and cereals. The absorption is slower and the functional strain minimal.

Avoidance of infection entails all that goes with maintaining a high standard of health. Good hygiene is important; cleanliness and care of the body, outdoor exercise and adequate rest and relaxation.

Exposure to infectious diseases through contact with sick persons should be avoided when possible. Specific methods of known value in preventing infections should be utilized; *i. e.*, vaccination against smallpox and immunization against diphtheria and typhoid fever. One can give reasonable assurance that a child exposed to measles will have only a

mild attack with no complications if given a small injection of an immune parent's blood. Susceptibility to cold infections is sometimes overcome by vaccine treatment when other methods fail. Resistance to infection may be increased by the regular use of cod-liver oil, particularly in children.

Eradication of infection in the nasal passages, accessory nasal sinuses, nose and throat is desirable. Care of the teeth should receive special consideration. Proper selection of foods will avoid deficiencies which cause malnutrition, lowered resistance to infection and poor teeth. Infected tonsils should be removed. They may be dangerous without being large, red, or painful. Other foci of infection should receive appropriate treatment. Gall-bladder disease requires special mention. It is frequently a forerunner of diabetes. The focus of infection in itself is injurious as well as the infection which is carried along the biliary and pancreatic passages to set up an inflammation in the pancreas (pancreatitis). Neglected gall-bladder disease invites diabetes. When medical treatment fails, surgical measures should be considered. A diseased appendix should be removed by the surgeon. Neglected, it increases the likelihood of diabetes.

Forewarned is forearmed. Periodic examinations are prophylactive agents in attracting attention to errors in living. Prevention of pneumonia by treating an ordinary "cold" is analogous to the prevention of severe diabetes by treating the mild form. If the diabetes is mild, control it and prevent severe diabetes and complications; or, if the diabetes is severe, control it and prevent complications.

The well-informed diabetic has ample opportunity to do missionary work among his relatives and overweight friends by influencing them to adopt the following precautionary plan: (1) Have a careful initial examination for the primary purpose of excluding diabetes. This will include a blood analysis, as well as a urine test. (2) Have an annual examination in order that any deviation from normal may be recognized and corrected in its incipiency. (3) Avoid becom-

ing overweight, particularly after thirty-five years of age. (4) Do not ignore the advantages that are to be derived from at least one-half hour of active outdoor exercise each day.

Diabetes occasionally makes its appearance in the child before it develops in the parent who has transmitted the tendency. Parents of a diabetic child should adopt the same preventive measures as descendants of a diabetic family.

THE TREATMENT OF DIABETES MELLITUS.

The measures used in the treatment of diabetes are diet, insulin, exercise and general care. Special diet is of vital value in every case of diabetes. Insulin is essential for some, advisable for others and not required by the majority. The object of treatment is always the same; *i. e.*, restoration of normal metabolism. By this is inferred the maintenance of a normal blood sugar and freedom from glycosuria. Furthermore, the undernourished will gain in weight; the overweight will reduce, and finally normal health and strength will be regained.

How are these ends best accomplished? Is hospitalization imperative? Careful observation and study are essential. Education of the patient is of equal value if the ground gained during the initial standardization period is to be maintained and further progress made. When these ideals are unobtainable otherwise, there is no alternative; hospital treatment is necessary. On the other hand, home treatment is allowable if the necessary studies can be made and the patients can be instructed by a corps of well-trained "dietitian nurses."

During the past seven years, many of my patients with uncomplicated diabetes have not been hospitalized. They have had from a few days to two weeks private tutoring by one of our "dietitian nurses."

The dietitian must be especially qualified for this work.

She remains in the patient's home on twenty-four-hour duty. She prepares the diet, gives the insulin, and tests the urine specimens for the first few days. Subsequently, she supervises these duties executed by the patient; she communicates with the physician-in-charge each evening for instructions, based on her report, regarding changes in diet or insulin for the next day; she brings the patient to the physician's office twice weekly, when feasible, during the initial control period; she gives the patient a concentrated course on diabetes, and finally she starts a written record (page 73) to be continued indefinitely by the patient.

This plan of instruction has worked well. Its chief advantages are: the diabetes is controlled under the patient's normal atmosphere and conditions; the patient continues with his occupation uninterrupted; the amount of individual instruction creates in the patient an investigative interest; and finally an accurate conception of home conditions is obtained.

The object lessons which attend hospital treatment are desirable and necessary for some, but are inadvisable for others.

The Training of the Patient.—This feature is entered into in some detail, as upon its application hangs the future of many diabetics. It is presented in this fashion to acquaint the reader with the program of instruction which I have found to be of greatest value.

What Should the Patient Know About Diabetes?—(A) *A General Knowledge of the Problems of Diabetes.*—The patient must, from the first, learn that diabetes must be treated every day and that the success of this treatment depends on how familiar he or she is with the subject. It is not possible to remain in a hospital permanently, to have a dietitian perpetually, or to have a nurse to make the urine tests and give the insulin if needed. The home may replace the hospital after a short time and the patient can be his own dieti-

tian and nurse quite effectively. He should be taught certain rules and procedures to enable satisfactory control of the diabetes. To go through a routine each day without knowing why would be a dull affair. My advice to the patient is: "Read and study. Ask your doctor questions, your nurse, dietitian and chemist. Read several of the excellent manuals on diabetes now easily obtained. Your physician will suggest those which he prefers to have you read first. Reread them. You will find the study a fascinating one; all studies of the magnificent workings of the human body are. The fruits of your reading will be, I hope, first: a general knowledge of diabetes; second: what to do and how to do it; third: the realization of the necessity of complete coöperation with your physician. You cannot get along without him. These ideals accomplished, you need not fear. 'He is free from danger, who, even when he is safe, is on his guard'—Publilius Syrus."

(B) *Diet Chart Calculation.*—One must be familiar with a few facts in order to arrange a menu of appropriate foods, and yet meet the requirements of the diet prescription.

The metric system, because of the convenience of the decimal plan, is used in calculating the diet charts.

The diet is prescribed in grams: so many grams of protein, of fat, and of carbohydrate. When the values of the protein, carbohydrate and the total calories are given, the amount of fat is evident.

TABLE 10.—THE CHIEF SOURCES OF THE PROTEIN, FAT AND CARBOHYDRATE IN THE DIABETIC'S DIET.

Protein.	Fat.	Carbohydrate.
Meat (lean)	Butter	Fruits
Fish	Cream	Vegetables
Eggs	Meat (fat)	Cereals
Milk	Salad oil	
Cottage cheese	Lard	
Peas, soy bean	Nuts	
Nuts	Egg-yolks	
Gluten, gelatin	Cheese (cream)	

Calories,[1] units of heat, are evolved as food is used by the body tissues. For practical purposes, let us consider that in their combustion in the human body—

1 gram protein liberates 4 Calories.
1 gram carbohydrate liberates 4 Calories.
1 gram fat liberates 9 Calories.
1 gram alcohol liberates 7 Calories.

For purposes of illustration, a diet of 70 grams protein, 105 grams carbohydrate and 2100 Calories is prescribed. The protein provides 280 and the carbohydrate 420 Calories, or both 700 Calories. The remaining calories, 1400, are provided by fat, 155.5 grams. For the sake of simplicity, this diet is divided into three equal meals.

The protein, fat and carbohydrate values of the different foods, as presented in the Appendix, are given in percentages.

Moderate variations in food values may be found in comparing several food lists. Owing to the normal fluctuations, the values are approximate at best. They are, nevertheless, quite accurate enough to permit smooth control of the most severe case of diabetes. It is well to adopt one list to the exclusion of all others for best results.

In actual calculation of the diet chart, it is simpler to estimate first the carbohydrate from the carbohydrate-containing foods, because, in most instances, they carry some protein. The protein is balanced second, as most protein foods contain some fat. The fat is balanced last—usually with butter or oil.

Chart figuring is made easier for the beginner if he memorizes two simple rules, adopted at the Physiatric Institute. Their application will be made clear as we proceed.

Rule No. I.—*To find the value, multiply the value of 1 gram by the desired quantity.*

Rule No. II.—*To find the weight, divide the value desired by the value of 1 gram.*

[1] A Calorie is the amount of heat required to raise the temperature of a liter of water 1° C. This is the large Calorie.

Assume that the patient selects for breakfast: grapefruit, oatmeal, toast, eggs, bacon, butter, cream and coffee. As oatmeal is the food with the highest carbohydrate value, it is estimated first. An average helping of oatmeal is 15 grams (dry weight). By applying Rule No. I, we calculate the carbohydrate in this amount. Referring to the food table, it is found that the carbohydrate value of oatmeal is 66 per cent. Accordingly, 1 gram of oatmeal contains 0.66 grams of carbohydrate, and 15 grams contain 9.9 grams of carbohydrate. The protein and fat contents are estimated in the same manner. In like fashion, it is found that 100 grams of cream (20 per cent) will yield 3 grams protein, 22 grams fat, and 3 grams carbohydrate. Proceeding with the calculation: 2 eggs supply 14 grams of protein and 10 grams of fat.

TABLE 11.—INCOMPLETED CHART. THE CARBOHYDRATE, PROTEIN AND FAT COLUMNS ARE NOT COMPLETE.

	P.	F.	C.
Per day	70.0	155.5	105.0
Per meal	23.3	51.8	35.0
Grapefruit (?)			
Oatmeal, 15 grams (dry weight)	2.4	1.0	9.9
Eggs (2)	14.0	10.0	
Bacon (?)			
Cream, 100 grams	3.0	22.0	3.0
Toast, 24 grams (white bread)	2.1	.....	12.7
Butter (?)			

The grapefruit has been reserved purposely to complete the carbohydrate, bacon to complete the protein, and butter to complete the fat column. There are already provided 25.6 grams of carbohydrate, 21.5 grams of protein, and 33 grams of fat. This leaves 9.4 grams of carbohydrate to be provided by the grapefruit. Rule No. II is now applied. Referring to the food list, it is found that grapefruit contains 10 per cent carbohydrate. The carbohydrate value of 1 gram is 0.10 grams. By dividing 9.4 by 0.10 we find that 94 grams will supply the necessary quota.

TABLE 12.—INCOMPLETE CHART. THE CARBOHYDRATE HAS BEEN BALANCED BUT THE FAT AND PROTEIN QUOTAS ARE LACKING.

	P.	F.	C.
Per meal	23.3	51.8	35.0
Grapefruit, 94 grams	..	..	9.4
Oatmeal, 15 grams	2.4	1.0	9.9
Eggs (2)	14.0	10.0	
Bacon (?)			
Cream, 100 grams	3.0	22.0	3.0
Toast, 24 grams	2.1	..	12.7
Butter (?)			
			35.0

By similar calculation it is found that 16 grams of bacon are needed to complete the protein allowance. This amount of bacon also supplies 10.4 grams of fat. The fat column is then balanced with butter. The completed chart for breakfast is presented in Table 13. The other meals are calculated in an identical fashion.

TABLE 13.—COMPLETED CHART FOR ONE MEAL.

	P.	F.	C.
Per meal	23.3	51.8	35.0
Grapefruit, 94 grams	..	..	9.4
Oatmeal, 15 grams	2.4	1.0	9.9
Eggs (2)	14.0	10.0	
Bacon, raw, 16 grams	1.8	10.4	
Cream, 100 grams	3.0	22.0	3.0
Toast, 24 grams	2.1	..	12.7
Butter, 10 grams	..	8.4	
	23.3	51.8	35.0

CLASSIFICATION OF FRUITS AND VEGETABLES ACCORDING TO THEIR CARBOHYDRATE CONTENT.

For the sake of simplicity and for practical purposes, the fruits and vegetables have been more or less roughly classified according to their carbohydrate content into 3, 6, 9, 12, 15 and 18 per cent groups, in Table 14. The average carbohydrate value, reasonably accurate, is designated. In chart making

the protein content of the 3, 6 and 9 per cent groups, those used most freely in the diabetic diet, may be ignored.

Calculations based on these values are quite permissible for the great majority of diabetics. I advocate, however, the use of the individual food values as listed in the Appendix as being more accurate when there is any difficulty in controlling the diabetes or when the severity of the disorder warrants 3 doses of insulin daily.

TABLE 14.—THE CARBOHYDRATE PERCENTAGE OF FRUITS AND VEGETABLES.

3 per cent.	6 per cent.	9 per cent.
Vegetables.	*Vegetables.*	*Vegetables.*
Asparagus, fresh or canned	Beans, scarlet runner	Artichokes, Globe or French
Beans, green, wax, fresh or canned	Beans, snap	Beets
Beet greens	Beets, canned	Brussels sprouts
Broccoli	Chives	Carrots
Cabbage	Collards	Onions
Cauliflower	Dandelion greens	Peas, very young
Celery	Eggplant	Peas, canned
Chard	Kohlrabi	Rutabagas
Cucumbers	Lambsquarters	
Dock	Leeks	*Fruits.*
Endive	Okra	Blackberries
Fennel	Peppers, green or red	Cranberries
Lettuce	Pumpkin	Currants
Mung bean sprouts	Squash, winter	Currant juice
Mustard greens	Tomato, puréed, canned	Gooseberries
Okra, canned	Turnips	Grapefruit
Radishes		Grapefruit juice
Romaine	*Fruits.*	Lemons
Sauerkraut, fresh or canned	Blackberry juice	Lemon juice
Sorrel	Muskmelon, including cantaloupe and honeydew	Limes
Spinach	Strawberries	Lime juice
Squash, summer	Strawberry juice	Loganberry juice
Tomatoes, fresh or canned	Watermelon	Raspberry juice
Tomato juice, fresh or canned		Tangerines
Turnip tops		
Watercress		
Fruits.		
Rhubarb		

TABLE 14.—THE CARBOHYDRATE PERCENTAGE OF FRUITS AND VEGETABLES. (*Continued.*)

12 per cent.	15 per cent.	18 per cent.
Vegetables.	*Vegetables.*	*Vegetables.*
Beans, lima, canned	Corn, green, very young	Beans, baked
	Parsnips	Beans, red kidney, cooked
Fruits.	Peas, medium	Corn, canned
Apple juice	Salsify	Potatoes
Apricots		Succotash, canned
Cherries, sour	*Fruits.*	
Oranges	Apples	*Fruits.*
Orange juice	Blueberries	Cherries, sweet
Peaches	Blueberry juice	Crabapples
Peach juice	Grapes	Figs
Pineapple	Loganberries	Grape juice, unsweetened
Pineapple juice, fresh	Nectarines	
Plums (excluding prunes)	Pears	
Raspberries		

The data for this classification are taken from Bulletin 587 (October 15, 1934), Food Composition Section, Bureau of Home Economics, United States Department of Agriculture, Washington, D. C.

The fruits in these groups represent fresh material. In estimating the weight of a serving of fruits canned by the special water-pack method, "the solid portion and its proportional part of liquor must be considered together. Usually canned foods are somewhat lower in carbohydrate content than the corresponding fresh material due to dilution by added water or brine in canning."

Vegetables and fruits may be measured either before or after cooking, with the exception of applesauce and rhubarb. These must be measured before cooking.

It is with the purpose of isolating a suitable list of foods which the diabetic can consult with safety that Table 15 is presented. In appropriate amounts all diabetic diets can be selected from this list, while the more complete list in the Appendix includes many foods which have no place in the diabetic diet.

(C) *How to Weigh the Diet.*—Whether the diet need or need not be weighed should not deter the patient from becoming familiar with the practice which is so essential under some circumstances.

Diets are prescribed in grams and the foods which make up the diet are weighed in grams. The dial on the scale is graduated in grams. Drop one United States Buffalo five-

cent piece on the pan and the pointer moves along a distance representing 5 grams. Add another five-cent piece and the diet advances another 5 grams. Additional coins of this denomination may be added in testing a scale for accuracy.

TABLE 15.—COMPOSITION OF FOODS SUITABLE FOR DIABETICS.

Food.	Weight, grams.	Approx. measure.	P.	F.	C.	Cals.
Cereal:[1]						
Cooked	120	½ cup	3	..	16	76
Dry	20	½ cup	3	..	16	76
Shredded Wheat	28	1 biscuit	3	..	21	96
Bread	30	1 slice	3	..	16	76
Bread	15	½ slice	1.5	..	8	38
Crackers, soda	6	2 biscuits (2″ x 2″)	1	1	4	29
Milk, whole	240	1 cup	7	10	12	166
Milk, skimmed	240	1 cup	7	..	12	76
20 per cent cream	120	½ cup	4	24	4	248
40 per cent cream	120	½ cup	2	48	2	448
3 per cent vegetable	100	½ cup, 1 serving	2	..	3	20
6 per cent vegetable	100	½ cup, 1 serving	2	..	6	32
9 per cent vegetable	100	½ cup, 1 serving	3	..	9	48
12 per cent vegetable	100	½ cup, 1 serving	4	..	12	64
15 per cent vegetable	100	½ cup, 1 serving	4	..	15	76
18 per cent vegetable	100	½ cup, 1 serving	5	1	18	101
3 per cent fruit	100	½ cup, 1 serving	..	..	3	12
6 per cent fruit	100	½ cup, 1 serving	..	..	6	24
9 per cent fruit	100	½ cup, 1 serving	..	..	9	36
12 per cent fruit	100	½ cup, 1 serving	..	..	12	48
15 per cent fruit	100	½ cup, 1 serving	..	..	15	60
18 per cent fruit	100	½ cup, 1 serving	..	..	18	72
Egg	50	1	7	5	..	73
Meat and chicken	30	1 ounce	7	5	..	73
Fish, fresh	30	1 ounce	6	2	..	42
Cheese, American	30	1 ounce	9	11	..	135
Cheese, cream	30	1 ounce	8	10	1	126
Cheese, cottage, skim	30	1 ounce	6	..	1	28
Gelatin	3	1 teaspoonful	3	..	..	12
Bacon, lean	15	3 thin strips, crisp	3	8	..	84
Butter	10	2 teaspoonsful	..	8.5	..	77
Oil	10	2 teaspoonsful	..	10	..	90
Mayonnaise	14	1 tablespoonful	..	12	..	108
Cocoa	5	2 teaspoonsful	1	1	2	21

The comparative household measure and weights of average servings. One serving of food represents a small sauce dish. (5¼ inches over all; 3¼ inches across bottom; 1¼ inches deep.)

[1] Rolled oats, Wheatena, Mead's Cereal, Cream of Wheat, Farina.

The scales,[1] Hanson and the Chatillon, are best adapted for weighing food. Each is equipped with a movable dial which greatly simplifies the weighing. Consider that 100 grams of meat have been allowed. A plate is placed on the pan and the dial revolved until the pointer rests at zero. Enough meat is placed on the plate to bring the pointer to 100 grams. The plate and meat are removed from the scale. Consider that 30 grams of cream are allowed. A glass is placed on the scale and the dial rotated until the pointer rests at zero. Cream is poured into the glass until the pointer registers 30 grams. The actual weight of any food may be read at a glance without the subtraction of the weights of containers.

TABLE 16.—SUBSTITUTION LIST.

May have:		In place of:	
Bread	30 gm. (1 slice)	Cereal	20 gm. (½ cup)
Potato	90 gm. (1 small)	Bread	30 gm. (1 slice)
3% veg.	200 gm. (1 cup) 2 servings	6% veg.	100 gm. (½ cup) 1 serving
9% veg.	175 gm. (1 scant cup) 2 small servings	Bread	30 gm. (1 slice)
12% veg.	70 gm. (⅓ cup) 1 small serving	9% veg.	100 gm. (½ cup) 1 serving
18% veg.	100 gm. (½ cup) 1 serving	9% veg.	200 gm. (1 cup) 2 servings
Meat	30 gm. (1 oz.)	Egg (1)	
Mayonnaise	14 gm. (1 tablespoonful)	Butter	15 gm. (1 tablesp.)

(D) *How to Test the Urine for Sugar (Benedict's Test).—Equipment:* 1. Qualitative Benedict's Solution.[2] 2. Test-tubes marked at 5 cc. and at 2½ cc. levels. 3. Medicine dropper. 4. Water-bath.

Technique of Test.—1. Put 5 cc. (approximately 1 teaspoonful) of Benedict's Solution[2] in a test-tube.

[1] These scales can be obtained from Hanson Brothers Scale Company, 525 N. Ada Street, Chicago, Ill., and John Chatillon & Sons, New York City, respectively.

[2] When purchasing testing solution, specify *Qualitative* Benedict's Solution, as Benedict's Quantitative Solution does not change color when boiled with sugar.

2. Add *8 drops only* of the urine to be tested.[1] Hold pipette perpendicularly while adding drops.

3. Shake tube to mix urine and Benedict's solution thoroughly.

4. Put the tube in a water-bath of boiling water and boil for five minutes.

5. Let cool and read reaction.

Interpretation of the Test.—Clear blue solution: no sugar.

Light greenish-yellow: faint trace of sugar.

Yellow to orange: moderate amount of sugar, about 1 per cent.

Chocolate-brown or brick-red: large quantities of sugar, over 2 per cent.

To aid the beginner in interpreting this test, the following crude but, nevertheless, convenient and satisfactory standard may be used. One drop of orange juice boiled in 5 cc. of Benedict's solution gives a color representing a trace of sugar, while 3 drops of orange juice gives a moderate reaction, and 9 drops a heavy reaction for sugar. In keeping home notes the following abbreviations may be used: T, Trace; M, Moderate; H, Heavy.

(E) *How to Meet Emergencies.*—Emergencies which diabetics may be called upon to meet are:

1. Infections.
2. Insulin reactions.
3. Acidosis.
4. Gangrene.
5. Vomiting.
6. Diarrhea.
7. Broken needle under skin.
8. Accidents.

These emergencies are dealt with in their respective chapters. They are mentioned here for the purpose of presenting them collectively. Patients are best prepared who familiarize

[1] One-half these quantities may be used; *i. e.*, $2\frac{1}{2}$ cc. Benedict's Solution and 4 drops of urine; boiling for five minutes is still necessary.

themselves with the first-aid management of these complications.

(F) *How to Keep Informative Records for the Doctor.*—The patient will do well to learn what the doctor wants to know at each visit, and keep a record. Valuable time is saved if "Home Notes" are concise and accurately dated. A space should be reserved for questions and for the physician's written answers. Such records are valuable. Recently, I have been asking my patients to mail, or bring, a loose-leaf copy of their respective diaries to me once a month. This plan has worked admirably. Up-to-date notes are always at hand. It eliminates much needless investigation on my part and makes office calls more profitable for the patient.

A sample sheet of one of these diaries belonging to a boy, nine years of age, is shown on page 73. Note that dated records have been kept of the *diet, insulin, urine tests, body weight, infections* and *general feelings.*

(G) *How to Administer Insulin.*—The technique of insulin administration being the same as other subcutaneous therapy further comment is unnecessary.

Diet.—There are several "diet treatments" for diabetes. References are given below to those receiving most attention at the present time. They represent various extremes which I purposely avoid discussing in my aim for clarity as against confusion.

There are supporters of (*a*) the Newburgh-Marsh[1] and Petren[2] régime—using low-carbohydrate, low-protein and high-fat diets; (*b*) Sansum, Blatherwick and Bowden,[3] Geylin,[4] and Porges and Adlersberg,[5] using high carbohydrate (200 to

[1] Newburgh, I. H., and Marsh, P. L.: Arch. Int. Med., **26**, 647, 1920.
[2] Petren, K.: Jour. Metab. Res., **3**, 5, 1924; Münch. med. Wchnschr., **74**, 1123, 1927.
[3] Sansum, W. D., Blatherwick, N. R., and Bowden, R.: Jour. Am. Med. Assn., **86**, 178, 1926.
[4] Geylin, H. R. Cecil: Text Book of Medicine, Philadelphia, W. B. Saunders Company, p. 619, 1931.
[5] Porges, O., and Adlersberg, D.: Med. Klin., No. 40, 1932.

TABLE 17.—A SAMPLE PAGE FROM "HOME NOTES."

Name..... Tel. No.....
Address.....

NOVEMBER, 1932.

Date.	Diet.				Insulin.			Urine tests.				Remarks.
	P.	F.	C.	Total calories.	A.M.	NOON.	P.M.	A.M.	NOON.	P.M.	10 P.M.	
1	70	180	120	2400	9	..	7	0	..	0	0	Weight 70 lbs.
2	70	180	120	2400	9	..	7	0	..	0	0	
3	70	180	120	2400	9	..	7	0	..	0	0	
4	70	180	120	2400	9	..	7	0	..	0	0	
5	70	180	120	2400	9	..	7	0	..	0	0	
6	70	180	120	2400	9	..	7	0	..	0	0	
7	70	180	120	2400	9	..	7	0	..	0	0	
8	70	180	120	2400	9	..	7	0	..	0	0	
9	70	180	120	2400	9	..	7	0	..	0	0	
10	70	180	120	2400	9	..	7	0	..	0	0	
11	70	180	120	2400	9	..	7	0	..	0	0	
12	70	180	120	2400	9	..	7	0	..	0	0	
13	70	180	120	2400	9	..	7	0	..	0	0	
14	70	180	120	2400	9	..	7	0	..	T	M	Temp. 99°; "head cold"
15	70	180	120	2400	10	2	7	0	..	0	0	Insulin increased
16	70	180	120	2400	10	..	7	0	..	0	0	Insulin reduced
17	70	180	120	2400	9	..	7	0	..	0	0	Former dosage
18	70	180	120	2400	9	..	7	0	..	0	0	
19	70	180	120	2400	9	..	7	0	..	0	0	
20	70	180	120	2400	9	..	7	0	..	0	0	
21	70	180	120	2400	9	..	7	0	..	0	0	
22	70	180	120	2400	9	..	7	0	..	0	0	
23	70	180	120	2400	9	..	7	0	..	0	0	
24	70	180	120	2400	9	..	7	0	..	0	0	
25	70	180	120	2400	9	..	7	0	..	0	0	
26	70	180	120	2400	9	..	7	0	..	0	0	
27	70	180	120	2400	9	..	7	0	..	0	0	
28	70	180	120	2400	9	..	7	0	..	0	0	
29	70	180	120	2400	9	..	7	0	..	0	0	
30	70	180	120	2400	9	..	7	0	..	0	0	Weight, 71 lbs.

To be filled out and mailed to Dr.....the last of each month.
T = trace, M = moderate, H = heavy, reactions for sugar.

400 grams carbohydrate daily); (*c*) students of Joslin[1] and Allen,[2] employing a midway course; *i. e.*, moderate protein (60 to 90 grams) moderate carbohydrate (70 to 150 grams) and restricted total calories; and (*d*) Rabinowitch,[3] giving high carbohydrate with restricted calories.

An open mind, clinical experience, scientific proof, and time to season one's judgment will go far toward crystallizing the belief that no 2 patients require exactly the same treatment, but that in general some one of the procedures referred to above will give best results. In arriving at a conclusion, one may be aided by keeping in mind the following questions: Is the patient enjoying normal health and strength? Is the diabetes milder than it was a year ago? Has the insulin need increased or decreased? Is the blood sugar uniformly normal, and is there continued freedom from glycosuria? With which program do the degenerative changes develop with greatest, and on which the least frequency? Which treatment seems most helpful in preventing and overcoming complications? Other factors such as the behavior of the body weight, changes in total calories and complications deserve consideration.

I have adhered fairly closely to the Allen and Joslin diet formulæ. It is along these lines that the calculation of the diet will be directed. The reader is referred to what has been said already regarding protein, fat and carbohydrate (Chapter III) as the introduction of this section on treatment.

The reason for the proportioning of the diet outlined below may be summed up in Allen's words, "The food which tends most strongly to produce glycosuria is carbohydrate. Protein comes second, and its glycosuria action in average cases is not equal to its theoretical glucose value. Fat seems to be important chiefly through the calories furnished by it,

[1] Joslin, E. P.: Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, p. 567, 1928.

[2] Allen, F. M.: New England Jour. Med., p. 1133, December 4, 1930.

[3] Rabinowitch, I. M.: Canadian Med. Assn. Jour., **26**, 141, 1932.

rather than as a theoretical direct source of glucose. *The most important factor governing the insulin requirement with an ordinary plan of diet is not the carbohydrate content, but the total caloric content.*" A striking example of the effect of reducing the total calories is presented below.

Case M. P. (No. 34848), male, aged fifty-eight years, was admitted to the hospital on June 18, 1934, for treatment of obesity and arterial hypertension. His weight was 97 kilograms (213 pounds) and height 65 inches. He was unaware that he had diabetes until a fasting blood sugar of 0.303 per cent was found.

TABLE 18.—THE EFFECT WHICH A REDUCED CALORIC INTAKE, WITH A CONSEQUENT LOSS OF WEIGHT, HAS ON REDUCING THE BLOOD SUGAR OF AN OVERWEIGHT DIABETIC.

Date, 1934.	Diet. P.	F.	C.	Calories.	Blood sugar.	Weight, kg.
June 19	80	53	100	1200	303	97
20	80	53	100	1200		
21	80	53	100	1200		
22	80	53	100	1200		
23	80	53	100	1200	150	
24	80	53	100	1200	...	94
25	80	53	100	1200		
26	80	53	100	1200		
27	80	53	100	1200		
28	80	53	100	1200	101	
29	80	53	100	1200	...	93

A diet of 80 grams of protein, 53 grams of fat and 100 grams of carbohydrate (1200 Calories) was prescribed, see Table 18. With this low-calorie diet the body weight fell and the blood sugar was promptly restored to normal without the aid of insulin. This case illustrates the response obtainable in practically all uncomplicated overweight diabetics by merely utilizing, temporarily, an undernutrition diet.

Protein Content of Diet.—To maintain nitrogen equilibrium $\frac{2}{3}$ gram of protein per kilogram of body weight will suffice for the adult. The allowance is increased to 1 to 1.5 grams per kilogram in the permanent diet. Growing children require more protein in proportion to their weight, 1.5 to 2.5 grams and higher per kilogram, than adults.

Carbohydrate Content of Diet.—The carbohydrate quota is variable. The initial diet—if it is probable that insulin will not be needed—may contain 70 to 90 gram of carbohydrate. This may be increased as the tolerance permits to 100 or even 120 grams. The patient who obviously needs insulin from the beginning may have more liberal carbohydrate at the outset—90 to 110 grams. As progress permits more is allowable, probably as much as 160 grams. The carbohydrate allowance for children need not be less than 100 grams at any time. Increases above 180 grams have not been considered advisable in uncomplicated diabetes.

Total Calories of Diet.—The caloric value of the diet is determined largely according to the body weight. If the patient is underweight, and a gain is advisable, a liberal diet may be allowed at once—30 to 35 Calories per kilogram of body weight. A patient whose weight is about the desirable level should be given less during the first days of treatment—25 Calories per kilogram. The overweight will be reduced by a lower diet—15 or 20 Calories per kilogram. Overweight patients above fifty-five years of age should be reduced slowly.

Suitable changes may be made as the individual characteristics assert themselves. These changes should be directed in such a manner as to reduce or increase the weight, as the need may be, until it reaches a level about 5 per cent below the accepted normal average.

With the protein, carbohydrate and total calories decided upon, the amount of fat is evident.

Insulin.—The physiological action of insulin in the treatment of diabetes is to reduce the blood sugar. This effect is observed only when the insulin is given parenterally. The influence on the blood sugar is noted in about one-half hour and is continued from four to six hours after the insulin is administered. By sparing the reserve insulin supply in the milder diabetic, its apparent effect is much more prolonged. Insulin may be taken indefinitely without deleterious effect.

It is not cumulative in its action. It is not habit forming, nor is it a cure for diabetes.

The optimum dosage is variable in one and in different patients. One person may need over 75 units daily, while another whose degree of diabetes is less severe may do well with 6 or 8 units. The problem is to determine the amount and distribution which will most closely imitate the action of the normal pancreas. With a satisfactory diet—satisfactory in amount, make-up and distribution—one can cautiously increase or decrease the insulin until the requirement is determined. The amount of insulin needed by a patient rarely remains stationary from year to year. It is subject to influences which will be mentioned in greater detail in the following pages.

Glucose and Total Calorie Equivalent of Insulin.—The glucose equivalent per unit of insulin is exceedingly variable. Illustration: Case 71214 (Pennsylvania Hospital, Philadelphia), female, aged forty-five years, needed no change in the dosage of insulin (14 units in the morning and 12 at night) when the diet was changed from protein 70 grams, carbohydrate 90 grams, and 1400 Calories; to protein 70 grams, carbohydrate 200 grams, and 1400 Calories. The blood sugar remained normal and there was no reduction in the insulin when the former diet was resumed. *Note that the total calories were unchanged.* Allen has proved that with the total calories constant, large increases in the glucose equivalent of the diet can be made, with little, if any, change in the insulin requirements. This fact doubtless accounts for the present tendency to allow higher carbohydrate diets. Startling increases in the demand for insulin may ensue when the total calories are added to. Note the prompt reduction in sugar loss in Case L. H. (Pennsylvania Hospital), Fig. 6, when the total calories were reduced, yet the glucose equivalent remained stationary. Prior to the observation in Fig. 6, this patient had been under continuous hospital observation for over six months and the diet had been unchanged from

January 30th until April 12th. It is interesting and significant that earlier in this study, from March 5th to 12th, 100 units of insulin (3 doses) daily were needed to rid the urine of sugar and reduce the blood sugar to 0.125 per cent. In this instance a reduction of 1000 Calories was quite the equal of 100 units of insulin in effect. It is difficult to understand Newburgh's stand that the insulin requirement is in direct proportion to the glucose equivalent of the diet.

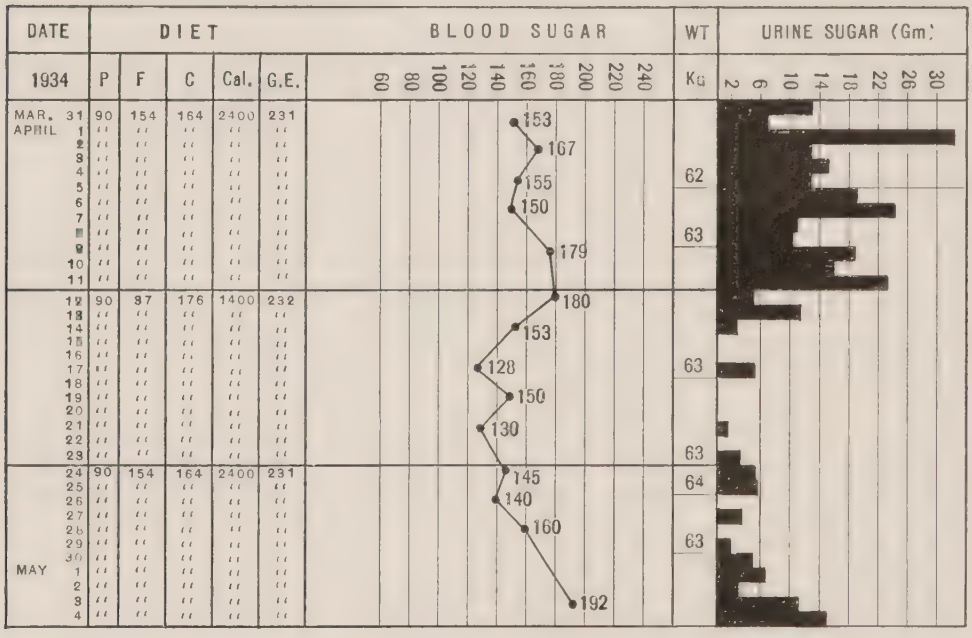

Fig. 6.—Illustrates prompt effect on the glycosuria and the blood sugar which followed a reduction in the total calories, despite the fact that the glucose equivalent of the diet remained constant. Note the opposite effect when the higher diet was resumed. (P. = protein; F. = fat; C. = carbohydrate; Cal. = calories; G.E. = glucose equivalent.)

The insulin requirement increases out of all proportion to the increase in the total calories if they exceed the needs of the body. The reverse is true as the calories are reduced below the maintenance requirement.

Indications for Insulin. — Persons with uncomplicated, mild diabetes do not need insulin. The contrary is true when severe diabetes or complications are present. Insulin is harmless no matter what is the severity or mildness of the

diabetes, unless too much is given. While it is unnecessary in mild diabetes, it may be used, temporarily, to hasten the control of the diabetes, relieve the pancreatic islands of their burden most quickly, and to shorten the patient's stay in the hospital. Also, the patient becomes accustomed to the technique of self-administration of insulin. This may seem unnecessary, but even the mild diabetic, if he is later afflicted with an infection, must either take insulin or sacrifice some of his islands of Langerhans and bring himself closer to the necessity of using insulin for an indefinite time. It may at first appear paradoxical that taking insulin is often the best insurance against having to take it later.

The severe diabetic always needs insulin. He has no longer enough pancreatic islands to provide sufficient endogenous insulin. The waning supply must be supplemented from outside to cover his need. Most children with active diabetes require insulin in order to cover the requirements of growth.

The problem of whether insulin should or should not be given, resolves itself into the questions: Is the diabetes mild or severe and are there complications; and how is one to determine the severity of the diabetes? A few facts can be given. The remainder of the problem must be solved by deduction. *The diabetes is mild if the patient who has never taken insulin is considerably overweight.* This is true irrespective of the level of the initial blood sugar. I cannot agree with Grafe that a patient necessarily has a severe diabetes if the blood sugar is 0.3 per cent. One of my overweight patients had a fasting blood sugar of 0.4 per cent, yet the diabetes was readily controlled by slowly reducing her weight by 5 kilograms (11 pounds). See also case M. P. on page 75.

The diabetes is severe if in the absence of complications the severely undernourished patient has a persistently high fasting blood sugar. Body weight which increases while using insulin loses its value as an indication of the severity of the diabetes.

Between the extremes referred to above, we find appar-

ently mild degrees of diabetes proving eventually to be severe and *vice versa*. In deducing the severity of a case, we cannot rely on any one factor. The level of the blood sugar, its response to changes in body weight, the response to diet, the effectiveness per unit of insulin, the influence of exercise, the age of the patient, and complications are all to be considered.

Certain complications, particularly ketosis and those causing fever, obscure the true degree of the native diabetes. They make a mild diabetes appear severe. They cause the diabetes to become progressively worse if adequate relief by diet, insulin and other appropriate treatment are not forthcoming.

Dosage and Distribution of Insulin.—The amount of insulin needed to control the diabetes cannot be calculated in advance. The dosage must be determined empirically for each patient. For purposes of clarity we shall assume that the diet is satisfactory and remains unchanged in quality and distribution while we deal with the insulin dosage and its division.

The initial amount of insulin and the number of doses given will vary with the apparent degree of diabetes and the urgency of the demand. It can be safely assumed that any diabetic needing insulin can tolerate 4 units of insulin once daily. This single dose is given about twenty minutes or one-half hour before the morning meal. It will spare the pancreatic reserve accumulated overnight and tend to prevent a high blood sugar after the three meals coming in fairly close succession. This small dose may suffice to control the diabetes. The resulting gain in tolerance will allow it to be discontinued within a short period.

Blood sugar estimations guide the changes in insulin after the glycosuria has been corrected. Urine tests, while there is glycosuria, serve as an excellent guide in increasing the insulin. I employ fractional urine tests for this purpose. These tests are made on specimens voided at 7 A.M., 11 A.M.,

4 P.M., and 10 P.M. when 2 or more doses of insulin are given. While sugar continues to appear in the 11 A.M. specimen, it is safe to add 1 or 2 units daily to the dose before breakfast. When this dose reaches 12 or 14 units, or if the 11 A.M. specimen becomes free from sugar while the other specimens contain sugar, it is well to divide the dose. It may be given as follows: 8 units before breakfast and 6 units twenty minutes or one-half hour before the evening meal. It is often well to make no increase in the total dose at the time it is divided. The mere splitting of the dose has the same effect as an increase. The smaller the dose the more effective is each unit.

Further increases of 1 or 2 units daily are made to the morning dose while glycosuria persists at 11 A.M. and to the evening dose if there is glycosuria at 10 P.M. or in the overnight collection. It is arbitrary when a third dose should be started. I prefer a third dose, given before lunch, when the morning and evening doses reach proportions about 16 and 12 units respectively. The division may be as follows: before breakfast, 12 units; before lunch, 6 units; and before supper, 10 units. Small additions, 1 or 2 units, may be added to the dose corresponding in time to the one which precedes the appearance of glycosuria. Glycosuria at 4 P.M. indicates that the noon insulin is insufficient, while absence of sugar would require no change. This applies, also, to the other doses and specimens. An occasional patient does better with a small third dose given at bedtime instead of before lunch. Illustration: J. W. (Case No. 13169, Pennsylvania Hospital), male, aged sixty-six years, had repeated attacks of hypoglycemia in the daytime and hyperglycemia in the morning until the following unusual timing and distribution of insulin were adopted: 22 units at 6 A.M., none before lunch, 5 units at 5 P.M. and 7 units at 11 P.M.

The diabetes in the majority of patients needing insulin is controlled by some one of the stages suggested above. There is, however, a more severe group in which a point is reached

when, if additions are made to any one of the 3 doses of insulin, a hypoglycemia results and yet a hyperglycemia occurs in the morning. This is due to 3 large doses fairly close together on one hand, and a long night period without insulin on the other. Allen[1] has suggested lengthening the day periods between doses and shortening the night period without insulin by giving the morning insulin one hour earlier and the evening insulin one or two hours later—after supper. The timing of the noon dose remains unchanged. When the severity of the diabetes calls for this plan, there need be no fear of a hypoglycemia during the night. A portion of the supper may be taken at bedtime if a safeguard seems necessary. For illustrative case see page 83.

Case Report.—B. W. (No. 34878 Pennsylvania Hospital), male, aged forty-one years, height 65 inches, weight 65 kilograms (143 pounds) has had diabetes since 1922 and has taken insulin since 1924. The amounts taken prior to the last admission were 55 units before breakfast, 20 before lunch and 20 before supper. Each dose was taken twenty minutes before the meal.

When seen in June, 1934, he was having occasional insulin reactions late in the day and yet there was heavy glycosuria every morning and the fasting blood sugar was high. Two estimations in June were 0.315 and 0.342 per cent. On one occasion the blood sugar was 0.038 per cent during an insulin reaction.

On admission to the hospital on June 21st the fasting blood sugar was 0.266 per cent and most of the day's sugar loss was in the morning specimens.

Believing the insulin doses to be too close together leaving a long night period without insulin we changed the distribution as well as reducing the amount given, see Table 19. The morning dose was given one and a half hours before breakfast and the evening dose at 8 P.M. for one day and at 9 P.M. thereafter. The timing of the noon dose remained unchanged.

[1] Allen, F. M.: Jour. Am. Med. Assn., **82**, 1937, 1924.

He was allowed to save a small portion of each meal to be taken midway between meals if he wished.

TABLE 19.—THE EFFECT OF GIVING THE INSULIN EARLIER THAN USUAL IN THE MORNING AND LATER THAN USUAL IN THE EVENING TO A MODERATELY SEVERE DIABETIC.

Date, 1934.	Diet.				Insulin.						Glycosuria.				Bl. sug.	Wt., kg.
	P.	F.	C.	Cal.	6 A.M.	7 A.M.	11.30 A.M.	5 P.M.	8 P.M.	9 P.M.	7 A.M.	11 A.M.	4 P.M.	10 P.M.		
June 20	80	89	120	1600	..	40	20	20	..	..	+4	+4	+1	0		
21	80	89	120	1600	..	40	20	20	..	..	+3	+1	+1	+1	266	65
22	80	89	120	1600	..	40	20	..	22	..	+1	0	+1	0		
23	80	76	100	1400	..	46	20	..	..	24	0	0	+3	+1		
24	80	76	100	1400	40	..	20	..	..	30	0	0	0	0		
25	80	76	100	1400	40	..	20	..	..	30	0	0	+2	0	67	
26	80	76	100	1400	38	..	20	..	..	26	0	0	0	0		
27	80	76	100	1400	36	..	20	..	..	24	0	0	0	0		
28	80	76	100	1400	34	..	18	..	..	22	0	0	+2	+1	..	64
29	80	76	100	1400	34	..	14	..	..	22	0	0	+2	0		
30	80	76	100	1400	31	..	14	..	..	22	0	0	0	0		
July 1	80	76	100	1400	29	..	14	..	..	22	0	0	0	0		
2	80	76	100	1400	27	..	14	..	..	22	0	0	0	0		
3	80	76	100	1400	25	..	12	..	..	22	0	0	0	0	111	
4	80	76	100	1400	25	..	8	..	..	20	0	0	+1	0		
7	80	76	100	1400	25	..	8	..	..	20	0	0	..	..	136	64

Prompt control of the diabetes ensued; the morning hyperglycemia was prevented; mild insulin reactions forced reductions in the insulin with the result that when the patient was discharged, July 11th, he was taking 53 units daily in place of 95 units—the pre-admission dose. He was free from insulin reactions and had regained the confidence he had lost when he was in constant jeopardy of either a hyperglycemia or a hypoglycemia.

When a fourth dose is necessary as occasionally occurs in severe diabetics, or during infections, it is well to give it at midnight with a small amount of nourishment (5 to 10 grams of carbohydrate). The other 3 doses, in event of the fourth dose being needed, should be given prior to the respective meals. The fourth dose is usually needed for a short period only.

Frequent doses, every three or four hours, are needed during emergencies. This is true in dealing with ketosis,

acute infections, and surgical conditions. They will be dealt with under their respective headings.

The amount of insulin needed is not relative to the degree of hyperglycemia with any constancy nor can it be calculated according to the amount of sugar in the urine. If glycosuria exists more insulin is needed; that is the extent of the information provided by this finding.

The insulin needed cannot be computed according to the so-called glucose equivalent in the diet. Case No. U 5805 on Dr. Elmer Funk's service at the Jefferson Hospital illustrates this nicely: With a blood sugar of 0.205 per cent she received 50 units of insulin when the total glucose of the diet was 95 grams. Three days later on a new diet, with a total glucose of 146 grams, 46 units reduced the blood sugar to 0.165 per cent. The total calories remained constant.

One to 4 doses of insulin may be obviously necessary from the outset. I believe it is a good plan to make the initial dosage less than it is known will be needed and by adopting the method of increasing the doses as suggested, one can quickly arrive at the correct timing and amount of the insulin necessary to bring the disorder under control. Mild insulin reactions will be prevented by appropriate reductions. This feature will be dealt with in detail later.

The need for insulin will be increased by overeating, gain in weight, loss of tolerance due to inadequate control of the diabetes, infection, lack of exercise, and intoxications. Among the last mentioned are included sunburns and reactions from deep Roentgen-ray therapy. Increased need for insulin should always be satisfied with suitable changes in the dosage. Otherwise loss of tolerance will ensue. There is a tendency to need less insulin after the diabetes is controlled, after loss in weight due to a restricted diet, after reduction in the total calories, after exercise, and after eradication of infection or intoxication. Reduction of the carbohydrate may spare insulin for a time, but if the total calories are not also reduced, this effect is gradually lost.

Diabetes characterized by emaciation, such as tuberculosis and cancer, may instead of increasing the insulin demand occasionally make rapid reductions necessary. This improvement in tolerance is due to an unwanted undernutrition. Illustrations: M. W. (Case No. 13228, Pennsylvania Hospital), male, aged fifty-four years, required 21 units of insulin daily until the emaciation due to carcinoma of the pancreas made its discontinuance imperative. L. B. (Case 99, private series), female, aged forty-eight years, needed 11 units of insulin (6 in the morning and 5 in the evening) while her weight was 155 pounds (70 kilograms). When it fell rapidly to 142 pounds (64 kilograms) due to a fulminating pulmonary tuberculosis, it was necessary to stop the insulin to prevent attacks of hypoglycemia. This is contrary, however, to the usual behavior of tuberculosis patients. I suspect that the case reported by Grafe[1] belonged to this group.

Insulin Reaction (Hypoglycemia).[2]—An insulin reaction is characterized by an abnormally low blood sugar (see page 47). Dr. Henry John has drawn attention to a group of patients who manifest symptoms similar to those due to insulin overdosage, while the blood sugar is quite within, or even above normal. In these cases, the symptoms are probably due to a rapid lowering of the blood sugar.

The prominent symptoms which usually occur when the blood sugar falls below 0.05 per cent are: weakness, profuse perspiration, most noticeable on the forehead at the hair margin, and excessive hunger while faintness, vertigo, trembling, feeling of tenseness, diplopia, cardiac palpitation, coldness of the extremities, difficult speech (voice may become guttural), and loss of control of the leg muscles with difficult locomotion may be complained of. Some patients experience a numbness and pins and needles sensation of certain areas,

[1] Grafe, E.: Metabolic Diseases and Their Treatment, Philadelphia, Lea & Febiger, p. 325, 1933.

[2] Note that I have not referred to hypoglycemia as an "insulin shock." This is a misnomer. Clinical evidences of a hypoglycemia are not those of shock.

particularly in the tongue and buccal regions. Occasionally a non-productive cough is incited. They may experience the sensation of floating on air and have a desire to toss their arms about and shout, lapsing into quietness, resenting interruptions as the reaction deepens. Headaches usually accompany, or follow, prolonged but mild reactions.

Emotional outbursts, periods of melancholia with difficult cerebration and curious eccentricities may characterize reactions in certain patients. One patient insisted on trying to solve cross-word puzzles on the occasion of a hypoglycemia; another invariably grasped a pencil and began making meaningless calculations on paper; another would stand on the street corner with his head tilted as though in deep meditation, while others have attacks similar to epilepsy. Experiences and chagrin to which these patients may be subjected is illustrated by case 32599: S. H. (Pennsylvania Hospital), who, while out walking, felt quite warm and experienced slight difficulty in controlling his legs. Knowing from past experiences that these were premonitory symptoms of a severe hypoglycemia, he entered a restaurant, purchased some food, but before he was able to partake of it his legs gave away and he collapsed on the floor. He was unable to arise. Believing him to be intoxicated, two attendants rather roughly ejected him. His anger was aroused at this treatment to which he offered considerable resistance. It is interesting that at this point his symptoms began to subside; he presented a police officer with his diabetic identification card; he returned, with the officer, to the restaurant, had his money refunded and walked half a block, unaided, to another restaurant where he secured some orange juice.

The stimulating effect which anger has on the adrenal glands may be exemplified clinically in this instance.

Objectively, the hypoglycemic patient may exhibit signs ranging from slight transitory moments of confusion to complete unconsciousness. With a moderately severe reaction pallor is noticeable, occasionally with dark rings under the

eyes and usually with beads of perspiration on exposed parts of the body. The blood-pressure, contrary to the prevalent belief, is normal or elevated. This is particularly true of patients over forty years of age. Illustration: Case No. 1887, on Dr. McCrae's service at the Pennsylvania Hospital: A man, aged forty-five years, was known to have had a normal blood-pressure shortly prior to admission in October, 1928, yet when brought to the hospital comatose from a hypog ycemia, following an accidental overdose of insulin, his blood-pressure was 160 systolic and 100 diastolic. On discharge five days later, it was 112 systolic and 76 diastolic. This, and a similar case, have been reported elsewhere.[1]

The pupils are usually dilated during a hypoglycemia. The pulse is full and rapid and the skin is moist. A functional systolic murmur at the cardiac apex may be heard. The reflexes tend to be increased, an extensor response of the great toe to plantar stimulation may be elicited and in children typical carpopedal spasm may occur. Muscle twitchings are late signs, as are convulsions which are rare. Transitory signs of a hemiplegia are occasionally noted. Dr. J. Vander Veer is about to report 2 such cases.

Coma, due to ketosis, may be mistaken for an insulin reaction, though one is the antithesis of the other in a number of respects. The dry skin (if the skin is wet, the coma is not due to ketosis), the desperately ill appearance with a gradual onset (at least twelve, usually over twenty-four hours), the sunken eyes, the decreased intra-ocular tension, the low blood-pressure, and the air hunger with a prompt and heavy reaction for sugar and acetone in the urine, acetone in the plasma, and a high blood sugar, serve to identify coma due to ketosis (see Table 20).

The hypoglycemia or insulin reaction produces quite a different history and picture. The patient or a relative may state he was perfectly well for a period after the last meal,

[1] Duncan, G. G., and Polk, S.: Medical Clin. of North America, **13**, 1013, 1930.

but that later he felt weak, complained of hunger, became anxious, dizzy, confused, excited and began to perspire profusely, particularly across the forehead and at the hair margin. Colored patients seem less apt to perspire during insulin reactions. The hypoglycemic patient may stubbornly resist treatment.

TABLE 20.—HYPOGLYCEMIA AND KETOSIS COMPARED.

	Hypoglycemia.	Ketosis.
Cause	Too much insulin	Too much food or not enough insulin
General appearance	A well person who has fainted	Very ill (to the inexperienced appears hopelessly ill)
Breathing	Normal	Rapid and deep (air hunger)
Onset	Rapid (minutes)	Slow, at least twelve hours
Hunger	Great	Anorexia
Thirst	None	Great
Vomiting	Rare	Common
Eyes	Staring, and pupils dilated	Sunken
Disturbed vision	Diplopia and difficulty in focussing	Haziness
Headache	Common	Absent
Intra-ocular tension	Normal	Decreased
Skin	Wet (especially forehead)	Dry
Tissues	Normal	Dehydrated
Pulse	Full and rapid	Weak and rapid
Blood-pressure	Elevated or normal	Subnormal
Cardiac palpitation	Frequent	Absent
Constipation	None	Present
Muscular twitching	Common	Absent
Nervousness	Common	Absent
Babinski's sign	May be present	Absent
Complicating infections	Absent	Common
Abdominal pain	Absent	Common
Urine sugar	None (after residual urine is discarded)	Present
Blood sugar	Below normal	Above normal
Acetonuria	Absent	Present
Response to treatment	Rapid (minutes)	Slow (hours)

The nutrition of the hypoglycemic patient is apparently not disturbed. He is not dehydrated. There is no evidence

of a prolonged illness; there is no sugar in the second specimen of urine obtained, and the blood sugar is subnormal.

Occasionally, consciousness is lost suddenly without any warning. The thin person with severe diabetes, who has a narrow safety zone, is more exposed to this type of onset.

The night sweats of the tuberculosis patient may simulate an insulin reaction. Blood and urine analyses alone provide sufficient evidence to differentiate between the two.

Treatment of Insulin Reactions.—(*a*) *Immediate.* — Well-nourished, muscular young patients can tolerate mild insulin reactions without treatment. Hypoglycemia carries an element of danger for the thin patient with severe diabetes and a small glycogen reserve, while to the patients with advanced arterial changes, especially coronary artery disease, a low blood sugar presents a genuine hazard. This rough classification will serve to emphasize the relative need of prevention and the urgency for corrective treatment when an insulin reaction is under way.

By far the majority of insulin reactions are promptly corrected by taking 10 grams of carbohydrate (100 cc. orange juice) by mouth. Carbohydrate in any form will suffice though the monosaccharides are absorbed with greatest speed. This is an advantage which orange juice has over cane sugar.

Loss of consciousness and the inability to administer carbohydrate by mouth may make feeding by a nasal tube or intravenous administration of glucose imperative. If sterile glucose is not available and nasal feeding is decided against, corn syrup or glucose, suitably diluted with warm water may be given by rectum. The administration may be by the Murphy drip or the intermittent method. It is agreed, I believe, that the hypoglycemic individual will absorb glucose when given by enteroclysis, even though at other times no absorption may take place.

Sterile glucose (10 grams) may be given in a 50 per cent solution intravenously. This may be repeated. It is pref-

erable, however, to use a 10 per cent solution if a second administration is necessary. This should be given *very slowly*. The solution should be tepid. It may be given continuously until sugar appears in the urine. It is a wise precaution to use the 10 per cent solution when the patient is past middle age and if the blood-pressure is high, a common but temporary finding during a hypoglycemia.

Epinephrine has been used to combat insulin reactions. The dosage usually employed is 0.5 cc. given subcutaneously. It is most effective in well-nourished patients, less effective in the thin patient with severe diabetes, while I believe it is decidedly dangerous in the arteriosclerotic type of patient when the blood-pressure is elevated. For this reason and the fact that patients with good nutrition do not need it, I see little indication for it.

Pituitary extract (pituitrin), owing to its neutralizing effect on insulin, is helpful in these cases. Given subcutaneously in doses of 0.5 cc., it is effective and yet its untoward influence on the blood-pressure is considerably less than that of epinephrine.

(*b*) *Prevention of Insulin Reactions.*—A recurrence of the insulin reaction may be prevented by merely reducing the insulin or increasing the diet on the following day. The reduction, 2 to 8 units, should be taken from the dose corresponding in time to that which preceded the reaction. It is not always wise to reduce the insulin before determining the cause of the fall in the blood sugar content. Unusual and strenuous exercise might quite readily account for a low blood sugar. Unless such exercise was to be repeated, no reduction in insulin would be indicated. Similarly, failure to eat a meal, vomiting or diarrhea, are not indications for a reduced insulin dosage on the subsequent day if normal conditions are restored.

Insulin reactions directly attributable to improving tolerance warrant a reduction in one or all doses. When a gain

in tolerance is correctly anticipated by appropriate reductions in the insulin, reactions never occur.

The appropriate timing and distribution of the insulin administration is important if both reactions and hyperglycemia are to be prevented. The safety zone for children may be increased by giving some of their lunch, milk, or an orange, in the mid-forenoon and some of their supper allowance midway between lunch and supper time.

Eye Symptoms Due to Insulin.—Some patients, the young ones especially, who require large doses of insulin, complain of dimness of vision and difficulty in focussing their eyes properly after beginning insulin treatment. These symptoms are entirely separate from those commonly reported during hypoglycemia reactions. Furthermore, they subside entirely after the first few weeks of treatment. This assurance which can well be given as routine to all young patients starting out on a heavy insulin program will spare the patient concern, needless examinations of the eyes, and the expense of obtaining new glasses.

Correction of disturbances of vision in no way connected with the diabetes is, of course, advisable; but examinations preparatory to prescribing glasses should be delayed until two months have elapsed after the beginning of insulin treatment. By this time all of the temporary effects which insulin may have had on the eyes will have disappeared, not to occur again.

CHAPTER VII.

COMPLICATIONS OF DIABETES MELLITUS.

DIABETIC GANGRENE.

Diabetic gangrene is, for the most part, a complication of a longstanding but mild diabetes. In the strict sense, it develops on the basis of arteriosclerosis. It affects males more frequently than females and it selects for its victims those who are over forty years of age.

Gangrene is recognizable in its early and impending stages. Furthermore, it is largely preventable. Nevertheless, it is today the most common cause of death for the diabetic.

The lower extremities are most susceptible to gangrene though other parts of the body—buttocks, genitalia, back, neck, upper extremities, nose, eyes and lungs—have been involved in isolated instances. Gangrene in the diabetic is usually a local manifestation of a general arteriosclerosis. The vessels of greatest predilection to sclerosis are those of the distal extremities, the coronary arteries and the aorta.

Causes of Diabetic Gangrene. — (*a*) *Predisposing.* — The mechanism of the development of arteriosclerosis in the diabetic is unknown. The comparison of a group of adult diabetics with non-diabetics of a similar age leaves no doubt that the disturbances in metabolism which characterize diabetes have an etiological relationship to the development of this abnormality in these patients. There are evidences that the increased blood lipids play a part. The experiments of Anitschkoff and the clinical observations of Joslin and Rabinowitch would leave no great uncertainty in this respect if other factors could be eliminated. Hyperglycemia is being relegated to a place of secondary importance. Is it right that it should be?

The increased carbohydrate content of the present-day diabetic diet with the lower fat will no doubt prevent, to a large extent, the lipid influence on the development of sclerosis. If the sole etiological factor, or even the most important factor is thus removed, we can anticipate a decrease in the frequency of diabetic gangrene. This decrease would not become perceptible until the increase, due to prolonged life permitted by insulin, has reached its peak. If, on the other hand, hyperglycemia is of chief etiological importance, the prevalent tendency to allow moderate elevations of the blood sugar and even glycosuria will militate against any reduction in the prevalence of diabetic gangrene. I have been much impressed by the extreme rarity with which gangrene developed in Dr. Allen's patients. Is this attributable to Allen's insisting on a normal blood sugar, or is it due to the low lipid content of the blood that usually accompanies the normal sugar level, or both? Both factors seem to influence the prevalence of gangrene. I have no fear in reducing the blood sugar, in arteriosclerotic patients, to normal and keeping it there providing the reduction is made *slowly*, over a period of a few weeks, and providing there is ample carbohydrate (125 to 150 grams) in the diet.

(*b*) *Exciting Cause.*—Injury is the exciting cause of gangrene. The reaction from a slight knock may be all that is needed to occlude a sclerosed vessel. Minute injuries from paring corns, cutting toe nails, poorly fitting shoes, exposure to cold, excessive dryness, and cracking of the skin and epidermophytosis, rank among the most frequent inciting influences.

Arteriosclerosis prepares the ground for the development of gangrene. It develops insidiously. Many years of actual disease of the arteries may pass before subjective symptoms manifest themselves. Lipids, particularly the cholesterol esters, have been deposited in the depths of the intima. Hyaline, degenerative, hyperplastic thickening of the intima with a corresponding reduction in the lumen of the affected

vessels have ensued. Secondary atrophy of the media may occur. Deposits of lime may lead to the Mönckeberg type of sclerosis. The tissues dependent on the affected vessels become impoverished.

The outcome will be: (*a*) reëstablishment of the circulation by collateral vessels—a slow process requiring many months or years—or (*b*) occlusion of the main vessel with gangrene of the area normally supplied by it, or (*c*) invasion of the impoverished tissue by infecting organisms having gained entrance through a minute wound. The poorly nourished, cold tissues have little resistance to infection. A minute break in the continuity of the skin will not heal. It remains a portal of entry for pathogenic bacteria which are always present. The local swelling, accompanying the inflammatory reaction to the invading organisms, goes further in obliterating the small vessels. Local death of tissue results. Inadequate circulation may prevent localization. The infection spreads upward by the lymphatics, along the veins, and pursues the course of the tendon sheaths. As the area of necrosis increases the bones are involved, osteomyelitis and loss of bone structure ensue. If unchecked, death follows from septicemia.

Embolic Gangrene.—This type of gangrene in the diabetic is comparatively rare. It appears suddenly. The pain is severe. Collateral circulation is lacking and the prognosis is bad.

Senile Gangrene.—Senile gangrene develops slowly. There is little or no attempt at establishing collateral circulation. The slow cutting off of the blood supply leads to mummification of the field affected. Amputation may be necessary for relief from pain even in the absence of actual necrosis.

Estimating the Circulation in the Feet.—The circulation is good if the feet are warm, free from pain and give a good dorsalis pedis and posterior tibial pulsation. The circulation is bad if pain in the extremities is a prominent symptom, if the feet are cold to the touch, and if there is no palpable

dorsalis pedis pulsation. Objectively, the temperature of the limb, changes in color and nutritional changes give the most information. A foot which, when elevated, pales promptly and which, when returned to the horizontal position, colors slowly has a poor main and collateral circulation. The foot with good circulation retains a normal color when hanging in a dependent position, while a wine-colored discoloration which blanches on pressure indicates extensive vascular disease. There may be no dorsalis pedis or posterior tibial pulsation, yet a well established collateral circulation may keep the limb quite warm and well nourished. Oscillometer and roentgen-ray studies are not informative where collateral circulation is concerned. The latter has its greatest value in determining the extent of calcification of the main vessels, and in this way aiding in the selection of the site of amputation.

Skin temperature readings are of special value in evaulating the nutritional supply to the affected parts. Drs. John Gibbon, Jr., and Ferdinand Fetter are studying this aspect in our patients. We have not employed the histamine test[1] as a routine, but are now making a comparative study of this test and skin temperature changes.

Onset of Gangrene.—*Objective Signs.*—A slight bluish discoloration on one of the toes, about a corn or callous, or on the heel, may be the first sign of gangrene. Frequently, a vesicle appears first without any apparent cause. See illustrative case on page 100. In one or two days the underlying tissues reveal the ominous change in color—the evidence of tissue necrosis. The extent of tissue death depends (1) on the lack of main and collateral circulation, and (2) on the presence of secondary infection. The gangrene spreads until it is bounded by areas fertile in blood supply. Demarcation and mummification may ensue until the affected areas are hard and black. Toes thus affected may, in time, drop off.

[1] Starr, I., Jr.: Am. Jour. Med. Sci., **180**, 149, 1930.

The presence of infection makes the outcome a speculation at best. Osteomyelitis, toxemia and septicemia ensue with great frequency if seasoned judgment is not exercised.

Subjective Symptoms. -Pain, constant or as intermittent claudication, may antedate the onset of gangrene by months or years. It is, nevertheless, more localized, more intense and persistent when actual death of tissue occurs. As the local disorder spreads, evidences of toxemia become manifest.

Prevention of Gangrene.—The control of the diabetes is the chief essential in preventing gangrene in these patients. The progressive arterial changes can be, in this fashion, largely avoided or kept in check. A good physical condition maintained by observing the principles of good hygiene will go far in preventing degenerative changes. The weight should conform closely with, or be a trifle below, that of the normal average.

The care of the feet may not need further emphasis. The importance of the subject, however, justifies repetitions.

It is the physician's duty to keep before the patient the necessity of (*a*) cleanliness of the feet; (*b*) foot exercises; (*c*) eradication of infections, particularly epidermophytosis; (*d*) avoiding injuries, and (*e*) special measures.

(*a*) *Cleanliness of Feet.*—1. Warm (never cold) foot bath each evening.

2. Anoint feet with toilet lanolin several times a week.

3. Clean under toe nails gently with an orangewood stick.

4. Wear clean hose each day.

(*b*) *Foot Exercises.*—1. Practice ending each step, while walking, on toes instead of on the ball of the foot.

2. Pick up 20 medium-sized marbles with toes morning and night.

3. *Gentle* massage of legs and feet each evening.

(*c*) *Eradication of Infection.*—Epidermophytosis (tinea trichophytina infection) is usually readily controlled by applying an ointment containing benzoic and salicylic acids

once daily. I have prescribed freely for the dry, scaly stage of the disease the following:

Salicylic acid	1.00 part
Benzoic acid	1.65 parts
Soft paraffin	10.00 parts
Cocoanut oil	22.00 parts

For the acute vesicular pustular type on the plantar surface and the acute eczematoid type between the toes, compresses of saturated boracic acid solution are helpful. Applications of warm potassium permanganate 1 to 4000 are of value.

Reinfection may be largely prevented by immersing the feet in a 0.5 per cent solution of sodium hyposulphate before and after bathing in public places, as suggested by Osborne, or by applying boracic acid powder to the interdigital and plantar surfaces each morning. It is well to sterilize the bedroom and bathroom floors with antiseptics known to have fungicidal properties. Fumigation with formaldehyde candle is effective. Shoes, slippers, socks and mats should be placed in the room about to be fumigated. Shoes may be fumigated by putting a blotter, on which 1 dram of strong formaldehyde solution (40 per cent) has been poured, in each shoe, wrapping tightly in paper and leaving undisturbed for twenty-four hours.

(*d*) *Avoiding and Treating Injuries.*—The possible manners in which the feet may be injured are obviously manifold.

1. Shoes should fit properly.
2. New shoes should be broken in gradually.
3. Corns should be treated diligently by applying a mixture of salicylic acid ℥i and collodion ℥i each evening for four or five treatments. In most instances, the corn will then separate readily without tissue injury. It if does not, the treatments may be repeated.
4. Callouses may be removed by soaking feet in warm soapy water for twenty minutes each evening.
5. Daub minor injuries in which the skin is broken with a

pledget of cotton soaked with Hexylresorcinol S.T. 37. (Do not use irritating antiseptics.)

6. Avoid exposing feet to extremes of temperature.

7. Avoid crossing the knees. Avoid use of circular garters, or any form of clothing which might interfere with the circulation of the feet.

(*e*) *Special Measures.—Alternate Suction and Pressure on Blood Flow to the Lower Extremities.*—This treatment, suggested by Landis and Gibbon,[1] merits a trial over long periods. The blood flow has been increased in the presence of advanced organic obstruction, the cold limb becomes warmer, and the artificially heated extremity cools more slowly under this form of treatment. Unfortunately the expense of the equipment precludes its general adoption.

Immersion of Forearms in Warm Water.—Vasodilatation in the lower extremities is secured by this simple procedure when disturbed circulation is due to vascular spasm.[2] Immersion of one foot in warm water causes vasodilation and increased skin temperature in its fellow.

Patients with vascular spasm, determined by skin temperature studies, should be given the advantage of this treatment. It can be carried out when direct bathing of the feet may be impractical. The two may be alternated: bathing of feet for twenty minutes each evening and immersion of hands and forearms for ten minutes each morning. Electric heating pads wrapped around the arms are equally effective.

Treatment of Gangrene.—*Non-operative.*—The response to non-operative treatment depends largely on the active vascularity of the extremity involved. Passive congestion is prevented by rest in bed and by slightly elevating the affected foot. Warmth plays an important part. It may be provided by a baker with adequate protection between the bulbs and the foot, insuring against any likelihood of too

[1] Landis, E. M., and Gibbon, J. H., Jr.: Jour. Clin. Invest., **12**, 925–961, 1933.

[2] Gibbon, J. H., Jr., and Landis, E. M.: Jour. Clin. Invest., **11**, 1019–1036, 1932.

much heat. The cradle should be high enough to allow free movement of the limb without danger of injury. The temperature about the foot should be that which provides maximum comfort. *Too much heat is worse than none at all.* A thermoregulated foot cradle[1,2] providing optimum temperature between 30° and 34° C. is ideal.

McKittrick and Root advise irrigating necrotic areas with a dilution of hyclorite with cold water. They protect the surrounding skin by following Farr's procedure of painting it with a mixture of rubber tire cement and ether in the proportions of 1 to 3. Great care is necessary in removing the gangrenous slough to prevent even the slightest injury. Direct exposure of the gangrenous ulcer to the sunlight, or to artificial ultra-violet rays, with due caution against over exposure, may stimulate a better tissue response. Applications of dressings soaked with insulin seemed to benefit two of my patients. The non-irritating and germicidal properties of Hexylresorcinol S.T. 37 make it valuable applied as a wet dressing. A mixture of equal parts of tincture of green soap and hydrogen peroxide is useful in cleansing and deodorizing gangrenous ulcers.

For patients with gangrene of one or more toes with a secondary infection I recommend the prone position with the lower third of the leg supported on a pillow. The affected foot extends beyond the pillow with the toes in a dependent position. This position is valuable in preventing a proximal extension of the infection along the course of the tendon sheaths.

Operative.—When a limb becomes a peril to life, it should be amputated. With pain a prominent symptom, coldness of the affected foot as contrasted with its fellow, and with evident extension of a secondary infection, surgery is indicated. Septicemia, so common if permission to operate is delayed, is the most common cause of death in these cases.

[1] Starr, I., Jr.: Am. Jour. Med. Sci., **187**, 502, 1934.
[2] Sevringhaus, E. L.: Am. Jour. Med. Sci., **187**, 509, 1934.

For details of the operations I refer the reader to McKittrick and Root's excellent presentation.[1] The site for amputation is chosen by the surgeon. My only suggestion in this respect is that if there is any question about a satisfactory outcome with a low operation, and there usually is, a high one, *above the knee*, should be resorted to.

An illustrative case of gangrene requiring operation is presented, in detail, below.

Surgical Case (Gangrene and Amputation of a Leg).

F. H., female, aged sixty-seven years, was admitted to the Pennsylvania Hospital on March 2, 1934, for the treatment of diabetes, diabetic gangrene and a lump in her left breast. She complained of severe pains in her legs. Her family history is unimportant and her only past illness was pneumonia in childhood.

Present Illness.—In 1931, after a minor injury to her right great toe, a vesicle appeared at the site of injury. The entire toe became inflamed. Glycosuria was found and a diagnosis of diabetes with gangrene was made. A special diet and insulin were given and the patient was confined to bed for five weeks with good results.

Five days prior to admission another vesicle appeared on the fifth toe of the left foot. The underlying tissues became black. At this time an ulcer appeared on the postero-lateral surface of the distal third of the right leg.

The positive findings on physical examination were: undernutrition, marked thickening of the peripheral arteries, arterial hypertension, retraction of the left nipple with an irregular mass, which proved to be a benign tumor, in the left upper quadrant of the breast, emphysema with fine crackling râles at the base of each lung and mitral insufficiency with enlargement of the heart. There was a feeble pulsation in both dorsalis arteries and the feet were cool to

[1] McKittrick, L. S., and Root, H. F.: Diabetic Surgery, Philadelphia, Lea & Febiger, 1928.

the touch. The affected toe was gangrenous, emitting a foul odor and a purulent discharge.

The patient was considered a poor surgical risk. Watchful waiting was advised by the surgeons.

Insulin was begun again on May 4th and was steadily increased. In May and June the gangrene extended involving the plantar surface of the foot with profuse purulent discharge. There was a continued febrile reaction. Radical amputation was decided upon.

TABLE 21.—CASE F. H. ILLUSTRATES THE EFFECT OF A SURGICAL COMPLICATION ON A MILD DIABETES. NOTE THE LIBERAL AMOUNTS OF CARBOHYDRATE ALLOWED, THE LARGE DOSAGE OF INSULIN BEFORE AND THE DECREASE AFTER THE OPERATION, AND THE EASE WITH WHICH NORMAL TESTS WERE MAINTAINED BY FREQUENT FEEDINGS AND INSULIN ADMINISTRATIONS.

Date, 1934.	Time.[1]	Diet.				Insulin.	Bl. sug.	Glycosuria.	
		P.	F.	C.	Cal.				
June 4	..	70	36	200	1400	26–24–25–25–23	..	0—0—0—0	
5	..	70	36	200	1400	26–24–25–25–23	..	0—0—0—0	
6	7	12	7	33	243	26	98	...	Liquid diet
	10	12	7	33	243	24			
	11.57	..	..	..	...	10			
	12.20	..	..	..	...	.....	..	.....	Leg amput.
	12.35	..	..	25	100	.....	..	.....	Glucose by
	4	..	..	60	240	20	67	Negative	vein
	8	12	7	33	243	22	..	Negative	
	12	12	7	33	243	15			
7	4	12	7	33	243	15	130		
	8	12	7	33	243	15	..	Negative	
	12	12	7	33	243	15			
	4	12	7	33	243	15	..	Negative	
	8	12	7	33	243	15			
	12	12	7	33	243	15			
8	..	70	36	200	1400	12–12–12–12–12–12	122	0—0—0—0	House diet
9	..	70	36	200	1400	9– 9– 9– 9– 9– 9	121	0—0—0—0	(6 meals)
10	..	70	36	200	1400	7– 7– 7– 7– 7– 7	133	0—0+1—0	
11	..	70	36	200	1400	6– 6– 6– 6– 6– 6	..	0—0—0—0	
12	..	70	36	200	1400	6– 6– 6– 6– 6– 6	126	0—0—0—0	
13	..	70	36	200	1400	6– 6– 6– 6– 6	181	0—0—0—0	5 meals
14	..	70	36	200	1400	6– 6– 6– 6– 6	133	0—0—0—0	
15	..	70	36	200	1400	9– 9– 9– 9	152	0—0—0—0	4 meals

[1] Italic figures indicate P.M.

Control of the diabetes was maintained by gradually adding to the insulin, which was given in 5 doses, and with a diet of 70 grams of protein 36 grams of fat and 200 grams of carbohydrate (1400 Calories) (see Table 21). The diet

was given in 5 equal feedings evenly distributed throughout the twenty-four hours.

On the day of operation, June 6th, the usual amounts of insulin were given before liquid meals at 7.00 A.M. and 10.00 A.M. At 11.45 A.M. a spinal anesthetic (neocaine) was administered and at mid-day 10 units of insulin were given. The left leg was then amputated at the mid-thigh level by Dr. A. Walkling. Following the operation 250 cc. of a 10 per cent solution of glucose were given intravenously. This was repeated at 4 P.M. with 20 units of insulin. Ginger ale and orange juice were given freely.

The liquid meals, 6, equally spaced, in twenty-four hours, were resumed at 8 P.M., each being preceded by 22 units of insulin. House diet of appropriate values was allowed on June 8th. A rapid decrease in the insulin need followed the operation. On June 13th the feedings and insulin doses were reduced to 5 in number and on June 15th to 4. Uneventful recovery ensued.

The amputated limb, on examination, revealed marked thickening of the arteries with partial occlusion of the popliteal artery, extensive gangrene about the heel and plantar surface of the foot (the original site of the gangrene had healed) with accumulations of pus in the ankle and tarsal joints and chronic osteomyelitis of the malleoli, astragalus, calcaneus, and scaphoid and cuboid bones.

SUMMARY.—This case illustrates: (1) the age occurrence of gangrene; (2) that the appearance of a vesicle is often the first sign of gangrene; (3) the insulin resistance in the presence of gangrene and infection; (4) the effectiveness of dividing the diet and insulin into 5 and 6 equal amounts distributed at equal intervals throughout the twenty-four hours during the course of the toxemia and febrile disturbance; (5) the prompt decrease in the insulin requirement, from 123 units to 36 units daily, following the riddance of the infection and toxemia.

DIABETIC COMA (KETOSIS).

Ketosis is an intoxication due to an accumulation in the body of the intermediary products of fat and, to a limited extent, protein metabolism. The poisoning may vary from the first and apparently innocent stage, in which only traces of acetone appear in the urine (ketonuria), to that of a profound toxemia characterized by large quantities of diacetic acid and β-hydroxybutyric acid in the urine and accumulation of demonstrable amounts of these ketone bodies in the blood. These bodies produce the condition usually known as diabetic coma.

Source and Disposal of Ketone Bodies.—The ketone bodies, acetone, diacetic and β-hydroxybutyric acid, are derived from fat and protein. In diabetes the insulin lack is responsible for their incomplete combustion which normally is carried on to the production of CO_2 and H_2O with the liberation of heat. Milder disturbances of this nature may be produced even when insulin is present in abundance. Starvation is of special significance in this respect as is inadequate carbohydrate intake and ketosis produced by certain drugs.

Acetone is the first to appear in the urine. It may be lost in small quantities over long periods without harm. Increased accumulation of acetone in the blood precedes its appearance in the form of gas which is excreted by way of the lungs giving to the expired air the distinctive acetone odor sometimes described as a sweet or fruity odor. It is likened to the odor of new-mown hay which odor is pleasing and invigorating while that of acetone certainly is not. A combination of over-ripe fruits emits an odor which closely resembles that of acetone.

Diacetic acid is second to appear as the ketosis deepens. It is definitely injurious and is believed to be the cause of death in clear-cut cases of diabetic ketosis. The last to appear is the β-hydroxybutyric acid. It is in this form that

most of the acids are eliminated. Its appearance in the urine is an index of the gravity of the intoxication.

These two acids, diacetic and β-hydroxybutyric acid, are lost only by way of the kidneys. The reaction of the urine is acid, but neither this nor the degree of ketonuria is a reliable indication of the severity of the ketosis.

As excretion fails to keep up with the production, ketone bodies accumulate in the body. In consequence the alkali reserve is diminished; the carbonate or carbonic acid content of the serum is reduced and replaced by the ketone bodies, hence the decreased CO_2 combining power of the plasma.

The CO_2 combining power of the plasma is measurable. A reliable indication of the severity of the ketosis is thus available. Van Slyke[1] gives as the normal bicarbonate reserve, plasma bicarbonate CO_2, 80 to 53 volumes per cent; mild ketosis, 53 to 40; moderate ketosis, 40 to 30, and severe ketosis, below 30 volumes per cent.

Another and much simpler test, that of Rothera and Wishart, is a qualitative, and, at the same time, roughly quantitative examination for the plasma acetone and diacetic acid content. I have employed this test repeatedly at the bedside and consider it an excellent guide in the treatment of diabetic coma. The details of this examination are presented on page 140.

Clinical Aspect.—Diabetic coma, formerly the most dreaded complication of diabetes and the most common cause of death among diabetics, has been rendered curable and preventable by insulin. Nevertheless, deaths still occur from diabetic ketosis and are largely attributable to delay on the part of the patient in obtaining medical assistance. Properly informed diabetics know the penalties of delay. It is the new diabetic, the patient who did not know he had diabetes, and the careless diabetic that swell the total of deaths from ketosis.

Young diabetics are most susceptible to ketosis, though

[1] Van Slyke, D.: Jour. Biol. Chem., **33**, 271, 1918.

any febrile disturbance, medical or surgical, or other factors (such as thyroid disease) which accelerate metabolism may expose any diabetic to the dangers of ketosis.

Severe diabetics owe their liberal diets largely to the insulin they are taking. They are eating beyond their own native resources. If the insulin is omitted for even a few doses with the diet unchanged, ketosis will ensue. It may be precipitated with amazing rapidity. It is a type of onset of ketosis unknown before insulin was discovered.

One young patient with severe diabetes omitted her insulin and was beyond aid within eighteen hours. In pre-insulin days this patient would have been on a much lower diet, and she would have had less fat to contribute to the development of ketosis. She might have escaped ketosis entirely. In any event the onset would have been gradual—over a period of days.

In the pre-insulin era, all diabetics were reduced in weight and, by virtue of the ensuing lowered metabolism and decreased fat, were in less danger of rapidly developing ketosis. The diabetic of today, if allowed to become overweight, is many times more apt to develop ketosis if for some reason his insulin should be stopped; or, if with loss of appetite he makes matters worse by stopping the insulin, see page 113. The sudden omission of large doses of insulin without simultaneous reduction of the diet is dangerous, and irregularities in the diet, excess fat in the diet, excess fat distributed throughout the body and overeating are dangerous. *It is folly to overnourish any diabetic.* It is advantageous to keep the weight a trifle below the accepted average and the insulin dosage small, though adequate.

The other chief exciting causes of ketosis—infection, gangrene, vomiting, diarrhea and intoxications—will be dealt with under their respective headings.

Manner of Onset.—Recognition of the onset of ketosis is not always easy. The onset is so variable, in fact, that any suggestion of ill health in a diabetic should at once suggest

the possibility of ketosis. Air hunger (Kussmaul breathing), anorexia, fatigue and increased thirst have occurred with greater frequency than any other group of symptoms in the cases of ketosis which I have seen. Drowsiness, polyuria, and nausea are also common as are vomiting, abdominal pain (due to dilatation of the stomach, rarely to acute pancreatitis), restlessness and irritability. In the presence of fever, weakness and the desire to sleep may be the only symptoms of approaching coma.

Recognition of Diabetic Coma.—The history of the symptoms mentioned above, given by the patient or by a relative, will aid in making a tentative diagnosis. Positive reactions for sugar, acetone and diacetic acid in the urine are further confirmatory evidences. A high blood sugar, usually above 0.3 per cent, a low CO_2 combining power, below 25 volumes per cent, with positive tests for acetone and diacetic acid on the blood plasma confirm the diagnosis. Occasionally the CO_2 combining power has been artificially raised by the administration of alkali. In this event, the CO_2 combining power ceases to be of great prognostic value. Patients in coma may die of ketosis with a normal CO_2 combining power. It is for this reason that I value the reactions for acetone on the plasma in treating these patients. Decreasing plasma acetone is an index of genuine improvement, and its disappearance means that the patient is out of immediate danger from the ketosis *per se.*

I have purposely mentioned the findings of greatest diagnostic significance first. Examination of the urine will invariably reveal a high specific gravity. Albuminuria is fairly constant and there may be showers of hyaline and granular casts. Further study of the blood will reveal a lipemia, a high cholesterol content, a low sodium chloride value, and a leukocytosis, frequently unexplained, is usual. A high urea concentration may be found. This is doubtless due to the decreased blood volume concurrent with the dehydration. Prompt return to normal accompanies treat-

ment except when a true diffuse glomerular nephritis exists. A high red cell count, over 5,000,000, is the rule. This, with the low blood-pressure, serves to differentiate diabetic coma from the coma of uremia.

Physical Findings.—The patient appears desperately ill. He may be restless or stuporous. The distressing hunger for air often accounts for the frantic tossing about. The deep respirations with unusually great respiratory excursion of the thoracic and abdominal walls is striking. The alæ nasi expand with each inspiration. The sweet, fruity odor of acetone may permeate the room. The skin is dry—*the skin is always dry in the coma of diabetic ketosis*—in contradistinction to the coma of hypoglycemia. The dehydration is very noticeable. The nasal passages, tongue, mouth and throat are dry and there is an unquenchable thirst. The tongue, from a patient's description, "feels like a hot, dry, rough piece of leather." Sordes on the lips, and dry, dark pigmentation on the teeth are common. The throat is red. The state of the pupils is variable, though contraction is the rule. The intra-ocular tension is greatly decreased, so much so that the orbit may feel like pulp to the palpating fingers.

The heart-rate is rapid, the sounds are distant, and blood-pressure is low—*the blood-pressure has been low in every case of established coma of diabetic ketosis that I have seen*—the extremities are cold, the pulse is rapid, and of poor force and volume. The temperature is often subnormal. In oncoming and early ketosis, fever due to infection, may be present. With the onset of unconsciousness the temperature may fall below normal. A patient of Dr. Charles Tait's, whom I saw in diabetic coma with a concurrent lobar pneumonia, had a typical pneumonic type of fever until the onset of severe ketosis. The temperature then fell below normal, 96° F., but promptly resumed its previous level after the ketosis was controlled. Fever in advanced coma is usually due to a septicemia. The abdomen may be tender, particularly in the epigastrium. There may be some muscular

rigidity due to dilatation of the stomach or to an acute pancreatitis (rare). The descending colon may be distended with hard, dry feces. There is no uniformity in the behavior of the reflexes.

It is common to find the exciting cause of the ketosis while conducting the physical examination. Gangrene, with secondary infection, carbuncles, furuncles and systemic infections are the common contributors. Too much food and too little insulin may be entirely responsible, however.

Differential Diagnosis.—A hypoglycemia, from an overdose of insulin, may be confused with the coma of ketosis. The moist skin, the absence of dehydration, a normal intraocular tension, the normal breathing, a normal or elevated blood-pressure, the absence of glycosuria and acetonuria with the history of a recent—within a few hours—and rather rapid onset serve to identify a hypoglycemia. The blood analysis reveals a subnormal blood sugar. A more complete differentiation of these two disorders is recorded on page 88.

Uremia may accompany diabetic coma. Occasionally there is a renal block with a rapidly ensuing nitrogen retention. The evidences of disturbed kidney function due to the ketosis alone and not to a preëxisting glomerular nephritis, quickly subside with proper treatment. The uncomplicated uremia is readily distinguishable from the coma of diabetic ketosis by the absence of a great increase in the blood sugar, a low red cell count, a high blood-pressure and a negative reaction for plasma acetone.

Cerebral hemorrhage may in some respects simulate diabetic coma. Intra-ventricular hemorrhage may be especially confusing. The blood sugar may be considerably elevated and sugar may appear in the urine and there may be acetonuria with mild reactions for plasma acetone. It will be noted, however, that the degree of coma is out of proportion to the elevation of the blood sugar, the blood-pressure is usually elevated, the skin is moist, the face is flushed and the reflexes are usually increased, though they may be absent.

Furthermore, the onset is sudden and the spinal fluid may contain gross blood. I have seen, recently, 3 such cases in each of which a tentative diagnosis of diabetic coma had been made.

Careful examinations, physical and chemical, will remove any difficulty in differentiating between diabetic coma and alkalosis, drug poisoning, acute infections and injuries and accidents which may complicate diseases of the cardio-vascular system.

Treatment.—The treatment of coma due to diabetic ketosis may be summed up by mentioning the main essentials which are—adequate insulin, ample carbohydrate, fluids, warmth, enema, cardiac stimulation, sodium chloride with gastric lavage and alkali if needed.

Each case of coma is an individual problem. No routine treatment is applicable to all. Constant supervision by a capable nurse is indispensable and the physician should see the patient hourly until the danger period is past.

A skeleton outline for the treatment of coma is presented on pages 138–140. It is employed for the "B" service patients at the Pennsylvania Hospital. It, of necessity, permits moderate elasticity.

Insulin.—Insulin has made it possible to save practically all coma patients. It is best employed in moderate doses *given at frequent intervals.* Fifty units as the initial dose is probably the minimum, while in only a few instances have I given 100 units. It is well established that the effectiveness per unit decreases with the increasing size of the dose. Added benefit is gained by giving smaller doses more frequently, every half hour, than large doses at longer intervals. With correction of the ketosis the effectiveness of the insulin is greatly increased.

The insulin may be given subcutaneously and intravenously but *not intravenously alone.* Reliance should not be placed on the insulin given by vein yet the promptness with which it may exert a beneficial effect makes it advisable in

cases of severe coma to use this route in conjunction with the subcutaneous therapy. The insulin given intravenously is more effective if administered very slowly (Fitz).

Carbohydrate.—Some authorities, notably Joslin, spare or give no carbohydrate in the treatment of coma. The excess blood sugar is considered sufficient to aid in the complete oxidation of the ketone bodies when insulin is given. Carbohydrate is given and the insulin decreased as the blood sugar approaches a low level. The results on this program have doubtless been good.

My feeling, governed by the fact that it is the ketosis and not the hyperglycemia that threatens life, is that the more sugar metabolized the better. In the critical stages of coma, therefore, little attention is given to the degree of hyperglycemia, but ample carbohydrate is given at least until the blood plasma gives a negative reaction for acetone bodies. This procedure is probably further justified when one considers that the total blood sugar in a case of coma may not exceed 25 grams, and that the liver is practically free of glycogen.

I believe that the administration of carbohydrate in the severe stages of coma increases the margin of safety, particularly in inexperienced hands. The difference in the total amounts of insulin used with and without simultaneous glucose administration is strikingly small.

Glucose, 60 grams in a 10 per cent solution, is given preferably by the intravenous route at the outset of treatment when oral administration is not practical. The solution must be kept warm and it should be given very slowly. For information regarding subsequent glucose therapy, consult the outline on page 139.

Fluids.—A liberal fluid intake is of great value. If not retained by mouth, liquids may be given as 10 per cent glucose (see above) and normal saline, 500 cc. by the intravenous route, or the saline solution, 1 liter, by hypodermoclysis and by rectum. When given by rectum the Murphy drip method is the most satisfactory.

When mouth feeding is feasible, broth, well salted, may be taken freely. Following the initial fluid intake by vein and subcutaneously (glucose solution and saline) 200 cc. may be taken each hour for the first six hours of treatment, though one-half this quantity is preferable if cardiac weakness is noted. Orange juice diluted with water, gruel, ginger ale (non-effervescent), coffee and tea may be given. Liquids, in most instances, are retained after giving sodium chloride and bicarbonate of soda, āā grs. xxx in a glassful of water, even though this mixture may be promptly expelled.

Gastric Lavage.—The advantages of gastric lavage have been emphasized by Joslin. The stomach tube should be passed and the stomach emptied if a history of abdominal pain is given, if there is rigidity of the abdominal muscles, or if there is some doubt as to whether some acute surgical condition exists. Emptying the stomach of its contents gave relief from acute abdominal pain and saved 2 patients, to my knowledge, from laparotomies. Vomiting, which persists after the administration of the sodium chloride and bicarbonate of soda, which is comparatively rare, indicates the need of lavage. A saline solution (℥i sodium chloride to a pint of water) is used for this purpose.

Alkalis.—It is with reluctance that one uses alkalis in the face of advice to the contrary from an authority as great as Dr. Joslin. It is difficult, however, to erase the apparent life-saving effect which the intravenous administration of a 3 per cent solution of sodium bicarbonate had on one of Dr. Allen's patients (Physiatric Institute Series, Case No. 1) who was apparently moribund. The same is true of Case No. 63 of the Rockefeller Series. We have not used alkali as a routine measure except for a single dose of soda bicarbonate and sodium chloride to prevent or stop vomiting. A single dose, 300 cc. of a 3 per cent solution in normal saline, given intravenously at the outset of treatment of a profound coma, also seems justified. Since boiling changes bicarbonate into the carbonate, solutions may be prepared by taking

clean sodium bicarbonate, preferably from a freshly opened package of a chemically pure brand, with sterile apparatus into sterile water or salt solution, without further sterilization.[1]

One remarkably good result obtained by the intravenous use of the molar sodium *r*-lactate solution recommended by Hartman and Senn[2] has come to my attention. I have had no experience with this preparation but suspect that its value will also be greatest in cases of profound coma. It need hardly be stated that mild and moderate degrees of ketosis are readily corrected without alkalis.

Warmth.—Warmth may be supplied by hot liquids, blankets and hot-water bottles. Due precaution against any danger of burning should be exercised—the patient may be insensitive to pain.

Enemata.—It is important to empty the bowel by enema. Clinical improvement in some instances begins only after thorough intestinal evacuation. Emptying the colon will facilitate absorption of saline given by enteroclysis.

Cardiac Stimulation.—The myocardium is exposed to the toxic effects of the ketosis and usually, if the patient is over thirty-five years of age, to the effects of some coronary artery disease. The burden of large quantities of fluid intravenously should be avoided. (See page 111.)

For supportive treatment, caffeine sodium benzoate is used freely. Indications for employing digitalis may present themselves. I have not used epinephrin to increase the blood-pressure.

Diabetic Coma (Severe).

O. S. (No. 6621), female, aged thirty-nine years, was admitted to the Pennsylvania Hospital, Philadelphia, in diabetic coma on August 15, 1928.

[1] Magnus Levy, A.: Ueber subkutane Infusionen von Mononatriumkarbonat, Therap. Monatsh., **27**, 838–843, 1913.

[2] Hartman, A. F., and Senn, M.: Jour. Clin. Invest., **11**, 341–344, 1932.

Family History.—Two of her maternal aunts suffer from diabetes and her father has heart trouble and hay fever. Her four children are living and well.

Past Illnesses.—Measles, mumps, frequent sore throat in childhood, influenza in 1918 and grippe several times comprised her past illnesses except an attack of nausea after overeating at a picnic on July 17, 1926. She vomited at short intervals and gradually became stuporous. She was taken to a hospital where a diagnosis of diabetes with impending coma was made. After treatment for several weeks she left the hospital taking 60 units of insulin daily.

Present Illness.—She was well until August 13, 1928 when she had an attack of diarrhea followed by nausea. Owing to loss of appetite she discontinued the insulin. General weakness, restlessness, extreme thirst and polyuria followed and at 4 A.M. on the date of admission, she was found in a comatose state. The family physician, Dr. C. C. Sheets, of Paulsboro, N. J., instituted treatment by giving 40 units of insulin and 10 grams of carbohydrate at 6.40 A.M. The insulin was repeated with 15 grams of carbohydrate one hour later.

When admitted at 10 A.M. she was in deep coma exhibiting marked air hunger with an acetone odor on the breath. Her skin was dry and there was considerable cyanosis. There was a pronounced reduction in the intra-ocular tension and the tongue was dry and fissured; the pharynx was dry and hyperemic; the body temperature, taken by rectum was 96.5° F. The blood-pressure was 56 systolic and 42 diastolic. At 11.30 P.M. it had increased to 84 systolic and 56 diastolic, and on August 16th to 94 systolic and 68 diastolic. The pulse-rate was extremely rapid and there was severe dehydration. There was incontinence of urine for the first twenty-four hours of treatment. A moderate amount of albumin with granular casts leukocytes and sugar was present in the urine.

On admission 20 units of insulin were given and when the

blood sugar was found to be 0.842 per cent (11.00 A.M.) 60 units, 20 intravenously and 40 subcutaneously, were given, see Table 22. Another dose of 60 units followed in one-half hour when the blood sugar was lower, 0.551 per cent. It will be observed in Table 22 that the insulin was given at half-hourly intervals until it was quite cer-

TABLE 22.—CHART OF MRS. O. S. (NO. 6621) ILLUSTRATING THE TREATMENT AND ITS EFFECT IN A CASE OF PROFOUND DIABETIC COMA.

Date, 1928.	Time.	Diet.				Insulin.	Blood sugar.	Glycosuria.				Wt., kg.
		P.	F.	C.	Cal.			7 A.M.	11 A.M.	4 P.M.	9 P.M.	
Aug. 15	6.40 A.M.	..	..	10	40	40	..	Heavy				
	7.30	..	..	15	60	40	..	Heavy				
	10.00[1]											
	10.10	..	..	..	...	20	842					
	10.30[2]											
	11.00	..	..	..	...	60[3]						
	11.30	..	..	..	...	60	551					
	12.00	..	..	..	...	20						
	12.30 P.M.	..	..	..	...	20						
	1.00	..	..	20	80	20						
	1.30	..	..	20	80	20						
	2.00	..	..	20	80	20	356					
	2.30	..	..	20	80	20						
	3.00	..	..	20	80	20						
	3.30	..	..	20	80	20						
	4.00	..	..	20	80	20						
	6.00	..	..	20	80	10						
	9.00	..	..	20	80	20						
	11.30	..	..	40	160							
16	4.00 A.M.	..	..	20	80	10						
	8.00	13	13	43	341	20	59	+1				
	12.00	13	13	43	341	20						
	5.00 P.M.	13	13	43	341	20	..	+1				
	12.00	..	..	20	80	12						
17	....	40	38	150	1100	20–20–20–12	..	+4	+3	+2	—	
18	....	40	38	150	1100	20–20–20–20	319	+4	+3	+1	—	
19	....	70	47	100	1100	30–24–16– 0	..	0	0	0	0	
20	....	..	..	..	...	24–24–12– 5	..	0	0	0	0	
21	....	..	..	..	...	24–20–12– 5	..	0	0	0	0	
22	....	..	..	..	...	24–20–12	180	+1	+3	+1	—	55.5
23	....	..	..	..	...	24–18–14	..	+3	+3	0	—	
24	....	70	107	90	1600	26–14–16	..	0	+1	0	0	
25	....	..	..	..	...	28–10–16	98	0	0	0	0	55
26	....	..	..	..	...	26–10–18	..	+1	+1	0	0	
27	....	..	..	..	...	28–10–18	..	0	0	0	0	
28	....	..	..	..	...	28– 8–18	..	0	0	0	0	
Sept. 1	....	..	..	..	...	26– 6–22	100	0	0	0	0	56
12	....	70	120	110	1800	25– 3–14	105	0	0	0	0	55

[1] Admitted to the hospital.
[2] Normal saline solution subcutaneously.
[3] Twenty units intravenously and 40 subcutaneously.

tain that the blood sugar was approaching normal; that the carbohydrate was given with each dose of insulin after the first few doses; that the blood sugar was below normal on the morning of August 16th though no symptoms of a hypoglycemia were noticeable and that in the first twenty-four hours of treatment 440 units of insulin were given.

In addition to insulin and carbohydrate, hot liquids—tea and well salted broths—were given by mouth when feasible. Heat was applied to the extremities and the patient was well covered.

The heart was supported by giving caffeine sodium benzoate, 2 grains every half hour, while the patient was critically ill. The tincture of digitalis, 15 minims, was given every four hours.

A soap water enema was given early and also a hypodermoclysis of 500 cc. of normal saline. This was repeated.

On August 17th the patient, being free from symptoms, insisted on leaving the hospital. A dietitian accompanied her and completed the instructions regarding diet, insulin and urine tests at home.

Points of special interest in this case are: (1) The coma was precipitated by stopping a moderately large amount of insulin; (2) diarrhea with anorexia were the symptoms leading to the patient's decision to stop insulin; (3) the profound coma indicated unusually large amounts of insulin; (4) subjectively the patient was well but the diabetes was not controlled on the second day after admission; (5) the diabetes was controlled, after the immediate effects of the ketosis had subsided, with 42 units of insulin daily. This is compared with 60 units needed before the attack. A smaller diet doubtless explains the apparent gain of tolerance; (6) this patient no doubt owes her life to her family physician who recognized the diabetes and had the courage to take vigorous steps to control it.

Impending Coma.

G. T., male, aged sixteen years, was admitted to the Pennsylvania Hospital, Philadelphia, on July 9, 1934, complaining of increasing drowsiness, loss of weight, appetite and strength, and an unquenchable thirst with frequent passing of large quantities of urine for four weeks prior to admission.

Family History.—One sister has diabetes.

Past Illnesses.—He had measles in childhood and in 1930 a diagnosis of hypopituitarism (dystrophia adiposogenitalis) was made at the Pennsylvania Hospital. On that admission he had glycosuria which cleared up in the first twenty-four hours of treatment.

Present Illness.—Four weeks before admission he lost his desire for cigarettes and at the same time weakness, thirst, polyuria, dryness of the skin, constipation and anorexia became noticeable. These symptoms increased in severity until admission. One month previously his weight was 82 kilograms and on admission it was 71 kilograms.

The physical examination revealed pronounced drowsiness, dry skin, good nutrition, apparently normal intra-ocular tension and diseased tonsils. The heart, lungs, abdomen, reflexes and genitalia were normal and the blood-pressure was 120 systolic and 80 diastolic.

There were 4 plus reactions for sugar, acetone and diacetic acid in the urine with a 1 plus albuminuria. The initial blood sugar was 0.263 per cent. There was a pronounced lipemia and there was a strongly positive reaction for acetone and diacetic acid in the plasma. Additional laboratory data are recorded in Table 23.

He improved steadily, subjectively and objectively. The tests for plasma acetone and diacetic acid became negative and the lipemia subsided within the first eight hours of treatment.

The insulin was increased daily until the fasting blood sugar was normal. Further adjusting of the insulin distribu-

tion was necessary to overcome the glycosuria. A remarkable gain in weight occurred, from 69 kilograms on July 10th to 77 kilograms on July 22d. This is doubtless accounted for, largely, in the correction of the dehydration though a hypopituitarism factor may have played a part.

TABLE 23.—ILLUSTRATING THE TREATMENT AND THE RESPONSE IN A CASE (G. T.) OF IMPENDING COMA.

Date, 1934.	Time.	Diet.				Insulin.	Bl. sug.	Glycosuria.					Wt., kg.
		P.	F.	C.	Cal.							Gm.	
July 9	6.30 P.M.	..	..	24	96	20	263	Heavy					
	8.30	..	..	24	96	20	..	Heavy					
	10.45	..	..	12	48	20	..	Heavy					
	12.45 A.M.	..	..	32	128	20							
10	....	85	47	160	1400	12–10–14– 8	..	+3	+3	+3	+3	42.6	69
11	....	85	47	160	1400	12–10–18–12	200	+4	+4	+4	+4	50.2	
12	....	85	47	160	1400	16–14–18–12	199	+4	+4	+4	+4	46.1	
13	....	85	47	160	1400	20–16–22–12	183	+4	+4	+4	+4	30.8	
14	....	85	47	160	1400	24–20–26–16	169	+1	+3	+1	+3	15.6	
15	....	85	47	160	1400	24–20–26–16	..	+3	...	+3	+2	14.4	
16	....	85	47	160	1400	27–20–29–19	146	+3	+3	+1	+3	18.0	71
17	....	85	47	160	1400	27–20–33–23	..	+3	...	0	0	2.4	
18	....	85	47	160	1400	31–22–33–20	100	0	+4	0	+1	7.2	

SUMMARY.—This case is of special interest because it depicts (1) the gradual onset of ketosis as is usual in the absence of other complications, especially fever, diarrhea, vomiting and the stopping of insulin; (2) the marked loss of weight and its recovery with treatment; (3) the classical symptoms of impending coma; (4) the response to insulin in moderate doses given at two-hourly intervals in contrast to case O. S., page 114, in which the insulin was given every half hour, and (5) the rapid decrease of the plasma acetone, diacetic acid and lipemia.

INFECTIONS.

Infections, no doubt, play a part in causing diabetes. They frequently bring a latent or potential diabetes to the fore. They tend to impair the carbohydrate and total food tolerance. They increase the need for insulin. They stimu-

late metabolism, and they often jeopardize life by precipitating a ketosis.

The treatment of the infection should be the same in the diabetic as in the non-diabetic. Diabetes, in the presence of infection with fever, is best dealt with by increasing the carbohydrate, reducing the fat and keeping the total calories a trifle on the side of undernutrition, thus minimizing the danger of ketosis. The insulin should be increased as warranted by the fractional urine tests and blood examinations. Frequent and small doses are more effective than infrequent and large doses. Alleviation of the infection brings with it a lessened need for insulin. The rapid loss of weight in tuberculous patients may decrease the need for insulin in isolated instances.

Tuberculosis.—Root's[1] recent exhaustive survey of tuberculosis and diabetes brings surprise to those of us who from observing smaller numbers of patients have obtained the impression that tuberculosis in the diabetic has decreased with the use of insulin. This apparently is not the case. According to Root, deaths from pulmonary tuberculosis among diabetics have increased instead of declined, and diabetic children are at least 10 times as apt to acquire tuberculosis as normal school children. Furthermore, in 85 per cent of 245 tuberculous diabetics, the onset of the tuberculosis was subsequent to the onset of the diabetes. In 8 per cent of cases recovering from coma tuberculosis developed within three years.

DEGENERATIVE CHANGES.

Degenerative changes are common and are progressive in the presence of neglected diabetes. Under this terminology I choose to list general arteriosclerosis, local arterial changes

[1] Root, H. F.: New England Jour. Med., **210**, 1–12, 78–92, 127–147, 192–206, 1934.

of grave import—in the coronary arteries and arteries of the lower extremities especially—cataract and retinitis.

With effective treatment the arterial changes are largely checked; the retinitis is halted and moderate improvement is the rule. These desirable results have not been obtained, in my experience at least, unless a normal blood sugar is maintained. Mild degrees of hyperglycemia doubtless contribute to the progressiveness of degenerative changes. In this connection it seems worthwhile to comment on Case No. 24 (private series), a male, aged forty-two years, seen by me in 1926 and a mild diabetes then found. Notes emphasizing the good circulation of the extremities were made. The patient was lost sight of but reappeared in June, 1932, suffering with attacks of angina pectoris on the slightest provocation. The feet were cold. When the legs were allowed to hang in a dependent position, a wine-colored cyanosis appeared promptly. No pulsation was made out in either of the dorsalis pedis or posterior tibial arteries.

This patient, though he had been taking insulin, was not taking enough. The amount was slowly increased from 20 units daily in 2 doses to 81 units given in 4 doses.

In general, the prognosis is bad in this type of case. In speaking with patients we should emphasize the following: "Bear in mind that diabetes is controllable, but when neglected, its complications may not only be incurable but are beyond control."

Cataract operations are successfully conducted. The end-results depend, not a little, on whether or not the diabetes is controlled.

SKIN DISORDERS.

Carbuncles.—Carbuncles are among the most serious surgical complications of diabetes, but, fortunately, are not common. The mortality is high. That this is largely

due to delay in obtaining treatment is beyond question. The fatal issue is usually attributable to septicemia.

Hospitalization is imperative. The local treatment is pre-eminently the task of the surgeon. He should be consulted early. The treatment may be as follows: hot compresses or poultices, free crucial incision or excision of the infected area, irrigation with Dakin's solution, ultra-violet light, and roentgen-ray therapy. Roentgen-ray treatments are of outstanding value and deserve special emphasis.

The internist will increase the resistance to infection and often save life by controlling the diabetes. Adequate carbohydrate, 150 to 175 grams daily, with restricted total calories, is advisable. At least four urine specimens should be examined each day to provide guides for increasing the insulin. Enormous doses may be necessary. With improvement a prompt decrease in the insulin requirement ensues. Daily reductions should be made while the urine continues to be free from sugar. The carbohydrate may be reduced to the level used for the non-complicated diabetes after an afebrile period of three days. The danger of ketosis will then be past.

Furuncles.—Furuncles have long been associated with diabetes. Often there are no other signs of the diabetes. They become serious if tampered with. It is a good practice to include in the routine instructions for all diabetics the following: *Do not squeeze, pick or cut a pimple or a boil.*

Essential for successful treatment is the control of the diabetes. Good hygiene, cleanliness of the skin, regular intestinal elimination and eradication of foci of infection are important. Locally, hot compresses, ultra-violet ray, and roentgen-ray therapy, release of pus when fluctuation is evident and frequent dressing are employed. Vaccines, particularly autogenous preparations, are sometimes effective. Active immunization with staphylococcic toxoid may be tried. Cleansing of the field surrounding the infection with effective antiseptic solutions, such as Hexylresorcinol

S.T. 37, aids in preventing contamination of fingers and clothes.

Pruritus.—Little need be said about diabetic pruritus, as recognition of the cause will automatically indicate appropriate treatment. Control of the diabetes yields prompt relief. Bathing of the genitalia, using an unirritating soap or with boracic acid solution, followed by applying a bland ointment or mineral oil, goes far in relieving pruritus vulvæ while systemic treatment is getting under way. Every case of pruritus, general or local, should suggest diabetes as the possible etiology.

Xanthoma Diabeticorum.—This rare skin condition occurring in diabetes is characterized by yellowish papules, varying in size from one-half to a full-sized pea, with a red periphery. They may be widespread over the body but are most numerous on the posterior aspect of the forearm, the hands and about the elbows and knees. They disappear with the checking of the diabetes.

Xanthochromia.—This yellow tinting of the skin, seen best in the palms of the hands in about 1 per cent of diabetics, is due to a lipochrome. The diabetic diet is particularly rich in carotine, one of these pigments. Restriction of egg-yolk, butter and carrots, and at the same time, overcoming the lipemia by controlling the diabetes, restores the normal color.

Fatty Atrophy of the Skin.—Pitting of the skin by fat necrosis following repeated insulin injections in the one location has been reported. I have seen but one instance in our clinic. There is first a painless indurated area and later an actual necrosis of the subcutaneous tissues. Faulty instruction on insulin administration is responsible. At least two weeks should subside after an injection before the same area is again used for this purpose.

Local Insulin (Allergic) Reactions.—The reactions, appearing from six to twelve hours after the insulin administration, are not uncommon among patients receiving insulin for the first time. They have been attributed to minute quantities

of protein in the insulin. I have seen similar reactions to alcohol or impurities in the alcohol when the syringe was not thoroughly dried before measuring the insulin. It is interesting that non-diabetics, particularly tuberculosis patients, are more frequently sensitive to insulin protein than are diabetics. Urticarial eruptions are uncommon, but present a real problem when they occur. The local and more common reaction appears in the form of a swelling about the site where the insulin was injected. The areas, varying in size from a bean to a walnut or even larger, become indurated, tender, hot and itchy with hyperemia of the overlying skin. The swelling disappears in two to three days. Within a few weeks a tolerance is established and the reactions gradually subside. In 1 patient these reactions became a serious problem. With each succeeding injection the areas about previous injections became angry, swollen and intensely itchy. Insulin of another pharmaceutical house was used with the result that there were no local reactions. The simple expedient of changing the brand of insulin usually proves effective. Should it fail, Hajek's[1] suggestion of giving ephedrine sulphate grain $\frac{3}{8}$ and calcium lactate grains 5 by mouth 3 times daily should be tried.

Occasionally it is possible to omit the insulin. This remains the treatment of choice for allergic reactions to insulin when suitable reduction in the total calories and carbohydrate will prevent untoward progress of the disease.

When omission of insulin would jeopardize life, very small but frequent doses may be tried. A few of these patients, especially those with urticarial eruptions, are remarkably resistant to insulin, but the practice of giving rapidly successive doses (every two hours if necessary) will permit a large total dosage and, at the same time, hasten desensitization. In certain cases, it is necessary and advisable to continue increasing the insulin even to great proportions until a response is obtained.

[1] Hajek, Joseph: Jour. Am. Med. Assn., **96**, 192, 1932.

Karr *et al.*[1] have suggested active desensitization. Their procedure, though advisable, is not always feasible.

In my experience allergic reactions have been due chiefly to sensitiveness to insulin obtained in part or whole from pork. Insulin prepared exclusively from beef is obtainable and should be given a trial. *Special insulin* has been prepared for these patients by Eli Lilly & Co.

Bathing of the local reactions with sodium bicarbonate solution is soothing. Epinephrine, in 0.5 cc. doses, is helpful especially in those with urticarial manifestations.

NEURITIS.

Diabetic neuritis is common. It is encountered in patients over thirty-five years of age. Directly attributable to the diabetes, it may prove very intractable until the cause is recognized and corrected. In the case of sciatica, the trouble may be bilateral. The pain is intense. This disorder afflicts chiefly the mild diabetic and the unrecognized diabetic with but slight hyperglycemia. One of my patients had consulted several physicians without relief. It was when one physician had a blood analysis made that a hyperglycemia, insufficient to cause glycosuria, was discovered. Prompt and complete recovery from the neuritis ensued with the control of the diabetes.

Diabetic neuritis *per se* is always cured by controlling the diabetes. The blood sugar must be kept constantly below 0.12 per cent. It is not sufficient merely to prevent glycosuria. Overweight diabetic patients with neuritis quite often suffer an exaggeration of the symptoms during the early part of treatment. This may be due in part to the restriction in calories to which they are subjected. Analgesics may be used to provide immediate relief. Salicylates and pyramidon may account for false reactions for glycosuria

[1] Karr, W. G., *et al.*: Jour. Lab. and Clin. Med., **18**, 1203–1211, 1933.

(see page 43). Dilaudid and codeine are helpful. Morphine should be used infrequently, if at all.

A neuritis which does not subside within three or four weeks from the time the diabetes is controlled is due to some other cause. A renewed effort to identify foci of infection should be made. Teeth, sinuses, tonsils and prostate gland especially, should be examined with care.

DIABETES MELLITUS AND SURGERY.

Reparative, prophylactic and emergency surgery are successfully conducted in the presence of diabetes. Insulin, although it has increased tremendously the margin of safety, has not simplified the management of the diabetes in these cases. No other complications call for more experience and skill with insulin. Simultaneous medical and surgical attention is essential. A surgeon might better ignore Lister's contributions to surgery than to be oblivious to the need of coöperation with the internist.

Concurrent medical and surgical study of every patient needing surgery is therefore the first step toward obtaining best results. The surgeon is in charge of the surgical aspect. He decides when the operation should be done and the method of procedure, as well as supervising all postoperative local treatments. The internist will prepare the patient for operation from the metabolic standpoint. He will be present at the operation and he will conduct the postoperative medical and dietary treatment. The efforts of the most skilled surgeon may be futile if he lacks adequate assistance from the internist.

Rarely is it necessary for the internist to delay the operation. The conditions which make operations necessary usually cause the disturbances in metabolism which immediately imperil life. When rid of them, correction of the disturbed metabolism is a relatively simple matter.

The need to delay operation, when present, is indicated

by a heavy reaction for plasma acetone and diacetic acid, or by a CO_2 combining power of the plasma below 35 volumes per cent. I can think of but few major operations in which the delay of one, two or three hours would add to the dangers presented by these circumstances. The level of the blood sugar in the absence of ketosis is no deterrent to operation. The preparation of the acidotic surgical diabetic for operation is conducted similar to the treatment of impending coma (page 139). Excess glucose may be given to replenish the glycogen supply and to insure against hypoglycemia. It is ketosis, not the hyperglycemia, that threatens life.

No single outline of treatment will prove suitable for all cases. I have, however, drawn up a skeleton plan, page 141, for use at the Pennsylvania Hospital, which is meant to serve as a guide only. The features of preoperative, operative and postoperative treatment which contribute most to success may be summarized as follows:

1. Coöperation of surgeon and internist.
2. Adequate carbohydrate.
3. Sufficient insulin, given in *frequent doses.*
4. Liberal quantities of fluid.
5. Recognition of special demands of the diabetic.

Every patient operated upon for gangrene should be considered to have coronary artery disease—also, no tourniquet should be used. This practice will reduce the incidence of gangrene of the stump.

Choice of Anesthetic for the Surgical Diabetic.—Spinal anesthesia, when practical, is the anesthesia of choice. Diabetics tolerate nitrous oxide well. Ether may be used in addition for abdominal surgery when complete muscular relaxation is needed. Ethylene and oxygen may be used during an entire operation, particularly if the period of deep anesthesia is short.

For local anesthesia novocaine gives best results. Ethyl chloride and chloroform should never be employed in the diabetic. Avertin behaves like ether and chloroform (Grafe).

Hence its field of usefulness in the diabetic is practically *nil.* My experience with avertin is quite limited. Liver disease should be excluded in every case in which its use is proposed.

PREGNANCY AND DIABETES MELLITUS.

Diabetes is no longer incompatible with pregnancy. It is not a contraindication to pregnancy, nor does it by itself justify therapeutic abortions or the induction of labor. Diabetics conceive less frequently than the normal. The babies tend to be large; polyhydramnios is relatively common; and the frequency of still-births is still too high. This may be corrected as the need of adequate control of the diabetes during gestation is fully recognized. Pregnancy often brings to light the objective signs of diabetes. A true diabetic glycosuria may persist, if allowed to, throughout pregnancy and promptly subside after confinement.

White, Joslin, and others report an economy of insulin during the latter months of gestation. They believe this is due to insulin supplied by the fetal pancreas.

My diabetics, on the contrary, who have become pregnant, have without exception required more insulin to keep the blood sugar normal. The non-insulin diabetic became an insulin diabetic during pregnancy. The need for insulin increased during the first trimester, the period of greatest metabolic readjustment. It remained fairly stationary during the second trimester and increased again during the third trimester, the period of greatest increase in body mass. A prompt fall in the need for insulin has been the rule after delivery. A publication[1] on this subject has recently appeared. For this paper Dr. F. Fetter has reviewed from the literature 78 cases of diabetes and pregnancy in which the changes in insulin were recorded. To these we added 5 cases. Of the total 83 patients, 46 (55.5 per cent) required more insulin during gestation than before or after. In 16

[1] Duncan, G. G., and Fetter, F.: Am. Jour. Med. Sci., **187**, 347, 1934.

(19.3 per cent) instances the insulin need remained essentially unchanged, and in 21 (25.3 per cent) less insulin was required during pregnancy.

Treatment of Diabetes Complicated by Pregnancy.—The coöperation of the accoucheur and the internist is the first essential. Without it two lives are in jeopardy. The usual hygiene and care of the expectant mother should be observed. Outdoor exercise is important, though fatigue should be prevented. A complete analysis of the urine should be made bi-monthly and a record of the regular daily tests for sugar should be presented to the physician at each fortnightly visit. Blood sugar analysis once a month, if the diabetes is of moderate severity, is usually advisable. The danger of ketosis should always be borne in mind.

Diet.—The diet should contain adequate calcium and vitamins. It should be restricted in total calories to prevent undue gain in weight. A restricted diet, during the last six weeks in particular, will go far in preventing a large baby. The carbohydrate should be ample, 1.75 to 2 grams per kilogram of the normal body weight. The protein should not be stinted, 1 to 1.5 grams per kilogram is advisable.

Insulin.—The insulin should be gradually increased, if need be, to prevent hyperglycemia. It does not seem fair to the mother or child to allow hyperglycemia merely to safeguard against insulin reactions. Proper control of the diabetes will attain the same result without a sacrifice of tolerance. Diabetics who do not need insulin in the non-pregnant state are better fortified by its use in small doses while pregnant.

During labor each urine specimen should be examined for sugar and acetone. If the labor is prolonged, carbohydrate in liquid form may be given by mouth, and insulin given in frequent, but small doses. Intravenous glucose (10 per cent solution) may be necessary if liquids are not retained by mouth.

Case Report.— *Diabetes Complicated by Pregnancy.*— Mrs. T. A., aged thirty-eight years, height 63 inches, weight 117 pounds (53 kilograms), had diabetes since 1924. Insulin was begun in April, 1925. The patient gave a history of one previous pregnancy. The baby died at two weeks of age. Except during the first pregnancy, there had been no disturbance in menstruation. Her mother had glycosuria of undetermined cause. The only past illness was scarlet fever in childhood. Her general physical condition was excellent. The pregnancy began in September, 1927. Before this time her daily dosage of insulin was 40 units, at the end of the third month it was 82 units, at the end of the sixth month 82, and at the end of the ninth month 98. Following a normal delivery there were severe insulin reactions and the insulin requirement dropped at once to 44 units. She did not nurse the baby which at birth weighed 9 pounds, 6 ounces.

DIABETES MELLITUS AND HYPERTHYROIDISM.

Hyperthyroidism and diabetes occasionally co-exist. Of the two, thyroid disease usually makes its appearance first.

The effect of thyroid disease on sugar metabolism must be appreciated if an unwarranted diagnosis of diabetes is to be prevented. Mild degrees of hyperglycemia, 0.135 per cent (fasting) to 0.18 per cent (after food), often accompany hyperthyroidism without diabetes. These patients frequently have glycosuria.

Diabetes is made more severe by the presence of hyperthyroidism and insulin is less effective per unit. Conversely, the correction of the thyroid disturbance improves the carbohydrate tolerance and permits a proportionate decrease in the insulin dosage.

DISTURBANCE OF SEXUAL CHARACTERISTICS.

Disturbed or absent menstruation, with early menopause, are frequent in women with untreated diabetes. With control

of the disorder, catamenia is restored in patients under thirty-five years of age. Pregnancy is not common in diabetics as a class, but is especially rare in the severe diabetic requiring much insulin. Abortions and polyhydramnios are relatively frequent.

Properly supported by good treatment, I do not believe there is any need for pregnancy to be a harmful strain on the carbohydrate economy. Neither do I believe that pregnancy should be prevented or interrupted on the grounds that the mother's life is in greater danger than the normal pregnant woman's.

I have found no logical reason why the diabetic mother should not nurse her baby.

The chief sexual disturbance in the male diabetic is impotence. This derangement is rather frequent. Curiously enough this group, in my experience, after receiving insulin experiences a loss of libido. This is not in agreement with Grafe's[1] observations, nor is the fact that I do not recall a single case of impotence corrected by improving the diabetic condition.

INSULIN REFRACTORY AND INSULIN RESISTANT DIABETES.

There is some confusion as to the exact identity of insulin refractory and insulin resistant patients. I prefer to use both terms for purpose of contrast and clarity, labeling as refractory to insulin the patient who shows no response to its use. In contradistinction to this is the insulin resistant diabetic who may require large doses, even several hundred units daily for a short time, but who is definitely benefited by it.

Diabetics unaffected by insulin are rare. Some complication and not a peculiarity of the diabetes is responsible. Gathering facts about such cases from the literature, especi-

[1] Grafe, E.: Diseases of Metabolism and Their Treatment, Philadelphia, Lea & Febiger, p. 335, 1933.

ally from the reviews by Root[1] and by Joslin,[2] we can classify these groups employing the terminology mentioned above with a fair degree of precision.

TABLE 24.—FACTORS DETRACTING FROM THE EFFECTIVENESS OF INSULIN.

Insulin Refractory Group:
1. Progressive destruction of islets of Langerhans
   (*a*) Late hemochromatosis
   (*b*) Invasion of pancreas by neoplasm
2. Certain diseases of liver
   (*a*) Cirrhosis
   (*b*) Unexplained
3. Overwhelming sepsis

Insulin Resistant Group:
1. Ketosis
2. Increased total metabolism
   (*a*) Obesity
   (*b*) High-calorie diet
   (*c*) Fever, infections and toxemias
   (*d*) Pregnancy
3. Skin disorders
   (*a*) "Sunburn"
   (*b*) Reaction to deep Roentgen-ray therapy
   (*c*) Eczema and pruritus
   (*d*) Aseptic skin wounds
4. Allergy
5. Cardiovascular disease
   (*a*) Atheromatous changes in arteries
   (*b*) Myocardial insufficiency with edema and enlarged liver
6. Liver disease
7. Disturbance of other endocrines

Insulin Refractory Group.—1. *Progressive Destruction of the Pancreas.*—Ineffectual insulin therapy has been especially noted in cases of hemochromatosis in which progressive loss of functional island tissue goes hand in hand with the increasing deposits of hemofuscin in the pancreas. Even when all the islands are lost it is difficult to believe that this loss alone should preclude *all* effect from 1680 units in twenty-four hours (Root's case). Surely this exceeds the amount of insulin ordinarily consumed. In cases of hemochromatosis, liver damage may play an important rôle in determining the degree of insulin inefficacy though this is probably not

[1] Root, H. F.: New England Jour. Med., **201**, 201, 1931.
[2] Joslin, E. P.: Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, p. 633, 1928.

so when the island tissue is destroyed by the invasion of malignant growths.

2. *Liver Damage.*—Certain diabetics with cirrhosis of the liver are refractory to insulin. The case reported by Mohler and Goldburgh[1] was not benefited by 1100 units in one day.

3. *Sepsis.*—It is not understood how sepsis may make a diabetic refractory to insulin. It is confusing, also, that some cases of profound sepsis are merely resistant to insulin.

Insulin Resistant Group.—1. *Ketosis.*—During an attack of ketosis the insulin need may be many times that ultimately required to maintain control of the diabetes. Barring other complications, insulin is effective, nevertheless.

2. *Increased Total Metabolism.*—Obesity: It is logical to consider obesity, gain in weight and high calorie diets together. Singly or combined they account for increased need for insulin. If insulin, for purpose of study, is given to a mild diabetic who weighs 120 kilograms and who has a blood sugar of 0.2 per cent, a larger dose will be necessary to depress the blood sugar than in the case of a severe diabetic weighing only 60 kilograms, but with an identical blood sugar. The difference is in the total metabolism which when high greatly reduces the apparent effectiveness of insulin and *vice versa.* This is the secret of controlling the diabetes in overweight patients—by merely reducing their weight the total metabolism is decreased.

One patient, a middle-aged overweight diabetic, presumably belonging to the insulin-resistant class by virtue of an insulin dosage of several hundred units daily, began to have hypoglycemic manifestations following the removal of fat from the diet. The carbohydrate was increased simultaneously. The effectiveness of the insulin was also enhanced by giving frequent small doses.

Fever, infections and toxemias, especially hyperthyroidism,

[1] Mohler, H. K., and Goldburgh, H. L.: Med. Clin. North America, **15**, 343–352, 1932.

all increase the total metabolism and in so doing force increases in insulin.

Pregnancy: All are agreed that the insulin requirement of the pregnant diabetic increases in the first trimester of pregnancy, while in the last three months, judging from the literature, 56 per cent of the cases need additional insulin.[1] My own experience has been that with the diabetics under perfect control all (100 per cent) require larger amounts of insulin in the final trimester.[1]

3. *Skin Disorders.*—The prevalence of "sun burns" and the unfavorable effect they have on the insulin action deserve mention. Skin reactions following deep Roentgen-ray therapy create a similar effect which persists for a fortnight or more. Aseptic wounds affect the insulin adversely. A search for a broken needle in the subcutaneous tissues of a young diabetic nearly doubled the insulin requirement, yet there was not the slightest evidence of infection. Joslin mentions pruritus of old age as having a tendency to neutralize the force of the insulin. This is true too of some cases of eczema and allergic manifestations.

4. *Allergy.*—A small number of patients in whom allergic reactions to insulin have deprived it of much of its therapeutic value have been reported. The frequency of this complication is steadily decreasing with the higher purification of insulin. Minor allergic reactions do not appreciably affect the insulin dosage.

5. *Cardiovascular Disease.*—Marked atheromatous changes in the arteries occasionally account for an apparent depression on insulin activity. Large doses are sometimes needed in this group.

Cardiac insufficiency effects a similar result when edema is prominent, and when the liver is enlarged. Poor absorption of the insulin, plus an unexplained hepatic influence, are probably at fault.

[1] Duncan, G., and Fetter, F.: Am. Jour. Med. Sci., **187**, 347, 1934.

6. *Liver Disease.*—Atrophic cirrhosis of the liver, enlargement of the liver and hepatic insufficiency, with or without icterus, all increase the need for insulin in the diabetic. Advanced atrophic cirrhosis may cause the patient to become refractory to insulin. The part played by the liver in these refractory and resistant to insulin groups is, I believe, significant. The exact relationship is unsolved. Luetic infection causing insulin resistance, which is corrected by anti-syphilitic treatment, acts in all probability through a disturbed liver function.

7. *Disturbance of Other Endocrines.*—The inhibitory neutralizing or antagonistic effect of excessive thyroid, suprarenal and pituitary secretions play the dominant rôle. As in all the resistant group increasing amounts of insulin are necessary, but they are not without effect.

CHAPTER VIII.

THE CLINIC FOR DIABETICS AND WARD ROUTINE.

The outline, *vide infra*, followed in the metabolic clinic "B Service," at the Pennsylvania Hospital is presented to give a general idea of our routine. It is to be remembered that each patient must be individualized, and on no account are the routine measures forced to fit every patient.

It will be noted that the initial carbohydrate allowance is relatively low. Increases are made gradually as the patient's tolerance improves. Non-insulin patients are rarely allowed more than 130 grams at any time and non-complicated insulin patients not more than 150 grams of carbohydrate.

We have found it unnecessary to hospitalize non-complicated diabetics. The alternative has been to request weekly or bi-weekly visits until the diabetes is controlled and the patient is adequately instructed. Others have no doubt shared our experience that out-patient diabetics do well if seen often, while the reverse is true, in general, if six weeks or two months elapse between visits.

Drs. Fetter, Durkin, Fish and I see many of our patients each fortnight. When a patient's home record (urinalyses) is good, and the blood sugar value is normal, he is not requested to have a blood analysis on the succeeding visit. This simple practice has encouraged the patient, improved our results, and reduced the laboratory work.

DIABETIC CLINIC ("B" SERVICE), PENNSYLVANIA HOSPITAL.

1. The patients are admitted to the diabetic clinic through the general medical clinic or referred from the wards.
2. Blood and urine specimens are obtained in the morning. The reports are on hand for the clinic later in the day.

3. Observation diet.

Protein	60 to 80 grams	Adult: 0.6 to 1 gram per kilogram of body weight. Children 1.5 to 3 grams per kilogram of body weight.
Carbohydrate		70 to 90 grams if insulin is not used. 90 to 110 grams if insulin is needed.

Total calories—estimated to reduce the overweight and add to the undernourished (see page 76).

4. The dietitian teaches patients in class and individually:
   (*a*) Diabetes in general and the diet.
   (*b*) Patients not needing insulin, or but 1 dose, are taught household measures. Those requiring 2 or more doses are instructed in weighing their food. Intelligent patients are taught to compute diet charts.
   (*c*) Which specimens the patients should test. Non-insulin patients and those needing 1 dose of insulin are instructed to test the 8 P.M. specimen daily, the patients using 2 or more doses are to test the 7 and 11 A.M., 5 and 9 P.M. specimens and bring a written record of each to the clinic.
5. Nurse instructs patients in:
   (*a*) Care of feet of all over thirty-five.
   (*b*) Insulin administration.
   (*c*) General hygiene.
6. Instructions for subsequent visits.
   (*a*) "Insulin patients" *do not delay* insulin and breakfast on account of the blood test (see page 45).
   (*b*) Non-insulin patients are to have fasting blood sugars until these are normal, after which the tests may be taken after breakfast.

On all subsequent visits, the patient is seen first by the dietitian who estimates and records the diet actually taken

by the patient. After seeing the physician the patient returns to the dietitian for instructions which may be made necessary by changes in diet.

Patients referred from Dr. McCrae's ward service, in addition to being standardized, are instructed by the Outpatient Department nurse and dietitian before they leave the ward.

Benedict's test for glycosuria is used. Thirty drops of this solution, and 4 drops of urine, are used instead of the usual teaspoonful and 8 drops respectively.

Insulin equipment and testing apparatus are available. Patients may obtain food scales by paying a nominal weekly rental to the hospital for same.

ROUTINE MANAGEMENT OF NON-COMPLICATED DIABETES ON ADMISSION TO THE WARD.

1. *Initial Observation Diet.*

   Protein $\frac{2}{3}$ to 1 gram per kilogram of body weight.
   (Children 1.5 to 3 grams per kilogram.)

   Carbohydrate 70 to 90 grams if insulin is probably not needed.
   90 to 110 grams if insulin is obviously necessary.

   Total calories 35 Calories per kilogram if patient is emaciated.
   25 Calories per kilogram if patient is normal weight.
   15 Calories per kilogram if patient is obese.

   Individual characteristics will indicate appropriate changes during hospitalization. The permanent diet should contain 1 to 1.5 grams protein per kilogram. Of this two-thirds should be animal protein.

2. *Insulin.*

   Underweight adults and children usually need insulin while those who are overweight do not.

When insulin is decided upon, the following *rough guide* may be followed:

(*a*) If the fasting blood sugar is between 180 and 220 milligrams 12 units are given once daily, twenty minutes to one-half hour before breakfast.

(*b*) If blood sugar is 200 to 260 milligrams, 12 units are given before breakfast and 8 units before supper.

(*c*) If blood sugar is above 260 milligrams, 12 units are given before breakfast, 5 units before lunch, and 8 units before supper.

While glycosuria persists in any of the fractional tests, 2 or 3 units of insulin are added daily to each corresponding dose which preceded the appearance of glycosuria on the previous day.

3. *Analyses.*

(*a*) The fasting blood sugar is taken on admission, and repeated every four days unless otherwise indicated.

(*b*) Daily twenty-four-hour urine collections are made for routine examinations and quantitative sugar estimation.

Fractional specimens for qualitative sugar examination:

I. From non-insulin patients, and those taking only 1 dose of insulin, the 8 P.M. specimen is collected.

II. From patients taking 2 or more doses of insulin, 7 A.M., 11 A.M., 4 P.M., and 9 P.M. specimens are collected, and tested for sugar.

4. *Instruction of Patient.*

The dietitian and nurse who instruct the diabetics should be notified as soon as the patient may receive instructions. One week's teaching is usually desirable. No diabetic is to be discharged until he, or a relative, is familiar with:

(*a*) Measuring or weighing the diet as the case may demand.

(*b*) How to test the urine and which specimens to test. (See Out-patient Department Outline, page 135.)

(*c*) Insulin administration (when necessary).

(*d*) General hygiene.

(*e*) Special hygiene—care of the feet.

5. *Discharge of Patient.*

I. The patient is given a written record of his diet, insulin dosage and distribution, and an appointment for the next "B" Service Metabolic Clinic (except when he is being referred directly to his family physician, in which case no appointment need be made).

II. The patient, on discharge, must be equipped to test the urine for sugar, to give insulin (if needed) and weigh the diet when necessary.

TREATMENT OF DIABETIC COMA.

1. Urine (catheterized specimen if necessary) is examined for sugar and acetone.
2. Blood (15 cc.) is taken for: (1) acetone; (2) sugar; (3) CO_2 combining power; (4) urea determination.
3. When the clinical diagnosis is verified by glycosuria, plasma acetone, and a high blood sugar, insulin is given at once followed by glucose.

   Initial insulin dosage, 40 units subcutaneously and 20 units intravenously.

   Glucose, 60 grams. This may be given in part by mouth and the remainder or all in a 10 per cent solution (warm) intravenously, slowly.
4. One-half hour after the initial dose of insulin, 30 units of insulin are given subcutaneously.
5. One hour after initial dose of insulin, 30 units of insulin

are given subcutaneously, and 30 grams glucose intravenously, or by mouth or nasal tube.

6. One and a half hours after first dose, 20 units of insulin may be given without glucose. The treatment of impending coma may be begun at this point and carried out as outlined below.
7. Thereafter at two-hourly intervals *until the plasma is free from acetone:*
   (*a*) 20 units of insulin and 10 grams carbohydrate are given while heavy glycosuria persists.
   (*b*) 10 units of insulin and 10 grams carbohydrate, if glycosuria gives only a moderate reaction.
   (*c*) A dose of insulin and glucose are eliminated if a *mild* reaction for glycosuria.
   (*d*) 10 grams of carbohydrate are given and a dose of insulin omitted if the urine is sugar-free.
8. When the plasma is free from acetone, the insulin is reduced to a *safe level.* It is given in 4 doses (such as 14, 8, 12 and 5 units). Subsequent increases are then made as indicated by fractional urine tests. Ten grams of carbohydrate are given in conjunction with the midnight dose. Liberal carbohydrate (150 grams daily) is allowed for at least forty-eight hours after the disappearance of the plasma acetone.

NOTE: When more radical treatment seems indicated, the physician on service is consulted.

Additional Measures:

Liquids.—If fluids are retained by mouth, 200 cc. or more are given every hour—hot bouillon (Steero or Oxo cubes, or 2 teaspoonsful of salt in 1 quart of broth are excellent), tea, coffee, lemonade, orangeade and oatmeal gruel.

If fluids are not readily retained and dehydration is considerable, 1 liter of normal saline (warm) is given by hypodermoclysis, and repeated if necessary in four hours.

Warmth.—Blankets, hot-water bottles, and hot liquids employed. Warmth is important.

Gastric Lavage.—If the patient complains of abdominal pain, or if vomiting continues after giving ½ dram sodium chloride and ½ dram bicarbonate of soda by mouth, the stomach is washed with normal saline. Eight ounces of the solution are left in the stomach.

Enema.—A soap water enema is given.

Stimulation.—For cardiac stimulation, caffeine sodium benzoate, grains v. q. 3 h., is given when indicated.

NOTE.—Blood (10 cc.) is taken for sugar and acetone analyses every two hours until the patient is out of immediate danger.

Bedside test for plasma acetone (Rothera-Wishart).

Two drops of plasma are placed in a Wassermann tube and supersaturated with ammonium sulphate crystals and shaken. Two drops of approximately 5 per cent sodium nitroprusside solution are added and shaken. Two drops of ammonia water are added and shaken.

Permanganate color	=	trace of plasma acetone:
Light blue	=	moderate.
Deep blue or almost black	=	heavy reaction for plasma acetone.

DIABETES MELLITUS WITH OTHER COMPLICATIONS.

1. Diet in the presence of fever. (Liquid or soft.)
   Protein, 1 gram per kilogram of body weight.
   (Children, 1 to 2.5 grams per kilogram.)
   Carbohydrate, 2 grams per kilogram.
   Total Calories, 20 to 30 per kilogram.
2. Insulin—*Insulin is always given to the febrile diabetic* and increases are guided by fractional analyses.
   If the blood sugar (fasting) is between 180 and 220 milligrams:
   12 units are given before breakfast, and
   10 units are given before supper.

If blood sugar is above 220 milligrams 3 doses are given:

12 units in A.M.

5 units at noon.

8 units at night.

A small dose, about 5 units, is often necessary at midnight along with 10 grams of carbohydrate. Appropriate increases are based on the fractional urinalyses.

During acute infections I advocate the equal division of the diet and insulin into 5 or 6 meals and doses, respectively, distributed at equal intervals throughout the twenty-four hours. For example see surgical case, page 101.

3. Tests.

Blood sugar estimations are made daily unless otherwise indicated.

Fractional urine tests.

Twenty-four-hour urine collections for quantitative studies.

THE SURGICAL DIABETIC.

1. *Preparation for Operation (Major):*

(*a*) When immediate operation is not imperative:

1. For three days preceding operation the following diet is given:

Protein $\frac{2}{3}$ to 1 gram per kilogram.

Carbohydrate 2 grams per kilogram.

Total calories 25 per kilogram.

2. Insulin—regulated as in the diabetic with fever (see page 140).

3. Daily blood sugar, twenty-four hour and fractional urinalyses.

(*b*) Day of operation.

1. Three hours before time set for operation, the usual carbohydrate content of 1 meal is given in liquid form, preceded by the usual dose of insulin. (If feeding is undesirable, give 200 cc. of a 10 per cent solution intravenously.)
2. An enema is given.
3. Immediately before operation, 10 units of insulin are given to thin patients and 15 units to the well nourished.
4. Immediately after operation, 200 cc. of a 10 per cent solution of glucose are given intravenously, slowly.
5. On return to the ward, 10 units of insulin are given to thin and 15 units to the well nourished patient.
6. Two hours after return to the ward, blood is taken for sugar, acetone, and CO_2 combining power estimations.
7. Fluids are given freely by enteroclysis, hypodermoclysis, and by mouth when permissible.
8. When regular feedings are permissible the diet (liquid) and insulin are equally divided and distributed as illustrated on pages 101 and 102.

2. *Emergency Operations on Diabetics.* — These patients are dealt with exactly as the impending coma patient, page 139. The postoperative treatment is no different from those for which the time of operation can be planned several days in advance (see p. 102).

Diabetics with a CO_2 combining power below 35 volumes per cent or with a heavy reaction for plasma acetone and diacetic acid are not allowed to undergo major surgical operations. The operation is delayed two to four hours while preparations for operation are made by treating similarly to a patient in impending coma.

CHAPTER IX.

LABORATORY METHODS.

Benedict's Qualitative Test for Glucose in the Urine.[1]— The technique of this test is described on page 70. The reagent and its preparation are as follows:

	Gm. or cc.
Copper sulphate (pure crystallized) . .	17.3
Sodium or potassium citrate	173.0
Sodium carbonate (crystallized) . . .	200.0
Distilled water to make	1000.0

"The citrate and carbonate are dissolved together (with the aid of heat) in about 700 cc. of water. The mixture is then poured (through a filter if necessary) into a large beaker or casserole. The copper sulphate (which should be dissolved separately in about 100 cc. of water) is then poured slowly into the first solution, with constant stirring. The mixture is then cooled and diluted to 1 liter.

"This reagent is about 10 times as sensitive to sugar in the urine as is Fehling's or Haines' solution, and unlike these latter solutions is not appreciably reduced by creatinin, uric acid, chloroform or the simple aldehydes. The mixture may be kept indefinitely in uncolored glass or cork-stoppered bottles."

Benedict's Quantitative Titration for Glucose in the Urine.[2]— "Sugar estimations are conducted as follows: The urine, 10 cc. of which should be diluted with water to 100 cc. (unless the sugar content is believed to be low), is poured into a 50 cc. burette up to the zero mark. Twenty-five cc. of the reagent (see below) are measured with a pipette into a porcelain evaporation dish (25 to 40 cm. in diameter), 10 to 20 grams of crystallized sodium carbonate (or one-half the weight of the anhydrous salt) are added, together with a small quantity of powdered pumice stone or talcum, and

[1] Benedict, S. R.: Jour. Am. Med. Assn., **57**, 1193, 1911.
[2] Idem: Ibid.

the mixture heated to boiling over a free flame until the carbonate has entirely dissolved. The diluted urine is now run in from the burette rather rapidly until a chalk-white precipitate forms and the blue color of the mixture begins to lessen perceptibly, after which the solution from the burette must be run in a few drops at a time, until the disappearance of the last trace of blue color, which marks the end-point. The solution must be kept vigorously boiling throughout the entire titration. If the mixture becomes too concentrated during the process, water may be added from time to time to replace the volume lost by evaporation. The calculation of the percentage of sugar in the original sample of urine is very simple. The 25 cc. of copper solution are reduced by exactly 50 milligrams of glucose. Therefore the volume run out of the burette to effect the reduction contained 50 milligrams of the sugar. When the urine is diluted 1 to 10, as in the usual titration of diabetic urines, the formula for calculating the percentage of sugar is the following: $\frac{X}{0.050} \times 1000 =$ per cent in original sample, wherein X is the number of cubic centimeters of the diluted urine required to reduce 25 cc. of the copper solution.

Reagent.

	Gm. or cc.
Copper sulphate (pure crystallized) . .	18.0
Sodium carbonate (crystallized)[1] . . .	200.0
Sodium or potassium citrate	200.0
Potassium sulphocyanate	125.0
Five per cent potassium ferrocyanide solution	5.0
Distilled water to make a total volume of	1000.0

[1] One-half the weight of the anhydrous salt may be used. With the aid of heat, dissolve the carbonate, citrate and sulphocyanate in enough water to make about 800 cc. of the mixture, and filter if necessary. Dissolve the copper sulphate separately in about 100 cc. of water and pour the solution slowly into the other liquid, with constant stirring. Add the ferrocyanid solution, cool and dilute to exactly 1 liter; of the various constituents, the copper salt only need be weighed with exactness. Twenty-five cc. of the reagent are reduced by 50 mg. of glucose.

Rothera Test for Aceto-acetic Acid and Acetone.[1]—"Take a little urine in a test-tube and add a large excess of ammonium sulphate crystals; add a few drops of fresh 5 per cent sodium nitroprusside solution, and finally a few drops of ammonia water. Through all these steps the tube should be shaken to maintain full saturation with ammonium sulphate, and some crystals should still remain in the bottom at the end of the process. A positive reaction consists in a permanganate color, ranging from the palest perceptible tint to almost black. It is necessary to wait almost five minutes to make sure that the maximum intensity of color is developed. Quantitative judgment is based upon the quickness with which the color develops as well as its intensity. For economy, when numerous tests are performed, it is satisfactory to use only 2 or 3 drops of urine in the smallest size test-tube (so called Wassermann tubes) and add 1 or 2 drops of nitroprusside solution and 1 or 2 drops of ammonia. A fresh nitroprusside solution means one possessing its original red color, which is lost on standing; this change is slower in a dark and cool place, and the solution may be kept for some days. Though this reaction is given by acetone, it is so much more sensitive to aceto-acetic acid, and the latter so predominates over acetone in fresh urine, that the test should properly be regarded as one for aceto-acetic acid. It is valuable as being the most delicate indication of ketosis and one purpose in treatment is therefore to keep this reaction continuously negative. As it is sensitive to 1 part of aceto-acetic acid in 20,000, while ferric chloride reacts only to about 1 part in 8000 and in urine is often indistinct in its fainter degrees, comparison of the two tests is useful. If the nitroprusside reaction is heavy, and the ferric chloride negative or faint, there is only slight ketonuria."

This test was applied to the blood plasma by Mary B. Wishart. The reliability of the test and the expediency with

[1] Allen, F. M.: Diabetes Mellitus, in Nelson's Loose-Leaf Medicine, **4**, 77, 1920. (Out of print.)

which it may be executed, as well as the lack of an intricate apparatus, places in the hands of the practitioner an excellent means of following the progress of the acidotic patient.

A detailed discussion of blood analyses required in the every-day treatment of diabetes is beyond the scope of this book. Benedict's recent quantitative test for blood sugar and Van Slyke's method of determining the CO_2 combining power of the blood plasma are advocated.

The blood specimen may be taken from any convenient vein, usually the median basilic. Six cubic centimeters are sufficient for a sugar analysis, 10 cc. when a CO_2 combining power determination is also requested, and 15 cc. when a more complete chemistry (sugar, acetone, CO_2 combining power, cholesterol and urea) is desired.

A minute quantity of potassium oxalate thoroughly mixed with the blood will prevent clotting. One drop of commercial formalin (40 per cent) solution added to each 5 cc. of blood will preserve the specimen for at least two days.

Blood specimens obtained for the purpose of determining the CO_2 combining power are aspirated into a centrifuge tube which contains a little powdered potassium oxalate and some paraffin oil. The tube is subjected to a minimum of agitation. Immediate examination is essential.

PART II.

OBESITY.

CHAPTER X.

INTRODUCTION.

Life is, in few instances and at rare intervals, the diapason of a heavenly melody; oftenest the fierce jar of disruption and convulsions, which, do what we will, there is no disregarding. —Carlyle.

It has been estimated that one-fifth of the American people are overweight.

The coöperation of the public with the medical profession in stamping out infectious diseases is in striking contrast to their toleration of this cause of physical impairment and suffering. If this national handicap was prevented as successfully as typhoid fever, smallpox, and diphtheria—as indeed it can be—the prolongation of life resulting would surpass in importance any scientific triumph in the field of medicine in recent years. The economic gain would be incalculable.

The means already exist for preventing and abolishing obesity in general. When people choose to apply these means thoroughly, a new epoch of preventive medicine will have begun. Until then, obesity will continue to exist. It will continue to be an impediment to active vigorous life and a threat to health and longevity.

Definition.—Obesity is an abnormal state. It is a metabolic imbalance; a derangement characterized by overweight due to excessive deposits of fat throughout the body. The sur-

plus fat for which the body has no immediate use is thus stored.

The terms obesity, adiposity and corpulency are synonymous. Overweight infers obesity but it may, in fact, be due to other causes, notably accumulation of fluids in the tissues or in the serous cavities.

Fat in moderate amounts is a normal equipment of every individual. It is potential food utilized if the needs of the body are not sufficiently supplied by the food intake. Partial starvation, sickness and increased physical exercise cause withdrawals from the stored fat. On the other hand, when the withdrawals are few and light and the additions are many, obesity is likely to develop. The normal regulatory influence of appetite, the satiety effect of food and exercise on the food intake, and the increased oxidative effect of excess food regulate body weight with a striking degree of accuracy. Were it not so, obesity would be more prevalent. We know that the body weight may not vary more than a trifle for many years without any conscious effort on the part of the patient. If the activities are reduced the appetite is proportionately less. The anorexia of confinement is well known. It is a part of the perfect regulation or defense mechanism which keeps the patient in equilibrium and prevents the laying on of fat. It is when the appetite increases, or the energy expenditure decreases without the proper regulation of the opposing function, that the automatic mechanism fails to keep the weight constant. It may be that, before the increased oxidative processes resulting from overnutrition of one day have subsided, those of the succeeding day are superimposed and lead to an accumulation of nourishment and eventually to obesity. (Grafe.)

Bernhardt[1] observed that increases in the metabolic rate in the obese are followed by periods of depressed metabolism, resulting in the annulment or neutralization of the influence

[1] Bernhardt, F. R.: Ergebn. d. inn. Med., Berlin, Julius Springer, **36**, 1, 1929.

of exercise on the metabolic rate. These observations lack confirmation in this country.

The degree of obesity is usually calculated by comparing the actual weight with that of the normal average or so-called standard weight. The ideal weight may differ from the normal average weight, the computation of which included large and small individuals as well as those with well developed and those with poorly developed bones and musculature. Gouty persons, diabetics and patients with heart disease and other afflictions have not figured especially in the preparation of these averages. Frequently, we are called upon to calculate the approximate ideal weight for persons in ill health. If one is aware of the malady with which the patient is affected, a glance at his physical make-up will give information of more value than that which can be gained by consulting a table of average weights. For purposes of illustration, the adult diabetic should weigh less than the usually accepted average weight. The same is true of the person with gout and the patient with chronic heart disease, while the tuberculous and nervous individuals do better with their weight a trifle above the normal average.

In isolated cases, poor health may be precipitated by reducing the athletic type or the elderly patient to conform with the normal average. These remarks should not be misconstrued as a license for anyone to remain obese. Obesity, after all, is a relative affair.

Normal average weights, charts of which appear in the appendix, are rough guides at best. They are intended as such only and are not to be adhered to rigidly. *The average weight is not always the best weight.* The fact that the normal average weights tend to increase each decade after thirty years of age is not proof that this is best for one's health. The hazards of life are better withstood and life expectancy is increased when the body weight is a trifle above the normal average before thirty and a trifle below after thirty-five years of age.

Types of Obesity.—Obesity may be conveniently classified into two groups: (*a*) simple or exogenous; and (*b*) endocrinal or endogenous obesity, in which some irregularity in the glands of internal secretions predominate.

When obesity is spoken of without designating the particular type, simple obesity is inferred. It is by far the more common form of overweight.

It is not rare to see apparent combinations of simple and endogenous obesities. Some believe that endogenous obesity is sometimes an outcome of simple obesity.

CHAPTER XI.

SIMPLE OBESITY. (EXOGENOUS.)

Simple obesity, also referred to as alimentary or indolence obesity, is prevalent. The overweight accrues from sheer excess food, too little exercise, or both. There is, in effect, a positive energy balance. Too often obesity denotes self-indulgence, indolence and lack of determination of purpose. It is at first thought difficult to picture a fat person adhering to a reducing diet when he has already allowed obesity to develop. It is frequently true, nevertheless, that overweight results from an ignorance of food properties and that its correction, though desired, is denied for the same reason. Small, imperceptible but habitual excesses in diet have a profound influence on body weight.

Simple obesity is curable. The pitfalls to which it predisposes are avoidable in the early stages. Readjustment of certain habits of living will bring about the desired decrease in weight. Prolonged and increasing insults to the vital organs, on the other hand, will cause irremediable damage.

THE ETIOLOGY OF SIMPLE OBESITY.

Predisposing Causes.—The most prominent influences which predispose to obesity are heredity, age, sex, race, occupation, illness, temperament, and general habits.

Heredity.—Heredity was traceable in 60.7 per cent of Anders[1] obese patients and 88 per cent of Bauer's. Inherited peculiarities of the digestive and assimilative powers are, it is believed, responsible rather than inherited habits and customs. The inherited tendency to obesity is more common

[1] Anders, J. M.: Osler's Modern Medicine, Philadelphia, Lea & Febiger, **3**, 209, 1926.

in the female. It usually manifests itself early, though, lacking an exciting cause, it may not do so until middle life. A greater degree of overweight may be carried with impunity if due to hereditary predisposition and not only to habits of living.

Age.—In childhood simple obesity is rare. It is uncommon, too, in early adult life. The tendency to gain in weight in an abnormal fashion becomes manifest when the fourth decade is reached. This is due, in part, to changes in habits. At this age, financial independence is usually greatest, and it is probably the period of greatest contentment. In consequence, physical activity is curtailed and new luxuries are indulged in.

Children of the well-to-do might be expected to be overweight. As a rule, this is not the case. Children have a delicately balanced relationship between hunger, body weight, and energy expenditure. When a child eats poorly the exercise is automatically reduced to prevent loss in weight. On the other hand, a large food intake is counteracted by increased physical activity.

The precision of this balance is lost in the adult over forty years of age, who tends to become obese. This loss is due largely to inherited influences and to repeated violations of the laws of nutrition. The habits of living may, singly or in combination with the direct causes of obesity, develop a vicious circle of overeating, gain in weight, disinclination to exercise, lack of exercise, inability to exercise, persistent increase in the fat deposits, and complications. Each additional degree of obesity, in one sense, predisposes to further gain until the individual becomes enormous or until treatment is begun. It seems that once having lost the governor or natural balance between the appetite and nutritional need it can never be fully restored; *i. e.*, the fat person who reduces successfully cannot rely on his appetite to dictate nutritional needs only. Continued restraint is essential if the return of the habit of overeating is to be avoided.

Race.—Obesity is common among certain races, notably Hebrews, southern Italians, Orientals, and certain African races. In the case of the Hebrews, this appears to be a true racial characteristic, while in certain other races obesity is deliberately cultivated. Geographical characteristics influence the habits of man and in this fashion play a part in causing overweight. Warm climates encourage while cold climates discourage obesity.

Sex.—Obesity is more common in the female than in the male. This may be due to less exercise, indulgence in sweets, and a poorer oxidation of carbohydrate. Women, for the most part, become obese after forty-five years of age. This may follow changes in endocrinal function. As children mature and assume responsibilities of the home, the mother, relieved of these duties, promptly gains in weight. Obesity is more prevalent among mothers of large families than among women with no children.

It is sometimes difficult to differentiate between the obesity which develops in women at or after the menopause due to endocrinal influence—ovarian rest—and the true simple obesity. There may be a changed, a slower physical reaction to stimuli at this age independent of ovarian function. It seems quite possible that this is an age or wear-and-tear influence on the mechanism which has to do with the appetite and exercise equilibrium and its effect on the regulation of body weight.

Occupation.—Sedentary occupations predispose to obesity. This tendency is exaggerated in the placid, slow moving, phlegmatic, indolent, unemotional person with a calm demeanor. It is least marked or absent among the alert, physically active and nervous individuals. Representatives of these two groups can be observed in any public conveyance or gathering. The former economizes at every turn and objectives are reached with the least exertion. The latter do not stand or sit quietly—they are keenly alive and sus-

ceptible to external stimuli about them. They move with vigor and animation.

Enforced idleness—from sickness and accidents—often accounts for the development of corpulency. In the young person the overweight is readily lost when the normal occupational status is restored.

General habits play an important part in causing obesity. The person who rises late each morning, who partakes of large and frequent meals, who does not masticate his food thoroughly, who has frequent rest periods in the day, who economizes on energy expenditure, who takes liquid nourishment to promote sleep or to obtain relief from digestive disturbances, or in the attempt by this means to strengthen himself physically, and to overcome the stupefying effects of overweight, who wears too much clothing and who has developed other habits which characterize indolence, is likely to join in the ranks of the obese.

Exciting Causes.—The exciting cause of simple obesity is the persistent ingestion of food in excess of the requirement to maintain a constant, normal weight. To the person predisposed to obesity, a dietary excess of as little as 100 or 200 Calories daily will gradually exert its influence. In the final analysis the total caloric value of the diet is responsible for increasing the deposits of fat.

To deal with obesity Dr. Burgess Gordon has advocated restriction of the higher starchy foods, substituting dextrose, with little, if any, reduction in the total calories. The dextrose is given between meals, preferably while the patient is exercising. The apparent success of this plan of treatment suggests that carbohydrate in starchy form becomes largely available for storage and not for combustion. I am not prepared to say that the slow release and prolonged absorption of monosaccharides derived from starches enhance storage while the rapid absorption of dextrose taken as such encourages prompt combustion, but, if the experiments under way confirm Gordon's clinical observations, we shall

be obliged to recognize additional influences which isocaloric diets may exert on body weight.

THE NATURE AND PATHOLOGY OF SIMPLE OBESITY.

In obese persons deposits of fat, far in excess of the normal, are stored throughout the body. They represent dietary surfeit beyond the physiological need. These deposits are derived from the fat, the carbohydrate, and the protein of the diet. The fat foods of the diet are absorbed as fatty acids, which are resynthesized to fat. The excess fat is stored, not consumed. Carbohydrate foods, absorbed as simple sugars (monosaccharides), replenish the glycogen stores and when a surplus exists they are changed to and stored as fat. The fattening of cattle and hogs on carbohydrate foods exemplify this metabolic transformation as do the people who have grown obese through excess sweets and starchy foods. Protein adds least to the fat stores. It is calculated that 58 per cent of the protein is utilizable as carbohydrate. As such it may contribute to the fat accumulation. The specific dynamic action of protein is less pronounced in overweight than in normal persons.[1,2]

Obesity, in the early stages, is an accentuation of normal physiological processes. The subcutaneous fatty deposits are multiplied. The abdominal girth is increased by fat in the abdominal wall and by accumulation of fat in the omentum.

The heart becomes overlaid with fat resulting in increased work and embarrassed function. There is marked accumulation of fat along the course of the arteries of the heart. Fat is also deposited about the kidneys and lungs and in the liver. The distribution of fat characteristic of the different types of obesity is dealt with elsewhere.

True fatty infiltration of the heart, kidneys and lungs eventually ensues if not prevented by appropriate treatment.

[1] Rolly, F.: Deutsch. med. Wchnschr., **47**, 887, 1921.
[2] Wang, C., *et al.*: Arch. Int. Med., **34**, 573, 1924.

THE SYMPTOMS OF SIMPLE OBESITY.

The person possessing a mild degree of adiposity is free from symptoms, though the inherent tendency to gain in weight has been created. Shortly, as the omental fat increases, a sense of fullness about the abdomen is noticed, especially after meals. The sensation of being burdened ensues and shortly there is dyspnea following exertion. Physical ability is reduced, fatigue is prominent and, in consequence, exercise is reduced. A more rapid gain in weight follows. Once obesity is established to a marked degree, the patient is upon the threshold of the complications which his condition tends to create.

Anders describes the plethoric and anemic forms of obesity. In the former, the blood may reveal a red cell count above 6,000,000. Better health is enjoyed for a longer period by this group than those of the anemic class.

In the anemic group, composed largely of women, exhaustion, shortness of breath, and cardiac palpitation are prominent symptoms. They are due not only to embarrassment of the heart and other organs, by unusual deposits of fat, but to the anemia. The hemoglobin averages about 70 per cent, though much lower percentages are obtained. The red cell count is low, as is the color index.

In addition to the symptoms already mentioned, the following are frequent: excessive perspiration, irritation of the skin (intertrigo), eczema, furuncles, joint discomforts, neuritis, swelling of the ankles, dysmenorrhea, amenorrhea, sterility, poor resistance to infections, constipation, visceroptosis, night attacks of difficult breathing and coughing, decreased urine output and finally dropsy.

THE RECOGNITION OF SIMPLE OBESITY.

Obesity in its pronounced stages is recognized at a glance. Simple or alimentary obesity is readily identified though it may complicate other forms of overweight. The etiological

identification is rendered difficult when disturbances in the glands of internal secretion change the individual's habits and mode of living in such a way that simple obesity is added to the overweight of endocrinal origin.

The physical signs presented by an obese patient may indicate any degree from the slightest overweight to the most advanced with its ever present complications. Many of the objective signs have been referred to already. They will bear repetition. The patient appears overweight. The facial features have become coarse. Many of the body surfaces have a rounded contour. The bony prominences are obscured. The cheeks are round, the dimples deep and the customary facial lineaments are lost. The eyelids are partially closed. The double chin is present and the neck is massive. The skin is moist, soft, smooth and, in some cases, the face appears congested. The mucous membranes present a rosy hue but when cyanosed reveal an unsatisfactory state of the circulatory system. The chest wall may be tremendously thickened. The breasts in both sexes are enlarged by fat deposits.

The breath sounds on auscultation are often distant, particularly in the apices. Fat is a poor conductor of sound. Heckel has described a "basitis" as a clinical sign of hepatico-omental obesity. It has been interpreted as a forerunner of generalized obesity. On careful auscultation, it is recognized by finding a patch of fine crepitant râles at the base of one lung, most frequently the right. The râles are best heard at the end of inspiration.

The cardiac impulse may not be obtained on inspection and palpation, and the heart borders are determined with difficulty. The area of dullness is increased, due to muscle hypertrophy and to pericardial accumulations of adipose tissue. The heart sounds are distant.

As the condition becomes extreme evidences of myocardial weakness are more pronounced. The blood-pressure may fall and edema become prominent. A falling blood-pressure

without treatment points to a failing heart muscle. It is, however, a common and gratifying sign when correction of an arterial hypertension accompanies an otherwise satisfactory response to judicious treatment.

Abdominal prominence is one of the first signs of overweight. There may be a slight thickening of the wall, a moderate degree of rotundity, or a pendulous mass of fat. The usual physical landmarks are distorted. Striæ may be present. The shifting of the omentum laden with fat may deceive one who is not on the alert into believing that fluid is present.

The legs become cylindrical. Varicosities are common and edema, visible or invisible, is present in all cases of established obesity.

Albuminuria, attributable to passive congestion, is found frequently. It clears up readily with proper treatment of the obesity.

THE PROGNOSIS OF SIMPLE OBESITY.

In summarizing the outlook for the obese person: the willingness and sustained effort with which the patient coöperates during the course of treatment are important considerations. A person unwilling to reduce will not be reduced, neither does willingness achieve success without determined and continued effort. A slave to habit and taste has little chance of being restored to normal.

A cure of the obesity is possible in the great majority of instances. Obesity of long standing and of severe degree offers more obstacles than do mild degrees of short duration. The former may be cured yet irreparable damage may have occurred in which case the prevailing complications in the individual case determine the outcome.

Untreated obesity, no matter of what type, exacts a penalty. It is a physical burden. It exhausts physiological reserves and exposes its possessor to organic diseases and

infective processes. It shortens life and adds misery to this shortened existence. Fig. 7 illustrates the bearing which obesity has on mortality. It represents the experience of 34 insurance companies. The lowest point reached by each curve represents the best weight for the respective age groups.

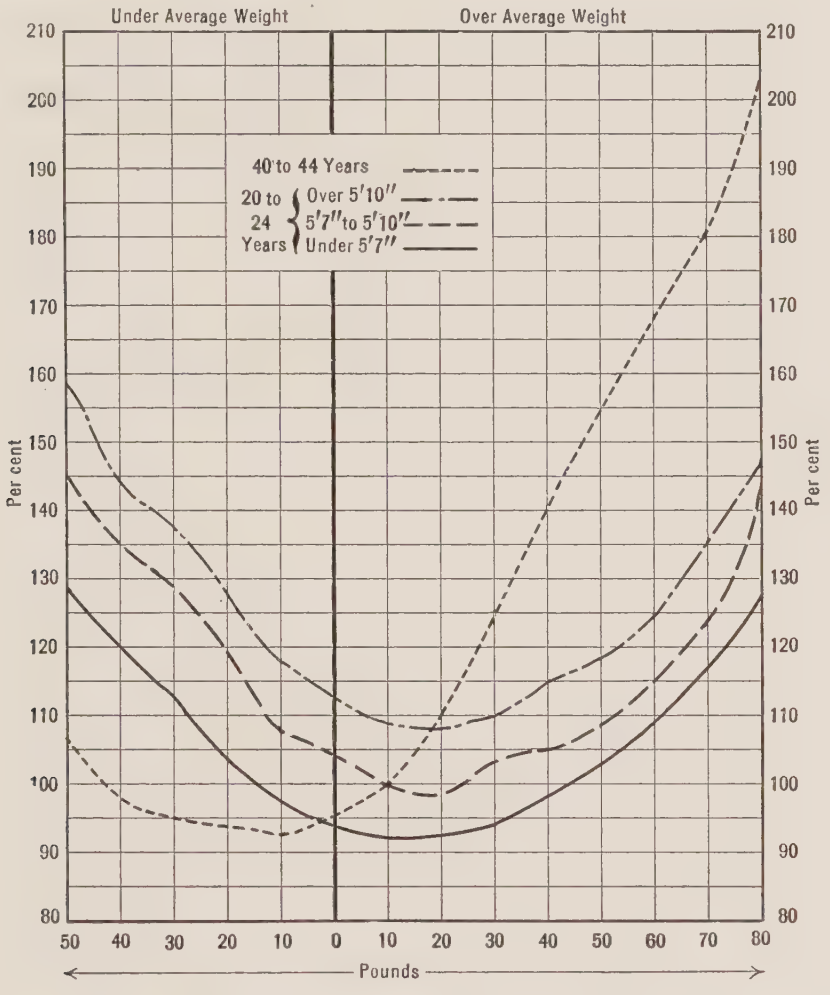

FIG. 7.—Mortality according to height and weight.[1]

COMPLICATIONS OF SIMPLE OBESITY.

The complications of this disease result from mechanical embarrassment, infiltrative and degenerative changes and functional overstrain.

[1] Medico-actuarial Mortality Investigation, vol. 2, 1913.

Foremost of the complications are diseases of the circulatory system. Myocardial decompensation with its many signs is predominant. The progressive changes in the arteries leading to arteriosclerosis and angina pectoris follow closely in frequency. The death-rate from diseases of the arteries in the extreme overweights is nearly 4 times that in the underweights.

High blood-pressure, or the ominous falling blood-pressure, cerebral hemorrhage and anasarca are complications of considerable frequency.

Diabetes and less frequently nephritis and gout are, from the metabolic standpoint, the prominent complications. Diabetes develops from 10 to 20 times more frequently in fat people than in those of normal weight. It is more prevalent among the obese who are subject to gall-bladder disease. The relationship between these three disorders—obesity, gall-bladder disease and diabetes—has been dealt with already.

Whether or not obesity upsets the harmony between the various endocrinal glands is not certain. There are instances in which characteristics of endocrinal disturbances promptly disappear as the result of treatment directed to correct simple obesity. That this is due to restored harmony between the endocrines appears probable.

Obesity influences unfavorably the prognosis in the case of acute infections and surgical operations.

The fat-laden great omentum, besides interfering with the free play of the diaphragm, predisposes to visceroptosis and intestinal stasis, and hemorrhoids.

Among other, probably less serious but nevertheless common complications, there are: skin infections, especially boils and carbuncles, eczema, varicosities, herniæ, neuritis and joint disorders.

CHAPTER XII.

THE PREVENTION AND TREATMENT OF SIMPLE OBESITY.

THE PREVENTION OF SIMPLE OBESITY.

To prevent obesity I know of no better practice than that of receiving and acting upon the results of a carefully conducted physical examination and medical advice once each year. The weight curve will attract attention and other signs of relative or absolute overweight will be identified during the early insidious symptom-free stage. It is then that very slight changes in diet or exercise will be most effective in retrieving the patient from the pathological path. Symptoms having once developed, obesity is not alone. The integrity of the perfect functioning parts of the body, hitherto unheeded, is at stake.

Regularity of good habits—regular and adequate daily exercise, moderation in eating, bathing, prevention of undue fatigue (exhaustion distorts tastes and is a forerunner to pernicious habits of eating) and the prevention of imprudence in drinking—will go far in warding off obesity. Anemia, when present, should be corrected.

Individual study, while always desirable, is most important in those patients to whom obesity would be a special peril. The person with gout, with diabetes or with chronic heart disease, should retain his or her leanness, if necessary, at the cost of treatment similar in principle to that employed for the correction of mild degrees of obesity. This is true, too, of persons predisposed to obesity by heredity. Sustained effort and self-denial are conditions precedent to success. When the new mode of living becomes the habit and custom of the individual most of the difficulties disappear.

THE TREATMENT OF SIMPLE OBESITY.

The Selection of Patients Who Should Reduce.—The urgency of treatment will depend on the type, the degree of obesity, the age of the patient and complications. To many, a failure to reduce means a sacrifice of good health. There are others who should not be reduced while a third group benefit by a very gradual loss of weight.

Just as no 2 consecutive patients have like needs to reduce neither will they respond similarly to a given program of treatment. Careful study and observation are essential for the identification and the application of the specific needs in the individual case.

Young patients—under thirty years of age—do well if their weight is allowed to exceed the average weight for their sex, age, and height, by 5 to 10 per cent. They are more resistant to infection, they enjoy a higher standard of health and life expectancy is increased. When overweight exceeds plus 10 per cent, restrictions in diet, commensurate with the need to reduce, should be observed. The reduction need not be rapid. I have seen the moral of patients destroyed and success prevented by too energetic treatment. A slow decrease is the best aim, particularly with very young and old patients.

Between the ages of thirty-five and fifty-five years a determined effort should be made to keep the weight a trifle below (5 to 10 per cent) the accepted average. The possible exceptions to this rule are those who have been obese for many years, those who have large bones and well developed musculature, particularly athletes, those who have a family history of obesity, those who are of a nervous type, and those who have, or are frequently exposed to, tuberculous infection. In these instances a plus 10 per cent weight is not only permissible but is desirable.

Over fifty-five years of age a reduction should be obtained, but with caution. It is not advisable to reduce the diet

radically or increase the exercise greatly. Further gain should, of course, be prevented. For these patients a diet and exercise program which will cause a reduction of 5 to 10 pounds yearly will prove harmless and will be satisfactory.

Patients who feel badly because of the treatment are being reduced too rapidly, or too steadily, or are exercising too much, or they belong to the group already referred to—who should not be reduced to conform with the calculated standard weight.

When tuberculosis complicates obesity, a very slow decrease in weight achieved by changes in diet may be helpful. Exercise should not be employed as a reducing agent in these cases. Neither should they be reduced below 5 per cent above the average weight.

The need to overcome obesity is especially increased in the presence of heart disease, diabetes, gout, dyspepsia and diseases of the gall-bladder, the kidneys and the joints, or when a family history of diabetes, heart disease or gout is obtained.

Diet.—Special diet holds a prominent place in the treatment of all types and degrees of obesity. The source of the fat deposits is attacked when the food intake is decreased. With the reduction of the food below the level necessary to carry on the body functions, the stored fat is drawn upon. A reduction in weight ensues.

Any measure which will increase the body's nutritional needs, or stimulate metabolism, will hasten the dissolution of the fat accumulations. It is known that exercise will produce this effect; so also will certain medications, notably thyroid extract. Fevers also exert this influence.

Obesity can therefore be approached with two weapons: (1) a reduced intake of food, and (2) an increased expenditure of nourishment.

The hardship imposed is much less if the reduction is made slowly. The undernutrition régime may be interrupted by allowing a maintenance diet for short periods from time to

time. This practice breaks the monotony of the treatment and allows the tissues, particularly the skin and abdominal muscles, to become readjusted to the decreased body mass; unsightly relaxation of the skin and visceroptosis are prevented and the general weakness is avoided.

Much can be done for the comfort of the patient during treatment. The appetite should be satisfied with a bulky diet of maximum satiety value. Those familiar with the undernutrition treatment of diabetes in the pre-insulin days will have no trouble in making a diet of 800 or 1000 Calories appear quite large.

Thorough and slow mastication of the food and decreased amounts of liquids with meals will enhance the satisfying effect of the food. Food-free fillers—bran wafers, broths, cocoa nibs infusion and mushrooms—may be added to the diet. The broth and cocoa nibs infusion are permissible between meals to avoid distressing hunger.

McLester suggests the wearing of a tight abdominal binder or belt as an aid in overcoming the feeling of emptiness. I have not employed this practice but believe it is good.

Calculation of the Diet.—The total diet is expressed in calories or units of heat (1 gram protein yields 4 Calories; 1 gram fat, 9 Calories; and 1 gram carbohydrate, 4 Calories). Theoretically, it is possible to calculate the number of calories which will serve to hold the weight constant or allow a reduction, as the indication may be. Practically, we find the response to the diets thus calculated varies considerably in different patients, and that some juggling of the diet is usually necessary to meet the individual requirements.

The calculation of the diet is based on the nutritive requirements. The estimation of the basal diet, which represents the heat production of the body while completely at rest and in the postabsorptive state, is the starting point. Over and above the basal caloric need there is the heat expenditure for work done.

For clinical purposes it may be assumed that the basal

requirement of adults, who are not underweight, is *25 Calories per kilogram of actual body weight.*

Table 25 shows roughly the occupational influence on the caloric requirement for the maintenance of body weight. The man doing laborious work may have a basal requirement of only 1800 Calories, yet the diet that is necessary to keep his weight constant may be 100 per cent larger (3600 Calories), or even more. Under these conditions a reduction in weight would be accomplished by reducing the increment above the basal diet from plus 75 to 100 per cent to plus 25 to 50 per cent.

TABLE 25.

Occupation.	Approximate caloric requirement for maintenance of weight.	Caloric allowance on reduction program.
Hard labor	Basal diet plus 75 to 120 per cent	Basal diet plus 25 to 50 per cent.[1]
Light labor	Basal diet plus 40 to 60 per cent	Basal diet plus 10 to 25 per cent.
Sedentary occupation	Basal diet plus 20 to 30 per cent	Basal diet.
Idleness	Basal diet plus 5 to 10 per cent	Basal diet minus 5 to 10 per cent.
Patients refractory to low calories	Basal diet or less	Basal diet minus 10 to 25 per cent.

[1] The basal diet referred to here is 25 Calories per kilogram of the actual weight. In the more refractory cases, or when a more rapid reduction is wanted, 25 Calories per kilogram of the desired weight is suggested.

At the other extreme we find that some patients actually gain in weight on a basal diet. Endocrine disturbance or disturbed water exchange should be suspected when this is encountered. A reduction in the diet to 10 or even 25 per cent below the calculated basal requirement may be necessary to overcome the excess weight. Restriction of the salt in the diet will aid in preventing water retention.

The information given in Table 25 may be used as a guide only in estimating the total calories. If the régime selected is too harsh and causes too quick a reduction, the calories should be increased, while if no reduction follows further decrease in calories is desirable. The rate at which weight

is lost will be the best indication of the adequacy of the diet. Two to 5 pounds reduction per month is satisfactory.

As a general rule it can be said that a man doing heavy work—day laborer, stevedore, blacksmith, farmer, lumberjack—will reduce weight satisfactorily on a diet of 35 Calories per kilogram of the ideal weight; that a man doing light labor—carpenter, painter, tinsmith, plumber, mechanic, street car conductor, gardener, will lose weight on a diet of 25 to 30 Calories per kilogram; and that a person with a sedentary occupation, office work, will need as little as 20 to 25 Calories per kilogram. When lower diets, 15 to 20 Calories per kilogram are necessary, it is because of endocrinal disturbances.

Women require approximately 10 per cent less total calories than men. An equivalent reduction in calories should be observed when the correction of overweight is being attempted.

Protein.—The reduction in weight should not be at the expense of body (endogenous) protein. There is no need to reduce the protein below that contained in a normal diet which for the adult varies between 100 and 125 grams. It is desirable, unless some complication such as nephritis is present, to allow from 1.0 to 1.5 grams of protein per kilogram of the calculated ideal weight.

Diets liberal in protein aid in preventing anemia and they have a high satiety value. This is especially true of the protein of high biological value—eggs, lean meat and milk.

The need for protein is increased by the undernutrition régime. This is due to the reduction in the sparing influence which liberal carbohydrate, and to a less extent the fat, exerts on protein metabolism.

There is no advantage in giving large excesses of protein. The specific dynamic action of protein cannot be depended upon as a reducing agent. It is but mildly operative in individuals who are overweight.

Carbohydrate.—Carbohydrate is the most readily available source of energy; it is essential for the normal combustion of fats and it has a high satiety value.

A diet low in fat does not reduce the need for carbohydrate below a certain limit. This limit is decided upon by the total fat metabolism—that is the fat in the diet or the exogenous fat plust he tissue or endogenous fat which supplements the low diet to meet nutritional needs.

Assuming that in a given case 100 grams of protein, 300 grams of carbohydrate and 133 grams of fat, yielding 2800 Calories, is a maintenance diet and an undernutrition diet of 100 grams protein, 300 grams carbohydrate and 45 grams fat, affording 2000 Calories is prescribed, there is to all intents and purposes no difference in the total fat metabolized. The source of the fat only is different; the 88 grams reduction in exogenous fat is theoretically made up by endogenous fat.

It has been estimated that 1 gram of carbohydrate is sufficient for the metabolism of 1.5 grams of fatty acid, without danger of ketosis, page 34. The carbohydrate content of the reducing diet need never be restricted to the degree of making this calculation necessary. When the estimation is made, however, the total and not only the exogenous fat metabolized should receive consideration.

I have adopted the practice of allowing carbohydrate in a reducing diet to provide calories equivalent to one-third of the calculated maintenance requirement.

A patient, whose maintenance diet is 2400 Calories, is therefore allowed 800 Calories in the form of carbohydrate (200 grams) even though the undernutrition diet is as low as 1600 Calories.

When very low diets, such as 600 and 800 Calories, are necessary, the rule mentioned above is not practicable. In these instances, 50 per cent of the diet should be in the form of carbohydrate.

The bulky carbohydrate foods are best suited for low diets. Of these the 3, 6, 9 and 12 per cent vegetables and fruits, see page 67, are especially desirable. These are amply illustrated in the diet charts on page 171.

Fat.—Fat is the large calorie producer. Thus the restrictions in diet affect this form of food chiefly. Unlike protein and carbohydrate, fat is not essential to normal nutrition. For this reason, the calculation of the fat has been left to the last. The total calories, the protein and the carbohydrate, have been estimated already. The calories not provided by the protein and carbohydrate are made up by fat.

The sample charts, page 171, exemplify very well the absence of or the reduced quantities of fat foods in reducing diets. Butter, cream cheese, fat meat, and salad oil are especially reduced or eliminated. Mayonnaise of practically no food value may be made with mineral oil. It satisfies the desire for fats quite well. Mineral oil may also be used in cooking. Bran wafers and mineral oil have a place in the low-calorie diet. Cooking pans may be greased with mineral oil.

Illustration of the diet calculation: C. A., female, aged forty-two years, a housewife, height 66 inches and weight 194 pounds (88 kilograms) was seen on October 1, 1927. Her complaints were: overweight, feeling of fullness in the abdomen, most pronounced after eating, fatigue and shortness of breath on exertion.

The physical examination revealed: patient comfortable while at rest, overweight, face full and fairly round, no wrinkles, some fullness of neck, breasts enlarged, chest wall thick, area of cardiac dullness increased to the left (12 cm. from the mid-sternal line in the fifth costal interspace), on deep inspiration a few fine crepitant râles heard at the base of the right lung posteriorly, abdomen obese, legs cylindrical, and there was slight pitting on pressure over the tibiæ.

Diagnosis: Simple (exogenous) obesity.

Treatment:

I. *Diet.*

(*a*) *Total calories, 1800.* This is approximately a basal diet based on the ideal weight (159 pounds or 72 kilograms) according to Table 25 (25 Calories per kilogram).

(*b*) *Protein, 90 grams.* This is approximately 1 gram of protein per kilogram of actual body weight or 1.25 grams per kilogram of the desired weight.

(*c*) *Carbohydrate, 150 grams.* This figure was determined by taking one-third (600) of the total calories and dividing this number by 4, to obtain the number of grams of carbohydrate.

(*d*) *Fat, 93 grams.* Fat provides the balance after deducting the calories provided by the protein and carbohydrate (960 Calories) from the total calories, 1800. There are therefore, 840 Calories provided by the fat. This is equivalent to 93 grams.

(*e*) Salt restricted in moderation.

This diet corresponds to diet No. 4 on page 171 with the added salt restriction.

II. *Exercise.* A ten minute walk night and morning daily. This was extended to one-half hour twice daily after two weeks of treatment.

Progress notes: There was prompt relief from the edema and the patient rapidly became free from symptoms.

Weight: October 1, 1927, 190 pounds (86 kilograms); October 15, 187 pounds (85 kilograms); November 27, 1927, 183 pounds (83 kilograms); December 4, 183 pounds (83 kilograms); January 6, 1928, 179 pounds (81 kilograms); June 25, 164 pounds (75 kilograms).

The diet was increased on June 25 to protein, 90 grams;

carbohydrate, 175 grams; fat, 111 grams; and the total Calories, 2059. This diet corresponds to diet No. 5, on page 171.

Fasting.—Obese persons who do not respond to the usual measures are benefited by short fasts. One day a week without food is a common practice in Europe. No harm results from these short fasts. The patients who need them are better subjectively and objectively because of them. Folin and Denis consider repeated fasting effective and safe when due consideration is given to the possibility of ketosis.

The occasional tendency to weakness on the fast days may be largely overcome by allowing protein in the form of skimmed milk, albumin water and lean meat.

In the event of a mild acidosis, a rare occurrence, carbohydrate may be allowed in small quantities. Orange juice, ginger ale, grapefruit and other fruits may be used. Glucose given in tablet form as advocated by Dr. Burgess Gordon will serve the same end, and has the added advantage of a high satiety effect. It postpones extreme hunger effectively.

Fast days are preferable and more effective than the fashionable practice of omitting one or two meals daily. The latter provides a false feeling of security; false because the omitted meal is usually added to the other one or two meals of the day.

The danger of causing deficiency disorders—from lack of vitamins and mineral salts—should be guarded against. Raw fruits and vegetables are valuable vitamin carriers. When adequate exposure to the sun's direct rays is not obtained irradiated ergosterol may be prescribed in preference to cod-liver oil with its high caloric value.

Fluids.—Fluids may be used freely by the obese person free from complications. They should be taken, largely between meals, as with food they detract from the satiety effect. When edema or ascites is present, a restriction of the total fluid intake per twenty-four hours to 1 quart is a good practice.

TABLE 26.—THE FIRST DIET (900 CALORIES) IS THE SKELETON DIET. EACH SUCCEEDING DIET IS EQUIVALENT TO THE PRECEDING DIET WITH CERTAIN ADDITIONS TO PROVIDE THE SPECIFIED INCREASE IN CALORIES.

	1. 900 Calories.		2. 1200 Calories.		3. 1500 Calories.		4. 1800 Calories.		5. 2100 Calories.		6. 2400 Calories.		7. 2700 Calories.	
	P-65. F-32. C-90.		P-80. F-53. C-100.		P-80. F-75. C-125.		P-90. F-93. C-150.		P-100. F-111. C-175.		P-110. F-129. C-200.		P-110. F-151. C-225.	
BREAKFAST:	Wt. gm.	Meas.	Wt. gm.	Meas.	Wt. gm.	Meas.	Wt. gm.	Meas.	Wt. gm.	Meas.	Wt. gm.	Meas.	Wt. gm.	Meas.
1. Milk	skim 120	½ c.	skim 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 120	½ c.
2. Eggs	..	1	..	2	..	2	..	2	..	2	..	2	..	2
3. 9% Fruit	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.
4. Bread	30	1 slice	30	1 slice	30	1 slice	30	1 slice	30	1 slice	30	1 slice	30	1 slice
5. Butter	..	..	5	1 tsp.	10	2 tsp.	15	1 tbsp.	15	1 tbsp.	10	2 tsp.	10	2 tsp.
6. Sugar	..	..	..	..	..	..	5	1 tsp.	5	1 tsp.	10	2 tsp.	15	1 tbsp.
7. Cereal	..	..	..	..	..	..	..	..	120	½ c.	120	½ c.	None	None
8. Cream	..	..	..	..	..	..	..	..	15	1 tbsp.	30	2 tbsp.	120	½ c.
9. Bacon	..	..	..	..	..	..	..	..	15	3 strips	15	3 strips	15	3 strips
NOON MEAL:														
10. Milk	skim 120	½ c.	skim 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 240	1 c.	whole 240	1 c.
11. Meat, fish, chicken	60	2 oz.	90	3 oz.	75	2½ oz.	90	3 oz.	90	3 oz.	105	3½ oz.	105	3½ oz.
12. 3% Vegetable	100	1 serv.	100	1 serv.	100	1 serv.	200	2 serv.	200	2 serv.	100	1 serv.	100	1 serv.
13. 9% Vegetable	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.
14. 12% Fruit	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	None	None	None	None
15. Butter	..	..	5	1 tsp.	10	2 tsp.	15	1 tbsp.	15	1 tbsp.	10	2 tsp.	15	1 tbsp.
16. Bread	..	..	..	..	30	1 slice	30	1 slice	30	1 slice	30	1 slice	30	1 slice
17. Cream	..	..	..	..	..	..	..	..	15	1 tbsp.	30	2 tbsp.	None	None
18. 18% Fruit	..	..	..	..	..	..	..	..	..	..	100	1 serv.	100	1 serv.
19. Oil	..	..	..	..	..	..	..	..	..	..	10	2 tsp.	10	2 tsp.
20. Sugar	..	..	..	..	..	..	..	..	..	..	15	1 tbsp.	15	1 tbsp.
21. 18% Vegetable	..	..	..	..	..	..	..	..	..	..	..	..	100	1 serv.
EVENING MEAL:														
22. Milk	skim 120	½ c.	skim 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 120	½ c.	whole 120	½ c.
23. Meat, fish, chicken	90	3 oz.	90	3 oz.	90	3 oz.	90	3 oz.	90	3 oz.	120	4 oz.	105	3½ oz.
24. 3% Vegetable	100	1 serv.	200	2 serv.	100	1 serv.	150	1½ serv.	200	2 serv.	100	1 serv.	100	1 serv.
25. 9% Vegetable	100	1 serv.	None	None	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.
26. 12% Fruit	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	100	1 serv.	None	None	None	None
27. Bread	..	..	30	1 slice	30	1 slice	30	1 slice	30	1 slice	30	1 slice	30	1 slice
28. Butter	..	..	5	1 tsp.	10	2 tsp.	15	1 tbsp.	15	1 tbsp.	10	2 tsp.	15	1 tbsp.
29. 18% Vegetable	..	..	..	..	..	..	100	1 serv.	100	1 serv.	None	None	100	1 serv.
30. Cream	..	..	..	..	..	..	..	..	15	1 tbsp.	30	2 tbsp.	None	None
31. Sugar	..	..	..	..	..	..	..	..	10	2 tsp.	15	1 tbsp.	15	1 tbsp.
32. 18% Fruit	..	..	..	..	..	..	..	..	..	..	100	1 serv.	100	1 serv.
33. Oil	..	..	..	..	..	..	..	..	..	..	..	..	10	2 tsp.

Serv. = serving; tbsp. = tablespoon; tsp. = teaspoon; c. = cup.

Salt.—Elimination of salt from the diet will prove a valuable aid in correcting edema and ascites. It will do away with the need of diuretics in many cases and, though slower of action, will prove of superior value. Salt restriction brings about very striking reductions in weight in those patients in whom disturbed water balance accounts for obstinate response to restricted calories.

Diets Suitable for Reducing Weight.—Table 26 depicts seven sample diets of different food values. Suitably selected they will prove of value in preventing and overcoming obesity. It will be noted that the carbohydrate provides at least one-third of the total calories. Furthermore, there are adequate protein, vitamins and mineral salts (calcium, iron and phosphate). In selecting the fruits and vegetables Table 14 may be consulted.

Lists of foods of low, medium, and high caloric value are presented in Table 27. Quite often the attraction of the patient's attention to the column of foods which tend to increase the body weight with greatest ease and rapidity, and to those foods which are least effective in this respect, serves to prevent obesity or to correct mild degrees of overweight.

TABLE 27.—FOOD VALUE.

(Calories.)

Low.	*Medium.*	*High.*
Asparagus	Parsnips	Beans (dried)
Bean sprouts	Peas	Corn
Broccoli	Apples	Potatoes, white
Cabbage	Apricots	Potatoes, sweet
Cauliflower	Blueberries	Bananas
Celery	Cherries (sour)	Sweet cherries
Chard	Grapes	Figs
Chinese cabbage	Huckleberries	Grapejuice
Cucumber	Loganberries	Prunes
Egg plant	Mulberries	Dried fruits

TABLE 27.—FOOD VALUE.—(*Continued.*)

(Calories.)

Low.	*Medium.*	*High.*
Endive	Pears	Griddle cakes or waffles
Greens, mustard	Pineapple	Pastries; *i. e.*, cake, cookies, pie
Greens, beets	Plums	Cereal
Kohlrabi	Raspberries	Macaroni
Lettuce	Lean meat, 3 ounces	Spaghetti
Okra	Lean fish, 3 ounces	Rice
Peppers	Lean chicken, 3 ounces	Noodles
Pumpkin	Egg	Bread
Radish	Cocoa	Crackers
Spinach	Whole milk	Sugar
String beans	Evaporated milk	Molasses
Summer squash		Honey
Tomatoes		Ice cream
Turnips		Jelly
Watercress		Jams
Beets		Pudding
Brussels sprouts		Nuts
Carrots		Gravies
Dandelion greens		Sauces
Leeks		Chocolate
Onions (juicy)		Malted Milk
Rutabagas		Oil
Sauerkraut		Mayonnaise
Winter squash		Salad dressing
Fruits.		Butter
Honeydew melons		Oleomargarine
Lemon juice		Lard
Muskmelon		Cream
Rhubarb		Fat meat
Strawberries		Cheese

TABLE 27.—FOOD VALUE.—(*Continued.*)

(Calories.)

Low.	*Medium.*	*High.*
Watermelon		Canned salmon
Blackberries		Canned sardines
Cranberries		
Currants		
Gooseberries		
Grapefruit		
Lime juice		
Oranges		
Orange juice		
Peaches		
Tangerines		
Beef bouillon		
Buttermilk		
Skim milk		
Gelatin		
Whey		

Exercise.—Exercise is, in most cases, second only to diet in importance as a reducing agent. It should be carried out under medical supervision for the first few weeks, at least. Employed judiciously, it carries no risks and all cases of obesity at some stage are benefited by it. The peripheral circulation is improved, carbohydrate assimilation is increased, a sense of general well-being is created and the physical condition is vastly improved.

The very fat person, however, should not only be deprived of exercise but should be confined to bed until the advantages obtained by special diet make it safe to begin graduated exercises. Sudden fatalities will be averted by observing this rule in all cases of suspected or obvious myocardial degeneration or coronary artery disease.

In these cases, passive exercises and massage may be started early, followed by gradually increasing bed gymnastics—wrist, arm, shoulder, foot, leg and abdominal exercises, dumb-bells and pulley weights. With further progress, short walks on the level are allowed. Inclines and steps should come later. Overweight places a great burden on the myocardium. This influence is increased by exercises which require climbing. After increasing gradually the length of walks on the level for several weeks, slight inclines may be tried. Calisthenics, particularly those supplying exercise to the abdominal muscles, are good. Climbing steps and golf are eventually advised, and the younger patients (below thirty-five years) are free to gradually take up gardening, cycling, tennis, swimming and basketball.

Fatigue is not a necessary precedent to a satisfactory result. Spasmodic and vigorous exercise carry a needless element of danger while gradually increasing daily exertions prove most helpful, not only in correcting obesity, but in preventing a recurrence and in promoting a normal physiological state. If one enjoys gymnasium exercises and adopts a regular routine, benefit will accrue. The "daily dozen" is a splendid practice to cultivate. It may be needless to emphasize that the program of exercise should not be abandoned when the obesity is cured.

It is obvious that minor degrees of obesity do not require the same caution as the severe, in which re-education of the muscles is part of the scheme of treatment. Individual study will determine the initial amounts of exercise advisable.

Hydrotherapy.—Special baths carry no virtue that hot or cold bathing, suitably prescribed, do not. Cold showers or baths stimulate metabolism and are advisable for those whose skin responds with a normal redness or glow. They produce an exhilarating effect which encourages increased physical activity. For these patients, cold showers or baths are helpful. There are those, however, particularly the endocrinal group, whose body temperatures are below normal,

and who respond with a pallor of the skin following a cold bath. There is a sensation of depression rather than exhilaration. Hot baths are preferable and are seemingly helpful to these people. There is a definite stimulation of metabolism if the body temperature is increased.

Medication.—*Thyroid preparations* have a powerful influence in increasing the metabolic rate. They are employed to advantage in stubborn cases of obesity which have failed to respond satisfactorily to diet restriction and exercise. Thyroid extract (desiccated) in doses of $\frac{1}{2}$ to 2 grains 3 times daily is usually sufficient, except in *bona fide* cases of hypothyroidism when more may be needed.

Dinitrophenol and *Allied Preparations.*—These remedies are still in the strictly experimental stage. They accelerate cellular metabolism to a remarkable degree, but as reports of grave toxic effects multiply without, as yet, any antidote or satisfactory method of detecting and avoiding persons susceptible to the drug, it will be sufficient to caution the practitioner against their use and to refer him to the recent review of the subject by Poole and Haining.[1]

Iron, given by mouth, in large doses (ferrous carbonate, gr. xc daily) is a valuable adjunct in the treatment of obesity when a secondary anemia co-exists.

Salyrgan, by virtue of its diuretic effect, is especially valuable in combatting overweight in which water retention is prominent.

[1] Poole, F. E., and Haining, R. B.: Jour. Am. Med. Assn., **102**, 1141, 1934.

CHAPTER XIII.

ENDOGENOUS OBESITY.

ENDOGENOUS obesity is attributable to, and is usually traceable to, disturbances in the glands of internal secretion. Decreased secretion of the posterior lobe of the pituitary gland is especially accountable for juvenile obesities, but it is no means confined to the young. In the adult, the pituitary obesity is usually due to a bilobar—anterior and posterior deficiency. Inadequate thyroid secretion, as well as the absence—partial or total—of sex hormones, may also lead to obesity, as does cortical disease, particularly adenomata, of the adrenal glands. The so-called pancreatic obesity is believed by Falta to be due to increased islet activity.

Obesity accompanying disorders of the pineal body is not clearly understood. The present tendency is to attribute it to secondary involvement of the hypophysis or of the hypothalamic region.

Dercum's disease (adiposis dolorosa), occurring chiefly in women, is characterized by nodular accumulations of fat which are exquisitely painful especially on pressure. Muscular weakness, mental and nervous disorders are associated symptoms. The etiology of this disease is not clearly understood. A derangement or an unbalance of the endocrine glands is probable.

The perfection of the function of these endocrine glands is that their collective activities seem as one. When this harmony is disturbed the discord may proclaim itself by the development of overweight.

When the fundamental rate of oxidation is below normal, as revealed by a low basal metabolic rate, a normal food intake is excessive and will tend to obesity. There are,

however, obese persons with endocrinal disturbances who have a normal basal metabolism, who do not eat in excess of the normal calculated requirement, who exercise freely, and yet gain in weight or fail to lose on a diet which, under normal conditions, would cause a reduction. Is this due entirely to disturbed water metabolism, or does an anomaly of intestinal absorption of carbohydrate play a part? Changes in the basal metabolic rate are not accountable for this ready-to-gain-and-loath-to-lose phenomenon. As yet the underlying mechanism is undetermined.

An abnormal transformation of carbohydrate to fat is found by Hagedorn and the decreased ability of the obese persons to use fat (Wang and Strouse) go further in confirming the belief that obesity of the type under discussion is due to a qualitative irregularity of metabolism.

To maintain the proper perspective of the various types of overweight, it is well to bear in mind that obesity of endocrinal origin comprises approximately 3 per cent of the overweights; that pluriglandular disturbances are seen more often than uniglandular; that characteristics of one glandular disturbance may obscure those of another, and that simple obesity may be added to any one or group of glandular abnormalities giving rise to a complicity of characteristics. Many times signs suggesting endocrinal disturbance are misleading. When the treatment is directed to the correction of simple obesity these evidences often disappear, thus disclosing the true nature of the disorder. Miss A. H., aged twenty-two years, Figs. 8 and 9, illustrates this response. When first seen in November, 1931, she weighed 111 kilograms (244 pounds). A diagnosis of obesity and hypothyroidism was made and was supported by a basal metabolic rate of −17 per cent. Specific therapy (thyroid extract, grains $\frac{1}{2}$ three times a day) was not well tolerated. It was discontinued after the first week. Following a restriction of the total calories and a gradual increase in exercises, the weight responded satisfactorily. She weighed 75 kilograms

(165 pounds) in September, 1932. The basal metabolic rate was returned to normal.

The prevention of endocrinal obesity resolves itself into the early recognition of the underlying disorder and the application of general and specific treatment.

FIG. 8.—Miss H., November, 1931.

FIG. 9.—Same patient, July, 1932.

Illustrates the effect of a reduction in caloric intake plus increased exercise.

The endocrine obesities tend to be resistant to treatment. Thyroid obesity is the one exception to this rule. It yields readily and the ground gained may be maintained by appropriate therapy.

The results of treatment of the remaining endocrinal group are on the whole disappointing. However, no case should be approached with the feeling of despair. Many prove by their response to treatment to belong to the simple

obese class; and those who fail to reduce on the adoption of the usual measures and specific treatment can be greatly benefited. The tendency to gain in weight ceases and the development of incurable complications can be largely stopped.

HYPOTHYROIDISM.

Overweight, due to hypothyroidism, is not common. It does not reach the extreme degree as in the case of faulty pituitary secretion or simple obesity, unless two or all three of these disorders are combined. There are, in fact, many patients with decreased function of the thyroid gland who are but a trifle overweight. Other signs of this disorder are often more noticeable.

Decreased thyroid secretion should be suspected in all new born babies weighing over 8 pounds. Cretinism is a form of infantilism due to inadequate thyroid secretion during the period of developmental growth; while myxedema is hypothyroidism with its onset after maturity.

The puffiness of the face, thickening and dryness of the skin, sensitiveness to cold, mental apathy, and the constant low basal metabolic rate suffice to identify reduced thyroid function. Weakness, pallor, secondary anemia, low blood-pressure, and constipation are also noted. Increased fat deposits are mostly general in distribution. The abdomen may be a trifle prominent and pads of fat in the supra-clavicular region and at the ankles in the vicinity of the malleoli are frequent. The response to specific therapy is striking.

It is unwise, at the beginning of the treatment, to attempt to administer thyroid preparations in proportion to the degree of lowered metabolism. A patient with a basal metabolic rate of −15 per cent may be greatly benefited by thyroid extracts grains $\frac{1}{2}$ twice daily, while 2 grains, 3 times daily might exceed the tolerance for the drug.

No harm will come if a small dose, $\frac{1}{2}$ grain (30 mg.) of

desiccated thyroid substance, twice daily, is given at first. Each fortnight an increase may be made if a satisfactory response is not obtained and if no evidences of overdosage appear. A pulse-rate above 90, nervousness, heart consciousness, headache and tremors, appearing alone or combined, necessitate stopping the drug for a few days. When it is resumed the dosage should be low. It should be kept below that which produced symptoms of intolerance. When more than 6 grains of the desiccated thyroid gland daily is tolerated indefinitely, it is probable that there is either poor absorption, or that the product is impotent.

Basal metabolism studies, from time to time, are well worth while, though not essential to good results.

Overweight is a fertile field for quack remedies. The reduction in weight while taking these preparations is usually due to the restrictions in diet, which are almost invariably outlined on the accompanying folder. If the medication itself causes the weight to decrease, it is due to contained thyroid extract, dinitrophenol or related remedies.

Patients should be emphatically warned against the continued use of thyroid preparations without medical supervision. After normal health is restored, the intermittent use, possibly every third week, of appropriate thyroid therapy, may be necessary to control the myxedema.

HYPOPITUITARISM.

Obesity of hypophyseal origin is attributed to hyposecretion of the posterior lobe of the pituitary gland in juvenile cases, and to bilobar insufficiency in the adult. The dystrophia adiposogenitalis, or Froelich's syndrome, is due to an interference of the secretory function of the pituitary gland as a whole.

Deficiency of the posterior lobe accounts for 70 to 80 per cent of juvenile obesities (Engelbach). Importance attaches itself to the early recognition of this type of overweight

because (1) it responds well to specific treatment, *i. e.*, with posterior lobe preparations, and (2) if unrecognized and untreated before adolescence secondary anterior lobe involvement, with faulty development of the genital system, is likely, though there are more adults with pure posterior lobe deficiency than is usually conceded.

The characteristics of posterior lobe insufficiencies in the young are: (1) obesity: the adipose tissue being diffusely distributed and giving, in some cases, a dimpled appearance to the skin; (2) round face, giving the appearance of an unusually round head sitting directly upon a spherical body; (3) polyphagia; (4) somnolence, most marked at or after adolescence, and (5) delayed development of the secondary sexual characteristics. This sign may be the first indication of associated anterior lobe insufficiency. These patients are particularly free from care, are quite happy, lack normal initiative, and usually play with children younger than themselves.

In the adult, pituitary lack (Froehlich's syndrome) is recognizable by the absence of catamenia, rapidly developing girdle deposits of fat, pendulous puckered masses between elbows and shoulders, huge amounts of adipose tissue being distributed between the diaphragm and the knees, leaving the shoulders, girdle, hands, wrists, forearms, lower leg, ankles and feet disproportionately small. The female takes on a masculine outline, and the male becomes effeminate. As the anterior lobe deficiency progresses atrophy of the genitalia occurs and the pubic and axillary hair disappears. Furthermore, the tolerance for carbohydrate is increased, and the body temperature tends to be subnormal. Headache and somnolence are common symptoms. Contraction of the field of vision and disease, usually a tumor, in the region of the sella turcica, as revealed by Roentgen-ray examination, are relevant when present.

These patients are often mentally alert. Physically, too,

they are more capable than those of the simple obese group with the same degree of adiposity.

Pituitary disease as a primary cause of obesity has been discredited by several investigators.[1,2] Obesity of the generally accepted pituitary type has been reproduced by slightly injuring the tuber cinereum with the hypophysis remaining intact while careful hypophysectomy without brain injury has not caused overweight. Evans reports invariable production of adiposity by slight injury to the brain adjacent to the hypophysis, while discrete injury to the hypophysis resulted in no such development.

Cushing describes a rare type of obesity caused by basophilic adenomata of the anterior lobe of the pituitary gland, occurring in the second and third decade of life. Secondary changes in the suprarenal and thyroid glands contribute to produce the picture of a polyglandular dysfunction. The obesity develops rapidly. Painful, tense deposits of fat accumulate in the face and abdomen. The abdominal enlargement is like that of a full term pregnancy with purplish pigmented striæ. The extremities are spared, making them appear disproportionately small. In the female, amenorrhea and regression of the uterus to the infantile type; and in the male, impotence, loss of libido, and atrophy of the testes result. Hirsutism, affecting particularly the chin and face, is outstanding. Development of a kyphosis is the rule, and pain in the thoracic region is common.

Glycosuria and hyperglycemia are present; the basal metabolic rate exceeds normal; the red blood cells number 5,000,000 or more, giving the patient a plethoric appearance; the blood calcium is low and there is definite decalcification of the body structure; the blood-pressure is elevated; a marked tendency to bruise easily exists and there is pronounced susceptibility to infections.

[1] Camus, J., and Roussy, G.: Jour. d. physiol. et gén., **20**, 535, 1922; ibid., **20**, 507, 1922.

[2] Evans, H. M.: Jour. Am. Med. Assn., **101**, 430, 1933.

The average duration of life in Cushing's collection of 12 cases was five years. One patient, a male, was benefited by Roentgen-ray radiations to the pituitary gland.

In the so-called cerebral obesity, hypophyseal insufficiency and a series of congenital deformities are characteristic. The latter are retinitis pigmentosa and disturbed mental development, poly- and syndactylia, skull deformities, peculiar digestive disturbances and even atresia ani. (Grafe.[1])

Cerebral injury from encephalitis lethargica is a cause of obesity. This is believed by Raab[2] and Wertheimer[3] to result from disturbance of a fat regulating center in the forebrain.

Pituitary Preparations.—At best, this form of therapy is unsatisfactory but the effect obtained in the juvenile cases, and occasionally in adults, warrants its trial.

Pituitrin, a posterior lobe preparation, given subcutaneously, has the advantage of complete absorption; it is more uniformly effective than if administered by mouth. The initial dosage of 5 minims, once daily, is advocated. Additions of 1 minim every third day may be made until the point of intolerance is determined. Given by mouth, larger doses are employed, 20 to 25 minims. Increases of 2 or 3 minims, twice weekly, may be made. For infants and children, Engelbach advocates an initial dosage of 1 minim, or less.

The symptoms which identify the onset of intolerance to the drug are sensations of unrest in the abdomen, followed by cramps and diarrhea.

For the adult with bilobar insufficiency, the extract of the entire gland may be given by mouth in doses of 10 grains after each meal. Lacking favorable response, the dosage may be doubled or even trebled.

Combined pituitary and thyroid therapy is indicated by

[1] Grafe, E.: Metabolic Diseases and Their Treatment, Philadelphia, Lea & Febiger, p. 154, 1933.

[2] Raab, P.: Ztschr. f. exper. Med., **49**, 179, 1926.

[3] Wertheimer, F.: Pflueger's Arch., **213**, 262, 1926.

evidences of insufficiency of these two glands, or in pituitary deficiency alone when it fails to respond to uniglandular treatment.

Williams has emphasized the need of ridding the body of foci of infection, supplying adequate vitamins in the diet and the perseverance of treatment over a period of weeks for best results from pituitary therapy.

DEFICIENT SEX HORMONES.

Obesity frequently develops when the sex hormones become diminished or are absent entirely. This is noticeable only after twenty-five years of age, in contrast to the juvenile obesity of pituitary disease. It is a type of overweight which does not respond in a satisfactory manner to specific therapy. Reliance on the usual measures, special diet and exercise, is justified, however.

OBESITY OF THE MENOPAUSE.

The tendency for women to lay on fat at the menopause is well known. The cessation of ovarian function may be responsible. The fact that some of these patients promptly reduce when supplied with a potent preparation of ovarian extract is evidence in favor of the endocrinal cause.

Decreased physical activity, and lessened responsibility without proportionate changes in the desire for food tend to confuse the picture by adding simple alimentary obesity to that of endocrinal origin.

Ovarian Preparations.—The extract of the whole ovary given in large doses, 10 to 30 grains 4 times daily, is sometimes useful in overcoming the obesity following the menopause, natural or artificial. The drug is not always effective, though failure of success in the past may have been partly due to the custom of prescribing small doses. When given subcutaneously, ovarian substance of the whole gland is used in doses of 1 to 6 cc. daily. (Engelbach.)

APPENDIX.

Composition of Foods.

Lists of the common foods with their protein, fat and carbohydrate values are obtainable in pamphlet and book form. There are considerable discrepancies on food values by different authors. In this compilation, an average of the different values has been adopted in some instances, while in others the latest analyses or those considered most likely to be correct are accepted.

For the most part, the values have been taken from Atwater and Bryant's Monograph, "The Chemical Composition of American Food Materials," Bulletin No. 28, Revised Edition. Reprints of this excellent monograph can be secured by sending with a request, ten cents, to the Superintendent of Documents, Washington, D. C.

The U. S. Dept. of Agriculture has published more recent figures on the composition of vegetables, fruits and beef: the values of Chatfield and Adams, "Proximate Composition of Fresh Vegetables," circular No. 146. The figures for the fruits are taken from Chatfield and McLauflin, "Proximate Composition of Fresh Fruits," circular No. 50. From the bulletin published in 1926, "Proximate Composition of Beef," circular 389, values have been taken on beef.

These may be obtained from the Superintendent of Documents, Washington, D. C.

Many of the values of special foods for diabetics may be obtained from the Thirty-first Report on Food Products, issued by Prof. E. M. Bailey from the Connecticut Agricultural Experiment Station at New Haven, Conn.

Key to Sources of Data Quoted.

A. Bulletin No. 28—Revised Edition—U. S. Dept. of Agriculture—"The Chemical Composition of American Food Materials"—Atwater and Bryant.

B. Circular No. 389, U. S. Dept. of Agriculture—"Proximate Composition of Beef"—Chatfield.

C. Circular No. 50, U. S. Dept. of Agriculture—"Proximate Composition of Fresh Fruits"—Chatfield and McLaughlin.

D. Circular No. 146, U. S. Dept. of Agriculture—"Proximate Composition of Fresh Vegetables"—Chatfield and Adams.

E. Bulletin No. 286, Connecticut Agricultural Experiment Station—"The Thirty-first Report on Food Products," Part I—E. M. Bailey.

Table 28.—Animal Food. Edible Portions Unless Otherwise Stated.

I. *Beef*

A. Beef (fresh)	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
Loin—med. fat	B	17	25	0
Loin—porterhouse steak	A	22	20	0
Loin—fat	B	16	31	0
Neck—medium	B	18	19	0
Round—medium	B	19	13	0
Rump—medium	B	16	31	0
Miscellaneous cuts, free from all fat	A	22	3	0
Heart	A	16	20	0
Kidney	B	15	8	0
Liver	A	20	5	2
Sweetbreads (as purchased)	A	17	12	0
Suet (as purchased)	A	5	82	0
Tongue	A	19	9	0

TABLE 28.—ANIMAL FOOD. EDIBLE PORTIONS UNLESS OTHERWISE STATED.—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
I. *Beef*				
B. Beef (cooked)				
Boiled (as purchased)	A	26	35	0
Roast (as purchased)	A	22	29	0
C. Beef (canned)				
Corned beef	A	26	19	0
Dried, salted and smoked beef	A	30	7	0
Tongue, whole (as purchased)	A	20	23	0
D. Beef (corned and pickled)				
Corned beef	A	16	26	0
Tongues, pickled	A	13	21	0
II. *Veal* (fresh)				
Leg	A	21	7	0
Loin, chop, med. fat	A	20	11	0
Heart (as purchased)	A	17	10	0
Kidneys (as purchased)	A	17	6	0
Liver (as purchased)	A	19	5	0
III. *Lamb*				
A. Lamb (fresh)				
Breast or chuck	A	19	24	0
Leg	A	19	17	0
Loin without kidney and tallow, chops	A	19	28	0
B. Lamb (cooked)				
Chops, broiled	A	22	30	0
Leg, roast	A	20	13	0
Tongue, spiced and cooked	A	14	18	0
IV. *Mutton*				
A. Mutton (fresh)				
Leg, hind, medium fat	A	19	18	0
Loin, without kidney or tallow	A	16	36	0

TABLE 28.—ANIMAL FOOD. EDIBLE PORTIONS UNLESS OTHERWISE STATED.—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
IV. *Mutton*				
A. Mutton (fresh)				
Loin, free fat removed	A	24	19	0
Heart (as purchased)	A	17	13	0
Kidneys (as purchased)	A	17	3	0
Liver	A	23	9	5
B. Mutton (cooked)				
Leg, roast	A	25	23	0
V. *Pork*				
A. Pork (fresh)				
Ham, lean	A	25	14	0
Ham, medium fat	A	15	29	0
Loin (chops, medium fat)	A	17	30	0
Side, lard and other fat included	A	9	62	0
Fat back (as purchased)	A	4	90	0
Heart (as purchased)	A	17	6	0
Kidney (as purchased)	A	16	5	0
Liver (as purchased)	A	21	5	1
B. Pork (pickled, salted or smoked)				
Ham, lean smoked	A	20	21	0
Ham, medium fat, smoked	A	16	39	0
Ham, smoked and boiled (as purchased)	A	20	22	0
Ham, luncheon, boiled	A	23	21	0
Pig's tongue	A	18	20	0
Pig's feet, pickled	A	16	15	0
Salt pork, clear fat (as purchased)	A	2	86	0
Salt pork, lean ends	A	8	67	0
Bacon, smoked	A	11	65	0

TABLE 28.—ANIMAL FOOD. EDIBLE PORTIONS UNLESS OTHERWISE STATED.—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
V. *Pork*				
C. Sausage				
Bologna	A	19	18	0
Frankfurt (as purchased)	A	20	19	1
Pork (as purchased)	A	13	44	1
Salami	A	24	40	0
Wienerwurst (as purchased)	A	28	22	2
VI. *Poultry*				
A. Chicken (fresh)				
Broilers	A	22	3	0
Fowls	A	19	16	0
Heart (as purchased)	A	21	6	0
Gizzard (as purchased)	A	25	1	0
Liver (as purchased)	A	22	4	2
B. Chicken (cooked)				
Capon	A	27	12	0
Fricasseed	A	18	12	2
C. Turkey (cooked)	A	28	18	0
D. Goose, not including giblets	A	16	36	0
VII. *Fish*				
A. Fish (fresh)				
Bass, black	A	21	2	0
Bluefish	A	19	1	0
Butterfish	A	18	11	0
Catfish	A	14	21	0
Cod	A	17	0	0
Flounder	A	14	1	0
Haddock	A	17	0	0
Halibut	A	19	5	0
Herring	A	20	7	0
Mackerel	A	19	7	0

TABLE 28.—ANIMAL FOOD. EDIBLE PORTIONS UNLESS OTHERWISE STATED.—(*Continued.*)

VII. *Fish*	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
A. Fish (fresh)				
Perch	A	19	4	0
Salmon	A	22	13	0
Shad	A	19	10	0
Trout, brook	A	19	2	0
Trout, lake	A	18	10	0
Whitefish	A	23	7	0
B. Fish (preserved, canned)				
Cod, salt, boneless (as purchased)	A	28	0	0
Herring, smoked	A	37	16	0
Mackerel, salt	A	21	23	0
Salmon, canned	A	22	12	0
Sardines, canned	A	23	20	0
Sturgeon, Russian, dried	A	32	10	0
Tunney (Tuna), canned in oil (as purchased)	A	24	20	1
C. Shell-fish, etc. (fresh)				
Clams, round, removed from shell (as purchased)	A	11	1	5
Crabs, hard shell, whole	A	17	2	1
Lobster	A	16	2	0
Mussels in shell	A	9	1	4
Oysters solids (as purchased)	A	6	1	3
Scallops (as purchased)	A	15	0	3
D. Shell-fish, etc. (canned)				
Crabs (as purchased)	A	16	2	1
Lobsters (as purchased)	A	18	1	1
Oysters (as purchased)	A	9	2	4
Shrimp (as purchased)	A	25	1	0

TABLE 28.—ANIMAL FOOD. EDIBLE PORTIONS UNLESS OTHERWISE STATED.—(*Continued*).

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
VIII. *Amphibia*—Frog's legs . . .	A	16	0	0
IX. *Eggs* (raw)				
Hens' eggs, whole	A	13	10	0
white	E	12	0	0
yolk	E	16	33	0
X. *Dairy Products*				
A. Milk				
Milk, whole, cow's . .	A	3	4	5
Condensed (evaporated, concentrated), unsweetened	A	10	9	11
Sweetened, condensed (sweetened, evaporated) (sweetened, concentrated)	A	9	8	54
Skimmed	A	3	0	5
Buttermilk	A	3	1	5
Cream, "heavy," whipping (approx. 40%) .	E	2	41	2
Cream, "light," table cream (approx. 20%) .	E	3	22	3
Milk powder (whole milk)	E	25	25	38
Malted Milk	E	14	7	72
Butter	A	1	85	0
B. Cheese				
American, pale . . .	A	29	36	0
Cheddar	A	28	37	4
Cottage, skim milk . .	A	21	1	4
Full cream	A	26	34	2

TABLE 28.—ANIMAL FOOD. EDIBLE PORTIONS UNLESS OTHERWISE STATED.—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
X. *Dairy Products*				
B. Cheese				
Limburger	A	23	29	0
Roquefort	A	23	30	2
Swiss	A	28	35	1
C. Ice cream, typical	E	4	13	20
XI. *Miscellaneous, as purchased*				
Gelatin	A	91	0	0
Lard, refined	A	0	100	0
Beef juice	A	5	1	0
Oleomargarine	A	1	83	0
Salad oils and cooking fat, typical	E	0	100	0

TABLE 29.—SOUPS—CAMPBELL'S.*

I. *Canned*			
Asparagus	1	1	7
Bean	6	2	14
Beef	6	1	8
Bouillon	3	0	1
Celery	1	2	7
Chicken	1	1	5
Chicken-gumbo	3	1	9
Clam chowder	3	4	10
Consommé	3	0	1
Julienne	3	0	1
Mock turtle	6	1	6
Mulligatawny	3	1	11
Mutton	5	1	5
Oxtail	4	2	8
Pea	5	2	12
Pepper pot	5	3	8

* Values supplied by Campbell Soup Company, Camden, N. J.

TABLE 29.—SOUPS—CAMPBELL'S.—(*Continued.*)*

I. *Canned*	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
Printainier		4	0	2
Tomato		2	1	9
Tomato-okra		2	1	9
Vegetable		3	1	10
Vegetable-beef		8	2	6

TABLE 30.—BREAD, FLOUR, CEREALS.

I. *Bread*				
Graham	A	9	2	52
Rye and wheat	A	12	0	52
Wheat, average of many analyses	A	9	1	53
Wheat, whole	A	10	1	50
Rolls, all analyses	A	9	4	57
Zwieback	A	10	10	74
Crackers, butter	A	10	10	72
graham	A	10	9	74
oyster	A	11	11	71
pretzels	A	10	4	73
Saltines	A	11	13	69
soda	A	10	9	73
II. *Flour, Meals, etc.*				
Hominy	A	8	1	79
Oatmeal	A	16	7	66
Rice	A	8	0	79
Soy-bean flour	E	43	20	24
Wheat flour, entire	A	14	2	72
Wheat flour, graham	A	13	2	71
Wheat flour, patent, average	A	11	1	75
Gluten	A	14	2	71
Cornmeal, unbolted	A	8	4	66
Cornmeal, granular	A	9	2	75

* Values supplied by Campbell Soup Company, Camden, N. J.

TABLE 30.—BREAD, FLOUR, CEREALS.—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
III. *Cereals*				
A. Barley, pearled	E	10	1	76
B. Corn preparations				
Jersey corn flakes	E	9	0	82
Kelloggs	E	6	0	79
Post toasties	E	7	0	79
Quaker hominy grits	E	8	1	78
C. Oat preparations				
Mother's Crushed Oats	E	16	6	65
Rolled oats	A	16	7	66
D. Rice preparations				
Kelloggs Rice Flakes	E	10	0	81
Quaker Puffed Rice	E	8	0	80
E. Rye—Rye Krisp	E	14	2	74
F. Wheat preparations				
Farina	A	11	1	76
Force	E	11	1	74
Grape Nuts	E	12	1	74
Kelloggs Krumbles	E	12	1	72
Macaroni	A	13	1	74
Noodles	A	12	1	76
Pettijohns	E	9	2	75
Puffed wheat	E	13	2	70
Ralston	E	12	2	72
Shredded wheat	E	11	1	75
Spaghetti	A	12	0	76
Wheatena	E	11	3	74
IV. *Miscellaneous Preparations*				
Tapioca	A	0	0	88
Starch, corn starch	A	0	0	90

TABLE 31.—VEGETABLES, FRESH (UNLESS OTHERWISE STATED).

I. *Fresh*	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
Artichokes	D	3	0	9
Jerusalem	D	2	0	16
Asparagus	D	2	0	3
Basella	D	2	0	3
Beans				
Lima	D	8	1	22
Sprouts	D	3	0	3
String (carbohydrate range, 4 to 10%)	D	2	0	6
Beets (carbohydrate range, 6 to 10%)	D	2	0	9
Borage (salad plant)	D	3	0	0
Brussels sprouts	D	4	1	8
Broccoli	D	3	0	4
Cabbage (carbohydrate range, 3 to 6%)	D	1	0	4
Chinese	D	1	0	2
Carrots (carbohydrate range, 6 to 11%)	D	1	0	8
Cauliflower	D	2	0	4
Celeriac	D	2	0	7
Celery	D	1	0	3
Chard, leaves only	D	3	0	4
Chayote (tayete) fruit	D	1	0	6
Chicory, leaves, Italian	D	2	0	2
Collards	D	4	1	6
Corn (green)	D	4	1	20
Cucumbers	D	1	0	2
Eggplant	D	1	0	5
Endive	D	2	0	3
Greens, beet, cooked	D	2	0	4
dandelion	D	3	1	7

TABLE 31.—VEGETABLES, FRESH (UNLESS OTHERWISE STATED).—(*Continued.*)

I. *Fresh*	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
Greens				
mustard	D	2	0	3
turnip tops	D	3	0	4
Garlic	D	4	0	19
Ginger	D	2	2	10
Kale	D	4	1	6
Kohlrabi	D	2	0	6
Lamb's quarters	D	4	1	6
Leeks	D	3	0	7
Lettuce	D	1	0	2
Mushrooms	D	0	0	0
Okra	D	2	0	6
Onions (carbohydrate range, 4 to 14%)	D	1	0	10
Orach	D	5	0	4
Oyster plant	D	4	1	14
Parsley	D	4	1	7
Parsnips	D	2	1	16
Peas, green, shelled	D	7	0	16
Peppers, red	D	1	0	7
sweet, green	D	1	0	4
Potatoes				
Raw	D	2	0	19
Cooked, chips	A	7	40	47
Sweet	D	2	1	27
Pumpkins	A	1	0	6
Radishes	A	1	0	4
Rhubarb	C	1	0	3
Rutabagas	D	1	0	8
Sauerkraut	A	2	1	4
Soy-beans, green, shelled	D	14	6	11
Spinach	D	2	0	3

TABLE 31.—VEGETABLES, FRESH (UNLESS OTHERWISE STATED).—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
I. *Fresh*				
Squash—Summer	D	1	0	3
Winter	D	2	0	7
Tomatoes, ripe	D	1	0	3
unripe	D	1	0	3
Turnips	D	1	0	6
Watercress	D	2	0	3
Yams	D	2	0	23
II. *Dried*				
Beans, navy	A	23	2	55
lima	A	18	2	66
Lentils	A	26	1	59
Peas	A	25	1	58
III. *Canned*				
Asparagus	A	2	0	2
Beans, string	A	1	0	3
wax	A	1	0	3
Corn	A	3	1	18
Peas	A	4	0	9
Tomatoes	A	1	0	4
IV. *Pickles, condiments, etc.*				
Catsup, tomato	A	2	0	12
Horseradish	A	1	0	11
Mustard, prepared	E	5	4	5
Olives, green	A	1	28	12
ripe	A	2	26	4
Pickles, cucumbers	A	1	0	3
Vinegar, cider	E	0	0	0
distilled	E	0	0	0
malt	E	0	0	1
Tarragon	E	0	0	0
wine	E	0	0	0

Table 32.—Fruits, Berries, Nuts, Etc.

I. *Fresh*	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
Apples	C	0	0	14
Apple juice	C	0	0	13
Apricots	C	1	0	12
Avocados (alligator pears), West Indian	C	1	8	7
South American	C	2	17	4
Bananas	C	1	0	22
Blackberries	C	1	1	8
Blackberry juice	C	0	0	7
Blueberries	C	1	1	14
Cherries, sour	C	1	1	13
sweet	C	1	1	17
Cranberries	C	0	1	10
Currants	C	2	0	10
Figs	C	1	0	18
Gooseberries	C	1	0	8
Grapefruit	C	1	0	10
Grapes, American	C	1	1	14
European	C	1	0	16
Grape juice, American	C	0	0	19
Huckleberries	C	1	1	14
Lemons	C	1	1	8
Limes	C	1	0	12
Lime juice	C	1	0	8
Logan blackberries	C	1	1	14
Mulberries	C	1	1	13
Muskmelons, all varieties	C	1	0	5
Nectarines	C	1	0	16
Oranges	C	1	0	11
Orange juice	C	0	0	9
Payayas	C	1	0	9
Papaws	C	5	1	17

TABLE 32.—FRUITS, BERRIES, NUTS, ETC.—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
I. *Fresh*				
Peaches	C	1	0	11
Pears	C	1	0	14
Persimmons, American	C	1	0	32
Pineapple	C	0	0	13
Pineapple juice	C	0	0	12
Plums, excluding prunes	C	1	0	12
Pomegranates	C	2	1	17
Prunes, fresh	C	1	0	21
Quinces	C	0	0	12
Raspberries, black	C	2	2	12
red	C	1	1	12
Rhubarb	C	1	0	3
Strawberries	C	1	1	7
Watermelons	C	1	0	6
II. *Dried*				
Apples	A	2	2	66
Apricots	A	5	1	63
Citron	A	1	2	78
Currants	A	2	2	74
Dates	A	2	3	78
Figs	A	4	0	74
Prunes	A	2	0	73
Raisins, seedless	A	3	3	76
III. *Nuts* (analyses are of edible portion)				
Almonds	E	21	55	15
Brazil nuts	E	17	69	5
Butternuts	E	28	61	4
Chestnuts	E	6	5	40
Cocoanuts—shredded	E	6	57	32
Filberts	E	16	65	13
Hickory nuts	E	15	67	11

TABLE 32.—FRUITS, BERRIES, NUTS, ETC.—(*Continued.*)

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
III. *Nuts* (analyses are of edible portion)				
Peanuts	E	26	39	22
Peanut butter	E	29	47	17
Pecans	E	10	71	15
Pistache	E	24	51	14
Walnuts, California English	E	18	64	12
Black	E	28	56	10
California soft shell	E	17	63	14

TABLE 33.—BEVERAGES.

I. *Alcoholic*				
Distilled liquors (whisky, gin, rum, brandy)	E	0	0	trace
Wines, dry (carbo. range, trace to 4%)	E	0	0	0
Wines, sweet (carbo. range, 0 to 41%)	E	0	0	8
Cordials (crème de menthe, kümmel, benedictine, anisette, chartreuse)	E	0	0	30
Beer, near (average of several brands)	E	0	0	5
Ale	E	0	0	5
Malt, extract, commercial	E	0	0	11
true, concentrated	E	0	0	71
Cider	E	0	0	5
II. *Other Beverages or Beverage Material*				
Carbonated drinks (bottled soda, sarsaparilla, birch beer, root beer, ginger ale)	E	0	0	8
Chocolate (as purchased)	E	12	52	25
Cocoa (as purchased)	E	18	27	38

TABLE 34.—CAKES, COOKIES, HONEY, JELLY.

	Source.	Protein, per cent.	Fat, per cent.	Carbohydrate, per cent.
I. *Cakes and Cookies*				
Sponge	E	6	11	66
Ginger snaps	E	7	9	75
Lady fingers	E	9	5	70
Macaroons	E	7	15	64
II. *Honey*	A	0	0	81
III. *Jelly, cherry*	A	1	0	77

TABLE 35.—JUNKET DESSERTS—JULLICUM.[1]

I. *Flavors*				
Almond	[1]	0	0	66
Butterscotch	[1]	0	25	22
Caramel	[1]	0	0	66
Chocolate	[1]	0	5	17
Coffee	[1]	0	0	33
Orange	[1]	0	0	44
Raspberry	[1]	0	0	48
Vanilla	[1]	0	0	44
II. *Plain, unflavored*		0	0	0

VITAMINS.[2]

Vitamin A (Anti-ophthalmic. Anti-infective).

I. *Function:*

Prevents xerophthalmia;
Promotes growth and longevity;
Increases body resistance to infection;
Promotes fertility and successful lactation.

[1] May be obtained from Samuel B. Kirk, 1724 Cayuga Street, Philadelphia. The values of this product are provided by the manufacturer.

[2] This summary is compiled largely from Pattee's Dietetics, 1933, through the courtesy of A. F. Pattee.

Vitamin A (Anti-ophthalmic. Anti-infective).—(*Continued.*)

II. *Source:*

Butter, cream, whole milk;
Whole milk powder;
Whole milk cheese;
Egg-yolk;
Fish oils (salmon, tuna, cod, halibut);
Liver and kidney;
Green leafy vegetables—spinach, chard, lettuce, escarole, kale, cabbage, etc.;
Yellow vegetables—carrots, sweet potatoes;
Tomatoes.

Vitamin B (Anti-neuritic. Anti-beri-beri).

I. *Function:*

Prevents beri-beri;
Promotes growth;
Stimulates appetite;
Aids in maintenance of gastro-intestinal tone and secretions;
Promotes fertility and successful lactation.

II. *Source:*

Eggs;
Yeast (dry, extract, powder);
Beans—kidney, navy, soy;
Peas, dried and fresh;
Whole milk;
Milk powder;
Whole grain cereals—wheat germ;
Vegetables;
Fruit.

Vitamin C (Anti-scorbutic).

I. *Function:*

Prevents scurvy;
Promotes growth;
Promotes good tooth and bone development;
Increases resistance to infection.

Vitamin C (Anti-scorbutic).

II. *Source:*

Citrus fruits—oranges, lemons, limes, tangerines, raw or canned grapefruit, apples, bananas;
Tomatoes, raw and canned;
Cabbage, raw;
Lettuce, cress;
Potatoes;
Commercially canned peas and spinach.

Vitamin D (Anti-rachitic).

I. *Function:*

Prevents rickets;
Promotes good tooth and bone development.

II. *Source:*

Fish oils (salmon, tuna, cod, halibut);
Egg-yolk;
Milk;
Butter;
Irradiated ergosterol.

Vitamin E (Anti-sterility).

I. *Function:*

Prevents nutritional sterility.

II. *Source:*

Wheat germ;
Lettuce;
Meat;
Whole grains.

Vitamin G (sometimes called Anti-pellagric).

I. *Function:*

Prevents condition similar to, if not identical with pellagra;
Promotes growth;
Aids in digestion;
Increases resistance to infection;
Improves health throughout life;
Increases longevity.

Vitamin G (sometimes called Anti-pellagric).—*(Continued.)*

II. *Source:*

Yeast (dry, brewer's);
Wheat germ;
Heart, liver and kidney;
Lean muscle meat;
Leafy vegetables;
Milk;
Egg.

NORMAL AVERAGE HEIGHTS AND WEIGHTS.

Tables of the average height and weight of members of both sexes of all ages over one year are presented on the following pages. While these figures provide a good guide they should not be adhered to rigidly. This is especially important in cases where individual characteristics such as unusually great musculature or large bones and, on the other hand, small muscles or small bones, justify a normal weight above or below the average, respectively.

TABLE 36.—HEIGHTS AND WEIGHTS OF CHILDREN BETWEEN ONE AND FOUR YEARS OF AGE (WITHOUT CLOTHES).[1]

5602 boys			4821 girls	
Height, inches.	Weight, pounds.	Age, months.	Height, inches.	Weight, pounds.
26.5	18.0	6	25.9	16.8
27.3	19.1	7	26.5	17.4
27.6	19.8	8	27.0	18.3
28.1	20.4	9	27.6	19.1
28.5	20.9	10	27.9	19.5
29.0	21.4	11	28.4	20.1
29.4	21.9	12	28.9	20.8
29.9	22.9	13	29.4	21.0
30.3	23.0	14	29.5	21.6
30.8	23.6	15	30.1	21.9
31.1	24.1	16	30.5	22.6
31.4	24.5	17	30.8	22.9
31.8	24.6	18	31.1	23.4
32.3	25.5	19	31.5	23.8
32.6	25.8	20	32.0	24.1
32.9	25.8	21	32.3	24.8
33.3	26.9	22	32.6	25.3
33.6	27.0	23	32.9	25.6
33.8	27.1	24	33.4	26.4
34.0	27.9	25	33.8	26.9
34.1	28.3	26	33.9	27.3
34.8	29.0	27	33.9	27.3
35.1	29.1	28	34.6	27.8
35.4	29.3	29	34.8	27.8
35.4	29.5	30	34.9	28.3
35.5	30.5	31	35.1	28.8
36.0	30.6	32	35.4	29.0
36.1	30.6	33	35.6	29.1
36.5	31.1	34	36.5	30.1
36.8	31.9	35	36.5	30.3
37.1	32.3	36	36.8	30.5
37.4	32.3	37	36.8	30.8
37.5	32.4	38	37.0	31.0
37.9	33.1	39	37.3	31.6
38.5	33.5	40	37.5	32.0
38.6	33.6	41	37.8	32.3
38.6	33.8	42	38.0	32.5
38.8	33.8	43	38.3	32.8
38.9	34.3	44	38.5	33.0
39.0	34.5	45	38.5	33.5
39.0	34.8	46	38.8	33.5
39.3	35.8	47	38.9	33.5
39.5	35.9	48	39.0	33 8

[1] Crum, F. S.: Quarterly Publication of the American Statistical Association, Boston, September, 1916, N. S., No. 115, **15**, 332.

TABLE 37.—HEIGHTS AND WEIGHTS OF BOYS BETWEEN FIVE TO FOURTEEN YEARS OF AGE (WITHOUT CLOTHES).[1]

BOYS

Weight in Pounds — Without Clothes

Height in Feet and Inches — Without Shoes

AGE	3-3	3-4	3-5	3-6	3-7	3-8	3-9	3-10	3-11	4	4-1	4-2	4-3	4-4	4-5	4-6	4-7	4-8	4-9	4-10	4-11	5	5-1	5-2	5-3	5-4	5-5	5-6	5-7	5-8	5-9	5-10	5-11	6	6-1
5	35	38	39	41	42	46																													
6		38	39	41	42	44	48	48																											
7					42	43	46	48	49	54																									
8							45	48	50	53	54	57	59																						
9									50	53	55	58	60	62	62	65																			
10										53	55	58	60	62	65	68	69	71																	
11													61	61	65	68	71	77	77	78															
12													63	67	70	75	76	79	84	84	85														
13														67	71	75	78	80	85	86	91	98	99	100											
14														67	71	76	79	82	86	90	94	97	103	107	114	122									
15																	79	82	87	91	95	99	106	112	118	119	121	128	133						
16																					90	98	104	112	120	122	125	129	133	134	136				
17																							104	110	117	122	125	128	130	136	140	140			
18																								115	120	120	126	131	136	139	143	146			
19																									120	126	129	134	136	139	144	146	149		
20																										125	130	132	136	139	145	148	154	165	

TABLE 38.—HEIGHTS AND WEIGHTS OF GIRLS BETWEEN FIVE TO FOURTEEN YEARS OF AGE (WITHOUT CLOTHES).[1]

GIRLS

Weight in Pounds — Without Clothes

Height in Feet and Inches — Without Shoes

AGE	3-3	3-4	3-5	3-6	3-7	3-8	3-9	3-10	3-11	4	4-1	4 2	4-3	4-4	4-5	4-6	4-7	4-8	4-9	4-10	4-11	5-0	5-1	5-2	5-3	5-4	5-5
5	34	37	38	41	41	45																					
6	35	37	39	41	43	45	48																				
7			39	42	44	45	47	50																			
8					42	45	47	49	51	53	56																
9								49	51	53	56	59	63														
10										54	57	58	62	64	69												
11												60	62	63	68	70	75										
12													63	66	69	71	75	78	83	88	94						
13														65	68	73	76	80	86	89	94	99	104				
14																	78	83	88	93	96	100	104	107	112	114	
15																			89	97	100	102	106	109	118	118	
16																				100	104	109	111	116	116	121	
17																					109	109	110	110	117	125	
18																					103	108	107	112	114	120	
19																					99	105	111	113	119	123	
20																					99	111	114	114	115	125	

[1] Wood, T. D.: The ninth yearbook of the National Society for the Study of Education, Part I, Health and Education, Chicago, 1910, p. 34.

TABLE 39.—HEIGHTS AND WEIGHTS OF 221,819 MEN FIFTEEN OR MORE YEARS OF AGE (WITH CLOTHES).[1]

Age.	Graded average weight in pounds with clothes.																	
	Feet and inches with shoes.																	
	5–0	5–1	5–2	5–3	5–4	5–5	5–6	5–7	5–8	5–9	5–10	5–11	6–0	6–1	6–2	6–3	6–4	6–5
15	107	109	112	115	118	122	126	130	134	138	142	147	152	157	162	167	172	177
16	109	111	114	117	120	124	128	132	136	140	144	149	154	159	164	169	174	179
17	111	113	116	119	122	126	130	134	138	142	146	151	156	161	166	171	176	181
18	113	115	118	121	124	128	132	136	140	144	148	153	158	163	168	173	178	183
19	115	117	120	123	126	130	134	138	142	146	150	155	160	165	170	175	180	185
20	117	119	122	125	128	132	136	140	144	148	152	156	161	166	171	176	181	186
21	118	120	123	126	130	134	138	141	145	149	153	157	162	167	172	177	182	187
22	119	121	124	127	131	135	139	142	146	150	154	158	163	168	173	178	183	188
23	120	122	125	128	132	136	140	143	147	151	155	159	164	169	175	180	185	190
24	121	123	126	129	133	137	141	144	148	152	156	160	165	171	177	182	187	192
25	122	124	126	129	133	137	141	145	149	153	157	162	167	173	179	184	189	194
26	123	125	127	130	134	138	142	146	150	154	158	163	168	174	180	186	191	196
27	124	126	128	131	134	138	142	146	150	154	158	163	169	175	181	187	192	197
28	125	127	129	132	135	139	143	147	151	155	159	164	170	176	182	188	193	198
29	126	128	130	133	136	140	144	148	152	156	160	165	171	177	183	189	194	199
30	126	128	130	133	136	140	144	148	152	156	161	166	172	178	184	190	196	201
31	127	129	131	134	137	141	145	149	153	157	162	167	173	179	185	191	197	202
32	127	129	131	134	137	141	145	149	154	158	163	168	174	180	186	192	198	203
33	127	129	131	134	137	141	145	149	154	159	164	169	175	181	187	193	199	204
34	128	130	132	135	138	142	146	150	155	160	165	170	176	182	188	194	200	206
35	128	130	132	135	138	142	146	150	155	160	165	170	176	182	189	195	201	207
36	129	131	133	136	139	143	147	151	156	161	166	171	177	183	190	196	202	208
37	129	131	133	136	140	144	148	152	157	162	167	172	178	184	191	197	203	209
38	130	132	134	137	140	144	148	152	157	162	167	173	179	185	192	198	104	210
39	130	132	134	137	140	144	148	152	157	162	167	173	179	185	192	199	205	211
40	131	133	135	138	141	145	149	153	158	163	168	174	180	186	193	200	206	212
41	131	133	135	138	141	145	149	153	158	163	168	174	180	186	193	200	207	213
42	132	134	136	139	142	146	150	154	159	164	169	175	181	187	194	201	208	214
43	132	134	136	139	142	146	150	154	159	164	169	175	181	187	194	201	208	214
44	133	135	137	140	143	147	151	155	160	165	170	176	182	188	195	202	209	215
45	133	135	137	140	143	147	151	155	160	165	170	176	182	188	195	202	209	215
46	134	136	138	141	144	148	152	156	161	166	171	177	183	189	196	203	210	216
47	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
48	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
49	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
50	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
51	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	205	212	218
52	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	205	212	218
53	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	205	212	218
54	135	137	139	142	145	149	153	158	163	168	173	178	184	191	198	205	212	219
55	135	137	139	142	145	149	153	158	163	168	173	178	184	191	198	205	212	219

[1] Association of Life Insurance Directors and Actuarial Society of America, New York, 1912, p. 38. Published by a committee. Allow 1 inch for shoes and 10 pounds for clothes.

TABLE 40.—HEIGHTS AND WEIGHTS OF 136,504 WOMEN FIFTEEN OR MORE YEARS OF AGE (WITH CLOTHES).[1]

Age.	Graded average weight in pounds with clothes.																
	Feet and inches with shoes.																
	4–8	4–9	4–10	4–11	5–0	5–1	5–2	5–3	5–4	5–5	5–6	5–7	5–8	5–9	5–10	5–11	6–0
15	101	103	105	106	107	109	112	115	118	122	126	130	134	138	142	147	152
16	102	104	106	108	109	111	114	117	120	124	128	132	136	139	143	148	153
17	103	105	107	109	111	113	116	119	122	125	129	133	137	140	144	149	154
18	104	106	108	110	112	114	117	120	123	126	130	134	138	141	145	150	155
19	105	107	109	111	113	115	118	121	124	127	131	135	139	142	146	151	155
20	106	108	110	112	114	116	119	122	125	128	132	136	140	143	147	151	156
21	107	109	111	113	115	117	120	123	126	129	133	137	141	144	148	152	156
22	107	109	111	113	115	117	120	123	126	129	133	137	141	145	149	153	157
23	108	110	112	114	116	118	121	124	127	130	134	138	142	146	150	153	157
24	109	111	113	115	117	119	121	124	127	130	134	138	142	146	150	154	158
25	109	111	113	115	117	119	121	124	128	131	135	139	143	147	151	154	158
26	110	112	114	116	118	120	122	125	128	131	135	139	143	147	151	155	159
27	110	112	114	116	118	120	122	125	129	132	136	140	144	148	152	155	159
28	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160
29	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160
30	112	114	116	118	120	122	124	127	131	134	138	142	146	150	154	157	161
31	113	115	117	119	121	123	125	128	132	135	139	143	147	151	154	157	161
32	113	115	117	119	121	123	125	128	132	136	140	144	148	152	155	158	162
33	114	116	118	120	122	124	126	129	133	137	141	145	149	153	156	159	162
34	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163
35	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163
36	116	118	120	122	124	126	128	¶131	135	139	143	147	151	155	158	161	164
37	116	118	120	122	124	126	129	132	136	140	144	148	152	156	159	162	165
38	117	119	121	123	125	127	130	133	137	141	145	149	153	157	160	163	166
39	118	120	122	124	126	128	131	134	138	142	146	150	154	158	161	164	167
40	119	121	123	125	127	129	132	135	138	142	146	150	154	158	161	164	167
41	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	165	168
42	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	166	169
43	121	123	125	127	129	131	134	137	140	144	148	152	156	160	163	167	170
44	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171
45	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171
46	123	125	127	129	131	133	136	139	142	146	150	154	158	162	165	169	172
47	123	125	127	129	131	133	136	139	142	146	151	155	159	163	166	170	173
48	124	126	128	130	132	134	137	140	143	147	152	156	160	164	167	171	174
49	124	126	128	130	132	134	137	140	143	147	152	156	161	165	168	172	175
50	125	127	129	131	133	135	138	141	144	148	152	156	161	165	169	173	176
51	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
52	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
53	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
54	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177
55	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177

[1] Association Life Insurance Directors and Actuarial Society of America, New York, 1912, p. 67. Published by a committee. Allow 1½ inches for shoes and 6 pounds for clothes.

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