1935

The quantitative relationship between calcium, cholesterol, phosphorus, sugar, and plasma proteins in diabetic blood

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Graduate School
Thesis
The Quantitative Relationship between Calcium, Cholesterol, Phosphorus, Sugar, and Plasma Proteins in Diabetic Blood.
by
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(B. S. in Ed., State Normal School at Framingham, 1927)
submitted in partial fulfilment of the requirements for the degree of Master of Arts 1935
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proteins, and cholesterol occurring in the blood of diabetic patients, with the blood tests to be varying tests. These levels are to be determined by both pure and complicated cases, with the hope of discovering any deviations from normal or change in relationships, caused by the disease or the co-existing illnesses. Furthermore, I wish to examine the effect of these deviations on the other usual complications of diabetes.

There are but few records in the literature of such studies on diabetic patients, although many on normals or in other disease conditions, in which these factors are studied, indicates the possibility of interesting relationships. One cholesterol level is possibly an exception, since Behinowitch (34), Joslin and his associates (35), and Ricor and co-workers (31) have made intensive surveys on its connection with blood sugar, and Rosenthal (30) has done some experimental work bearing on this problem. Peters and his associates have studied blood proteins in patients with diabetes.
Statement of Problem.

The purpose of this study is to determine the amounts of serum calcium, inorganic phosphorus, plasma proteins, and cholesterol occurring in the blood of diabetic patients, when the blood sugar is at varying levels. These levels are to be determined in both pure and complicated cases, with the hope of discovering any deviations from normal or change in relationships, caused by the diabetes or the co-existing disease. Furthermore, I wish to evaluate the effect of these variations on some of the usual complications of diabetes.

There are but few records in the literature of such studies on diabetic patients, although work on normals or in other diseased conditions, in which these factors are changed, indicates the possibility of interesting relationships. The cholesterol level is possibly an exception, since Kabinowitch (45), Joslin and his associates (23), and Bloor and co-workers (4) have made intensive surveys on its connection with blood sugar, and Mosenthal (33) has done some experimental work bearing on this problem. Peters and his associates have studied blood proteins in patients with diabetes
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and found that their concentration varies with the state of hydration in the blood (44), and Sunderman, Austin, and Williams have found that massive doses of insulin given to fasting diabetic persons, caused a drop in the amounts of inorganic phosphorus and cholesterol (51). Wiener and Wiener, in a study of plasma proteins in many diseases, give calcium, protein, and cholesterol values for a series of diabetics (58). They show protein levels within normal limits in uncomplicated cases but a changed ratio of the protein fractions in infection, high normal or slightly increased calciums, and cholesterol mostly within normal limits.

Experimental work on other than diabetic people suggests possible changes in the levels of these constituents. Taubenhaus and Steinig found a variation of proteins with glucose ingestion (52), while Greenberg and Gunther (18), Darrow, Hopper, and Cary (11), and Peters and Riserson (43) found direct relationship between calcium and protein. The administration of glucose or glucose and insulin causes a drop in phosphorus and a rise in calcium (13), (30), while Peters and Riserson discovered that along with the phosphorus balance the concentration of the calcium varies directly with the concentration of
the protein (43). Stearns and Knowlton found a lack of relationship between these three in normal children (50). With this information in mind, it will be of interest to determine whether in the diabetic, with a mounting hyperglycemia, there will be a lowered phosphorus and an increased calcium or whether he will react more nearly as did Markowitz's depancreatized dogs (30). These and other suggestions, such as the cholesterol and protein levels, the relation of proteins to edema, etc., indicate an extensive field for study.

*These dogs did not show the usual reduction in urinary phosphates found in normal dogs following the ingestion of glucose (30).
Procedure.

Blood studies were done on an unselected group of out-patients sent from the diabetic clinic. These included cases of complicated and pure diabetes and those with and without insulin medication. All the patients when studied were in a fasting condition and insulin cases came without the morning dose. An attempt was made to do more than one series on each case so that it would be possible to watch relationships with the blood sugar at varying levels. In two instances there was an opportunity to determine some of these factors during a glucose tolerance test.

Samples of 25-30 cc. of blood were taken, and the following determinations made: sugar, non-protein nitrogen, plasma proteins (fractioned), plasma cholesterol, serum calcium, inorganic phosphorus, blood cell count and hemoglobin to detect any anemia, and plasma volume % to show the state of hydration. The sugars and non-protein nitrogens were done by the

#The inorganic phosphorus determinations were made on serum in all but a few cases in which plasma was substituted.
Folin-Wu method (16). The plasma proteins were fractioned by a modification of Howe's method (21), but after digestion, the ammonia was distilled into N/50 HCl and titrated with N/50 NaOH rather than nesslerized. Bloor's method for cholesterol (5), the Kramer-Tisdall method for serum calcium (26), and the Benedict and Theis method for inorganic phosphorus (21) were used. The hemoglobins were determined on a Haden-Hausser hemoglobinometer and Haden's standard of 15.4 gm. equal to 100 % utilized in calculating the percentage (20). Plasma volume % was found by centrifuging a known amount of blood in a graduated tube and calculating the per cent. All values unless otherwise indicated are in mg. per 100 cc.

A study of the patients' records was made to aid in evaluating the results. The history, physical examination card, and reports of calls at the clinic were read to give a knowledge of the general physical condition, the diet in use, the insulin dosage if any, complicating conditions or diseases, and any other factors of importance.

A routine examination of the urine was also carried out to detect the presence of glycosuria, acidosis,
kidney involvement, or any other abnormalities shown here.

The combined study of the blood findings, case records, and urine examination gives a fairly well defined picture of the condition of the patient.
### Results of Blood Studies

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- **M** = male patient.
- **F** = female patient.
- *p* = patient on insulin medication except at time.
- † = patient not in fasting state.

**Remarks:**
- Increased Icteric Index 30 - glycosuria - slight acetonuria.
- Varicose veins - glycosuria 1 %.
- Icteric Index 30 - diet often inadequate - poor nutrition - in second study recovering from coryza and congested ear.
- Albuminuria - recovering from gastric upset.
- Hyaline casts.
- Glycosuria - abdominal pain, cause not determined.
- Glycosuria - sl. kidney involvement a few months ago.
- Many dietary irregularities.
- Polyuria - glycosuria - albuminuria - controlled syph.
- Acrongeal features - Scant. pit. 7 yr., post. pit. lry.
- Polyphagia - polydipsia - polyuria - glycosuria - mercury treatment for syphilis.
- Sl. albuminuria - careless about diet - recovering from coryza - hypertension - early hypertensive arthritis.
- Albuminuria - coryza - arteriosclerosis - calcified aortic ring - senescent heart.
- Rather persistent glycosuria - acetonuria - albuminuriasome dietary irregularities.
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### Patient I - 100 gm. Glucose.

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<td>1 hr.</td>
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<td>27.2</td>
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<td>7.09</td>
<td>.857</td>
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<td>9.2 65.9</td>
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Records show: Woman, 60 yrs. of age. Hypertension case.
Hemoglobin 73% - slight albuminuria - occasional glycosuria.
History of Diabetes Mellitus of ten years duration
Controlled by diet.

### Patient II - 100 gm. Glucose.

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<td>11.6 52.8</td>
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<tr>
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<td>30.0</td>
<td>9.850</td>
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<td>28.4</td>
<td>8.256</td>
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<td>8.6 53.4</td>
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</table>

Records show: Woman about 50 yrs. of age.
Hemoglobin 86 - glycosuria - albuminuria.
History of Diabetes Mellitus of 9-10 years duration.
Heart involvement - probably early myocardial impairment due to coronary thrombosis.
No regular diet at time of study.
<table>
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<th>Patient I - 700 mm. Hg.</th>
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1. Blood Sugar in mg. per 100 cc.
2. Plasma Volume %.
3. Plasma Proteins %.
4. Serum Calcium in mg. per 100 cc.
Results of Blood Studies.

The detailed account of each study is listed in the adjoining charts and graphs, which when interpreted, tend to explain some of the questions set forth in the earlier part of the paper. Before attempting to evaluate these data, we should consider the type of patient studied. Perhaps cases 1, 3, 5, 10, 13 might be classed as the true pancreatic type of diabetes and most of the rest as the senile or mild form found in middle and late life. From these two groups we may expect some difference in reaction since in that of old age there is probably loss of sugar tolerance through poor utilization rather than entirely through lack of available insulin. The fasting blood sugar levels would suggest poor control in some cases, but it must be remembered that this group is composed of out-patients, who come to the clinic only about once a month or at longer intervals, in most cases, and who are in general very poor, in fact some cannot buy insulin and find it difficult to obtain the proper diet. Others, as you will note, are very negligent about keeping their diets. Also in the cases under insulin medication hyperglycemia would prevail since the last dose
Page 10

Features of Brain Growth

The cerebral cortex of an early fetus is largely in the
state of differentiation and change, making new interpretations
to apply to some of the concepts and features of the living
brain. The role of the brain...
of insulin was taken at least 14-15 hours prior to the
time of study, whereas the maximum effect of insulin
takes place in about 3-6 hours normally. Complications
such as obesity, infection, hyperfunction of the
pituitary, etc. undoubtedly alter the glycemic level in
some of the patients (55), (56).

The type of diet in use should also be mentioned
here. A standard diet of 1700 calories, carbohydrates
73 gm., proteins 67 gm., fats 127 gm. was used as a basis
and modified in some instances where not tolerated.

Most of the values reported are within normal limits
but when examined for small variations yield some
information not seen at first glance. A majority of the
plasma protein levels, ranging from 7.53-9.14 % (serum
proteins where no fibrinogen is reported), are within
high normal limits according to the ordinary standards of
6.5-8.2 % used by Hawk and Bergeim (21), and all but one
within the upper limit if the figures of 5.5-9 % of
Osgood and Haskins (39) are utilized. They are all much
higher than the normal range of 5.6-6.9 % as given by
Wiener and Wiener (58). This seems to be due in part to
the state of hemoconcentration in many of my cases, as
shown by the plasma volume % and high hemoglobin and
erythrocyte count. Wieners' cases show the plasma volume from 53-64 % with many in the upper levels (58). The normal limits of fibrinogen are given by Hawk and Bergeim to be .3-.6 % (21), by Osgood and Haskins .2-.4 % (39), and by Wiener and Wiener .22-.28 % for males, for females .25-.33 % (58). From this it is seen that the majority of my values tend to be high, and in nearly half of the cases increased even above the high normal given by Hawk and Bergeim (21). The normal range for albumin is generally quoted as 4.6-6.7 % (21), although Wiener and Wiener offer 4.2-5 % (58), the globulin values 1.2-2.3 % (21), 1.3-3.3 % (39), 1.5-1.9 % (58), and the albumin-globulin quotient at 2.2-3.3 (58). Thus it is easily seen that while the albumin and globulin values on these patients may lie within the extreme limits of this range, there is a tendency toward a low albumin and a high normal or increased globulin which makes the ratios much lower, but which can be explained in part, by the complicating factors. The plasma proteins, for the most part, are in inverse proportion to the degree of hydration. This is also true of the albumin fraction when determined on a series on the same individual, although Lepore (28) has shown, with his dogs, that they
vary directly with the blood volume. Chang (9) too, found that in patients with edema from nephrosis or malnutrition that the plasma proteins and blood volume run in parallel. Peters, Kydd, and Eisenman (44) seem to agree with my findings when they suggested that the high protein concentration of the blood, found in diabetic acidosis, was due to hemoconcentration. In a series of tests on the same patient, the plasma proteins vary inversely with the sugar, since hyperglycemia induces relative hydremia and the proteins vary inversely with the state of hydration.

The serum calcium and inorganic phosphorus, since they are so closely related, may be studied together. The ordinary normal for calcium is given as 9-11 mg. by Nicholson (37), 9-14 mg. by Osgood and Masek (39), Boynton males 10.3 mg., females 10.01 mg. (6), and Mull and Bill females 10-11.5 mg. (34). The phosphorus levels are taken as 3-4 mg. by Hawk and Bergeim (21), 2.5-4.5 mg. by Todd and Sanford (53), and by Mull and Bill, for women under 30 years 3.2-4.4 mg. and for women over 30 years 2.6-4.2 mg. (35). My calcium results are, for the most high normals which is in agreement with Wieners' work (58). Inorganic phosphorus also is within normal limits in my
many filaments with the strongest affinity for the chromosomal proteins.

To understand the nature of these interactions, we examined the relationship between
the number of filaments and the concentration of the chromosomal proteins.

We found that as the concentration of the chromosomal proteins increased, the number of filaments also increased.

This result suggests that the chromosomal proteins are not simply bound to the DNA, but that they form a complex with the DNA.

The exact nature of this complex is not yet clear, but further studies are underway to elucidate this aspect of the chromatin structure.
cases. There seems to be only slight correlation of calcium with the protein, contrary to some other reports (43), but this fact rather agrees with the views of Stearns and Knowlton, who found a lack of relationship between them in normal children (50). The inverse proportion of calcium and phosphorus described by Peters and Eiserson (43) is corroborated by my work in most cases.

Part of the cholesterol values fall within the upper limits of normal and the rest are slightly increased when judged by Joslin's normal range of 125-230 mg. (23) but by most standards they are too high (39), (37). Rabinowitch considers 180 mg. the top level of normality in his series of cases (45). Since both Joslin (23) and Rabinowitch (45) regard the cholesterol content as an index of the control of the patient's diabetic condition, these patients of ours, despite the high blood sugars, show a fair, although not perfect, degree of adjustment. There seems to be no close correlation between the blood sugar and the cholesterol which is what Mosenthal proved in his tolerance tests (33), although Joslin believes that there is in the mild cases (23). Another possible correlation might be the compensatory rise in cholesterol when there is a low protein value in lipemia. Rabinowitch attributes this
The text on the page appears to be a excerpt from a legal or formal document, discussing legal or administrative matters. The text is not clearly legible due to the quality of the image.
concept to Fishberg, but, himself, believes that cholesterol may aid in increasing osmotic pressure through increasing the permeability of the cell membranes rather than by exerting a pressure of its own (47). While patients 3 and 5 are not in a state of lipemia, there is a definite correlation of the proteins and cholesterol level.

Some of the apparent abnormalities of these cases may be explained through the medium of the experimental work of others. First, when glucose or glucose and insulin are injected in normal people, the phosphorus drops and the calcium rises, due to some part the stimulation of insulin plays, probably causing the formation of hexose-phosphate in the muscle (13). The principal effect is in the phosphorus, and the calcium is a secondary compensatory factor. The same takes place with the ingestion of only glucose but there is a delay due to the necessity of first stimulating the insulin production with the glucose and then the phosphorus and calcium phenomenon takes place (13). Markowitz has attempted to do this with depancreatized dogs with little or no success although he studied the change in urinary phosphates rather than in the blood (30). We may apply
The text on the page is not legible or clear enough to transcribe accurately. It appears to be a continuous line of text, possibly a paragraph or a set of instructions, but the characters are not legible due to the quality or condition of the image.
the calcium-phosphorus theory to the diabetics, but fortunately their pancreas is still partly functional, so that the continuous hyperglycemia may stimulate some insulin production in varying degrees and so lower the phosphorus. This coincides fairly closely with our results and accounts for the persistently high calciums found both in this study and in that of Wiener and Wiener (58). In patient 3 the apparent reversal may be explained by the fact that in the second study the patient had a cold and congested ear, which apparently lowered his sugar tolerance, as shown by the increased glycemias. Infection is accompanied by a lowered ability to utilize insulin, both natural and injected, so that the lessened insulin effect failed to lower the phosphorus and therefore there was no compensatory rise of calcium.

In case 10 the sugar tolerance is very low, and the diabetes is not well controlled. This is accounted for by the fact that patient 10 is a new case recently referred to the clinic. Furthermore, the patient has syphilis, and Wiener and Wiener have found that syphilitics have a low albumin-globulin quotient (58). That was found to be true in this case. It indicates an infectious reaction which would also affect the insulin usage.
Patient 13 also appears to be rather poorly controlled and so has a low glucose tolerance with a probable defective insulin mechanism. Therefore we do not see the decided drop in phosphorus in these. Note that cases 10, 13, and 3 belong to the group of acute diabetics, rather than the senile type, which indicates a real insulin deficiency, but case 3, being an insulin treated patient, has acquired the characteristic low phosphorus level. All the insulin patients listed here show a high level of calcium, which is indicative of this phenomenon. In 6F this rise in calcium might be explained as due to the stimulation of insulin production by the food. (14)

In case 5 F the change in the albumin-globulin ratio may be due to some obscure infectious process since she is referred to another clinic for a diagnosis of abdominal pain.

In cases 7 and 8 the hemoconcentration seems almost the only apparent cause for such high protein values. The low albumin-globulin ratios of cases 11 and 12 appear to be due to the effects of upper respiratory infections, which fact is in agreement with the findings of Wiener and Wiener (58).
The two glucose tolerance tests do not prove a great deal as they are incomplete, but they do suggest a parallelism between the level of blood sugar and the degree of hydration, which in turn is inversely proportional to the plasma proteins. The calcium figures are not conclusive, but the variation is probably due to the difference in sugar tolerance. The low albumin-globulin ratio in Patient II may possibly be attributed to the cardiac lesion as the albumin is often low in such cases (40).

Although this work is highly suggestive, more extensive study is needed to furnish conclusive proof. Not all of these cases reported here are complete, due in some to lack of sufficient blood, or in others to hemolysis in a sample, etc. More studies on each patient for comparison are required. Then, too, work on hospitalized cases will yield material from patients more completely under control. As time permits more glucose tolerance tests and some insulin tolerance tests will be carried out to show the effect on these blood constituents.
The need for accurate reference texts is of vital importance. A poor or faulty reference may lead to incorrect or misleading conclusions. Therefore, it is essential to ensure the accuracy and reliability of the reference used. Any reference material should be cross-verified to confirm its accuracy. The reference should be relevant and up-to-date. It should be comprehensive and provide a clear understanding of the topic. The reference should also be credible, coming from reputable sources. Any information obtained from the reference should be cross-checked with other sources to ensure its validity.
Organization of Material.

The significance of the calcium and phosphorus levels is so closely related it seems advisable to discuss them together. In this study the calcium and phosphorus levels are in inverse ratio in the patients on insulin medication and patients with some degree of tolerance, which of course is at variance with the work of Markowitz on depancreatized dogs as these dogs had lost all tolerance for glucose (30). The effect of hyperglycemia or glucose and insulin medication causes a drop in phosphorus and increase in calcium in the majority of cases as in the experimental work of many others (13), (14), (39), (43). This is particularly outstanding in that most of the values for calcium are high normals in both mine and Wieners' (58). Cowan and Wright working on experimental hyperglycemia in dogs, found an increase in calcium following sugar rise, rather than simultaneously (10). These fixed ratios do not always hold, even without the problem of sugar tolerance, as shown by Stearns and Knowlton in non-nephritic children (50), by Osgood and Haskins, when they pointed out a high phosphorus level in nephritis (39), by Farquharson and Ribbetts when they showed a temporary change after food ingestion (14), and
The importance of the clinical and occupational environments is on occasion overlooked. If there is little objective evidence of change,

and observations to date indicate the need to maintain our attention on the potential importance of these factors. In addition to the need for awareness of the role of environment in occupational performance and productivity, there is a need to ensure that the workplace is safe and healthy.

In the case of performance (26), the effects of physical and mental stress on performance and productivity are significant. In these cases, it is important to consider the potential impact of these factors in order to improve performance and productivity. The role of the workplace in facilitating the development of skills and the promotion of health and well-being cannot be underestimated (27). These include factors such as job satisfaction, job control, and social support.

The importance of the socio-economic and cultural factors in the workplace cannot be overlooked (28). In addition to the need for awareness of the role of environment in occupational performance and productivity, there is a need to ensure that the workplace is safe and healthy.
by Greenwald, when he tried to make a definite formula for the ratio of calcium, phosphorus, and proteins (19). Greenberg and another believe that the diffusible or ionized calcium is the part linked to the phosphorus (18).

Other men have put a different interpretation on the action of insulin on calcium. Nalib found either a rise or a fall in calcium when insulin was administered to rabbits (43). He also found a lowering of the calcium in hypoglycemic shock and believes that convulsions from this cause stand in etiological relation to calcium variation produced by insulin. Langeron and associates in France, in calcium balance experiments, claim a decalcifying action for insulin (27).

Högl er and Zell sought to determine if parathormone would affect both calcium and sugar since they often move in parallel (22). However parathormone had no effect on sugar metabolism other than to enhance, occasionally, the effect of insulin in animals not otherwise susceptible.

Another possible correlation of sugar and calcium, of doubtful value, lies in the relationship of guanidine, sugar, and calcium levels. Synthalin, a guanidine derivative, has been used to lower blood sugar level (54), and Andes and Meyers report an increase of guanidine in some
parathyroid tetany where there is a low calcium (1). Thus both low sugar and calcium are compatible with increased guanidine content, and Minot and Cutler state that calcium will raise the blood sugar in guanidine poisoning (32), while previously cited references found a rise in calcium value with glucose increase.

Berlinger has advocated the use of calcium salts in heart disease. He includes a review of the work of several men who have attempted to attribute the calcium effect to a stimulation of the sympathetic or vagus nerves (3). The best hypothesis seems to be that calcium is amphoteric, since there has been so much variation in its action. In small doses it is sympathomimetic and tends toward a condition of hypertension, hyperglycemia, etc. In larger doses it acts in the same way as does a stimulation of the vagus causing hypoglycemia. Brachomejew reports that vagus stimulation depresses the blood sugar but does not change the calcium (7). Also Santenoise and Vidacovitch treat their patients with "vagotonine" and find that it lowers the blood sugar (49), while Friedenwald and Feldman working on vagotomized dogs found no constant change in sugar metabolism (17). If the vagus does affect the blood sugar, and the calcium in large doses
simulates vagus stimulation, is the beneficial effect of calcium directly through nerve stimulation, or does it increase the glucose and develop superior nutrition when used in heart disease? Conversely, does the helpful action of a high carbohydrate diet in heart disorders (46) act through improving nutrition entirely, or by causing increased calcium which acts directly on the organ?

In the cases studied here there seems to be little relationship between calcium and protein levels, although Fishberg states a definite ratio between calcium, protein, and phosphorus (15), and Darrow, Hopper, and Cary state that calcium and proteins vary directly (11), while others feel that they are not always proportional (50), (31). Greenberg goes one step further and links the non-diffusible inert calcium with the proteins and the diffusible calcium with the phosphorus (18).

The cholesterol determinations done on my patients lie slightly above the normal limits in the majority of the cases. Since Joslin (23), Rabinowitch (45), and Nicholson (37) all believe that the height of cholesterol parallels the control of the disease and is perhaps a better index than the blood sugar, an examination of the levels in the patients here shows a fairly high average
for the type of patient studied. They believe a high cholesterol indicates a faulty fat metabolism or infection. Mosenthal by tolerance tests found that cholesterol does not necessarily parallel blood sugar, but varies often inversely (33). Sunderman, Austin, and Williams found that a fall in glucose from insulin caused a fall in cholesterol (51).

Diet is an important factor in controlling the level of cholesterol in the blood. Okey and Stewart studied the effects of feeding a diet high in cholesterol to normals and found the total and free cholesterol content higher than with the control diet (38). Joslin stresses the damage done by a high fat diet and believes the lowered cholesterol in patients of the past few years a result of a leaning toward a higher carbohydrate-low fat diet (23). He believes a high fat diet injures the sugar tolerance and if persisted in may cause fatty infiltration of the liver (23). Rabinowitch too is highly in favor of high carbohydrate diets if the patient is carefully controlled and the fat content kept low (46).

The importance of the relation of protein and cholesterol lies in its effect on colloid pressure. Fishberg states that with the fall of proteins and the
consequent lowering of the osmotic pressure there is a rise of serum lipids to compensate, and in the lipemic blood the osmotic pressure per gram of protein is higher (15). Mosenthal in discussing the relation of cholesterol to the osmotic pressure believes the inverse ratio of blood sugar and cholesterol is to help to preserve this equilibrium (33). Rabinowitch in his explanation of the cholesterol effect on this pressure suggests that lipoids act by reducing the permeability of the cell membranes and so facilitating the passage of fluid. He adds that in lipemic blood the general hydrostatic pressure is greater. In edema there is often a high cholesterol (47).

Another very important relation of the cholesterol content is its probable role in the causation of arteriosclerosis. Bloor and his co-workers (4), Rabinowitch in 1933 (45), and Joslin in several papers (23), (24), (25) all feel that there is a very close parallelism between a high cholesterol and the high incidence of sclerotic changes and warn against the high death rate from this cause now that the diabetic has been rescued from a coma death. The solution seems to be careful control and a normal cholesterol limit.

The plasma proteins from these patients studied show
a high normal level, which seems to be due to the hemoconcentration of most of the bloods. Many of the albumin-globulin ratios are rather low, but that is undoubtedly due to the presence of various types of infections such as coryza, which Wiener and Wiener have said will have such an effect. (58). They also state that there is generally an increase in fibrinogen during infection. These fraction levels in infection are possibly due to changes in permeability of the capillaries because of disease. Variation in size of the different protein molecules accounts for the retention of some and loss of others, as, for example, the albumin is smaller and so possibly goes first, or as in nephrosis, increased permeability releases additional fibrinogen and cholesterol. These men mention Sorensen's theory of the addition of pseudoglobulin and lipid to give the fraction known as euglobulin. Twoensgaard and Koendahl are also quoted as assigning great importance to the cholesterol-globulin linkage and ascribing the greater viscosity of euglobulin to the lipid addition.

The relation of protein to sugar levels in the bloods of single patients does show some coordination, as shown in the glucose curves, but the general levels of the group
are not necessarily proportional. Comparing this with experimental glycemia let us examine the work of Taubenhaus, who, by the ingestion of glucose in normals, showed a definite lowering of the total proteins and fractions at the time of the rise of the blood sugar and at the time of recession of the blood sugar a definite increase of albumin and the albumin-globulin ratio (52). Cavett doing sugar tolerance tests on normals found no change in protein relations (8).

The relation of protein level to nutrition is an important one. Lui, Chu, Wang, and Chung report nutritional edema due to low protein level in the blood caused by inadequate protein in the diet (29). They found by experiment that 1 gm. of animal protein per kg. was superior to an equal amount of vegetable protein. Another group working with diabetic patients found the plasma proteins reduced in chronic malnutrition (42). Weech correlates low albumin with nutritional edema (57). All these workers admit its close parallelism with the edema of nephrosis.

Wiener and Wiener, in their studies of renal diseases in cases of diabetes found all types of protein levels but a low albumin-globulin ratio (58). Muntwyler, Way, Binns, and Myers reported a low protein and colloid osmotic
are not developmentally appropriate.

Another common misconception is that achievement in science is a result of innate ability or intelligence.

However, research has shown that the development of scientific thinking and problem-solving skills can be significantly enhanced through effective teaching strategies and instructional approaches.

One key factor in promoting scientific thinking is the use of hands-on activities and experiments that allow students to engage with the material in a concrete, tangible way.

Incorporating real-world applications and relevant examples also helps students see the relevance and importance of scientific concepts in their daily lives.

Furthermore, fostering a growth mindset within the classroom is crucial. Teachers should encourage students to embrace challenges, learn from mistakes, and view obstacles as opportunities for growth and improvement.

Encouraging collaborative learning and group discussion promotes critical thinking and peer learning, which are essential components of scientific inquiry.

Incorporating technology, such as interactive simulations and virtual laboratories, can also enhance student engagement and deepen their understanding of complex concepts.

By implementing these strategies, educators can help students develop the foundational skills necessary for success in science and foster a lifelong appreciation for the subject.

It is important to recognize that everyone is capable of mastering scientific concepts with the right support and guidance.
pressure associated with the edema of nephritis (36), while Peters, Buckman, Eisenman, Hald, and Wakeman found the edema eliminated when the protein was above 4% (41). This was an accompanying deficiency of albumin. They mentioned that the low protein is due not only to altered blood volume but to loss through albuminuria and diet deficiency, as the edema disappeared when the protein intake was raised (41). Barnett, in plasmaphoresis experiments, found that mere loss of protein without the interference of a regeneration mechanism was not sufficient to cause low plasma protein (2). In heart failure edema there is generally an albumin deficit (40).

In discussing the relation of proteins to the blood volume the figures indicate a decrease of protein with a rise in plasma volume. Chang stated that the volume change in nephrosis and nutritional edema is confined mostly to the plasma. He feels that the proteins, plasma volume, and edema run nearly in parallel and that protein concentration is a regulating factor of circulatory volume (9). Lepore limited this to the concentration of plasma albumin as one factor concerned in regulating the blood volume (27).

When the diabetes is complicated by severe acidosis
the serum protein is within or above normal and falls during recovery (44). The hemoconcentration is partly due to a loss of water and partly due to fluid loss into the tissues. Peters, Kydd, and Eisenman believe clinical improvement is better correlated with serum protein than with blood sugar. They believe that the state of shock and hemoconcentration contribute to the cause of coma, and in cases of coma it is possible to reduce the sugar and ketonuria and have the condition not improve until the serum fluid rises (44). In mild diabetes without ketosis or malnutrition the protein is normal (42).
Summary.

The levels of sugar, calcium, cholesterol, phosphorus, and plasma proteins in diabetic blood were determined on a group of fasting patients. The sugar values varied between 166-454 mg. with the majority in the upper levels.

The total plasma proteins were nearly all within high normal levels, running from 7.53-9.14 %.

The values of the protein fractions show a tendency to vary from the normal. The fibrinogen is generally slightly higher, the albumin at low normal level with the globulin often slightly increased making the albumin-globulin quotients, for the most part, below 2.

The majority of the serum calcium values group themselves as high normals.

The inorganic phosphorus values are within normal limits.

The cholesterol values are in the high normal group or slightly increased in the majority of the cases.

The plasma proteins tend to be in inverse proportion to the state of hydration.

The calcium and phosphorus values are in inverse
proportion in most cases.

The higher levels of phosphorus occur in the cases not under as good therapeutic control.
The effect of this process on the data.

The effect on the data.
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-Experiment:

1. Add equal volumes of water, vitamin C, and glucose to the blood sample.

2. Heat the solution to cause an oxidation of the glucose.

3. Prepare a standard solution of glucose in water.

4. Place the standard and sample solutions in a spectrophotometer.

5. Record the absorbance at 260 nm.

6. Repeat the experiment with different concentrations of glucose.

7. Calculate the concentration of glucose in the blood sample.

8. Repeat the experiment on another day.

9. Calculate the mean and standard deviation of the absorbance readings.

10. Compare the results with the standard solution.

11. Calculate the percentage error in the experiment.
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