Levels of sugar in the blood considerably lower than those found in man and the laboratory animals commonly studied have been repeatedly observed in goats in our laboratory. The normal resting blood sugar of non-fasted goats has, as a rule, been found to be below 50 mg. per 100 cc. Frequently the levels are lower than those at which other animals show symptoms of hypoglycemic shock. It seemed that such low sugar levels might be indicative of a further peculiarity in the manner in which the goat utilizes carbohydrate. Consequently, a study of a number of phases of the carbohydrate metabolism of these animals has been undertaken. The present paper includes the results of an investigation of the following points: (1) the difference in sugar content of arterial and venous blood; (2) the renal threshold for sugar; (3) the mobilization of sugar following excitement, or administration of adrenalin; (4) the hyperglycemia resulting from administration of glucose; (5) the effects of insulin and the resulting hypoglycemia; and (6) the changes in the level of the inorganic phosphates in the blood which result from the administration of glucose, adrenalin, or insulin.

Normal Blood Sugar—We have made 150 determinations of the normal resting blood sugar in twenty-six goats. The figures range from 24 to 65 mg. per 100 cc. The majority of the figures are be-
It was found that if reasonable care was exercised to prevent exciting the goats before taking the samples, the levels were nearly always below the latter figure. The average of the figures is 46 mg. per 100 cc.

Only two earlier references to the normal blood sugar level of the goat have been noted. Abderhalden (1) reports a concentration of sugar of 0.829 part per 1000, and Bang (2), one of 0.08 part per 100 in the blood of the goat. These figures are considerably higher than those which we are reporting, but were determined by methods which are not at the present day considered accurate.

The goats used in our studies were obtained from four different localities, and were of various breeds. Normal males, castrated males, and females, both lactating and non-lactating, were included. The low blood sugars were persistent whether the goats had been at pasture or had been kept for several months in the laboratory on a diet of oats and hay.

The sugar in the blood was determined routinely by Benedict's method (5). However, because the figures obtained were unusual, they were repeatedly checked by the use of several other well established methods. Folin's ferriyanide method (11) and the method of Shaffer and Hartmann (18) gave figures which checked very well with those obtained by Benedict's method. Moreover, approximately the same figures were obtained whether the determinations were carried out on protein-free filtrates prepared by the use of the Folin-Wu tungstic acid precipitation procedure (12) or the zinc sulfate protein precipitation of Somogyi (19). Typical figures obtained by these various methods are presented in Table I.

There is apparently no substance in goat blood which interferes with the determination of glucose, as is indicated by the fact that glucose added to the blood can be quantitatively recovered.

The factor of loss of sugar due to rapid glycolysis has been ruled out in several ways. In the first place, data to be presented later show that glycolysis occurs exceptionally slowly in goat blood. In the second place, glycolysis was prevented in most of the samples used for sugar determination, either by such rapid handling that not even an anticoagulant was needed, or by the addition of sodium fluoride to the blood. Parallel determinations on fluorized and non-fluorized portions of the same samples showed no significant differences in sugar content, even when the samples were allowed to stand at room temperature for an hour.
The figures presented above, therefore, apparently indicate the true level of reducing sugar in the blood of goats. They do not, however, preclude the possibility that additional sugar may be present in a non-reducing form, yet is available to the animal for metabolic purposes.

**Arterial-Venous Difference in Sugar Content**—The figures presented above were obtained on venous blood. In several cases, samples were taken as nearly simultaneously as possible from the saphenous vein and from the left ventricle of the heart. Comparative sugar determinations on these samples show sugar levels in the ventricular blood only 2 to 4 mg. per 100 cc. higher than those in venous blood. These differences are wholly in accord with those observed in other animals. Moreover, we found that insulin, which increases the utilization of sugar, does not cause the arterial venous difference of sugar content in the blood of the goats to increase beyond the normal limits. Therefore, the low sugar concentration in venous blood cannot be explained on the basis of an unusually rapid withdrawal of sugar from the blood by the tissues.

**Renal Threshold for Sugar**—An extremely low renal threshold is not the cause of the low blood sugar. This is indicated by the fact that numerous samples of urine taken from goats more or less at random did not contain sugar. Further evidence was obtained by experiments on four goats in which the renal threshold for sugar was determined. We were not able to catheterize goats and were forced to use anesthetized animals. Amytal was found

<table>
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<th>Benedict method, mg. per 100 cc.</th>
<th>Folin method, mg. per 100 cc.</th>
<th>Sample</th>
<th>Benedict method, Folin-Wu filtrate, mg. per 100 cc.</th>
<th>Benedict method, Somogyi filtrate, mg. per 100 cc.</th>
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to be unsatisfactory for maintaining anesthesia in goats, and we therefore resorted to barbital. This anesthetic had only a slight effect on the blood sugar, as evidenced by the fact that the levels after anesthetization and cannulation of a ureter were only slightly higher than those obtained before the procedures were instituted. Before the anesthetic was given, the blood sugar levels of the four goats were 45, 44, 35, and 46 mg. per 100 cc. After the operation they were 61, 46, 44, and 47 mg., respectively.

The renal threshold was determined in the following manner. Urine was obtained from the ureteral cannula and immediately tested for sugar by Benedict's method (4). A small dose of glucose, about 0.06 gm. per kilo, was then injected intravenously. A blood sample was taken immediately and the urine examined for sugar at 2 to 5 minute intervals for about 30 minutes. If the urine did not give a positive test for sugar, a slightly larger dose of glucose was given and the procedure repeated. After sugar appeared in the urine, tests were made as frequently as possible, and as soon as sugar-free urine was again obtained, another blood sample was taken. Thus, we were able to determine the approximate levels of blood sugar at which sugar appeared in, and disappeared from, the urine.

In the four goats, sugar was noted in the urine at blood sugar levels of 130, 81, 112, and 115 mg. per 100 cc., and had disappeared at 80, 67, 89, and 87 mg., respectively. These levels indicate a threshold considerably lower than that reported for the dog, the rabbit, and man. The threshold in the goat is, however, almost as much higher than the normal blood sugar level as it is in other animals. Excretion of sugar in the urine, therefore, cannot be the direct cause of the low blood sugar.

Mobilization of Sugar—Having established the fact that the goat is able to maintain its normal activity with an unusually low concentration of sugar in the blood, we wished to know whether in an emergency it can draw upon its carbohydrate reserves in a normal manner. The administration of large doses of adrenalin to most animals is followed by an increase in blood sugar. Likewise, fright or excitement results in hyperglycemia. We have found that goats respond to the administration of adrenalin and to excitement with a hyperglycemia which is comparable to that seen in the dog. In Chart 1, typical curves are given which illustr-
trate the rise in blood sugar that occurs in the goat after the subcutaneous injection of 0.1 mg. of adrenalin per kilo and after moderate excitement.

The figures obtained from these procedures indicate that though the goat maintains normal metabolism with a very low blood sugar,

![Chart 1: Effect of adrenalin and excitement on the blood sugar of goats](image)

**Chart 1.** Effect of adrenalin and excitement on the blood sugar of goats

it is like other animals in being able to call into the blood stream reserves of sugar in an emergency.

*Administration of Sugar*—To investigate the rate at which goats remove excess sugar from the blood stream, we administered glucose, either orally or by vein, and made subsequent determinations of the blood sugar concentration at short intervals. When sugar is given by mouth to goats, the resulting hyperglycemia is slight
Carbohydrate Metabolism in Goat

and rather late in appearing. One of the factors influencing the blood sugar level after the oral ingestion of glucose is the rate of absorption from the gastrointestinal tract. The goat is a ruminant and it is possible, therefore, that the rate of absorption is relatively slow. If so, this may explain why the blood sugar rise is so slight and so late in appearing.

**Chart 2.** Effect of oral and intravenous administration of glucose on the blood sugar of goats.

When comparable amounts of glucose are administered by vein to the goat and the dog, the blood sugar response in the two animals is similar. The abrupt initial rise is followed by a return to the normal level in 1½ to 3 hours. In Chart 2 the blood sugar changes in the goat after oral and intravenous administration of glucose are illustrated. From the results of these experiments...
we may conclude that in the goat excess sugar can be removed from the blood at a normal rate.

Effects of Insulin—The reaction of the goat to insulin is unusual in two respects: (1) exceptionally large doses of insulin are required to produce shock; and (2) shock occurs only after a blood sugar level between 10 and 20 mg. per 100 cc. has been maintained for a period of 5 to 8 hours.

The smallest dose of insulin with which we have produced shock in the goat is 4 units per kilo. Even larger doses than this have frequently failed to produce symptoms. Scott, Ferrill, Rogoff, and Barnes (17), in a recent study on the sensitivity of dogs to insulin, reported that 2 units of insulin per kilo produced convulsions in dogs in nearly every case, and that smaller doses would suffice in certain dogs. Therefore, at least twice as much insulin per kilo of body weight is required to produce shock in the goat as in the dog.

When large doses of insulin are administered to goats, the blood sugar falls rapidly, within 1 or 2 hours, to a level between 10 and 20 mg. per 100 cc. At this stage, the animals appear perfectly normal in every respect, and continue to do so for some time. The blood sugar usually remains at approximately the same low level for several hours. If, within 4 or 5 hours, it begins to rise toward its normal level, no symptoms are ever noted in the animal. If, however, the dose of insulin is sufficient to keep the blood sugar concentration well below 20 mg. per 100 cc. for 5 to 8 hours, symptoms of shock will be noted. Although we have sometimes used extremely large doses of insulin, we have never been able to produce shock in the goat without this 5 to 8 hour period of hypoglycemia. In two cases, doses of 10 units per kilo and 12 units per kilo were administered, but symptoms appeared only 8 and 9 hours, respectively, after the insulin was given. We can, as yet, offer no explanation of why the goat is able to maintain his normal activity for several hours with a blood sugar so remarkably low, and then without further lowering, manifests shock.

The symptoms of shock in the goat are those of apathy and sluggishness, followed by coma. We have never seen convulsions, and only in a few cases, slight signs of restlessness in the early stages. The animals usually salivate profusely. The symptoms can be relieved promptly and completely by injection of glucose, and as far as can be observed, there are no after effects.
The hypoglycemia resulting in the goat from injection of insulin and its relationship to the onset of symptoms are illustrated in Chart 3.

The studies of the blood sugar have not, thus far, revealed the nature of the abnormality in the carbohydrate metabolism of the goat. The peculiarity of the reaction of this animal to insulin is, however, still further suggestive of the existence of such an abnormality. Therefore, another criterion for the comparison of the carbohydrate metabolism of the goat with that of other animals was sought.

Numerous reports in the past decade have indicated that phos-
phorus plays an important rôle in carbohydrate metabolism. One type of evidence that this is so is found in the fact that the changes in blood sugar which result from the administration of glucose, adrenalin, or insulin are accompanied by characteristic changes in the level of the inorganic phosphates of the blood. Therefore, we have studied the changes produced by these procedures in the level of the inorganic phosphorus in the blood of the goat.

The normal concentration of the inorganic phosphate in the blood of the goats which were used for these studies was considerably higher than that in the blood of the dogs used as control animals. Our figures for goat blood range from 3.2 to 11.1 mg. of phosphorus per 100 cc. with an average of 6.0 mg., while those for dog blood vary from 2.2 to 4.9 mg. per 100 cc. with an average of 3.2 mg. The determinations were made by Briggs' modification (8) of the Bell-Doisy method (3). We believe that the high levels in the goat blood result, at least in part, from the diet. The figures were always considerably higher when the animals had been kept at pasture for some time than when they had been receiving the diet of oats and hay furnished in the animal quarters. The soil in this region is rich in phosphates, so that it is probable that the animals kept at pasture received a comparatively large amount of these salts.

Effect of Administration of Glucose on Inorganic Phosphate—Harrop and Benedict (13) reported in 1924 that the hyperglycemia resulting from the oral administration of glucose was followed by a marked reduction of the inorganic phosphate of the blood. Bolliger and Hartman (7) showed that the same change occurs after intravenous injection of glucose in normal animals, but that no such change takes place in depancreatized subjects. Hartman and Foster (14), as well as McCullagh and Van Alstine (15), have studied the changes in the inorganic phosphate of the blood after the administration of glucose to large numbers of patients. Both groups of investigators found that certain abnormalities of carbohydrate metabolism are reflected in an abnormal curve of the inorganic phosphate.

In our experiments, glucose was given intravenously to both goats and dogs in doses of 0.4 gm. per kilo. The intravenous route was chosen in order to avoid variations in the rate of intestinal absorption. Blood samples for the determination of sugar and
inorganic phosphate were taken 10, 30, 60, 120, and 180 minutes after the injection.

In the blood of both species, the abrupt initial rise in blood sugar which results from the injection of glucose is followed by a marked reduction of the inorganic phosphate. The fall continues for 40 minutes to 2 hours, following which there is a return toward the normal level. The rise in phosphate does not usually begin until the blood sugar has fallen to a level only slightly in excess of the normal. The phosphate level is, as a rule, still somewhat depressed as long as 3 hours after the administration of glucose. In Chart 4, typical curves are presented of the inorganic phosphate

**Chart 4. Effect of intravenous injection of glucose on the inorganic phosphate of the blood of the goat and the dog.**
of the blood of the dog and the goat after the intravenous injection of 0.4 gm. of glucose per kilo. The changes which occur in the goat blood do not differ from those in dog blood and are similar to those reported in the literature.

![Chart 5. Effect of adrenalin on the inorganic phosphate in the blood of the dog and the goat.](chart.png)

**Effect of Injection of Adrenalin**—Perlzweig, Latham, and Keefer (16), Vollmer (21), and Bolliger and Hartman (7) reported that the injection of adrenalin results in a marked fall in the inorganic phosphate of the blood. Yamada (23) was unable to confirm this observation.

In Chart 5 are presented typical curves illustrating the changes in sugar and inorganic phosphate of the blood which result from
the subcutaneous injection of adrenalin in dogs and goats. Adrenalin was given in doses of 0.1 mg. per kilo. Blood samples were taken hourly, following the injection, for 6 to 8 hours. The resulting curves in the two species are similar. Following the injection of adrenalin the blood sugar rises rapidly at first and then more slowly for 3 or 4 hours. During the same period the

![Chart 6. Effect of insulin on the inorganic phosphate in the blood of the goat.](chart)

inorganic phosphate falls markedly. Both constituents then begin to return toward their normal levels.

**Effect of Injection of Insulin**—A marked fall in the inorganic phosphate of the blood following the administration of insulin was reported by Wigglesworth, Woodrow, Smith, and Winter (22). This observation has since been confirmed by many investigators (6, 9, 10, 13, 20, 23). Wigglesworth *et al.* found that the low level of the inorganic phosphate persists in the blood for many hours.
after the hypoglycemic convulsions have been relieved by glucose. Yamada (23) reported, however, that during unrelieved insulin convulsions the inorganic phosphate rises again to approach the normal level.

The large dose of insulin required and the greater severity and duration of hypoglycemiam necessary to produce shock in goats make difficult any exact analysis of the comparative effect of insulin in goats and dogs. However, the marked fall in the inorganic phosphate of the blood which has been observed in other animals after the injection of insulin takes place also in the goat. The initial fall of both sugar and inorganic phosphate in goat blood is about equally great whether or not the dose of insulin is large enough to produce shock. When shock does not occur, the inorganic phosphate begins to rise at about the same time that the sugar starts to return to a more normal level. When shock occurs, the inorganic phosphate remains low until symptoms have set in and have been relieved by administration of glucose (Chart 6).

The data presented indicate that the inorganic phosphate of goat blood is altered in response to the administration of glucose, adrenalin, and insulin in the same manner as that observed in other animals. Not enough is yet known regarding the significance of the changes in inorganic phosphate in relation to the metabolism of carbohydrate to make it possible to say that these observations indicate a normal type of carbohydrate metabolism in the goat. They do not, however, furnish any evidence of metabolic abnormalities.

**SUMMARY**

The normal resting blood sugar of goats has been found to be between 24 and 65 mg. per 100 cc. The low blood sugar is not to be explained by an unusually efficient utilization of sugar by the tissues, nor by a remarkably low renal threshold. The blood sugar changes following excitement, the administration of adrenalin, or the administration of sugar are similar to those observed in the dog. Unusually large doses of insulin are required to produce shock in goats, and shock is manifested only when blood sugar levels between 10 and 20 mg. per 100 cc. have been maintained for 5 to 8 hours. The inorganic phosphorus of goat blood is
markedly lowered by the administration of glucose, adrenalin, or insulin.

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