

LIVER FUNCTION AND BLOOD PLASMA PROTEIN FORMATION

NORMAL AND ECK FISTULA DOGS

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The experimental data given below support the thesis that the liver is actively concerned with the fabrication of the plasma proteins. One of the plasma proteins (fibrinogen) takes its origin from the liver and the evidence (5, 3, 8) for this statement is now generally accepted. There is a reserve store of protein material in the liver (1, 7), and some of this or other material is thrown into the circulation after a rapid and extreme plasma depletion (6) to effect a sharp rise in total plasma protein concentration. Liver injury and the Eck fistula abolish this sharp reaction. Disease of the liver in man may show a low plasma protein concentration (12).

The *Eck fistula* permits the portal blood to flow directly into the vena cava and excludes it from the liver so that the blood supply of the liver is then wholly arterial and probably reduced to 25 to 35 per cent of the normal combined portal and arterial flow. Under such circumstances we may have a clinically normal dog, active and lively, with a good appetite, constant weight, and normal gastro-intestinal activity. These dogs often have more or less conspicuous transient clinical disturbances, which become familiar to laboratory workers. Abnormal thirst and diuresis may appear (2). At first dogs may be intoxicated with meat feeding but this abnormality usually disappears. There may be a slight icteric tinge in the blood plasma. The liver is distinctly smaller than normal and we have evidence that liver function may be subnormal (15). It has been shown that the blood ammonia in such dogs on a high protein diet may be increased. Further-

more blood ammonia values after ammonia administration are higher in Eck fistula dogs than in normal controls (11). This indicates that the ability of the liver to form urea is subnormal in the Eck fistula dog. Abnormalities related to the function of the liver in carbohydrate metabolism have been recognized.

Perhaps it is surprising that the Eck fistula liver with its limited blood supply can carry on so effectively its metabolic duties. The well known margin of safety of the liver is probably responsible. It seemed that an extra burden placed on such an Eck fistula liver might well bring out its incompetency and we planned to test its plasma protein-forming capacity by means of careful plasma depletion. Before this could be done it was found that one Eck fistula dog (33-180) was unable to form enough plasma protein for *maintenance* of a normal plasma protein concentration on our basal diet used during former plasma depletion studies (4). Relatively large amounts of protein in the diet were required to keep this dog at the low normal level of plasma protein concentration.

Dog 33-180 (Eck fistula) was active and normal in appearance. This dog showed excessive thirst and diuresis. A biopsy showed some abnormalities of the liver and the clinical evidence indicates no other organ abnormality. The Eck fistula means an inefficient liver and we assume all the *evidence points to the liver* as responsible for the conspicuous difference between this dog and control animals. The dog is alive at this time and is the subject of continued study.

It is not clear why other Eck fistula dogs do not show all these abnormalities. We may argue that development of collateral circulation in some dogs may improve the circulation in the liver lobules. It is not difficult to believe that some dogs may tolerate this Eck fistula abnormality with less disturbance than others—for example, a young dog is apt to do better than an old one.

It has been recognized that *protein deficient diets* can bring about in the dog a definite decrease in the amount of plasma protein. Weech, Goettsch, and Reeves (16), using a carrot-rice-lard diet containing roughly 0.5 gm. of protein per kilo body weight per day, demonstrated in a number of dogs an average of about 2 gm. per cent drop in the plasma protein concentration in 80 days. This drop corresponds roughly to that shown by Dog 33-180 (Table 24), when twice as much

protein was being consumed. The potato-bran diet used in the present experiments, *for the length of time tested* appears to be adequate in protein for the maintenance in normal dogs of a plasma protein concentration within normal limits.

Methods

In the first experiment, three dogs with Eck fistulas and four normal dogs were studied. Later experiments were concerned with one dog (33-180) only. The basal diet consisted of boiled potatoes, canned tomatoes, Post's bran flakes, Karo, cod liver oil, cottonseed oil, and the McCollum-Simmonds (9) salt mixture. The diet was adjusted in all instances except in one normal dog to supply 0.7 to 1 gm. of protein and 80 to 100 calories per kilo of body weight per day. Plasma protein analyses were made the day before the diet was started, and frequent determinations were made during the course of the experiment on all dogs except two of the normal ones (33-11, 33-324), on which determinations were made at the beginning and at the end of the allotted time periods. Nitrogen determinations were made by the micro-Kjeldahl method with steam distillation, as modified by Goebel (13). This was checked from time to time with the macro-Kjeldahl method. The determinations on the Eck fistula dogs and on one normal dog (35-124) were carried out on oxalated plasma in duplicate and triplicate. Determinations on other dogs were carried out on citrated plasma. In all instances the dilution was corrected by appropriate factors. Albumin and globulin were determined by Howe's method as described by Peters and Van Slyke (13) using 22 per cent sodium sulfate at 37°C. Triplicate analyses were carried out, and the nitrogen determined with the micro-Kjeldahl apparatus. Urinary nitrogen was determined on the total weekly output, using measured amounts of concentrated H₂SO₄ as a preservative. For the determination of fecal nitrogen, stools were collected in concentrated H₂SO₄. This mixture, representing the weekly output was stirred mechanically for 24 hours and aliquot samples were analyzed for nitrogen by the macro-Kjeldahl method. Plasma non-protein nitrogen determinations were done by the macro-Kjeldahl method using trichloroacetic acid for precipitation (13).

EXPERIMENTAL OBSERVATIONS

Table 21 indicates the changes in the amounts of circulating plasma protein in four normal dogs, and in three Eck fistula dogs. All of these dogs were given the potato-bran basal diet for the periods of time indicated.

In the normal dogs, there was a slight drop in the circulating plasma protein level. The drop was greatest in Dog 32-58, but the final level of this animal (6.1) is well above the lower normal limits.

The two Eck fistula dogs (34-206, 29-328) show decreases which are quite similar to those of the normal dogs. Table 21 may be misleading, in that it suggests that the drop in plasma protein concentration is uniform and gradual. This is not correct except in the case of 33-180. The most marked drop occurs during the first 2 weeks; from that time, further diminution rarely occurs. In fact some animals showed a slight increase in concentration following an initial drop.

The Eck fistula dog (33-180, Table 21) shows a totally different picture. The first period 33-180 (1) followed a long interval of kennel

TABLE 21

Effect of Potato-Bran Diet on Plasma Protein Concentration in Normal and in Eck Fistula Dogs

Dog No.	Condition	Time	Daily protein intake	Initial plasma protein level	Final plasma protein level	Initial weight	Final weight
			<i>days</i>	<i>gm. per kg.</i>	<i>gm. per cent</i>	<i>gm. per cent</i>	<i>kg.</i>
33-324	Normal	14	0.7	5.9	5.5	11.2	10.6
35-124	Normal	63	1.0	5.6	5.5	12.3	15.2
33-11	Normal	65	0.8	5.3	5.0	13.1	11.6
32-58	Normal	77	4.2	7.8	6.1	5.8	—
29-328	Eck fistula	42	1.0	5.2	4.9	12.3	11.8
34-206	Eck fistula	63	1.0	7.3	6.1	21.0	21.6
33-180(1)	Eck fistula	6	1.0	5.3	3.8	17.4	18.0
33-180(2)	Eck fistula	79	1.0	5.4	3.9	17.4	15.4

diet (table scraps) which is adequate in all respects. During the 6 days of this period there was a sharp fall in the plasma protein concentration from 5.3 (low normal) to 3.8 gm. per cent (close to the edema level). Obviously at this time this dog had no available reserve store of plasma protein building material. There was a slight gain in weight. The diet was supplemented with kidney to bring the plasma protein concentration up to a safe level. During this period there was no evidence of clinical abnormality. Obviously this potato-bran diet did not furnish sufficient protein for this dog to maintain its plasma protein level above the danger line.

The second period of this Eck fistula dog (Table 21, Dog 33-180 (2)) was much longer (79 days) (see also Table 24) and followed an

anemia period of 20 weeks (see Table 23) during which time the dog received a high protein diet (salmon bread, salmon, and liver (16)). It is not easy to say why this dog during this second period was able to maintain its plasma protein above the danger level for 79 days (Table 24) in contrast to the first period (Table 21). During the anemia period (Table 23) the mechanism which produces hemoglobin was rendered active and functioned efficiently, and it is possible that this general anemia reaction is concerned with the better production of plasma protein in the subsequent period. However, inefficient

TABLE 22

Effect of Diet Protein on Plasma Protein Formation (Dog 33-180 Eck Fistula)

Period	Time days	Diet	Total protein intake		Average output of plasma protein on same diet by normal dog	Average plasma protein concentration	Urinary nitrogen	A/G ratio	Weight	R.B.C. hematocrit
			gm. per day	gm. per day						
1	6	Potato-bran basal	18	0.68	3.6	5.5-3.8	2.3	1.1	17.7	38.4
2	9	Potato-bran + kidney	33	0.28	6.6	4.1	2.2	1.1	17.4	35.9
3	8	Potato-bran + kidney	25	0.26	5.0	4.3	2.4	1.1	18.1	36.5
4	7	Potato-bran + liver	33	0.23	5.9	4.3	3.5	0.9	17.7	37.1
5	7	Potato-bran + beef heart	33	0.17	5.5	4.2	2.6	0.8	18.6	38.0
6	7	Potato-bran + beef heart	50	0.20	7.6	4.3	3.5	0.9	19.3	38.9
7	7	Potato-bran + soy bean	50	0.20	10.0	4.2	5.0	1.0	19.2	38.1

kidneys have periods of improvement and a similar reaction on the part of this abnormal liver may account for this improvement in the capacity to produce plasma protein on the limited potato-bran diet. One may consider the possibility that this dog *stored* protein building materials during the period of heavy protein intake (anemia period, Table 23) and from this store was able to contribute to the circulating plasma proteins during the periods given in Table 24.

During this experiment (Table 22) plasma samples were taken daily. The column indicating protein removed shows the amount contained in such samples. The average plasma protein concentration in

column 7, indicates an average of the daily determinations during the given interval. Other values are determined in the same manner.

Table 22 shows the striking difference between the normal dog and the Eck fistula Dog 33-180. The Eck fistula animal cannot maintain its plasma protein concentration on the standard basal ration and we note a fall which nears the edema level (period 1). The potato-bran basal diet is continued throughout the seven periods at 18 gm. protein intake daily. Supplementing the basal diet with 15 gm. kidney protein per day (period 2) brought the plasma protein concentration level above 4.1 and the protein was then reduced giving only 7 gm. of

TABLE 23

Protein Metabolism during Bleeding and Anemia (Dog 33-180 Eck Fistula)

Period, 7 days	Diet	Protein intake	Plasma protein removed	Average plasma protein concentration	Urinary nitrogen	A/G ratio	Weight	R.B.C. hematocrit
		gm. per day	gm. per day	gm. per cent	gm. per day		kg.	per cent
1	Salmon bread-salmon-Hamburger	72	2.54	5.9	7.1	—	17.0	25.2
2	Salmon bread-salmon-Hamburger	75	2.31	6.3	8.2	—	16.9	25.6
3	Salmon bread-salmon	68	1.46	6.3	8.4	—	17.0	24.1
4	Salmon bread-liver	103	0.32	6.1	11.0	0.9	17.4	27.1
5	Salmon bread-liver	106	3.6	5.9	10.1	1.0	17.7	27.2

kidney protein in period 3. The diet was adjusted so that a plasma protein concentration was maintained at about 4.0 to 4.2 gm. per cent which is the plasma depletion level maintained in our plasmapheresis experiments. It might be assumed that this low plasma protein level would stimulate the body to form more plasma protein, as is true for the normal dog. As the food protein is increased the urinary nitrogen rises slowly and the body weight increases. The A/G ratio shows no significant change.

A normal dog depleted by plasmapheresis on these various diets would form 4 to 10 gm. of new plasma protein per day or 30 to 70 gm. per week as recorded in other experiments (10). This dog barely

maintained its plasma protein level at 4.0 gm. per cent. A normal dog shows potency ratios of 5 to 8 for these various diet mixtures while this Eck fistula dog shows a potency ratio of approximately 150. The latter figure is not accurate, as it does not take into consideration the *maintenance factor*. This maintenance factor is present of course in a normal dog but it is a relatively small factor compared with the large net plasma protein production as measured by plasmapheresis and plasma removal.

During the 20 week period while Dog 33-180 was being made anemic, the protein metabolism is of interest. 5 consecutive weeks during the middle of this period are shown in Table 23. In this period considerably greater amounts of protein were fed in order to insure maintenance of an adequate plasma protein concentration, in spite of the amount of protein being removed in the bleeding. In comparison with Table 22, it is obvious that the animal at this time was utilizing a higher protein intake in amounts sufficient to maintain a relatively high plasma protein concentration. The plasma protein concentration has risen from 4.2 gm. per cent to 6 gm. per cent in spite of the daily removal of 2 to 3 gm. of plasma protein, a significant change from this animal's previous state (Table 22). It is realized that this table does not indicate the true protein-forming ability of the animal at this time, and in order to measure it, plasmapheresis in addition to the bleeding would have to be done. This table is not included for that purpose, however, but rather to indicate that under different conditions with an extremely high protein diet, the animal was able to manufacture adequate amounts of plasma protein.

This Eck fistula dog had no reserve supply of plasma protein building materials at the start of the anemic period. The dog was put in the anemia colony and anemia produced by blood withdrawal (Dr. Robbins). The bleeding was more cautiously done than in a normal control but it became apparent that the dog did have a *considerable reserve store* of materials out of which new hemoglobin could be fabricated. This indicates that *reserve stores* which contribute to hemoglobin are independent of those which go to form plasma protein. The dog also produced a low normal output of new hemoglobin in this anemic period when fed liver. These data will be published in detail elsewhere.

Table 24 shows nine consecutive weekly intervals following the anemic period. At this time the protein intake has again been diminished to the basal level, and the amount of protein removed is only that necessary for chemical analysis. It is seen that the red blood cell percentage, as indicated by the hematocrit, slowly increased to within the original normal limits for this dog. The plasma protein

TABLE 24

Protein Metabolism during Recovery from Anemic Period—Potato-Bran Diet (Dog 33-180 Eck Fistula)

Period 7 days	Diet	Protein intake	Plasma protein removed	Average plasma protein concentration	Urinary nitrogen	A/G ratio	Weight	R.B.C. hema- tocrit
		<i>gm. per day</i>	<i>gm. per day</i>	<i>gm. per cent</i>	<i>gm. per day</i>		<i>kg.</i>	<i>per cent</i>
1	Potato-bran basal	17.5	0.35	5.3	3.28	0.8	17.4	30.9
2	Potato-bran basal	17.5	0.26	5.1	2.07	0.8	16.9	33.6
3	Potato-bran basal	17.5	0.24	4.7	2.35	0.7	16.5	34.5
4	Potato-bran basal	18.3	0.22	4.7	2.98	0.6	16.8	38.4
5	Potato-bran basal	18.3	0.22	4.9	1.98	0.5	16.5	38.8
6	Potato-bran basal	18.3	0.14	4.8	2.90	0.5	16.5	38.4
7	Potato-bran basal	18.3	0.19	4.7	2.04	0.4	16.5	40.1
8	Potato-bran basal	18.3	0.18	4.5	1.80	0.4	16.4	39.0
9	Potato-bran basal	18.3	0.12	4.3	1.83	0.3	16.1	38.8

TABLE 25

Urine Volume and Plasma Volume of Dog 33-180

Period, 7 days.....	1	2	3	4	5	6	7	8	9
Urine volume, liters.....	22.3	18.3	18.2	21.6	16.5	20.1	15.4	15.6	15.7
Plasma volume, cc.....	948	857	817	790	784	808	795	899	774

concentration gradually diminished. It is also of interest that the A/G ratio, which heretofore in this animal had been quite constant, gradually fell off from 0.8 to 0.3. Judging from other experience we were fortunate that this dog did not pick up some serious infection. A steadily falling A/G ratio usually means trouble which fortunately this dog escaped.

The diuresis and plasma volume of Dog 33-180 are shown in Table

25. This table represents the same successive periods that are shown in Table 24. A striking feature is the abnormally high urine volume with no conspicuous departure from normal noted in the plasma volume. Normal dogs of this weight will eliminate 3 to 4 liters of urine per week. It is evident that there was a diminution of water turnover in the last weeks and that the plasma volume during the whole interval diminished somewhat. This would indicate that dilution of plasma played no part in the drop in the plasma protein concentration during this period. In fact, the absolute decrease in total plasma protein would be somewhat greater than the *percentage* figures indicate, due to the slight plasma concentration. Crandall and Roberts (2) have recently reported that a number of Eck fistula dogs showed excessive water intake and urine output, and ascribe the phenomenon to interference by the Eck fistula with the "water storage function of the liver." The condition has been noted in a few Eck fistula dogs in this laboratory but has not been studied in detail.

Determinations of fecal nitrogen on the different diets showed a variation of from 15 to 18 gm. of nitrogen per week with no correlation with the amount of nitrogen in the ingested food. Plasma non-protein nitrogen determinations were done from time to time and varied between 21 and 36 mg. per cent. These figures are not of sufficient magnitude to make any appreciable difference in the figures given as plasma protein. In the estimation of plasma protein an arbitrary figure of 20 mg. was deducted from the determined total plasma nitrogen, before multiplication by 6.25.

Clinical Histories

Clinical History.—Dog 33-180. An adult male brindle bull mongrel weighing 18.5 kg. An Eck fistula was made on Dec. 28, 1933. For the next year it was used for cholesterol studies, being on a diet of table scraps (kennel diet), which was supplemented from time to time with substances high in cholesterol. For 3 months previous to the beginning of the present studies no supplements had been added to the diet. 3 months prior to the time when the present experiments were started there was evidence of a slight *intoxication* which lasted for 3 days. The blood plasma from the time of the operation had always showed a slight trace of bile pigment.

On Jan. 27, 1935, the animal was put in a metabolism cage and fasted 1 day. On the 2nd day the standard potato-bran basal ration was started. It had been planned to lower the plasma protein level by means of plasmapheresis, but during

the next few days the plasma protein level dropped so rapidly that this procedure was abandoned. It was noted that excessive amounts of urine were being excreted. Tests for sugar and albumin in the urine were done at that time, and have subsequently been repeated and these substances have never been demonstrated. 8 days from the beginning of the experiment the plasma protein concentration fell to a dangerous level (3.83), and protein in the form of cooked kidney was added to the diet. The plasma protein level rose in a few days to 4.1 to 4.2.

For the next 8 weeks various food substances whose plasma protein-regenerating qualities were known were tested on the animal. During this period its clinical condition remained excellent. For 3 months experiments were discontinued, the dog being fed during this interval the basal diet plus 150 gm. of liver daily. The next period of 20 weeks was used for hemoglobin regeneration studies, the results of which will be included in another publication. During this interval the dog was fed a relatively high protein diet (80 to 100 gm. per day), derived from salmon and salmon bread, and was bled sufficient amounts to render it anemic. Protein studies were resumed at the end of this 20 week period, at which time the plasma protein level was 5.52 and the hemoglobin percentage was 45. The clinical condition was excellent.

Potato-bran basal diet was again instituted, with addition of liver. The liver was gradually diminished over a period of 2 weeks, from which time only the basal diet was fed. This furnished 1 gm. per kilo body weight per day of vegetable protein, and 90 to 100 calories. This was continued for 10 weeks, during which time complete protein studies were done. During the latter part of this interval ulcerative lesions appeared on the buttocks but the animal remained in good general condition. Fasting was then carried out for 2 days, and at the end of this period the dog was fed the equivalent in liver of 140 gm. of protein. After a short and abrupt rise in the plasma protein level, it dropped off after 3 more weeks on the basal diet to 3.89. These data will be published separately.

At this point the dog developed considerable edema of the neck, associated with a thrombosed jugular vein, and appeared to be quite sick. The plasma was jaundiced. Large intravenous doses of dog plasma and glucose solution were given, whereupon the edema almost immediately disappeared. A high protein diet was resumed and the animal again became active and clinically normal. Within 2 weeks the plasma protein rose to 5.3 per cent. During this last experimental period of some 4 months, the weight dropped from 17.5 kg. to 15.4 kg.

Two months following this episode a *biopsy of the liver* was taken. At time of operation the liver appeared smaller than normal. It was quite yellow, and the surface was very slightly granular. Microscopic study showed moderate increase of deep red staining hyalinized connective tissue about the bile ducts and portal vessels. There was moderate round cell infiltration about some of the portal areas. In the mid-zonal regions of some liver lobules there were small foci of round cells along with a few connective tissue nuclei. The liver cells were large, pale, swollen and contained numerous tiny vacuoles. In the liver cells near the portal zones the vacuoles were much larger. By appropriate staining these large

and small vacuoles were shown to be of a fatty nature. There was no evidence of acute hepatic injury. At present the animal is in excellent condition.

Clinical History.—Dog 29-328. An Eck fistula was produced in an adult male coach mongrel on Jan. 21, 1934. The year following this operation the animal was used for hemoglobin studies and remained in excellent condition throughout this period. At the time (Feb. 27, 1935) when the present experiments were started the animal was in good condition, though moderately anemic. Potato-bran basal diet was given for a period of 44 days, during which time the plasma proteins were determined at frequent intervals (Table 21). During this period the weight dropped from 12.3 to 11.8 kg. When the experiment was terminated, the dog was in excellent condition. The red blood cell percentage, as determined by the hematocrit, had risen from 30.1 to 38.1 (Table 21).

Clinical History.—Dog 34-206. An adult male, short haired, brown mongrel, weighing 21 kg. An Eck fistula was done on June 12, 1935. The post-operative course was uneventful. Until the time when the present experiment was started, Aug. 8, 1935, the animal had been on a diet of table scraps and had shown no evidence of intoxication. Potato-bran basal diet was started on Oct. 16, 1935, and continued for 9 weeks. Frequent plasma protein determinations were made during this interval. The weight of the animal was maintained, and at the end of the period, the clinical condition was excellent. During subsequent experiments the animal died with interstitial bronchopneumonia. At autopsy the liver was small, brownish yellow. The Eck fistula was patent and the portal vein above the fistula occluded by ligature. Microscopic examination of the liver showed marked fatty change with atrophic liver cells and engorged bile canaliculi. There was hyalinization of the periportal connective tissue, but the amount of this tissue was not increased.

Clinical History.—Dog 33-11. An adult female bull mongrel, was given a potato-bran basal diet containing 0.8 gm. protein per kilo body weight over a period of 65 days. The weight during this interval was maintained, and the animal was in apparently excellent condition at the end of the period.

Clinical History.—Dog 33-324. An adult male mongrel terrier, was given potato-bran basal diet for a period of 2 weeks. The animal maintained its weight and at the end of this time was in good clinical condition.

Clinical History.—Dog 32-58. An adult female mongrel, was given potato-bran basal diet for a period of 77 days. The average daily protein intake was 4.2 gm. per kilo body weight. The dog was in good condition at the end of the period.

Clinical History.—Dog 35-124. A young mongrel collie, was given potato-bran basal diet for a period of 63 days, receiving 1 gm. per kilo body weight daily. The weight rose from 12.3 kg. to 15.2 kg. during this period and the dog was normal.

DISCUSSION

We are dealing with an Eck fistula dog which has difficulty in producing plasma protein sufficient to maintain the plasma protein

concentration above the dangerous edema level on standard low protein diets. Apparently this dog is normal in all respects but for the Eck fistula, related thirst and diuresis, and certain anatomical changes in the liver, shown by biopsy. Presumably the inability of the animal to maintain a normal plasma protein concentration lies somewhere in the chain of metabolic processes between the ingestion of food and the final elaboration of the finished product of plasma protein. It appears reasonable to assume that this dog's inadequacy in forming plasma proteins is related to an abnormal and inefficient liver.

We use the term *maintenance factor* as related to plasma proteins and indicate by that term the unknown amount of plasma protein which must be supplied day by day to take care of the "wear and tear" of the circulating protein. We assume that this maintenance factor may include certain contributions which the plasma protein may make to the body proteins, as it has been shown (14) that the fasting dog can be kept relatively close to nitrogen equilibrium by means of plasma protein given by vein. The amount of plasma protein "wear and tear" per day is probably a matter of a few grams and in this connection we note the rapid fall in plasma protein (Dog 33-180, period 1, Table 21) from 5.3 to 3.8 gm. per cent in 6 days. This amounts to 2 gm. plasma protein loss per day using the plasma volume of this dog as 800 cc. (Table 25). There is no reason to assume that the Eck fistula dog uses up more plasma protein than do normal dogs.

A point of interest in this dog is the relationship of hemoglobin formation to the decrease in plasma protein. During the interval when the plasma protein was on a decrease (Table 24), hemoglobin was being readily formed. At this time, one complex protein substance was increasing, while another protein was decreasing. Was hemoglobin being formed at the expense of plasma protein? We believe the evidence is against this hypothesis and it has been noted above that the "reserve store" of plasma protein building materials is independent of the store of hemoglobin building materials.

SUMMARY

Normal dogs and two Eck fistula dogs, receiving a daily diet containing an average of 1 gm. of vegetable protein per kilo of body weight, showed after average intervals of 7 to 9 weeks, slight decreases in amounts of circulating plasma protein (Table 21).

A third Eck fistula dog under similar circumstances was unable to maintain its plasma protein concentration above the edema level. This dog by biopsy was shown to have an abnormal liver and the evidence indicated that the other organs were normal. The animal showed active thirst and diuresis as compared with controls (Table 25).

This Eck fistula dog had less than one-tenth the capacity of the normal dog to form new plasma protein when various food proteins were added to the basal diet, and no significant quantitative differences in the relative potency of these foods (liver, kidney, heart muscle, soy bean, salmon) could be distinguished (Table 22).

It appears that the liver abnormality is responsible for this abnormal reaction. This observation gives strong support to the thesis that the liver is actively concerned with fabrication of new plasma protein.

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