

CONCENTRATION AND SEDIMENTATION RATES OF BLOOD FROM THE SPLENIC ARTERY AND VEIN

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It was observed by Gawrilow [1928] that splenic vein blood in some instances sedimented more rapidly than blood from the general circulation, and in other cases more slowly. Berglund [1930] found that the sedimentation rate of splenic vein blood of horses was very much less than that of the artery. Stephens [1938*a*] observed a progressive diminution in the sedimentation rate of successive samples taken from the splenic vein when the splenic artery was clamped.

Sedimentation rates are greatly influenced by the red cell concentration of the blood, the greater the number of red cells per unit volume the less the sedimentation rate, other factors being equal. Now blood in the spleen pulp is more concentrated in red cells than that in the general circulation [Cruickshank, 1926; Feldberg & Lewin, 1928; Barcroft & Florey, 1928]. Moreover, it was found in the present experiments that the spleen may concentrate with great rapidity the blood supplied to it. This factor must therefore be considered first.

IMMEDIATE CONCENTRATION OF BLOOD BY THE SPLEEN

The spleens of cats were emptied via a cannula in the main splenic vein, then allowed to refill with the vein cannula closed, and the splenic artery clamped when the filling was complete. The subsidiary veins and arteries were ligated. The filling process required from 3 to 5 min. By faradic stimulation of the splenic nerves or of the spleen itself the contents were then expelled and the sequence of haematocrit values of splenic vein blood compared with that of the artery. The samples were taken in a 1 c.c. syringe graduated to 0.01 c.c., the blood being diluted with one-quarter its volume of 5% sodium citrate. Haematocrit values were determined on 100 mm. columns of citrated blood in Wintrobe tubes, all tubes being centrifuged together under standard conditions.

Table II shows typical haematocrit values for samples obtained in 5 min. from a cat spleen which required 4 min. to fill under nembutal anaesthesia.

TABLE I

	mm.
Splenic artery	28.5
1st splenic vein sample	17.0
2nd ,,	29.0
3rd ,,	33.5

The low haematocrit value of the first splenic vein sample is evidently due to corpuscles being retained in the spleen and released in the later samples. For another cat Fig. 3 (lower photograph, tubes *a, d, e, f* and *g*) shows the haematocrit values obtained in a similar experiment. Such results were obtained in seven cats and three dogs under anaesthesia, by nembutal, ether or urethane (two cats only).

Apparently the concentration of the blood occurs chiefly in the first 2 or 3 min. during filling. In fact, the overflow from the first refilling after emptying of cats' spleens could be seen with the naked eye to be dilute in red cells. When the spleen had been at rest untouched for some time this blood impoverished in red cells had evidently moved on.

Another mechanism by which the spleen concentrates blood by removing fluid via the lymphatics, described by Barcroft & Florey [1928], did not seem to be the important factor in the present experiments. Only by supposing that the spleen had retained the red cells and allowed the plasma to pass on can the haematocrit value of the first splenic vein sample, much lower than that of the artery, be accounted for. Moreover, concentration due to lymphatic drainage would seem to be excluded by the following further experiments. The spleens of cats were first emptied and refilled, the entire splenic mesentery, including artery, vein and lymphatics, then clamped, the splenic vein cannulated and samples withdrawn. These samples showed the same progression of haematocrit value with an initial value much below that of splenic arterial blood. The same precautions were observed in centrifugation. The errors of haematocrit determinations, admittedly rather large, could not account for the phenomena observed.

This latter method of performing the experiment affords the easiest method of demonstrating the effects.

Fig. 1 shows the haematocrit values of splenic vein blood from another type of experiment in cats, the splenic artery being untouched, a cannula placed in the splenic vein and samples taken from this during stimulated contraction of the spleen and during a phase of passive

dilatation. Contraction and dilatation were caused to occur as rapidly as possible, and in the example shown 3-5 min. elapsed between each sample. All the samples were centrifuged together. The maximum error in haematocrit estimations of this sort is of the order of 1 mm. as determined by successive estimations on the femoral vein.

Rapid concentration of the blood by arrest of the corpuscles during filling of the spleen affords part of the explanation of the fact that whilst Cruickshank [1926] found that the red cell concentration of splenic vein blood showed first an increase and then a decrease as successive samples were taken, Feldberg & Lewin [1928] found no such variation. The time interval between the filling of the spleen and the taking of the blood samples is evidently a factor here. Fig. 2 shows the rise and fall referred to by Cruickshank, but in Figs. 3 and 5 a rise only is shown. In yet other experiments the progression was the inverse of that described by Cruickshank, with lower haematocrit values in the middle samples than at either the beginning or the end. The lower haematocrit value of terminal samples, when found, is probably due to the fact that the discharges from different regions of the spleen do not reach the vein simultaneously but in succession, the terminal discharge from one segment being followed by the initial discharge from another segment. Splenic innervation is segmental [Tait & Cashin, 1925].

A time lag of 3 or 4 sec. between the moment of releasing a clip on the splenic artery and the commencement of flow in the vein was noticed when the spleens of cats were in the contracted state. The flow gave the impression of fluid percolating through a sponge.

SEDIMENTATION RATES OF BLOOD FROM SPLENIC ARTERY AND VEIN

Methods

Experiments in which the sedimentation of splenic arterial blood was compared with that of successive samples taken from a cannula in the main splenic vein, the entire splenic mesentery being clamped, were

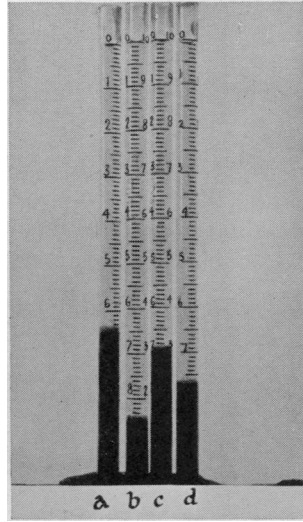


Fig. 1. Immediate concentration of blood by the spleen. *a*, spleen contracting; *b*, dilating; *c*, contracting; *d*, dilating. 3-5 min. intervals.

performed in twenty-six cats and seven dogs. By faradic stimulation of the splenic nerve or of the spleen itself the terminal contents of the spleen were disgorged, after the initial free flow had ceased. Clamping of the splenic artery is necessary as Cruickshank [1926] showed to prevent mixture of splenic pulp blood with that by-passed directly from the artery. Accordingly, the entire mesentery was clamped in order to close all the arteries and veins simultaneously. A useful point of technique for experiments of this and other types described, is to clamp the entire splenic mesentery with a long rubber-jawed bowel clamp before the vein samples are taken. Further entry of blood from small adventitious arteries is thus avoided.

The blood samples were obtained by withdrawal into sodium citrate as already described for the blood concentration experiments. Sedimentation was observed in Wintrobe tubes 100 mm. in length and 2.5–3 mm. bore. Haematocrit values were obtained by centrifuging the same specimens in the same tubes upon which sedimentation rates were observed, the tubes being centrifuged together. The tubes were filled by pipetting from the collected samples, and it was arranged that the inside wall of the tube above the column was wet with the blood. These factors of technique influence sedimentation rates.

The effects observed were independent of the type of anaesthesia, except that when ether was employed the spleen contained so little blood that it was necessary first to fill it by pressure on the splenic vein. Nembutal gives at laparotomy a dilated spleen engorged with blood; urethane gives less engorgement; with ether it is usually contracted.

Results

These were as follows:

(a) In blood from the resting spleen there was a much lower sedimentation rate in the splenic vein than in the artery, and also a small progressive decrease in the sedimentation rate as the later vein samples were reached [Stephens, 1938*a*].

(b) When the spleen had been recently refilled with blood the progressive decrease in the sedimentation rate of the later vein samples became extremely marked. Immediately after refilling, moreover, the initial vein samples had a sedimentation rate much greater than that of the artery.

(c) When the spleen was emptied and refilled and then left for some time with the vein alone clamped, the results were indistinguishable from those found with resting spleens.

In two cats the first vein sample obtained showed a lesser sedimentation rate than the artery, followed by a rate greater than the artery and then by a progressively lesser rate. Pressure on the spleen followed by refilling probably accounted for this sequence, an explanation in accord with the corresponding haematocrit values.

The general result obtained on resting spleens is typified in Fig. 2. In dogs the normal blood sedimentation rate is from 0.5 to 1.5 mm./hr., but the splenic vein sedimentation rate is so low that several hours are

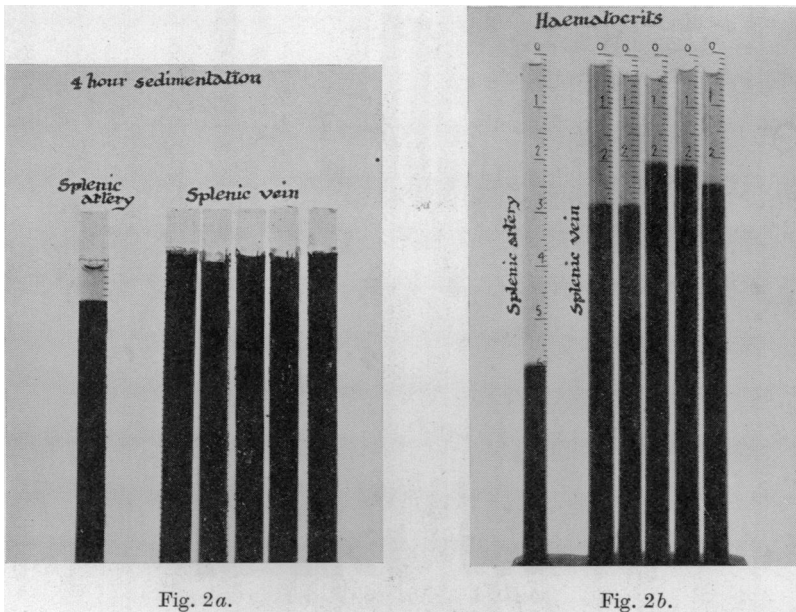


Fig. 2. Resting spleen. Normal dog. Haematocrits of same specimens as 4 hr. sedimentations. No measurable sedimentation of splenic vein blood in this time. (Nembutal anaesthesia.)

necessary before any measurable sedimentation can be seen. After 4 hr. the arterial blood sedimented 5 mm. in this case, whilst the vein blood was quite unsedimented. The haematocrit values of the same blood specimens is also shown in Fig. 2. (The photograph of these haematocrits was unavoidably delayed in this case so that some evaporation has occurred.) The maximum haematocrit value in the splenic vein was, as shown, almost exactly twice that in the artery, viz. 41 and 79.5 mm. respectively.

It is possible that the results mean nothing more than that splenic pulp blood becomes increasingly more concentrated in erythrocytes as the

deeper samples are reached. A reciprocal relationship between sedimentation rate and haematocrit values for splenic vein blood was found in every case, well within the limits of accuracy of sedimentation rate and haematocrit measurements. Anomalies occurred, however, when the values for splenic vein blood were compared with those of the artery.

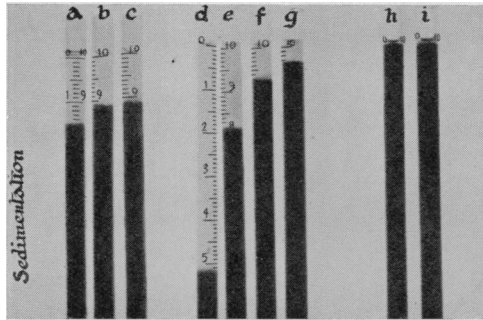


Fig. 3a.

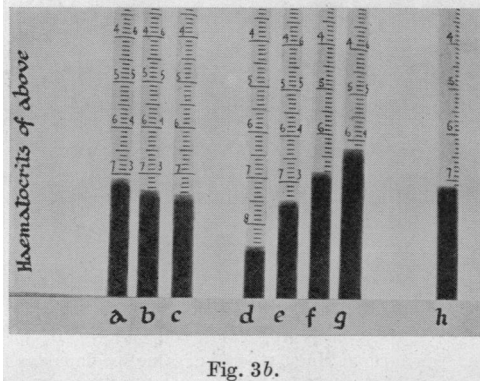


Fig. 3b.

Fig. 3. Immediately after refilling spleen. Pregnant cat. $2\frac{1}{2}$ hr. sedimentation of: *a*, splenic artery at time of filling spleen after emptying; *d* to *g*, splenic vein samples taken in quick succession, artery clamped; *h* and *i*, foetal blood; *b* and *c*, splenic artery $\frac{1}{2}$ and 1 hr. later showing effect of continued urethane. Below: haematocrits of same tubes, *i* removed. Sedimentation tubes set up from *i* to *a* at approximately 1 min. intervals.

ANAESTHESIA AND SEDIMENTATION RATE

Fig. 3 shows the effect of urethane anaesthesia on the sedimentation rate of cat blood from the splenic artery. There is a progressive decrease from the normal value (*a*), to (*c*), that after 1 hr. anaesthesia. Ether gave a similar result. Similar effects of chloroform anaesthesia have been observed by Rourke & Plass [1928] and with various anaesthetics by

Hino [1934]. In the case of ether and urethane it was not possible to explain these effects in the present experiments on the basis of increased red cell concentration of the peripheral blood. The haematocrit value became less as the anaesthesia proceeded, and yet the sedimentation rate decreased. Chloroform is known to produce a diminution of the blood sedimentation rate due to interference with fibrinogen production by the liver [Rourke & Plass, 1928].

In this connexion brief mention may be made of the fact that ether or chloroform and ether anaesthesia of cats and dogs was observed to produce an increase in red cell electrophoretic speed which became very marked after prolonged anaesthesia. Under nembutal or urethane the speed was practically unchanged. The electrophoretic speed and sedimentation changes under anaesthesia are evidently related to each other, and are probably due to altered plasma composition.

In order, therefore, to eliminate any effect due to the anaesthetic not being applied equally to splenic artery and pulp blood, in some experiments the spleen was first emptied by stimulation of the nerves and then allowed to fill with blood corresponding to the first splenic artery sample. Identical results were obtained. Progressive effects of the anaesthetic on the spleen pulp blood was, of course, improbable after the splenic artery was clamped. Moreover, the effects of anaesthesia on the sedimentation rate were very much smaller than the marked changes observed in splenic blood.

EFFECT OF REFILLING, PLASMA ALTERATION AND ANAEMIA

Four variations of the experiment were next performed:

(1) The splenic vein samples were taken immediately after emptying and refilling, and after the spleen had been left refilled for periods up to 1 hr.

Sampling immediately after refilling

When the initial splenic vein sample was taken immediately after refilling it showed a higher sedimentation rate than the splenic artery. (The two exceptions, already mentioned, were probably due to manipulation of the spleen.) This initial high rate is shown in Fig. 3. The corresponding haematocrit values showed that this was due to red cells being retained in the spleen and released in the later samples.

Sampling delayed after refilling

There were no significant differences when the blood was left in the spleen for 1 hr. with the entire splenic mesentery clamped. The initial high sedimentation rate, low haematocrit value and progressive sequence

were found as before. It was desirable, however, that these experiments of delayed sampling after refilling should be extended with precautions to ensure that the lymphatic drainage was free.

Accordingly in four cats the spleen was emptied by stimulation, the principal vein alone ligated, and the spleen then left for periods from $\frac{3}{4}$ to 1 hr. During this time the lymphatic drainage was presumably free, and, what is perhaps equally important, the spleen pulp was exposed to the arterial blood pressure.

Marked differences were then found between the splenic vein samples thus obtained and those immediately after refilling. The results were now indistinguishable from those seen when the spleen had been at rest for long periods, resembling those shown in Fig. 2. The splenic vein haematocrit values were all approximately double that of the artery, whilst their sedimentation rates were all much less than that of the artery without any marked characteristic sequence.

Table II shows typical values after the vein had been ligated for 45 min. in a cat under nembutal.

TABLE II

	Haematocrit mm.	Sedimentation rate (1 hr.) mm.	Sedimentation rate (5 hr.) mm.
Splenic artery	26.5	23	42
1st splenic vein	50	less than 0.5	1.0
2nd "	50	less than 0.5	1.5
3rd "	46	less than 0.5	3.0
4th "	47	less than 0.5	3.0

Three factors must be considered in accounting for this effect:

- (a) Lymphatic drainage causing further concentration of the blood.
- (b) Drainage of blood impoverished in red cells via the small accessory veins which were not ligated.

(c) Red cells retained in the deeper regions of the spleen pulp may have moved on, perhaps aided by the pulsations of the spleen [Roy, 1881], and the arterial pressure. In any case, this would seem to be the most probable explanation of the marked increase in concentration of the first vein sample.

In order, therefore, to ascertain the part played by lymphatic drainage, it is necessary to ligate the numerous small veins in the splenic mesentery without damage to the lymphatics. This work is proceeding.

It is significant that persistent contraction of the splenic vein could cause concentration of the entire contents of the spleen by a mechanism similar to that involved in this experiment of ligating the main splenic

vein alone. The marked contractility of this vessel, and its persistent contraction for an hour after stimulation, have been described by Tait & Cashin [1925].

(2) In cats with initial high blood sedimentation rate due to pregnancy the splenic vein samples collected immediately after filling the spleen showed the same progression. Fig. 3, upper photograph, shows the sequence for 2¼ hr. sedimentation in a pregnant cat. In this experiment the entire splenic mesentery was clamped after the spleen had refilled following emptying by faradic stimulation, the blood samples collected and set up as nearly as possible at the same time, but commencing with the tubes on the right-hand side of the photograph. The sedimentation differences shown are therefore rather less than those actually occurring.

The 1 hr. values in this case are shown in Table III.

TABLE III

	Sedimentation rate (1 hr.) mm.	Haematocrit (citrated blood) mm.
Splenic artery	6	27.5
1st splenic vein sample	23	14
2nd "	7.2	25
3rd "	2.5	30.5
4th "	1.5	36.5
Foetal blood	less than 0.5	28
Splenic artery ½ hr. later	5	25
Splenic artery 1½ hr. later	4.5	24.5

The first splenic vein sample after refilling has thus nearly four times the sedimentation rate of blood from the splenic artery, whilst the last vein sample has only one-quarter the sedimentation rate of the artery. The above table also shows the effect of urethane anaesthesia (no ether was used) and the reciprocal relationship between sedimentation rate and haematocrit value for splenic vein blood. Tubes *h* and *i* in Fig. 3 also show the extremely low sedimentation rate of foetal blood. Tube *i* was placed aside and observed for 8 hr., in which time the blood sedimented 3.5 mm. only. A similar result was obtained in other specimens of cat foetal blood, and by analogy with human foetal blood may be ascribed to its low plasma protein content.

(3) The sedimentation rate was artificially raised by intravenous injections of 10% gelatin solution (10-15 c.c./kg.). The splenic vein samples behaved as before.

(4) Two dogs were given an anaemia by a single large haemorrhage of ½ of their body weight 4 days previously. The results were unaltered.

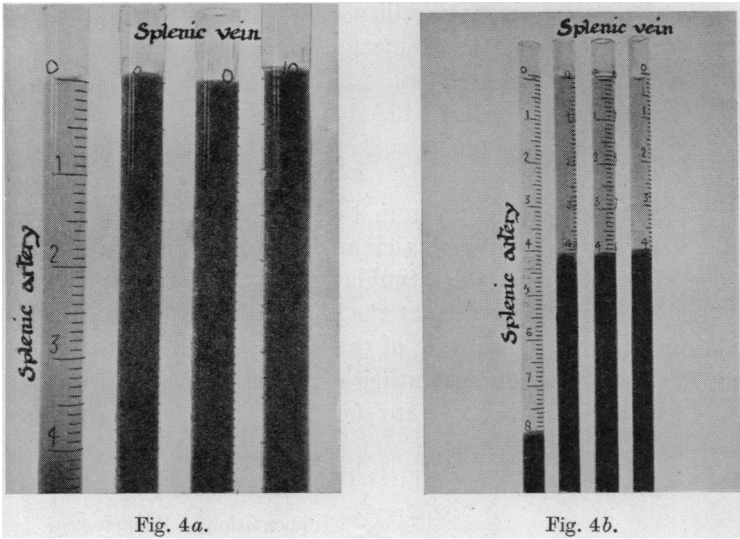


Fig. 4. Resting spleen. Dog after haemorrhage. Left: 2 hr. sedimentation. Right: haematocrits of same tubes. (Nembutal.)

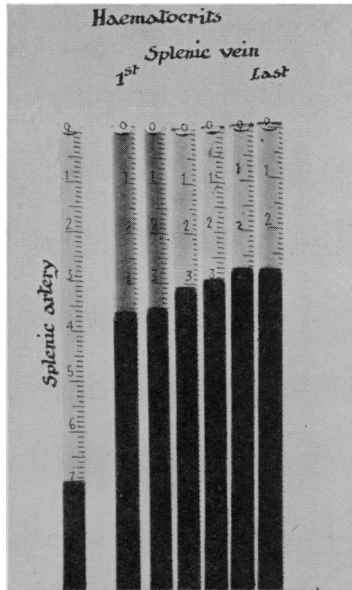


Fig. 5. Resting spleen. Haematocrits of splenic artery and vein blood of dog after haemorrhage 4 days previously. (Nembutal.)

Fig. 4 shows the sedimentation and haematocrit results in one of these animals (nembutal anaesthesia). The values are shown in Table IV.

TABLE IV

	Haematocrit mm.	Sedimentation rate (1 hr.) mm.
Splenic artery	18	30
1st splenic vein sample	57	less than 0.5
2nd "	58	less than 0.5
3rd "	59	less than 0.5

The diffuse upper level of the arterial sedimenting column after haemorrhage, as shown in Fig. 4, is due to the presence in this diffuse zone of immature red cells [Stephens, 1938*b*].

Altogether twenty-four samples were taken from the splenic vein in each dog. In Fig. 5 the haematocrits over the full range of splenic vein samples of the second dog are shown.

ANAEMIA AND RED CELL CONCENTRATION BY THE SPLEEN

It is worthy of mention that the spleens of dogs apparently concentrate the blood to at least the same relative extent after haemorrhage when the red cell count of the general circulating blood is low, as when the blood count is normal. This can be seen by comparing Figs. 4 and 5 from anaemic blood with Fig. 2 from normal blood. These haematocrit values are shown in Table V.

TABLE V

	Splenic artery haematocrit mm.	Maximum splenic vein haematocrit mm.
Typical normal dog, Fig. 2	41	79.5
Anaemic dog, no. 1, Fig. 4	18	59
Anaemic dog, no. 2, Fig. 5	29.5	69

The spleens of these animals were not disturbed, and the entire splenic mesentery was clamped immediately at laparotomy under nembutal anaesthesia. All these spleens and those of other normal dogs under nembutal were observed to be extremely dilated. Their colour was dark violet, approximately the colour of reduced blood, the general appearance being the same in all cases. The actual dimensions of the spleens were surprisingly large but these are probably the dimensions of the spleen in a living normal dog at rest [Barcroft & Stephens, 1927]. The spleens could not be weighed without interfering with the experiment. The maximum thickness was between 3 and 4 cm. in each case, the other dimensions being shown in Table VI.

TABLE VI

	Body weight kg.	Size of spleen at laparotomy (cm.)	
		Max. length cm.	Max. width cm.
Normal dog	14.5	26.5	16.5
Anaemic dog, no. 1	17.5	27	14
Anaemic dog, no. 2	22	29.5	14.5

The fact that the spleens were thus engorged with blood under conditions where a haemoglobin deficiency in the general circulation is to be presumed is perhaps surprising. There is, however, no reason to attribute the phenomena to the anaesthesia, as the result accords with the observation of Shen [1928] that anaemia does not cause contraction of the spleen. Although ether anaesthesia does not produce such marked splenic engorgement, its vasodilator action could account for the difference, vasodilators causing marked splenic contraction.

CAUSE OF SEDIMENTATION RATE DIFFERENCES BETWEEN SPLENIC ARTERIAL AND VENOUS BLOOD

The low sedimentation rate of splenic vein blood is possibly due, not only to the concentration of red cells, but partly to splenic influence upon it. It is difficult rigorously to separate the two factors by experimental means.

In three of five cats in which the principal splenic vein and several of the smaller veins were ligated, anomalies were found which would seem to be outside the limits of experimental error. The indications were that the plasma protein concentration had been increased, simultaneously with the increase in the red cell concentration. Thus the values shown in Table VII were found 70 min. after the spleen had been emptied and the veins ligated:

TABLE VII

	Sedimentation rate (90 min.)	Haematocrit
	mm.	mm.
Splenic artery	41	22.0
1st splenic vein	43	32.5
2nd "	16	35.0
3rd "	17	33.0
4th "	4	41.0
5th "	less than 0.5	52.0

The first splenic vein sample has thus a sedimentation rate slightly greater than that of the artery, but its haematocrit value is nevertheless also greater by 50%. Cases of this sort may occur more frequently than stated above but be concealed by mixing of blood on emergence from

different regions of the spleen or in the cannula. (The cat from which the data given in Table VII were obtained exhibited an anaemia and high sedimentation rate for which no cause could be assigned.)

A simple interpretation of these anomalies to mean that the plasma protein composition has been altered is not, however, possible. Alteration of red cells and of their surfaces by the spleen must be taken into account here and also in explaining the abnormally low sedimentation rate of splenic vein blood. In the latter case Bergenhem & Fåhraeus [1936] suggest the action of a lysolecithin-like substance. The question as to whether red cells of some particular type have selectively been arrested in the spleen pulp will be considered subsequently.

SEDIMENTATION FACTORS IN THROMBOSIS OF THE SPLENIC VEIN

In two cats whose blood had high sedimentation rates of 20.5 and 23.0 mm./hr. (normal value 3 mm./hr.), it was noticed that a sedimented deposit formed inside the splenic vein when the blood had lain stagnant for approximately 10 min. after the vein and arteries were clamped. This was seen in the course of experiments in which the spleen had been refilled immediately before the vessels were clamped, and the cannulation purposely delayed. In these cases the vein, approximately horizontal, was occupied above by clear plasma with a sedimented deposit of corpuscles below. Formation of red cell aggregates *in vivo* in conditions of stasis is well known and is discussed by Fåhraeus [1929]. The present phenomena represented the later stage of sedimentation after aggregate formation.

When, later, the splenic vein blood was withdrawn, the initial sample showed haematocrit values of 17 mm. in one animal and 20.5 mm. in the other, the splenic artery haematocrit values being 29 and 30 mm. respectively. Evidently the low red cell concentration and increased plasma protein content (presumed from the high sedimentation rate of the general circulating blood) were the two factors causing the rapid *in vivo* sedimentation in these cases.

In another cat in which the principal and several of the accessory veins had been ligated for some time, the blood sedimented 2-3 mm. inside the splenic vein cannula of 6 mm. bore, within approximately 3 min. between the taking of samples.

It is conceivable that the frequently occurring thrombosis of the splenic vein in the human subject arises from similar rapid sedimentation in conditions of stasis brought about by contraction of the splenic vein.

CONCENTRATION AND SEDIMENTATION RELATIONSHIPS IN
DENERVATED EXTERIORIZED SPLEEN

In one dog only have these measurements been made. The nerves of the dorsal portion of a dog's spleen were cut, care being taken to ensure that the nerves entwining the blood vessels supplying this region were divided. The innervation of the ventral half of the spleen was not disturbed. The spleen was then exteriorized, the experiment thus being similar to that previously described [Barcroft & Stephens, 1927].

Blood samples were taken 15 days later by puncture of the spleen, and for this purpose no anaesthetic was necessary. It was possible to obtain samples for sedimentation measurement only from the denervated end. Clotting always occurred in blood from the other end of the spleen. It was noticed, moreover, that when the denervated end was punctured, blood flowed out quite readily, but from the end with the nerves intact a slow oozing only appeared.

The following measurements were made:

	Sedimentation rate (1 hr.) mm.	Haematocrit mm.
Femoral vein	33	29.5
Denervated spleen	18.5	32

In this experiment there was very little concentration of blood by the denervated spleen. The low sedimentation rate of the splenic blood may be considered anomalous, the haematocrit difference probably not accounting for it.

SUMMARY

1. Concentration of red cells occurs within a few minutes during filling of cats' and dogs' spleens. The cells are strained out of the blood and the plasma passes on. In cats a further concentration ensues when the principal splenic vein alone is clamped.

2. In anaemia the spleen of the dog concentrates blood to the same relative extent as normally.

3. Blood from the splenic vein of resting spleens of cats or dogs has a much lower sedimentation rate than blood from the artery.

4. Immediately after refilling the spleen the first vein sample shows a much greater sedimentation rate than the artery, sometimes four or five times as great. This is due to red cells being retained in the spleen, impoverishing the initial samples and enriching the later ones.

5. The results are unaltered when the sedimentation rate of the general circulation is abnormally high, or in anaemia.

6. Most of the sedimentation differences between splenic artery and vein may be adequately explained by the varying red cell concentration. Altered splenic vein plasma composition or red cell surface changes may also occur.

7. Ether or urethane diminish the sedimentation rate of the general circulating blood, probably due to altered plasma composition. Ether or chloroform and ether anaesthesia produce a marked increase in red cell electrophoretic speed.

8. Thrombosis of the splenic vein in the human subject may be due to the high sedimentation rate of some portions of the emergent blood, in addition to stasis caused by contraction of the vein.

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