

VARIATIONS EXPERIMENTALLY PRODUCED IN THE SPECIFIC GRAVITY OF THE BLOOD. BY C. S. SHERRINGTON, M.A., M.B., AND S. MONCKTON COPEMAN, M.A., M.D., *late Research Scholar of the British Medical Association.* Plate IV.

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THE ingenious method devised by Roy¹ for estimating the specific gravity of the blood puts into possession of the physiologist a means of making rapid and accurate observations at the expense of the withdrawal of a single drop, or even a fraction of a drop of blood. After a little experience of the method it seemed to us that it might be worth while to study in this way results which follow the injection of quantities of saline fluid into the circulation². We are induced to place our observations on record here, although in some respects their extent is too limited, because circumstances render it unlikely that we shall have opportunity to further pursue the subject together.

Roy's method is now so well known that we need not explain it here in detail, except in so far as to refer to the particulars and precautions followed in our own experiments. Briefly stated, his method consists in determining the specific gravity of the blood by observing whether a drop of it rapidly withdrawn from the circulation, and placed in a solution of known specific gravity, rises, sinks, or remains stationary in that solution.

The first step in carrying out such observations is the preparation of the solutions which are to serve as standards of specific gravity. We prepared a series of solutions ranging from a specific gravity of 1025 to 1070, one member of the series corresponding to each unit of the third place of decimals.

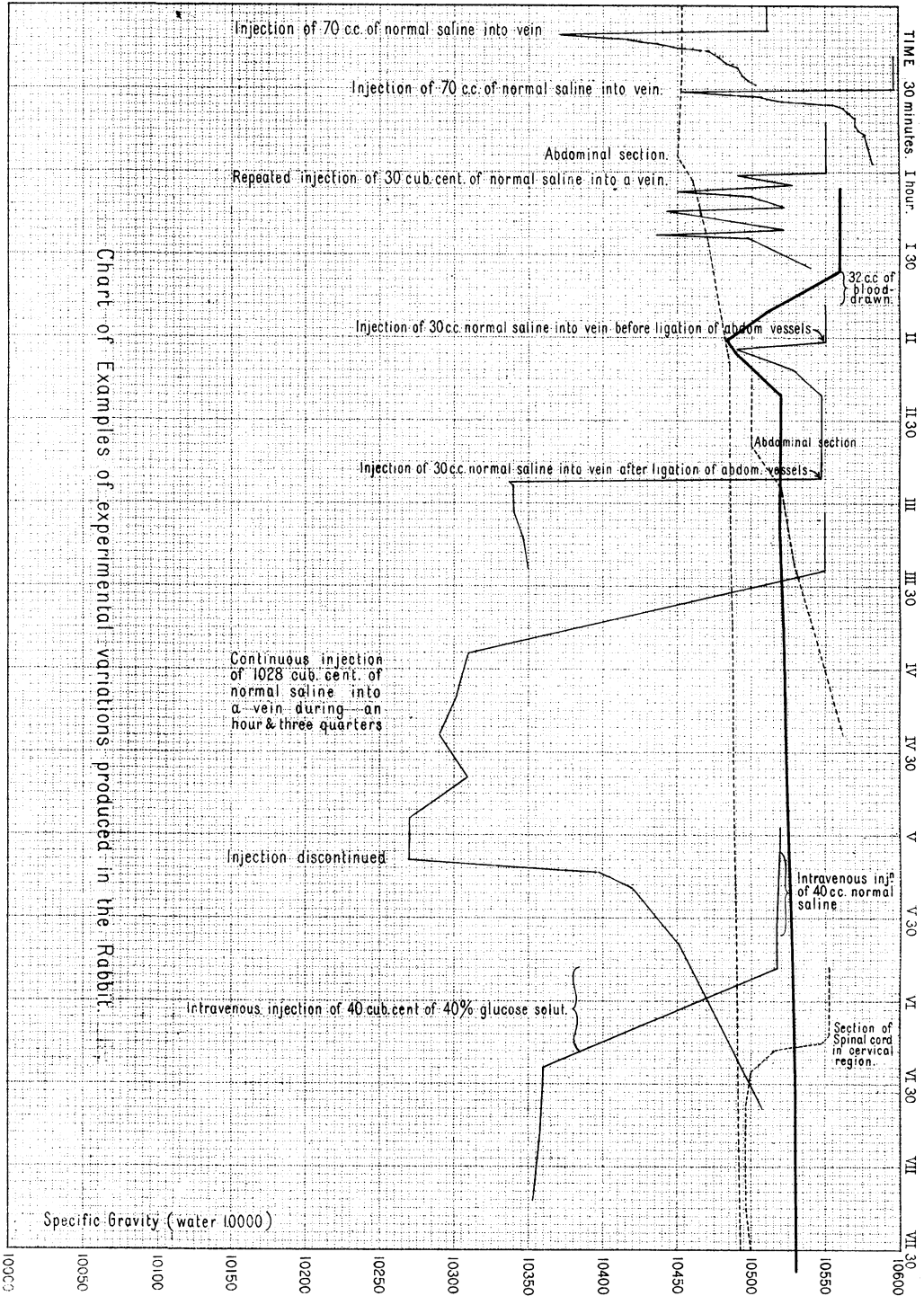
The solutions were prepared by weighing, and tested by an accurate hydrometer made by Dring and Fage. The solution employed was of Barff's boroglyceride, glycerin and magnesium sulphate in distilled water with the addition of a small quantity of mercuric perchloride solution.

From a solution of these with a sp. gr. of 1.040 the series of fluids was prepared by the addition of distilled water on the one hand or of glycerin on the other.

¹ This *Journal*, Vol. v. p. ix.

² Several of the results dealt with in the present paper were the subject of a short communication made to the Physiological Society in May 1890, cf. *Proc. of the Phys. Soc.* No. III. 1890.

Chart of Examples of experimental variations produced in the Rabbit.



A large quantity (2 litres) of each unit of the series was made up, and these fluids retained their specific gravity throughout the somewhat extended period over which our work has been spread. The constancy of the series was several times verified by going over it unit by unit with the hydrometer and also by the method of weighing.

Blood does not clot very rapidly in these solutions and that desideratum it was, coupled with the antiseptic properties, which led us after some previous trials to adopt this slight modification of Roy's original mixture. Lloyd Jones¹ also has employed corrosive sublimate for the preservation of the fluid. At first we were careful to observe the temperature of the room at the time of making the observation, but this precaution was found to be needless and was afterwards discontinued.

Inasmuch as actually the same fluids have been used throughout the work, and have kept well, our series of observations are completely serviceable for comparison among themselves. But it may be well to furnish some guide for an estimate of the absolute values our figures possess in relation to those recorded by other observers, especially by those who have used the same method as ourselves. The following is a list of estimations of the specific gravity of the blood of healthy animals of various species recorded by the authorities appended.

Species	Specific gravity	Observer
Frog (winter)	Highest of 14 observations	1·053 Lloyd Jones ²
	Lowest " "	1·034 " "
Blackbird ♂		1·066 " "
	♀	1·062 " "
Sparrow ♂		1·074 " "
	♀	1·0635 " "
Rabbit	1·046–1052	Gschleiden ³
Dog	1·059	Nasse ⁴
"	1·048–1068	Pflüger ⁵
Man ♀	1·045–1056	Davy ⁶
"	1·054	Nasse ⁷
"	1·054–1060	Becquerel & Rodier ⁸
"	1·050	Schmidt ⁹
"	1·058–60	Quincke ¹⁰

¹ This *Journal*, Vol. VIII. p. 1.

² This *Journal*, Vol. XII. p. 306.

³ *Unters. a. d. physiol. Lab. zu Würzburg*, II. p. 151, 1868.

⁴ Quoted by Gschleiden, *Physiol. Méthodique*, p. 328.

⁵ *Archiv*, Vol. I. p. 75, 1868.

⁶ *Researches on Physiological Anatomy*, Vol. II. p. 15.

⁷ *Wagner, Handwörterbuch*, Vol. I. p. 131.

⁸ *Recherches sur la composition du sang*, p. 22, 1844.

⁹ *Caractéristique du Epidém. Cholera*, p. 31.

¹⁰ *Virchow's Archiv*, Vol. LIV. p. 541, 1872.

Species	Specific gravity	Observer
Man ♀	about 1.055	Lloyd Jones ¹
"	1.0562	Schmaltz ²
♂	1.052-60	Davy ³
"	1.055	Nasse ⁴
"	1.058-62	Becquerel & Rodier ⁵
"	1.060	Schmidt ⁶
"	1.058	Lloyd Jones ¹
"	1.0591	Schmaltz ²

Specific gravity of the blood in various animals, observed by ourselves.

Name	Date	Sex	Weight	Age	Blood from	Condition	Sp. gr.
Frog	Nov. 5/88	—	—	—	aorta	—	1.0556
Snake	Feb. 17/90	—	—	—	caudal artery	—	1.0550
Fowl	"	M	—	—	comb	—	1.0640
"	"	F	—	—	comb	—	1.0636
Pigeon	"	—	—	—	leg	—	1.0673
Mouse	Oct. 14/89	F	—	—	ear	—	1.0590
Rat	"	—	—	—	tail	—	1.0560
Guinea-pig	Feb. 21/89	F	—	—	ear	large, advanced in pregnancy	1.0510
"	"	—	—	fœtus in utero	—	—	1.0603
"	Oct. 13/89	F	—	—	lip	—	1.0580
"	Feb. 11/90	M	—	—	ear	—	1.0590
"	" 14/90	—	—	—	"	—	1.0560
Rabbit	Nov. 14/87	M	4 lbs. 15 oz.	—	—	—	1.0526
"	" 15/87	M	5 " 0 "	—	nose	—	1.0530
"	" 21/87	M	4 " 13 "	—	ear	—	1.0496
"	" 23/87	—	4 " 2 "	—	"	—	1.0516
"	" 30/87	—	—	—	"	large & fat	1.0576
"	" 30/88	—	2.7782 kilos	—	"	—	1.0576
"	Feb. 7/88	—	5 lbs. 6½ oz.	—	"	—	1.0543
"	" 15/88	—	2.289 kilos	—	"	—	1.0556
"	Mar. 10/88	—	2.884 "	—	"	—	1.0556
"	Aug. 2/88	—	5¼ lbs.	—	"	—	1.0506
"	" 4/88	—	—	—	"	—	1.0463
Monkey	Sep. 25/88	—	2.161 kilos	—	cutaneous vessel of arm	—	1.0516
Rabbit	Oct. 25/88	—	—	—	—	large	1.0520
"	Nov. 2/88	—	7 lbs. 4¼ oz.	—	ear	"	1.0546
"	" 9/88	—	—	—	—	"	1.0490
"	" 11/88	—	—	—	—	small	1.0473
"	" 13/88	—	—	half-grown	ear (vein)	"	1.0426
"	" 16/88	—	3 lbs. 5 oz.	very young	" "	—	1.0446
"	" "	—	—	"	" "	—	1.0436
"	" "	—	3 lbs. 0½ oz.	"	" "	—	1.0446
"	" "	—	2 " 15¼ "	"	" "	—	1.0456
"	" 28/88	—	3 " 12 "	"	" "	—	1.0490
"	" "	—	3 " 4½ "	"	" "	—	1.0450
"	" 20/88	—	2.451 kilos	not half-grown	ear	—	1.0446

¹ *loc. cit.*

² *Deutsche medic. Wochenschr.* No. 16, 1891.

³ *Researches on Physiological Anatomy*, Vol. II. p. 15.

⁴ Quoted by Gschleiden, *Physiol. Méthodique*, p. 328.

⁵ *Recherches sur la composition du sang*, p. 22, 1844.

⁶ *Caractéristique du Epidém. Cholera*, p. 31.

SPECIFIC GRAVITY OF BLOOD.

Name	Date	Sex	Weight	Age	Blood from	Condition	Sp. gr.
Rabbit	Nov. 26/88	—	3 lbs. 5 oz.	—	ear	—	1.0470
"	" 16/88	—	3 " 2 "	—	"	—	1.0446
"	" 27/88	—	1.0615 kilos	—	"	—	1.0506
"	Dec. 4/88	—	—	—	ear (artery)	—	1.0450
"	" 18/88	—	3.514 kilos	—	ear	very large	1.0463
"	Jan. 10/89	F	7 lbs. 10 oz.	—	"	—	1.0580
"	" 15/89	F	3.478 kilos	—	ear & thigh	—	1.0580
"	" 23/89	M	6 lbs. 4 oz.	—	ear	very good	1.0586
"	" 24/89	M	1 " 3 "	7 weeks	"	—	1.0490
"	" "	M	1 " 8 "	"	"	—	1.0506
"	" "	F	1 " 11 "	"	"	—	1.0523
"	" 29/89	M	1 " 4 "	—	"	—	1.0476
"	" "	M	1 " 13 "	—	"	—	1.0506
"	" "	F	1 " 12½ "	—	"	—	1.0500
"	" 30/89	—	.878 kilo	8 weeks	"	—	1.0526
"	Mar. 19/89	F	5 lbs. 4 oz.	—	—	poor	1.0490
"	" "	—	5 " 1 "	—	ear (arterial)	—	1.0500
"	" "	M	4 " 13 "	—	—	—	1.0520
"	" 29/89	—	—	—	ear	—	1.0490
"	April 6/89	—	6 lbs. 8½ oz.	full grown	"	—	1.0576
"	" 26/89	—	5 " 5¾ "	—	"	—	1.0480
"	" "	—	2.182 kilos	young	ear (arterial)	—	1.0513
"	May 7/89	F	6 lbs. 2½ oz.	—	ear	—	1.0573
"	" 11/89	M	4 " 4¾ "	young	"	—	1.0516
"	" 21/89	—	4 " 0¾ "	—	"	—	1.0460
"	" 24/89	M	2 " 7 "	—	"	—	1.0453
"	" 29/89	M	—	—	"	—	1.0530
"	June 4/89	M	—	—	"	med. size	1.0533
"	" 11/89	—	—	—	"	large	1.0493
"	" "	—	—	—	"	—	1.0500
"	" 14/89	—	—	—	"	small	1.0500
"	" 15/89	—	—	—	"	small poor condition	1.0446
"	—	M	7 lbs. 15 oz.	—	"	—	1.0540
"	July 21/89	—	—	—	"	small	1.0553
"	" 22/89	—	4 lbs. 15 oz.	—	"	—	1.0510
"	Sep. 3/89	F	8 " 12 "	—	"	—	1.0520
"	" 4/89	M	4 " 10 "	—	"	—	1.0510
"	" 10/89	M	5 " 6¾ "	—	"	—	1.0566
"	" 11/89	F	4 " 8½ "	—	"	—	1.0523
"	" 12/89	F	4 " 2½ "	—	"	—	1.0500
"	" 15/89	F	7 " 4 "	—	"	poor	1.0456
"	" 17/89	M	—	—	"	good	1.0570
"	" "	M	4 lbs. 8 oz.	young	"	—	1.0546
"	" 18/89	M	4 " 9 "	"	"	—	1.0516
"	" 20/89	—	6 " 6 "	—	"	—	1.0526
"	" "	—	8 " 15 "	—	"	—	1.0563
"	" 24/89	M	4 " 15 "	—	"	—	1.0493
"	Feb. 19/90	F	6 " 13 "	—	"	—	1.0560
"	" 25/90	—	5 " 6 "	—	"	—	1.0530
"	" 28/90	F	5 " 6 "	—	"	—	1.0520
"	Mar. 1/90	M	6 " 7 "	—	"	—	1.0520
"	" 5/90	—	—	—	"	—	1.0533
"	" 14/90	—	—	—	"	—	1.0530
"	" 12/90	F	—	—	"	small	1.0510
"	" 17/90	M	7 lbs. 1¾ oz.	—	"	—	1.0546
"	" 13/90	—	—	—	"	—	1.0576
"	" 29/90	M	6 lbs. 7½ oz.	—	"	—	1.0540

Name	Date	Sex	Weight	Age	Blood from	Condition	Sp. gr.
Rabbit	Mar. 31/90	M	—	—	ear	—	1-0550
"	Apr. 1/90	—	—	—	"	large	1-0576
"	" 22/90	M	—	—	"	small good	1-0580
"	" 24/90	—	—	—	ear (right)	—	1-0560
"	" 29/90	F	5 lbs. 14 oz.	—	ear	—	1-0490
"	May 6/90	F	—	—	"	well-fed	1-0526
"	" 10/90	M	3572 grms.	—	jugular vein	good	1-0520
Cat	Mar. 20/88	F	—	—	ex. jugular v.	pregnant	1-0550
"	Feb. 7/90	F	6 lbs. 5½ oz.	adult	ear	—	1-0506
"	" 20/90	F	6 lbs. 6½ oz.	adult	"	—	1-0516
"	Mar. 22/90	—	—	—	"	—	1-0553
"	May 12/92	—	—	—	"	—	1-0603
Dog	Jan. 18/88	M	9579 grms.	young	small artery	large	1-0550
"	Feb. 5/89	—	—	—	—	—	1-0630
"	Apr. 2/89	F	—	—	—	very large Bst. hnd	1-0620
"	" 3/89	M	—	under 12 months	—	—	1-0620
"	June 17/89	—	—	—	ear	small	1-0566
"	Oct. 27/89	—	7943 grms.	9 months	"	—	1-0566
"	Nov. 2/89	F	—	puppy	"	—	1-0520
"	" 7/89	F	—	9 months	"	—	1-0570
"	Dec. 1/89	F	—	puppy	"	—	1-0526
"	Feb. 7/90	F	—	3½ months	"	—	1-0496
"	" 7/90	F	—	"	"	—	1-0510
"	" 10/90	M	38 lbs. 3½ oz.	10 months	"	—	1-0610
Goat	May 6/91	—	—	—	—	—	1-0620
Horse	Mar. 8/90	F	—	old	jugular vein	emaciated	1-0510
Calf	May 10/91	—	—	—	—	—	1-0583
Monkey	Dec. 17/88	—	4819 grms.	—	ear	large	1-0566
"	Jan. 4/89	—	—	—	"	—	1-0566
Man	1888	—	—	29	finger	healthy	1-0561
"	"	—	—	24	"	"	1-0540
"	"	—	—	31	"	"	1-0562
"	"	—	—	18	"	"	1-0550
"	"	—	—	19	"	"	1-0580
"	"	—	—	36	"	"	1-0562
"	"	—	—	28	"	"	1-0530
"	"	—	—	19	"	"	1-0563
"	"	—	—	19	"	"	1-0566
"	"	—	—	27	"	"	1-0605
"	"	—	—	24	"	"	1-0600
"	"	—	—	23	"	"	1-0593
"	"	—	—	19	"	"	1-0600
"	"	—	—	27	"	"	1-0596

Certain precautions have to be observed in the manner of withdrawal of the specimen of blood and in its transference to the standard solution. The drop of blood must not be taken from any portion of the circulation subjected, in the least degree, to obstruction from the venous side. A very small degree of venous obstruction suffices to increase to a quite detectable extent, the specific gravity of the blood. Mistakes from this cause can be easily avoided in the rabbit, by taking the blood from a vessel in the ear when the neck is not tightly stretched and is free

from compression. Care must also be taken to avoid admixture of the drop of blood with lymph; but in a part where the course of the vessels can be easily seen, as in the ear of the rabbit, this source of fallacy is not difficult to avoid, especially if, as was done in most of our experiments, the sympathetic trunk in the neck be divided as a preliminary.

The portion of the blood which is expelled from the pipette latest is not infrequently of a sp. gr. some '0005 above that of the portion expelled first. This is owing partly to capillary action in filling, and partly to friction of the blood against the wall of the pipette. The difficulty is overcome by using the same relative portion of each drop withdrawn.

We have followed Lloyd Jones in using a capillary pipette for transferring the minute quantity of blood to the standard solution. A fresh pipette, recently drawn in the blow-pipe flame, was used throughout our work for each single observation in order to avoid any trace of admixture of two successive drops of blood and to avoid the rapid clotting which goes on in the drops if received into a pipette in which blood has previously been received. A further precaution which we also found necessary was to see that the pipettes were carefully dried, as moisture tended to condense within them, during their cooling after they were drawn. To make an observation, small quantities of the standard solutions likely to be used in the observation were placed in each of a row of little glass cylinders so that the specimen of blood could be with ease placed in any one of them as desired.

It is hardly necessary to lay stress on the fact that in any experiment dealing with the specific gravity of the blood it is of extreme importance to avoid hæmorrhage, because even a slight loss of blood causes a diminution of the specific gravity of the blood quite sufficient to disturb the observation.

The method employed determines of course only the specific gravity of the blood considered as a mixed and complicated whole. What particular factor, or factors, in each case caused in our experiments an alteration in the specific gravity remains to some extent a matter of conjecture. It is obvious that the alteration might be due to one, or two, or all of the following causes:

1. An increase or diminution in the number of corpuscles in a given volume, the specific gravity of individual corpuscles and of the plasma remaining unchanged.
2. An increase or diminution in density of the plasma, the specific gravity and the number of the corpuscles remaining unaltered.

3. A simultaneous increase or diminution in density both of corpuscles and plasma, with or without alteration in the number of corpuscles in a given volume of the blood.

Schmaltz from observations with his capillary pycnometer concludes that broadly speaking the sp. gr. of the blood varies directly with the percentage of hæmoglobin, but is largely independent of the number of red corpuscles. Lloyd Jones expresses somewhat the same opinion. Some experiments we carried out, in which the number of corpuscles in a specimen of blood, as determined by the hæmacytometer, was compared with simultaneous observations on the specific gravity.

For this purpose a ligature was passed round one limb of a rabbit, so as to induce venous obstruction and thus cause a considerable rise of specific gravity in the blood of the ligatured part after a longer or shorter interval.

Some of the observations obtained are shown in the following table :—

Experiment	Specific Gravity of Blood before Ligature	Specific Gravity after Ligature	Number of Corpuscles before Ligature per Cubic Millimetre	Number of Corpuscles after Ligature per Cubic Millimetre
1	1057	10606	6,550,000	8,465,000
2	10573	1062	6,625,000	8,966,000
3	1058	10686	6,322,000	10,289,000
4	10586	10583	6,183,000	6,093,000

In the fourth experiment the ligature, more tightly applied, appears to have hindered the arterial as well as the venous flow, as when a drop of blood was removed from the part below the ligature it was of an extremely dark purple colour, while, as is shown in the table, both the specific gravity and also the number of corpuscles had fallen slightly instead of rising, as in the other cases. The experiment is quoted, however, as it forms a useful control to the others, in which, apparently, the venous flow only was obstructed.

In experiments on rapid injection of saline solution into the vascular system, the fall of sp. gr. observed must go hand in hand with a diminution in number of the red corpuscles per unit volume of blood. Thus in the rabbit in one instance the blood having a sp. gr. of 1·057 possessed 6,550,000 corpuscles per cubic mm., in another 1·0573 gave 6,625,000, in a third 1·058 gave 6,332,300, and in the course of experimental dilution, when the sp. gr. had fallen to 1·0495, the number of corpuscles had fallen to 3,900,000, and again when 1·039 gave 1,800,000 per cubic mm.

In a similar way, in cases of paroxysmal hæmoglobinuria, when during the paroxysm the red corpuscles are broken up and the dissolved hæmoglobin has escaped from the blood, the diminution in number of

the corpuscles is accompanied by a concurrent lowering of the specific gravity of the blood, as the following observations show.

Man	(before paroxysm)	10523	3,910,000}
„	after „	10515	3,680,000}
„	before „	1057	3,710,000}
„	after „	10505	3,440,000}
„	before „	10516	3,270,000}
„	after „	10506	2,970,000}
„	after „	1047	2,760,000

At the same time it is certain that the sp. gr. of the plasma itself was also lowered, and this not only in the experiments on injection into the vessels but in those in which the sp. gr. of the blood as a whole was lowered by hæmorrhage¹ or by the injection of solutions of glucose, sodium sulphate, etc. It seems certain also that the substance of the coloured corpuscles has its share of the additional amount of water, and those corpuscles themselves also become of less specific gravity than previously.

We have also examined the specific gravity of the blood in a number of cases in which anæmia was a prominent symptom of disease, about a hundred cases having been observed. Our observations on other diseases have not been numerous, but the results are given that they may be of use for purposes of comparison. The observations were for the most part taken at the same time of day, about 11 A.M., a point which Lloyd Jones has shown to be of importance. In the table we have placed beside our own results, for purposes of comparison, some obtained by Quincke and others working with the older methods, as well as some of those by Lloyd Jones, who used Roy's method.

In the table the numbers on either side of a hyphen denote the maximum and minimum of the observations relating to that particular disease; where one number only is given, that is the only one that has been recorded. It is worth noting that it is not possible in some cases to form at all a correct judgment of what the specific gravity of the blood is likely to be from the appearance of the patient, as under certain circumstances, which are at present but ill-understood, the tint of the skin does not necessarily form an index of the poorness or the reverse of the circulating blood. This fact has also been noted by

¹ Popp, *Ueber die Beschaffenheit* &c. 1845. V. Lesser, *Arch. f. Anat. u. Phys.* 1878, p. 41.

Oppenheimer¹, who, in the course of a series of observations on the enumeration of the blood corpuscles with the hæmacytometer, frequently came across such apparent discrepancies, the anomaly being explained, according to him, by the theory of an irregular circulation.

Specific Gravity of the Blood in Various Diseases.

Disease	Ourselves	Quincke	Becquerel and Rodier	Lloyd Jones
Anæmia : Chlorosis ²	1041—1043	1035·2—1049·1 (probably included cases of pernicious anæmia)	1045·8 (mean of observations on six chlorotic girls)	1032—1045 (severe cases)
Pernicious anæmia	1027—1034	—	—	1029—1040
Leucocythæmia	1048·5—1051 (1 case in last stage) = 1032	— 1044·3	— (1036—1049·5 Robertson) range of five cases	—
Gastric ulcer	1038 (very anæmic)—1050·5	—	—	—
Lymphadenoma	1062	—	—	—
Hæmoglobinuria	1050·3—1052	—	—	—
Cardiac (none congenital)	1033—1052	—	1052·5 (mean of series of 24 cases) 1050·2 (mean of series of 31 cases in third stage)	compensated 1054 uncompensated 10516 congenital 1061—1072
Diabetes	1058—1061	1054·9—1059·5	—	1054—1061
Cirrhosis of liver with ascites	1046—1052	1049·6 (with hæmophilia)	—	—
Acute nephritis	1041—1057	—	—	1038—1060
Chronic nephritis	1054·5—1060	1047·3—1048·7	—	10345—1060
Uræmia	1052	1050·5	—	—
Tuberculosis (of kidney)	1048·5	—	—	—
Tubercular peritonitis	1057—1059	—	—	—
Chorea	1050—1054	—	—	—
Chronic hip disease	1042—1047	—	—	—
Dysentery	1049—1052	—	—	—
Chronic plumbism	1031	—	—	—
Myxœdema	1508—1062	—	—	—

Fœtus.

Lloyd Jones has shown that the blood of the newly-born child is of very high specific gravity, whereas the maternal blood during pregnancy is of somewhat low specific gravity. It seemed interesting to observe whether the blood in the fœtal circulation is of a different specific

¹ *Deutsche med. Wochenschr.* 1889, 42—44.

² Schmaltz, using his capillary pycnometer, found the blood in chlorosis possess p. gr. of 1·030—1·049 (29 cases). But he apparently includes cases of pernicious anæmia.

gravity to the blood in the maternal circulation. Experiments on two guinea-pigs showed that the specific gravity of the two bloods does actually differ. Great care was taken to avoid any interference with the circulation in the foetus during the observations.

EXPERIMENT. *Feb.* 21, 1889. Ether and chlor.

1.45	P.M.	blood from ear of mother	10523
1.46	"	" mesenteric vein of mother	1053 (5,090,000 red corpuscles per cub. mm.)
1.48	"	" abdominal wall of foetus	1060 (5,556,000 red corpuscles per cub. mm.)
1.50	"	" mesenteric vein of foetus	1060
2.20	"	" " mother	1054
2.22	"	" " foetus	> 1060

These results are not in accord with the statement of Scherrenziss¹ who found the foetal blood of lower specific gravity than that of the adult.

Age.

The specific gravity in half-grown rabbits is lower than in adult; in the following observations the range in twenty-two young rabbits extended from 1.0426 to 1.0546, while in twenty-two consecutive observations on full-grown adults the range extended from 1.0506 to 1.0580.

Specific gravity in young rabbits.

10426	10506	10490	10500
10436	10513	10450	10516
10446	10546	10446	10516
10546	10493	10506	10446
10490	10453	10476	10473
10523	10446		

(10426—10546).

Specific gravity in old rabbits.

10520	10530	10520	10576
10526	10560	10520	10543
10570	10560	10530	10556
10550	10580	10530	10556
10576	10540	10576	10506
10546	10530		

(10506—10580).

¹ *Dorpat. Inaug. Dissert.* Dorpat, 1888.

The effect of intravenous injections of .7% NaCl solution on the specific gravity of the blood.

When a quantity of normal saline solution is injected rapidly into the circulation, the specific gravity of the circulating blood is at once diminished, but this diminution of the specific gravity persists for a short time only, indeed the blood almost immediately begins to return towards its previous specific gravity.

There can be little doubt but that this is due to the speedy escape from the circulation of the saline injected. In illustration of the rapidity with which it is usual for this return toward the previous specific gravity to take place, the following examples may be quoted:—

Example. Rabbit. 4 lbs. 8 oz. Chloroform and ether.

1.20 P.M.	Sp. gr. of blood from ear =	1.0596.
1.25 P.M.	70 c.c. NaCl .7% injected per ven. submaxil. in 40".	
	40" after end of injection sp. gr. =	1.0453
	60" later " " "	1.0486
	60" " " " "	1.0506
	60" " " " "	1.0520
	60" " " " "	1.0536
	60" " " " "	1.0556
	60" " " " "	1.0563
	120" " " " "	1.0566
	120" " " " "	1.0570
	120" " " " "	1.0570
	120" " " " "	1.0573
1.45 P.M.	" " " "	1.0576
1.55 " "	" " " "	1.0586

Rabbit. 4 lbs. 9 oz. Chloroform and ether.

12 noon.	Sp. gr. of blood from ear =	1.0510.
12.7.	70 c.c. NaCl solution .7% injected per ven. jug. ext. sinist. in 20".	
	40" after end of injection sp. gr. =	1.0370
	60" later " " "	1.0400
	60" " " " "	1.0416
	60" " " " "	1.0426
	60" " " " "	1.0436
	60" " " " "	1.0446
	60" " " " "	1.0460
	60" " " " "	1.0470

60"	later end of injection	sp. gr.	=	1·0476
120"	"	"	"	1·0483
120"	"	"	"	1·0490
120"	"	"	"	1·0493
120"	"	"	"	1·0496
12.37	P.M.	"	"	1·0503

It will be noted that the rate of return is most rapid immediately after the injection and gradually diminishes. When the injections are repeated even at short intervals, the recovery of the specific gravity of the blood may be exhibited several times in rapid succession, as the following experiment shows, but the recovery is not quite as rapid after the later, as after the earlier injections.

Rabbit. Chloroform and ether.

1·20	blood from ear	1·0550	
1·30	"	"	1·0550
1·40	"	"	1·0550 30 cc. .7 % NaCl sol. by ext. jug. in about 30".
1·41	"	"	1·0490
1·45	"	"	1·0526 30 cc. .7 % NaCl as before.
1·47	"	"	1·0450
1·49	"	"	1·0500
1·51	"	"	1·0513
1·53	"	"	1·0523 30 cc. .7 % NaCl as before.
1·54½	"	"	1·0443
2·03	"	"	1·0523 30 cc. .7 % NaCl as before.
2·04½	"	"	1·0436
2·07	"	"	1·0496
2·17	"	"	1·0540

It is noticeable, however, that even after a single injection of 33 c.c. of the saline into a rabbit of medium size, although the blood returns rapidly to very near its original specific gravity, it does not quite regain it, there being always a slight dilution of more permanent character. The method of Roy is sufficiently delicate to afford evidence that the nett result of the injection, as concerns the circulating blood, is a somewhat lasting slight dilution to the extent of sometimes not more than 0·0003 where water is 1·0000.

What is the channel by which the diluting fluid so rapidly passes from the circulation? In the capillaries of what vascular area or areas does the escape occur? It cannot be accounted for in the renal areas, as is seen from the following experiments, in which the kidneys had been previous to the injection of the saline solution removed from the circu-

lation by ligation of the renal vessels. Ligation of the renal vessels produced no obvious difference in the rate of recovery of the specific gravity of the blood.

Example. Aug. 2. Rabbit, weight < 6 lbs. Ether and chlor.

12.53. Sp. gr. from ear 1.0506 Inject. of 30 cc. saline into vein.

12.57 " " 1.0480

1.10 " " 1.0500

Right and left renal vessels ligatured; at 1.20 inject. of 30 cc. as before.

1.23. Sp. gr. from ear 1.0470

1.35 " " 1.0500

In other experiments the amount of urine entering the bladder after the saline injection was observed by collecting it through cannulæ placed in the ureters near the kidneys. The amount of urine passed did not nearly account for the fluid that had escaped from the vascular system.

Example. Rabbit. 5½ lbs. Cannulæ in ureters. Chloral-Ether. Sept. 14, 1888.

11 A.M. Sp. gr. of blood from ear = 1.0520.

11.15 " " " 1.0520.

11.30 " " " 1.0520.

30 c.c. of .7% saline per ext. jugular dext.

11.33 " Sp. gr. of blood from ear 1.0500.

11.45 " " " 1.0520 (slightly less).

30 c.c. of .7% saline per ext. jug. dext.

12.00 " Sp. gr. of blood from ear 1.0513.

30 c.c. of .7% saline per ext. jug. dext.

12.15 P.M. Sp. gr. of blood from ear 1.0513. The urine from 11.30 to 12.15 collected, measured less than 6 cub. cent. although 90 c.c. of water had disappeared from the blood vessels in that time.

Nor would it appear that the capillaries of the limbs are the channel of rapid escape of the injected saline in any considerable quantity. The ligation of the blood vessels of all four limbs retards the rate of escape no more appreciably than does the removal of the kidneys.

Example. Rabbit ♂. 7 lb. 1¾ oz. Chloral and ether.

2 P.M. Section of right cervic. sympathetic.

Sp. gr. of arterial blood from ear = 1.0546.

2.45 P.M.	Loops round the two axillaries, and the two femorals both artery and vein.	
3.35	Sp. gr. of arterial blood from ear	1.055.
	Cannula into external jugular (left).	
4.0	Sp. gr. from ear =	1.0546.
4.2	30 c.c. .6 % saline at 38° C. in 60".	
4.4.30	Sp. gr. of blood from ear =	1.0490.
4.12	" " " "	1.052.
4.32	" " " "	1.0546.
4.40	Ligatures round limb vessels drawn tight.	
4.50	Sp. gr. of blood from ear	1.0546.
4.53	30 c.c. .6 % saline in left ext. jug. in 60".	
4.55.30	" " " "	1.0450.
5.03	" " " "	1.0513.
5.13	" " " "	1.0523.
5.30	" " " "	1.0540.

The post-mortem examination of a rabbit, into the circulation of which saline solution has been introduced in quantity, offers some clue as to the way in which the injected fluid is disposed of. The intestines are then usually found distended with a thin watery fluid and often very greatly. The lymphatic vessels and glands in the mesentery and the spaces in the retro-peritoneal tissue are also distended to a striking degree, although not constantly so. Watery fluid lies free in some quantity in the peritoneal chamber itself and to a less extent in the pericardial and the pleural cavities. The gall bladder is frequently distended with thin watery bile. On the other hand the spleen, we have seen diminished rather than increased in size, and we have never noticed the subcutaneous tissue or the muscles to be œdematous.

The fluid introduced into the circulation would therefore appear to escape in chief part at least from the capillaries of the abdominal area. The following experiment tends to bear out this suggestion.

In a rabbit, round a loop of the small intestine, three ligatures *A*, *B*, and *C*, were placed at equidistant intervals of ten centimetres. Each of the loops having been carefully emptied of its contents by light compression with the fingers, the mesenteric vessels supplying the intestine between *B* and *C* were ligated. The ligatures round the intestine were drawn tight at 3.15 p.m. At 3.50 examination of the two pieces *in situ* without opening them appeared to show that they were both empty. 70 c.c. of normal saline solution of the body temperature were then introduced into the circulation by the right external jugular vein, reducing the

specific gravity of the blood $1\frac{1}{2}$ minutes after the injection from 1.0523 to 1.0380. At 4.30 the animal was killed and the intestine examined, when the piece included between the ligatures *A* and *B* was found to contain 6 c.c. of watery fluid, the piece between *B* and *C* being absolutely empty. The bladder was full of urine. The small intestine was distended with watery fluid, the large intestine at its lower part contained the usual scybala but little watery fluid, nor were the contents of the cæcum or stomach obviously abnormal.

Again, the effect of ligation of the abdominal aorta points in the same direction.

<i>Example.</i> Rabbit. 7 lbs. 2 ozs. Chloroform and ether.			
4.0	P.M.	Sp. gr. of blood from ear	= 1.0550.
4.2	„	30 c.c. NaCl solution .6% injected per ven. jug. ext. in 60'.	
		90'' after end of injection sp. gr.	1.0490.
		$8\frac{1}{2}$ minutes later „	1.0526.
		10 „ „	1.0546.
5.53	P.M.	Ven. cav. sup. and aorta abd. clamped simultaneously just above diaphragm.	
5.54	„	Sp. gr. of blood from ear	1.0546.
5.55	„	30 c.c. NaCl solution .6% injected per ven. jug. ext. in 60'.	
		$1\frac{1}{2}$ minutes after end of injection	
		Sp. gr. of blood from ear	1.0336.
		$2\frac{1}{2}$ mins. after inj. sp. gr. of blood from ear	1.0340.
		10 minutes later „ „ „	1.0340.
		10 „ „ „ „	1.0346.
		10 „ „ „ „	1.0350.

Thus the saline injected seems in large quantity to escape from the circulation in the abdominal area. It will be remembered that Worm Müller¹ gives reasons for believing that saline injected in large quantity into the circulation of the dog becomes distributed in the capillary region of all parts of the body fairly equally; in the limbs for instance just as in the abdominal area.

The above experiment as to the destination of injected saline in the rabbit stands so far in complete harmony with the lucid summary of facts concerning hydræmia given by Cohnheim in the *Allgemeine Pathologie*². Cohnheim and Lichtheim³ showed that when a huge

¹ *Ludwig's Arbeiten*, 1874, p. 159.

² Vol. 1. p. 430, 2nd edition.

³ *Virchow's Archiv*, Vol. LXIX. p. 106.

quantity of normal saline solution is injected into the vascular system of the dog a considerable portion of it escapes in a comparatively short time from the circulation, and that the portion which escapes is recoverable not from the muscles, or skin, or lungs, but from the peritoneal chamber and the intestines. A certain difference between our own experiments and the previous ones exists in the smaller quantities of normal saline used in the former. For Cohnheim's observations relatively huge injections were made, and though he points out that with these injections hardly a half of the fluid introduced remained at all lastingly in the circulation, from his summary in the *Vorlesungen* it is clear that he supposed that with smaller injections of saline the quantity introduced would not escape, but would be found room for in the vascular system, remaining, but causing no lasting increase in the blood pressure although a decided increase in the mean rate of blood flow. Our experiments indicate that in the rabbit when a quantity of normal saline varying from 2.5 % to 25 % of the body weight is injected into the circulation rapidly, e.g. in less than 60", two-thirds of the injected quantity has usually passed out of the circulation again by the end of the first five minutes succeeding the injection.

Although no doubt the exit of the injected saline solution takes place chiefly through the walls of the capillary blood vessels, there is reason to think that it may also partly occur through the walls of veins, even of large veins. This seems to be the case even with the wall of the inferior vena cava of the rabbit, as the following experiment indicates.

Rabbit small ♂. Ether and chlor.

Sp. gr. of blood from ear = 1058.

5.16 P.M. 3 ligatures that had previously been placed round inf. ven. cava pulled tight simultaneously.

5.30 ,, Ligated portions of vein removed and the blood in them at once examined in the two compartments.

The blood in one piece had sp. gr. = 1063.

Blood in other piece ,, = 1063.

No clot was found in the vein ; and there was no side branch of the vein between the two end ligatures.

The relation between the rate of exudation of fluid from the blood vessels and the mean arterial blood pressure obtaining for the time is a subject that has been so much elucidated by various experimental workers in the laboratories of Ludwig and Heidenhain, that it is not necessary to enter upon the question here ; but we have several times

had occasion to remark that the rapid injection into the circulation of a rabbit of 30 to 60 c.c. of saline solution does not usually cause even a transient alteration in the mean arterial pressure as registered from the carotid artery. And we have several times ascertained the somewhat to us surprising fact that a previous complete section of the spinal cord in the cervical region does not detectably alter the rate of escape from the circulation of saline solution injected rapidly per venam of the rabbit.

Rabbit ♂.	6 lbs. 7 ozs.	Ether and chlor.	
12.40 P.M.	Sp. gr. of blood from ear =	10516.	
12.42 "	30 c.c. of saline solution into jugular at 35° C.		
12.44 "	Sp. gr. of blood from ear	10486.	
12.49 "	" " "	10510.	
1.10 "	" " "	10513.	
1.20 "	Spinal cord completely divided above atlas vertebra almost without hæmorrhage.		

Artificial respiration.

1.23 "	Sp. gr. of blood from ear =	1047.
2.20 "	" " "	10466.
2.40 "	" " "	10466.
2.42 "	30 c.c. saline solution into ext. jugular at 35° C.	
2.44 "	Sp. gr. of blood from ear =	10403.
2.54 "	" " "	1045.
3.0 "	" " "	1046.
3.30 "	" " "	10466.

A fact that was constantly brought home to us was that towards the end of a lengthy experiment, when doubtless the arterial blood pressure had become low, the specific gravity of the circulating blood, even although no saline had been injected during the course of the experiment, nor any hæmorrhage occasioned, became lowered slightly but distinctly. Just before death so constantly did a slight and rapid diminution in the specific gravity of the circulating blood occur, that we have been accustomed in our laboratory notes to refer to this as the lethal fall.

As to the influence which the nature of the saline solution injected has upon its rate of escape from the vascular system, this is so large a subject that we have only attempted to deal with it in a limited and incidental manner. It seemed of interest to enquire whether if instead of the 7% sodium chloride solution (the so-called normal saline of the

laboratory) there were substituted for injection distilled water, the escape of it from the vascular system would take place with greater rapidity than in the case of the normal saline solution. Zuntz and Cohnstein in working at the exchange of fluid between the blood vessels and the tissues and using another method than ours, suggested that this would be the case¹, and indeed it seems to be so, although the difference is at any rate not a great one, that is to say, in less than 15 minutes after the injection of 30 c.c. of water into a quite small rabbit, the specific gravity of the circulating blood had ceased to be more than dubiously less in specific gravity than it was before the injection, a speed of return to normal of the specific gravity which we have seen nearly but not quite equalled in any of the experiments in which we have injected normal saline. The above experiment may be compared with, for instance, the following, which was made on the same day on a rabbit under apparently the same conditions in which a relatively smaller quantity of saline was injected in the same way.

Rabbit.	4 lbs. 12 ozs.	Ether and chlor.
10.42 A.M.	Sp. gr. of blood from left ear =	10510.
10.43 "	30 c.c. distilled water at 38° C. into ext. jugular in 30".	
	30" after end of injection	
	Sp. gr. of blood from ear =	10453.
	60" later " " "	> 10466.
	60" " " "	10480.
	60" " " "	10486.
	120" " " "	10493.
	120" " " "	10496.
	120" " " "	10500.
	120" " " "	10503.
	120" " " "	< 10506.
	120" " " "	10506.

Rabbit ♂.	7 lbs. 15 ozs.	Ether and chlor.
11.40 A.M.	Sp. gr. of blood from ear =	10550.
11.54 "	30 c.c. of .75% NaCl aqueous solution at 37° C. into ext. jug. in 15".	
	30" after end of inj. sp. gr. of blood from ear =	10490.
	60" later " " "	10496.
	60" " " "	10506.
	90" " " "	10510.
	90" " " "	10516.

¹ *Pfugers Archiv*, Vol. XLII. p. 303, 1888.

3'	later end of inj.	sp. gr. of blood from ear	=	10523.
3'	"	"	"	10533.
3'	"	"	"	10536.
30'	"	"	"	> 10540.

Continued Dilution.

The repeated injections of small quantities of saline solution into the vascular system do not, as may have been inferred from the above descriptions, perceptibly lower the specific gravity of the blood, unless the interval of repetition be very small relatively to the amount injected. And even in the latter case no permanent dilution of the blood is brought about. To give an instance, the injection of 5 c.c. of normal saline per venam into a medium-sized rabbit repeated twelve times, once every third minute, thus introducing 60 c.c. into the circulation in a little over half-an-hour, causes a lowering of the specific gravity of the blood of less than a unit in the third place of decimals.

On three occasions only have we allowed a continuous flow of saline solution to enter the circulation at a slow rate for a considerable time. The effect of the slower and continued injection in the rabbit was found quite similar to the results recorded by Dastre and Loye¹ in their experiments on the dog. The publication of those experiments appeared when we were commencing similar work on the rabbit, and accorded so well with what we had seen ourselves that it did not seem worth while to prosecute our own investigation further in that direction. One point deserving attention is not alluded to in Dastre's paper. That is, the remarkable speed with which at the end of a long-continued injection when the specific gravity of the blood has been kept down even by .025 degrees of the empirical scale, the blood turns toward its previous specific gravity, not however regaining it completely for a time.

Example. Oct. 25th., 1888. Large rabbit. Chloral ether.

Cannula into branch of left femoral and connected with pressure bottle containing normal saline.

4.0 P.M. Injection commenced.

Sp. gr. of blood = 1.0520.

4.30 " " " 1.0440.

4.45 " " " 1.0400.

5.0 " " " 1.038.

Inject. discontinued. 559 cub. cent. had been injected.

¹ *Arch. de Physiol.* p. 253, 1889, and *Com. Rend. Soc. de Biol.* March 31, 1888.

5.10 P.M.	Sp. gr. of blood =	1.0450.
5.20 "	" "	1.0480.
5.30 "	" "	1.0490.
5.45 "	" "	1.0500.
6.30 "	" "	1.0506.
8.30 "	" "	1.0506.
10.30 "	" "	1.0503.
11.30 "	" "	1.0503.

Example. May 2nd, 1888. Rabbit. 7 lb. 5 ozs. Chloral ether.
Cannula into left submental vein, and connected with pressure bottle containing normal saline.

4.45 P.M. Injection commenced.

Sp. gr. of blood from ear = 1.0550.

5.15 "	" "	" "	1.0310.
5.30 "	" "	" "	1.0303.
5.45 "	" "	" "	1.0290.
6.00 "	" "	" "	1.0310.
6.15 "	" "	" "	1.0270.
6.30 "	" "	" "	1.0270.

Injection discontinued. 1028 cub. cent. had been injected.

6.35 P.M. Sp. gr. of blood from ear = 1.0396.

6.40 "	" "	" "	1.0420.
7.00 "	" "	" "	1.0450.
8.00 "	" "	" "	1.0506.

By continued injection of normal saline solution the specific gravity of the blood of the rabbit may be therefore kept for more than an hour at a degree of dilution nearly amounting to what would be reached by admixture to it of an equal volume of water, and this dilution is maintained without production of obvious signs of circulatory, respiratory or nervous distress. The urinary, intestinal, and salivary secretions, as pointed out by Dastre and Loye, and in the case of saliva by Langley and Fletcher¹, become very greatly increased and watery in character.

Estimation of the quantity of blood in circulation.

By observing the alteration in specific gravity of the blood on rapid injection of a known volume of saline solution it is evident that a means is obtained for gauging the volume of blood in the circulation of

¹ *Phil. Trans.* CLXXX. B. p. 109, 1889.

the animal receiving the injection. It is only necessary if the specific gravity of the blood of an animal have been already measured to add to the circulating blood a definite quantity of an innocuous fluid of known specific gravity and then to determine once more the density of blood admixed with the fluid injected. Adopting this plan we sought to determine the quantity of blood in the circulation under varying conditions of *age, diet, etc.*

In order to approach accuracy, certain precautions have to be taken in the performance of the experiment. Some of these are obvious, and some are less so. Sufficient time must be allowed for the injected fluid to become thoroughly mixed with the circulating blood to which it is added. The time which is estimated for the completion of the circulation in the rabbit is 7 secs.¹ The amount of fluid which we injected was generally 30 c.c., occasionally it was 90 c.c. or even more. If 30 c.c. be thrown into the circulation in 15 seconds, the usual time in our experiments, it would be able to completely traverse the vascular circuit six or seven times before the lapse of half a minute from the end of the injection, and might be supposed to be completely mixed with the blood at the end of that time. To test the probability of this assumption we, after injecting saline solution into the jugular vein of one side in the direction of the heart, took observations of the specific gravity of the blood obtained from a small vein in the opposite ear at various successive intervals after the completion of the injection. These observations showed us that the blood so obtained was of a less specific gravity, thirty to forty-five seconds after the completion of the injection, than it was either before or after that interval of time had elapsed, seeming to confirm the supposition that the mixing was complete in something less than a minute from the commencement of the injection of the 30 c.c.

A second source of error has to be remembered, viz. the rapid escape of the injected saline solution from the circulation. This escape is rapid, as the experiments quoted in the previous section abundantly prove. An observation taken 30 seconds after the completion of the injection can, we think, allow time for the escape of about 2 c.c., but inasmuch as the rate of disappearance seems to be somewhat variable, and the quantity must always be small, it seems better to avoid dealing with it further than to remember that its influence will be in the direction of rendering our estimation of the quantity of circulating blood a little larger than is really the case. In order to further obviate

¹ Vierordt, *Stromgeschwindigkeiten des Blutes*, p. 130, 1858.

as far as possible the fallacy due to escape of the saline, the injection of the small quantity employed has always been made as nearly as possible at the same rate and in the same space of time, that is to say, the 30 c.c. have been injected in 15 seconds.

A further precaution consists in the avoidance of taking the drops of blood to be examined from any part of the circulation that is in the least degree exposed to obstruction from the venous side, and this point was carefully attended to in the course of our somewhat numerous experiments. Loss of blood causes a marked diminution of the specific gravity of the blood, as is well known, but where, as in the method of Roy, a fraction of a drop is sufficient for determining the specific gravity, a fallacy arising from hæmorrhage can be strictly prevented. It has seemed to us that the specific gravity of circulating blood varies slightly according to local conditions of flushing or constriction of blood vessels. In order to free our observations from possible error of that nature the drop of blood for estimation has always been taken under conditions of particularly free local circulation. For instance, previously to taking blood from the ear, section of the sympathetic nerve in the neck has been practised as a matter of routine.

Physiological saline solution containing .75% NaCl seemed to us the best fluid to employ for dilution on account of its comparatively innocuous quality and its low specific gravity. We injected the solution at a temperature of 38° C., at which it possesses a specific gravity of 1.0046.

With observance of these precautions the method of experiment runs as follows:—

In a rabbit the weight of which is known and to which no solid food has been given for 30 hours before the experiment, the cervical sympathetic is divided. A cannula is inserted into the proximal end of a vein; the external jugular, the submental, and the anterior tarsal have been employed by us. A drop of venous blood taken from the right ear is then determined by the method of Roy to be of a certain specific gravity. Then 30 c.c. of .75% NaCl solution are injected per venam in the space of 15 seconds; thirty seconds after the completion of the injection a drop of blood is again taken from a venule in the right ear and the specific gravity of it estimated as before. The requisite data for the calculation have been then obtained. The following experiment will illustrate the method.

In a rabbit, anæsthetized with chloral and chloroform, the right

cervical sympathetic was divided; a drop of arterial blood taken from the right ear was then shown to be of a certain specific gravity (in this experiment 1.0520); 30 c.c. of .75 NaCl solution having a specific gravity of 1.0046 at a temperature of 38° C. were then injected into the external jugular vein in 15". 30" later a drop of arterial blood was again taken from the right ear and the specific gravity of it estimated as before (found in this experiment to be 1.0470). The weight of the animal before the injection was 3572 gram.; no solid food had been given for 30 hours before the experiment. On two assumptions, (i) that the blood and injected fluid were thoroughly mixed together in the 30"—45", (ii) that only a negligible quantity had escaped from the

Table of estimations by previous observers.

Species	Ratio of blood to body-weight	Observer	Species	Ratio of blood to body-weight	Observer
Lizard (<i>L. agilis</i>)	5.9 %	Welcker	Rabbit	6.6—5.26	Heidenhain
Dog ♂	8.3—7.14	Heidenhain	"	4.97	Gscheidlen
" Adult	8.9—1	Steinberg	"	7.14—6.25	Brozeit
" young	6.17—5.61	"	"	8.13—7.52	Steinberg
Dog ♀ not pregnant	7.87	Speigelberg & Gscheidlen	Guinea-pig	4.78	Gscheidlen
" at beginning of gestation	7.81	"	"	8.3—8.13	Steinberg
" at end of gestation	10.63	"	Cat	7.52	Brozeit
Dog (young)	8.3	Panum	" young	9.61—8.4	Steinberg
Dog	8.46	Colin	" very young	5.61	"
"	8.2—5.5	Jollet & Laffont	Ox	5.78—5.43	"
Pig (fatted)	4.6 %	Heissler	Sheep	7.71	Heissler
			Horse	8.01	"
				9.75	"

Table of estimations by ourselves.

Animal	Weight in grms.	Quantity of saline injected	Sp. grav.		Weight of blood as % of body weight
			before	after	
Rabbit (young)	1871.1	14.5 c.c.	1.0510	1.0470	7.59
"	2289	30 c.c.	1.0556	1.0470	6.9
"	same + 30 grm.	same	1.0550	1.0460	6.4
"	2884	30 c.c.	1.0516	1.0446	6.6
" (very young)	1061	30 c.c.	1.056	1.0436	16.55
"	3478	40 c.c.	1.0550	1.0460	6.7
"	3572	30 c.c.	1.0520	1.0470	7.49
" (young)	2041	70 c.c.	1.0606	1.0453	9.675
Dog	9957	30 c.c.	1.0593	1.0566	6.9
" (young)	6293	100 c.c.	1.0620	1.0553	12.77
"	7943	80 c.c.	1.0566	1.0496	6.84
"	8760	70 c.c.	1.0526	1.0473	6.776
Monkey (young)	1948	50 c.c.	1.0530	1.0420	9.018
" (rather young)	2161	30 c.c.	1.0510	1.0450	7.35

circulation in 30"—45", the calculation ran as follows :

$$30 \cdot 1\cdot0046 + x \cdot 1\cdot0520 = (30 + x) \cdot 1\cdot0470,$$

$$x = 254\cdot4 \text{ c.c. weighing } 267\cdot6 \text{ gm.}$$

$$\frac{267\cdot6}{3572} = 7\cdot49\% \text{ of body weight.}$$

In our experiments we believe that the method employed yielded results which are at least reliable for comparison one with another. It would appear from them that the amount of blood in a well-fed adult rabbit, dog, or monkey is somewhat less than 7% of the total body-weight.

Comparing these estimations with the results obtained by other observers using various other methods, in every case involving however the slaughter of the animal, we find that they accord most nearly with those of Heidenhain¹.

It is a matter of interest that in the case of the young animals the estimated quantity of blood relatively to the body-weight is larger than the estimated quantity in the adult animal, and the difference is considerable. Heissler² however in his observations could find no evidence that age has any influence on the proportion of blood to body-weight; and our result is contrary to that obtained by Welcker³, but in accord with that of Malassez⁴.

We have attempted to repeat the classical observation⁵ that during a period of prolonged fasting the blood shares but slightly in the wasting of bulk undergone by the tissues of the body as a whole.

EXPERIMENT. Dog. 17th November. After 10 days very low diet, with free allowance of water. Specific gravity blood from ear = 1·0563.

72 cc. NaCl sol. 7% per ven. subment. gave 60" after injection a specific gravity of 1·0503.

And again 30' later same injection reduced blood to 1·0500.

Therefore there were 508 c.c. blood in the circulation, weighing 536 grammes.

The weight of animal before injection was 6690 gm.

The blood weighed therefore considerably less than $\frac{1}{12}$ th of the body-weight.

Thirteen days later, Nov. 30th, after a very free and nourishing diet for

¹ *Disq. crit. et exper. de sanguinis quantitate.* Halis, 1857.

² *Arbeiten a. d. pathol. Institut. zu München,* edited by Bollinger, 1886, p. 322.

³ *Zeitsch. f. Rat. Mediz.* 1858.

⁴ *Archives de Physiol.* 1874, 1875.

⁵ Valentin, *Repertorium*, III, 289. Panum, *Virchow's Archiv.* xxix. 256. Bidder and Voit, *Zeitsch. für Biol.* 1866, II, 307.

that period the specific gravity of the blood was 1·0530. 72 c.c. of the ·7% saline solution were then injected as before. Sixty seconds after end of the injection the specific gravity of the blood was 1·0473, and one hour later the same observation was again obtained. The carcase, deducting the weight of the contents of the stomach and intestine and 144 grammes for the two saline injections, weighed 8384 grammes. The amount of blood, as shown in the two observations, must have been 584 c.c. or by weight 615 grammes. The blood weighed therefore considerably less than $\frac{1}{13}$ th of the total body-weight. The return of weight after the fasting period had brought the weight up to somewhat more than the weight before the fasting. In that thirteen days' period of return 76 c.c. were added to the volume of the blood, or by weight 79 grammes, the additional fluid having a specific gravity of about 1·0395, probably with proteids to the extent of about 5% in it. Of the 1694 gram. added to the weight in the 13 days of liberal diet succeeding the low diet not so much as $\frac{1}{3}$ rd part had been contributed as blood.

The experiment, and a second which gave results in perfect harmony with it, confirm the view that there is a larger percentage of blood to body-weight after a prolonged fast than on a free diet. During a period of free diet after fasting, other tissues gain in bulk more than does the blood. The relative increase in the bulk of the blood during fasting seemed however hardly so great as might be inferred from older experiments; that is to say, the volume of blood in the body seems to remain hardly so stable a quantity during fasting as has been sometimes supposed.

A point worthy of mention in connection with the effect of a protracted fast upon the blood came clearly into evidence. After commencement of the fasting period the blood of the animal under experiment at first became of lower specific gravity than it had been under the previous normal diet. The specific gravity later regained its previous level, and then continued steadily to rise until it finally had become much higher than it had been before the commencement of the experiment. In each of three experiments of this kind the same result was obtained. We quote the following example:—

Sp. gr. of blood on normal diet, animal weighing 19 lbs. 4 ozs. = 1·0530.

Next day spare diet commenced with free allowance of water.

24 hours later, sp. gr. of blood = 1·0505.

” ” ” 1·0510.

” ” ” 1·0515.

” ” ” 1·0515.

24 hours later, sp. gr. of blood =	1·0525.	
” ” ”	1·0530.	
” ” ”	1·0545.	
” ” ”	1·0555.	
” ” ”	1·0560.	
” ” ”	1·0563.	Weighs 14 lbs. 13 ozs.
Free diet commenced.		

24 hours later, sp. gr. of blood =	1·0530.	
” ” ”	1·0535.	
” ” ”	1·0530.	
” ” ”	1·0525.	
” ” ”	1·0525.	
” ” ”	1·0525.	
” ” ”	1·0525.	
” ” ”	1·0525.	
” ” ”	1·0525.	Weighs 19 lbs. 6½ ozs.

In another experiment in a period during which the body-weight fell from 6 lbs. 5½ oz. to 5 lbs. 1 oz., the specific gravity of the blood rose from 1·0500 to 1·0566, water being allowed freely throughout. In twenty hours after return to liberal diet the specific gravity of the blood had fallen to 1·0520.

Buntzen observed that the corpuscular richness of the blood seemed increased rather than diminished by inanition¹.

Bizzozero has noted an increase in the solids of the blood serum in the first days of fasting²; Luciani and G. Bufalini have noticed that during fasting the percentage of hæmoglobin in the blood becomes increased³. Fränkel and Röhmann have recorded the same fact⁴.

In a case of marked neurasthenia in a young woman aged 30, we had opportunity to examine the blood, and found its specific gravity 1·047; the degree of emaciation she presented was extreme. Her height was 5 ft. 2 ins., and her weight was 4 stone 5 lbs. The observation indicates a difference in the character of the blood in what may be called chronic fasting as compared with acute fasting. As regards change in specific gravity of the blood during a period of rapid increase in weight the following example is of interest. A man, aged 45, recovering from severe dysentery and much emaciated, height 6 ft. ½ in.

¹ *Om Ernäringsens &c.* Copenhagen, 1879, p. 66.

² *Atti della R. Accad. d. Scienze di Torino*, Vol. xvi.

³ *Archivio p. l. Scienze mediche*, Vol. v. 20.

⁴ *Zeits. f. physiol. Chemie*, iv.

Nov. 7, 1889, weight 9 stone 11 lbs.

spec. grav. of blood from finger, at 6 p.m., 1.0520.

Nov. 22, 1889, weight 11 stone 1 lb.

spec. grav. of blood from finger, at 6 p.m., 1.0576.

Lloyd Jones observed that the specific gravity of Succi's blood on the 39th day of his fast was slightly higher than it had been on the 10th day (1063—1061).

As to the conditions which influence the passage of water through living animal membrane, the tendency of modern work is to show that these conditions are intimately dependent upon characters associated with the membrane considered as protoplasm, meaning by protoplasm material endowed with life.

The work of Heidenhain¹ upon the intestinal wall, and of Tigerstedt² upon the bladder of the frog, and of Reid³ on the skin of the frog, have shown that the physical processes of filtration and osmosis are, as it were, overridden by and subservient to, the living nature of the cells forming those membranes, and that those membranes when alive react quite differently to the same membranes when dead in regard to filtration and osmosis.

It has been of interest to us to carry out a few experiments upon the nature of the conditions determining the escape of the fluid we injected into the blood vessels through the walls of the capillaries; that escape, as we have given reason to think, taking place largely in the capillaries of the abdominal cavity.

Zuntz and Cohnstein have suggested that water injected into the circulation must escape from it with far greater rapidity than does 'physiological' saline solution, but they made no comparative experiments. We compared the rate of escape of distilled water and of physiological saline from the circulation and have already quoted an example of our results. We quite failed to find any great difference between the rate of passage of the pure water and of water containing NaCl to the extent of .75 %.

Although of course it is abundantly shown by the experiments of Heidenhain and others, that conditions which are too subtle for

¹ *Pflüger's Arch.* Vol. XLIII. Supplem. p. 49 &c. also Röhmann, *Pflüger's Arch.* Vol. XLI. p. 411.

² *Mittheil. v. physiol. Labor. in Stockholm*, iv. 20, 1886.

³ *This Journal*, Vol. XI. p. 312, 1890.

adequate examination by ordinary physical methods, conditions that Heidenhain himself considers best expressed by the term "vital," determine very largely the osmotic and filtration equivalents for membranes of which living cells form the component parts, the fact must not be lost sight of that living cells when put under stress beyond certain limits, instead of overriding and controlling the physical laws of filtration and osmosis, give way before them and react in obvious obedience to them. This may be because by the very extremity of the conditions under which they are placed, the state of the living cells has been somewhat approximated to that of non-living matter, that is to say injured and its vitality lowered.

The following experiments serve as examples, and are in harmony with experiments of Klikowicz¹, of v. Brasol², and of Hamburger³.

Example. Rabbit ♀. 4 lbs. 3 ozs. Oct. 12, 1889. Chloral and ether.

12.50 P.M. Sp. gr. of blood from ear = 1.0500.

12.52—12.57 Injection of 12 c.c. of 10% Na_2SO_4 in water at 35° C. per venam subment.

12.58 P.M. Sp. gr. of blood from ear = 1.0480.

1.10 " " " " 1.0480.

1.20 " " " " 1.0473.

1.30 " " " " 1.047.

4.10 " " " " 1.0486.

Example. Rabbit ♂. 5 lbs. 6 ozs. Oct. 10, 1889. Chloral and ether.

1.30 P.M. Sp. gr. of blood from ear = 1.0523.

2.30 " " " " 1.0520.

2.39—3.9 Injection of 40 c.c. .7% NaCl solution at 35° C. per ven. subment. ; the solution injected was of about 1.005 sp. gr.

3.4 P.M. Sp. gr. of blood from ear = 1.0516.

3.17 " " " " 1.0516.

3.21 " " " " 1.0516.

3.22—3.52 Injection of 40 c.c. of 40% aq. solution of glucose at 35° C. per venam subment. ; the solution injected had itself a sp. gr. of more than 1.022.

3.58 P.M. Sp. gr. of blood from ear = 1.0370.

4.22 " " " " 1.0366.

4.40 " " " " 1.0363.

¹ *Archiv f. (Anatomie u.) Physiologie*, 1884, p. 211.

² *Archiv f. (Anatomie u.) Physiologie*, 1886, p. 518.

³ *Zeitschrift f. Biologie*, Vol. xxvii., p. 259, 1890.

Example. Young dog ♂. Weight 7943 gramme. Oct. 27, 1889.

12.35 P.M.	Sp. gr. of blood from ear =	1.0553.
1.43 "	" " " "	1.0550.
1.44 "	Rapid injection of 80 c.c. of 7% NaCl solution at 35° C. per ven. submaxill.	
1.52 "	Sp. gr. of blood from ear =	1.0523.
2.04 "	" " " "	1.0540.
2.15 "	" " " "	1.0546.
2.17—2.20	Injection of 40 c.c. of 25% NaCl solution at 35° C. per ven. submaxill.	
2.22 P.M.	Sp. gr. of blood from ear =	1.0420.
2.23 "	" " " "	1.0430.
2.43 "	" " " "	1.0490.
3.16 "	114 c.c. of pale urine passed.	
3.47 "	Sp. gr. of blood from ear	1.0533.

The blood was now examined with the spectroscope for methæmoglobin, but no evidence of that compound found.

Example. Rabbit ♂. Mar. 13, 1890.

2 P.M.	Sp. gr. of blood from ear =	1.0576.
2.33 "	" " " "	1.0576.
2.37 "	45 cub. cent. of 2.2 sol. of glycogen at 37° C. introduced through small opening into the abdom. cavity.	
2.45 "	Sp. gr. of blood from ear	1.0583.
3.45 "	" " " "	1.0603.
5.00 "	" " " "	1.0600.

At death 38 c.c. of fluid found in the abdominal cavity; this fluid contained both sugar and glycogen.

Example. Rabbit ♀ small. Mar. 11, 1890.

3 P.M.	Sp. gr. of blood from ear =	1.0500.
3.7 "	30 c.c. normal saline injected per venam jug. ext.	
3.27 "	Sp. gr. of blood from ear =	1.0483.
4.15 "	30 c.c. of 2.2% glycogen sol. injected at 35° C. into external jugular. Rapid injection.	
4.18 P.M.	Sp. gr. of blood from ear	1.0416.
4.30 "	" " " "	1.0410.
4.32 "	No sugar in some urine voided.	
4.50 "	Sp. gr. of blood from ear	1.0450.
5.50 "	" " " "	1.0470.

Example. Rabbit. 4 lbs. 13 oz. Mar. 19, 1888. Ether and chlor.

12.30 P.M.	Sp. gr. of blood from ear =	1.0520.
12.45 "	" " " "	1.0520.
12.46—12.51	55 c.c. of fresh defibrinated rabbit's blood containing also 2 grms. Na_2HPO_4 introduced into peritoneal chamber at 35° C.	
12.55 P.M.	Sp. gr. of blood from ear =	1.0550.
1.20 "	" " " "	1.0563.
2.40 "	" " " "	1.0563.
3.50 "	" " " "	1.0566.
4.30 "	" " " "	1.0566.
5.20 "	" " " "	1.0563.
8.30 "	" " " "	1.0536.
10.0 A.M.	" " " "	1.0510.
8.30 P.M.	" " " "	1.0476.
10.30 A.M.	" " " "	1.0496.

It will be noticed in the experiment on injection of glyose that the lowering of the specific gravity of the blood was relatively very great. It is natural to suppose that this experiment, showing somewhat lasting dilution caused by the strong glucose solution injected into the blood vessels, has to a certain extent its converse in the experiment of adding glycogen to the inter-vascular fluid of the body; and it was always noticed that carbohydrate solution introduced into the abdominal cavity raised the specific gravity of the blood. So also did defibrinated blood.

The experiments with 10% solution of sodium sulphate throw some light upon the experiments made with the same solution by Klikowicz under Ludwig's guidance¹. Working with the dog, Klikowicz injected per venam a quantity of a 10% solution of sodium sulphate sufficient when mixed with the whole mass of the blood of the animal to raise the percentage of sodium sulphate in the entire mixture up to .75. He calculated the quantity of sodium sulphate requisite for this purpose on the basis of the classical estimation of the total weight of blood in the animal being equal to 6% of the body-weight. The injection was carried out fairly slowly—i.e. in five minutes, and exactly two minutes after the completion of the injection 160 c.c. of blood were again drawn from the carotid artery. He found that the percentage of the sulphate in that

¹ *Archiv f. (Anatomie u.) Physiol.* 1886.

blood was '3, '46, '24. Previous to the injection he found the sodium sulphate in the blood to be '42, '44, '68, from analysis of 100 c.c. withdrawn from the carotid. He considered that were there no escape of the salt from the circulation within the seven minutes elapsing between the introduction of the salt and the obtaining of the specimen of blood for examination, he should have found the following percentages: '88, '88, '87. He concluded that the salt injected escaped in large quantity from the blood in the seven minutes' interval.

It must be admitted we think that in this experiment the data for the calculation are complicated by the fact that the introduction of 10% solution of sodium sulphate causes a rapid and extreme dilution of the blood. Further in Klikowicz's experiment the loss of the large quantities of blood he withdrew from the circulation would of itself induce still further dilution¹. His experiment therefore fails to show that in the short space of from two to seven minutes even half of the salt injected had disappeared from the circulation. It merely shows that sodium sulphate, like the chloride and the nitrate, when injected per venam in strong solutions produces considerable dilution of the blood.

Towards the end of a lengthy experiment it is extremely common to find that the specific gravity of the blood becomes lower, and when death occurs this diminution may amount to two or three units in the third place of decimals. The explanation of this does not appear clear, but considerations that may throw light upon it are the following:—

Very soon after death the specific gravity of the blood no longer remains equal in all parts of the body, but local differences in it become obvious.

Examples of this are seen in the following observations:

Rabbit. Four minutes after death.

blood from external jugular = 1·044.

„ mesenteric vein 1·038.

Guinea-pig. Five minutes after death.

blood from facial vein 1·0496.

„ mesenteric vein 1·0380.

¹ Pflüger has stated (*Archiv*, Vol. I. p. 71) that 300 c.c. of blood can be withdrawn from a dog weighing 20 kil. without the sp. gr. of the blood falling more than a unit in the third place of decimals. Our observations on this point have shown a fall much greater than that. *Vide infra*.

	Five minutes later.	
	blood from left renal vein	1·0526.
	„ inferior vena cava	1·0570.
	„ left external jugular	1·0390.
Rabbit.	Seven minutes after death.	
	blood from right ext. jugular	1·0590.
	„ mesenteric vein	1·0573.
	„ pulmonary vein	1·0650.

The clotting that rapidly sets in, in the larger vessels, may help to explain some of these variations, but it would appear that in large measure they must be due to transference of the watery matters of the blood through the walls of the vessels in some areas and a passage of watery matters into the blood from outside the vessels in other areas. It may be that towards the end of a lengthy experiment the latter process has been commenced where, from the above observations, it seems sometimes to occur markedly after death, namely, in the mesenteric area, and that thus what we have in our note-book been accustomed to refer to as the lethal fall of specific gravity of the blood is at the end of a protracted experiment thus produced.

Shock.

One circumstance which has appeared somewhat remarkable may now be referred to. We desired to ascertain what influence, if any, the ligation of the splenic vein would exert upon the specific gravity of the circulating blood. Through a small opening in the linea alba a ligature was quickly and carefully adjusted around the main splenic vein of the rabbit. The specific gravity of the blood from the ear was then taken, and subsequently the ligature round the splenic vein was drawn tight. It was found that in a quarter of an hour's time the specific gravity of the blood from the ear was obviously greater than it was before, and in one hour and ten minutes it was no less than ·005 higher, ultimately rising in the course of eight hours by as much as ·0073. The experiment was repeated several times, and each time yielded similar though sometimes less striking results. It was found however that similar though less marked rise in the specific gravity of the blood could be induced by simply allowing the ligature to lie loosely round the splenic vein without permitting it in any way to impede the circulation along the vein. It was further found that simply incising the linea alba sufficed to increase the specific gravity of the blood, especially if at the same time the abdominal contents were in any way disturbed. The effect of simple

incision of the linea alba upon the specific gravity of the blood was however less certain to cause an increase than was the placing of a ligature upon any portion of the mesentery

Example. Rabbit ♀. Small. Ether and chlor.

10	A.M.	Sp. gr. of blood from ear =	1.0500.
10.15	"	" " " "	1.0500.
10.30	"	" " " "	1.0500.
		Abdomen opened by incision along linea alba, and edges of incision then readjusted.	
10.45	"	Sp. gr. of blood from ear	1.0520.
11.15	"	" " " "	1.0530.
1.15	P.M.	" " " "	1.0563.

As forerunner or accompaniment of the increase of specific gravity of the blood thus produced we noticed symptoms of circulatory disturbance which were very constant in their appearance. The ears would become anæmic, although on the side on which the cervical sympathetic had been divided as a matter of precaution the anæmia was not enough to interfere with the observations on the blood. Breathing became rapid and shallow; examination of the mesentery showed it to be very hyperæmic; the pulse became abnormally frequent. Indeed the symptoms agreed broadly with those which the surgeon denominates as indicating "shock." To study the condition further, graphic records of the aortic blood pressure and of the respiration were taken in rabbits alongside of the observations on specific gravity of the blood. The recording of the blood pressure, involving as it does the admixture of some strong saline solution with the blood, seemed to diminish very much in every case the rise in the specific gravity otherwise obtained; this difficulty was partly met by using normal saline in the junctional cannula; the other features of the experiments resembled accurately those in which no actual blood pressure record was employed. The following is quoted as typical of the observation when graphic records were employed.

Example. May 8, 1890. Rabbit ♀. 6 lb. 4 oz. Ether. R. cervic. sympath. divided.

11	A.M.	Sp. gr. of blood from right ear =	1.0563.
		Aortic blood pressure 122 mm. Hg. Respiratory oscillations	
		18 mm. Hg. Pulse rate 21 in 10". Respirat. rhythm 25	
		per minute.	
11.5	"	Same.	

- 11.35 A.M. Sp. gr. of blood from right ear = 1.0560.
Aortic blood pressure 124 mm. Hg. Respiratory oscillations 19.5 mm. Hg. Pulse rate 20 in 10". Respiratory rhythm 26 per minute.
- 11.36 to 11.36.51 Incision along linea alba from xiphoid to pubes. During the first 4 seconds of the operation the blood pressure fell from 124 to 114; in the next six seconds it rose from 114 mm. to 127 mm., in the next 12 secs. it fell to 122 mm., in the next 29 to 112 mm. The extent of the respiratory oscillations of the blood pressure fell during the operation from 20 mm. to 15 mm. The pulse-rate and respiratory rhythm were but slightly affected, the former at the end of the operation being 19 in 10" instead of 20, the latter 33 per minute instead of 27.
- 11.37.50-11.38 Aortic press. 111 mm. Respirat. oscillations 16 mm. Hg. Pulse-rate 19 in 10". Resp. rhythm 36 per minute.
- 11.38.50-39 Aortic pressure 106 mm. Resp. oscill. 14 mm. Pulse 19 in 10". Resp. 38 per min.
- 11.39.50-40 Aort. press. 97 mm. Resp. oscill. 15 mm. Pulse 24. Resp. 39.
- 11.40.50-41 Aort. press. 86 mm. Resp. oscill. 8 mm. Pulse 35. Resp. 53.
- 11.41.50-42 Aort. press. 76 mm. Resp. oscill. 6 mm. Pulse 36. Resp. 58.
- 11.42.50-43 Aort. press. 70 mm. Resp. oscill. 5 mm. Pulse 38. Resp. 60.
- 11.43.9 Blood pressure reached its lowest, 67 mm. Pulse then being 40, i.e. 240 per minute, the respiration 66 per minute.
- 11.43.50-44 Aort. press. 74 mm. Resp. 5 mm. Pulse 39. Resp. 63.
- 11.44.50-45 Aort. press. 79 mm. Resp. 4 mm. Pulse 41. Resp. 63.
- 11.45.50-46 Aort. press. 87 mm. Resp. oscill. 6 mm. Pulse 39. Resp. 62.
- 11.46.50-47 Aort. press. 78 mm. Resp. oscill. 6 mm. Pulse 40. Resp. 62.
- 11.47.50-48 Aort. press. 72 mm. Resp. 5 mm. Pulse 38. Resp. 66.
- 11.48.50-49 Aort. press. 80 mm. Resp. 6 mm. Pulse 37. Resp. 65.
Sp. gr. of blood from ear = 1.0566.
- 11.58.50-11.59 Aort. press. 88 mm. Resp. oscill. 6 mm. Pulse 38. Resp. 64.
- 12.9.50-12.10 Aort. press. 97 mm. Resp. oscill. 4 mm. Pulse 38. Resp. 68.
Sp. gr. of blood from ear 1.0570.
- 12.19.50-12.20 Aort. press. 95 mm. Resp. oscill. 4 mm. Pulse 38. Resp. 72.
- 12.39.50-12.40 Aort. press. 96 mm. Resp. oscill. 4 mm. Pulse 38. Resp. 75.
Sp. gr. of blood from ear 1.0570.

On one occasion we introduced the whites of two fresh eggs with, dissolved in them, one gramme of magnesium sulphate, the

solution warmed to a temperature of 38° C. The blood of the dog, which had been of a specific gravity of 1·0563 at each observation in the previous two hours, in half-an-hour rose to 1·0586, an hour later was 1·0590, and remained at that height till the end of the experiment four hours later. The increase in the specific gravity of the blood in this and the previous similar experiments is doubtless due to inspissation (anhydræmia, Cohnheim). Wegner¹ and Maas² attributed the effect on the blood entirely to the high osmotic equivalent of the solution placed in the abdomen, and Cohnheim follows them in this. W. Hunter in an interesting paper describes a similar effect following the introduction of defibrinated blood into the peritoneum³.

We think that in interpreting the increase of the specific gravity of the blood following introduction of solutions into the abdominal cavity some caution is necessary before concluding that they act in other ways than as mere agents which by irritation produce a very great increase in the amount of blood supplied to the splanchnic area; that this caution is necessary is shown by the effect of introducing water or normal saline into the peritoneal chamber.

Example. Rabbit ♂. Rather large. Mar. 31, 1890. Ether and chlor.

10.0	A.M.	Sp. gr. of blood from ear =	1·0553.
10.10	"	" " "	1·0550.
10.15	"	Small incision in linea alba; opening into periton. chamber not being more than 5 mm. long.	
10.18	"	Sp. gr. of blood from ear	1·0553.
10.50	"	" " "	1·0560.
11.10	"	" " "	1·0560.
11.15	"	90 cub. cent. of sterilised distilled water at 37° C. into abdomen in five minutes through the incision.	
11.22	"	Sp. gr. of blood from ear	1·0556.
11.32	"	" " "	1·0560.
11.42	"	" " "	1·0566.
12.10	P.M.	" " "	1·0580.
1.10	"	" " "	1·0580.
3.0	"	" " "	1·0570.
5.0	"	" " "	1·0563.
7.0	"	" " "	1·0560.
12	midnight	" " "	1·0556.

¹ *Langenbeck's Archiv*, xx. p. 51.

² *Ctbl. f. Chirurgie*, No. 20, 1881.

³ This *Journal*, Vol. xi. p. 115, 1890. Our own observation was published *Proc. Physiol. Soc.* May, 1890.

Other similar experiments showed that 100 c.c. of water placed in the peritoneal cavity of a rabbit may disappear from it completely in eight hours without a lowering of the specific gravity of the circulating blood, except to the extent of half a degree for a varying number of minutes immediately after the placing of the fluid in the peritoneal cavity; the water is however during the eight hours largely if not entirely got rid of in the urinary and intestinal secretions. In the following the removal of the fluid from the abdominal cavity was particularly rapid.

Example. Rabbit ♂, large. Chloral and ether.

6.5	P.M.	Sp. gr. of blood from ear =	1.0573.
6.10	„	Small opening made in linea alba.	
6.15	„	Sp. gr. of blood from ear	1.0580.
6.25	„	„ „ „	1.0580.
6.30	„	100 c.c. distilled water at 37° C. into peritoneal chamber in 4½ minutes.	
6.35	„	Sp. gr. of blood from ear	1.0570.
6.48	„	„ „ „	1.0580.
6.58	„	„ „ „	1.0583.
8.00	„	„ „ „	1.0586.
10.30	„	„ „ „	1.0576.

Animal killed. No urine had been passed, but 32 c.c. found in bladder. The retro-peritoneal tissue seemed oedematous. The intestines contained some not particularly fluid contents. By careful collection 8 c.c. fluid could be obtained from the abdominal and pleural sacs all together. It is noticeable that in this experiment the rise of specific gravity of the blood was comparatively slight.

It would appear therefore that a considerable quantity of water can be transferred from one part of the body to another, presumably by means of the circulation, without there being during the time that the transference is taking place any at all obvious dilution of the circulating blood; at least without any detectable lowering of the specific gravity of the blood.

Hæmorrhage.

It is well known that the effect of withdrawing any considerable quantity of blood from the circulation is to cause the remaining blood to be poorer in solid matters, and that this alteration in the quality of the blood is so marked and takes place so rapidly that in venesection the latter portions of the blood drawn are more dilute than are the

earlier¹. In the method of Roy we have a delicate means of easily detecting this, and even if the quantity withdrawn be quite small the resulting dilution is quite obvious. So great is this dilution resulting from hæmorrhage that we must suppose that it invalidates somewhat the calculations of observers who, like von Brasol and Klikowicz, withdrew considerable quantities of blood in order to obtain their data. Examples of lowering of the specific gravity of the blood by hæmorrhage are afforded by the following:—

Example. Guinea-pig ♀. Large. Ether and chlor.

10.30 A.M.	Sp. gr. of blood from ear =	1.0583.
11.0 "	" " " "	1.0583.
11.5 "	5 c.c. blood drawn from femoral art.	
11.15 "	Sp. gr. of blood from ear	1.0560.
11.25 "	" " " "	1.0560.

Example. Guinea-pig. Weight 608 grms. Ether and chlor.

7 P.M.	Sp. gr. of blood from ear =	1.0555.
7.1–7.5	8.5 cub. cent. blood from jugular vein.	
7.8 P.M.	Sp. gr. of blood from ear	1.0503.
7.12 "	" " " "	1.0480.
7.15–7.20	10 cub. cent. more blood withdrawn.	
7.22 P.M.	Sp. gr. of blood from ear	1.0420.
7.25 "	" " " "	1.0370.

Example. Rabbit ♀. 6 lb. 13 oz. Feb. 19, 1890. Ether and chlor.

12.35 P.M.	Sp. gr. of blood from ear =	1.0560.
1.5 "	" " " "	1.0560.
1.8–1.18	32 cub. cent. blood withdrawn from femoral vein.	
1.20 P.M.	Sp. gr. of blood from ear	1.0510.
1.25 "	" " " "	1.0496.
1.30 "	" " " "	1.0483.
1.35 "	" " " "	1.0490.
1.40 "	" " " "	1.0500.
1.45 "	" " " "	1.0510.
1.50 "	" " " "	1.0520.
2.00 "	" " " "	1.0520.
2.45 "	" " " "	1.0520.
6.00 "	" " " "	1.0530.
8.20 "	" " " "	1.0530.

From a number of experiments of this kind it seemed that the

¹ Popp, *Ueber die Beschaffenheit des Blutes*, 1845, p. 89.

reduction of specific gravity of the blood due to hæmorrhages such as these reaches its maximum from 15 to 25 minutes after the cessation of the hæmorrhage. The amount of dilution caused by withdrawal of 30 c.c. of blood was greater than that caused by injection of more than 90 c.c. of water into the blood vessels, and was of long duration. Vierordt¹ showed more than 40 years ago that the number of corpuscles in the last blood drawn in a severe venesection might reach only 42 per cent. of that drawn at the beginning. Lesser found that the dilution caused by hæmorrhage was not prevented by ligation of the thoracic ducts; but he nevertheless argues that it can only in part be explained by reabsorption of extra vascular fluid into the circulation; his argument on this point is however not very convincing. He found the dilution as marked immediately after the hæmorrhage, i.e. one minute after, as at any time later, but of this we have in our own observations not found confirmation. On the other hand our own observations do not agree on this point with those by Bizzozero and Salvioli² who found the dilution at its maximum 24—28 hrs. after the hæmorrhage. The dilution in this case cannot be presumed to be due to a fall in the general blood pressure because, as is well known, the abstraction of far larger quantities of blood than those that suffice to cause a fall in the specific gravity do not produce any lowering of blood pressure.

Indeed it would seem that the abstraction of even a small quantity of blood from the circulation is sufficient to largely diminish or even reverse the balance of that exchange through the capillary wall between the blood and the inter-vascular fluids, the sum of which, under normal conditions, is in favour of the extra-vascular fluid.

Specific gravity of venous blood.

Lloyd Jones has found that the specific gravity of blood from a vein is higher than that of blood taken from an artery, a fact in harmony with the observations of J. G. Otto³. We have made a very large number of observations, and in comparing, for instance, the specific gravity of blood from the jugular vein with that of the carotid artery, or femoral vein and artery, we have most frequently observed them to differ from one another by only so slight an extent as to leave the existence of an actual difference dubious.

¹ *Archiv f. physiol. Heilkunde*, XIII. p. 249.

² *Archivio p. l. scienze mediche*, 1880, IV. p. 273.

³ *Pflüger's Archiv*, Vol. XXXVI. p. 57.

Frequently specimens of blood taken from the two vessels have appeared to us to possess exactly the same specific gravity. When a difference has been present it has been extremely slight, the venous being sometimes the heavier. At the same time it must be remembered that it is quite true that even a very slight degree of obstruction to the local circulation on its venous side occasions an easily detectable increase of specific gravity in specimens of blood taken from the obstructed area. So sensitive is this reaction, that in determining the specific gravity of the blood great care has to be exercised to avoid any hindrance to the venous circulation¹. If the obstruction be considerable the increase in the specific gravity may be very great indeed; thus after an elastic band had been placed somewhat tightly round the thigh of the rabbit for ten minutes the blood in the limb had a specific gravity of 1·055, while the blood circulating elsewhere had a specific gravity of only 1·046; in another instance the blood in the limb was 1·059 while the blood circulating elsewhere was only 1·050; in another instance, after a ligature had been applied to the left thigh for 15 minutes, the blood in that thigh was 1·066, while the blood circulating in the other thigh and in the ears was 1·049. Again, in a small young rabbit in which, by copious injection of saline solution, the specific gravity of the blood had been lowered from 1·044 to 1·042, and in which the saline injected had, as has been shown above to be usually the case, rendered the abdominal tissues œdematous, compression of the portal vein for 3 minutes raised the specific gravity of the portal blood to 1·049, although the radicles of the vein must have been at the time bathed in unusually watery lymph. The amount of local inspissation may be so great that if the area obstructed be a large one, on removing the obstruction and allowing the blood, the specific gravity of which has been artificially increased in the local area, to again enter the general circulation, the admixture of it with the rest of the circulating blood causes a detectable increase in the specific gravity of the whole blood of the body. In this way the amount of fluid that has escaped from the obstructed areas can be approximately measured, for, as we have shown above, observations with the hæmacytometer, made concurrently with observations on specific gravity, show that the increase in density of the blood in a passively congested area is at least in the first quarter of an hour of obstruction a matter of escape of fluid without escape of red corpuscles (the leucocytes not being taken into consideration).

¹ Cf. Heidenhain, Cohnstein and Zuntz, Krüger.

Example. Small rabbit.

- Sp. gr. of drop of blood from ear = 1·0473.
- 11 A.M. Ligatures placed round all four limbs.
- 11.20 ,, Drop of blood from ear, sp. gr. = 1·0476.
- ,, ,, right thigh, sp. gr. 1·0673.
- All ligatures then loosened.
- 11.23 ,, Drop of blood from ear, sp. gr. 1·0496.

It was noticeable in experiments on passive congestion that the increase of specific gravity of the blood in the obstructed area was considerably greater in the first 5 minutes of obstruction than in the second.

Of course these results are but another aspect of the fact nowhere better evidenced than in the original experiments of Paschutin and Emminghaus, viz. that obstruction of the circulation from the venous side produces a great and immediate increase of lymph-flow from the obstructed region. This increase, which Heidenhain has lately brought forward reasons for believing to be the result of a secretive rather than a filtration process, although related chiefly to the smaller vessels, is not necessarily entirely due to them; in it the walls of even the largest veins may have a share. If in the rabbit a length of a large vein¹ be ligated between two ligatures which enclose between them a piece of the vein in which no side branches exist, the blood contained in the included lengths usually soon becomes of higher specific gravity than it was at the time of ligation. Sometimes the alteration does not occur, or not detectably. In making the experiment it is necessary to avoid any increase of distension of the vein by the tying of the ligatures, and to be sure that clotting has not set in in the blood contained.

Severance of Spinal Cord.

That the important factor in the inspissation of the blood in an area of obstructed venous flow is not the mere distension of the capillaries and venous radicles and veins, and the heightened pressure in them, seems indicated by the very different effect on the specific gravity of the blood which section of the cervical spinal cord occasions. Section of the cervical spinal cord can in the rabbit and monkey be performed with only trifling hæmorrhage, and, as is well known, causes venous congestion of the great splanchnic region of the circulation. Yet so far from giving an increase in the specific gravity of the blood it is an operation followed by a fall in the specific gravity of the blood.

¹ Vide *supra*, p. 67.

Example. Rabbit. 8 lb. 14 oz. Chloral, ether. Artif. respiration.

1	P.M.	Left cervic. symp. divided.	Sp. gr. of blood from ear = 1·0556.
1.10	„		Sp. gr. of blood from ear = 1·0553.
1.22	„	Cord exposed behind 2nd cervic. nerve, hæmorrhage being very slight in the operation.	
1.25	„	Sp. gr. of blood from ear	1·0553.
1.26	„	Cord divided completely.	Hæmorrhage insignificant.
1.28	„	Sp. gr. of blood from ear	1·0546.
1.31	„	„ „ „	1·0516.
1.39	„	„ „ „	1·0500.
1.50	„	„ „ „	1·0496.
2.00	„	„ „ „	1·0496.
2.15	„	„ „ „	1·0496.

Example. Rabbit ♀. 7 lbs. 4 ozs. Ether and chlor.

1.40	P.M.	Sp. gr. of blood from ear = 1·0456.	
1.44	„	Spinal cord divided by thermo-cautery opposite 6th cervical nerve without any considerable hæmorrhage.	
1.48	„	Sp. gr. of blood from ear	1·044.
1.54	„	„ „ „	1·044.
4.40	„	„ „ „	1·0413.
6.40	„	„ „ „	1·042.

It is not obvious why a fall in the general arterial pressure such as is produced by division of the cervical spinal cord should produce a lowering in the specific gravity of the blood. Inasmuch as the capillary blood pressure must have been increased in the great visceral areas it might have been supposed that the transudation of fluid from the capillaries in that area would have been increased and the blood for the time being have become of higher specific gravity.

We met with no instance however in which section of the cord was succeeded by increase in the specific gravity of the blood. The following are further examples of the contrary result.

Example. Rabbit. Weight 5 lb. 6 oz. Chloral and ether. Feb. 25, 1890.

11	A.M.	Right cervical symp. divided.	Artific. resp. at 70 per minute.
			Sp. gr. of blood from right ear = 1·053.
11.25	„	Cord prepared between occiput and atlas.	
		Sp. gr. of blood, right ear	1·0526.
11.40	„	„ „ „	1·0523.
11.55	„	„ „ „	1·0523. Temp. in rectum 33·2° C.

12.05 P.M.	Sp. gr. of blood, right ear	1·0526.	
12.15 "	" " " "	1·0526.	Temp. in rectum 33·1° C.
12.24 "	" " " "	1·0526.	
	Cord divided at 1st cervical with very slight hæmorrhage.		
12.30 "	Sp. gr. of blood, right ear	1·0490.	Temp. in rectum 34·2° C.
12.35 "	" " " "	1·0480.	Anal reflex sharp.
12.45 "	" " " "	1·0476.	" "
1.00 "	" " " "	1·0476.	Temp. in rect. 32·8° C.
1.10 "	" " " "	1·0476.	
2.10 "	" " " "	1·0480.	
3.10 "	" " " "	1·0480.	Anal reflex brisk.
4.10 "	" " " "	1·0480.	Temp. in rect. 29·3° C.
5.10 "	" " " "	1·0480.	

Example. Rabbit. 6 lb. 7 oz. Chloral and ether. Feb. 28, 1890.

9.30 A.M.	Sp. gr. of blood from ear =	1·052	after division of cerv. symp.
9.38 "	Artificial respiration commenced, and the cord between atlas and axis prepared.		
9.55 "	Sp. gr. of blood from ear =	1·0516.	
10.55 "	" " " "	1·0516.	
11.55 "	" " " "	1·0516.	
12.40 P.M.	" " " "	1·0516.	
12.42 "	30 c.c. of ·75% NaCl sol. per ven. jug. ext.		
12.44 "	Sp. gr. of blood from ear	1·0486.	
12.49 "	" " " "	1·0510.	
1.15 "	" " " "	1·0513.	
1.20 "	Cord divided behind atlas, very little hæmorrhage.		
1.23 "	Sp. gr. of blood from ear	1·047.	
2.20 "	" " " "	1·0466.	
2.40 "	" " " "	1·0466.	
2.42 "	30 c.c. injected as before.		
2.44 "	Sp. gr. of blood from ear	1·0403.	
2.54 "	" " " "	1·045.	
3.04 "	" " " "	1·0460.	
3.30 "	" " " "	1·0466.	
4.00 "	" " " "	1·0466.	
6.00 "	" " " "	1·0466.	
7.00 "	" " " "	1·0466.	
	" "	from mesenteric vein	1·0470.
	" "	from inferior vena cava	1·0470.
	" "	from hepatic vein	1·0470.

It will be seen from the last example that section of the cord at the

top of the cervical region seemed to slightly affect the speed of recovery to previous specific gravity of the blood diluted by a rapid injection of saline solution per venam, checking the return a little, but not markedly. The return before the cord had been severed was in 10' as far as 1·0510 on the way to 1·0516, and after severance in the same time as far as 1·0450 on the way to 1·0466; but part of that difference might well be due to the fact that of necessity the second injection followed on a first, although at two hours' interval.

Local differences in the specific gravity of the blood.

Considering the rapidity of the circulation and the large amount of effect that can be produced by the continuous action of organs the results of whose activity in any short space of time is quite inconsiderable, it might seem surprising that the blood circulating freely should in any one part of the body detectably differ in specific gravity from the rest, yet it appears to do so. In view of the accredited fact that the blood of the splenic vein contains a different ratio of white corpuscles and red to that obtaining in the blood of the splenic artery, we desired to compare the specific gravity of the blood taken from those two sources, and we early became aware that there is often a distinct difference of specific gravity between the two, and Krüger¹ has lately shown that the blood of the splenic vein is richer in solids and pigment than is the arterial blood.

Examples:

Sp. gr. of blood from ear,	mesenteric artery,	splenic vein,	renal vein
1·0560	1·0560	1·0573	1·054
1·0496	1·0496	1·0510	
1·0533	1·0530	1·0550	1·0526.

Often there is however no detectable difference between the specific gravity of the blood in these veins and of the blood in the arterial system. In the case of the spleen the existence of difference in specific gravity of the blood entering and leaving the organ appears to be associated with a contracted condition of the organ, although in two cases a difference existed when the organ was not markedly contracted in appearance. More surprising than the increased specific gravity of

¹ *Zeitsch. f. Biologie*, xxvi. p. 452, 1890. Our own observation was published in May, 1890.

blood leaving the spleen is the lowered specific gravity of blood leaving the kidney; nor did we find this latter difference of so regular occurrence as that of the splenic vein and artery. But again the observation is in consonance with analyses by Krüger, and had been noticed in the course of our experiments previous to the appearance of Krüger's paper. We have several times compared the specific gravity of the blood of the hepatic vein with that of the blood in the portal vein, and have not been able to detect a difference between the two.

To examine the point further, comparison was instituted between the blood of the thyroid vein and thyroid artery during flushing and during blanching of the gland. The cervical sympathetic when stimulated causes extreme constriction of the blood vessels of the thyroid gland¹. After section of the cervical sympathetic the corresponding half of the gland is markedly flushed with blood. We found that the specific gravity of the blood leaving the thyroid is usually not detectably higher than that of the blood going to the gland; sometimes it is just detectably higher. After section of the cervical sympathetic it was never possible to detect a difference between the specific gravity of the ingoing and outgoing blood. On the other hand, after five minutes or even three minutes of excitation of the upper end of the cervical sympathetic the blood of the thyroid vein was in each of six experiments of distinctly higher specific gravity than the blood of the thyroid arterial.

<i>Example.</i> Rabbit. 6 lb. 8 oz. Chloral, ether. April 6, 1890.			
11	A.M.	Sp. gr. of blood from ear	1·0553.
11.15	"	" " from thyroid vein (left)	1·0556.
	"	" " from facial artery	1·0553.
11.20	"	Left cervical sympathetic divided.	
11.23	"	Thyroid on left side of isthmus is much flushed.	
11.30	"	Sp. gr. of blood from thyroid vein	1·0553.
	"	" " from twig of thyroid artery	1·0553.
11.40—11.44		Excitation of upper end of divided cervical sympathetic.	
11.45	A.M.	Sp. gr. of blood from thyroid vein	1·0560.
	"	" " from facial artery	1·0560.
11.50—11.54		Excitation as before.	
11.55	A.M.	Sp. gr. of blood from thyroid vein	1·0563.
11.57	"	" " " " "	1·0553.

Careful observations with the Zeiss-Thoma hæmatocytometer showed

¹ Cf. Sherrington. *This Journal*, Vol. XIII. p. 700.

that the number of red corpuscles per cubic mm. of blood was increased in the thyroid vein during excitation of the cervical sympathetic, and was greater after the excitation than in the blood of the facial artery or the thyroid artery.

Examples :

	Artery	Thyroid vein
after excitation	4313000	4438000
” ”	4126000	4198000}
before excitation		4086000}
after excitation	4634000	4712000}
after relaxation		4620000}
before excitation		4576000}
after excitation	4569000	4710000}

Lloyd Jones and Roy have shown that a vaso-constriction in the rabbits' ear perceptibly increases the specific gravity of the blood obtainable from the ear. We can confirm their observation from our own experience, but with us the phenomenon although the rule was subject to exceptions, which we failed to account for.

The difference thus observed in the specific gravity and corpuscular richness of blood leaving certain organs during the existence of vaso-contraction in them seems comparable in a certain degree to the result of retardation of the blood-flow by slight mechanical obstruction which, as shown above, causes in like manner an increase in the specific gravity of the blood in the part and an increase in its corpuscular richness. The observations of G. N. Stewart, recently communicated to the Physiological Society, which show that the "circulation time" of the blood passing through an organ is much lengthened by vaso-constriction occurring in the organ, lend new interest to such venous variations of the quality of the blood as are illustrated above, and may probably lead to their explanation.

June, 1892.

PLATE IV.

Chart illustrating examples of variations experimentally produced in the specific gravity of the blood. All are examples taken from experiments on the rabbit. The time is expressed in intervals of 3 minutes each along the abscissa line. The specific gravity of the blood is indicated on ordinates starting with the specific gravity of water below and reaching 1.0600 at the top of the chart.