high counts. In addition to those shown in the chart there were 3 diabetic cases showing 10 particles per 100 cubic micra and one showing 45 particles. When the clinical records of the patients who showed very high counts were examined, it was found that the samples of blood were taken before their diabetes was well regulated.

We can conclude, therefore, that controlled diabetics have a fasting chylomicron count about the same as that of normal persons. The unregulated diabetics have a higher count than normal.

In the majority of cases cholesterol determinations were done on the blood. There was no correlation with the chylomicron count, very high counts being found in some instances with low normal cholesterol values, and low counts being obtained in cases with moderately high cholesterol values. The determinations of total lipid have not been made on the material.

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Effect of Pituitrin Injection in Rabbits on Serum Osmotic Pressure and Blood Picture.

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Dodds and Noble[1] reported that a single massive subcutaneous dose of pituitrin in rabbits resulted in a severe anemia on the 4th to 5th day after injection. This anemia was macrocytic, hyperchromic and accompanied by a marked leucocytosis, reticulocytosis, and an increase in bile. Dodds and Noble are inclined to entertain the possibility "that the control of blood destruction by the reticulo-endothelial system may be vested outside the system and may reside in the posterior lobe of the pituitary gland."

In view, however, of the well-known antidiuretic action of pituitrin, and the high water content of a rabbit's normal diet, it was thought that this anemia might well be due to serum osmotic changes resulting from water retention, rather than to a "hemoclastic principle" of the posterior pituitary.

In over 20 preliminary experiments on 15 healthy adult rabbits, pituitrin was injected subcutaneously in the dose reported by Dodds,

[1] Dodds, E. C., and Noble, R. L., *Nature*, 1935, **135**, 788.

200 units/kg. of body weight (10 cc. pituitrin* per kilo). The animals were kept in individual metabolism cages on a diet of cabbage, carrots and lettuce *ad libitum*. At frequent intervals the serum osmotic pressure values were determined by the vapor pressure method of Hill,[2] and serum specific gravity alterations were followed by the falling drop method of Barbour and Hamilton.[3] Complete blood counts were frequently taken, and the reticulocyte, hematocrit, fragility to hypotonic saline solutions, icteric index and mean cell diameter values were closely followed. Urines were tested for hemoglobin and urobilinogen, and stools for occult blood. Body weight, urine volumes and specific gravities were recorded daily.

The essential data of our experiments have been briefly summarized as average figures in Table I.

TABLE I.
Average Urine and Blood Changes* in Rabbits Following Subcutaneous Pituitrin.

	Normals	Post-injection value	% change	Max. change noted on:
				day
Urine volume, 24 hr.	500 cc.	35 cc.	—93	3
Urine specific gravity	1.011	1.029	+164	3
Serum osmotic pressure†	0.866%	0.642%	—26	5
Serum specific gravity	1.0221	1.0178	—20	4
Red blood corpuscles	5.39 mil.	3.19 mil.	—40	7
Hemoglobin	12.0 gm.	8.0 gm.	—33	8
Hematocrit	34.0%	20.0%	—40	7
Fragility				
Hemolysis Begins	0.50% NaCl	0.42% NaCl	16	—
Hemolysis Complete	0.40% NaCl	0.27% NaCl	33	—

*Figures representing the maximal changes observed in each experiment are averaged in this table.

†Expressed as percentage concentration of an isosmolar NaCl solution.

It is clear from this table that accompanying the evident anemia, there is also a marked decrease in urine output, a definite blood dilution, an abnormally low level of osmotically active substances in the serum and interesting alterations in the *in vitro* fragility of the red corpuscles.

Body weight was variable, representing a balance between gain due to water retention and loss resulting from poor appetite which often followed the injection of pituitrin. As a rule the icteric index

*This pituitrin, CE1138-D, was kindly furnished by Dr. Oliver Kamm of the Parke, Davis & Company.

[2] Hill, A. V., *Proc. Roy. Soc.*, 1930, **127**-A, 9.

[3] Barbour, H. G., and Hamilton, W. F., *J. Biol. Chem.*, 1926, **69**, 625.

remained well under the value for clinical jaundice. The reticulocyte increase was not marked unless the anemia was severe.

The most marked anemia so far encountered is depicted in Table II.

TABLE II.

Adult rabbit; ♂; pre-injection weight: 1.92 Kg.; Pituitrin subcutaneously, 200 units per Kg.

	Pre-Inject. Value	Max. Change to:	3 Weeks after Inject.
Body weight	1.92 Kg.	1.52 kg.	1.66 Kg.
Urine volume, 24 hr. spec.	>500 cc.	40 cc.	>500
Urine specific gravity	1.010	1.020	1.010
Serum osmotic pressure*	0.880%	0.647%	0.868%
Serum specific gravity	1.0218	1.0172	1.0206
Red blood corpuscles	6.25 mil.	1.38 mil.	3.16 mil.
Hemoglobin	13.5 gm.—%	4.5 gm.—%	7.5 gm.—%
Hematocrit	34.5%	11.0%	25.0%
Fragility			
Hemolysis begins	0.52% NaCl	0.46% NaCl	—
Hemolysis complete	0.36% NaCl	0.28% NaCl	—
Reticulocytes	0.3%	49.7%	6.1%
Icterus index	6	10	6

*See note bottom Table I.

There is a definite parallelism between the decrease in serum osmotic pressure and the RBC count. Inasmuch as the specific gravity change observed, which is consequent upon the dilution of plasma proteins, corresponds in order of magnitude to that observed for the osmotic pressure change, the mechanism of osmotic dilution seemingly must result from water retention rather than electrolyte excretion. Furthermore, this plasma dilution due to water retention is far insufficient in itself to account for the marked reduction in cell count. At present we are inclined to interpret the anemia as a hemolytic one due to hypotonic plasma. That the plasma can become a decidedly abnormal environment for red cells after pituitrin administration is shown by the fact that in one experiment the serum osmotic pressure was reduced to such a striking extent as to be isosmolar with a NaCl solution of 0.561%.

The recovery from the anemia occurs gradually and parallels increased urine output and the slow return of serum osmotic pressure to normal.

These experiments are still in progress as well as others designed to determine (1) the minimal and optimal pituitrin dosage, (2) the quantitative relationship between the *in vitro* fragility values and the level of plasma hypotonicity at which *intravascular* hemolysis occurs and (3) the prevention of the anemia by maintenance of a normal osmotic environment in the blood.