onary sinus blood oxygen content rose. This hemodynamic pattern is significantly different from that which has been reported in man for nitroglycerin(2,3) and erythrol tetranitrate(4), since neither of these agents produced an increase in coronary sinus blood oxygen content. Furthermore, after nitrates, left ventricular work and cardiac output are decreased(2,3,4) whereas after hexadylamine cardiac output increased significantly and left ventricular work tended to increase. Although nitroglycerin is reported to increase coronary flow of normal human subjects(2), no such change was observed in those with angina pectoris(3) in spite of the fact that their coronary blood flow can be increased as shown by the response during exercise(5). Erythrol tetranitrate did not increase coronary flow in either normal subjects or those with angina pectoris. In the present experiments, then, hexadylamine would appear to be significantly different from nitroglycerin and erythrol tetranitrate.

Whether hexadylamine will be effective in relieving anginal pain must be determined clinically, since at present there is no clear cut relationship between coronary blood flow and angina pectoris(5,6,7) and since hydralazine, which increases coronary blood flow and coronary sinus blood oxygen content(8) is prone to precipitate anginal pain in susceptible subjects.

Summary. 1. Systemic and coronary hemodynamics have been determined in a series of 10 intact anesthetized mongrel dogs by the Fick principle and nitrous oxide method respectively, before and during a constant intravenous infusion of hexadylamine (MRL 38, dicyclohexyl-piperidyl-ethylene hydrochloride). 2. Administration of hexadylamine produced peripheral and coronary vasodilatation, as well as increased cardiac output and coronary blood flow. 3. The coronary sinus oxygen content increased significantly, with narrowing of the myocardial arteriovenous oxygen difference. 4. Left ventricular work and myocardial oxygen consumption increased slightly but insignificantly.

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Amount of Residual Blood in Rabbit Organs After Acute Lethal Hemorrhage. (28101)

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Many studies with labelled proteins in recent years have been concerned with their partition between blood and extravascular space in man and in animals, this being determined by difference from measurements made in the plasma before and after equilibrium is established. It is highly desirable to extend these studies to individual organs so that a detailed picture of lymphatic distribution of proteins can be pieced together. Since it is seldom practical to wash out the blood trapped in organs we have preferred to introduce a second isotopic indicator injected just before death to measure its amount. During

TABLE I. Organ Weights, Residual Blood Volumes and Total and Extravascular Water Percentages in Rabbit. Values represent means and their standard deviations obtained from 6 rabbits with an avg body wt of 2.83 ± 0.25 kg. "Various" includes paws, ears, tail, endothelium of mouth and connective tissue.

Organ	Wet wt, g/kg body wt		Water content, g/100 g wet organ wt		Residual blood, ml/kg body wt		Extravascular water, g/100 g net organ wt*	
	Mean	± σ	Mean	± σ	Mean	± σ	Mean	± σ
Adrenal glands	.103	.033	—	—	.0117	.0029	—	—
Brain	3.50	.24	78.86	.71	.0499	.0060	78.80	.72
Diaphragm	2.45	.33	69.90	1.75	.2215	.0250	68.53	1.57
Eyes	1.87	.21	86.83	1.07	.0086	.0023	86.84	1.06
Fat	68.39	24.05	6.85	2.94	1.0486	.1600	5.55	2.79
Heart	2.06	.21	76.72	1.82	.2378	.0304	75.86	2.07
Hypophysis	.0075	.0008	—	—	.0010	.0001	—	—
Intestines, large	15.82	1.81	79.47	1.64	.3243	.1080	79.38	1.69
" , small	15.10	1.96	78.29	.88	.3008	.0690	78.18	.88
Kidneys	6.39	1.00	79.04	3.33	1.2496	.1730	78.01	4.23
Lacrimal glands	.68	.07	61.79	2.69	.0096	.0069	61.43	2.73
Liver	27.75	1.85	70.18	1.74	3.2991	.3790	68.38	1.79
Muscles and tendons	405.93	36.53	71.38	2.29	4.3789	.6190	69.89	2.56
Oesophagus	.65	.05	76.40	1.06	.0264	.0031	76.11	1.12
Respiratory system	4.46	.44	76.45	1.37	.5661	.0117	74.87	1.18
Skeleton	70.50	6.34	32.80	1.32	5.3963	.7015	28.47	1.34
Skin	108.82	4.80	67.96	3.05	1.2022	.4040	67.78	3.06
Spinal medulla	1.72	.10	69.36	.88	.0249	.0029	69.15	.88
Spleen	.62	.13	77.67	.59	.0989	.0196	76.61	.77
Stomach	6.38	.59	79.44	1.43	.2232	.0180	79.31	1.46
Submandibular glands	.52	.07	77.47	1.45	.0262	.0042	77.16	1.57
Testes	1.52	.11	84.68	.50	.0524	.0030	84.74	.44
Thymus	1.17	.59	55.86	12.53	.0464	.0389	46.97	29.24
Thyroid gland	.075	.019	—	—	.0021	.0002	—	—
Tongue	2.36	.29	73.43	1.61	.0742	.0097	73.11	1.66
Urinary bladder	.60	.14	77.48	3.91	.0260	.0074	77.15	4.26
Uterus and vagina	1.78	.41	79.62	1.16	.0694	.0207	79.49	1.21
Vermiform appendix	1.77	.35	82.04	.90	.0250	.0075	82.02	.92
Various	58.36	9.22	—	—	2.0511	1.6864	—	—

* Net organ wt = Wet organ wt − wt of trapped blood.

such experiments it became evident however that after acute hemorrhage values for the volume of trapped blood in the organs of rabbits are rather reproducible. These are reported separately here as being possibly of interest outside the field of protein metabolism.

Experimental. (a) *Preparation of radioactive labelled materials.* As an indicator of intravascular blood volume, ^{131}I-labelled rabbit albumin was used. This was prepared by fractionating rabbit plasma on polyvinylchloride (supplied by Guest Industrials, Sweden, under the trade name of Pevikon), frozen and dried. For each of the rabbits, 40 mg of this protein was iodinated by the method of McFarlane(2) using 3 moles inactive carrier iodine monochloride per mole of albumin. The free iodide was removed by dialysis against 0.9% sodium chloride. Doses injected were 400-500 μc per rabbit.

(b) *Bleeding procedures.* The rabbits were first bled from the xylol dilated marginal ear veins as long as a continuous flow could be obtained. This period, lasting up to 5 min, was followed by injection of the ^{131}I-labelled albumin. After 5 minutes 40 mg/kg of body weight of pentobarbital-Na were injected, the thorax opened quickly and the remaining circulating blood removed by puncture of the right heart.

(c) *Measurement of radioactivities.* Activities of large organs were measured in a ring counter(1) while the smaller organs were dissolved in their entirety in 10 N NaOH and counted in a well-type scintillation counter. A 5 ml sample of the total blood removed by heart puncture was also counted and its radioactivity used as a basis for calculating the blood remaining in the different organs. The statistical error of the counts did not exceed 5% in any case and in larger organs was always less than 3%.

(d) *Water content of the organs* was cal-

culated from the difference between wet weight and that found after drying the whole organ in an oven at 120°C. In the case of muscle, fat and skin representative samples of 20 to 30 g were dried. No water content estimations were made on the alkali-treated organs.

Results are given in Table I.

Summary. The data show that percentages of organ water due to trapped blood are generally small using this method of sacrifice and except in cases of spleen and thymus are satisfactorily constant. Variability in spleen values is probably due to variable blood discharge during hemorrhage. Comparison of spleen weights in Table I with those of spleens from unbled rabbits(4) suggests blood discharge volumes of about 2 ml. Profound vasoconstriction presumably explains the smaller percentages of blood in muscle and skin(3), the latter normally comprising one of the largest blood reservoirs in the living animal.

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In vivo Inhibition of Rat Blood Serum Xanthine Dehydrogenase by Semicarbazide.* (28102)

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It is known that xanthine oxidase (XO) from milk and from rat liver is inhibited *in vitro* by phenylhydrazine and semicarbazide, this inhibition being completely reversed by 2-methyl-1,4-naphthoquinone(1). Semicarbazide (SC) also inhibits 3 pyridoxal phosphate catalyzed enzymatic systems, *i.e.*, l-cysteine desulfhydrase, glutamic-aspartic transaminase and l-glutamic acid decarboxylase which is competitively reversed by pyridoxal phosphate(2). Further, it has also been shown that SC is able to inhibit the xanthine dehydrogenase activity (XD) of rat serum(3).

Semicarbazide is of great pharmacological and biochemical interest since it produces in animals seizures which simulate *grand mal* epilepsy. These seizures are preceded by a latent period after administration of the drug (4).

It is shown here that XD activity from rat serum is strongly inhibited *in vivo* by SC and that this inhibition could be reversed by propanone (a compound having a free carbonyl group) or by NaBr, a compound which increases the latent period preceding the seizures.

Methods. Male Wistar white rats weighing 100-150 g kept on a well balanced diet were used throughout the experiments. All drugs were injected intraperitoneally in aqueous solutions except for menadione (2-methyl-1,4-naphthoquinone) which was dissolved in propylene glycol. Doses used for 100 g body weight were as follows: semicarbazide, 50 mg; pentamethylenetetrazol, 10 mg; NaBr, 20 mg; acetone (2-propanone), 40 mg; and menadione, 2 mg. At the dosage used, SC produced seizures which appeared 45-60 minutes after injection of the drug. Blood samples were collected by heart puncture under light ether anesthesia and the clear serum

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