TABLE II.
Serological and Biochemical Studies of Resin and Oxalate Treated Blood.

Determination	Resin treated*	Oxalated*†
Sugar, mg %	111.2	114.0
Urea nitrogen, %	14.3	13.8
Uric acid, %	4.1	4.4
Total protein, g	7.31	7.25
A/G ratio	2.03	2.16
Albumin, g	4.90	4.75
Globulin, g	2.41	2.20
Fibrinogen	0.268	0.324
Non-protein nitrogen, mg %	29.1	26.4
Inorganic phosphorus, mg %	2.6	2.2
Sugar (24 hours), mg %	22.5	45.0
Specific gravity—whole blood	1.0623	1.0608
" " plasma	1.0285	1.0278
Oxygen capacity, cc	22.73	21.99
Cephalin-cholesterol flocculation test	Negative	Negative
Creatinine, mg %	1.2	1.2
Cholesterol, mg %	182.0	194.0
†Serology:		
Wassermann	Negative	Negative
"	++++	++++
Kahn	Negative	Negative
"	++++	++++
Mazzini	Negative	Negative

* Average of five samples.
† Serum for Serology.

logical and biochemical studies. Minimal alterations in cellular morphology were observed. 3. The resin is inexpensive and can be regenerated innumerable times and re-employed.

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Vaso-Excitor and -Depressor Substances as "Toxic" Factors in Experimentally Induced Shock*

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In our observations on the visceral circulation of animals in tourniquet and traumatic shock, capillary changes, in addition to those produced by generalized vasoconstriction, were noted remote from the site of injury. This and the fact that similar changes occurred in irreversible hemorrhagic shock led us to look for the presence in the blood of abnormal substances which would account for the observed reactions. Descriptions of the vascular reactions after these shock treatments involving fluid loss are being published.[1] They indicate that the changes are of the order of an initial hyper-reactive condition, suggesting the presence of vaso-excitors, and a

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1 Zweifach, B. W., Lee, R. E., Hyman, C., and Chambers, R., *Ann. Surg.*, in press.

TABLE I.

Animals	Treatment	Survival after treatment	Time of obtaining blood samples	Reaction of capillary bed in test rat
Dogs	Muscle trauma* (Gregersen's method)	>12 hr	4-6 hr after trauma	vaso-excitor or neutral
		6-8 hr	5-6 hr after trauma (1-1½ hr before death)	vaso-depressor
Rats	Noble Collip drum, 600 turns (no anesthesia)	45 min-2 hr	30-60 min after treatment (45-60 min before death)	,, ,,
Rabbits and Rats	Tourniquet,† duration 3-4 hr	>24 hr	1-6 hr after release	vaso-excitor
,,	Tourniquet,† duration 5-7 hr	3-5 hr	30-50 min after release	,, ,,
			1½-4 hr after release	vaso-depressor
Dogs	Graded hemorrhage‡	4-8 hr	Initial reversible period (1-3 hr after bleeding)	vaso-excitor
			Final irreversible period (4-8 hr after bleeding)	vaso-depressor

* Ether administered during period of pounding leg.

† Vascular occlusion of one hind limb. Rabbits were given sodium pentobarbital (20 mg/kg) prior to tourniquet application. Rats were similarly treated just prior to release of tourniquet to permit exteriorization of the mesoappendix.

‡ Bled to produce moderate, followed by drastic, hypotension culminating in a state irreversible to restoration of blood previously withdrawn. Pentobarbital (20-30 mg/kg) or morphine (2-12 mg/kg) administered prior to bleeding.

subsequent hypo-reactive condition in which substances possessing vaso-depressor properties predominate in the blood.

To obtain objective evidence for this, small quantities of blood, taken at intervals during the shock syndrome, were introduced into the blood of normal rats and the effect noted on the vessels of the normal mesoappendix. This test proved to be a discriminating one because of the highly specific pattern of responsiveness of these vessels.

The blood from the shocked animals was either heparinized or allowed to clot and the serum collected and refrigerated for 24 hours. The test rat, under nembutal, was prepared for blood pressure measurements[2] and its mesoappendix exposed for microscopic observation. About 0.5 cc of the blood or serum to be tested was then injected into the tail vein. The effect on the capillary circulation of the test rat was transient but was found to simulate many of the changes previously observed in the shocked animals. For control, it was found that normal and hemolyzed blood or serum of dogs and rabbits after 24 hours refrigeration exerted no specific effects.

The criteria looked for were: (a) altered appearance of the capillary flow with a shift toward either an ischemic or a hyperemic flow and a change in rate of the venular flow; (b) change in responsiveness to topical application of epinephrine; and (c) augmentation or diminution of the vasomotion of arteriolar vessels. The effect on blood pressure was not reliable as a test criterion.

Table I summarizes the types of shock to which the animals were subjected and the reactions of the capillary bed in the test rats to the injections.

The blood of the dogs with muscle trauma was collected by Drs. Gregersen and Root (College of Physicians and Surgeons). The reactions of the blood of dogs which they reported (personal communication) as surviving were either vaso-excitor or neutral. The blood taken 5 to 6 hours after the trauma from dogs which later died gave vaso-depressor reactions.

The fatality of the rats subjected to the Noble-Collip drum was chiefly due to gut injury[3] and the animals were completely comatose when the blood samples were taken.

It is to be noted that the blood samples of the non-fatal cases and the early blood

2 Duncan, G. W., Hyman, C., and Chambers, E. L., *J. Lab. and Clin. Med.*, 1943, **28**, 886.

3 Chambers, R., Zweifach, B. W., and Lowenstein, B. E., *Am. J. Physiol.*, 1943, **139**, 123.

samples of the fatal tourniquet and hemorrhagic cases were all vaso-excitor. This, in general, is the initial reaction to fluid loss.[4] On the other hand, the blood samples taken during the late periods of the fatal shock syndrome were all vaso-depressor.

The effects of known substances were compared with those of the shock depressor blood, noted above. The criteria were diminished responsiveness to epinephrine, loss of vasomotion with the dilator phase persisting and hyperemia.

Normal rats were given intravenous injections of histamine (0.5-3.0 mg/100 g rat), adenylic acid (0.2 mg/100 g), diphosphopyridine nucleotide (3 mg/100 g), Padutin Niphanoid (Winthrop) (5-10 mg/100 g), leukotaxin (1-10 mg/100 g), physostigmine and acetylcholine. All lowered the blood pressure and induced peripheral hyperemia but none gave all the effects of the vaso-depressor serum. For example, Padutin, a kallikrein, slowed the vasomotion, but had no effect on the epinephrine reactivity, while adenylic acid increased the vasomotion.

The vaso-depressor effect of shock plasma or serum was not destroyed by incubation with histaminase (Winthrop T360-N) for 24 hours. That the vaso-depressor was probably not a choline derivative was indicated by the fact that atropinized test rats still gave the vaso-depressor response.

In conclusion, the presence of vaso-excitor substances was demonstrated in the blood of animals during the early period of shock treatment involving fluid loss. Subsequently, when a hypo-reactive state of the capillary circulation occurred, the blood was found to contain vaso-depressor substances having properties which differed from those of a number of known tissue extracts.

[4] Zweifach, B. W., Lowenstein, B. E., and Chambers, R., *Am. J. Physiol.*, in press.

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Rancid Fat in Experimental Diets.

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The deleterious effects caused by the ingestion of rancid fats have been reviewed recently by Burr and Barnes.[1] The possible effect of small amounts of rancid fat in the diet on the toxic action of a drug has not been sufficiently emphasized by nutrition investigators. The seriousness of the presence of oxidized fat in the diet was observed in this laboratory when it was found that rats, fed an experimental diet in which corn oil was replaced by lard, developed a humped back and partial paralysis, followed by death. The condition was first noticed in rats fed a diet containing cadmium as a toxic agent; however, it later developed in the control animals of this same series. We observed this abnormal condition in rats fed 6% lard as well as in those fed 25% lard in the diet. In order to interpret our previous data from the cadmium experiment, it was thought advisable to determine what effect, if any, the lard had on the toxicity results.

Experimental. Twenty pairs of albino rats, 21 days of age and equally divided between the sexes, were placed on the following diet: Casein 18%, cornstarch 60%, brewer's yeast 5%, whole dried liver 5%, salt mixture (U.S.P. XII No. 2) 4%, cod liver oil 2%, and lard* or corn oil 6%. Dietary mixtures were prepared in sufficient quantities to last

[1] Burr, G. O., and Barnes, R. H., *Physiol. Rev.*, 1943, **23**, 256.

* The lard used in this experiment was obtained from the Beltsville Experiment Station of the U. S. Department of Agriculture. It was stored at 35°F and was used as needed within a year.