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Heparin Inhibition of Coagulating Agents Rendered Isocoagulant.

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In attempting to use serum rather than tissue extract for the coagulant in clotting heparin-plasma it was found that frequently a plasma rendered incoagulable with heparin could not be clotted with serum but could be clotted with tissue extract. This observation suggested that the coagulant in serum (thrombin) might be more sensitive to heparin than the coagulant in tissue extract (tissue fibrinogen).

One must consider the possibility of the concentration of coagulant in the tissue extract being greater than in the serum. This factor was controlled by rendering the 2 coagulants isocoagulant by dilution of the stronger of the 2 with physiological saline. They were regarded as isocoagulant when similar amounts of either shortened the coagulation time of a recalcified citrate plasma to the same extent.

The citrate plasma is from adult rabbits, citrated to 0.5%; serum is obtained from the clotted recalcified citrate plasma.

The tissue fibrinogen was kindly furnished by the Wm. S. Merrell Co. ("Fibrogen" for subcutaneous use).

In Experiment A. Table I, the plasma has a fairly long recalcification time of 13½ minutes; this is reduced to 3 minutes by 4 drops of either coagulant. The heparin concentrations are high at the start being reduced by dilution, the clotting time becoming consistently shorter for both coagulants. In each set the serum is more inhibited than the tissue fibrinogen. Control at the end shows the coagulants to be isocoagulant and within 15 seconds of the original value.

In Experiment B, the plasma has a recalcification time of 3½

TABLE I.

Citrate plasma and calcium chloride 1%, 2 drops in each test.

Exp.	Tissue Fibrinogen	Serum	Heparin	Water	Coag. Time	Remarks
A				6	13½ min.	Recalc. time plasma No. 136
	4			2	3 "	Isocoagulant pair
		4		2	3 "	
	4		1	1	22½ "	
		4	1	1	None 1 hr 42 min.	
	4		1	1	6½ "	Heparin diluted 1:3
		4	1	1	None 2 hr. 31 min.	" " "
	4		1	1	4¾ "	" " 1:5
		4	1	1	36+ "	" " "
	4		1	1	4¼ "	" " 1:9
		4	1	1	21 "	" " "
	4			2	3¼ "	Control on isocoag. pr.
		4		2	3¼ "	
B				6	3½ "	Recalc. time plasma No. 139
	2			4	2 "	Isocoag. pr.
		2		4	2 "	
	2		1	3	2 "	
		2	1	3	3¾ "	
			1	5	5¼ "	
	2		2	2	3¾ "	
		2	2	2	7 "	
			2	4	8 "	
	2		3	1	6¾ "	
		2	3	1	14¼ "	
			3	3	20½ "	
	2		4		10 "	
		2	4		30 "	
			4	2	50+ "	

minutes which is shortened to 2 minutes by either coagulant. The heparin concentration is here being increased; the effect of heparin on the recalcified plasma without any coagulant is also shown for each set. There is a consistent lengthening of the clotting time as heparin is increased. In each set serum is more inhibited. In each the order of clotting is tissue fibrinogen, serum, no coagulant. Serum, therefore, though strongly inhibited still exerts some effect; this is particularly noticeable in higher concentrations of heparin.

Some irregular results have been noted which suggest that tissue fibrinogen undergoes some change on standing after dilution which renders it unsuitable for use and that sera which fail to accelerate clotting after high dilution are also unsuitable.

The pipettes used in these experiments are calibrated to drop the same number of drops per cc. when held at the same angle and drop-

ping at the same rate. The concentration of blood fibrinogen is kept constant by working with a total volume of 10 drops.

These data are tentatively interpreted as indicating that thrombin is more sensitive to heparin inhibition than is tissue fibrinogen. The possibility that tissue fibrinogen suspension used might in some non-specific manner inactivate the heparin has to be considered.

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Volume of the Various Lobes of the Hypophysis During Pregnancy in the Rat.

SAM STEIN. (Introduced by A. T. Rasmussen.)

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Contrary to the general tendency of the hypophysis, and particularly the anterior lobe, to enlarge during pregnancy in many animals, it appears from the data on 86 albino rats tabulated below, that the organ, as a whole, does not enlarge. If anything, the whole organ is slightly smaller in the normal pregnant animals. No significant difference was found in the relative volume of the various lobes as determined by the paper weight method on serial sections.

TABLE I.

Condition of Animals	No. of animals	Average age	Average body length	Average body weight	Average weight whole gland	Relative Volume of Lobes		
						Pars Anterior Average	Pars Posterior Average	Pars Intermedia Average
		days	cm.	gm.	mgm.	%	%	%
Group I—Normal non-pregnant controls	20	109	20.0	185	10.67	87.42	7.73	4.86
Group II—Normal pregnant	28	135	19.9	175*	10.14	86.67	8.45	4.81
Group III—Pregnant vitamin E deficient	19	136	20.3	229	12.41	87.39	7.78	4.82
Group IV—Pregnant cured of vitamin E deficiency	19	153	20.3	241	12.79	87.77	7.60	4.61

* When impregnated.

All the animals used in these investigations were standard female albino rats reared under uniform conditions in the animal colony of the Department of Anatomy, University of Minnesota.