From 2 to 6 complete experiments on each tissue were averaged to give the recorded values. In addition to the general conclusions recorded in the summary, the following points may be noted. Dog liver was previously reported(1) to be free of this enzyme, but its presence could readily be demonstrated by the addition of methylene blue to the aerobic test system. The pigeon was the only species in which the liver was found to be completely free of xanthine oxidase; no activity was detected in any of 6 experiments with xanthine or p-hydroxybenzaldehyde as the substrate in the presence or absence of methylene blue.

The xanthine oxidase of mouse liver was unchanged by a total body x-ray irradiation of 600 r. Control mice had liver xanthine oxidases in the presence and absence of methylene blue of 36 and 20 cmm O_2/20 min. respectively, while the mice analyzed 3 to 6 days after irradiation‡ had corresponding values of 42 and 18.

Human livers obtained at autopsy after accidental or other deaths had little xanthine oxidase. In the usual determination, values of 0 to 5 cmm O_2/20 min. were obtained, and these were increased 2 fold by the addition of methylene blue.

Summary. A study of the xanthine oxidases in selected tissue homogenates from different species showed that the enzymes present in bird tissues was a dehydrogenase rather than an oxidase, since the aerobic activity of the enzyme was negligible in comparison with its activity in the presence of methylene blue. The enzyme present in mammalian tissues was an oxidase whose aerobic activity could generally be increased from 1.5 to 2.5 times by the addition of methylene blue to the aerobic test system. In all cases the aerobic activity of the xanthine oxidase was inhibited from 40 to 100% by antabuse, and this inhibition was completely overcome by the addition of methylene blue. Heating the tissue homogenate at 56° for 30 minutes gave decreased aerobic xanthine oxidase activities with rat and mouse liver but no change with most mammalian tissues; the antabuse inhibition was eliminated to varying degrees with different tissues. The dehydrogenase enzyme or the dehydrogenase portion of the mammalian xanthine oxidase complex was unaffected by antabuse or by the heating procedure, since the activity in the presence of methylene blue remained constant irrespective of what happened to the aerobic activity.

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Reactions of Albino Rats to Injections of Dextran. (18453)

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Dextran, a long-chain polysaccharide, in 6% concentration in physiological saline solution, has been used as a plasma substitute in the treatment of hemorrhagic and burn shock (1-4). In experiments with this substance in the albino rat, consistent reactions have been observed.

Reactions in 29 albino rats, 150-250 g, have been observed in our laboratory when 0.5 ml 6% Dextran per 100 g body weight was injected into the tail vein. All rats showed reactions, lasting for a period of 2 or

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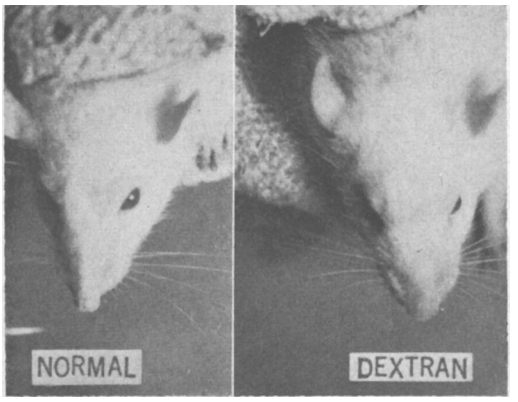

FIG. 1.
Showing swelling of snout in rat after injection of Dextran.

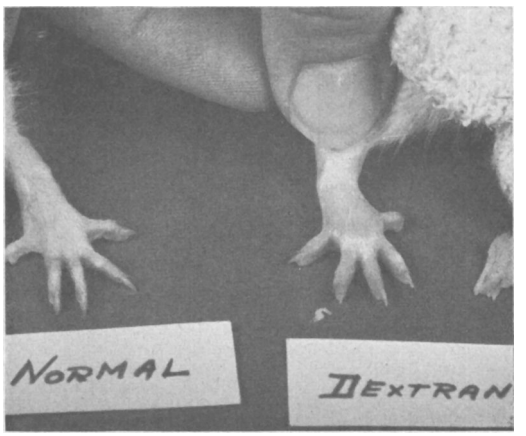

FIG. 2.
Showing swelling of paw in rat after injection of Dextran.

3 hours. Stupor, dyspnea and plethora of ears and feet was observed after 5 minutes, followed frequently by scratching. In 15 minutes swelling of snout and paws was evident. (Fig. 1,2.) The plethora, dyspnea and stupor subsided in 30 to 60 minutes and the swelling was diminished or absent after 2 hours. These reactions of the albino rat to Dextran have been observed in the laboratories of Dr. Walter Bloom(5) of Emory University and Dr. W. D. A. Maycock of the Lister Institute, London.

In another experiment, 27 rats were injected intraperitoneally with 6% Dextran, 1 ml per 100 g body weight. The reactions were prominent in every case and consisted of the same elements. The only difference noted was a 30-minute delay in the onset of reactions with those animals injected intraperitoneally.

To test the relation of rat reaction to human reaction, 3 pairs of rats were injected intraperitoneally, each pair receiving one of the following lots of Dextran: (1) from a bottle which had produced a reaction in a human; (2) from a lot which had not produced any reaction in human trials, and (3) from a lot which had not had a human trial. The reactions of these rats showed no significant variation.

To relate the molecular weight of Dextran to the reaction, 6% solutions of the following mean molecular weight fractions were employed: (1) 170,000; (2) 130,000; (3) 80,000; (4) 40,000; and (5) 25,000. One ml per 100 g body weight of each fraction was injected into 2 rats intraperitoneally. Equal amounts of 6% stock Dextran and isotonic saline were injected into control rats.

Table I shows that the reaction occurs between 15 and 30 minutes after injection with 25,000 molecular weight fraction, and between 30 and 45 minutes with stock Dextran and fractions 40,000 to 80,000 molecular weight. Rats receiving fraction 130,000 molecular weight showed the first reaction after 45 minutes, and those receiving 170,000 molecular weight fraction had no reaction until after one hour. In addition to slower onset, the reactions were not as severe when the intraperitoneal injection was with fractions of higher molecular weight. When these fractions were administered intravenously, following the same plan (Table II), the animals reacted to all fractions in the first 5 minutes. The reactions were as marked with the larger molecular weight fractions as with the smaller.

When Dextran was administered intravenously on subsequent days, the degree of reaction diminished (Table III). The diminution of the redness following the subsequent injections was striking. The most persistent sign of reaction on subsequent injections was the swelling of loose tissue on

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TABLE I. Dextran Reactions to Various Molecular Fractions Injected Intraperitoneally.

Fraction	II	III	IV	V	VI	Stock sol. dextran 170,000 to 40,000	Isotonic saline
Mean molecular wt	170,000	130,000	80,000	40,000	25,000		
Time after inj., min.							
15	0	0	0	0	0	0	0
30	0	0	0	0	+	+	0
45	0	0	++	++	++	+	0
60	0	+	++++	++++	++++	+++	0
75	+	++	++++	++++	++	++++	0
90	+++	+++	+++	++	+	++	0
105	+	++	++	++	+	+	0
120	+	++	++	++	+	+	0
135	+	++	++	+	+	+	0

+ to ++++ indicates severity of reaction (plethora, swelling, dyspnea, scratching).

TABLE II. Dextran Reactions to Various Molecular Fractions Injected Intravenously.

Fraction	II	III	IV	V	VI	Stock sol. dextran 170,000 to 40,000	Isotonic saline
Mean molecular wt	170,000	130,000	80,000	40,000	25,000		
Time after inj., min.							
5	++++	++++	+++	+++	+++	++	0
15	++++	+++	+++	++++	++	++	0
30	+++	+++	+++	++	++	+++	0
45	+++	++	++	++	++	++	0
60	++	++	++	++	++	++	0
75	++	++	++	++	++	++	0
90	++	++	++	++	++	++	0
105	++	++	++	++	+++	++	0
120	++	++	++	++	+++	++	0
135	++	+	+	++	+++	++	0

+ to ++++ indicates severity of reaction (plethora, swelling, dyspnea, scratching).

TABLE III. Severity of Reactions to Intravenous Dextran Administered on Subsequent Days.

Day / Rat	1	2	3	4	5
1	++	++	+	++	+
2	++	++	++	+	+
3	++	++	++	+	+
4	++	++	+	+	+
5	++	+++	+	+	+

+ to ++++ indicates severity of reaction (plethora, swelling, dyspnea, scratching).

face and paws.

Summary and Conclusions. Albino rats give a demonstrable reaction of redness, swelling of loose tissue, pruritis and stupor, when injected with doses of Dextran comparable to recommended doses for humans. Three different lots of Dextran gave the same reactions. Fractions of varying mean molecular weight all gave prompt reactions when administered intravenously. The delay in reaction following intraperitoneal injection may be related to the time required for the Dextran to enter the general circulation in sufficient quantity. The larger molecules pass more slowly into the circulating blood. Dextran reactions in rats following injections on subsequent days are diminished.

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