crease of GSH in various tissues.

Summary. Intradermal injection of GSH into healing sites of Arthus phenomenon produces a reactivation of the inflammatory process having the same aspect as the original reaction. The interval during which reactivation occurs is correlated with the susceptibility to GSH of a protease extracted from the healing sites, which decreases with the age of the lesion. Cysteine is less active *in vivo* than GSH but no difference was observed between the *in vitro* effects of the 2 thiol compounds.

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Effect of Endotoxin upon Total Iron-Binding Capacity of the Serum. (29266)

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The iron-binding property of transferrin is specific for this particular protein and is not exhibited by any of the other proteins of serum(1). It follows, therefore, that the capacity of serum for transport of iron is limited by its content of transferrin. This is called the total iron-binding capacity (TIBC).

A decrease in TIBC has been shown to occur during infections in humans and dogs (2), during turpentine inflammation in rats (3) and in protein deficiency in swine(4) as well as such diseases as hemolytic or aplastic anemia and malignant conditions(4). In some of these conditions the decrease in TIBC seems to be a part of a general change in plasma proteins(5). There is also some evidence that the balance between tissue oxygen supply and demand can be a regulating factor of the TIBC(6).

It was recently shown that when endotoxins were injected into normal rats a rapid decline in plasma iron concentration was produced(7). This decrease in plasma iron was not due to a more rapid loss of iron from the plasma, but seemed instead to be related to reutilization of iron from recently destroyed red blood cells(8). It was therefore of interest to see what effect the endotoxins had upon TIBC.

Materials and methods. Female Holtzman rats, 50 to 70 days old, weighing 180-200 g were used in these experiments. Lipopolysaccharide from *Escherichia coli* 055:B5 was obtained from Difco Laboratories, Detroit, Mich. (Lot No. 460830).

Plasma bound iron and unsaturated iron-binding capacity (UIBC) were determined by the method of Schade *et al*(9). The bound iron and the UIBC were added to give the TIBC. The TIBC was also checked by the

TABLE I. Effect of an Intraperitoneal Injection of 100 μg of *E. coli* Lipopolysaccharide on Total Iron-Binding Capacity of Rat Serum.

Interval after inj (hr)	No. of animals	Bound iron	UIBC	TIBC
		μg %		
0	35	282 ± 5*	157 ± 8	439 ± 7
2	8	223 ±25	216 ±34	439 ±16
4	8	156 ±13	248 ±15	404 ± 9
6	12	80 ± 9	281 ±13	361 ±10
8	11	39 ± 4	312 ±12	351 ±11
12	9	39 ± 3	320 ±10	359 ± 7
16	8	49 ± 6	304 ± 7	353 ± 7
24	12	83 ±11	249 ± 9	332 ± 4
48	6	262 ±18	148 ±16	410 ±14
72	6	285 ±16	195 ±19	480 ±18

* Mean ± S.E.

method of Morgan and Carter(10). Since the results were similar by these two methods, they were combined in the experiments to be reported.

Total blood volume determinations were made by injecting a known volume of washed, Fe^{59} labeled, red blood cells. The plasma proteins were separated by solution electrophoresis in barbital buffer pH 8.6 with the Perkin-Elmer model 38A. Total protein was determined by the method of Lowry *et al* (11).

Results. The effect of an intraperitoneal injection of 100 μg/animal of endotoxin on the TIBC of rats is shown in Table I. Bound iron began to decrease shortly after injection of endotoxin and reached a minimum 8-12 hours later. The TIBC decreased more slowly than the bound iron and did not reach a minimum until 24 hours after endotoxin injection. By this time the bound iron had started to increase. The TIBC was generally above normal values for the rat 3 to 6 days after endotoxin injection.

By increasing the dose of endotoxin, a further decrease in TIBC was found as shown in Table II. These results also indicated that the decrease in TIBC did not parallel the decrease in plasma iron. The 1 μg dose of endotoxin produced a marked decrease in plasma iron but very little effect on TIBC.

TABLE II. Effect of Dose of Endotoxin on Total Iron-Binding Capacity.*

Dose of endotoxin, μg %	No. of animals	Bound iron	TIBC
		μg %	
1	9	68 ± 3	407 ± 9
100	9	45 ± 8	362 ± 8
1000	9	32 ± 4	325 ± 7

* Plasma iron was measured 12 hr after injection of endotoxin.

One possible explanation for the decrease in TIBC after a single injection of endotoxin would be an increase of the blood volume after injections of endotoxin. However, it was found that the hemoglobin concentration was 0.5 to 2.0 g% higher than normal during the interval in which the TIBC was decreasing. Further indication that changes in blood volume would not explain the decrease in TIBC was obtained by finding that the blood volume of normal rats, rats 6 hours after receiving endotoxin and rats 24 hours after endotoxin was 5.07 ± .06, 5.07 ± .15 and 4.84 ± .08 ml/100 g body weight respectively.

Some indication that rapid changes can occur in the serum proteins of the rat after an injection of endotoxin is illustrated in Fig. 1. The endotoxin injections produced a significant alteration in plasma proteins which reached a maximum 24 hours after the injection.

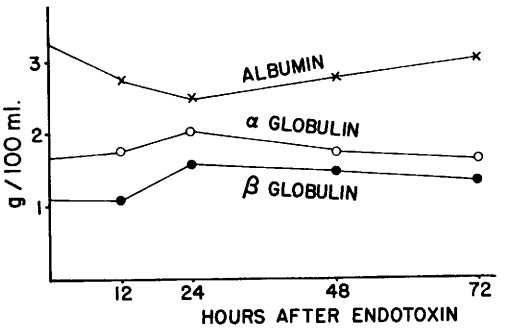

FIG. 1. Effect of endotoxin upon plasma proteins. One mg of *E. coli* lipopolysaccharide per rat.

Discussion. An abnormally high transferrin level is regularly observed in chronic iron deficiency(4). A low transferrin level occurs in pathologic conditions which impair the synthesis of plasma proteins(1,2,3,4,5). Generally, in those pathologic conditions which produce a decrease in albumin concentration, a decrease in transferrin will also occur. It was, however, somewhat surprising to find that these conditions occurred so rapidly after an injection of endotoxin.

Mitchell *et al*(12) proposed that transferrin occurs in two phases: one in the plasma and the other sequestered at cellular sites. Transferrin has also been found attached to immature red cells(13). A longer period of attachment of the transferrin at cellular sites or to the immature red blood cells might explain the decrease in TIBC after endotoxin. Bound iron was shown to be decreased(7) without an increased removal of iron from the plasma(8). It therefore follows that lower than normal amounts of iron were entering the plasma and that less than normal amounts of bound iron would be available to displace transferrin. Jandl and Katz(13) have suggested that transferrin containing iron was selectively attached to cellular sites or immature red blood cells and was then displaced by another molecule containing iron.

If the changes in TIBC after endotoxin were due to an inhibition of protein synthesis the half life of transferrin in the rat must be much shorter than the 6-10 days found in humans(14,15).

Summary. A decrease in total iron-binding capacity of the serum of rats was found to occur after injection of *Escherichia coli* lipopolysaccharide. The decrease was apparently not due to an increased blood volume and was accompanied by other alterations of the serum proteins.

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Incidence of Endogenous Lipoprotein Lipase Activity in Human Plasma.* (29267)

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The mechanisms involved in removal of triglycerides from the bloodstream are being intensively investigated as they are of physiologic interest and also clinically relevant to some lipid abnormalities involved in the genesis of atherosclerosis. There is much evidence, summarized elsewhere(1), that the heparin-activated lipolytic enzyme, lipoprotein lipase, has a major physiologic function in fat transport. This point of view has been disputed, however, and one of the counter-arguments is that the enzyme has only been demonstrable in the plasma of a small percentage of individuals without prior injection of heparin. In a previous study of 482 normal subjects circulating endogenous lipoprotein lipase activity was found in 15-20% of the group(2).

More recent observations indicated that the enzyme was sometimes inactivated by

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