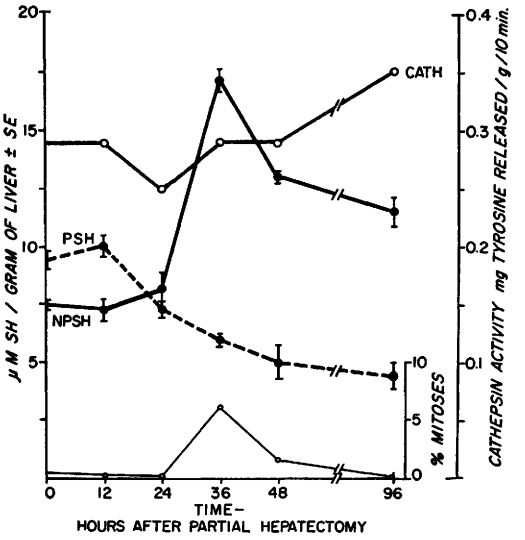

FIG. 1. Fluctuations in non-protein sulfhydryl (NPSH), protein sulfhydryl (PSH) levels, cathepsin (Cath) activity and mitotic activity in regenerating liver. The S.E. for cathepsin activity was too small to be displayed on a graph of this scale.

lationships seems to be a likely area for further investigation. Change in protein structure, (not synthesis) including the cell wall (9), might well be the basic phenomenon, with fluctuating SH levels a tangible result of this change.

Cathepsin activity seems to follow a pattern exhibited by many enzymes in regenerating liver; an initial decrease followed by an increase(10,11). On the basis of these findings no case for a unique relationship between cathepsin activity and cell division in regenerating liver can be made.

Summary. Cell division in regenerating liver is associated with a high sulfhydryl level showing a maximum at peak mitotic activity.

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Translocation of Bacteriophage Across the Intestinal Wall of the Rat.* (27146)

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Particulate matter and large molecules introduced into the lumen of the intestine appear in the blood stream and other body fluids. The particle size varies from that of bacteria(1,2) to that of botulinum toxin(3, 4) and native proteins in food(5).

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Keller and Engley(6) showed that bacteriophage for *Bacillus megaterium* appears in blood within minutes after being administered *per os,* to mice. These workers left open the question as to the primary mode of entry of this phage into the blood. In the work presented here phage is shown to enter primarily into the intestinal lymph, and only sporadically and in small numbers directly into portal blood.

Methods and materials. Rats (Long-Evans

TABLE I. Recovery in Rat Lymph and Blood of Phage Introduced into Intestines.

Rat No.	pfu/ml instilled*	pfu/ml of sample collected over indicated time intervals (min.) Lymph 0-10	Lymph 10-20	Blood 20-25	Lymph 20-30	Blood 25-26
1	8.8×10^{10}	8.8×10^{1}	5.3×10^{2}	0	4.9×10^{2}	0
2	"	0	0	0	9.4×10^{1}	0
3	7.0×10^{10}	1.9×10^{4}	1.3×10^{3}	0	10^{5}	0
4	8.7×10^{10}	1.4×10^{3}	3.7×10^{3}	0	—†	0
5	"	10^{5}	10^{5}	0	3.1×10^{4}	0
6	8.8×10^{10}	1.3×10^{3}	1.5×10^{4}	0	2.3×10^{4}	0
7	"	2.0×10^{3}	10^{5}	0	10^{5}	0
8	6.3×10^{10}	0	0	18	0	3
9	"	8.2×10^{1}	3.4×10^{2}	0	9.9×10^{2}	27
10	"	5.8×10^{1}	5.3×10^{1}	—	3.4×10^{1}	9
11	1.3×10^{11}	3.2×10^{2}	6.2×10^{2}	6.2	9.2×10^{3}	9
12	"	3.8×10^{3}	3.2×10^{2}	0	4.7×10^{2}	0
13	"	8.1×10^{1}	2.2×10^{1}	0	0	0

* 2.0 ml instilled in all instances. † Not done.

strain), 250 to 300 g weight, were used. Introduction of phage suspension (2.0 ml) into the small intestine and recovery of lymph was carried out as described(4). The lymph flow from the small intestine was collected from the *cisterna chyli*. To the extent that collection of lymph from the *cisterna chyli* is complete there can be no spill-over into blood of the lymph flowing from the intestine. A portion (0.2-0.3 ml) of portal blood was collected slowly 20 minutes after administration of the phage (rats 1 through 13). Twenty-five minutes after phage administration all the blood flowing in the portal vein was collected over a 1-minute period (0.6-1.5 ml). In 2 other rats, blood and lymph were collected over earlier and shorter time intervals as described below. Heparin was used as an anticoagulant for both fluids.

Escherichia coli strain B and coliphage, strain T_1, were used throughout. The phage was harvested from nutrient broth cultures, with titers of 10^9 to 10^{10} plaque forming units (pfu) per ml. Suspension of phage were rendered bacteria-free by filtration through membrane filters.

The Gratia technic(7) for phage counting was used, with Bacto nutrient agar as the base medium. Overlay plates were incubated at 20-25°C for 18-20 hours. The volume of lymph or blood collected was measured by a 0.1-0.2 ml pipette. To this was added 1.0 ml nutrient broth and 1.0 ml *E. coli* culture, 4-5 hours old. These mixtures were incubated at 37°C for 5-10 minutes prior to assay. Lymph and blood samples taken prior to introduction of phage were likewise assayed. The possible existence of anti-phage activity of lymph, blood, and heparin was tested by adding small (0.04 or 0.05 ml) volumes of titered phage suspension to samples of these fluids and incubating for periods up to 2 hours prior to quantitative titration for residual phage.

Results and discussion. Of 15 rats used, phage was demonstrated to be in the lymph of 14, and in the blood of 4. In one rat, phage was present in blood, but not lymph. However, the amount of phage recovered in these 2 fluids differed greatly (Table I), and in 3 of the 4 instances where it was recovered in blood samples, circumstances lead us to suspect the possibility of inadvertent experimental contamination. In 2 rats, lymph was collected for 2 periods of 5-6 minutes each, from the time of instillation of phage. These samples contained phage in concentrations similar to those shown in the table for period 0-10 minutes. Blood samples taken over several intervals of 1-2 minutes from time of instillation were found to be uniformly free of phage. Times of appearance of the phage in the lymph closely paralleled those of bacteria (Hildebrand, unpublished). Use of mixtures of *Serratia marcescens* and phage substantiated these findings.

No evidence was found for a phagocidal action of rat blood or lymph (both *in vitro*), even with periods of up to 2 hours exposure. Heparin was likewise nonphagocidal. Con-

trol samples of blood and lymph were free of phage.

Samples of small intestine contents of 3 rats were taken after collection of blood and lymph was completed. Titration indicated that phage was not being inactivated by intestinal fluids, the counts ranging from 95 to 100% of the count of the phage suspension introduced.

These results clearly demonstrate that the primary path of translocation of coli phage T_1 through the intestinal walls is into the intestinal lymph rather than directly into the intestinal blood. These findings agree with those for bacteria and large protein molecules.

The number of particles appearing in the lymph is not impressive, considering the numbers administered. However, the fact that translocation occurs at all may be of significance in the pathogenesis of certain infections, allergic states and intoxications(5).

Summary. In the rat, coli phage strain T_1 has been shown to be translocated from the lumen of the intestine to the blood *via* the regional lymphatic system.

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Inhibition of Coagulase Reaction of Pathogenic Staphylococci by Heparin *in vitro*.* (27147)

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Since the first description of staphylocoagulase by Loeb in 1908, numerous attempts have been made to ascribe a role to this reaction in the pathogenesis of staphylococcal infections and to link the process with that of normal human clotting, but no definitive answers have been given to either of these problems. It was felt that demonstration of significant inhibition of the coagulase clotting mechanism by a known thrombin inhibitor would provide both a key to the sight of action of coagulase and a useful tool with which to define its role in pathogenesis of staphylococcal infections.

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Materials and methods. Overnight broth cultures (Nutrient or Trypticase Soy Broth, Difco) of coagulase positive staphylococci were employed as a source of coagulase. Staphylococci of various bacteriophage types, isolated from 30 patients were utilized. Standardized Normal Human Plasma (Dade), Coagulase Rabbit Plasma (Baltimore Biological Laboratories), fresh human plasma, or fresh rabbit plasma was used to assay coagulase activity. Heparin (Upjohn) was employed as the thrombin inhibitor with all strains. In addition, heparin (phenol-free and Organon) was used with strains HE and 17262. The 0.5% phenol in commercial heparin did not interfere with growth of staphylococci in the assay system when the heparin was diluted 1:10 in 0.85% NaCl. Furthermore, Elek(1) has reported that coagulase