TABLE IV. Statistical Analysis of Combined Experiments.

	High dose*	Low dose†	Treated	Control	
	Treated *vs* control	Treated *vs* control	High dose *vs* low dose	High dose *vs* low dose	Treated *vs* control
Chi square	8.98	10.90	4.30	7.50	18.60
Prob.	<.005	<.005	.50–.025	<.005	<.005

* High dose = 1000-1100 cells/animal. † Low dose = 200-600 cells/animal.

in the gamma globulin of cystic fibrosis patients. Potter and Stollerman(13) have demonstrated that adsorption of human gamma globulin (in particular Cohn Fraction II) to bentonite particles results in marked enhancement of phagocytosis of the particles by human leukocytes *in vitro*.

Experiments are in progress to identify the specific antibody or antibodies in gamma globulin protective against this cutaneous route of infection.

Summary. The technic of subcutaneous implantation of sutures infected with *Staphylococcus aureus* was used to assay protection of mice by pooled human gamma globulin. The mice which received 1 ml each of gamma globulin in divided doses showed 30 to 35% fewer purulent skin lesions than controls. The infected sutures, however, were not freed of viable staphylococci. This model system is regarded as being sufficiently satisfactory to warrant its continued use in experiments toward elucidation of critical factors in pathogenesis and protection.

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Stop Flow Analysis of Renal Tubular Site of Reabsorption of Radioiodide in Dogs.* (27091)

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The renal excretion of iodide in dog and man is believed to involve glomerular filtration and tubular reabsorption(1,2). Giebisch *et al.*(1) suggested on the basis of the failure of water diuresis to cause increased ioduresis that 95% of filtered iodide is reabsorbed at a tubular site proximal to that of facultative water reabsorption. The stop flow technic of Malvin *et al.*(3) has offered a more direct means to localize the site of reabsorption of this anion.

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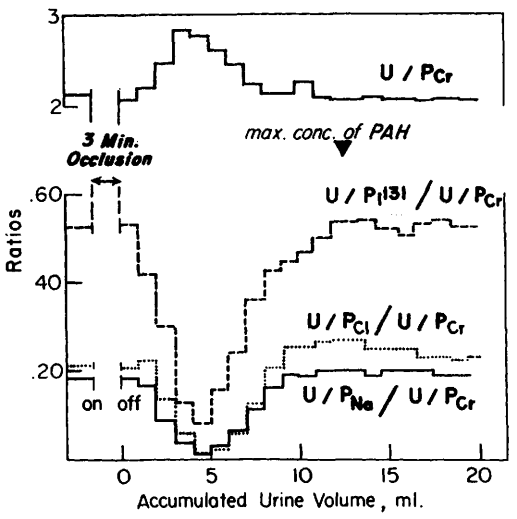

FIG. 1. Urinary stop flow patterns for sodium, chloride, creatinine and I^{131}.

Methods. Stop flow experiments were performed on 8 female mongrel dogs weighing 7-14 kg. Sodium pentobarbital, 30 mg/kg, was administered intravenously. The left ureter was catheterized with polyethylene tubing and a Foley catheter placed in the urinary bladder to allow urine from the other kidney to drain freely. An infusion containing 20% mannitol, .1-.3% creatinine, 30 mg% p-aminohippuric acid (PAH), 10^{-3} M methimazole (Tapazole) and 3.33 μc/ml of radioiodide (I^{131}) was administered at the rate of 8-10 ml/min. *via* the femoral vein. A priming dose of creatinine (80 mg/kg) and PAH (4 mg/kg) was given at the time the infusion was started. Creatinine was used to estimate water reabsorption, PAH to localize the proximal segment, sodium to localize the distal segment, methimazole to prevent organic binding of I^{131} in the thyroid and I^{131} to estimate iodide excretion. Blood samples were taken before and after each occlusion *via* a cannulated femoral artery. Free flow urine samples were also collected before and after each occlusion. Ureteral occlusions were performed only after urine flow from the catheterized ureter stabilized at more than 7 ml/min., and duration of the occlusion was always 3 min. Creatinine was determined by the method of Kennedy *et al.*(4), PAH by the method of Smith *et al.*(5), chloride by the method of Brun(6), sodium by means of a Coleman flame photometer and I^{131} with a well-type scintillation counter. The terms "proximal" and "distal" are used in this paper as defined elsewhere(3,7).

Results. Fig. 1 shows the typical stop flow patterns obtained for I^{131}, sodium, chloride and creatinine. The patterns were the same in all of the 8 experiments carried out. Data are plotted as ratios of urine to plasma concentrations (U/P) divided by ratios for urine to plasma concentrations for creatinine (U/P_{Cr}), as described by Pitts *et al.*(7). These values will be referred to as the "ratios" for the different ions. The pattern for I^{131} is qualitatively similar to that for chloride, which was measured in the experiment depicted, and to that for sodium, which was determined in all experiments. (Earlier observations(8,9) have shown qualitative and quantitative similarity between patterns for sodium and chloride in stop flow experiments.) Ratios for I^{131} and chloride exhibit a marked reduction in the same distal area where the lowest ratio for sodium is found and ratios for both anions reach a plateau in the proximal segment. While the patterns are similar qualitatively, quantitative differences are apparent. The ratios for I^{131} exceeded those for sodium along the entire nephron by a factor of 1.5 or more (Table I). Previous studies concerning the renal excretion of iodide have also led to the conclusion that the clearance of iodide is greater than that of chloride or sodium(2,10,11). Our results indicate that under conditions of stop flow a higher per cent of filtered chloride or sodium than of iodide is reabsorbed in both the proximal and distal segments. These findings are not necessarily opposed to those of Giebisch *et al.*(1) who reported that the bulk of I^{131} was reabsorbed proximal to the site of facultative water reabsorption inasmuch as excretion of I^{131} was not affected by water diuresis. Our findings indicate only that some I^{131} is reabsorbed in a distal area. This area of distal reabsorption could lie in a proximal section of the distal tubule and hence not be greatly affected by water diuresis.

Halmi *et al.*(12) found that perchlorate in the rat causes a marked increase in excretion

TABLE I. Comparison of Minimal Distal and Average Proximal Stop Flow $U/P_{I^{131}}/U/P_{Cr}$ and $U/P_{Na}/U/P_{Cr}$ Ratios before and after Administration of Stable Iodide, Perchlorate or Thiosulfate.

Dog No.	Treatment	$U/P_{Na}/U/P_{Cr}$ Minimal distal	$U/P_{Na}/U/P_{Cr}$ Avg* proximal	$U/P_{I^{131}}/U/P_{Cr}$ Minimal distal	$U/P_{I^{131}}/U/P_{Cr}$ Avg* proximal
3	Control	.01	.17	.07	.36
	Perchlorate	.02	.23	.11	.47
5	Control	.01	.09	.05	.49
	Perchlorate	.03	.13	.10	.54
4	Control	.02	.19	.08	.48
	Stable iodide	.03	.20	.12	.40
7	Control	.02	.20	.06	.31
	Stable iodide	.01	.18	.08	.31
8	Control	.02	.23	.11	.54
	Thiosulfate	.05	.24	.09	.45

* Avg of ratios for the 3 samples in which concentration of PAH was greatest.

of I^{131}. They suggested that perchlorate may be blocking a tubular transport mechanism for iodide in this animal(11). It was therefore decided to test this agent in the dog. After a control stop flow experiment 10 meq of sodium perchlorate were administered intravenously and a second stop flow experiment was performed. This resulted in a slight increase in the ratios for I^{131} in both proximal and distal segments (Table I).

If the reabsorption of iodide in either the proximal or distal segments did involve transport, loading with iodide might be expected to affect the stop flow pattern by saturating the carrier for iodide. In 2 experiments 10 meq of stable iodide were administered intravenously after a control stop flow experiment (Table I) and ratios for I^{131} in both distal and proximal segments were found not to be greatly altered by this treatment. Both these findings and those obtained with perchlorate contrast greatly with those reported in rats(11) in which comparable (on a body weight basis) doses of these anions given in an isotonic medium increased the clearance of I^{131} 5-30-fold without changing urine flow or clearance of endogenous creatinine-like chromogen. This suggests a species difference and is in agreement with the interpretation of Giebisch *et al.*(1) that renal tubular reabsorption of iodide in the dog is by simple diffusion, as in man(2), and does not involve transport as it appears to do in the rat. The inside of the renal tubules is electronegative compared with the outside (13). Because of this, simple diffusion of anions suffices as an explanation for their tubular reabsorption unless it can be shown that a mechanism susceptible to specific inhibition and/or saturation is involved. The doses of perchlorate and stable iodide given to our dogs were high enough to cause an abrupt rise of plasma I^{131} levels, undoubtedly owing to displacement of I^{131} (by block or saturation of iodide transport) from such sites as gastric juice, thyroid and saliva.

Giebisch *et al.*(1) reported that other anions could affect the renal excretion of iodide in a non-specific manner: anions more readily reabsorbed than iodide increased the excretion of iodide, while anions less readily reabsorbed decrease it. Such a passive displacement of iodide by perchlorate could explain the small effect we observed. In another experiment, a 10 meq dose of sodium thiosulfate produced a slight depression of the stop flow ratios of I^{131} (Table I). This is as expected since there is little or no net tubular reabsorption of thiosulfate, its clearance in the dog approximating that of creatinine(14).

Summary. The renal tubular site of reabsorption of iodide has been determined in the dog using the stop flow technic. The pattern for I^{131} was found to be qualitatively similar to that for chloride or sodium. However, I^{131} was reabsorbed to a lesser extent than

chloride or sodium in both distal and proximal segments. Administration of large doses of stable iodide, perchlorate or thiosulfate did not greatly affect the stop flow ratios of I^{131}. These experiments are interpreted as indicating passive reabsorption of iodide in both proximal and distal portions of the renal tubules of the dog.

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Comparative Stability of Trypsin and Chymotrypsin in Human Intestinal Juice. (27092)

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Intramuscular administration of trypsin and chymotrypsin is frequently resorted to in various inflammatory conditions. In view of its ease of administration, oral forms would be more desirable, providing that these enzymes are not destroyed in the gastrointestinal tract. Destruction of the proteolytic enzymes in the stomach need not be a problem, since tablets may be enterically coated so that they disintegrate in the small intestine. However, once the enzymes are released into the intestinal juice they must be stable for a sufficient length of time to permit absorption.

Pancreatic juice contains inhibitors which inactivate trypsin(1-6). This inactivation is very rapid(1,4,5) and is complete at a pH of 7 within one minute(4). The trypsin inhibitor complex is quite stable, having a dissociation constant of 2×10^{10}(4). Chymotrypsin is relatively unaffected by these inhibitors(2,3,5).

The results obtained from the study of pancreatic juice may not necessarily apply to intestinal juice because the latter is a mixture of pancreatic juice, gastric outflow, bile, and intestinal secretions. In view of the work cited above, the authors felt that a study of the stability of trypsin and chymotrypsin in complete human intestinal juice would be useful.

Materials and methods. Intestinal juice was obtained from 5 normal fasting humans by use of a Rehfuss tube. The end of the tube was positioned by fluoroscopy into the lower duodenum and pH was frequently determined during collection to insure that the tube was not withdrawn toward the stomach. In no case was the pH lower than 6.1. The aspirated juice was collected in an ice cooled container and was used within one hour after collection.

Tubes containing the weighed enzymes* were placed in a water bath at 37.5°C and 10 ml of the intestinal juice was pipetted into them under constant stirring. Solution was complete within one minute. Incubation of the intestinal juice, intestinal juice with chymotrypsin and intestinal juice with trypsin

* Trypsin and chymotrypsin used were supplied by Wampole Laboratories, Stamford, Conn.