TABLE I.
Acute Occlusion by Ligature of the Portal Vein in the *Macacus rhesus* Monkey.*
All recovered and present condition is normal.

Exper. No.	Vessels ligated	Sex	Days post-op.	Major collateral circulation
1	Portal vein	F	51	Splenic vein Inferior mesenteric vein Middle colic vein
2	" "	M	50	Same
3	" "	M	49	Same
4	Superior mesenteric vein	F	43	Middle colic vein Retroperitoneal vein Hepatic ligament vein
5	Portal vein Superior mesenteric vein	F	38	Middle colic vein Inferior mesenteric vein
6	Portal vein Superior mesenteric vein Splenic vein	F	23	Retroperitoneal vein Middle colic vein Omental vein
7	Same	F	16	Same

* Seven *Macacus rhesus* monkeys subjected to ligation of various segments of the portal venous system. Survival periods and chief systemic pathways of anastomosis are indicated in the column headed "Major Collateral Circulation."

creas. To date none of the animals has developed clinically detectable nutritional deficiencies or ascites. Table I outlines the seven experiments performed.

Summary and conclusions. Various segments of the portal circulation (including the portal vein) have been suddenly occluded by ligature in 7 adult *Macacus rhesus* monkeys. All of the animals have survived this procedure uneventfully and are in apparent good health from 16 to 51 days postoperatively. By means of portal venography anastomotic channels have been demonstrated by way of which blood is immediately returned to the systemic circulation in sufficient quantities to prevent these animals from succumbing to shock due to depletion of their circulating blood volume.

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The Ulcer-Inhibiting Action of Pyrogens.

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A series of urinary extracts under investigation for their ulcer-inhibiting action in the Shay rat, were found to contain a high concentration of pyrogens. Since Necheles[1] had shown that pyrogens suppressed gastric motility in dogs, it seemed desirable to study the inhibitory effect of purified pyrogens in the pylorus-ligated rat. Pyrogens prepared from cultures of *B. prodigiosus, Pseudomonas aeruginosa* and *E. typhi* were investigated.

Method. The assay procedure for estimating anti-ulcer activity was essentially that of Pauls, Wick, and MacKay.[2] Sprague-Dawley male rats of 150-170 g weight were fasted for 48 hours in cages with coarse mesh bottoms. Water was given *ad libitum.* After ether anesthesia, the duodenum was exposed, grasped lightly with fine forceps and ligated at the pyloric sphincter with braided silk thread. The incision was closed with metal clips and painted with collodion solution in order to avoid ingestion of blood residue from the wound.

[1] Necheles, H., *Am. J. Physiol.*, 1942, **137**, 28.

[2] Pauls, F., Wick, A. N., and MacKay, E. M., *Gastroenterology*, 1947, **8**, 774.

TABLE I.

Pyrogen	M.P.D.,* μg per kg	Nitrogen, %	Reducing substances, %	Glycosamine, %
B. prodigiosus	.005	.7	68.9	2.5
Pseudomonas aerugenosa	.02	1.1	64.5	4.2
E. typhi	.01	.8	58.7	3.1

* M.P.D. or minimal pyrogen dose refers to the minimal amount which will cause a temperature rise of 0.6°C in rabbits (U.S.P. XIII).

TABLE II.

Preparation	Dose range, μg	Route	Total No. rats	No. ulcerated	Ulcer index
Controls	—	Intrav.	56	53	315
Prodigiosus pyrogen	3-10	"	28	10	72
" "	15-20	"	24	7	55
" "	25-30	"	30	5	31
" "	35-50	"	20	1	15
" "	10-25	Intraper.	15	8	140
" "	50	"	10	2	80
" "	100-1000	"	15	0	0
" "	100-1000	Oral	3	3	367
Pseudomonas pyrogen	10-50	Intrav.	29	8	52
" "	100-500	"	11	0	0
Typhoid pyrogen	50-250	"	8	2	25

Pyrogens were dissolved in pyrogen-free dilute buffer and injected in 0.5 ml volumes intravenously in a tail vein or intraperitoneally just prior to pyloric ligation. In one experiment, pyrogen solution was given orally by stomach tube a few minutes following the operation when recovery from anesthesia was nearly complete. Control rats received 0.5 ml pyrogen-free buffer solution intravenously. Animals were sacrificed at the end of eight hours. Volume and free acidity of stomach contents were measured and recorded and the degree of ulceration scored using an arbitrary scale of +4 to +1 according to the number and size of lesions observed. Zero was recorded when no macroscopic abnormality was seen. The average score for each group was multiplied by 100 to give an "ulcer index" following the method of Risley, Raymond, and Barnes.[3]

Pyrogens. Pyrogens were prepared from pure cultures grown on synthetic medium[4] and isolated by a procedure to be described in a subsequent publication. Full analytical data on these pyrogens will appear later.[5] However, Table I gives the pertinent information on each of these highly purified preparations used in the experiments reported here.

Results. Experimental results are recorded in Table II which for brevity is tabulated in dose ranges of administered pyrogens rather than for separate dosages.

Among 56 control rats not treated with pyrogen, 53 showed ulceration at the end of 8 hours to an average degree of +3.15 or an ulcer index of 315. Intravenous doses of 3-10 μg prodigiosus pyrogen protected 18 of 28 rats and reduced the ulcer index to 72. Increasing doses increased the number of rats protected and reduced the ulcer index to a low of 15 at 35-50 μg doses. Intraperitoneally, corresponding amounts of this pyrogen are somewhat less effective than when given intravenously. However, doses ranging from 100-1000 μg offer complete protection, none of the 15 rats treated with this amount of pyrogen showing any ulceration. Orally this pyrogen appears to be completely lacking in protective activity against ulceration. The data, however, are too limited to allow gen-

[3] Risley, E. A., Raymond, W. B., and Barnes, R. H., *Am. J. Physiol.*, 1947, **150**, 754.

[4] Rodney, G., and Welcke, M., *J. Bact.*, 1945, **50**, 129.

[5] Rodney, G., and Devlin, H. B., to be published.

eralization with respect to this mode of administration.

Pseudomonas pyrogen was used in only 2 dose ranges of 10-50 μg in 29 rats and 100-500 μg in 11 rats. Critical examination of the individual protocols indicates that this pyrogen had slightly less inhibitory effect on ulceration than the prodigiosus pyrogen which correlated with the comparatively low pyrogenic activity as measured in the rabbit test.

Typhoid pyrogen was used only in the larger dose range, two of eight rats showing minor ulceration with this preparation.

Not shown in the table but deserving of mention are results with a non-pyrogenic polysaccharide prepared by the pyrogen isolation technic from pneumococcus type II cultures. This substance showed no anti-ulcer activity in 4 rats in doses up to 200 μg.

Also omitted are detailed data on gastric volume and free acidity. However, it may be stated that among all rats studied in these and related experiments, the mean gastric volume of 208 ulcerated rats was 8.9 $\pm$ 2.6 (S.D.) ml whereas in 94 non-ulcerated rats secretion amounted to 5.9 $\pm$ 3.2 ml. Likewise free acidity of gastric contents from ulcerated rats was equivalent to 5.3 $\pm$ 2.4 ml N/10 NaOH. Non-ulcerated rats showed values of 3.0 $\pm$ 2.3 ml. Among both groups of data the differences between the means from ulcerated and non-ulcerated rats are statistically significant.

Conclusion. As judged by response in the Shay rat, pyrogens from *B. prodigiosus, Pseudomonas aerugenosa* and *E. typhi* are highly active ulcer-inhibiting substances. Whether the presence of these substances in various tissue and urinary extracts may account for the reported anti-ulcer activity of these preparations remains to be investigated. The mode of action of pyrogens is not clear but may be associated with the obviously diminished acidity and volume of gastric secretion which occurs as a result of administration of these substances. There was observed no evidence, however, of any general "toxicity" in the animals which received purified pyrogens.

Summary. Intravenously administered purified pyrogens from cultures of *B. prodigiosus, Pseudomonas aeruginosa* and *E. typhi* possessed marked ulcer-inhibiting action in the Shay rat.

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Increased Requirement for Pteroyl Glutamic Acid During Lactation.*

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A series of experiments had been undertaken in an attempt to produce an anemia in fetal and newborn rats. One of the technics employed was the feeding of succinyl sulfathiazole (SS) to the maternal rats. During the course of the study, it was observed that the newborn rats from mothers receiving the diet containing SS, died within five days after birth. It was thought that this high mortality among the newborn might be due to either a toxic effect or to a failure of lactation.

Preliminary experiments indicated that SS or its hydrolysis products did not have any toxic effect on the newborn rats. Although SS passes through the alimentary tract substantially unchanged and is not absorbed, some small part of it is hydrolyzed to sulfathiazole which may be absorbed. On a diet containing 1% SS, rats were found to have a blood level of approximately 0.3 mg % sulfathiazole.[1] The administration of SS or

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