

Of the 9 untreated cases, 7 died (77.8%); whereas only 2 of the 9 treated cases died (22%).

Because many cases of human pneumonia come to the physician relatively late, further experiments are in progress to determine the efficacy of sulfonamide therapy in rat pneumonia which had been allowed to progress without treatment for various time periods.

Conclusions. *P*-aminobenzenesulfonamide therapy is effective in prolonging, and in many instances saving, the lives of rats infected intrabronchially with Type III pneumococci suspended in mucin.

9180

Filtration Studies on Pyrogenic Inulin.

CO TUI, M. H. SCHRIFT, K. L. MCCLOSKEY AND A. L. YATES.

From the Laboratory of Experimental Surgery, New York University College of Medicine.

In a previous report,¹ it was shown that the pyrogen or fever-producing substance in tap water and a sample of aquarium water which, upon intravenous injection produces a fever in dogs, was removable by filtration of the water through a 200-second Zsigmondy membrane filter or a Seitz Serum No. 3 filter.* Likewise removable is the pyrogen in glucose and physiological saline solutions found to be pyrogenic in patients upon intravenous injection.² Because the former filter acts mainly by sieving and the latter by adsorption, it is concluded that the pyrogen in these fluids was of a particulate nature of an order of magnitude larger than 50 m μ as well as adsorbable.

In the course of their work on inulin clearance, Goldring and Smith³ found that some samples of dahlia inulin injected intravenously gave a febrile reaction in man, characterized by chill, fever, headache, nausea, and lumbar pain. This symptomatology resembles closely that found in man following an intravenous injection of one of the pyrogenic fluids which we have investigated. One gram

¹ Co Tui, McCloskey, Schrift, and Yates, *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 297.

* Due to error in labelling, these filters were called "Seitz EK filters" in our previous communication.¹

² Co Tui, McCloskey, Schrift, and Yates, *J. Am. Med. Assn.*, in press.

³ Goldring and Smith, *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 67.

of a sample of inulin supplied us by Professor Smith was injected intravenously into a dog, resulting in fever, leucopenia, chill, nausea, and vomiting. This symptomatology likewise parallels that of dogs receiving pyrogenic infusion fluids intravenously.

In connection with the alleged toxicity of inulin, it may be mentioned that Nathan⁴ used it for the production of anaphylatoxin. By incubating a suspension of inulin with guinea pig serum and then injecting the mixture into guinea pigs, he found restlessness, dyspnea, convulsions and agonized breathing resulting in death (anaphylaxis). When inulin in solution was used, however, there was no such manifestation. He concluded that its ability to initiate this toxicity depends upon the physical state of the inulin. DeKruif and German⁵ found that inulin mixed in proportion 1:16 with normal rat serum produced a potent anaphylatoxin. Hanzlik and Karsner⁶ found that inulin, without serum, injected intravenously into guinea pigs produced symptoms of anaphylactoid shock, namely, marked dyspnea, shallow respiration, cyanosis, and restlessness. When the animals were killed, autopsy revealed collapsed and congested lungs and cardiac dilatation. It will be recalled that in none of these studies was the temperature curve of the experimental animals taken into consideration.

In view of the similarity of the manifestations of pyrogenic inulin in both dog and man to those of pyrogenic infusion fluids, it seemed desirable to submit pyrogenic inulin to a similar filtration study.

As in our previous work, the types of filter used here were: Berkefeld filter "W", Seitz Serum No. 3 filter, and Zsigmondy filter of graded porosity (ultrafiltration). Two samples of inulin (684 and 684A), which Pfanstiehl and Company kindly furnished, were used. These were made in 10% solution. Where ultrafiltration was performed, the entire solution was filtered through but one membrane, thus limiting adsorption to that membrane only.

Table I shows that the pyrogen from both samples passes through a Berkefeld filter as well as a 42-second Zsigmondy ultrafilter membrane, but is held back by filtration through 2 pads of Seitz Serum No. 3 filter. But while a 200-second Zsigmondy membrane filter removed the pyrogen in 684, it did not hold back that in 684A, and a 300-second filter had to be used. This would suggest that the pyrogen is of a different particulate size in the 2 samples. Since the pyrogen is held back by a 200-second Zsigmondy membrane filter in one

⁴ Nathan, *Z. f. Immunitätsf.*, 1914, **23**, 204.

⁵ DeKruif, P. H., and German, W. M., *J. Infect. Dis.*, 1917, **20**, 833.

⁶ Hanzlik and Karsner, *J. Pharm. and Exp. Therap.*, 1920, **14**, 449.

TABLE I.
Inulin.

Lot No.	Subject	Vol. Injected cc.	Filter Used	Final Concen- tration	Total Dose, Gm.	Temp. Changes	Blood Count Changes, WBC per cmm.
684	Dog	55.0	0	10.0	5.5	101.8-104.6	29,300- 4,900
	"	235.0	Berkefeld W	9.8	23.03	101.8-105.2	29,650- 2,600
	"	50.0	42-sec. Zsig.	9.9	4.95	101.4-104.2	16,500- 4,200
	"	250.0	200 " "	9.8	24.5	101.6-102.2	11,500-10,600
	Man	2.5	0	10.0	.25	98.2-102.2	8,600- 4,950
	"	250.0	200-sec. Zsig.	9.8	24.5	99.8- 99.8	9,600- 8,400
684A	"	260.0	Seitz (twice)	9.7	25.22	98.8- 99.2	
	Dog	10.0	0	10.0	1.0	102.0-104.8	17,500- 4,300
	"	15.0	Berkefeld W	9.8	1.47	102.0-104.6	18,200- 3,600
	"	250.0	200-sec. Z.	9.7	24.25	102.2-103.4	17,700- 8,600
	"	260.0	300 " "	9.6	24.95	101.6-101.8	21,200-20,800
	"	240.0	Seitz (twice)	9.6	23.04	102.2-101.8	18,500-19,200
	Man	2.5	0	10.0	.25	99.2-103.4	7,200- 3,600
	"	230.0	200-sec. Z.	9.8	22.54	99.4-101.8	10,200- 9,200
	"	250.0	300 " "	9.7	24.25	99.4- 99.2	
	"	250.0	Seitz (twice)	9.6	24.0	99.2- 98.8	10,200- 9,800

WBC = Leucocytes.

case and by a 300-second in the other, but not by a 42-second filter, it is concluded that the removal was accomplished by sieving rather than adsorption. On the other hand, the removal of the pyrogen by the Seitz Serum No. 3, because of the nature of the filter, is by adsorption. Smith and his associates⁷ have devised a method of purifying crude, toxic inulin into a non-toxic one with charcoal, probably utilizing the known adsorbing power of the latter substance.

Since after the treatment with charcoal by the Smith method, and after filtration through membranes as well as through an adsorptive filter, inulin can be injected into man and dogs without any symptoms, it is clear that the results obtained by Hanzlik and Karsner in the guinea pig are not reproducible in the human being or in the dog. The question arises whether the symptoms elicited by Hanzlik and Karsner as well as by Nathan and by DeKruif and German were not due to an artefact instead of to inulin itself.

Summary and Conclusions. 1. The febrile reaction elicited by intravenous injections of some samples of inulin is similar to that following the intravenous administration of pyrogenic infusion fluids in both dog and man. 2. The pyrogen in the inulin as well as that in the pyrogenic infusion fluid is filterable through a Berkefeld filter, but held back by filtration through 2 Seitz Serum No. 3 filter pads and by Zsigmondy membrane filters of from 200 to 300 seconds. 3. The pyrogen in inulin, like that in pyrogenic infusion fluids, is therefore of a particulate nature of a large order of magnitude. It is likewise adsorbable.

9181

Phosphorus Metabolism. VII. Course of Phosphorus in Alimentary Tract of the Rat.

GUY E. YOUNGBURG.

From the Department of Biological Chemistry, University of Buffalo Medical School.

The main object was to compare the concentrations of total P and its fractions in the stomach contents, small intestinal contents, large intestinal contents and colon, and feces, on a P-free diet, with the concentrations on a normal diet. This should indicate some changes taking place, particularly to what extent P compounds are excreted

⁷ Smith and associates. Personal communication.