

Serum Polysaccharide Levels in Experimental Inflammation.* (17412)

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The serum polysaccharide level has been shown to be elevated in malignancies, tuberculosis, and certain other pathological conditions. It has been suggested by Seibert, Seibert, Atno, and Campbell¹ that this rise is related to tissue destruction. They note that the α_2 globulin, which is especially rich in carbohydrate content, is elevated in tuberculosis and carcinomas. Since Shedlovsky and Scudder² have noted that a rise in α_2 globulin is associated with inflammation or tissue destruction irrespective of cause, one might postulate that a rise in serum polysaccharides is to be expected wherever inflammation occurs. In studies of human conditions this has, in general, proved to be true,³ although low results were found in some infectious diseases. It appeared that this problem might be further elucidated by a study of inflammation in experimental animals.

Experimental. Chemical methods. In this study non-glucosamine polysaccharide and protein were determined as previously described.⁴ Glucosamine polysaccharide was also determined on all samples, but as the results roughly parallel those for non-glucosamine polysaccharide, they are not given in this paper.

Inflammation due to infection. In order to

produce an infectious lesion which could be closely followed, 5 ml of a mixed culture of *Staphylococcus aureus* and *Streptococcus pyogenes* and mucin[†] were injected subcutaneously into the back legs of healthy mongrel canines. In several cases, large abscesses about 10 cm in diameter resulted. The abscesses usually ruptured spontaneously and drained on about the sixth day; the skin sloughed on the eighth day, leaving the abscess area lined with granulation tissue. The wounds granulated completely within 60 days. The temperature reached a maximal elevation on the third day, but did not return to normal until the sixth day. Clinically, there was no sign of septicemia, and the animals appeared greatly improved by the sixth day. The non-glucosamine polysaccharide level was elevated slightly on the first day, when expressed as a percentage of protein, but did not reach a maximum until the sixth day. The level then fell slowly, but it was still elevated appreciably on the 26th day and did not become normal until the 52nd day. Results obtained from the study of 3 dogs are depicted graphically in Fig. 1. Similar results were not obtained with all dogs, as some animals exhibited more resistance to the infectious agent and no apparent abscess was formed. In these cases the maximal polysaccharide level was not so high, and the return to normal occurred much earlier.

Turpentine Inflammation. Turpentine was sterilized for injection by filtering National Formulary grade turpentine through a Seitz filter by suction into a filter flask. The flask and filter were previously sterilized by auto-

* This work was supported by a grant from the American Cancer Society on the recommendation of the Committee on Growth of the National Research Council and by funds from the John Archer Hatchett Memorial Fund.

¹ Seibert, F. B., Seibert, M. V., Atno, A. J., and Campbell, H. W., *J. Clin. Invest.*, 1947, **26**, 90.

² Shedlovsky, T., and Scudder, J., *J. Exp. Med.*, 1942, **75**, 119.

³ Shetlar, M. R., Foster, J. V., Kelly, K. H., Shetlar, C. L., Bryan, R. S., and Everett, M. R., accepted for publication in *Cancer Research*.

⁴ Shetlar, M. R., Foster, J. V., Kelly, K. H., and Everett, M. R., *Proc. Soc. Exp. Biol. and Med.*, 1948, **69**, 507.

[†] The authors wish to gratefully acknowledge the aid of Dr. Florene Kelly and Dr. Homer Marsh, Department of Bacteriology, Oklahoma University School of Medicine, for their advice in planning the bacterial phase of this work and for their preparation of the culture used.

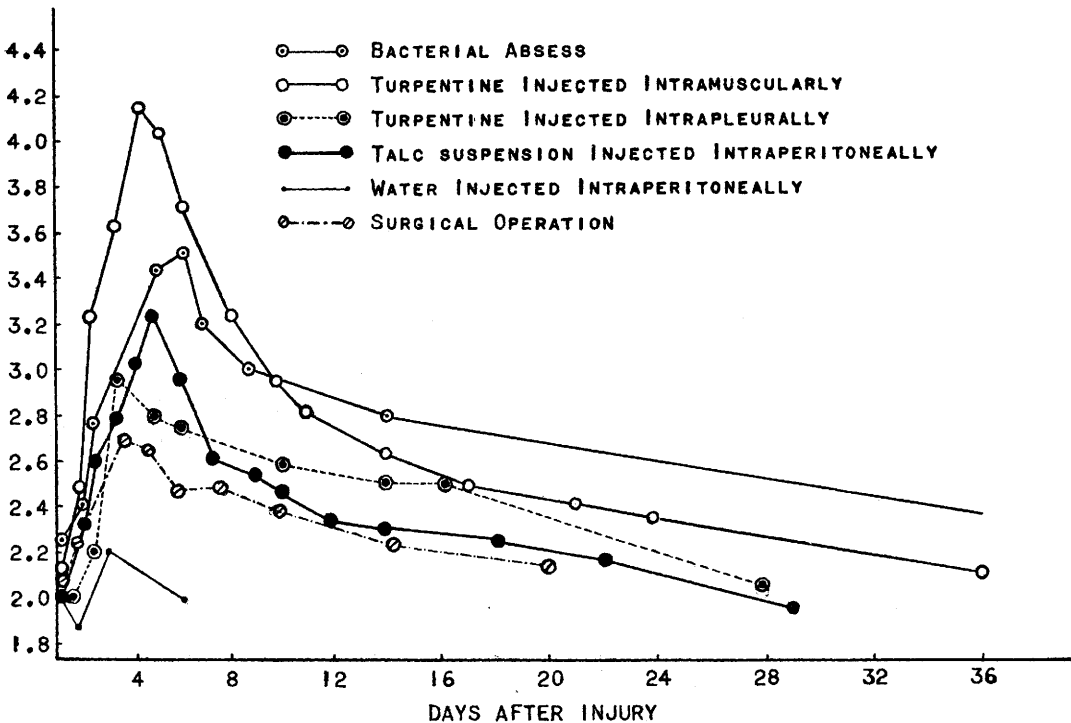


FIG. 1. NON-GLUCOSAMINE SERUM POLYSACCHARIDE OF DOGS EXPRESSED AS A PERCENTAGE OF SERUM PROTEIN FOLLOWING INJURY.

claving for 30 minutes at 15 lb pressure. The turpentine was then transferred to a syringe and injected into the experimental animals, using aseptic technic. In one series of studies the turpentine was injected into the pleural cavity, and in a second series it was injected intramuscularly. Opie⁵ describes the former type of injection as "resulting in serofibrinous inflammation which undergoes resolution, so that the pleural cavity is restored to normal in about 10 days; there is no destruction of tissue."

Intramuscular injection of turpentine on the other hand results in a sterile abscess which is filled with purulent material. In this case there is much destruction of tissue early in the course and repair by granulation and fibrosis after evacuation or absorption of the contents of the abscess. In our experiments, using mongrel dogs, swelling usually became apparent after 24 hours, reached a maximum at 48-72 hours, and was reduced after 5 days. The temperature was usually elevated after

24 hours, reached a maximum within 48 hours, and became normal by the fifth day. Abscess formation was noted in every case; in approximately one-half of the experiments the abscess ruptured spontaneously and drained about the fourth day. In these cases it was apparent that considerable tissue damage resulted; the formation of some repair tissue had taken place by the fourth day, when rupture occurred. Average results of the polysaccharide expressed as percentage of protein for 6 animals are expressed graphically in Fig. 1. In both types of injection the serum polysaccharide levels reached maximal elevation on the fourth day, however, the animals injected intramuscularly exhibited the higher maxima.

Talc Granuloma. A talc suspension for injection was prepared by suspending 20 g of talc in 80 ml of water. The suspension was sterilized, allowed to cool, resuspended and injected intraperitoneally into healthy mongrel dogs through a No. 15 needle, using aseptic technic. The signs of peritoneal ir-

⁵ Opie, E. L., *Arch. Int. Med.*, 1910, 541.

ritation usually subsided in about 3 hours. No appreciable temperature elevation occurred during the time the animals were studied. Extensive granulomatous lesions resulted in all cases but no attempt was made to correlate the extent with serum polysaccharide levels. Average results of studies using 4 dogs are depicted in Fig. 1. The serum polysaccharide reached a maximal elevation on the third or fourth day and was higher than normal even on the 20th day. Intraperitoneal injection of 100 ml of sterile water in a control experiment caused only a slight change in the serum polysaccharide as noted in Fig. 1.

Experimental Surgical Operation. Several experimental laparotomies were carried out under aseptic conditions on mongrel dogs, and the serum polysaccharide level was studied by serial determinations following operation. Since no tissue was removed during these procedures, the only tissue injury was that resulting from the incisions. Data obtained from these studies based on the results from 3 animals are presented graphically in Fig. 1. The maximal elevation of serum polysaccharide occurred on the fourth day. The elevation was not as great as that caused by severe bacterial infection or turpentine abscess. No significant temperature elevation was found.

Discussion. It is apparent from the data presented that an increase in serum polysaccharide follows the production of experimental inflammation regardless of the causative agent. As this response is a delayed one, with maximal elevation in 3 to 6 days after injury, the polysaccharide level does not appear to be directly correlated with tissue destruction. Furthermore, the same effect is produced by

inflammatory processes caused by injection of talc suspensions or by intrapleural injection of turpentine, conditions in which little tissue destruction is thought to occur. Fever is apparently not essential for the elevation, inasmuch as the serum polysaccharide rose in cases where no temperature elevation occurred. It is therefore possible that the elevation of polysaccharide may be correlated with tissue proliferation or repair.

The length of time which elapsed before the polysaccharide level became normal again seemed to have some connection with the extent of repair. The time required for the polysaccharide level to become normal in an animal with a large abscess resulting from bacterial action was much longer than for types of inflammation where less regeneration of tissue occurred. It seems unlikely that the continued high level could be the direct result of tissue injury, as signs of infection and trauma were absent after the eighth day.

Summary and conclusions. Studies were made of serum polysaccharide levels in dogs following the production of sterile turpentine abscesses, of bacterial abscesses, and of talc granulomas, the injection of turpentine intrapleurally, and experimental surgical operations. In all cases the polysaccharide level rose and the maximal level depended somewhat upon the type of inflammation. Elevation occurred both in the presence and absence of fever. The maximal elevation appeared within 3 to 6 days after the initial injury. The suggestion is made that this phenomenon is correlated in some way with tissue proliferation or repair.

Received July 25, 1949. P.S.E.B.M., 1949, 72.