these studies fails to inhibit the coagulation of rabbit blood; this holds true for the filtrate as well.

In conclusion, the foregoing preliminary data indicate that the localizing property of *Staphylococcus aureus* is probably referable not merely to the severe irritating property of the organism *per se,* but also to its additional ability to release a powerful soluble exotoxin-like product, identical in many respects with leucocidin, and capable in itself of inducing a sufficiently intense injury to cause obstruction of normal lymphatic drainage. *Pneumococcus* Type I and *Streptococcus hemolyticus,* on the other hand, fail to form any such detectable accessory substance able to cause damage to the lymphatic or capillary endothelium. Briefly, then, evidences obtained thus far are in accord with the writer's original view, that the delayed fixation of dye and hence the invasive capacity of hemolytic streptococcus is referable to the mild local effects of this organism in contrast to the pronounced injurious action of *Staphylococcus aureus.* These studies are being continued in an attempt to obtain more precise information concerning the chemistry and the rôle of leucocidin-like substances.

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Anticoagulants of the Blood.

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Any agent which inactivates or removes from blood, calcium, prothrombin, or thrombin is an anticoagulant. Theoretically, antifibrinogen and antithromboplastin are also possible but have never been convincingly demonstrated. The removal of calcium by oxalates, citrates, or fluorides is well known. As a type of antiprothrombin, aluminum hydroxide is an excellent example. On mixing and incubating oxalated plasma (0.5 cc.) with aluminum hydroxide cream (0.05 cc.) a plasma is obtained which after the removal of the aluminium hydroxide, will not clot on recalcification, whereas the untreated plasma clots in 2 minutes when calcium is added. The loss of clotting power is not due to removal of thromboplastin, for on adding an active preparation made from rabbit's brain, the normal clotting time is not restored. Furthermore, fibrinogen is not removed, for thrombin (fresh serum) will cause clot-

ting in 10 seconds. Prothrombin must be the constituent that is removed or inactivated by aluminum hydroxide. Significantly, this reagent does not remove or inactivate thrombin.

Hirudin is a type of true antithrombin. Heparin likewise appears to be an antithrombin as the following experiment demonstrates:

Fibrinogen 0.5% solution (cc.)	0.1	0.1	0.1	0.1	0.1
Fresh serum (cc.)	0.1	0.1	0.1	0.1	0.1
Heparin (mg.)	0.0	0.003	0.006	0.009	0.012
Clotting time (sec.)	15	60	300	No clot	

Heparin is not neutralized by thromboplastin. Even when excess thromboplastin is present, the clotting time is prolonged as the concentration of heparin is increased. Plasma containing 0.2 mg. of heparin per cc. will not clot, irrespective of the excess of thromboplastin.

Other substances, notably certain dyes, are antithrombic. Calcomine Fast Pink 2 B.L Unbl.* is a strong anticlotting agent.

Fibrinogen 0.5% solution (cc.)	0.1	0.1	0.1	0.1
Fresh serum (cc.)	0.1	0.1	0.1	0.1
Calcomine fast pink (mg.)	0.0	0.01	0.03	0.10
Clotting time (sec.)	10	15	30	300

There is no evidence that the presence of thrombin in the blood stimulates the production of antithrombin. On injecting 70 cc. of freshly defibrinated blood containing a high concentration of thrombin into dog (Body weight 13 kg.) no intravascular clotting occurred, but free thrombin was still present in the blood 40 minutes after the injection. On withdrawing 9 cc. of blood and mixing it with 1 cc. of M/10 sodium oxalate (an amount amply sufficient to prevent normal blood from clotting) a solid clot was formed in less than 24 hours by merely allowing the blood to stand. This must be attributed to the free thrombin still present.

* The dye, Calcomine Fast Pink 2 B.L. Unbl. was kindly furnished by The Calco Chemical Company.