

sistent findings with some definite increase in fibrous tissue about the periphery of each liver lobule and especially about the bile duct, a general infiltration of lymphocytes throughout this fibrous tissue and a little cloudy swelling of the cytoplasm of the liver cells.

Other liver function tests were done and many other observations on the blood serum carried out at this time, but the only parallelism existed between the Takata-Ara reaction and the sedimentation time which was materially reduced as the reaction became positive.

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Antigenicity of Streptofibrinolysin.*

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The low antifibrinolytic titer† of most commercial anti-streptococcus serums¹ suggests the possibility that the specific antihuman fibrinolysin formed or secreted by certain strains of *Streptococcus hemolyticus* is not antigenic.

To test this possibility, active antifibrinolytic immunization was attempted with rabbits. The selected vaccines were (a) centrifugates from 24-hour broth cultures of fibrinolytic streptococci, and (b) lytic enzymes isolated from such cultures by the alcohol-precipitation technic.² Control injections were made with (c) heat-killed streptococci centrifuged free from lytic broth. There were also available for comparison (d) a series of rabbit precipitins for the Lancefield streptocarbohydrate A. This specific capsular sugar is apparently genetically linked with the antihuman fibrinolytic function.³

Three methods of immunization were used with these rabbits. Six animals (Group A) received 3 subcutaneous, 3 intraperitoneal and 3 intravenous injections at 3 to 4-day intervals, followed by 6 intra-

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† There is no known parallelism between the antifibrinolytic titer and the therapeutic value of a streptococcus antiserum. (W. H. M.)

¹ Van Deventer, J. K., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1117.

² Tillett, W. S., and Garner, R. L., *J. Exp. Med.*, 1933, **58**, 485.

³ Madison, R. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 49.

venous injections at weekly intervals, the injection dose being: (a) 1,000 arbitrary units of the lytic enzyme, (b) 1 cc. (about 100 lytic units) of the centrifugate, or (c) equivalent amounts of lysin-free streptococci. Six rabbits (Group B) received the same vaccines intradermally (divided doses). Six animals (Group C) were given only one vaccine, the alcohol-precipitate, this was administered by means of a stomach tube, duodenal tube or enteric capsule.

Antiserums were withdrawn from all animals 10 days after the final vaccine dose. The average antifibrinolytic titer of each group of antiserums thus obtained is recorded in Table I.

TABLE I.
Antifibrinolytic Titers of Rabbit Antiserums

Each recorded number represents the average titer for the specified vaccine and animal group. The titrations were made with purified fibrinolysin, isolated human fibrin being used as the reaction index. For details of technic, see previous paper.¹

Vaccine	Average number of arbitrary antifibrinolytic units ¹ per cc. of antiserum			Normal rabbit serum	Normal human serum
	Group A	Group B	Group C		
(a) Centrifugate	80	80	—	30	60
(b) Alcohol-precipitate	80	80	80	40	50
(c) Heat-killed streptococci	80	80	—	30	40
(d) Carbohydrate A	30	—	—	20	80

Since none of the presumably immune rabbit serums had an antifibrinolytic titer more than 2 to 3 times that of normal rabbit serum, the conclusion seems justified that the antihuman streptofibrinolysin in itself is practically non-antigenic for rabbits.

It is conceivable that conjugation of the lytic factor with a colloidal "carrier" or even the establishment of an active focus of fibrinolytic infection may be necessary for the development of an effective antifibrinolytic immunity in this animal species.