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Lethality of a Forssman Antiserum for Mice.* (27754)

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It has been known for many years that the tissues of the mouse contain the Forssman antigen(1), and recently the precise localization of this material has been visualized by the fluorescent antibody technic(2). The mouse, however, unlike the Forssman positive guinea pig, has not succumbed to the injection of Forssman antibody(3,4,5), and the absence of fatal reactions has been used to support the claim that mouse tissue does not contain true Forssman antigen(5). The following data indicate that pertussis-inoculated mice which have an increased susceptibility to the lethal effects of anaphylaxis, histamine, serotonin, etc.(6) can easily be killed with a Forssman antiserum.

Material and methods. A rabbit was injected subcutaneously once or twice a week for a month with boiled guinea pig kidney (Difco). Forty mg of the antigen was suspended in 1 ml of saline and the suspension mixed 1:1 with complete Freund's adjuvant (Difco) prior to injection. Ten days after the last inoculation the rabbit was bled and its serum was found to hemolyze sheep cells in the presence of complement (titer >5120). Portions of the rabbit antiserum to boiled guinea pig kidney (anti BGPK) were absorbed with one of the following antigens: (a) Boiled sheep erythrocyte stromata, a Forssman positive tissue (method of preparation described(7)); (b) boiled sheep erythrocyte stromata extracted with absolute methanol at room temperature, a procedure which removes the Forssman antigen(1); (c) desiccated boiled rabbit kidney which does not contain the Forssman antigen(1); (d) beef cell antigen (Difco), a heterogenetic antigen distinct from the Forssman antigen(8).

Aliquots of rabbit antiserum to BGPK (3.5 ml) were absorbed 4 times with 25 mg (per absorption) of one of the aforementioned antigens. Each absorption, lasting 5-10 minutes, was performed at room temperature and was accompanied by gentle stirring of the suspension. Centrifugations following absorptions were carried out at 2500 rpm for 10 minutes.

Swiss-Webster 20-25 g female mice sensitized intraperitoneally with 5 billion *B. pertussis* organisms killed wth 1:10,000 Thimerosol were injected intravenously 5-7 days later with 0.5 ml of absorbed or unabsorbed rabbit antiserum to BGPK. Deaths were noted within 1 hour although the great majority occurred 15-30 minutes after challenge.

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TABLE I. Lethality of a Forssman Antiserum for Mice.

Mice injected i. v. with 0.5 ml of rabbit antiserum to boiled guinea pig kidney absorbed with	Deaths/Total
Nothing	19/21
Boiled sheep stromata	3/24
Boiled sheep stromata extracted with alcohol	11/12
Boiled rabbit kidney	5/5
Beef cell antigen	11/12

Results and discussion. The data in Table I demonstrate that a rabbit antiserum to boiled guinea pig kidney killed 19 of 21 pertussis-inoculated mice. The lethal property of this antiserum was removed by absorption with boiled sheep erythrocyte stromata (3 deaths out of 24 mice injected) but was unaffected by absorption with alcohol-extracted sheep erythroctye stromata, boiled rabbit kidney, or beef cell antigen. The failure of beef red cell antigen to remove the toxic effect from the rabbit antiserum to BGPK rules out the possibility that this effect might be due to heterophile antibodies of the infectious mononucleosis or serum sickness type(9). This finding, plus the loss of absorptive capacity of sheep erythrocyte stromata after extraction with alcohol (a procedure which removes the Forssman antigen), strongly suggests that the deaths observed in mice were actually due to presence of Forssman antibodies in the serum employed.

Although the injection of rabbit antiserum to BGPK into mice produces death with symptoms similar to anaphylaxis, we hesitate to describe this reaction as characteristic reversed passive anaphylaxis without additional studies on histamine release, mast cell destruction, etc. Humphrey and Mota(10) recently observed that Forssman antibodies would not cause mast cell degranulation in the guinea pig although this occurrs in anaphylaxis. Also, blood taken just before death of animals injected with Forssman antibodies contained no detectable histamine.

Redfern reported that the lungs of guinea pigs killed by Forssman antisera were hemorrhagic and edematous and fluid often extended into the trachea and exuded from the nose(11). Such signs and symptoms were not seen in mice injected with rabbit antiserum to BGPK but have been observed in mice injected with rabbit antisera to Ehrlich's ascites tumor(12). However, the lethal effect of the latter sera cannot be removed by absorption with sheep cells.

Summary. Mice can be killed by an intravenous injection of a rabbit antiserum to boiled guinea pig kidney. Evidence is presented that these deaths are due to Forssman antibodies.

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