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## Effects of Epsilon Amino Caproic Acid (EACA) on Survival of Fibrinogen $I^{131}$ and on Fibrinolytic and Coagulation Factors in Dogs.* (28794)

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Epsilon amino caproic acid (EACA) acts as an inhibitor of the activation of profibrinolysin, and, in higher concentrations, of fibrinolysin itself(1,2). These experiments were undertaken to determine whether or not large oral doses of EACA given to dogs would affect the coagulation mechanism, the fibrinolytic mechanism or the turnover rate of fibrinogen $I^{131}$.

*Methods and materials.* Methods for the assay of coagulation factors(3,4), fibrinolytic factors(5) and for turnover of fibrinogen $I^{131}$ (6) have been described. Eighteen mongrel dogs were used in the study. Twenty-four fibrinogen $I^{131}$ survival studies were carried out; 12 on dogs receiving EACA and 12 on dogs which had never received EACA or had received none for 4 weeks or longer. On 6 dogs 2 studies were done, one with EACA and one without. EACA was started 4 days before injection of fibrinogen $I^{131}$ and continued for 8 days thereafter. The dogs ingested 200 mg EACA per kg 3 times a day in meat balls. Coagulation studies were carried out before and after 4 and 12 days of EACA feeding in experimental dogs and, at the same periods, in control dogs. Fibrinolytic assays were carried out before EACA was started and just before fibrinogen $I^{131}$ was injected in the experimental dogs and at similar time intervals in the control group. The presence of $I^{131}$ in recipient plasma interfered with the fibrinolytic assays which, therefore, were not done at the 8-day post-fibrinogen $I^{131}$ period.

*Results. Coagulation factors.* No significant changes were observed in whole blood clotting time, serum prothrombin time, plasma prothrombin time, plasma thrombin time, platelet count or plasma levels of factors I, II, V, VII, VIII and IX.

*Fibrinolytic factors.* Fig. 1 illustrates the spontaneous fibrinolytic activity of plasmas and their euglobulin fractions from control and experimental dogs and from a group of 30 normal human subjects. An occasional dog plasma showed fibrinolytic activity (*i.e.,* ability to dissolve added iodinated purified bovine fibrin) which was greater than human. This was suppressed following EACA. Because dog euglobulin activates spontaneously, these fractions were prepared and tested as rapidly as possible. Significant fibrinolytic activity was found in 12 of 36

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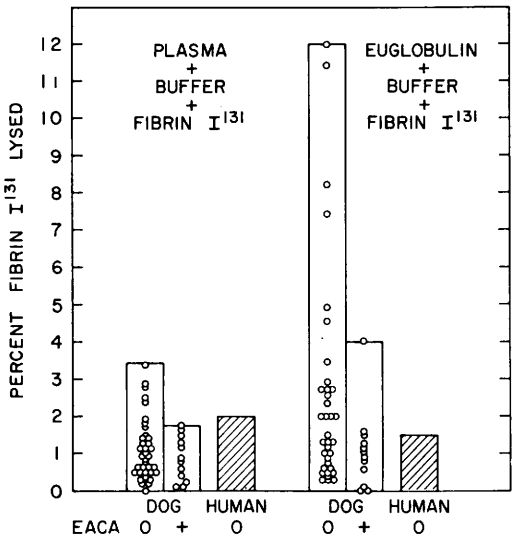


FIG. 1. Fibrinolytic activity of dog plasma and plasma euglobulin fraction before and after EACA treatment.

control samples and one of 12 samples from treated dogs. Neither profibrinolysin nor anti-fibrinolysin (progressive) concentrations were changed following EACA.

*Fibrinogen $I^{131}$ survival.* Table I illustrates the half-life of fibrinogen $I^{131}$ in control and experimental dogs. No increased survival was noted in the treated dogs. Half-life in the control dogs approximated our previous observation of 2.4 days(6).

*Comment and summary.* The average daily dose of EACA was 9.0 g, a very large amount as compared to the usual human dose of 10 to 20 g per day. *In vitro* tests (not illustrated) demonstrated that EACA inhibited dog fibrinolysin and SK-activation of profibrinolysin at concentrations of 0.02-0.06%. In the treated dogs the "spontaneous" fibrinolytic activity of the plasma and its euglobulin fraction were significantly lessened. No changes in coagulation factor levels or in survival of fibrinogen $I^{131}$ were noted.

TABLE I. Fibrinogen $I^{131}$ Half-Life (Days).

| Dog No. | No EACA | Dog No. | EACA | |
|---|---|---|---|---|
| 620 | 1.85 | 620 | 2.25 | (2)* |
| 547 | 2.05 | 547 | 3.3 | (1) |
| 545 | 2.2 | 545 | 2.1 | (1) |
| 696 | 2.45 | 696 | 2.05 | (2) |
| 538 | 2.65 | 538 | 2.0 | (2) |
| 525 | 3.3 | 525 | 1.7 | (2) |
| 542 | 1.75 | 622 | 1.75 | |
| 856 | 2.05 | 698 | 1.80 | |
| 611 | 2.25 | 619 | 1.90 | |
| 490 | 2.35 | 513 | 2.10 | |
| 700 | 2.55 | 576 | 2.05 | |
| 711 | 2.70 | 1770 | 3.05 | |
| Mean | 2.35 | | 2.17 | |

* Order of test in parentheses.

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## Serological Comparison with Rabbit Antisera of Hog Cholera Virus and Bovine Virus Diarrhea Virus.* (28795)

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Cross precipitin reactions by the diffusion technique(1,2) suggested an antigenic relationship between hog cholera(HC) virus and bovine virus diarrhea (BVD) virus. Comparison of these viruses, however, by cross neutralization, using convalescent BVD sera produced in cattle and convalescent HC sera produced in swine, indicated that the two viruses were different, although repeated inoculations of HC virus into swine allowed

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