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CROSS-PROTECTION STUDIES BETWEEN FELINE INFECTIOUS PERITONITIS AND PORCINE TRANSMISSIBLE GASTROENTERITIS VIRUSES

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ABSTRACT

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Cross-protection studies between the feline infectious peritonitis (FIP) and the porcine transmissible gastroenteritis (TGE) viruses were conducted in cats, pigs and pregnant gilts. Cats vaccinated with TGE virus developed neutralizing antibodies against TGE virus and low titer antibody against FIP virus detected by an indirect fluorescent antibody technique but were not protected against a virulent FIP virus challenge. Baby pigs and pregnant gilts vaccinated with FIP virus did not develop detectable antibodies to TGE virus. Nevertheless, it appeared that vaccination of swine with FIP virus conferred some immunity against TGE virus infection. Seventeen-day-old pigs vaccinated with two doses of FIP virus had a 67% survival rate following a virulent TGE virus challenge, and 75% of the 3-day-old pigs suckling either FIP or TGE-virus-vaccinated gilts survived virulent TGE virus infection in contrast to 0% survival of baby pigs suckling unvaccinated gilts.

INTRODUCTION

The porcine transmissible gastroenteritis (TGE) virus is serologically related to the canine corona virus (Binn et al., 1974), feline infectious peritonitis (FIP) virus (Osterhaus et al., 1977; Reynolds et al., 1977; Witte et al., 1977; Pedersen et al., 1978), and human corona virus 229E (Pedersen et al., 1978). Of these viruses, the antigenic relationship between TGE and FIP viruses is especially strong (Pedersen et al., 1978). Because of this strong antigenic relationship, it is logical to assume that infection with one virus might confer protection against infection with the other virus. Preliminary studies suggest that TGE virus will not protect cats against FIP virus infection (Witte et al., 1977), but no information is
available on the protective effect of FIP virus vaccination on baby pigs and pregnant gilts infected with virulent TGE virus.

The purpose of this report is to present information on the cross-protective effect of TGE virus vaccination on FIP infection of cats and FIP virus vaccination on TGE infection of swine.

MATERIALS AND METHODS

Viruses

The virulent Miller No. 3 strain of TGE virus \((2.5 \times 10^6\) plaque forming units (pfu)/ml) and an attenuated small plaque variant TGE virus \((2 \times 10^6\) pfu/ml) were used (Woods, 1978). The virulent UCD-1 strain of FIP virus was prepared as a homogenized suspension containing the equivalent of \(2\) g of liver per ml of suspension from kittens infected experimentally (Pedersen, 1976a). Bioassays have not been developed that permit an actual determination of the FIP virus content.

Experimental animals and vaccination

Two cats were given three doses of virulent TGE virus intraperitoneally (IP) according to the protocol given in Table I, and two cats were held as uninoculated controls.

TABLE I

| Days post-vaccination* | Antibody titer |
|------------------------|----------------|
|                        | VD5            | VF1            | VE2            | VF-2           |
|                        | TGE** | FIP*** | TGE | FIP | TGE | FIP | TGE | FIP |
| 0                      | < 4    | < 2    | <4  | < 2 | <4  | < 2 | <4  | < 2 |
| 10                     | < 4    | < 2    | <4  | < 2 | <4  | < 2 | <4  | < 2 |
| 16                     | 76     | < 2    | <4  | < 2 | <4  | < 2 | <4  | < 2 |
| 20                     | 101    | < 2    | 17  | < 2 | <4  | < 2 | <4  | < 2 |
| 29                     | 104    | < 2    | 18  | < 2 | <4  | < 2 | <4  | < 2 |
| 45                     | 309    | 8      | 67  | 2   | <4  | < 2 | <4  | < 2 |
| 48                     | 396    | < 2    | 98  | < 2 | <4  | < 2 | <4  | < 2 |
| 51                     | 360    | 32     | 78  | 16  | <4  | < 2 | <4  | < 2 |
| 54                     | 360    | 128    | 45  | 256 | <4  | < 2 | <4  | < 2 |
| 57                     | 443    | 128    | 52  | 256 | <4  | 8   | <4  | 32  |
| 63                     | 111    | 256    | 43  | 512 | <4  | 256 | <4  | 512 |

*Cats VD5 and VF1 were inoculated intraperitoneally with \(2.5 \times 10^6\) pfu of virulent TGE virus on day 0 and 13 and with \(6.5 \times 10^7\) pfu of virulent TGE virus on day 34. Cats VE2 and VF-2 were uninoculated controls. Cats were challenged on day 45 with feline infectious peritonitis (FIP) virus. All cats were euthanatized 18 days postchallenge because of near terminal FIP.

**Reciprocal of dilution resulting in a plaque reduction of 50%.

***Reciprocal of endpoint titration determined by indirect fluorescence antibody.
TABLE II

Immunity challenge of 27 6-h-old pigs vaccinated with feline infectious peritonitis (FIP) or transmissible gastroenteritis (TGE) virus

| Vaccine                  | Age when vaccinated (days) | Age when challenged (days) | TGE VN titer at challenge* | Survival rate** |
|--------------------------|----------------------------|----------------------------|----------------------------|-----------------|
| 2 × 10⁶ pfu TGE         | 0                          | 17                         | 125                        | 0/3 (0%)        |
| 0.3 g-equivalent FIP (in one dose) | 0                          | 17                         | < 4                        | 2/6 (33%)       |
| 0.3 g-equivalent FIP*** (in two doses) | 0 and 7                   | 17                         | < 4                        | 6/9 (67%)       |
| Controls                | --                         | 17                         | < 4                        | 2/9 (22%)       |

*Reciprocal of dilution resulting in a plaque reduction of 50%. Geometric mean titer of all swine tested.
**Number of survivors over number of pigs challenged.
***Vaccine administered 1/2 orally and 1/2 intraperitoneally in two equal doses.

A total of 27 newborn pigs, less than 6 h old, were tested (Table II). Of those, three were given orally (O) 2 × 10⁶ pfu of attenuated TGE virus. 15 were given 0.15 g-equivalents of FIP virus IP and 0.15 g-equivalents intranasally (IN); nine of those 15 pigs were given a second FIP dose 7 days later by the same protocol. The other nine pigs were held as uninoculated controls.

Two gilts were given 2 g-equivalents of FIP virus 8 and 2 weeks before parturition; one half of the dose was given O/IN and one half was injected into the mammary glands at four sites (Table III). Two gilts were given

TABLE III

Survival rate following transmissible gastroenteritis (TGE) virus challenge of 3-day-old suckling pigs born to feline-infectious-peritonitis (FIP) or TGE-virus-vaccinated and non-vaccinated gilts

| Gilt number | Vaccine*         | TGE VN titer at challenge** | Survival rate*** |
|-------------|------------------|-----------------------------|------------------|
| 811         | 2.0 g-equivalents FIP | < 4                         | 7/9 (75%)        |
| 5–3         | 2.0 g-equivalents FIP | < 4                         | 5/7 (75%)        |
| 817         | 2 × 10⁶ pfu TGE    | 2696                        | 5/6 (71%)        |
| 843         | 2 × 10⁶ pfu TGE    | 1240                        | 7/11 (71%)       |
| 815         | Control           | < 4                         | 0/8 (0%)         |
| 839         | Control           | < 4                         | 0/9 (0%)         |

*Administered 1/2 oral/intranasal and 1/2 intramammary approximately 8 weeks and 2 weeks before parturition.
**Reciprocal of dilution resulting in a plaque reduction of approximately 50%.
***Number of survivors over number of pigs challenged.
2 × 10^6 pfu of attenuated TGE virus by the same vaccination protocol. Two gilts were held as uninoculated controls.

**Challenge**

Pigs were 0 challenged with about 2000 pig infectious doses of virulent TGE virus. Cats were challenged IP with 0.5 g-equivalents of FIP virus (Pedersen, 1976a).

**Antibody titer**

Blood sera from cats, pigs and gilts were tested for their TGE antibody content by a plaque reduction technique (Woods, 1978). The FIP antibody content was determined by an indirect fluorescent antibody technique (IFA) (Pedersen, 1976b).

**RESULTS**

Cats VFI and VD5, vaccinated with virulent TGE virus, developed virus neutralizing (VN) antibodies (1:67–1:309) against TGE on day 45, after three injections of vaccine (Table I). These cats also developed FIP reacting antibodies (1:2–1:8) before exposure to the FIP virus. Following inoculation with FIP virus, both TGE-virus-vaccinated and unvaccinated cats developed effusive FIP and were killed 18 days post-challenge.

Pigs vaccinated with attenuated TGE virus developed VN antibodies against TGE, but unvaccinated pigs and pigs infected with FIP virus did not demonstrate TGE antibodies (Table II). The survival rate of pigs vaccinated with a single dose of FIP or TGE virus was 33 and 0%, respectively; that of pigs vaccinated with two doses of FIP virus was 67% and that of unvaccinated controls was 22%.

No clinical signs were observed in pregnant gilts vaccinated with either FIP of TGE virus. Two gilts vaccinated with attenuated TGE virus had VN antibodies against TGE virus, but the two gilts vaccinated with FIP virus and the two controls gilts did not have detectable VN antibodies against TGE virus (Table III). The survival rate of baby pigs suckling FIP-vaccinated gilts was 75%; that of pigs suckling TGE-vaccinated gilts was 71% and that of pigs suckling unvaccinated control gilts was 0%. A mild diarrhea was observed in about 60% of the protected pigs, but vomiting and dehydration were not observed. FIP and TGE-virus-vaccinated gilts did not develop clinical signs of TGE after their suckling pigs were O challenged. However, one of the unvaccinated control gilts did develop typical signs of TGE following infection of her suckling offspring.

**DISCUSSION**

The serological relatedness of these two coronaviruses has been previously shown, but this is the first reported attempt to use these viruses as
naturally occurring vaccine strains. Cats vaccinated with TGE virus developed high titers of VN antibody against TGE virus. TGE virus antibody cross-reacting with FIP virus was detectable at low titer only after three injections of TGE virus. The pronounced differences in the titers and speed of appearance of TGE VN antibody and FIP-virus-reacting antibody indicates that these two antibody activities differ from each other. TGE antibody that reacts with FIP virus in the IFA assay is probably not virus neutralizing, as cat sera with high IFA titers to FIP virus do not neutralize TGE virus (Osterhaus et al., 1977).

The fact that TGE-vaccinated cats developed antibodies that cross-reacted with FIP virus indicates that at least one antigen is shared by these two viruses. Not only did TGE-virus-vaccinated cats develop low levels of FIP virus reacting antibody, but they also underwent an anamnestic response when challenged with FIP virus. Cats vaccinated with TGE virus had high levels of FIP virus reacting antibodies 6 and 9 days post-challenge with FIP virus, while the unvaccinated control cats did not develop detectable levels of FIP antibodies until 12 days post-challenge.

Attempts to elicit active immunity in 6-h-old pigs with FIP or TGE virus produced inconclusive results. Protection, as measured by mortality, is difficult to evaluate in pigs over 14 days of age because of the rapid onset of resistance to TGE after this time (Moon et al., 1975). In this study, a single dose of FIP or TGE virus did not protect the pigs; whereas, two doses of FIP virus appeared to provide some protection against virulent TGE virus challenge. Because of the small number of pigs used in this study, these results need to be confirmed.

The survival rate of pigs suckling either FIP or TGE-vaccinated gilts was about 70%. Although this is lower than the survival rate of baby pigs born to sows that had undergone a natural infection, it is still high enough to merit further investigation. These results suggest that the FIP virus may confer some degree of colostral immunity against TGE virus infection of suckling pigs. It is hoped that these findings can be confirmed in larger numbers of pigs, and that methods can be developed that would allow quantitation of the FIP virus so more meaningful comparisons can be made.

The phenomena described in this report appears similar to that reported in swine with the Pestiviruses (bovine viral diarrhea (BVD) and hog cholera (HC)). The BVD–HC virus complex appears to be related to the strain of BVD immunizing virus and the Ames challenge strain of HC virus (Snowdon and French, 1968; Stewart et al., 1971). In unpublished studies using agar gel diffusion, at least one antigen shared by TGE and FIP was soluble. However, because this is a preliminary report and only one strain of FIP virus was used, much additional information needs to be generated to clarify the TGE–FIP complex.
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