

Infection of Pigs with Avian Hepatitis E Virus (HEV)

A.S. Leaflet R1982

C. Kasorndorkbua, graduate student,
P. J. Thomas, graduate student,
P. G. Halbur, professor,
College of Veterinary Medicine, Iowa State University;
D. K. Guenette, technician; F. F. Huang, graduate
student;
X.-J. Meng, associate professor,
College of Veterinary Medicine,
Virginia Polytechnic Institute and State University,
Blacksburg, VA;

Summary and Implications

It is now known that HEV can cross-species barriers. In the present study, we used a pig model to determine if HEV from chickens (avian HEV) or rats (rat HEV) was infectious to pigs. Thirty six, SPF pigs were randomly separated into 4 groups of 9 pigs each. Group 1 served as the sham-inoculated group. Group 2 was inoculated with rat HEV. Group 3 was inoculated with avian HEV. In the rat and avian HEV groups, 6 pigs were inoculated with the corresponding virus and 3 pigs remained uninoculated and served as contact controls. Group 4 was inoculated with the prototype swine HEV. Necropsy of 3 pigs from each group was performed on 7, 21, and 35 days postinoculation (dpi). In the rat and avian HEV groups, 2 inoculated and 1 contact control pigs were necropsied at each time point. Liver and bile from sham-inoculated pigs were negative for HEV throughout the study. Pigs in the sham and rat HEV group remained noninfected. Pigs inoculated with avian HEV and those inoculated with the swine HEV became viremic and shed HEV in feces. Both the avian and swine HEV infected pigs had mild-to-moderate lymphoplasmacytic hepatitis. The findings indicate that avian HEV is transmissible to pigs. This may open new areas of study in the epidemiology of HEV. Pigs may be an excellent model for comparative molecular and pathogenetic studies of different HEV strains.

Introduction

Hepatitis E virus (HEV) is the primary causative agent of acute, non-A, non-B hepatitis in humans. HEV is a recently discovered virus and the relatively large and diverse species prone to infection with HEV suggest that the virus may readily adapt to new hosts. Avian and swine HEV have certain similarities (24). Avian HEV recovered from chickens also has the ability to cross species barriers and infect turkeys; however, avian HEV was not transmissible to rhesus monkeys.

Anti-HEV antibodies have been found in rodents in the US and Japan. Laboratory rats have been shown to be susceptible to experimental infection by human HEV. Evidence of rat-to-human transmission of HEV was suggested in Nepal where Hepatitis E is endemic. However, HEV in US rats remains to be characterized in animal models.

Chickens, rats, and pigs are commonly found together on farms across the world. The aim of the present study was to determine if HEV recovered from chickens or rats is infectious to pigs.

Materials and Methods

Thirty-six, 6-week-old, SPF pigs were used in this study. All pigs were free of swine HEV in feces and seronegative to anti-HEV antibodies prior to inoculation. The experimental design consisted of 4 groups, including negative-control, rat HEV-, avian HEV-, and swine HEV-inoculated groups. Each group contained nine randomly selected pigs. The nine pigs in each of the rat and avian HEV group were randomly assigned to 2 sub-groups. Six pigs were inoculated with rat or avian HEV and the three remaining pigs served as uninoculated contact-controls. The inoculation route was intravenous for all groups. All pigs were monitored for clinical signs throughout the study. Rectal temperature was recorded every other day through 14 days postinoculation (dpi). Liver and bile samples were also collected from all pigs at necropsy. HEV infection was confirmed by the presence of HEV in feces, serum, liver, or bile by RT-PCR and anti-HEV seroconversion by ELISA. Necropsy was performed on 3 randomly selected pigs at one of 3 time points; 7, 21, and 35 dpi. In the rat and avian HEV groups, the three pigs for each necropsy comprised two inoculated and one contact-control pig.

Results and Discussion

There was no evidence of clinical disease in pigs in any of the inoculated groups. No remarkable gross lesions were observed in any of the sham-inoculated or HEV-inoculated groups. Microscopic lesions were confined to the liver. Mild-to-moderate, multifocal, lymphoplasmacytic hepatitis was present in 5 of 9 sham-inoculated, 7 of 9 rat HEV-inoculated, 7 of 9 avian HEV-inoculated, and 9 of 9 swine HEV-inoculated pigs. Swine HEV inoculated pigs had significantly more severe hepatitis lesion scores.

Results of the nested RT-PCR assays for HEV RNA in feces, serum, liver, and bile samples tested are summarized in Table 1. None of the liver and bile samples collected from the sham inoculated pigs contained HEV. HEV was not detected in fecal samples obtained from pigs inoculated with rat HEV. All nine pigs

inoculated with avian HEV shed HEV in feces and were viremic. HEV was detected in liver and bile in the avian HEV group which was viremic and shed HEV in feces and developed anti-HEV antibodies by 35 dpi. Pigs in the swine HEV group also became infected and shed HEV in feces from 7 to 28 dpi. Two pigs inoculated with swine HEV developed anti-HEV antibodies on 21 and 35 dpi. All pigs in the sham- or rat HEV-inoculated group remained seronegative throughout the study.

In summary, avian HEV was readily transmissible to pigs by intravenous inoculation. Direct contact appears to be the route that avian HEV was transmitted to uninoculated contact-control pigs. Rat HEV did not infect pigs. Infection of pigs with avian or swine HEV induced subclinical hepatitis.

Pigs and chickens are often raised in close proximity. Both swine and avian HEV are ubiquitous in their respective host populations. It is likely that natural exposure of pigs to avian HEV and likewise chickens to swine HEV occurs frequently in the field. Such conditions would provide opportunities for avian HEV to adapt for replication in pigs and vice versa. It currently remains unknown if swine HEV is transmissible to chickens.

Acknowledgments

The authors thank Drs. Suzanne U. Emerson and Robert H. Purcell of the National Institutes of Health for providing the rat and swine HEV inocula.

Table 1. HEV RNA in feces, serum, liver, and bile of sham- and HEV-inoculated pigs

Inocula	Sample	No. of positive inoculated pigs (no. of positive contact control pig) per no. tested on the following dpi;					
		0	7 ^a	14	21 ^a	28	35 ^a
Sham	Feces	0/9	0/9	NT ^b	NT	NT	0/3
	Serum	NT	NT	NT	NT	NT	NT
	Liver	NT	0/3	NT	0/3	NT	0/3
	Bile	NT	0/3	NT	0/3	NT	0/3
Rat HEV	Feces	0/9	0/9	0/6	NT	NT	0/3
	Serum	NT	NT	NT	NT	NT	NT
	Liver	NT	NT	NT	NT	NT	NT
	Bile	NT	NT	NT	NT	NT	NT
Avian HEV	Feces	0/9	6(3)/9	4(2)/6	4(2)/6	2(1)/3	0/3
	Serum	NT	5(3)/9	1(1)/6	1(1)/6	0/3	0/3
	Liver	NT	1(0)/3	NT	1(0)/3	NT	1(0)/3
	Bile	NT	2(1)/3	NT	1(0)/3	NT	1(1)/3
Swine HEV	Feces	0/9	4/9	6/6	5/6	1/3	0/3
	Serum	NT	0/9	0/6	1/6	0/3	0/3
	Liver	NT	0/3	NT	1/3	NT	0/3
	Bile	NT	2/3	NT	1/3	NT	0/3

^a dpi on which necropsy was performed.

^b Not tested, samples not collected or tested on this dpi.