ESTIMATION OF TRANSMISSION PARAMETERS OF HEV WITHIN AND BETWEEN PEN TRANSMISSION IN EXPERIMENTAL CONDITIONS

Aylaj, B., M. Andraud, Dumarest, M., Eono, F., Bailly, Y., Cariolet, R., Pavio, N. & Rose, N.

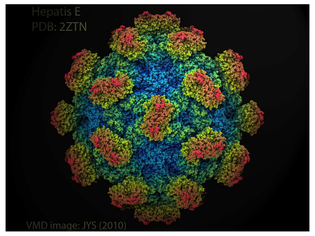
Anses - Laboratoire de Ploufragan - Plouzané, BP 53, 22440 Ploufragan - France

Universit Hassan II, Facult des sciences An Chock, B.P 5366 Maarif Casablanca 20100 Maroc

Correspondence e-mail: bouchra.aylaj@gmail.com

Background & Objective

- Hepatitis E virus (HEV) is a non-enveloped, single-stranded, positive sense RNA virus and is the causative agent of acute hepatitis E in humans.



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- In developed countries, a possible role for zoonotic transmission in the epidemiology of human HEV episodes has been suggested after viral RNA was detected in different animal species, and these viruses were found to be closely related to HEV strains found in humans (Pavio et al. 2010).
- HEV strains of genotypes 3 and 4 have since been detected in pigs in many countries, and these strains were found to be genetically related to HEV strains originating from humans in the same geographic region (Pavio et al. 2010).
- A nation-wide prevalence study showed that HEV was highly prevalent in French pig herds (Rose et al., 2011) and the great variability in within-herd seroprevalence suggested different transmission patterns according to farm structure.

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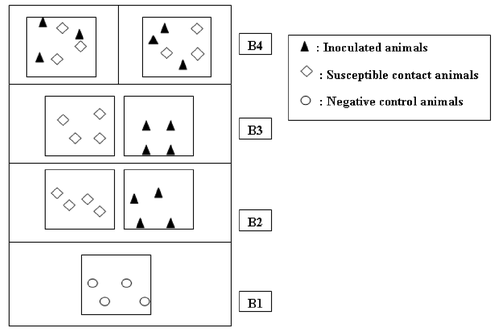
- In this present work :
  - HEV within- and between-pen transmission was quantified by estimating the daily transmission rate β, the infectious period and the basic reproduction ratio R_0 using a stochastic SEIR model fitted on experimental data.
  - The experimental study and the related mathematical model showed the important role of the environment in the transmission of hepatitis E virus. This study submitted for publication (see Andraud et al (2013)).

Material and methods

- Specific Pathogen Free (SPF) pigs, free from HEV have been inoculated through the oral route to mimic natural infection.
- Within-pen transmission was quantified by using four transmission trials of 3 infected and 3 SPF pigs having direct contact.
- Between-pen transmission was assessed using 4 infected and 4 susceptible pigs separated in 2 different pens 10 cm apart.



Results

- Transmission parameters within, β_w, and between, β_b, pens, were estimated using a maximum likelihood method based on the observed incidence of new infections in the contact groups ([1, 6]):

$$\log L(\beta_w, \beta_b) = \sum_i [C_i \log\left(\exp^{d_i\left(\beta_w \pi_{i,w} + \beta_b \pi_{i,b}\right)} - 1\right) - S_i\left(d_i\left(\beta_w \pi_{i,w} + \beta_b \pi_{i,b}\right)\right)]$$

  In this equation, π_w and π_b are the proportions of infectious animals within the same pen and in contact pens, with S_i and C_i the number of susceptible pigs and cases at each time interval i of duration d_i, respectively.
- Because R_0 represents the number of new infections caused by an infected pig during the entire infectious period, the duration of the infectious period needs to be estimated, μ.
- The infectious period μ was defined as the average number of HEV shedding days and was estimated using survival analysis from data on contact and inoculated pigs $\left(10.2 \text{ days } (6.54\text{-}15.73)\right)$.
- Between pen R_0 $\left(0.2(0.02\text{-}1.3)\right)$ was significantly lower than within pen R_0 $\left(3.4\ (1.6\text{-}7.3)\right)$

	Infectious period (μ)	Transmission rate (β)		R_0	
	(days)	within pens	between pens	within pens	between pens
Median	10.2	0.34	0.02	3.4	0.2
lower (95%) CI	6.5	0.18	0.002	1.6	0.02
upper (95%) CI	15.7	0.63	0.12	7.3	1.3

↪ These results showed that HEV is more likely to spread when contacts between pigs occur randomly.

↪ Therefore, segregation of pigs should considerably decrease transmission in pig herds.

Conclusions and Perspectives

- An experimental trial was carried out to study the main characteristics of HEV transmission between orally inoculated pigs and nave animals.
- In Andraud et al (2013) (submitted for publication), a mathematical models was used to investigate three transmission routes, namely direct and indirect contacts between pigs and an environmental component to represent oro-fecal transmission.
  ↪ The environment played an essential role in the transmission process.
- These results showed that direct transmission alone, can be considered as a factor of persistence of infection within a population, (i.e. $R_0 > 1$).
- Indirect transmission occurred to a lesser extent and could further a within- group process.
- The combination of these three transmission routes could explain the maintenance and high prevalence of HEV observed in pig populations.
- The reproduction ratio should be estimated for HEV transmission in pigs-farms.
- These estimates will be further used within a population dynamic model representing a farrow-to-finish herd to evaluate management strategies that could be used to decrease transmission and prevent from late infection of fattening pigs leading to viremic animals at slaughter age.

Acknowledgements

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References

[1] Andraud, M., Grasland, B., Durand, B., Cariolet, R., Jestin, A., Madec, F., Rose, N., Quantification of porcine circovirus type 2 (PCV- 2) within- and between- pen transmission in pigs, Vet Res 2008, 39:43.

[2] Andraud, M., Dumarest, M., Cariolet, R., Aylaj, B., Barnaud, E., Eono, F., Pavio, N., Rose, N., Direct contact and environmental contaminations are responsible for HEV transmission in pigs, submitted to Veterinary Research.

[3] Bouwknegt M., Frankena K., Rutjes, S.A., Wellenberg, G.J., de Roda Husman, A.M., van der Poel, W.H., de Jong, M.C., *Estimation of hepatitis E virus transmision among pigs due to contact-exposure*, Vet. Res (2008), 39:39-40.

[4] Pavio, N., Meng, X.J., Renou, C., *Zoonotic hepatitis E: animal reservoirs and emerging risks*, Vet. Res. (2010)41(6):46.

[5] Rose, N., Lunazzi, A., Dorenlor, V., Merbah, T., Eono, F., Eloit, M., Madec, F. & Pavio, N. (2011) *High prevalence of Hepatitis E virus in French domestic pigs.* Comp. Immunol. Microbiol. Infect. Dis. 34, 419-427.

[6] Klinkenberg, D., De Bree, J., Laevens, H. & De Jong, M. C. M. (2002) *Within- and between- pen transmission of classical swine fever virus: a new method to estimate the basic reproduction ratio from transmission experiments.* Epidemiol. Infect. 128, 293-299.