

Latest on PRV Control Program

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**The Reference
in Prevention
for Animal Health**

Aujeszky disease

Clinical signs

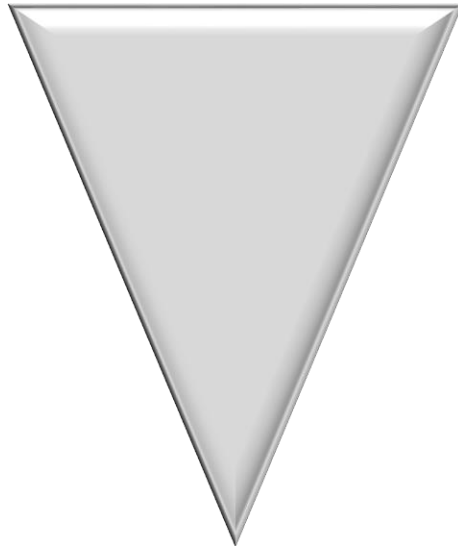
depends on:

- Virus strain
- Infective dose
- Age of the affected pig

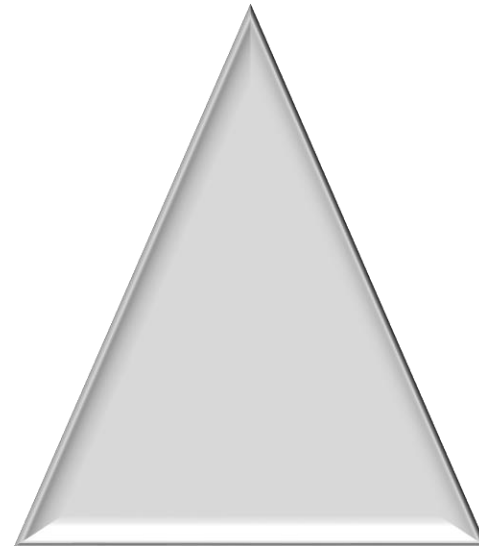
AGE

1
3
11
15
19
23
25

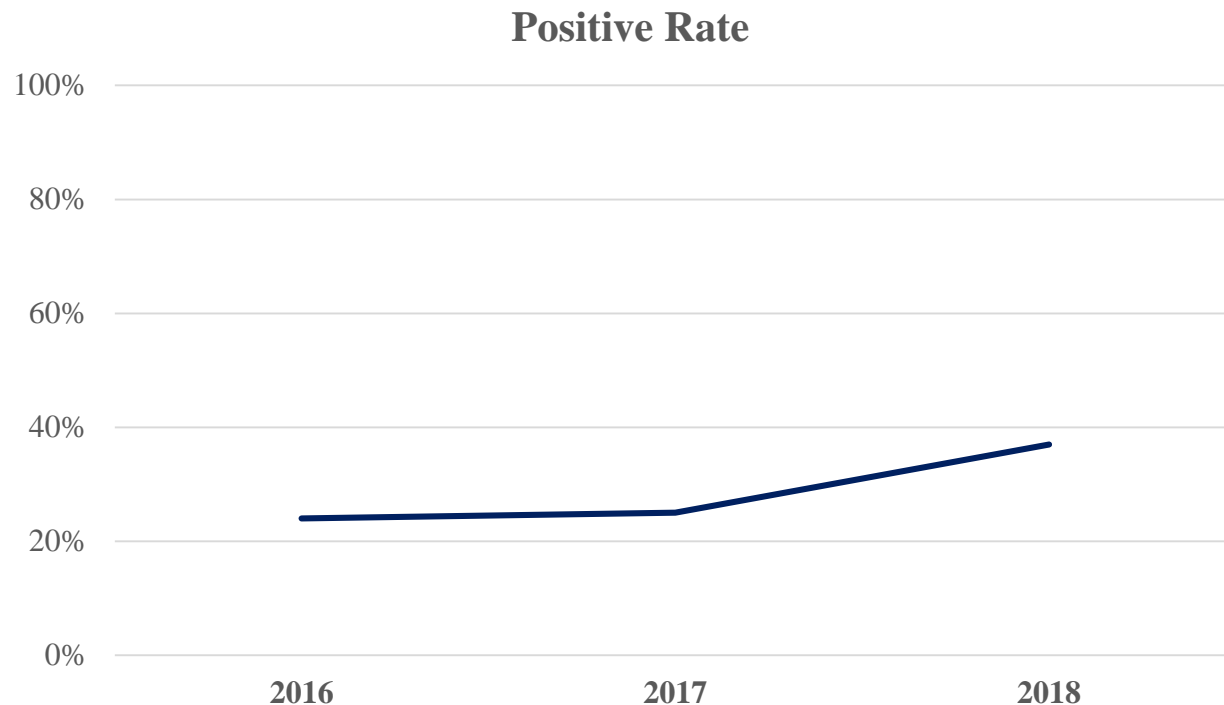
NERVOUS



RESPIRATORY



ADV prevalence in Philippines(by Hipra Lab)



	2016	2017	2018
Batangas	28%	43%	57%
Bulacan	43%	55%	58%
Pampanga	18%	32%	43%

Epidemiological HP-ADV in China

From 2011, outbreaks of AD have become headaches again in porcine industry in China



2015
All parts of China

Rui Wu et al 2013

Field condition

High mortality of piglets before weaning (even 12 week old age)

Pig Progress Feb 1, 2016



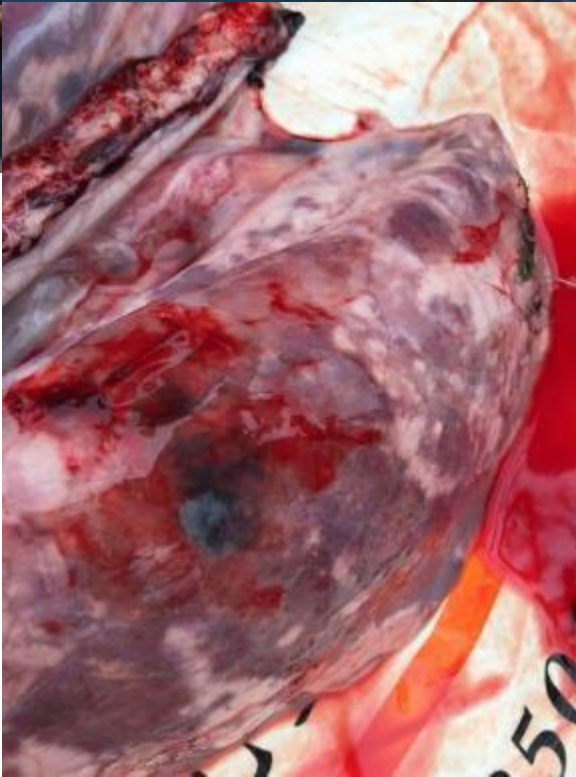
Conjunctivitis, Dyspnea, Salivation



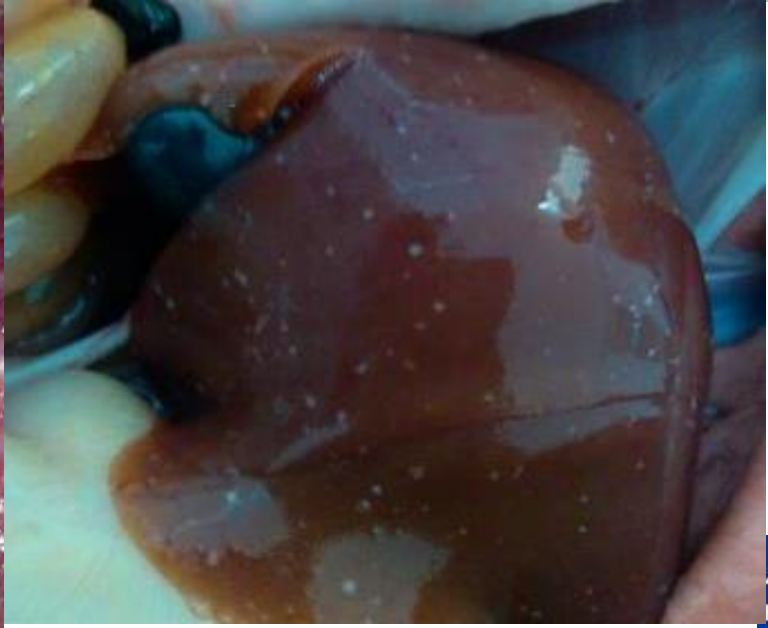
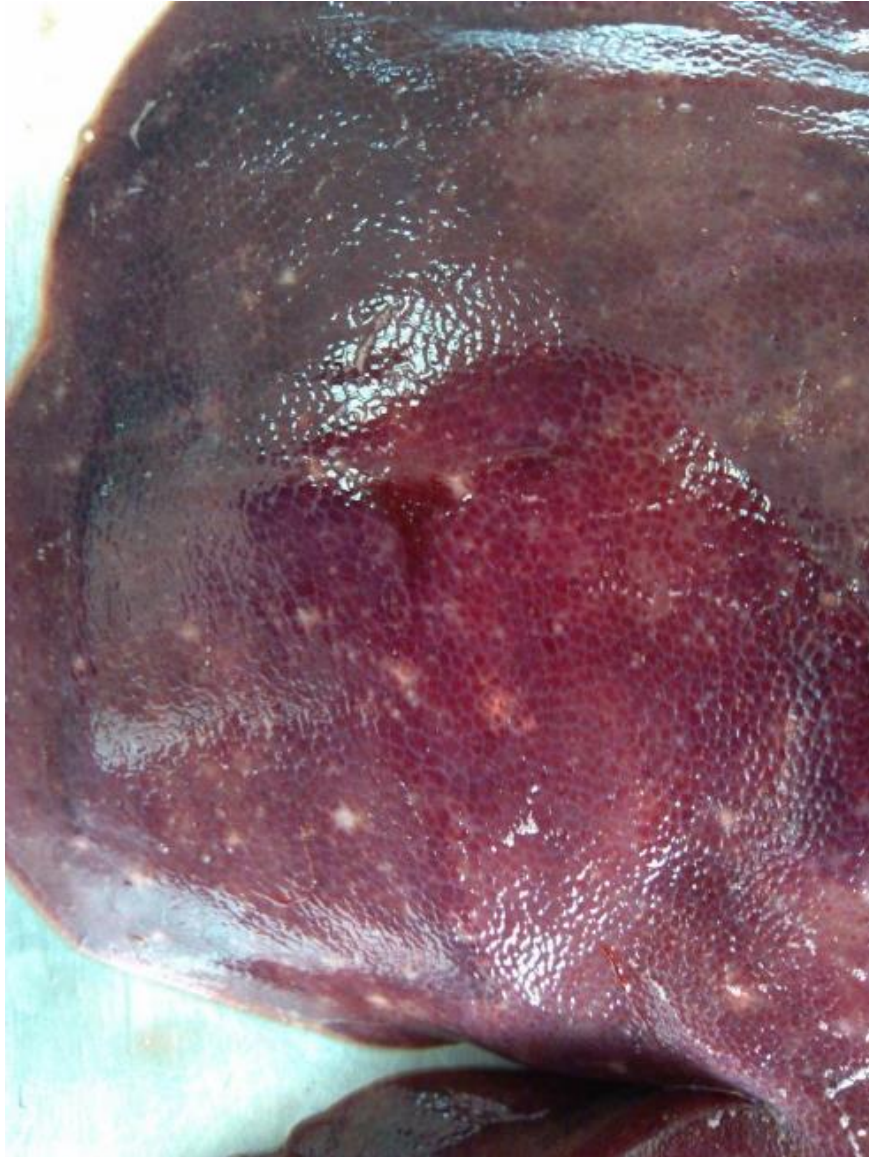
Nervous symptom– ataxia, tremors



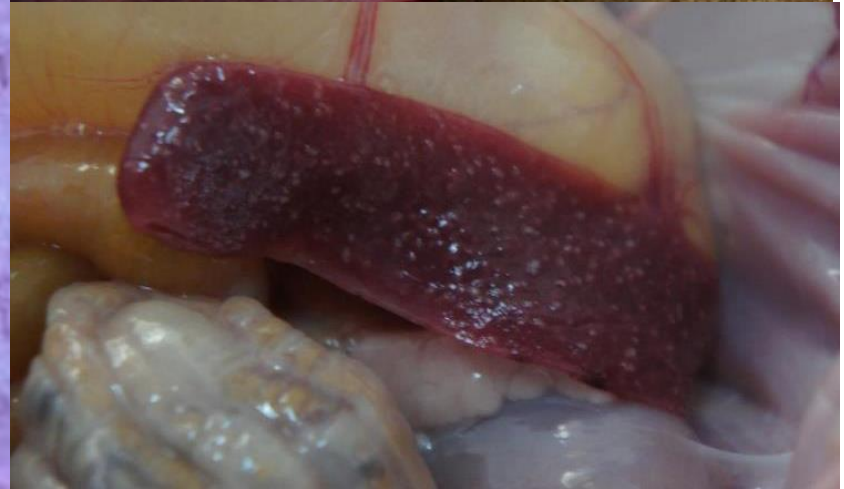
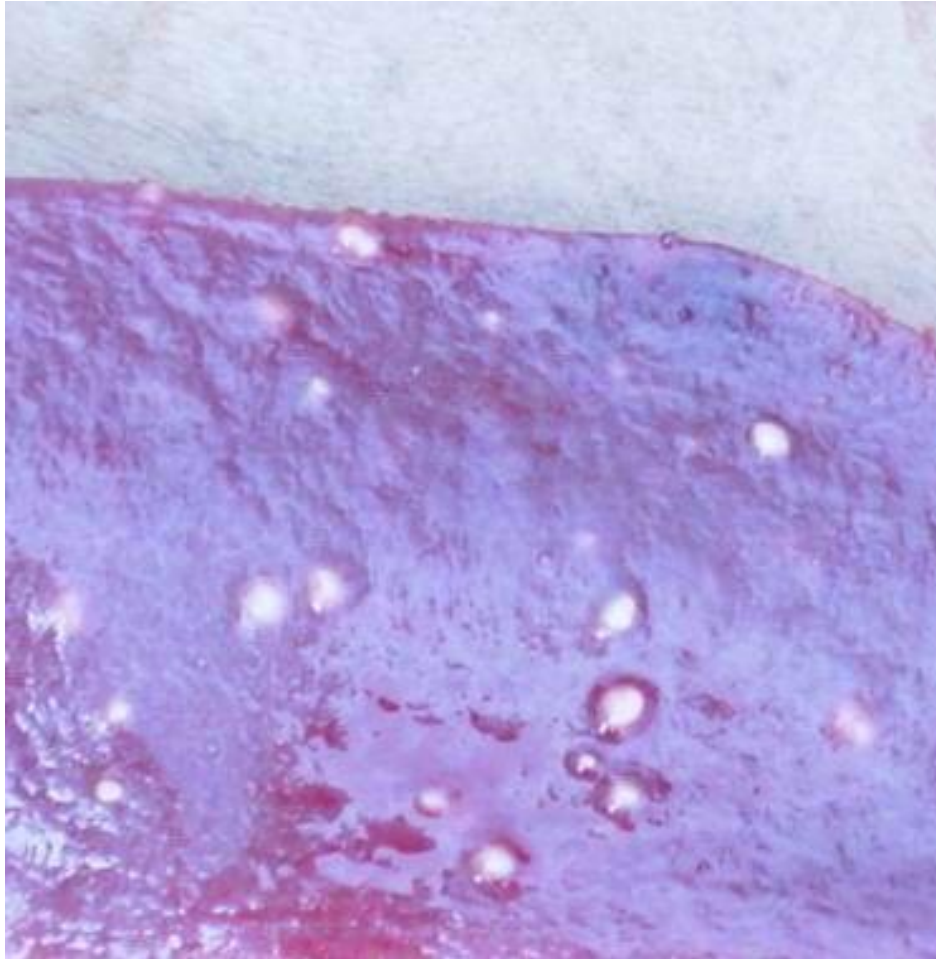
Fattening pig- coinfection with APP



Multifocal necrosis in organ



Multifocal necrosis in organ



Multifocal necrosis in organ



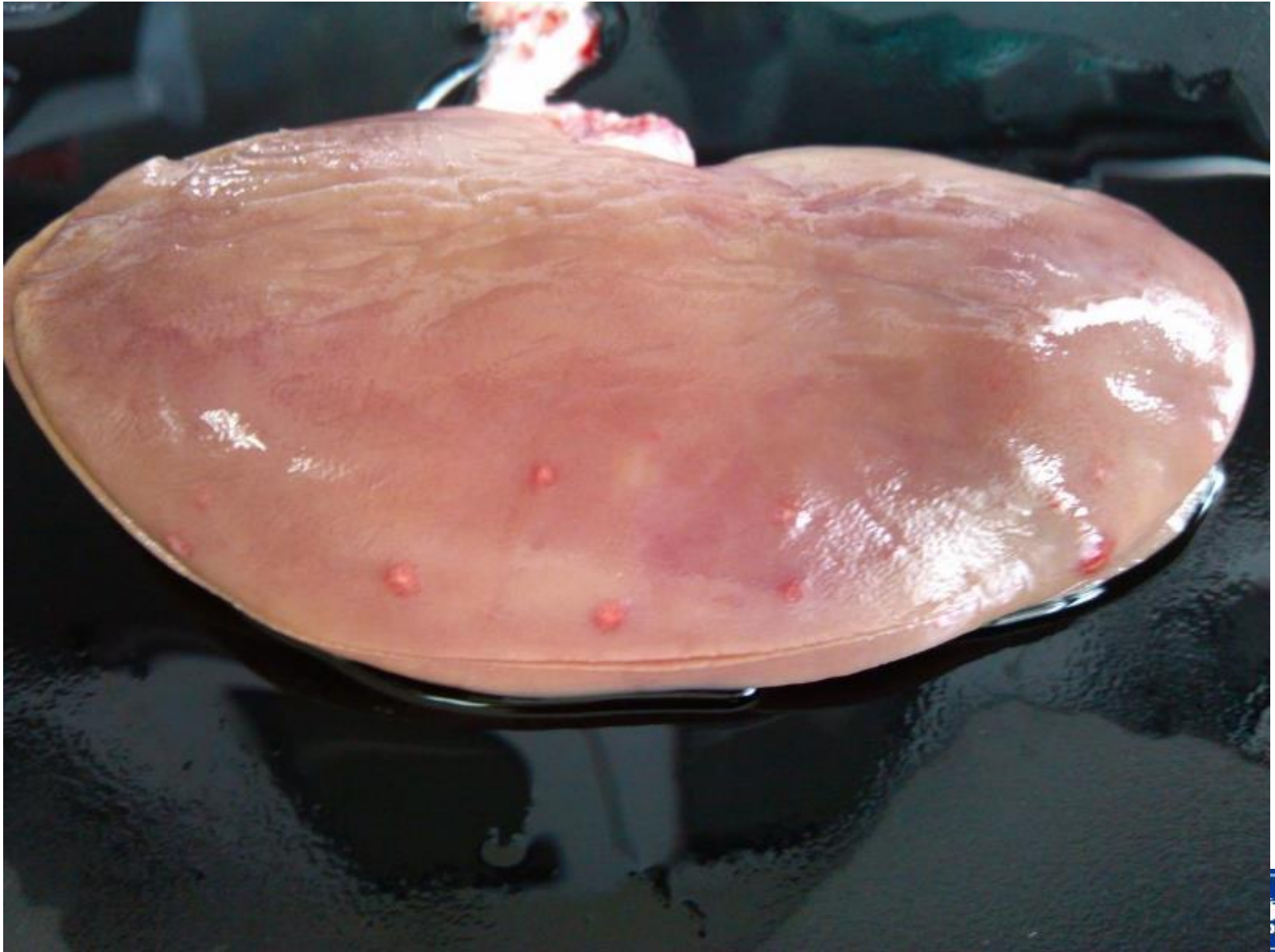
Multifocal necrosis in organ



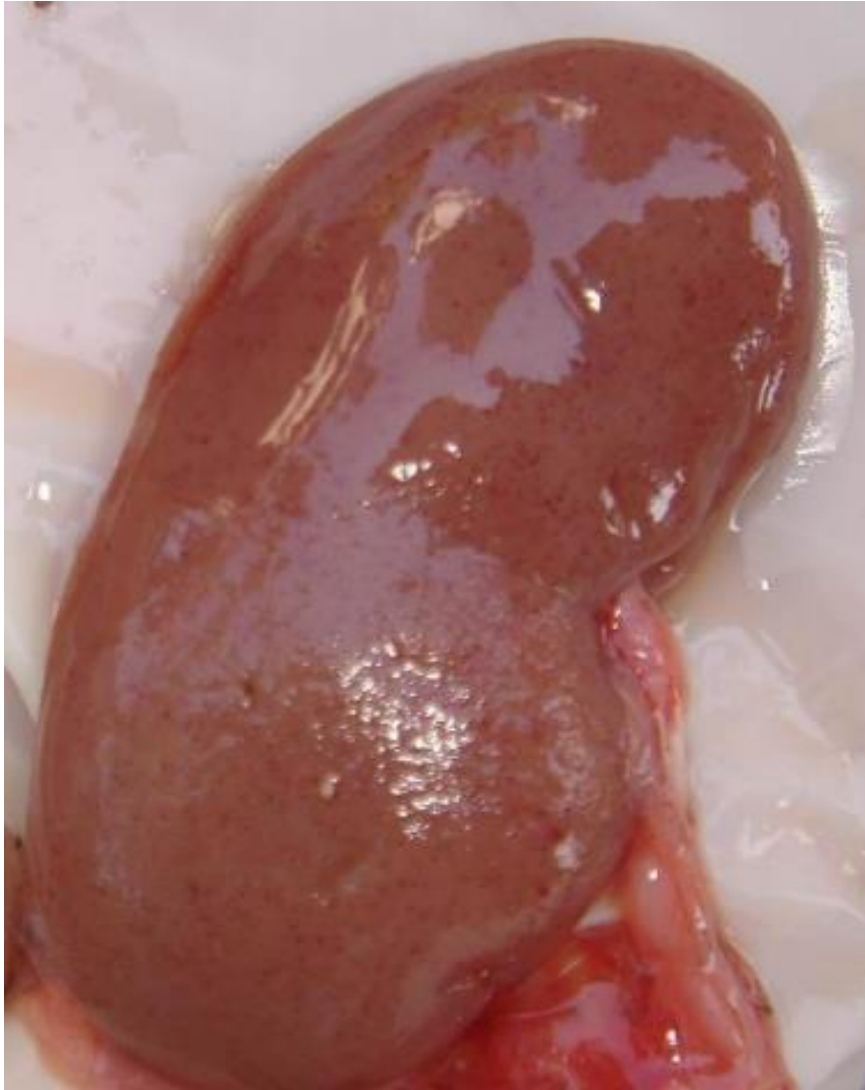
Multifocal necrosis in organ



Multifocal necrosis in organ



Hemorrhage in kidney



Sows-Reproductive problems



Reasons for outbreak?

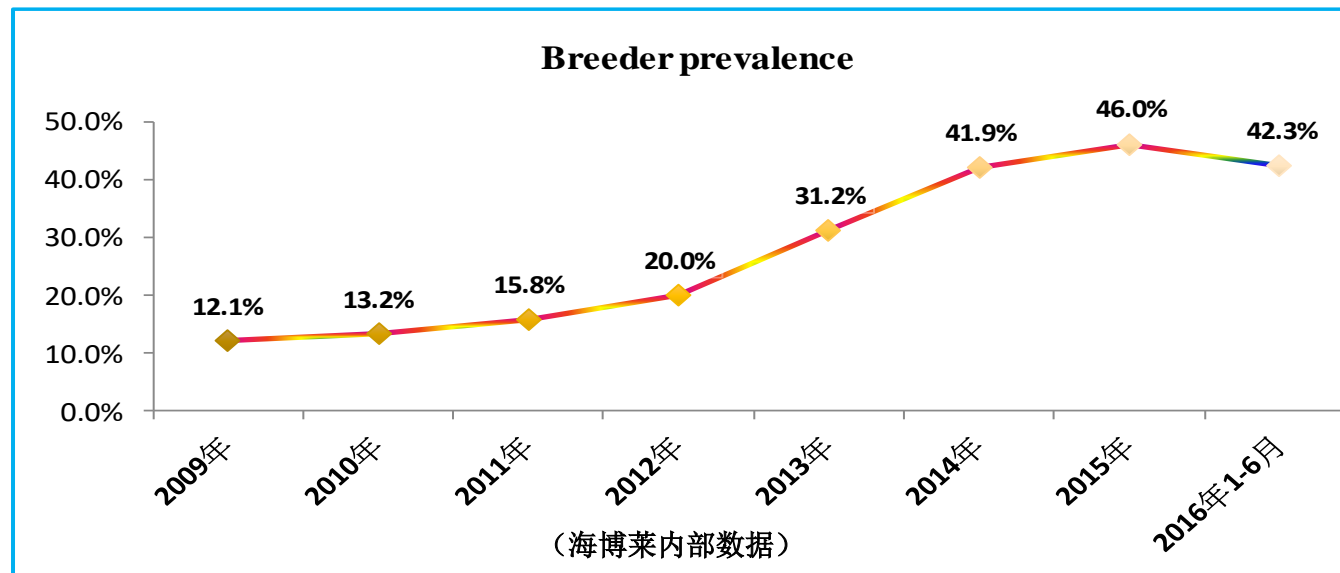
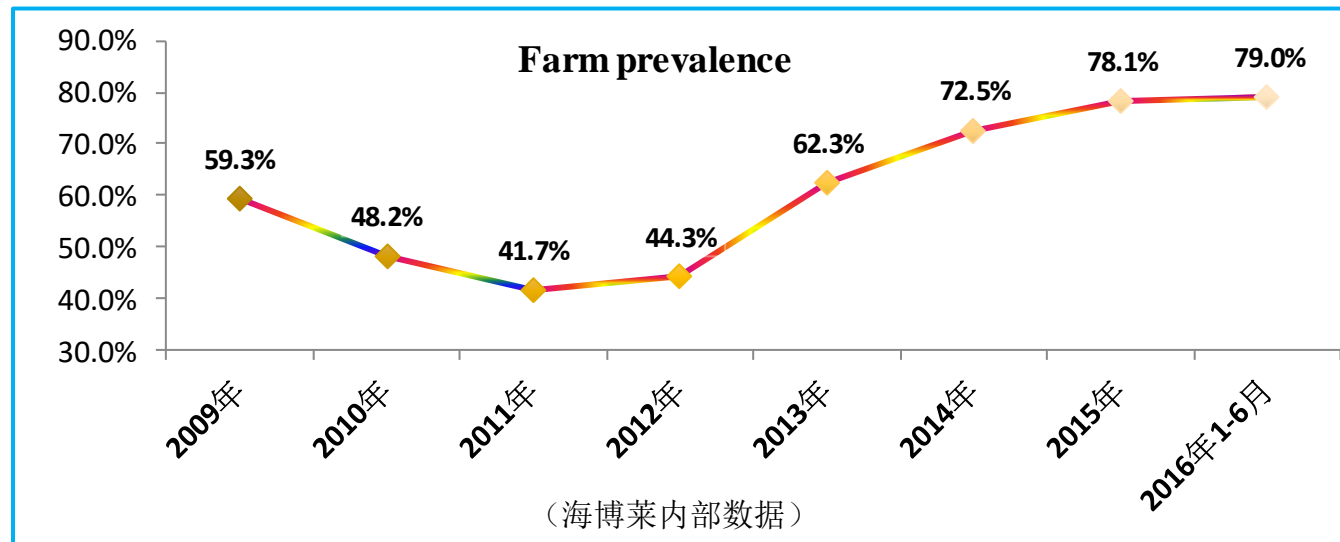
1. Reducing vaccination program

- ✓ No clinical syndrome
- ✓ Low prevalence

2. Facing high virulent wild strain

- ✓ 10^3 TICD₅₀ virulent China strain can infect pigs and have clinical sign (*Yimin Wang et al, 2015*)

Question- Strain mutant?

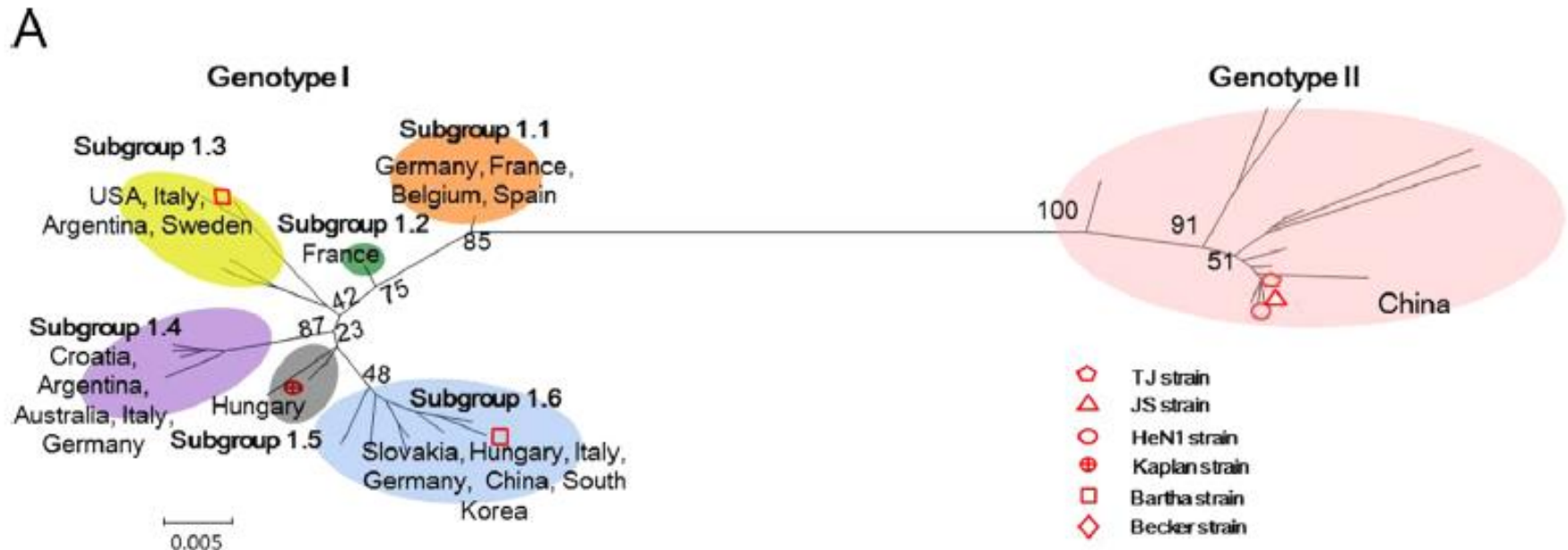


(HIPRA Lab, Beijing, 2016)



Question- Strain mutant? (genotype)

Based on gC gene partial sequences(phylogenetic tree)



(Ye *et al* , Virology, 2015)

Question- Strain mutant? (serotype)



AMERICAN
SOCIETY FOR
MICROBIOLOGY

genomeA[®]nnouncements



Complete Genome Sequence of Novel Pseudorabies Virus Strain HNB Isolated in China

Teng Yu,^a Fangzhou Chen,^a Xugang Ku,^b Yinxing Zhu,^a Hailong Ma,^a Subei Li,^b Qigai He^a

- HP-ADV all gene sequences compare to Bartha strain
90.6%-92.6%
- 5 known HP-ADV gene homologous around 96%



Question- Bartha strain cannot against HP-ADV?

Vaccine xxx (2014) xxx–xxx



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



A novel gE-deleted pseudorabies virus (PRV) provides rapid and complete protection from lethal challenge with the PRV variant emerging in Bartha-K61-vaccinated swine population in China

Chun-Hua Wang¹, Jin Yuan¹, Hua-Yang Qin¹, Yuzi Luo, Xin Cong, Yongfeng Li, Jianing Chen, Su Li, Yuan Sun*, Hua-Ji Qiu*

State Key Laboratory of Veterinary Biotechnology, Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Harbin 150001, China

Pigsin Group A (n = 3) were inoculated intramuscularly (i.m.) with one-dose (105TCID₅₀) of PRV Bartha-K61 strain vaccine ; One week post-immunization, all pigs were challenged i.m. with 105TCID₅₀PRVTJ in the neck.

Two out of three pigs in the Bartha-K61 vaccine group exhibited fever, depression, anorexia and retarded growth from 4 DPC.

- ✓ Challenge after one week vaccination
- ✓ Homologous better than heterologous protection?
- ✓ Vaccine brand? titers? adjuvant?



PRV vaccine AUSKIPRA® GN provide quick and strong protection against Chinese PRV variant

APVS, 2015

中國畜牧與獸醫期刊, 2015

Jichun Wang Ph.D, Professor, Group Leader



National Research Center of Veterinary
Biologicals Engineering and Technology
国家兽用生物制品工程技术研究中心

Trial protocol

- **3 times replicated trial**
- 20 heads, 4 week-old piglet, gE-/gB-
- randomly assign to 4 groups

Groups	Treatment	Volume	# of piglets
A: A3 solvent	AUSKIPRA [®] GN +A3	1dose, 2ml	5
B : RED solvent	AUSKIPRA [®] GN +RED	1dose, 2ml	5
C: Challenge Control	PBS	2ml	5
D: Placebo control	PBS	2ml	5

Challenge route : I.N.

Challenge virus : AH02LA strain $10^{7.1}$ TCID₅₀/mL, 2mL/dose

Results- ELISA antibodies against PRV gE/gB

Groups	Before vaccination		7 days post vaccination	
	gB	gE	gB	gE
A: A3 solvent	-	-	+	-
B : RED solvent	-	-	+	-
C: Challenge Control	-	-	-	-
D: Placebo control	-	-	-	-

“-” indicates negative for all samples; “+” indicates positive for all samples

- 7 days after vaccination, all piglets in vaccination group had gB antibodies sero-conversion

Results- Neutralizing antibodies(against AH02LA strain)

Groups	Before vaccination	7 days post vaccination
A: A3 solvent	<2	<2
B : RED solvent	<2	<2
C: Challenge Control	<2	<2
D: Placebo control	<2	<2

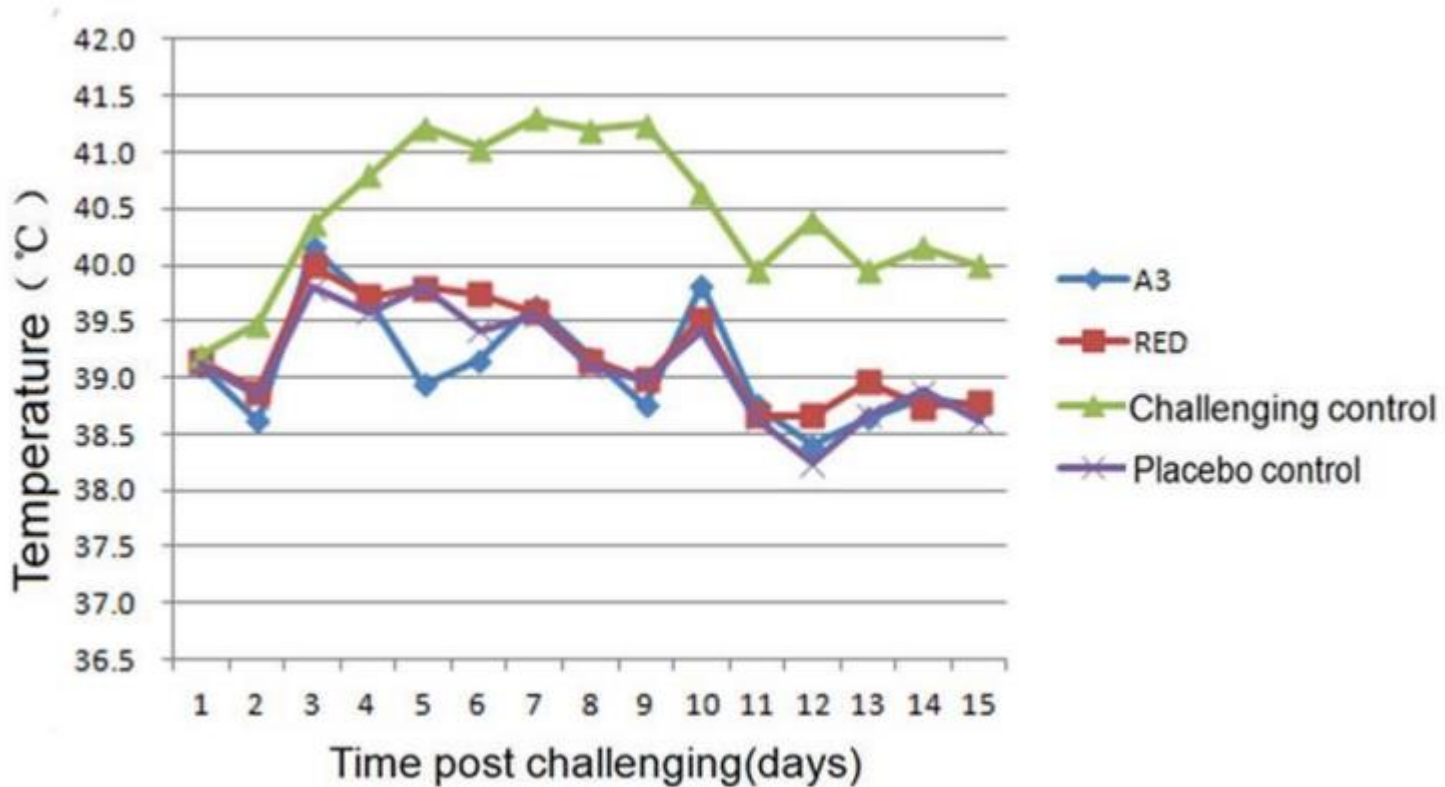
- No neutralizing antibodies were detected in all piglets, 7 days after vaccination

Results- Clinical signs

Groups	Before challenge	Post challenge	
		Morbidity	Mortality
A: A3 solvent	-	0/5	0/5
B : RED solvent	-	0/5	0/5
C: Challenge Control	-	5/5	3/5
D: Placebo control	-	0/5	0/5

- No clinic symptoms, no death in vaccination group after challenge
- 100% morbidity, 60% mortality in control group after challenge

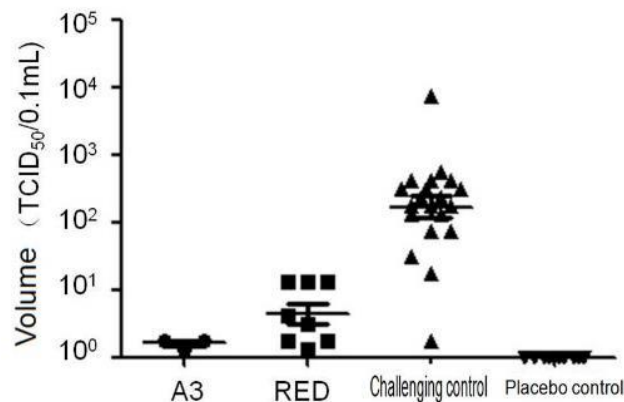
Results- Body temperature



- No fever in vaccination group after challenge

Results- Virus shedding in nasal swabs after challenge

Groups	Numbers	Duration(days)	Volume (TCID ₅₀ /0.1mL)
A: A3 solvent	3 ^a /5 ^b	1	10 ^{0.125} ~10 ^{0.25}
B : RED solvent	4/5	1~3	10 ^{0.25} ~10 ^{1.125}
C: Challenge control	5/5	3~5	10 ^{0.25} ~10 ^{3.875}
D: Placebo control	0/5	/	/



Frequency of virus shedding

A3:	3 ^a /70 ^b
RED:	8/70
Challenge control:	19/41
Placebo control:	0/70

- Less shedding titer and shedding time in vaccination group
- A3 group is better than Red solvent group

Results- Lung lesions post challenge

Groups	Results	
	-	+
A: A3 solvent	5	0
B : RED solvent	5	0
C: Challenging Control	0	5
D: Placebo control	5	0

- No lung lesion in vaccination group
- Serious lung lesion in control group

Conclusions

- AUSKIPRA® GN can provide quick and strong protection(7 days after vaccination already can provide protection)
- AUSKIPRA® GN can significantly reduce virus shedding titer and time once infection
- A3 improves the protection of AUSKIPRA® GN

For details, please refer to our publication:

WANG Ji-chun, ZENG Rong-yu, Torrents Daniel, Martinez Carlos, QIAO Yong-feng, GU Yi-qi, LIU Chang.
Protection Test of Pseudorabies Vaccine (Bartha K61 strain) for Pigs against Pseudorabies Virus Variant.
Animal Husbandry and Veterinary Medicine. 2015(12).

Adjuvant- Strong protection

Group (number)	Mean no. of days (\pm standard error of mean)			
	Virus excretion	Fever ($T \geq 40^\circ\text{C}$)	Clinical signs	MRDG7
MLV +A ($n = 3$)	0.0 ^a (0)	0 ^b (0)	0 ^b (0)	+ 0.8 ^c (0.2)
MLV ($n = 4$)	3.3 ^d (1.1)	0.3 ^b (0.3)	0 ^b (0)	+ 0.7 ^c (0.4)
IV +A ($n = 3$)	4.5 ^d (0.5)	5.5 (1.5)	5 (0)	-0.3 (0.4)
IV ($n = 4$)	4.5 ^d (0.6)	4.8 (0.3)	6 (0)	-0.2 (0.6)
Controls ($n = 4$)	9.8 (0.3)	6.3 (0.5)	6.3 (0.3)	-0.9 (0.2)

van Rooij, et al., 2004

Vet Immuno Immunopatho, 99: 113-125

MLV+A - No virus shedding
- No fever & clinical sign
- better weight gain

Adjuvant- Strong protection(A3 adjuvant)

Virus Genes (2015) 50:401–409
DOI 10.1007/s11262-015-1190-0



Molecular epidemiology of outbreak-associated pseudorabies virus (PRV) strains in central China

Yinbiao Wang^{1,2} · Songlin Qiao² · Xuewu Li² · Weitao Xie^{2,3} · Junqing Guo² ·
Qingmei Li² · Xiao Liu^{2,3} · Jie Hou^{2,3} · Yanqi Xu^{2,3} · Li Wang² · Chengliu Guo² ·
Gaiping Zhang^{1,3}

The use of Carbomer and Levamisole(A3) as adjuvants in the administered Bartha-K61 have been suggested to contribute to the observed improvement over the claimed incomplete protection in other studies [20]



Question: Why IN route to against virulent strain?

- High virulent wild strain
 - 10^3 TICD₅₀ virulent China strain can infect pigs and have clinical sign (*Yimin Wang et al, 2015*)
 - Early infection in farrowing unit
- Intra nasal vaccination
 - Avoid interfere of maternal AB
 - Occupied nerve sys → block latency infection
 - Build first line of protection(Mucosal immunity)
 - First choice when facing high virulent infection

Question: Why IN route to against virulent strain?

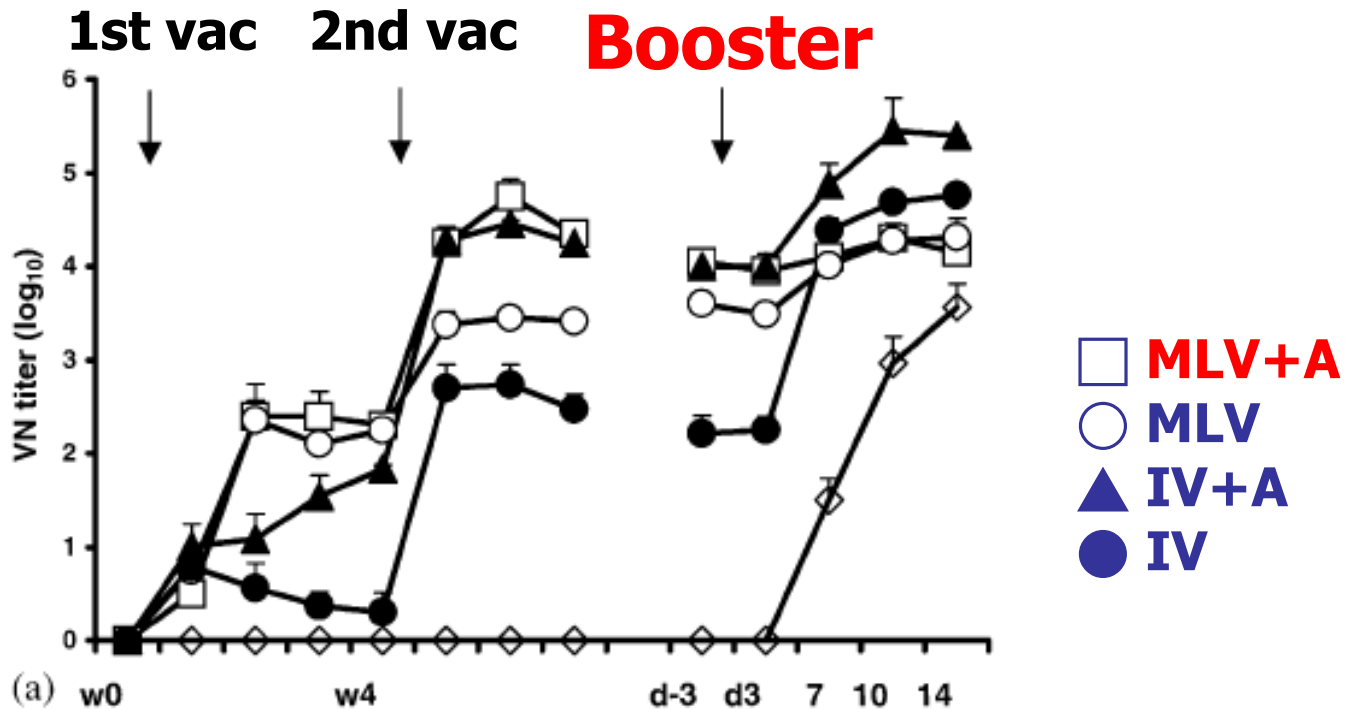
Comparison of different vaccination route of Bartha strain (IN Challenge after 4 wks of vaccination)

Vaccination route	SN	Virus shedding (day)	Virus shedding rate	Potential infection
IN	0	1.6 ± 1.7	5/7	11.1 ± 12.4
IM	1.5 ± 1.4	2.7 ± 1.7	6/7	31.3 ± 30.7

(Aivars Vilnis, et .1998.Vet.Microbiology 62 : 81-96)



Question: the advantage of killed vaccine



- ✓ Efficacy of vaccine with adjuvant is better than without adjuvant
- ✓ Booster of IV can provide higher VN titer than MLV

Question: the advantage of killed vaccine

Group A: 2 shot live vaccine

Group B: 2 shot live vaccine+ 1 shot killed vaccine

Bartha strain					HP China strain					
A group (30 heads)			B group (25 heads)			A group (30 heads)		B group (25 heads)		
SN titer	No. of gilt	%	No. of gilt	%	SN titer	No. of gilt	%	No. of gilt	%	
1:32	12	40.00%	25	100.00%	1:32	3	10.34%	25	100.00%	
1:64	5	16.67%	25	100.00%	1:64	0	0.00%	25	100.00%	
1:128	1	3.33%	19	76.00%	1:128	0	0.00%	25	100.00%	
Avg.		3.63	Avg.		Avg.		3.55	Avg.		7.68

(伍少钦, 2014)

Additional one shot of killed vaccine can increase the PR SN titer to against Barth strain and HP China strain



Vaccination program based on farm situation

Negative farm

- ✓ low infectious pressure

Piglet IM 10w+16w、 gilt 22w+26w、 sow and boar 3 time per year

- ✓ High infectious pressure

Piglet IN+IM(10w+16w)、 gile 22w+26w、 sow and boar 4 time per year

Positive farm

- ✓ Trade of positive rate decreasing

Piglet IN+IM(12w+18w)、 gilt 22w+26w、 sow and boar 4 time per year(live+killed)

- ✓ Still positive(Live+killed)

Piglet IN+IM(8w-killed+16w-live)、 gilt 22w+26w(killed)、 sow and boar 4 time per year(live+killed)

Case report-1

- Farrow to finish farm with 350 sows
- Vaccination program (Jun, 2016)
 - Sows and boars → 4 times per year
 - Piglets

Before → IN at birth + IM at 10 wks

After → IN at birth + 2 shot IM at 10 wks and 16 wks

APVS, 2017

EFFECT OF VACCINATION PROGRAM ON THE PSEUDORABIES VIRUS (PRV) INFECTION RATE IN FATTENING PIGS IN PRV POSITIVE FARMS

Wenyuan Xi, Rongyu Zeng*, Yicun Liu, Cong Li, Juan Li, Tingting Zhang

HIPRA CHINA, Beijing, China

*e-mail: carlos.martinezbenitez@hipra.com



Case report-1

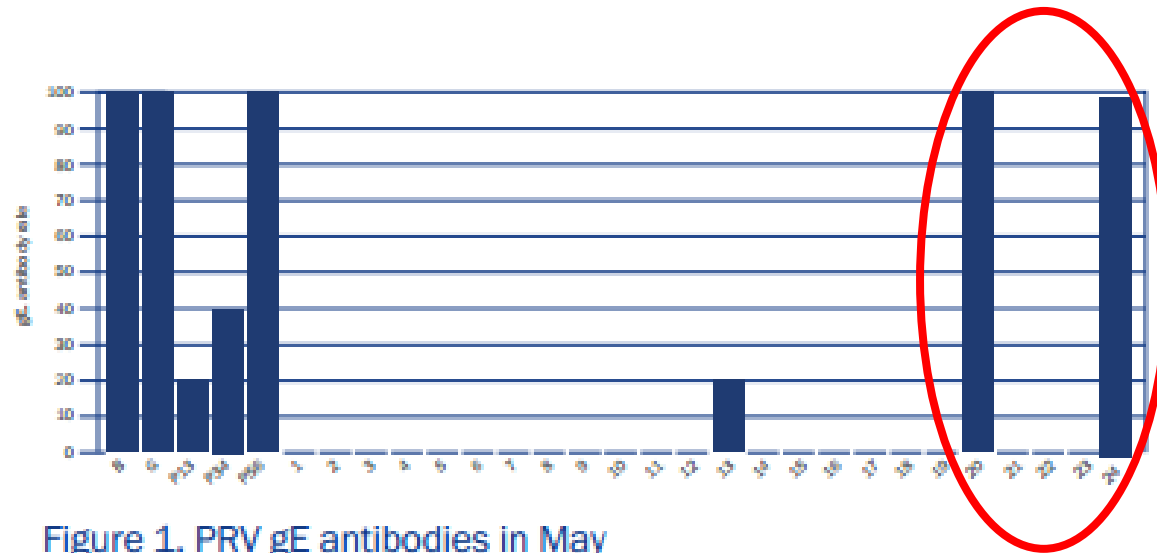


Figure 1. PRV gE antibodies in May

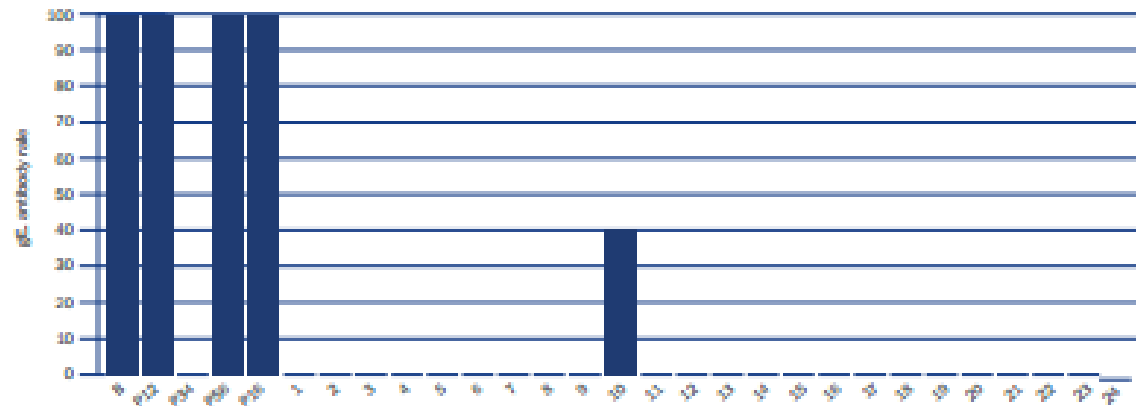


Figure 2. PRV gE antibodies in November

Case report-2

- 3000 sows farrow to finish farm

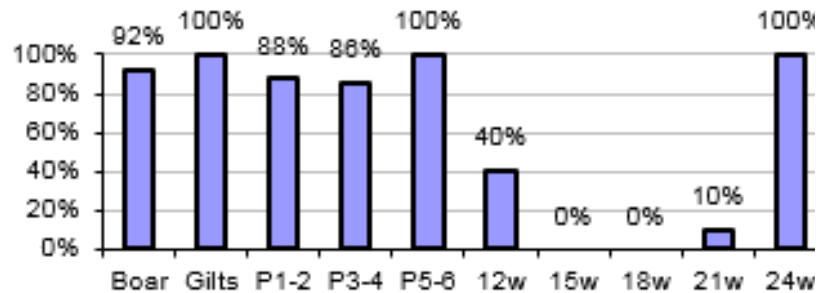


Fig 1 PRV ~~gE~~ antibody rate in May 2016

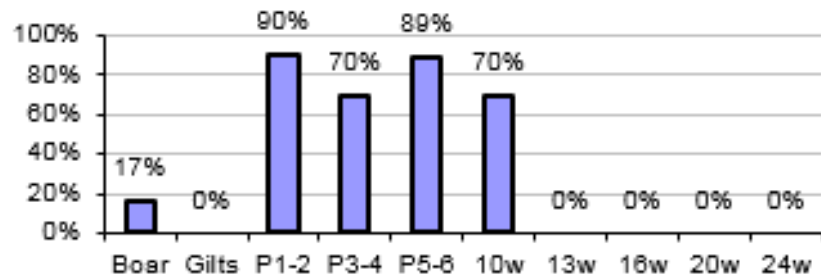


Fig 2 PRV ~~gE~~ antibody rate in Dec 2016

Group	Before	After
Breeder	Live, 4 times per year	BK before farrowing
Piglets	0(IN)+6W(L)+13W(L)	0(IN)+8W(IM,GN)+13W(IM,GN)

Case report-3

- Farrow to finish farm with 1,500 sows
- Vaccination program (Feb, 2016)

Group	Before Feb. 2016	After Feb. 2016
Boars	I.M. GN every 3 months	I.M. GN or BK every 3 months
Sows	I.M. GN every 3 months	I.M. GN or BK every 3 months
Gilts	22/26W I.M GN	22/26W I.M BK
Day 1 - 2	None	I.N. GN
Day 50	I.M. GN	None
Day 70	None	I.M. BK
Day 108	I.M. GN	I.M. GN

APVS, 2017

EFFICACY OF A NOVEL VACCINATION PROGRAM IN A PRV INFECTED FARM

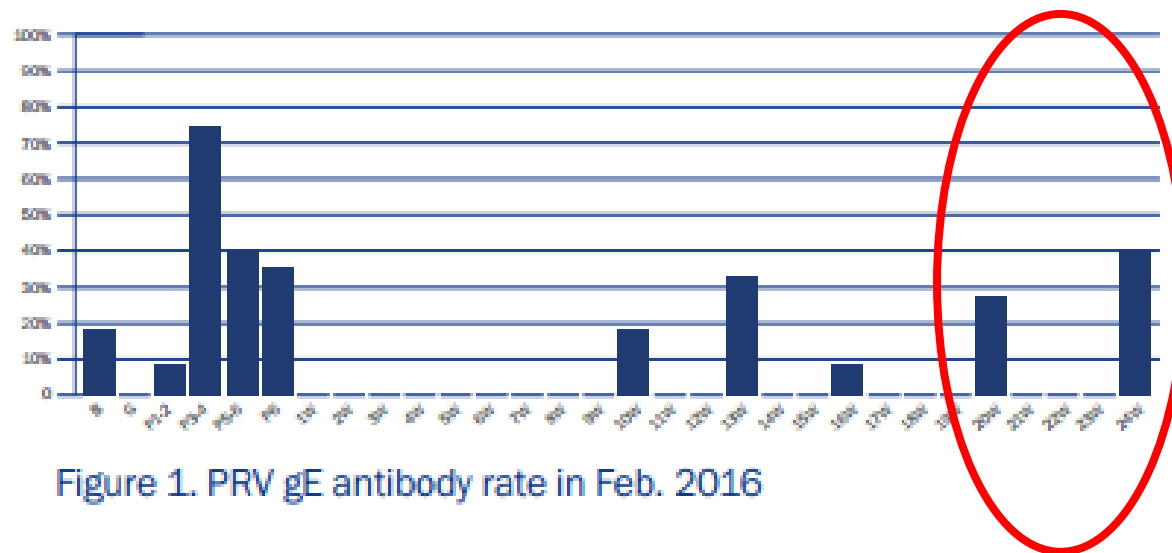
Huibo Ning¹, Xihua Hu², Rongyu Zeng^{1*}, Dong Zheng¹

¹HIPRA China, Beijing, 100086 ²Qingshan Breeding Company, Jinhua, Zhejiang, 21000

*e-mail: carlos.martinezbenitez@hipra.com



Case report-3

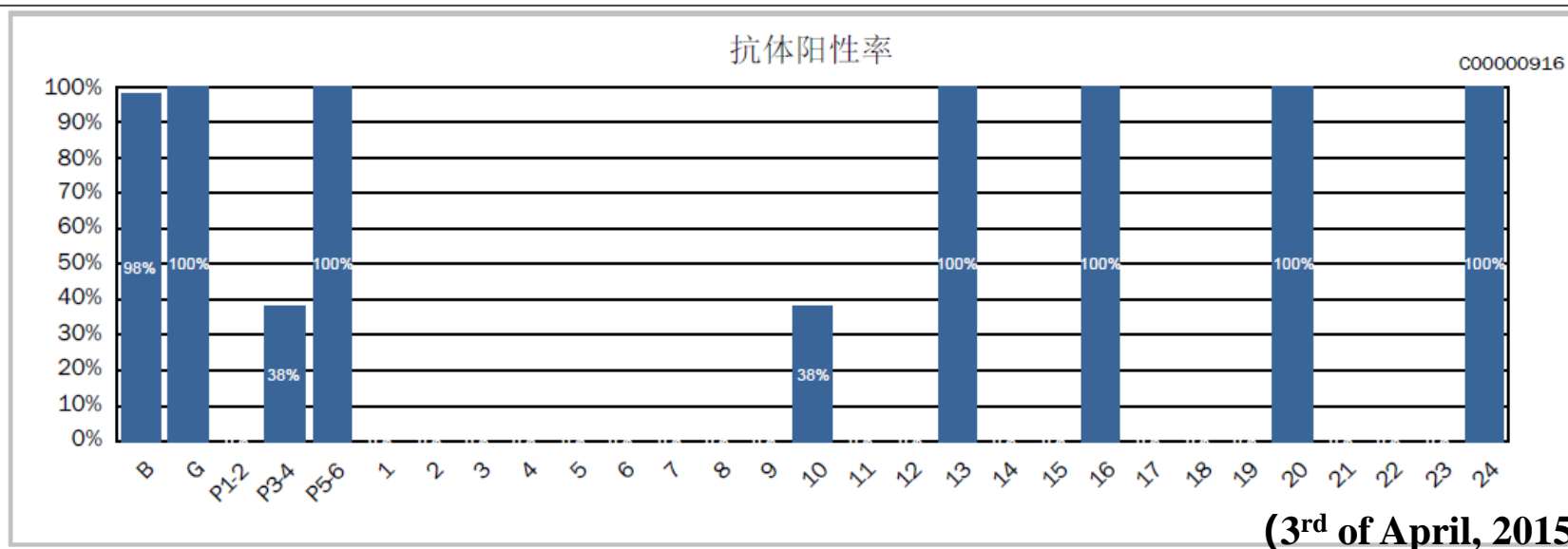


Case report-4

伪狂犬gE抗体

判界标准:

ELISA



Group	Before	After
Boar	Live, 3 times per year	GN+BK、 4 times per year
Gilt	2 live before farrowing	2 BK before farrowing
Sow	Live, 3 time per year	GN+BK、 4 time per year
Piglet	0(IN)+6W(L)+10W(L)	0(IN, GN)、 8W(IM, BK)、 15W(IM, GN)



Case report-4

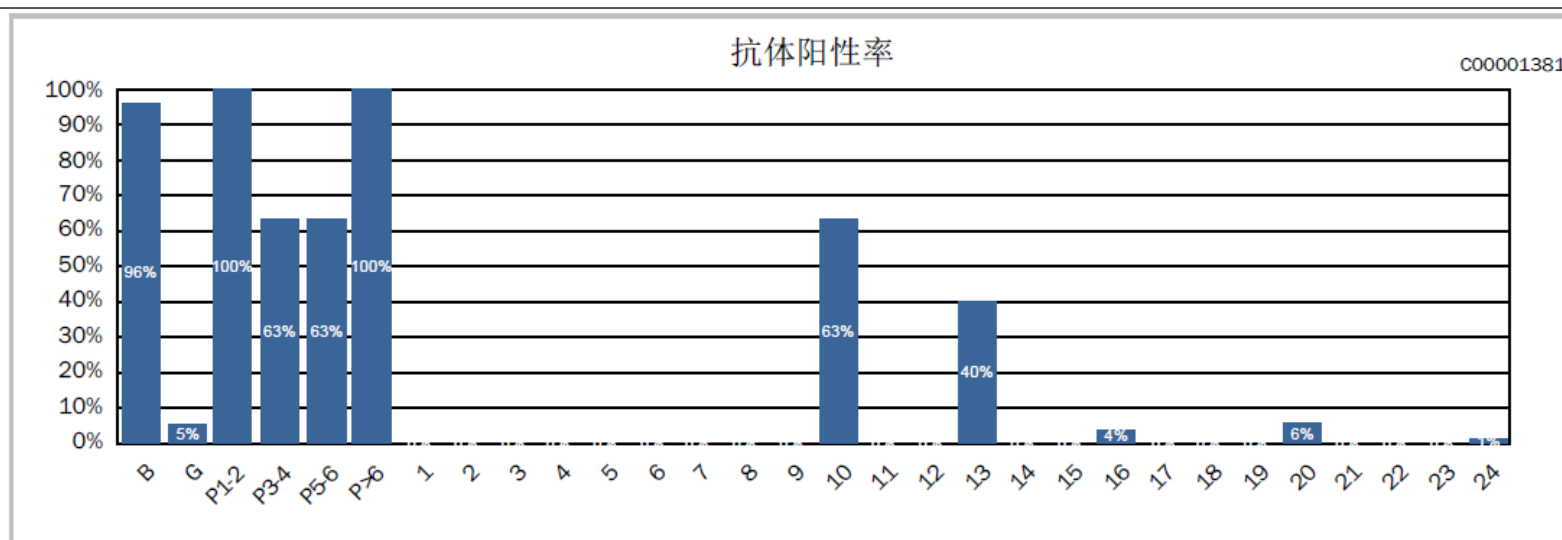
7 months later

Can produce negative finisher/gilt to market

伪狂犬gE抗体

判界标准:

ELISA



(26th of Nov, 2015)

Take home message

- ADV
 - Immune suppression and economic loss
 - One of the swine diseases can be eradicated with good vaccine and tool
 - Re-emergency disease
- HP-ADV in China
 - High infectious ability
 - Need IN route to prevent early infection

Thanks for your attention