The Effects of Biannual Equine Influenza Vaccine on Performance in Adult Horses

A Knowledge Summary by

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PICO question

In three day event horses, does biannual routine influenza vaccination compared to annual routine influenza vaccination reduce performance levels?

Clinical bottom line

There is no evidence that biannual equine influenza vaccination compared to annual booster vaccination in three day event horses is associated with reduced performance.

A group of five studies published over an 11 year period from one veterinary hospital were evaluated. In adult warmblood horses there is weak evidence that exercise in the 28 day period post booster vaccination for equine influenza and equine herpes virus 1 and 4 (EHV1&4), is associated with changes in physical and clinical pathophysiological parameters including total red blood cell (RBC) count, neutrophil and lymphocyte count, fibrinogen concentration and serum proteins. These changes occurred at variable time points in the 14 days post exercise and values were not outside the published reference ranges for the reporting laboratories where published. Athletic performance of the horses was not evaluated.

No recommendations for equine influenza vaccination protocols in three day event horses can be made from the evidence.

The evidence

There is no retrospective or prospective evidence examining performance in three day event horses after annual or biannual booster vaccination against equine influenza virus. There is no evidence examining performance levels in three day event horses after booster vaccination against equine influenza virus. There is a small amount of evidence, and the quality of the evidence is low, evaluating clinical and clinicopathological data that may relate to performance in adult warmblood horses undergoing booster vaccination and subsequent exercise. These five randomised controlled trials were conducted at one veterinary teaching hospital using a small number of adult warmblood horses over an 11 year period. The evidence evaluated may not be applicable outside the experimental group of 15 horses and some horses may have been included in more than one of the studies.

Summary of the evidence

(A) Gundasheva (2015)	
Population:	Adult Hanoverian geldings at one Bulgarian veterinary hospital
Sample size:	15 horses
Intervention details:	• Vaccinated for EHV1&4 and equine influenza virus (EIV) 12 months after initial vaccination [n=6] • Vaccinated for EHV1&4 and EI 12 months after initial vaccination and submitted to physical exercise for 4 days commencing 14 days after revaccination [n=6] • Control group of unvaccinated animals [n=3]

Study design:	Randomised controlled trial
Outcome studied:	Erythron parameters, heart and respiratory rates were determined 0h, 2h, and day 14 and 17 after booster vaccination and days 1, 2, 4 and 11 after commencement of exercise. Results were presented as mean +/- standard error of mean (SEM)
Main findings: (relevant to PICO question):	1. All erythron parameters of all groups remained within the published reference ranges for the study period 2. Heart rate and respiratory rate were significantly increased in the physical exercise group 0h and 2h post exercise 3. RBC count was statistically different between vaccine and vaccine plus exercise groups, increasing in the vaccine and exercise group on day 4 after cessation of physical exercise but not on day 2 or 11
Limitations:	• Small group sizes • Whether horses in the intervention groups had received primary and/or booster vaccinations against EHV1&4 and EIV is not reported • Randomisation process was not described • Reported reference ranges are laboratory specific • Prior vaccination status of the horses was not discussed in detail • Level of preceding fitness prior to study inclusion was not reported

Sotirov et al. (2004)	
Population:	Adult Hannovarian horses (4–9 years old) at one Bulgarian veterinary hospital
Sample size:	12 horses
Intervention details:	• Vaccinated for EHV1&4 and EI 12 month after initial vaccination (control group) [n=6] • Vaccinated for EHV1&4 and EI 12 months after initial vaccination and exercised for 4 days commencing 14 days after booster vaccination [n=6]
Study design:	Randomised controlled trial
Outcome studied:	Serum lysozyme, and magnitude of alternate pathway complement activation and classical pathway complement activation were determined on days 17, 18, 19, 21 and 28 after booster vaccination, corresponding to days 0, 1, 2, 4 and 11 after cessation of exercise. Values were reported as mean +/- SEM
Main findings: (relevant to PICO question):	1. Exercise post booster vaccination did not alter Lysozyme concentrations at any time point 2. Alternate complement pathway activation was statistically higher in the exercise group on days 4 and 11 post cessation of exercise
Limitations:	• Small group size • Randomisation process was not described

	• Level of preceding fitness prior to study inclusion was not reported for either group • Prior vaccination status of the horses was not discussed in detail

Goundasheva [sic] et al. (2005)	
Population:	Adult Hanoverian horses (4–9 years) at one Bulgarian veterinary hospital
Sample size:	12 horses
Intervention details:	• Vaccinated for EHV1&4 and EIV 12 month after initial vaccination (control group) [n=6] • Vaccinated for EHV1&4 and EIV 12 months after initial vaccination and exercised for 4 days commencing 14 days after booster vaccination [n=6]
Study design:	Randomised controlled trial
Outcome studied:	White blood cells (WBC), band neutrophils, segmented neutrophils, eosinophils, monocytes and lymphocytes, cortisol and antibody titers against EHV1&4 and EIV were determined on days 17, 18, 19, 21 and 28 after booster vaccination, corresponding to days 0, 1, 2, 4 and 11 after cessation of exercise. Results were presented as mean +/- SEM
Main findings: (relevant to PICO question):	1. Kinetics of antibody titers in response to booster vaccination were similar between groups 2. Lymphocyte counts increased in the vaccine only group on days 17, 18 and 28 after revaccination 3. In the vaccine and exercise group band neutrophils counts increased and segmented neutrophils decreased on day 18 after revaccination (day 1 after cessation of exercise)
Limitations:	• No data was presented for serum cortisol concentration other than 0h and 2h after cessation of exercise in the exercise group • Randomisation process was not described • Small group size • While trends in various leucocyte counts are reported, no comment is made as to whether these lie outside the published reference ranges for the appropriate laboratories • Level of preceding fitness prior to study inclusion was not reported

(B) Gundasheva (2015)	
Population:	Adult Hanoverian geldings (4–9 years of age) at one Bulgarian veterinary hospital intussusception within 3 days of initial surgical reduction.
Sample size:	15 horses

Intervention details:	• Vaccinated for EHV1&4 and EIV 12 months after initial vaccination [n=6] • Vaccinated for EHV1&4 and EIV12 months after initial vaccination and submitted to physical exercise for 4 days commencing 14 days after revaccination [n=6] • Control group of unvaccinated animals [n=3]
Study design:	Randomised controlled trial
Outcome studied:	Albumin, alpha, beta and gamma globulin serum protein fractions were determined in all groups on days 14 and 17, 18, 19, 21 and 28 after booster vaccination corresponding with days 1, 2, 4 and 11 after cessation of the exercise program. Results were reported as mean +/-SEM
Main findings: (relevant to PICO question):	Statistically significant difference were noted for albumin, alpha 2 and beta 1 and 2 globulins between booster, vaccinated and booster, vaccinated and exercised horses at individual time points but these differences did not persist over the timeframe of the study. Beta 2 globulins were reported as reduced in the exercise group at certain time points whereas all other parameters were increased in the exercising group. All parameters remained with the published reference ranges at all time points for the reporting laboratory.
Limitations:	• No data was collected during the first 14 days post booster vaccine • Small group size • Randomisation process was not described • Level of fitness of the horses included in this study prior to commencement of the trial was not discussed

Gundasheva and Georgieva (2015)	
Population:	Adult Hanoverian geldings (4–9 years of age) at one Bulgarian veterinary hospital
Sample size:	15 horses
Intervention details:	• Vaccinated for EHV1&4 and EI 12 months after initial vaccination [n=6] • Vaccinated for EHV1&4 and EI 12 months after initial vaccination and submitted to physical exercise for 4 days commencing 14 days after revaccination [n=6] • Control group of unvaccinated animals [n=3]
Study design:	Randomised controlled trial
Outcome studied:	Haptoglobin, fibrinogen and erythrocyte sedimentation ratio were evaluated in all groups on days 14 and 17, 18, 19, 21 and 28 after booster vaccination, corresponding with days 1, 2, 4 and 11 after cessation of the exercise program. Results were reported as mean +/-SEM

Main findings: (relevant to PICO question):	1. Plasma haptoglobin was not significantly different at any time point between the vaccinated, and the vaccinated and exercised groups. 2. Fibrinogen concentration was significantly different between the vaccinated, and vaccinated and exercised group at day 1 post cessation of exercise, increasing in the exercise group but not significantly different at any other time point during the study. 3. Haptoglobin and fibrinogen remained within the reference range for the laboratory in all horses throughout the study period. 4. Erythrocyte sedimentation rate (ESR) were significantly different between the vaccinated only and vaccinated plus exercised group, increasing in the vaccinated plus exercised group on days 1, and 4 after cessation of exercise, but not day 2. 5. Reference ranges for haptoglobin and fibrinogen concentrations were not presented.
Limitations:	• Randomisation process was not discussed • For horses in the revaccination only and revaccination plus exercise groups, it was unclear whether the prior vaccination 12 months preceding the commencement of the study, was a primary course or booster vaccination • Small group size • Level of preceding fitness prior to study inclusion was not reported

Appraisal, application and reflection

There is no evidence available comparing performance levels in three day event horses receiving either biannual or annual booster vaccinations against equine influenza virus. There is no evidence available evaluating performance levels in three day event horses receiving booster vaccination for equine influenza virus or placebo controls.

Only low quality evidence is available from a group of five papers from one veterinary teaching hospital evaluating a variety of physical and clinicopathological variables in adult warmblood horses after either booster vaccination against equine influenza virus and equine herpes virus and rest or booster vaccination followed by a controlled exercise program for 4 days commencing 14 days after vaccination. Variables evaluated included:

- heart rate*, respiratory rate* and total red blood cell count * (A - Gundasheva, 2015)
- Serum proteins (albumin*, alpha 1, alpha 2*, beta 1* and beta 2*, gamma globulins) (B - Gundasheva, 2015)
- Fibrinogen*, haptoglobin erythrocyte sedimentation rate (Gundasheva and Georgieva, 2015)
- Total white blood cell, eosinophil, neutrophil* and lymphocyte* counts (Goundasheva [sic] et al., 2005)
- Lysozyme*, classical and alternate complement activation* (Sotirov et al., 2004)

Statistically significant differences ($P < 0.05$) were noted in the above variables (*) at intermittent time points in the 14 days post exercise (corresponding to 18–31 days post booster vaccination.) Values were reported as means in all cases with mean plus standard error of mean in some publications. Confidence limits were not reported in any of the studies. Reported values remained within the published reference ranges for the conducting laboratories at all time points when these were reported in the studies. While the above variables are commonly evaluated in horses with reduced performance, athletic performance was not directly evaluated.

The study participants were reported as male (Goundasheva [sic] et al., 2005) (Sotirov et al., 2004), male entire (A - Gundasheva 2015) geldings (B - Gundasheva 2015) or not reported (Gundasheva and Georgieva 2015) and previous level of fitness prior to study inclusion was not discussed in any study. In all trials an exercise period of 4 days was used, which is likely to vary greatly to training programs for competing three day event horses. While all study horse were reported as being previously vaccinated for equine influenza virus and equine herpes virus 1&4 a year prior to inclusion in the trial, whether this was a booster or primary vaccine course was not discussed. All trials involved booster vaccination with an oil adjuvanted intramuscular vaccine and therefore these finding may not be relevant to horses receiving intranasal/immune stimulating complex (ISCOM) vaccines/vaccines containing varying influenza strain or vaccines containing equine influenza only.

Conclusions:

There is no evidence that biannual equine influenza vaccination compared to annual booster vaccination is associated with reduced performance in three day event horses. The quality of the data in adult warmblood horses in the 28 days period post booster vaccination where exercise occurred on days 14–17post vaccination is insufficient to determine whether athletic performance was affected during this period. More definitive conclusions on vaccination protocols in three day event horses cannot be drawn until higher quality evidence is available on the topic.

Methodology Section

Search Strategy	
Databases searched and dates covered:	PubMed NCBI Platform 1973–2018 Week 16 CAB Abstracts on OVID Platform 1973–2018 Week 16
Search terms:	PubMed 1. equine* or horse* or equus or equid* or mare or mares or pony or ponies or exp equidae/ or exp equus/ or exp horses/ or exp mares/ 2. 'three day event*' or 'show jump*' or dressag* or endur* or exercis* or sport* or compet* or athlet* or 'cross country' 3. exp show jumping/ or exp horse riding/ 4. (1 and 2) or 3 5. vaccin* or immunisation or immunization or inoculation or exp vaccination/ or exp immunization/ 6. influenza or flu or exp influenza/ 7. 4 and 5 and 6 CAB Abstracts 1. equine OR horse OR mare OR mares OR broodmares OR pony OR ponies 2. three day evening OR show jumping OR dressage OR endurance OR exercise OR sport OR sporting OR competition OR athlete OR athletic OR cross country 3. influenza OR flu 4. vaccine OR vaccination OR immunisation OR immunization OR inoculation 5. 1 and 2 and 3 and 4
Dates searches performed:	01 May 2018

Exclusion / Inclusion Criteria	
Exclusion:	Non English language papers Single case reports Book chapters and literature reviews without novel information Not relevant to the question
Inclusion:	Papers comparing physical or clincopathological data, in sports horses exercising after revaccination for equine influenza or equine influenza and equine herpes virus 1&4 were evaluated. Due to the absence of published data in sports horses after biannual vaccination for EI, varying vaccination protocols were included.

Search Outcome

Database	Number of results	Excluded – [Non English Language]	Excluded – [single case report]	Excluded – [Narrative review/opinion pieces]	Excluded – [not relevant to PICO]	Total relevant papers
CAB Abstracts	188	37	2	5	139	5
NCBI Pubmed	25	2	0	0	22	1
Total relevant papers when duplicates removed						**5**

CONFLICT OF INTEREST

The author declares no conflicts of interest.

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