Further research into equine joints is imperative for racehorses

In Flux

WHEN IT COMES TO JOINT ISSUES, TREAMENTS **CONTINUE TO EVOLVE**

By **AMANDA DUCKWORTH**

IDEALLY, A HORSE will never have joint issues, but that is not a reality for most. Osteoarthritis is a big concern for many owners, especially when it comes to racehorses, because the economic impact of lameness is not small.

The market is full of supplements and procedures to try to prevent or recover from common joint issues, but veterinarians have voiced concern about overuse of these approaches when combined with a lack of scientific understanding. Further research into the equine joint is imperative for the continued well-being of all horses, but especially racehorses.

According to the American Association of Equine Practitioners (AAEP) in its paper "Lameness & Joint Medications," traumatic joint disease in horses includes synovitis (inflammation of the fluid-producing membrane), capsulitis (inflammation of the fibrous joint capsule), articular cartilage and bone fragmentation, ligamentous tearing, and eventually, osteoarthritis. Studies have indicated that up to 60% of lameness in horses is related to osteoarthritis.

"In many cases the disease process primarily involves soft tissue overuse and microtrauma to the bone surfaces, and therefore it can be challenging to diagnose without diagnostic anesthesia," said Drs. Benjamin Espy and Justin Harper for the AAEP. "In addition to localizing pain to a certain joint with aide of diagnostic anesthesia, radiographs, ultrasound, computed tomography, magnetic resonance imaging (MRI) techniques and diagnostic arthroscopy have all been used to confirm causes of joint lameness.

"Trusting your veterinarian to decide when joint injections might be beneficial for your horse is prudent. There is no 'gold standard' for the diagnoses of preliminary joint disease in the horse as radiographic changes are usually indicative of irreparable harm."

Veterinarians are constantly striving to improve how they approach joint issues. In June 2021, *Equine Veterinary Journal* published "Current joint therapy usage in equine practice: Changes in the last 10 years." The objective of the survey was to document changes in clinical use of joint therapies over the decade while looking at how newly developed therapies have been added to routine clinical practice.

The survey was sent to members of AAEP, and 407 completed surveys were returned. The majority of respondents had decades of experience and work with racehorses and Warmbloods. The survey was a follow-up to one from 2009 but also included new questions. Responses were compared with those from the previous survey.

"There are clear differences in the use of joint therapies over time," researchers reported. "While some differences agree with the scientific evidence, others are not fully concordant or are in direct conflict with the scientific literature."

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Veterinarians are striving to improve how they approach joint issues in racehorses

Results showed that triamcinolone acetonide (TA) has remained the most common corticosteroid used to treat high-motion joints while methylprednisolone acetate (MPA) remains the most common corticosteroid to treat low-motion joints. However, the use of MPA for high-motion joints was significantly more common in 2009 than in 2019 while the use of biological therapies have become more popular in recent years. Overall, there was a general concern about overuse when it comes to joint treatments.

"The majority of the clinicians —66.4%—reported seeing frequent joint treatments as a problem in the equine industry," researchers said. "Furthermore, 75.8% reported believing that joints are harmed by overly frequent treatments. Regarding frequency of repeated intra-articular corticosteroid therapy, most clinicians, 50.4%, considered six months as the shortest interval between injections that they felt comfortable with, while three months was selected by 29.8%. Only one respondent reported believing that corticosteroids caused no harm, regardless of interval.

"For 45.7% of the respondents, the primary reason for choosing a biological therapy over corticosteroid for intra-articular use was long-term efficacy. Other reasons included safety, as selected by 19.4%; client request, as selected by 10.8%; and short-term efficacy, as selected by 5.6%. The majority of the respondents, 87%, said they had patients who benefited from intra-articular biological therapy."

As far as the biological therapy treatment, the vast majority, 83.3%, selected autologous conditioned serum (IRAP) while platelet-rich plasma was the second-most common treatment at 72.5%. From 2009-2019, the use of IRAP increased 54.1% among respondents.

"This study contributes to the understanding of how joint therapies are being used clinically," researchers said. "Compared with the survey data gathered in 2009, we were able to observe some differences in the use of intra-articular therapy.

"Of particular importance, in the intervening 10 years, there were differences in terms of the use of intra-articular corticosteroids, increased popularity of biological therapy, and increased frequency of use of intra-articular antibiotics. Some of these differences are in accord with recent evidence from scientific literature while others are not fully supported from the scientific perspective and appear to be related to anecdotal observation."

Continued scientific research is needed to help veterinarians decide on effective plans to treat joint issues. One recent study examined the efficacy of different treatment options when it comes to lameness in Thoroughbreds.

"A Double-Blinded Positive Control Study Comparing

ANNE M. EBERHARDT

the Relative Efficacy of 2.5% Polyacrylamide Hydrogel (PAAG) Against Triamcinolone Acetonide (TA) and Sodium Hyaluronate (HA) in the Management of Middle Carpal Joint Lameness in Racing Thoroughbreds" was published in the December 2021 edition of the *Journal of Equine Veterinary Science*. For the study, 31 Thoroughbreds with lameness grades of one to three (out of five) were used. All raced on the flat as opposed to jumps. They were randomly assigned for intra-articular treatment with either 2ml of 2.5% PAAG, 12 mg TA, or 20 mg HA. The HA group also received two further treatments. The horses were allowed to rest for two days after treatment before being returned to their unaltered training routines. All groups were reexamined at two, four, and six weeks while horses treated with 2.5% PAAG were monitored for 12 weeks.

"ULTRASOUND CAN DIRECTLY IMAGE CARTILAGE AND THE SUBCHONDRAL BONE MARGIN WITHOUT EXPOSURE TO IONIZING RADIATION."

—RESEARCHERS IN A RECENT STUDY PUBLISHED IN *IRISH VETERINARY JOURNAL*

"Significantly more joints treated with 2.5% PAAG were lame-free (83%) at six weeks compared to TA (27%) and to HA (40%)," researchers concluded. "There was no significant difference between TA and HA groups at any time. All the joints treated within 2.5% PAAG that were lame-free at six weeks (10/12) were still lame-free at 12 weeks. In conclusion, treatment with 2.5% PAAG led to statistically superior results compared to TA and HA in the management of selected middle carpal joint lameness in flat-racing Thoroughbreds, with therapeutic effects persisting up to 12 weeks."

While some might think osteoarthritis only becomes a problem once a horse is actively engaged in a sport or competition, anyone who has looked at radiographs at yearling sales knows that's not the case. While radiographs are standard protocol, researchers are looking into other ways to examine limbs, leading the *Irish Veterinary Journal* to publish "Ultrasound screening protocol for osteochondrosis at selected predilection sites in Thoroughbred yearlings" in April 2022.

"Radiography is currently the recognized gold standard for equine

orthopedic screening, particularly in the case of pre-purchase examinations," explain researchers. "A major limitation of radiography is the inability to distinguish cartilage from the other soft tissue opacities of the joint. In radiography, the deformation of the subchondral bone margins, change in opacity of the subchondral bone, and soft tissue swelling are signs of osteochondral disease. Subtle cases involving only the articular cartilage might be missed. Ultrasound can directly image cartilage and the subchondral bone margin without exposure to ionizing radiation."

Because of these limitations, researchers wanted to examine the practicality of using ultrasonography. For the study, 22 clinically normal Thoroughbred weanlings were used while veterinarians detailed the protocol of an ultrasonographic examination. These took place on the farm, and the horses were screened in areas known for osteochondral disease in young horses, including the carpal, metacarpophalangeal, stifle, tarsal, and metatarsophalangeal joints.

As the economic impact of lameness in racehorses is significant, horsemen constantly monitor for any issues

ANNE M. EBERHARDT

"Ultrasonography allows imaging of the articular cartilage and subchondral bone margins and has been shown to be more sensitive in identifying osteochondrosis lesions," said researchers. "However, the ultrasonographic technique for examining joints is operator dependent, resulting in highly variable examinations, thus affecting its reliability and reproducibility as a screening test.

"Two veterinary practitioners used the technique to illustrate the repeatability of the protocol. The step-by-step protocol provides a valuable, reliable, repeatable technique for veterinary professionals performing screening ultrasound in the field."

No matter how horses are examined, once they begin racing, the amount of stress on their limbs increases. In July 2022, *Scientific Reports* published "Relationship between Thoroughbred workloads in racing and the fatigue life of equine subchondral bone."

As the researchers explain, fatigue life (FL) is the number of cycles of load sustained by a material before failure. It is dependent on the load magnitude. For equine athletes, cycles correlate to number of strides, with load proportional to speed.

"Musculoskeletal injuries occur at various locations in Thoroughbred racehorses, but the metacarpo (/metatarso)-phalangeal (fetlock) joints, and in particular, the subchondral bone of the distal palmar aspect of the third metacarpal (/tarsal) condyles are most frequently affected," explained researchers. "Of all (these), the distal

limb is subjected to the highest stress, with vertical load on the limb amplified at the joint surface by the fetlock moment arm.

"The repeated high-joint surface loads result in fatigue failure of subchondral bone, with damage either spreading transversely across the joint surface (palmar osteochondral disease) or propagating proximally as parasagittal fractures. Given the high loads incurred on the fetlock joint, and the frequency of condylar disease/fracture, the condylar subchondral bone was the focus of this investigation."

For the study, retrospective speed and stride data—including stride length, duration—from Thoroughbred racehorses in Australia in 33,459 starts from January 2011-August 2016 were sourced.

"Models produced for different joint surface loads demonstrated that the proportion of fatigue life per race increased exponentially based on the magnitude of the scaled load, but there was substantial variation between horses," researchers concluded. "Moreover, unmeasured horse effects (i.e. innate qualities of individual horses) accounted for a large proportion of the variance in fatigue life consumed between race starts. Older horses, females, better finishing positions, firmer track surfaces, and longer race distances were estimated to accrue a greater percentage of fatigue life over each race start. Synthetic surfaces were associated with accrued fatigue life that was more similar to soft-rated than good-rated surfaces. The effect of race class on fatigue accumulation was dependent on the weight carried.

"The results presented here suggest that there is substantial variation across horse- and race-level factors for fatigue accumulation in Thoroughbred racing. There is also substantial inter-horse variation in fatigue accumulation based on individual horses' stride characteristics, which explains why horses with similar racing histories might have very different outcomes."

Researchers are working to understand better how Thoroughbred joints are affected, not only in race situations but also in training. In March 2022, the *Polish Journal of Veterinary Sciences* published "The effect of training on infrared thermographic images of the forelimb and hindlimb

When It Comes to Horse Health and Safety, Don't Hit the Easy Button

Many horse owners want to reduce the cost of treatment by reaching for a "compounded" version of altrenogest (a progestin used in veterinary medicine to suppress or synchronize estrus in horses) in long-acting injectable formulations. BUT AT WHAT COST TO YOUR HORSE?

A compounder simply mixes up a drug preparation and sells it without any required testing for purity and concentration. This has been illustrated many times by horses DYING from compounded medications that weren't tested before being sold. Compounded products require no proof of efficacy, so you have no proof the product is even altrenogest or is safe.

When you use only FDA-approved altrenogest products such as Altren® (altrenogest) Oral Solution manufactured by Aurora Pharmaceutical, the veterinarian and the horseman know the *i*ngredients have been tested for purity and the final product has been tested for purity and stability. NO EXCEPTIONS. Also, before any drug formula is approved by the FDA, it must pass rigorous research trials that prove it is safe and works for its intended purpose.

So, the question every equine enthusiast must ask is whether convenience is more important than the peace of mind that comes from using the approved and tested product in your expensive mare? The answer should always be NO. Your equine partner will thank you.

—Content provided by Aurora Pharmaceutical, Northfield, Minn.
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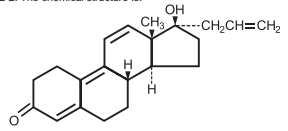
Altren®
(altrenogest)
SOLUTION 0.22% (2.2 mg/mL)

CAUTION:
Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:
Altren® (altrenogest) Solution 0.22% contains the active synthetic progestin, altrenogest. The chemical name is 17α-allyl-17β-hydroxyestra-4,9,11-trien-3-one. The CAS Registry Number is 850-52-2. The chemical structure is:



Each mL of Altren® (altrenogest) Solution 0.22% contains 2.2 mg of altrenogest in an oil solution.

ACTIONS:
Altren® (altrenogest) Solution 0.22% produces a progestational effect in mares.

INDICATIONS:
Altren® (altrenogest) Solution 0.22% is indicated to suppress estrus in mares. Suppression of estrus allows for a predictable occurrence of estrus following drug withdrawal. This facilitates the attainment of regular cyclicity during the transition from winter anestrus to the physiological breeding season. Suppression of estrus will also facilitate management of prolonged estrus conditions. Suppression of estrus may be used to facilitate scheduled breeding during the physiological breeding season.

CONTRAINDICATIONS:
Altren® (altrenogest) Solution 0.22% is contraindicated for use in mares having a previous or current history of uterine inflammation (i.e., acute, subacute, or chronic endometritis). Natural or synthetic gestagen therapy may exacerbate existing low-grade or "smoldering" uterine inflammation into a fulminating uterine infection in some instances.

PRECAUTIONS:
Various synthetic progestins, including altrenogest, when administered to rats during the embryogenic stage of pregnancy at doses manyfold greater than the recommended equine dose caused fetal anomalies, specifically masculinization of the female genitalia.

DOSAGE AND DIRECTIONS:
While wearing protective gloves, remove shipping cap and seal; replace with enclosed plastic dispensing cap. Remove cover from bottle dispensing tip and connect luer lock syringe (without needle). Draw out appropriate volume of Altren® solution. (Note: Do not remove syringe while bottle is inverted as spillage may result.) Detach syringe and administer solution orally at the rate of 1 mL per 110 pounds of body weight (0.044 mg/kg) once daily for 15 consecutive days. Administer solution directly on the base of the mare's tongue or on the mare's usual grain ration. Replace cover on bottle dispensing tip to prevent leakage. Excessive use of a syringe may cause the syringe to stick; therefore, replace syringe as necessary.

DOSAGE CHART:

Approximate Weight in Pounds	Dose in mL
770	7
880	8
990	9
1100	10
1210	11
1320	12

WHICH MARES WILL RESPOND TO ALTREN® (altrenogest) SOLUTION 0.22%:
Extensive clinical trials have demonstrated that estrus will be suppressed in approximately 95% of the mares within three days; however, the post-treatment response depended on the level of ovarian activity when treatment was initiated. Estrus in mares exhibiting regular estrus cycles during the breeding season will be suppressed during treatment; these mares return to estrus four to five days following treatment and continue to cycle normally. Mares in winter anestrus with small follicles continued in anestrus and failed to exhibit normal estrus following withdrawal.

Response in mares in the transition phase between winter anestrus and the summer breeding season depended on the degree of follicular activity. Mares with inactive ovaries and small follicles failed to respond with normal cycles post-treatment, whereas a higher proportion of mares with ovarian follicles 20 mm or greater in diameter exhibited normal estrus cycles post-treatment. Altrenogest Solution 0.22% was very effective for suppressing the prolonged estrus behavior frequently observed in mares during the transition period (February, March and April). In addition, a high proportion of these mares responded with regular estrus cycles post-treatment.

SPECIFIC USES FOR ALTREN® (altrenogest) SOLUTION 0.22%:

SUPPRESSION OF ESTRUS TO:

1. Facilitate attainment of regular cycles during the transition period from winter anestrus to the physiological breeding season. To facilitate attainment of regular cycles during the transition phase, mares should be examined to determine the degree of ovarian activity. Estrus in mares with inactive ovaries (no follicles greater than 20 mm in diameter) will be suppressed but these mares may not begin regular cycles following treatment. However, mares with active ovaries (follicles greater than 20 mm in diameter) frequently respond with regular post-treatment estrus cycles.
2. Facilitate management of the mare exhibiting prolonged estrus during the transition period. Estrus will be suppressed in mares exhibiting prolonged behavioral estrus either early or late during the transition period. Again, the post-treatment response depends on the level of ovarian activity. The mares with greater ovarian activity initiate regular cycles and conceive sooner than the inactive mares. Altren® (altrenogest) Solution 0.22% may be administered early in the transition period to suppress estrus in mares with inactive ovaries to aid in the management of these mares or to mares later in the transition period with active ovaries to prepare and schedule the mare for breeding.
3. Permit scheduled breeding of mares during the physiological breeding season. To permit scheduled breeding, mares which are regularly cycling or which have active ovarian function should be given Altren® (altrenogest) Solution 0.22% daily for 15 consecutive days beginning 20 days before the date of the planned estrus. Ovulation will occur 5 to 7 days following the onset of estrus as expected for non-treated mares. Breeding should follow usual procedures for mares in estrus. Mares may be regulated and scheduled either individually or in groups.

ADDITIONAL INFORMATION:
A 3-year well controlled reproductive safety study was conducted in 27 pregnant mares, and compared with 24 untreated control mares. Treated mares received 2 mL altrenogest solution 0.22%/110 lb body weight (2x dosage recommended for estrus suppression) from day 20 to day 325 of gestation. This study provided the following data:

1. In filly offspring (all ages) of treated mares, clitoral size was increased.
2. Filly offspring from treated mares had shorter interval from Feb. 1 to first ovulation than fillies from their untreated mare counterparts.
3. There were no significant differences in reproductive performance between treated and untreated animals (mares & their respective offspring) measuring the following parameters:
   - interval from Feb. 1 to first ovulation, in mares only.
   - mean interovulatory interval from first to second cycle and second to third cycle, mares only.
   - follicle size, mares only.
   - at 50 days gestation, pregnancy rate in treated mares was 81.8% (9/11) and untreated mares was 100% (4/4).
   - after 3 cycles, 11/12 treated mares were pregnant (91.7%) and 4/4 untreated mares were pregnant (100%).
   - colt offspring of treated and control mares reached puberty at approximately the same age (82 & 84 weeks respectively).
   - stallion offspring from treated and control mares showed no differences in seminal volume, spermatozoal concentration, spermatozoal motility, and total sperm per ejaculate.
   - stallion offspring from treated and control mares showed no difference in sexual behavior.
   - testicular characteristics (scrotal width, testis weight, parenchymal weight, epididymal weight and height, testicular height, width & length) were the same between stallion offspring of treated and control mares.

REFERENCES:
Shoemaker, C.F., E.L. Squires, and R.K. Shideler, 1989.

Safety of Altrenogest in Pregnant Mares and on Health and Development of Offspring. Eq. Vet. Sci. (9); No. 2: 69–72.

Squires, E.L., R.K. Shideler, and A.O. McKinnon. 1989.

Reproductive Performance of Offspring from Mares Administered Altrenogest During Gestation. Eq. Vet. Sci. (9); No. 2: 73–76.

WARNING:
For oral use in horses only. Keep this and all other medications out of the reach of children. Do not use in horses intended for human consumption.

HUMAN WARNINGS:
Skin contact must be avoided as Altren® (altrenogest) Solution 0.22% is readily absorbed through unbroken skin. Protective gloves must be worn by all persons handling this product. Pregnant women or women who suspect they are pregnant should not handle Altren® (altrenogest) Solution 0.22%. Women of child bearing age should exercise extreme caution when handling this product. Accidental absorption could lead to a disruption of the menstrual cycle or prolongation of pregnancy. Direct contact with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

INFORMATION FOR HANDLERS:
WARNING: Altren® (altrenogest) Solution 0.22% is readily absorbed by the skin. Skin contact must be avoided; protective gloves must be worn when handling this product.

Effects of Overexposure
There has been no human use of this specific product. The information contained in this section is extrapolated from data available on other products of the same pharmacological class that have been used in humans. Effects anticipated are due to the progestational activity of altrenogest.

Acute effects after a single exposure are possible; however, continued daily exposure has the potential for more untoward effects such as disruption of the menstrual cycle, uterine or abdominal cramping, increased or decreased uterine bleeding, prolongation of pregnancy and headaches. The oil base may also cause complications if swallowed.

In addition, the list of people who should not handle this product (see below) is based upon the known effects of progestins used in humans on a chronic basis.

PEOPLE WHO SHOULD NOT HANDLE THIS PRODUCT:

1. Women who are or suspect they are pregnant.
2. Anyone with thrombophlebitis or thromboembolic disorders or with a history of these events.
3. Anyone with cerebral-vascular or coronary-artery disease.
4. Women with known or suspected carcinoma of the breast.
5. People with known or suspected estrogen-dependent neoplasia.
6. Women with undiagnosed vaginal bleeding.
7. People with benign or malignant tumors which developed during the use of oral contraceptives or other estrogen-containing products.
8. Anyone with liver dysfunction or disease.

Accidental Exposure
Altrenogest is readily absorbed from contact with the skin. In addition, this oil based product can penetrate porous gloves. Altrenogest should not penetrate intact rubber or impervious gloves; however, if there is leakage (i.e., pinhole, spillage, etc.), the contaminated area covered by such occlusive materials may have increased absorption. The following measures are recommended in case of accidental exposure.

Skin Exposure: Wash immediately with soap and water.

Eye Exposure: Immediately flush with plenty of water for 15 minutes. Get medical attention.

If Swallowed: Do not induce vomiting. Altren® (altrenogest) Solution 0.22% contains an oil. Call a physician. Vomiting should be supervised by a physician because of possible pulmonary damage via aspiration of the oil base. If possible, bring the container and labeling to the physician.

Store at or below 25° C (77° F). Reclose tightly.

HOW SUPPLIED:
Altren® (altrenogest) Solution 0.22% (2.2 mg/mL). Each mL contains 2.2 mg altrenogest in an oil solution. Available in 1000 mL and 150 mL plastic bottles.

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Approved by FDA under ANADA # 200-620 04/2019

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Altren® (altrenogest) Solution 0.22% is contraindicated for use in mares with a previous or current history of uterine inflammation. Talk to your veterinarian about proper use and safe handling of Altren. Avoid skin contact and always wear protective gloves when administering. Pregnant women, or women who suspect they are pregnant, should not handle Altren. Refer to the package insert by visiting www.aurorapharmaceutical.com for complete product information.

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For more information on Altren® consult your veterinarian or equine health care professional

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A limitation of radiography is the inability to distinguish cartilage from other soft tissue opacities of the joint

Better scientific understanding of equine joints figures to provide better outcomes on the track

joints of healthy racehorses."

Study organizers wanted to evaluate the influence of training on body surface temperature on the joints of racehorses and did so by measuring temperatures with infrared thermography. Fourteen Thoroughbreds were used in the study, and they were monitored for three months. During that time each horse had six imaging sessions where the temperature of its forelimb and hindlimb joints was taken before training and just after training.

"Joint temperature of limbs increased significantly after training," concluded researchers. "Environmental temperature had a statistically significant influence on surface temperature over the joints. The lowest surface temperatures were recorded over the metacarpophalangeal and metatarsophalangeal joint and the highest temperatures in the shoulder, elbow, hip, and stifle joint.

"The metacarpophalangeal and metatarsophalangeal joints warmed the least during training but were influenced the most by differences in environmental temperature. The surface temperature difference before and after training is an important indicator of the thermoregulatory response to exercise in racing horses. Understanding surface temperature changes in response to regular training is necessary for future studies on diagnosing injuries of joints."

With better scientific understanding comes the opportunity for better outcomes. For individuals, it is important to work with a veterinarian to find the best path forward for a specific horse, as the information, technology, and treatment options available constantly evolve in terms of preventative and recovery measures. BH

TOP: ANNE M. EBERHARDT; BOTTOM: COGLIANESE PHOTOS

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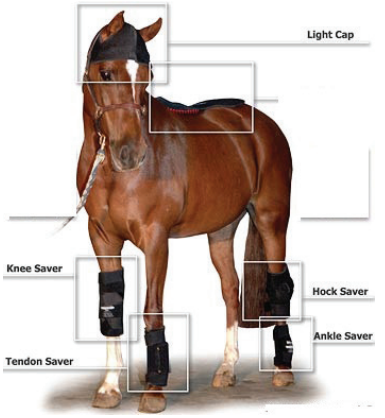

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