Review on cowdriosis (heartwater)

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Summary: Heart-water is a notifiable disease that listed by the World Organization for Animal Health. It is caused by *Ehrlichia ruminantium*, obligately intracellular gram negative bacteria in the order of *Rickettsiales* and family *Anaplasmataceae*. It is one of the most important diseases of livestock in Africa. Heartwater is readily introduced into new regions by infected animals or ticks. The known and potential host ticks are widely distributed and can be found on a variety of animals including reptiles. This disease is tick borne and most wildlife species appear to carry the organism asymptomatically and serves as reservoir. The most susceptible animals are those exotic breeds and immunocompromised pregnant animals, where as the endogenous breeds have adaptive immunity for cowdiriosis. Due to this reason, the disease has great economic importance in African countries including Ethiopia. Even though there is no enough research taken place, few researches indicates that cawdriosis is one of the most economic important of blood parasite (pathogen) in Ethiopia. The incidences of cawdriosis from 80 animals 30 of them develop *Ehrilichiosis* with an average incidence of 12.33 cases per annum or 15% of the herd. Its economic loses per three years of study can also reach up to 141,924.20 Birr (7884.67 USD). This disease cannot be diagnosed easily on a field as well as in laboratory. The most effective way to tackle the disease is prevention before occurrence, through tick control and vaccination rather than treatment. Generally, the disease hinders the modern farm system development in African countries, including Ethiopia. Therefore, this paper prepared to highlight the current status of Cowdriosis for alarming the professionals to emphasize on this disease.
[Gebrehiwot T, Endris A, Gashaw E, Oumer M, Tsehaye N, Andinet Y, Demeke D, Fentahun M, **A review on mechanism of anemia in trypanosomiasis.** *J Am Sci* 2017;13(8):99-106]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org. 12. doi:10.7537/marsjas130817.12.

Key Words: *Amblyoma verigatum, Cowdriosis, Ehrlichia ruminantium, Tick*

1. Introduction

Heartwater is a lethal bacterial disease of domestic and some wild ruminants. It is caused by the intracellular rickettsia *Ehrlichia ruminantium* which is transmitted by ticks of the genus *Amblyomma*, and the disease is prevalent wherever the tick vectors occur (Allsopp, 2015). The organism is transmitted by three host ticks of the genus *Amblyomma* (Mahan *et al.,* 2008**).**

The global Distribution of Cawdiriosis is in the geographical sites that are suitable habitat for *Amblyomma species* includes: Sub-Saharan Africa, Caribbean Islands and Tick introduction into U.S. also possible but in Asia Not reported (CFSPH, 2015). In tropical and subtropical areas, the disease is endemic and results in considerable economic losses due to loss of production, treatment costs and reduced initiatives for the upgrading of local breeds of livestock with more susceptible exotic breeds (Swai *et al*., 2008).

The disease in the sub-Saharan region is also one of the major causes of stock losses, and it has been that more than 150 million animals are at risk in the area (Minjauw and McLeod, 2003). In the horn of Africa except Djibutti Cowdriosis cases were reported in all of the countries currently.

In Ethiopia both the vector (*Amblyoma varigatum)* and the disease *(cowdiriosis)* are reported from different studies in different geographical areas like in and around Addis Ababa, Oromia region (Ahmed, 2016). The economic impact of *Cowdriosis* in Ethiopia includes expense for treatment of diseased animal, loss due to death (annul 8. 1%), due to reduction in milk production, as well as wastage for tick control. According to Achenef *et al.* (2014) approximately 141,924.20 Birr (7884.67 USD) was lost during the three year period of study. therefor livestock in Ethiopia is under the high risk of Cowdriosis Then the objective of this paper:

- To review current status of cowdriosis for alarming the professionals to emphasize on this disease and to state its social and economic impact.
- To highlight the existed prevention and control methods of the disease, its cause and the vector.

2. Cowdriosis (Heartwater)

2.1 Aetiology

2.1.1. The history of Cowdriosis and its namoculature

The disease was known in South Africa for nearly 90 years before the causative organism was identified in 1925 as a rickettsia, originally named *Rickettsia ruminantiu.* The name was later changed to *Cowdria ruminantium f*rom which arose the term '*cowdriosis*'. Molecular phylogenetic studies of the Rickettsiales in the 1990s uncovered the real evolutionary relationships within the order and the organism was reclassified *as Ehrlichia ruminantium* in the *Family* Anaplasmataceae (Dumler, 2001). *Ehrlichia ruminantium*, which is transmitted by Amblyomma ticks, is obligately intracellular, infects cattle, sheep, goats and some wild ruminants, and is frequently fatal. A comprehensive account of the history and biology of *E. ruminantiu* an be found elsewhere (Allsopp, 2010).

Codriosis is listed by the World Organization of Animal Health as a notifiable disease. Heart water is caused by *Ehrlichia ruminantium* (formerly *Cowdria ruminantium*) Order *Rickettsiales*, *Family Anaplasmataceae* which is Small, Gram negative, pleomorphic coccus, and obligate intracellular parasite. The Strains of *E. ruminantium* are very diverse and vary in virulence: while some strains are highly virulent, others appear to be less-pathogenic. *E. ruminantium* has a high level of genomic plasticity. Several different genotypes can co-exist in a geographical area, and may recombine to form new strains. It multiplies in vascular endothelial cells throughout the body to cause severe vascular compromise. And usually occurs in clumps of from less than five to several thousand organisms within the cytoplasm of infected capillary endothelial cells, and can be detected in brain smears by light microscopy (OIE, 2009). This rickettsia causes the blood vessels to "leak" that is why it has the name heartwater disease- fluid leaks out and fills the sack around the heart (Sornsin, 2005).

2.1.2. Characteristics of the agent

Temperature: Heat labile and loses its viability within 12–38 hours at room temperature. Infective stabilities can be cryopreserved in DMSO (dimethyl sulphide) or better yet in sucrose potassium phosphate-glutamate medium (SPG). Infective half-life of thawed stabilate kept on ice is only 20–30 minutes (OIE, 2009).

Ehrlichia ruminantium does not survive for long periods outside of a host. Blood exposed to sunlight will lose infectivity in ≤ 5 minutes. In a dead animal, the organism will typically begin to die in ≤ 6 hours. However, infectivity may be prolonged for as long as 72 hours under cold conditions (4°C [39.2°F]). *Ehrlichia ruminantium* is also susceptible to treatment with antimicrobials, particularly tetracycline derivatives (Thomas and Angela, 2010).

Therefore, the main source of the agent's are: *Amblyomma* ticks fed on an infected vertebrate host, Whole blood or plasma of vertebrate host during the febrile reaction, but highest levels of agent occur during the second or third day of fever as well as Colostrum containing infected cells (reticulo-endothelial cells and macrophages) has been speculated (OIE, 2009).

2.2 Species affected

Heartwater-endemic areas, populations of indigenous cattle (par-ticularly B indicus–type breeds), goats, and sheep typically are more resistant to infection than are non-indigenous breeds. (Yunker, 1996) This suggests that genetic factors are important in these ruminants for the de-velopment of immunity against heartwater. Immunity is probably maintained best in sheep; in contrast, immunity is of the shortest duration in cattle (Plessis, 1987).

Reports of possible fatal heartwater in an African elephant (*Loxodonta africana*) and a dromedary camel are unproven, and could have occurred from other causes **(**CFSPH, 2008).

2.3. Epidemiology

Factors relating to the tick vector, causative organism and vertebrate host are important in the epidemiology of heartwater. These include possible immunological strain differences of *E. ruminantium,* availability of wild animal reservoir hosts or vectors for the organisms, infection rate in ticks, age and genetic resistance of domestic ruminant populations, seasonal changes influencing tick abundance and activity, and the intensity of tick control (AU-IBAR, 2013).

Heartwater occurs only where its *Amblyomma* tick vectors are present. Where, are generally found at elevations from sea level to 2,590 m (8,497 feet). These species are more abundant during the rainy season and in environments typified by continuous high relative humidity. Because the seasonal reproductive activity of these ticks is regulated by rainfall and warm temperatures, heartwarter-endemic regions are found in a variety of habitats in sub-Saharan Africa and from wooded savanna to bushland to wooded grassland that comprise tropical, humid temperate, dry subhumid, semiarid, and arid climates. Outside of Africa, suitable habitat for *A. variegatum* ticks can be found in the Caribbean islands, southeastern United States, and Latin America (Thomas and Angela, 2010). But to date, heartwater has never been reported in Asia despite the presence of many species of *Amblyomma* ticks. The U.S. has two tick species, *A.maculatum* and *A. cajennense*, that have been shown experimentally to

be capable of serving as vectors of heartwater (Sornsin, 2005).

According to AU-IBAR (2011), cowdriosis is present in Africa south of the Sahara and the islands of the Comoros, Zanzibar, Madagascar, Sao Tomé, Réunion, and Mauritius. Many ruminants, including some antelope species, are susceptible (table1).

Table1. Cowdriosis reported from Ethiopian Neighbouring Countries (AU-IBAR report of 2011)

Country	Outbreaks	Cases	Deaths	Slaughtered
Eritrea	1	7	7	7
Kenya	60	94	5	0
Somalia	63	396	80	4
Sudan	4	106	47	0

Source: AU-IBAR (2013)

From the report stated at the table above Ethiopia is at the risk of Cowdriosis since itsneighbouring countries are affected with cowdriosis. The causative agent of Cowdriosis is extreme fragile, due to this case the principal mode of bringing the disease into an area is by introduction of infected ticks or carrier animals. It is not known for how long wild or domestic ruminants can be a source of infection for ticks in nature, but it may be many months. Ticks are a robust reservoir of *E. ruminantium,* and infection can persist in them for at least 15 months. Careful dipping and hand-dressing followed by inspection to ensure the absence of ticks is recommended for animals in transit to heartwater free areas (OIE, 2009).

2.4. Transmission

Heartwater is primarily transmitted by ticks of the genus *Amblyomma* (Family Ixodiae). At least twelve species of *Amblyomma* ticks have been shown to transmit *Ehrlichia ruminantium. A. variegatum* (tropical bont tick) is the most important transmitter of heartwater (Sornsin, 2005). Transracial transmission occurs in these ticks, which can remain infected for at least 15 months. Transovarial transmission is not thought to be epidemiologically significant in nature, although it has been demonstrated in the laboratory **(**CFSPH, 2015).

Amblyomma ticks are three-host ticks whose life cycles may take from 5 months to 4 years to complete. Because the ticks may pick up the infection as larvae or nymphs and transmit it as nymphs or as adults, the infection can persist in the tick for a very long time (Loftis *et al.,* 2006). The immature stages feed on a wide variety of livestock, wild ungulates, ground birds, small mammals, reptiles and amphibians (Bindy *et al, 2011*).

2.4.1 Vector biology

All the vectors of heartwater are three-host ticks which become infected within two to four days of feeding on infected hosts. Transstadial transmission of *E. ruminantium* takes place between nymphal and adult ticks but transovarial transmission does not occur in the field. Infected nymphs and larvae only become infective in the following instar, and infective nymphs or adults transmit *E. ruminantium* to susceptible hosts without losing the infection (Allsopp, 2015).

Fig 2. *A. variegatum* (*Bindy et al*., 2011).

2.5. Morbidity and Mortality

The mortality rate in susceptible livestock ranges from <10% to 90%, depending on the animal's species, breed and previous exposures. Morbidity and mortality rates are normally higher in non-native than indigenous breeds, and sheep and goats are usually affected more severely than cattle. For example, up to 80% of merino sheep may die, but the mortality rate can be only 6% in Persian or Afrikander sheep. Angora and Saanen goats are also very susceptible to heartwater, while Creole goats in Guadeloupe are resistant. In cattle, reported mortality rates can be as high as 60-80%, and *Bos indicus* breeds tend to be lessseverely affected than *Bos Taurus*. Genetic resistance has been demonstrated in some breeds. Young ruminants are resistant to heartwater **(**CFSPH, 2008).

2.6. Clinical signs

Infected domestic ruminants show a wide range clinical signs. The incubation period in natural infections is 2-3 weeks (Hein, 2005). Clinical signs depend on the stage of disease of the animal at the time of examination (ie, peracute, acute, subacute, or subclinical form) (Mahan, 2008). But the most common form of heartwater is the acute form. This is seen in both nonnative and indigenous domestic ruminants. Animals develop an acute high fever, loss of appetite, depression, respiratory distress and rapid breathing. Nervous system signs can soon follow and be seen as excessive chewing movements, eyelid twitching, and tongue protrusion, walking in circles and with a high stepping gait. Some animals may have convulsions. Galloping movements and

"moonstruck" (head tipped back and eyes rolled back) are commonly seen before death, which can occur in less than one week (Bindy *et al, 2011*). peracute form is relatively rare and has usually been observed in European breeds of cattle (B taurus), goats, and sheep introduced into heartwater-endemic areas of Africa. Furthermore, sudden death is a characteristic of the peracute form. However, livestock owners that closely and frequently observe their animals may find that high fever, respiratory distress, terminal convul-sions, and diarrhea may precede death during the per-acute form (Thomas and Angela, 2010).

Clinical signs of the subacute form include prolonged fever and coughing due to fluid in the lungs- pictured right along with fluid in the chest cavity. Animals may show mild incoordination and either recover in 1-2 weeks or die (Sornsin, 2005). Mild or subclinical infections may be seen in young calves, lambs or kids; partially immune livestock; some indigenous breeds; and some wild ruminants. Transient fever may be the only clinical sign in this form, which is known as **"**heartwater fever**"** (CFSPH, 2015**).**

Post-mortem lesions**:** The gross lesions in cattle, sheep, and goats are very similar. Heartwater derives its name from one of the prominent lesions observed in the disease, namely pronounced hydropericardium. The most common macroscopic lesions are hydropericardium, hydrothorax, pulmonary oedema, intestinal congestion, oedema of the mediastinal and bronchial lymph nodes, petechiae on the epicardium and endocardium, congestion of the brain, and moderate splenomegaly (Bezuidenhout *et al., 1994*). However, some or all of these signs may be absent and a final diagnosis depends on the observation of *E. ruminantium* colonies in the cytoplasm of brain endothelial cells. The normal procedure is to examine brain smears after staining with Diff-Quik (a commercial Giemsa-type stain) (Allsopp, 2015).

2.7. Diagnostic tests

Polymerase chain reaction (PCR) tests can identify *E.ruminantium* in tissues at necropsy, or in the blood of live animals from just before the onset of the fever to a few days after recovery. Whole blood in anticoagulant: In clinically ill animals, blood samples should be collected for PCR. Nucleic acids may sometimes be detected in the blood or bone marrow of carrier animals, but this is inconsistent. Loop-mediated isothermal amplification (LAMP) assays to detect *E. ruminantium* have also been published (CFSPH, 2008).

Observing *E.ruminantium* colonies in stained (Giemsa) smears from the brain or intima of blood vessels at necropsy also used for Cowdriosis diagnosing. The best samples to collect from the brain are well-vascularized portions such as the cerebrum, cerebellum or hippocampus. *E. ruminantium* occurs as clumps of reddish-purple to blue, coccoid to pleomorphic organisms inside capillaryendothelial cells. These organisms are often found close to the nucleus, and may be in a ring or horseshoe. But Colonies can be difficult or impossible to find in some animals that have been treated with antibiotics (Loftis *et al.,* 2006).

*E.ruminantium*can also be detected in formalin-fixed brain sections using immunoperoxidase techniques, including combined immunostaining and counterstaining with hematoxylin. These techniques are more likely to detect small numbers of organisms than the use of tissue stains alone **(**CFSPH, 2015). Serological diagnosis of heartwater is subjective and should be used only as a tool of investigation rather than for definitive diagnosis. Definitive diagnosis should be by demonstration of the organism on a smear, or by PCR amplification using the pSC20 nested PCR assay and corroborated by isolation of *E. ruminantium* in endothelial cell culture **(**(Mahan *et al.,* 2000).

2.8. Differential diagnosis

The peracute form of Heartwater can be confused with anthrax. The acute nervous form of Heartwater can be confused with rabies, tetanus, chlamydiosis, bacterial meningitis or encephalitis, cerebral trypanosomiasis, piroplasmosis or theileriosis, and various intoxications such as with strychnine, lead, organophosphates, or chlorinated hydrocarbons. Heavy helminth infestations may produce accumulations of fluid similar to those seen in Heartwater. Arsenical poisoning may resemble the enteric form of the disease, and certain poisonous plants (e.g., Cestrum laevigatum, Pachystigma spp., Pavetta spp.) (Loftis *et al.,* 2006).

2.9. Treatment

Tetracyclines are reported to be effective in the early stage of the disease. Prolonged treatment and/or larger doses may be needed if treatment is started later, and antibiotics are often ineffective once neurological signs appear. Sulfonamides also have activity against *E.ruminantium* but are less effective. Treated animals can remain carriers (CFSPH, 2008**).**

Antimicrobial drug treatmentalone is not always successful in later stages. Animals in to endemic areas may be protected by prophylactic treatment with tetracycline. In endemic regions, heartwater can be prevented by tick control and vaccination (Hein *et al*., 2005).

2.10. Prevention and control

There are various prevention and control methods that can be applied to heartwater Prevention. Preventative measures for heartwater include implementation of an effective tick control program

using acaricides which are products aimed at killing ticks as well as regular inspection of animals and pastures for ticks (Bindy *et al, 2011*). Vector control measures aimed at eradication of Amblyomma ticks by acaricide treatment of cattle and small ruminants has been successful in the context of small islands in the Caribbean but is not achievable in most situations and even not recommended. In endemic areas of Africa, tick levels are now allowed to remain at levels high enough to permit re-infection of immune animals to boost the immunity and develop endemic stability (Hein**,** 2005). Tick controle can be achive by several methods in Ethiopia such as biological methods (using predator birds), using acaricides, using mecanical removal, bu avoiding of vegetation suitable habitate for tick (Ahmed, 2016).

The establishment of endemic stability, using limited dipping to control ticks to manageable levels, can be highly successful, but if herd immunity breaks down then serious disease outbreaks can occur. This can happen if new immunotypes enter an area where immunity to the previously prevalent strains offers no or limited protection, and such a situation is very likely to occur as widespread genetic exchange is known to take place in the field between different strains of *E. ruminantium* (Allsopp and Allsopp, 2007).

E. ruminantium cannot survive outside a living host formore than a few hours at room temperature. For this reason, heartwater is usually introduced in infected animals, including asymptomatic carriers, or in ticks. In heartwaterfree countries, susceptible ruminants from endemic regions are tested before importation. Because serology is unreliable, the World Organization for Animal Health (OIE) currently recommends that the epidemiology of the importing herd be studied to determine that the animals and their resident ticks are free of *E. ruminantium*, and that the animals also be repeatedly tested by PCR ***(***Hassan and Salih., 2013***).***

2.10.1. Vaccination

Animals recovering from the natural disease or from artificial exposure to the organism are solidly immune for a variable period ranging from 6 months to 18 months. Animals exposed to reinfection during this period of resistance will have their immunity reinforced and will remain immune as long as they are periodically reinfected and there is now conclusive evidence that immunity to Heartwater is T-cell mediated (Plessis, 1991).

There are three possible types of improved vaccine each of which has received extensive attention from researchers: inactivated, live attenuated, and recombinant. We will survey recent developments and future prospects for all three types (Collins *et al.,* 2003**).**

Table 2. Immunising ability of attenuated *E. ruminantium*

Species	Dose of elementary bodies	Route	Challenge	Protection (%)
Merino sheep	1.1 x 105	iv	Homologous	100
Merino sheep	Various	iv	Heterologous (five different strains)	100
Merino sheep	6.7 x 105	sc	Homologous	83
Merino sheep	2.6 x 105	im	Homologous	80
Boer goats	Various	iv	Homologous	100
Angora goats	0.9 x 104–1.3 x 105	iv	Homologous	90
Friesian cattle	1.7 x 105–2.2 x 106	iv	Heterologous (Gardel)	83

Note: All animals were needle challenged with blood stabilates of virulent *E. ruminantium*
Source: (Zweygarth *et al*. 2008)

2.11. Zoonotic potential

Despite the ability of E ruminantium to infect human endothelial cells in vitro, (Tustin and Kriek, 1993) humans are thought to be resistant to E ruminantium infection. However, fatal *E ruminantium* infection has been reported (Louw *et al.,* 2005)). In 4 humans in South Africa all 4 of these people initially had clinical signs consistent with viral encephalitis. *Ehrlichia ruminantium* infection was strongly suggested on the basis of DNA-sequence evidence for this organ ism obtained from all 4 people and the presence of brain lesions that are typical of those seen in domestic animals infected with this rickettsia. Panola Mountain *Ehrlichia*, which may yet be proven to be another strain of *E ruminantium*, might also emerge as a cause of zoonotic disease in the United States within the geographic distribution of its tick vec -tor, *A americanum*. Recently, a human was infected with this disease agent after a tick bite. (Reeves *et al.,* 2008).

2.12. Economic and social importance

Heartwater is a serious economic problem wherever it occurs, in an enormous area covering most of sub-Saharan Africa, its offshore islands, and several islands in the Caribbean. The disease generally prevents livestock farmers from upgrading their herds to modern high-yielding breeds, as these

are more susceptible to infection than traditional stock breeds, which often have a measure of resistance (Allsopp, 2015). Losses in commercial systems were 25 times greater than losses in the communal system. The greatest components of economic loss were control (acaricide - used to kill ticks) costs (76%), followed by milk loss (18%) and treatment cost (5%). (CFSPH, 2006). Since heartwater is so common in the endemic areas of Africa, farmers are usually unwilling or unable to pay for definitive diagnoses, so it is difficult to quantify the economic impact of the disease. The only estimates in the literature apply to the Southern African Development Community, where total animal production losses from the disease are thought to average US$48 million annually (Allsopp, 2015**).**

3. Cowdriosis In Ethiopia

3.1 Epidemiology

Even though there is no enough research taken place, few researches indicates that cawdriosis is one of the most economic important of blood parasite (pathogen) in Ethiopia. The incidences of cowdriosis from 80 animals 30 of them develop *ehrilichiosis* with an average incidence of 12.33 cases per annum or 15% of the herd (Achenef *et al., 2014*). In another study taken place in Oromia region shows that from 120 Amlyoma ticks that has been collected from both exotic and indigenous cattles for the examination of *Ehrilichia ruminantum* with in the ticks using semi-nested PCR. 10 of them or 8.3% were positive for *ehrilichia ruminantum (*Gedyon *et al., 2014).* The major risk factors such as age, season and sex were considered as factors that may contribute for the occurrence of the disease (Achenef *et al., 2014*).

3.2. Economic impact

The economic impact of *Cowdriosis* in Ethiopia includes expense for treatment of diseased animal, loss due to death (annul 8. 1%), due to reduction in milk production, as well as wastage for tick control. According to Achenef *et al.* (2014) approximately 141,924.20 Birr (7884.67 USD) was lost during the three year period of study.

4. Conclusions

Cowdriosis is rhicketicial disease which is one of the OIE listed disease. The disease has a threat of heavy economic losses due to affecting the production and reproductivity of the high producing capacity of exotic breeds. It has also high waste of finance for treatment of affected animals as well as for controlling of *Amblyoma* tick distribution. Even though there is no enough research taken place, few researches indicates that Cowdriosis is one of the most economic important of blood parasite (pathogen) in Ethiopia. The incidences of Cowdriosis from 80 animals 30 of them develop *Ehrilichiosis* with an average incidence of 12 cases per annum or 15% of the herd. Its economic loses per three years of study can also reach up to 141,924.20 Birr (7884.67 USD). The disease is able to transport from one country to country by infected animals and recovered animals which are serve as reservoir. Wildlife are also serves as reservoir and spread the disease when the wildlife contact with the domestic animals during grazing time by the means of tick.

Based on the above conclusions the following recommendations are forwarded:

- Restrict animal movement from one area to another area.
- Importing animals should be certified by authorized veterinarian.
- Quarantine station should be available at the ports of import.
- Vaccination against the particular strain of endemics.
- Tick control strategy should be developing.
- Veterinarian and farmers as well as concerned bodies should report to the federal (national) authority imidatly during observing the sign of Cawdriosis.
- Rule and regulations should be settled and implemented against illegal livestock import and export practicesa.
- Avoid the contact between wild life and domestic animals which has still a little awareness in most of African societies.
- Careful dipping and hand-dressing followed by inspection to ensure the absence of ticks is recommended for animals in transit to heartwater free areas.

Acknowledgments

All praises be to God, the most gracious, merciful and self sufficient, master of the universe.

We would like to express our deep appreciation and heartfelt gratitude to our advisor Dr.Wudu Temesgen for his advice, motivation, suggestion and devotion of time for correcting this paper.

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8/25/2017