Review

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Toxoplasmosis in Nigeria: the story so far (1950–2016): a review

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Abstract: Toxoplasmosis is caused by intracellular protozoan parasite, *Toxoplasma gondii* (Nicolle et Manceaux, 1908). Cats and other felids are the definitive hosts. It could be transmitted to man and animals by consumption of infected undercooked meat and contaminated food items including drinking water. Results of toxoplasmosis epidemiological surveys in animals and humans in South-West, North-West, North-East and North-Central Zones of Nigeria have been reported with greater impact on the health of pregnant women and HIV-infected individuals. Meanwhile, studies in states within the South-South and South-East Zones are relatively scanty or non-existent. Overall, the seroprevalence of human toxoplasmosis in Nigeria is estimated at 32% with the following reports for North-West (32%), North-East (22%), North-Central (24%) and South-West (37%). Information on the genetic diversity of isolates of *T. gondii* in humans and animals including the role of the environment in transmission and maintenance of the disease are highly needed.

Keywords: *Toxoplasma gondii*, seroprevalence, humans, animals, environment, Nigeria

Toxoplasmosis is caused by an apicomplexan protozoan parasite, *Toxoplasma gondii* (Nicolle et Manceaux, 1908). This parasite infects warm-blooded animals and only felids (cats) harbour the sexually reproductive stage. Its medical and veterinary importance was not known for long time (Wolf et al. 1939).

Nigeria being a tropical country has a climate suitable for the survival of parasitic agents of most infectious diseases. Also, among other factors, its socio-economic state has enhanced the rate and distribution of most neglected tropical diseases. Data on toxoplasmosis are sparse (Hotez and Kamath 2009, Hammond-Aryee et al. 2014) and this is largely attributed to scanty epidemiological survey on the parasite and its associated signs and symptoms. Consequently, there are no control measure in place, the likely reason Nigeria might be highly rated on the toxoplasmosis scale burden among the league of endemic countries. This paper therefore reviews data from Nigeria and highlights areas that would require further investigation.

Clinical manifestations

Toxoplasma gondii can persist in the host for a long period even to an entire life of the host (Pusch et al. 2009). It rarely causes illness in an immune-competent person and only few infected individuals present signs or symptoms of infection (Remington 1974). Some of the signs and symptoms include listlessness, fatigue, headache, excessive sweating, muscle and joint pains. There may be self-lim-

iting fever, retinochoroiditis and sometimes maculopapular rash. These manifestations may last for one or several weeks (Benenson et al. 1982, Luft and Remington 1984, Bowie et al. 1997, Ho-Yen 2001).

Due to the overlap of symptoms of toxoplasmosis and other infectious diseases like malaria, influenza, viral syndromes and mononucleosis, acute toxoplasmosis is often undiagnosed and thus under-reported. A person is suspected to be infected with *T. gondii* if the forgoing symptoms are accompanied with a cervical lymphadenopathy (McCabe et al. 1987, Dubey and Beattie 2010). However, clinical manifestations are reportedly common among certain age-groups particularly < 15 years (Beverley et al. 1976).

Complications are pronounced in persons with compromised immunity with malignancies and anti-tumour therapy or acquired immune deficiency syndrome (AIDS). In individuals with AIDS, this disease could lead to death (Luft and Remington 1992, Luft et al. 1993). However, symptoms such as encephalitis, seizures hemiparesis, subacute focal deficits anxiety, loss of consciousness, headache and other mental disturbances could ensue following cyst rupture in the brain (Weiss and Kim 2007, Emeka et al. 2010, Philib-Ephraim et al. 2015).

In addition, the signs and symptoms of congenital toxoplasmosis are microcephaly or hydrocephaly, abortion, still birth, ocular malformation (such as chorioretinitis), hepatosplenomegaly, lymphadenopathy and central nervous system (CNS) abnormalities (Lynfield and Guerina 1997,

Martin 2000). In animals, anorexia, weight loss, fever and abortion have been reported (Pereira-Bueno et al. 2004, Dubey and Beattie 2010).

History of toxoplasmosis in Nigeria

The human population estimate for Nigeria is over 160 million. The landmass is divided into six Geopolitical Zones comprising 36 States and a Federal Capital Territory. Toxoplasmosis in Nigeria was first diagnosed and reported in a 3-year old boy on 3 February 1950 (Jelliffe 1951). He was diagnosed of macrocephaly, hydrocephaly with radiological evidence of intracranial calcification and cardiac enlargement. In 1972, a study reported a reaction rate of 95% to a dye test among Nigerians with chorioretinitis and 72% among control group. That study concluded that many cases of focal chorioretinitis were related to *T. gondii*. However, with the limitation of the dye test, it was impossible to confirm the causative agent of this clinical case (Olurin et al. 1972).

In 1973, Emejuaiwe and colleagues reported an increasing incidence of human toxoplasmosis in one of the South-East states (Emejuiwe et al. 1976). After that, there was an outbreak of animal toxoplasmosis in a buffalo ranch in the defunct Bendel state, now Edo and Delta states with 11 recorded deaths out of 200 animals (Falade 1978). In the midst of the outbreak, tissue cysts were found in the brain of a buffalo with appreciable levels of antibody in other examined animals (Falade 1978). In 1978, a report linked abortion in animals to toxoplasmosis and prevalence of 4% was recorded in goats from Oyo state (Falade 1978).

So far, several investigators have used an array of methods in screening for *T. gondii*. A recap of how it all started shows that the dye test developed by Sabin and Feldman (1948) was the first employed method in Nigeria (Jelliffe 1951, Iverson et al. 1960, Falade 1978, Arene 1984). The indirect haemagglutination test (IHA) was the second most applied method (Aganga and Ortese 1984). These two continued to be the choice diagnostic tools for almost four decades.

In recent times, the study of toxoplasmosis has employed serological methods like the enzyme linked immunosorbent assays (ELISA) or enzyme immunoassay (EIA), an indirect fluorescent antibody test (IFAT), modified agglutination test (MAT), haemagglutination test (HA), latex agglutination test (LAT) (Aganga and Ortese 1984, Ishaku et al. 2009, Kamanai et al. 2010a, Alayande et al. 2012a, Ogoina et al. 2013, Oyinloye 2014, Ayinmode et al. 2015) and Western blotting technique (Ayinmode et al. 2016a). Meanwhile, the use of molecular tools has been sparingly applied (Kamani et al. 2010b).

Prevalence among Nigerians

Several investigations have been carried out in Nigeria to ascertain the seroprevalence of *T. gondii* in humans. Some researchers have determined the seroprevalence in pregnant women and HIV/AIDS individuals as well as providing empirical data on the influence of certain demographic characteristics on the disease epidemiology. From

Fig. 1. Seroprevalence of infection with *Toxoplasma gondii* in humans according to geopolitical zones (2005–2015). Abbreviations: NW – North-West; NE – North-East; NC – North-Central; SW – South-West; SS – South-South; SE – South-East.

the first detection till now, varying seroprevalence has been reported in different parts of the country.

In association with pregnancy, reports of seropositivity have been documented (Olusi et al. 1996, Akinbami et al. 2010, Alayande et al. 2013, Oyinloye et al. 2014), including the isolation of *T. gondii* from placenta and/or amniotic fluid of women with frequent abortion histories. Other conditions resulting from *T. gondii* infection have been described to include neonatal deaths, prematurity, hydrocephalus, retained placenta and stillbirth (Aganga et al. 1990, Onadeko et al. 1996, Deji-Agboola et al. 2011, Alayande et al. 2013).

Recently, having analysed pooled reports across geopolitical zones in the last decade (2005–2015), South-West and North-West Zones showed high prevalence (Fig. 1). However, the prevalence in South-South and South-East Zones is largely unknown (Figs. 1, 2). Generally, in zones where reports of human seroprevalence were recorded, there is a mean prevalence of 32% and infection could be asymptomatic, chronic or acute.

In the Niger Delta region, 1 650 individuals were investigated for antibodies against *T. gondii*, 972 (59%) presented significant antibody titres with prevalence rate varying among different age groups. The highest prevalence occurred among 16–20 years age group (75%) and the lowest among individuals of over 50 years old. Children 1–5 years old had a relatively high prevalence rate of (66%) (Arene 1986a). Kamani et al. (2009) reported a positive correlation between the mean antibody titre and the age of the subjects with highest seroprevalence among age group 51–60 years and lowest in <21 years. More females (65%) were observed to be infected than males (53%) (Arene 1986a). An increased seroprevalence was observed in pregnant women in comparison to immunocompromised and immunocompetent individuals (Uttah et al. 2013).

Fig. 2. Studies of *Toxoplasma gondii* in humans and animals in Nigeria. Indicated on the map are the six geopolitical zones of Nigeria. **North-West:** Sokoto, Kaduna, Katsina, Kano, Zamfara, Kebbi, Jigawa, **North-Central:** FCT (Federal Capital Territory), Kogi, Kwara, Nassarawa, Niger, Benue, Plateau, **North- East:** Yobe, Borno, Gombe, Taraba, Bauchi, Adamawa, **South-West:** Ekiti, Oyo, Ogun, Lagos, Osun, **South-South:** Edo, Delta, Cross river, Rivers, Bayelsa, Akwa Ibom, **South-East:** Imo, Anambra, Abia, Enugu, Ebonyi.

Table 1. Prevalence of toxoplasmosis in North-West Zone.

Location	Number tested	Method	Prevalence (%)	Target	Study population/description	Reference
Kano	17	Dye test	88	H	Chorioretinitis patients	Iverson et al. 1960
Kano	751	Dye test	3	A	Goats	Falade 1978
Kano	829	HA	17	A	Goats, sheep and camel	Okoh et al. 1981
Kano	20	HA	35	H	Women attending antenatal care and male with various health histories	Okoh et al. 1981
Zaria	70	IHA	37	A	Horses	Aganga et al. 1983
Zaria	250	IHA	45	A	Chicken	Aganga and Belino 1984
Kaduna	834	IFAT	39	H	Pregnant women	Aganga et al. 1990
Kaduna	374	EIA	29	H	Pregnant women attending antenatal care	Ishaku et al. 2009
Sokoto	75	LAT	50	H	Abattoir workers	Alayande et al. 2012b
Sokoto	84	LAT	26	H	HIV infected individuals	Alayande et al. 2012c
Sokoto	200	LAT	7	A	Cats	Alayande et al. 2012a
Sokoto	173	LAT	28	H	Pregnant women with obstetric history	Alayande et al. 2013
Kaduna	219	ELISA	39	H	HIV-infected individuals	Ogoina et al. 2013
Kano	273	ELISA	34	H	HIV-infected pregnant women	Yusuf et al. 2016

HA – haemagglutination assay/test; IHA – indirect haemagglutination test; IFAT – indirect fluorescent antibody; EIA – enzyme immunoassay; LAT – indirect, latex agglutination test; ELISA – enzyme linked immunosorbent assays; H – humans; A – animals.

Table 2. Prevalence of toxoplasmosis in North-East Zone.

Location	Number tested	Method	Prevalence (%)	Target	Study population/description	Reference
Borno	180	ELISA	24	H	Indigenes of Maiduguri	Kamani et al. 2009
Borno	168	LAT	25	A	Dogs	Kamani et al. 2010c
Borno	105	LAT	36	A	Cats	Kamani et al. 2010a
Borno	76	PCR	0	A	Sheep and goats	Kamani et al. 2010b
Borno	168	LAT	25	A	Dogs	Kamani et al. 2010c
Borno	105	LAT	36	A	Cats	Kamani et al. 2010a
Borno	76	PCR	0	A	Sheep and goats	Kamani et al. 2010b
Borno	190	ELISA	22	H	HIV-infected individuals	Goni et al. 2012
Borno	90	ELISA	22	H	Pregnant women attending antenatal care	Oyinloye et al. 2014

ELISA – enzyme linked immunosorbent assays; LAT – indirect, latex agglutination test; PCR – polymerase chain reaction; H – humans; A – animals.

Table 3. Prevalence of toxoplasmosis in North-Central Zone.

Location	Number tested	Method	Prevalence (%)	Target	Study population/description	Reference
Niger	176	N/A	79	H	Hospital patients	Sixl et al. 1987
Benue	606	N/A	44	H	Child-bearing age women	Olusi et al. 1996
Plateau	363	N/A	32	H	HIV-infected individuals and apparently healthy individuals	Uneke et al. 2005
Plateau	144	ELISA	21	H	Indigenes of Kwal district	Uneke et al. 2007
Ilorin	60	ELISA	42	H	HIV individuals with related eye disease	Adepoju et al. 2007
Benue	360	ELISA	11	H	HIV/AIDS-infected individuals	Amuta et al. 2012
FCT	216	LAT	32	H	Pregnant women, immunocompromised and immunocompetent	Utah et al. 2013

N/A – not available; ELISA – enzyme linked immunosorbent assays; LAT – indirect, latex agglutination test; FCT – Federal Capital Territory; H – humans.

Table 4. Prevalence of toxoplasmosis in South-West Zone.

Location	Number tested	Method	Prevalence (%)	Target	Study population/description	Reference
Oyo	6	Dye test	84	H	Toxocara positive individuals	Wiseman and Woodruff 1970
Oyo	97	Dye test	4	A	Goats	Falade 1978
Oyo	162	ELISA	68	H	Patients with lymphoid neoplasia and controls	Ekweozor et al. 1994
Oyo	352	Dye test	75	H	Pregnant women	Onadeko et al. 1996
Oyo	1922	MAT	32	A	Food and companion A	Okewole 2007
Lagos	179	ELISA	41	H	Pregnant women	Akimbami et al. 2010
Lagos	460	EIA	50	H	HIV infected individuals and controls	Akanmu et al. 2010
Lagos	83	N/A	86	H	HIV infected individuals	Oshinaike et al. 2010
Lagos	276	EIA	33	H	Pregnant women attending antenatal	Deji-Agboola et al. 2011
Lagos	380	ELISA	54	H	HIV infected individuals	Osunkalu et al. 2011
Oyo	50	MAT	66	A	Free range chicken	Ayinmode and Dubey 2012
Oyo	512	ELISA	23	A	Cattle and pigs	Onyiche and Ademola 2013
Lagos	242	ELISA	41	H	HIV infected individuals	Okwuzu et al. 2014
Lagos	382	LAT	24	H	School children	Gyang et al. 2015
Lagos	840	ELISA	34	H	HIV infected individuals and controls	Okwuzu et al. 2015
Ekiti and Ondo	278	MAT	20	A	Slaughtered dogs	Ayinmode et al. 2015
Oyo, Osun and Kwara	226	MAT	4	A	Cats from animal markets	Ayinmode et al. 2016b
Oyo and Ogun	223	Western blot	19	A	Urban and rural dogs	Ayinmode et al. 2016a

ELISA – enzyme linked immunosorbent assays; MAT – modified agglutination test; EIA – enzyme immunoassay; N/A – not available; LAT – indirect, latex agglutination test; H – humans; A – animals.

Table 5. Prevalence of toxoplasmosis in South-South Zone.

Location	Number tested	Method	Prevalence (%)	Target	Study population/description	Reference
Rivers	300	Dye test	33–82	A	cattle, sheep, goats and pigs	Arene 1984
Rivers	1 650	Dye test	59	H	Indigenous Niger Deltans	Arene 1986a
Rivers	104	Dye test	100	A	Rodents	Arene 1986b

H – humans; A – animals.

In relation to co-infection with other parasites, there are limited studies from Nigeria (Wiseman and Woodruff 1970). However, with respect to infection with HIV, there are relatively more reported studies (Tables 1–5). HIV-positive patients with *T. gondii* have shown higher seropreva-

lence than only *T. gondii*-positive persons (Okwuzu et al. 2015). Similarly, in an earlier investigation, the prevalence of *T. gondii* in HIV-infected patients was higher than that of healthy individuals (Uneke et al. 2005). A study carried out in the capital city (Abuja) involving pregnant women,

HIV-infected, hepatitis patients and immuno-competent individuals showed a seroprevalence of 32% (Uttah et al. 2013). Studies have also revealed increased seroprevalence among the aged that are HIV positive (Osunkalu et al. 2011, Amuta et al. 2012, Okwuzu et al. 2015). Toxoplasmosis in HIV patients is majorly due to reactivation of latent infection with *T. gondii* due to immune suppressions that results in the activation of tissue cysts (Luft and Remington 1988).

Case reports

Case studies and reports from virtually all parts of the country have been documented, with severe mental complications linked to infection with *T. gondii*. This was observed in a case-control study carried out in Benin, a metropolis in Nigeria on patients presented to a mental facility on grounds of psychotic disorder. It was demonstrated that patients had a significantly higher IgG specific to *T. gondii* (see James et al. 2013).

In immunocompromised individuals positive of HIV, case reports of complications have also been linked to infection with *T. gondii*. One of such is a report of a stroke-like presentation of cerebral toxoplasmosis in two HIV-infected individuals. The first case revealed a markedly raised IgM and IgG in a 30-year-old right-handed Nigerian woman with a one week history of inability to move the left upper and lower limbs. The second case showed an increased IgG in a 35-year-old female with a two day history of left-sided weakness affecting her leg and arm and focal seizures involving her left upper limb (Philip-Ephraim et al. 2015).

A brain CT scan of the first case revealed a rounded ring enhancing hypodense lesion in the parafalcine zone of the right parietal cortex, while in the second case, hyperdense lesion with perilesional oedema in the right thalamus were highlighted (Philip-Ephraim et al. 2015). Cerebellar toxoplasmosis (Emeka et al. 2010), encephalitis caused by *T. gondii* and other central nervous complications have also been reported (Ogun et al. 2005, Adeniji-Sofoluwe 2014, Ogoina et al. 2014). Report of toxoplasmosis prevalence in South-East is scanty. Meanwhile, case report of a 17-month old with generalised lymphadenopathy, weight loss, ganglia calcification and microcephaly has been documented (Amadi et al. 2015). Other case control study on peripheral lymphadenopathy has been reported by Adenij and Anjorin (2000).

Prevalence in animals

Virtually all warm-blooded animals are susceptible to infection with *T. gondii*. From the very first record of toxoplasmosis in dog (Falade 1978), subsequent investigations have been carried out on other animals. Aganga et al. (1981) demonstrated *T. gondii* in cattle, sheep, goats and swine from northern Nigeria. *Toxoplasma gondii* in sheep, goats, pigs and camel from nomadic flocks, veterinary clinic and a ranch have been reported (Okoh et al. 1981). Of the 70 horses from Kaduna, Kano and Jos assembled in Zaria for the annual national polo games tournament, up to 26 (37%) were seropositive with the highest serological titre of 1 : 256. Afterwards, they reported a 45% prevalence

of 250 local breed of chicken from Zaria (Aganga and Belino 1984).

Similarly, reports among cattle, sheep, goats and pigs from the Niger Delta region indicated 33%, 75%, 82% and 69% seroprevalence rates, respectively (Arene 1984). There was also a report of 100% seroprevalence in West African rodent, *Thryonomys swinderianus* (Temminck), commonly called grass cutter, a highly cherished meat source (Arene 1986b). These are clear indications that these animals could be potential reservoirs of *T. gondii* (Arene 1984, 1986a,b).

In addition, the presence of antibodies specific to *T. gondii* in meat indicated an average prevalence of 17% (Osiyemi et al. 1985). Investigations of free-range chickens have also revealed infection with *T. gondii* (see Ayinmode and Dubey 2012). Recently, oocyst shedding potentials of cat were examined and it was reported that seropositive cats did not shed oocyst (Alayande et al. 2012a). The authors thus assumed that the cats may have concluded the process of oocyst shedding before being caught (Dubey 1994). Meanwhile, in another study, oocysts from faeces of 3 of 14 stray cats (21%) were isolated with seropositives of 13/15 (87%) (J.A.O. – unpubl. data). Kamani et al. (2010a) also reported seropositive cats from northwestern Nigeria with higher prevalence in older and stray cats. In sheep and goats, an investigation using Polymerase Chain Reaction (PCR) to detect *T. gondii* in a total of 327 tissues from 45 and 31 of the caprine and ovine aborted fetuses respectively were negative (Kamani et al. 2010b). A summary of the overall prevalence of *T. gondii* in animals from 1970 until now is thus documented in this review according to geopolitical zones (Tables 1, 2, 4, 5).

Risk factors

The high seroprevalence level in children has been shown and this is mostly due to their relatively frequent contact with contaminated soil (Gyang et al. 2015). In relation to occupation, farmers are at higher risk of acquiring infection than others (Deji-Agboola et al. 2011). Other occupational persons at relatively higher risk are abattoir workers who sometimes eat meat during evisceration (Alayande et al. 2012b), a practice that might allow ingestion of tissue cysts from infected animals.

Also, higher seroprevalence of antibodies against *T. gondii* was associated with the habit of eating rodents (Olusi et al. 1994). Accordingly, keeping of animals like cats and dogs could portend possible risk in the spread of the disease. For instance, a report has shown 46% seroprevalence of those persons that keep cats/dogs was significantly higher than those living without cats/dogs (16%) (Uttah et al. 2013). Also, public health implications have been argued by Okoli (1985) from the point that some ethnic groups in Nigeria could be at high risk of infection because they consume dog meat known to be susceptible. Additionally, the consumption of infected undercooked beef is a risk factor in acquiring *T. gondii* (see Akanmu et al. 2010). Other risk factors include source of water, drinking unpasteurised cow milk (Okwuzu et al. 2015) and consumption of raw vegetables (Deji-Agboola et al. 2011).

***Toxoplasma gondii* in the environment**

In Nigeria, there is a dearth of information on the level of environmental contamination by oocysts of *T. gondii* as very limited surveys have been carried out. Meanwhile, it has been shown that high seroprevalence of *T. gondii* in cats might be an indication of contaminated environment (Kamani et al. 2010b, J.A.O. – unpubl. data). Although oocysts of *T. gondii* are shed for a period of time during the life of the cat, millions of shed oocysts survive for months or even up to a year in the soil (Dubey and Beattie 2010). In addition, seroprevalence of *T. gondii* in free range chickens could also indicate soil contamination (Cañón-Franco et al. 2014). The role of the environment in the transmission and maintenance of the disease should be further explored.

Genetic diversity of strains of *T. gondii* in Nigeria

Worldwide genotypic analysis of isolates of *T. gondii* has identified a population structure consisting of three widespread clonal lineages termed types I, II and III (Howe and Sibley 1995, Ferreira Ade et al. 2006). However, recent studies have revealed a greater genetic diversity of *T. gondii*, particularly isolates from domestic animals in Brazil, China, Iran and wildlife in USA (Lehmann et al. 2006, Dubey et al. 2011, Khan et al. 2011, Su et al. 2012, Tavalla et al. 2013, Tian et al. 2014). It has been reported that strains of *T. gondii* are correlate with the parasite's clinical presentations and virulence (Howe and Sibley 1995, Dubey et al. 2014, Sánchez et al. 2014, Ferreira Ade et al. 2006). In Nigeria, there are no reports on the genetic diversity of strains of *T. gondii*. This information is critical to effectively tackle the disease. Presently, the use of molecular tools in the analysis of this parasitic infection is scantily applied. This is evident by the limited available literature (Kamani et al. 2010b). The reasons for the scanty application of molecular technique include lack of funds, poor electricity supply for specimen preservation and lack/

shortage of trained personnel. The use of this approach cannot be overemphasised giving the advantages it has over other diagnostic techniques (Ajmal et al. 2013, Wang et al. 2014, Palos Ladeiro et al. 2015, Shapiro et al. 2015).

From the available seroprevalence reports, it is obvious that toxoplasmosis is highly neglected as a human disease, being relatively under-studied among the numerous parasitic diseases endemic in Nigeria. Thus, there is need to evolve a comprehensive toxoplasmosis survey on both human and animal population across the country so that a near-accurate, reliable data are available. This is critical towards providing information on areas where control efforts should be prioritised and targeted. Meanwhile, clinical symptoms of this disease have been found to overlap with those of other infections, which often leads to misdiagnosis and increased morbidity. It is therefore suggested that diagnosis/test should be routine in health centres. Accordingly, due to limited resources, children and pregnant women should be given priority both in diagnosis and treatment. Critically, strains of *T. gondii* have been reported to correlate with different clinical presentations, it is necessary to investigate the genetic diversity of *T. gondii* in Nigeria. Studies have shown that water, food and soil are sources of infection (Du et al. 2012, Ajmal et al. 2013, Gotteland et al. 2014), but a dearth of information exists for Nigeria as regards the role played by these matrices in the disease epidemiology. More studies on environmental factors should be carried out to determine the degree to which these factors could influence transmission of *T. gondii*. Importantly, it is highly desirable to largely make available prevalence data of toxoplasmosis on humans and animals in the South-South and South-East Zones.

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