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REVIEW: "A LITTLE DRAGON-DRANCUCULUS MEDINENSIS" A SURPRISE IN THE MICROBIAL WORLD

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ABSTRACT

"Skin" the physical barrier which protects everyone from the external exposed environment.This review aim to discuss about the issue that, what happen when this barrier is used to get rid of a foreign body unnaturally by the parasite .Drancuculus medinensis have been well known and documented from thousands of years. The life cycle wheels of this parasite comprised of six development stages , which chooses a year to complete .Through worm pushes her way , which results in break open the blister to expel her larvae in external environment. At this point of time, the host's immune system begins to respond against infection.The inflammatory reaction, severe pain in infected site and crippling effects last for months and can become permanents, depending on where the worm emerges .The most interesting characteristics of this nematode infection is that, the in spite of having strong defensive immune system mechanisms of human this organism gets stay and grow for a year without any kind of recognition and realization by host.There is the probability that, this pathogen might be down-regulating the host's immune response and adapt very quickly to the responses thrown by the host's body.This organism can even use what body sends out to locate them to there advantage by disguising themselves as part of the host's body, or using the antibodies as a food source. This review focuses on the biological immunological information about the Dracunculiasis and also focus on the detection, diagnostics and treatment measure taken till date. We have also discussed in brief about the epidemiology of the disease, its social and economical impacts during outbreaks and theinitiative eradication program.It also summarizes the broader benefits uniquely linked to interventions against dracunculiasis. The latest biotechnology and bioinformatics techniques can be used to investigate this disease in more comprehensive way to develop the synthetic vaccine or drugs against this disease, to eradicate it completely.

Keywords: GWD,dracunculiasis Antigen, Immunoproteomics, Antigen, Antibody, Bioinformatics, Epitopes.

I. INTRODUCTION OF *DRACUNCULIASIS*

Dracunculiasis/ dracuncalosismost commonly known as Guinea warm disease .The parasite agent is *Dracunculusmedinesis.* These nematodes (round worm) is the largest tissue parasite and only species within the genus Dracunculuswhich infect humans.This bears the characteristics of the water borne filarial nematode.There are other human filarial nematods which is responsible for subcutaneous filariasis like *Loa loa* (the African eyeworm), *mansonellastreptocerca*and*Onchocerca volvulus* (river blindness).The first known mention of the disease worm in the Turin Papyrus in the fifteenth century BC by the Egyptian; it has been since described by ancient Greek, Roman,Arab,Persian and Indian physicians [Groove D.1900].The common name of Dracunculiasis is derived its prevalence on the Gulf of Guinea[Palmer P,Reeder M.2001].The single uterus of

female GWD parasite makes it different from other filarial parasite ,where as filarial have two.The outbreak of this disease is generally somehow associated with places where there is a lack of clean drinking water eg. Step wells in India, covered cisterns in Iran, and ponds in Ghana .The life cycle usually involves copepod intermediate host.They are parasite in the connective tissue or coelom of vertebrates.

1.1 Detection methods of Pathogen (GWD)

The realization of this disease becomes difficult because of its year and half incubation life cycle within the host body without showing any significant remarks and symptoms. After successful completion of the incubation period the mature female worm come towards the skin and startthe formation of a small round bulge on the skinby secreting an irritating chemical. This blisterappearance becomes the red flag of GWD infection. The blister rapture and the larvae starts releasing, this is only the point when the host's immune system recognizes themas parasite and as foreign and then an allergic reactionbegins. The symptoms expressions of the infection are highfever, redness, swelling, and pain (at the site of the worm's location on the skin, usually on the lower extremities) [Muller, (1979); Molyneux et al., (2004)]. Theadditional systemic symptoms include vomiting, nausea, diarrhea and dizziness. These symptoms can persist for several days and later on begin to diminish when the worm is manually forced out by slowly winding it onto a stick over several weeks to months [Molyneux, D., D. Hopkins, N. Zagaria. 2004].Sadly, but there is no other way of detecting this guinea worm disease other than the noticing a blister somewhere on the lower extremities. Till date thereis no confined assay tests has been design for its early onset stages detection.

1.2 Classification, Morhology and Biology of D. medinensis

The filarial nematode Dracunculus genus belongs to the **family:*Dracunculidae*,superfamily: *Dracunculoidea*, order: *spirurida*, class: *chromadorea*,phylum: Nematoda**.The *Dracunculidae*family consists of two genera *Dracunculus*and *Micropleura*. Furthermore, *Dracunculus* genus can be divided differently into 12 species:***Dracunculusbrasiliensis,Dracunculusdanomensis,Dracunculusdoi,Dracunculusfaelleborni,Dracunculusglobocephalus,Dracunculushoudemeri,Dracunculusinsignis,Dracunculuslutrae,Dracunculusmedinensis,Dracunculus mulbus,Dracunculusoesophageus, Dracunculusophidensis***[Muller ,R., 1971; Muller,R., 1979; Jones,h.I., and Mulder, E.,2007;Moravee,F, and Santos C.P, 2009].From all the *Dracunculus*species ,only *D.medinesis* (a little dragon from Medina) infects humans,causes**"Guinea Worm Disease"**.Whereas, other *Dracunculus*species generally resides in the internal tissues and body cavities of non-human mammals and reptiles(snake and turtles)[Bimi,L., et al., 2005].*Dracunculusmedinensis* taxon closely related to the *Filarioidea* under the order *Spiruida* .These two super-families members share similar type of general morphology and all are tissue dwelling parasites,ovoviviparous, and their intermediate hosts is arthropod.Frequently, these two taxa discussed broadly in filarial nematode group[HotezPJ., 2013].*Dracunculus*species can be described differently from true filarial nematodes based on certain specific morphological features, molecular phylogenies and life cycle .The relationship between Dracunculusspp. and other spirurids (*B.malayi* and *W.bancrofti*) can be distinguish based on the phylogenetic analysis of 18srRNA gene sequence .It has been seen that in spite of having similar morphological characteristics *D. oesophageus*reprents different species from human Guinea worm. The dracunculiasisprecisely denoted as both a disease of poverty and cause of poverty. Sometimes, due to outbreaks of this peculiar disease, large number of village population get into trap, which ultimately results in

agricultural productivity, maternal and child health and the school attendance [Ruiz-TibenE,HopkinsDR.,2006].In numberof all neglected tropical disease, it has a low mortality, but morbidity is considerably high due to huge disabilities which was physically and economically devastating[Ramakrishna J,Brieger WR, Adeniyi JD, Kale OO.(2006-2007);FeaseyN,Wansbrough-Jones M ,MabeyDC,SolomonAW.Neglected tropical disease.Br Med Bull 2010;93:179-200].The adult female worm measures upto one meter in length, whereas, the male measures about 2cm[*Molyneux, D., D. Hopkins, N. Zagaria., 2004]*.

1.3 Properties of *Dracunculus medinensis* Environments

Dracunculusmedinensis thrivesin fresh water habitats usually in stagnant waters such as ponds, reservoirs, dried up pools in riverbeds, and dug up water holes. Reason behind to thrives in these kind of environment is that ,that the water never gets disturbed or moved and the larvae can able to multiply in the stagnant waters without any external disturbance. This kind of natural territory are mostly the reservoirs for copepods- the vector of *Dracunculusmedinensis* . The copepods eat the larvae and get infected with the disease they carry. The infected larvae survival is only last for an about only three days in the water before it dies and doesn't harm to the copepods even if they eat the dead larvae. The known reported cases of dracunculiasis in sub-Saharan Africa where the climate is found dry at least part of the year,which is the most favorable environment for worm [*Greenaway, 2004]*. This parasite can be ranked as a xenophile ,an obligate thermophile, because of its habitat which has mostly observed in the dry, warm places like - sub-Saharan Africa.

II. BIOLOGY OF THE PARASITE

The stagnant contaminated drinking water with infected copepode is the transmission source of the Dracunculiasis .The cyclops(The small water fleas)are the one which act as the intermediate host of pathogenesis of GWD. The moment when populationconsume this unfiltered water from stagnant pods or open a shallow well which is contaminated with infected copepods withpathogenicDraculiasislarvae.After ingestion, the cyclops dies by the stomach digestive juices which interns results in larvae release. This larvae penetrate the digestive wall into the body cavityand get entry in abdominal cavity and retroperitoneal space .The larvae develop and mature into adults ;after copulationthe ovoviviparous female grows upto 1 meter(60-100cm/3 feet) length, but only 1 to 2mm thickness in the subcutaneous tissue of skin and have survival upto 12 to 19 months .Whereas male dies soon after copulation with few months[Greenaway C., 2004].No symptoms manifest till a year or so .With 12 to 14 months after infection female worm .By the time produced millions of eggs in its uterus,and it gravid with microfilariae migrateand predominantly localized in the lower extremities(80-90%).After an incubation period the female worm release which induces a painful blister (1 to 6cm diameter) on the skin of lower limbs ; the person develop a slight fever , local skin redness , swelling and severe pruritus around the blister .The presence of other symptoms like diarrhea, nausea, vomiting and dizziness has been seen .The blister burst within 1 to 3 days and female worms one or more slowely comes out from the wounds which causes an excoriating burning sensation and pain [Miillner A, Helfer A ,KotlyarD.Oswald J, EfferthT(2011)].Immersing or pouring water over the blister provide pain relieve. But this the moment that adult female exposed to the external environment [Ruiz-Tiben E, Hopkins DR.(2006].And while emerging the limbs

in open water sources it recognizes the temperature difference and releases the milky white liquid in the water which contains millions of immature larvae , when larvae released in water are ingested by copepods where they mount twice and become infective larvae within two weeks [IriemenamNC,Oyibo WA, Fagbenro-BeyiokuAF.(2008].The cycle begins a new shift if the contaminateds drinking water is ingested by any individuals.[Hopkins DR,Ruiz-Tiben E, Downs P,Withers PC jr,Roy S. (2008); Muller R.(1985)][Fig. 6& Table:1].Once the blister comes in contact with the water it bursts and kill the worm and the infected larvae comes out its mouth into the water and the host wound. This is only the time when immune system of the host body recognizes it as the foreign body and start producing the immune responses against it by sending eosinophils, basophils, and other specialized granular cells to the scene (where the larvae have been released). They release toxic chemicals in attempt to destroy the invader. B- Cells then make antibodies specifically for the parasite. The antibodies then attach to the invader and act as signals and communicate to other immune system cells to destroy them. There is some evidence which suggest that the antibodies are used as a food source, and that the worms are able to trigger the immune system to make more antibodies. They can even disguise themselves as part of the host's body by displaying different proteins on their surfaces that identify them as part of the host [Molyneux, 2004]. It is a pretty nasty parasite, and investigations on still being made to really understand the mechanisms of this organism.The treatment measures includes the extraction of the worm manually and painkiller medication to ease the pain. It can take months to recover from the extracting of the worm mainly because one's need to be very carefully while extracting the worm slowly. With this fevers and wells and pain and the other symptoms with accompany the process until the worm is completely out. Secondary bacterial infections are also a problem with the lesions; the bacterial infections cause increased pain and may lead to locked joints or permanent crippling [Molyneux, 2004]. The infection is resolved and back to normal when the worm is completely extracted. As the body recovers it is important not infect the wound, and to properly filter water when using it. The guinea worm disease is not communicable, so the chances of contracting the disease are at none from person to person. Treatment measures in Africa are being practiced to reduce the number of cases as well as trying to eliminate this preventable disease.

Table 1-Life cycle stages of GWD

Stages	Table 1: Description
Stage 1	The host becomes infected when drinking unfiltered or untreated water which contains copepods with infective larvae from a local well or pond.
Stage 2	In the host body , the copepods were destroyed by stomach acid which interns release of the parasitic larvae .These larvae travel and penetrate and cross the peritoneal cavity to the subcutaneous tissues of intestine. At this stage larvae survive at and adapt quickly to the stomachs pH of acid. The phenomenon of the larvae survival at high acidic pH is still not clear, but some researcher believes that it is triggered by the copepods response to the changing conditions of its surroundings. To reach to the maturation stage by fooling host immune system and utilizing host's antibody as nutrient source , its takes one year in the lining of the intestine [Molyneux, 2004].
Stage 3	The fertilized female worm then migrates to the subcutaneous tissues of the skin, usually in the lower extremities. Again this whole process takes about a year, and the body still has not recognized the foreign body.
Stage 4	The worm then travels to the surface of the skin and dies by erupting and casing the uterus to expels all its contents (infective larvae), from the uterus, through the mouth which releases millions of larvae in a milky white substance [Molyneux, 2004]. This happens when the host comes in contact with water and the infective larvae are then released in it. This is the official point where the body then recognizes the parasite.
Stage 5	Copepods in water consume the infected larvae, they see them by the wiggling of their bodies and see them as food. The larvae can live in the water up to three days, if not consumed within those three days the larvae won't be as affective in infecting the copepod that eats it.
Stage 6	Larvae undergo two molts inside the copepod and then become a mature larva. The copepod is now ready to be consumed again by the host. The cycle of the *Dracunculusmedinensis* disease is repetitive.

III. IMMUNITY /IMMUNOLOGY OF PARASITE

The presence of different transmissional season of dracunculiasis provides an absolute occasion to narrate the variations in the humoral immune responses of infected individuals in relation to seasonality, or in relation to the time of patency of infection .The earlier studies conducted in northern Ghana , it was noticed that the infected people by dracunculus in edemic area had level of *D.medinensis* –specific antibodies (total, IgG1 and IgG4) during the time of patency, which were significantly higher than the levels measured in the same individuals eight months later, except for a few individuals who had developed a new patent infection [Bloch P,Simonsen PE, Vennervald BJ,(1993)].Whereas, variation in the IgE value is relatively negotiable and constant before,during infection and after the recovery.There is possibility that variation in antibody production is regulated by infected larvae (i.e. by transmission) and / or by adult worms (i.e. by patency) is still need to be clear.It is possibility that increased production of IgG1,IgG4 during the time of patency plays a role in blocking/protecting immune responses otherwise it could have killed ingested infected larvae [BlochP,Simonsen

E.PAUL,(1998)].The recent studies on response profile of guinea worm –specific cellular cytokines and reactivity evaluation of parasite-specific antibody subclass shows that the antigen-specific depression found similar for IFN-gamma and T-helper type2 cytokines IL-10 production in patent, post-patent and control individual .Whereas the Il-5 production was always the highest in control[Knopp S, Amegbo IK, Hamm DM,Schulz-Key H,BanlaM,Soboslay PT.(2008)].While examine for presence and localization of human serum albumin and immunoglobulins by immunoelectrophoretic technique, it's found that anti-human albumin antibodies reacted to the both stages of parasite which was recovered from infected individuals. Moreover, antigens mimicking human albumin and human immunoglobulins(isotypes Ig G) were found on the surface of adult female worm while conducting investigation through direct fluorescence . This investigation suggest that there might be possibility that due to occurrence of host-like compound on the parasites may be the reason for the parasite survival in host body and adaptation[Bloch P,LundM,VennervaldBJ,Simonsen PE(1999)].There are different types of immunodiagnostic methods has been used to detect the antibody response of the pre-patent and patent *D.medinensis* infected individual .There are the possibility to detect the early asymptomatic infection six month in prior before worm emerges from the infected individual through ELISA immunodiagnostic method [BapnaS,Eenapurkar DM(1996].The other specific and sensitive methods like dot-enzyme-linked immunosorbent assay(dot-ELISA) [Prakash D,Parab PB, Sharma RN.(1993)] , The Falcon assay screening test-enzyme-linked immunosorbent assay(FAST-ELISA) and the enzyme-linked immunoelectrotransfer blot(EITB) in order to assess adult worm antigen and their potential value. [FagbemiBO,Hillyer GV(1990)], Immunoelectroblotting and ELISA to identify non cross –reacting antigenic compound proven to be possible immunodiagnostic method for the detection of infection [Garate T, Kliks MM , Cabrera Z,Parkhouse RM(1990)].The usual property of dracunculiasis compare to other parasite there is less facts on the acquired immunity .It is difficult to detect by most standard tests such as blood and skin biopsy in prior to rupturing of blister.It is important to understand that how this parasite conceal themselves for more than an year incubation period in spite of having strong human immune defense system .The usual symptoms which arise from the parasite infection are the result of the interactions between the immune system and the parasite.

3.1 The expression of Immune System against the parasitic infection

- Firstly , through inflammatory responses by the esinophils, basophils and other specialized granular cells release their toxic chemical to attempt to destroy the invader. Later on after activation of B cells starts making antibodies against the specific parasite .These antibodies get attached to invader and act like a signal flare, and communicate the signals to other immune cells to destroy the foreign antigen .The immune cells like phagocytes, which travel throughout the body to phagocytos the foreign body. Which are not recognized as body belonging .These cells are much more effective at destroying any worms/parasite that labeled by antibodies.
- Secondly,there are proteins like complement protein which make up complement system that are able to recognize some general characteristics.This protein rarely capable to kill targets by forming a membrane attack complex. The amazing partis the interaction of worm and immune system .Both play hide and seek for their own mutual benefits .There is the probability by which the worm hide themselves from immune system by degrading the antibodies that attach to them.

Some evidence suggests that these worms used antibodies as their food source and that the worms are able to triggerthe immune system to produce large amount of antibodies.The parasites identify themselves through displaying different proteins on their surfaces which is recognized as a part of host. The parasite approach to hide them from host immune system: (1) They avoid the complement proteins from attaching to their surface; (2) They avoid killer protein to destroy them by releasing different types of molecules that act as decoys; (3) They also produce other proteins which protect them from phagocytosis.Although the process of accomplishment is still unknown.Nematodes generally infect the digestive system, but mostly the infections are asymptomatic, which signifies that these worms are capable of down regulation of host's immune responses against them.The analysis on adult guinea worm was conducted and found that there were morphine and its active opiate, alkaloid metabolite morphine-6-glucoronide (M6G).There might be a chance that this substances is utilized by*D.medinensis* to evade immune system.The lack of immune response to the living host is due to release of opiate chemical.Morphine release from parasitic nematodes cause immune cell inactivation, and when the worm recognized the immune cells it is triggered to produce the morphine.This can be one of the way by which parasite can suppress the immune system[Zhu,W., et. Al (2002)]. The other study conducted via ELISA and western blot technique is used to identify and detect the antibody responses of total and isotypes of IgG1,IgM,IgA and IgE).to conduct this test sera is collected from infected person at early and late in the peak transmission period and as well as from persons with signs of the disease and after the infection had cleared.The ELISA absorbance values obtained from sera of the same individualvaried between the two transmission seasons with the highest titers were obtained towards the end of the peak transmission period .Western blots were obtained while detecting the isotype of IgG4 antibodies.This study suggest that parasites use antigenic cloaking, that the reason that response of antibody not observed until the larvae are about to release from the infected person which makes difficult to detect at early onset of the disease.The antigenic cloaking is observed when Guinea worm binds to the hosts proteins to its surface, so that the host's immune system will identify it as self.This investigation prove the theory that when the parasite first gets entry to the host it is hidden from the host immune system completely and with respect to the time (progression)progress the host body starts realizing the foreign body.Although the worm is good at cloaking itself, and immune system starts to breakdown [Bloch,P., Simonsen,P.E.(1998)].“Autoimmunity/Allergy and hypersensitivity” Journals, discuss about the strengthen ofimmune system response and the obviousness of most common symptoms , When IgE binds to FcY receptors on the surface of mast cells, basophils and eosinophils which causes smooth muscle contraction of surrounding the airways and the gut.The strong muscular contractions leads to expel the parasites from the gut or airways which in terns increased local blood flow and can help to flush parasites out from the body with the combination action of IgE, mast cell , basophils, and eosinophils.Eosinophils utilize its FcE receptors for direct action against multicellular parasites .Whereas phagocytic cells cannotphagocytos the whole worm because of its large size in spite of large number of phagocytes. The mast cells responses is most frequently seen as a disadvantage in humans who rarely encounter parasites, because its triggers allergies and asthma.This is part of the Hygiene Hypothesis.Individual with these conditions produces IgE in responses to relatively harmless substances called allergens.Some individual produces very specific IgE which can leads to massive degranulation of mast cell, which show anaphylaxis [Capton.M,Kinet,J.(2005)].

IV. CLINICAL ASPECTS OF DRACUNCULIASIS

Clinical manifestation and pathogenesis pre-emergent female worms can move very easily through the connective tissues, while emerges to the surface, a few larvae gets released into the sub-dermis through a rupture at the anterior end. The blister which burst later in few days gives a shallow ulcer and a marked inflammatory response against the cuticle of the entire worm, which prevent its removal. The bacteriologically sterile blister fluid contains larvae surrounded principally by polymorphonuclear neutrophils with macrophages,lymphocytes, and eosinophils [Muller R.(1976)] The thousands of larvae when expels at the end of worms dries up, and this process is repeated a few times with the complete worm being extruded in a few weeks andsoon after that the lesion heals quickly. It has been observed in most of the cases the unfortunate secondarily infection and patients incapacitated severely.Ghana study suggest that 28% of patients continue in pain for 12 to 18 months after emergence of worm and 0.5% had suffered from permanent physical impairment due to "locked" knees or other joints related issues[Hours,M., and S.aincross.(1994)] .The study in Benin suggest that there eas 0.3% mortality from tetanus and septicemia [Chippaux,J.P., and A.Massougbodji.(1991)].In few cases female worms burst in the tissues which results in large pus-filled abscess and severe cellulitis, whereas, infertile females or males elicit a slight inflammatory reaction and sometimes calcify, showing up on a roentgenogram.In the Dracunculiasis parasitic infection very little evidence of acquired immunity has observed and there are possibilities of number of reinfection of the same individual. The response to the extrusion of larvae is indicative of an Arthus reaction followed by a delayed hypersensitivity response [Muller R.(1976)]

V. DIAGNOSIS OF DRACUNCULIASIS

In the endemicity area patients have no doubt about the diagnosis when, or just before the blister from the local itching and then sharp pain and often general allergic symptoms including urticarial follow. When the blister burst, cold water encourages release of larvae, which can be observed under low power microscope. Due to lack of pre-paten serum samples it's difficult to go ahead with immunodiagnostic methods and it not useful in practice because prepaten infection detection is notpossible.Enzyme –linked –immunosorbent assay can be used to detect the antibodies using whole worm antigen of infected individuals.Immunoglobin G4 is the most specific reaction can be used for disease diagnosis [Bloch , P., P.E.Simonsen, and B.J.Vennervald.(1993)] . This test can detect prepatent infections upto 6 months before emergence [Bapna,S., and D.M.Renapurkar.(1996)], in which case it could have practical important. The presence of circulating antigen evidences has not been detected [Bloch,P.,B.J.Vennervald, and P.E.Simonsen.(1998)].

VI. MEDICAL CARE OF DRACUNCULIASIS

Till date there is no accurate and efficient curative drug of vaccine is available against dracunculiasis[Muller R.1985].Immunity is not developed by the infected individual [Cairncross S, Muller R, Zagaria N.(2002); Issaka –Tinogah A, magnussenp,BlochP,Yakubu A.(1994);Greenway C. (2004)].The 'traditional treatment" i.e-pulling out the worm gradually and manually by winding the worm a few inches/centimeters on a small wooden stick each day, which is usually a very distress procedure [Hopkins Dr, Ruiz-Tiben E, Downs P , Withers PC Jr, Roy S .(2008)]. The traditional treatment customarily taken weeks to months to shed the complete length worm,

during this period the infected individual become often severely incapacitated. Furthermore, approximately every infected individual become victim/sufferer of secondary bacterial infection. The untreated lesions may cause several complication without antibiotics treatments alike erysipelas/cellutitis, abscesses, sepsis,septic arthritis and even trismus (lock jaw caused by tetanus infection)[Iriemenam NC ,OyiboWA,Fagbenro-BeyiokuAF(2008)].The infected patients needs to be careful and avoid breakdown of the worm in manual extraction procedure , by any chance of worm breaking can leads to intense inflammation because the left out part of dead worm disintegrated in the affected limbs .Treatment includes winding up worms out on stick, combined with clean dressing and antibiotic ointment to prevent from secondary bacterial infection and pain killer drug [Magnussen,p.,A.Yakubu, and P.Bloch(1994)]. Till date there is no evidence of any chemotherapeutic agent has a direct action against guinea worms, although various benzimidazoles may have an anti- inflammatory action, aiding elimination [Nwoke, B. E. (1992)].Similarly, aspirin is equally effective (Muller,unpublished). Study suggests, the effectiveness of Ivermectin against other nematodes but it has no effect on this organism nor in experimental infections [Eberhard, M. L., F. H. Brandt, and A. Hightower. (1990); Issaka-Tinorgah, A., P. Magnussen, P. Bloch, and A. Yakubu. (1994)].Chippaux[Chippaux, J. P. (1991)] found that treatment with mebendazole was associated with aberrant migration of the worms, which were more likely than usual to emerge at places other than the lower limbs.

6.1 Precaution Measures

- By avoiding contaminated source of drinking water
- Filtering unsafe water with cloth and fine-mesh strainers before consumption
- Use of drinking water from improved sources and controlling the vectors of transmission.

VII. EPIDEMIOLOGY, ECONOMICAL AND SOCIAL IMPACT DUE TO DRACUNCULIASIS

Dracunculiasis affect the masses / people that depend on contaminated drinking water sources, stagnant water source such as ponds.The 15% to 70% of the whole population gets affected by Dracunculiasis who depend on the stagnant water as the water sources. This is quite threaten, slow down the economic development and life style of infected individuals [OjoTB,OjoKK. (2011)].Reason is that it mainly affects the most productive people (12-50 years old), sustaining the disease-provertycycle.The evidence of the incidence variation has been seen between gender,age, occupation usually identified based on their water resource that from where they use water for drinking purpose.This disease transmission has got a seasonal pattern and closely related to rainfall .In arid areas; people get infected during the rainy season, when surface water is available. Along with this its infections has also seen in the wet regions during the dry season, when the consuming water source become scarce and stagnant.The disease transmission pattern and seasonal clinical manifestations often coincides with harvest or planting seasons and significantly affects productivity of agricultural product.For an example in Nigeria, due to this disease an approximately 11.6% decrease in total rice production. Estimately, the infected individual loose 100days of works per year, school attendance gets affect due to GWD. The world bank has estimated that the economicsrate of return on the investment in GWEP will be about 29% per year once the disease is eradicated[RamkrishnaJ.BriegerWR,Adeniyi JD, Kale OO.(1985-86)].

7.1 Socioeconomics Impact

In current scenario, the understanding has been development the only biological and technical feasibility is not the only criterion to consider before launching an eradication program, simultaneously costs and benefits are no less important[Dowdle, W. R., and D. R. Hopkins. ed. (1998)].The condition benefits of dracunculiasis in contrast to those of smallpox and polio will accrue almost exclusively to the population in which the disease is endemic[Aylward, B., K. A. Hennessey, N. Zagaria, J.-M. Olivé, and S. Cochi. (2000)].Earlier the dracunculiasis cases went unreported due to number of reasons.Most health centers had very little to offer the patient besides palliative treatment; most patients live in poor, remove rural areas and are hindered by their disease from walking to a health facility; and most recover spontaneously after expulsion of the worm .Nerthe less , the endemicity of affected area and is social , economical and educational I consequences and the cost incurred by the individuals, households, and communities suffer from it and can be substantial.

7.2 Economic Impact

The economic impact can be estimated by disease is multiplied the number of days of labour lost by the mean value of production per day /by the wage rate.A study in Nigeria based on the survey of 87 households, concluded that the three states of southern Nigeria of rice- growing area substained an $ 20 million annual loss due to Dracunculiasis[de Rooy, C., and L. D. Edungbola.(1988)].But this simple arguments, mobilized the senior politician of Nigeria for the disease eradication[Edungbola, L. D, et al.,(1992)].This type of calculation method has been argued previously used as oversimplified approach and is likely to overestimate the coast [Guiguemdé, T. R., et al.,(1986);Paul, J. E. (1988)] as it doesn't permits for the various coping strategies by which households respond to illness(such as abandoning other tasks and using additional labour) found to be common in peasant farming [Brieger, W. R., S. Watts, and M. Yacoob. (1989);Chippaux, J. P., A. Banzou, and K. Agbede. (1992)].

7.3 Disability of Infected individual

Dracunculiasis is rarely found fatal; the generous study conducted in India on medical records suggest 0.1% [Imtiaz, R., D. R. Hopkins, and E. Ruiz-Tiben. (1990) ;Rao, C. K., and G. V. M. Reddy. (1965) ;Singh, J., and N. G. S. Raghavan. (1957)].The social Impact of Dracunculuiasis is majorly attributable to the temporary disability suffered by the patient.The study conducted in Nigeria [Bhatt, A. N., and K. H. Palan. (1978);Smith, G. S., D. Blum, S. R. A. Huttly, N. Okeke, B. R. Kirkwood, and R. G. Feachem. (1989)]. Suggest that 58 to 76% of Guinea worm disease suffering patients are unable to leave their beds for approximately a month during and after emergence of the worm.The secondary infection of the lesion is the more severe and protracted disability had observed in half of the cases [Nwosu, A. B. C., E. O. Ifezulike, and A. O. Anya. (1982); Wurapa, F. K., D. W. Belcher, and W. B. Ward. (1975)].This disease impact is leads to temporary disability and reinforcement by the patency period of worm transmission,often peaking at the stage of the agricultural year when the labour is in maximum demand.Indeed , it has been claimed that the effect of the disease on agricultural productivity can be identified in satellite photographs [Ahearn, S. C., and C. de Rooy. (1996)].'The disease of the empty granary' is referred by the Dogon people of Mali [World Health Organization. (1998)].The Guinea worm disease effect doesn't end when the worm comes out and the sufferer returns to their normal life style.The study in Ghana [Hours, M., and S. Cairncross. (1994)] suggest that between 12 to 18 months after the

emergence of worms, 34% of patient find difficulty in performing everyday activities, reason may be due to pain attributable by its location and the date of onset to the episode of Guinea worm disease.But this types of disability is not necessarily to be permanents, it extends beyond the incapacity occurring worm emergence.

VIII. THE INITIATIVE ERADICATION PROGRAMS

Dracunculiasis is the one of the promising candidate for the successful eradication after its first pointed registered report [Muller, R. (1979)].It's prevention in seasonal campaigns permits a more intensive focus because of its markedly seasonal out breaks. The extensive effort for its prevention and control was taken care by the members of the Centers for Disease Controland Prevention(CDC),who began the advocacy campaign in 1980 and sustained over more than a decades and highly succeeded in convincing former U.S. president Jimmy Carter, the United Nations Children's Fund (UNICEF) Executive Board, the 1989 African Regional Committee of the World Health Organization (WHO), and the 1990 World Summit for Children to take up the challenge. The World Health Assembly in 1991 declared the eradicating dracunculiasis by end of 1995.In order to establish the eradication programe and to advocate about the disease the efforts needed to be replicated by each country [Edungbola, L. D., et al.,(1992)] .India taken the first initiative step in 1982 for eradication of GWD. Later on, Pakistan, Ghana, Nigeria, and Cameroon in 1990 taken the initiative of the eradication programe .In duration of 5 years, all the other known countries of endemicity also established national eradication programs, and substantial and progressive reductions in disease incidence were recorded each year, particularly at the beginning of the campaign. UNICEF and WHO maintained a joint technical team based in Ouagadougou, Burkina Faso, to provide technical support to national program coordinators in the region and to external support agencies(From 1992 to 1996).The resultant of this type of extensive eradication program from different supported agencies and the organization led to a remarkable decline of the number of cases almost 98%, from an estimated 3.3 millionworldwide in 1986 [Watts, S. J. (1987)] to only 75,223 cases reported in 2000.In 2000, Only 14 countries, all in Africa, reported indigenous case [WHO(2001)].The number of dracunculiasis cases reported worldwide in 2013 declined by 73% compared with 2012, and by 71% during January–June 2014 compared with January–June 2013. Transmission remains endemic in four countries, with South Sudan accounting for 70% of all reported cases during January–June 2014.Table 2&3)[Donald R. Hopkins et al.,(2014)][Table:2].

Country	Year 2011	Year 2012	Year 2013	Year 2014	Year 2015
South Sudan	1,028	521	113	70	5
Mali	12	7	11	40	5
Ethiopia	8	4	7	3	3
Chad	10	10	14	13	9
Total	1058	542	148	126	22

TABLE 2. Number of reported cases of dracunculiasis(From 2011-2015)

8.1 Interventions

In the direction of the dracunculiasis prevention it is necessary to select and develop the most effective interventions andsimultaneously the apt of field experience is more reliable than only having the theory or basic biology .A number of intervention would seems to be taken into the consideration:

(i) Supply of a safe water

(ii) To remove Cyclops, one's should drinking filtrated water

(iii)Investigation and identification of the active cases patients and its proper management

(iv) Advocating and aware patients to avoid contact with ponds

(v) Shooting down or withdrawing cyclops from ponds

IX. FUTURE PROSPECTIVE

There is the need for more timely and comprehensive methods of monitoring and control of the infectious disease. The Identification, screening, classification and high throughput screening of nucleotide and protein sequences of nematode protein needs to be carried out to analyze the toxin's sequences which is responsible for the disease progression using computational biology, advanced biological databases and bioinformatics. Advanced database management system (DBMS) will use for data mining and data manipulation. It leverages from recent breakthroughs in high-throughput molecular profiling of pathogen and text mining as well as upon the growing electronic sources of knowledge about the molecular epidemiology of pathogens with epidemic potential.The pathogen profiling and biosurveillance focused text mining tools can enable integrated infectious disease outbreak detection and response environments based upon bioinformatics knowledge models and measured by outcomes including the accuracy and timeliness of outbreak detection.This concept can be used for effectively in public health and disease management .To find the high throughput screening of sequence, sequence analysis, computational modeling and patterns comparison of protein, expression analysis, functional annotation and target confirmation for disease profiling .Identification and high throughput screening ofsequence that are involve in disease progression and may be novel therapeutic target for disease. It is plausible that there are minor differences in toxin/protein expression profile based on the disease aggressiveness, which may be exploited for development of biomarkers for different stages of disease. The proposed study will establish that modulation of expression profiles of disease related proteins and may be better therapeutic approach for disease treatment. Bioinformatics is being increasingly used to support target validation by pro-viding functionally predictive information mined from databases and experimental datasets using variety computational tools .Application of structural and functional genomics and proteomics approaches allow high-throughput expression profiling in human disease Presently available immunoproteomics validation techniques and strategies can play an import role diagnosis and developing a therapeutic methods ,drug or vaccine against numerous pathogen /disease.Drug discovery depends on well integrated data management in order to identify drug targets and in determining drug-gene interaction. By determines the molecular processes involved in disease progression incisively and ultimately brings a new prospect in the field of therapeutic targets and treatments.

9.1 Abbreviations

Cyclops: The small water fleas

Dot-ELISA: dot-enzyme-linked immunosorbent assay

FAST-ELISA): Falcon assay screening test-enzyme-linked immunosorbent assay

EITB: Enzyme-linked immunoelectrotransfer blot

M6G: morphine-6-glucoronide

GWEP-Guinea worm eradication program

CDC: Centers for Disease Controland Prevention

WHO: World Health Organization

UNICEF: United Nations Children's Fund

DBMS: database management system

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