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REVIEW: CHAGAS DISEASE

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ABSTRACT

There are several species of trypanosomes, which are single-celled organisms. Some affect primarily animals, but some are a significant cause of human illnes. Trypanosomes are transmitted by insect bites; Chagas disease is transmitted by bites of the reduviid bug. It is estimated that 16 to 18 million people are infected with T. cruzi and that 30 to 40 percent will develop heart symptoms as a result of their infection. In parts of the world where Chagas disease is endemic, most notably South America, the disease is the largest single cause of cardiovascular death. Chagas disease is very rare in the United States; only eight cases have been reported, and all of these in Latin American immigrants.Conditions resulting from Chagas disease also include atrioventricular block, which is a failure of the normal conduction of the electrical impulses which control the heartbeat. Eighteen of the 25 patients with Chagas disease were under treatment for heart disease prior to their proper diagnosis. In one case, a patient had been treated for 10 prior to the diagnosis.

Keyword:- *Mal de Chagas-Mazza*, *Chagas*, Trypanosomes cruzi, American trypanosomiasis, Brazilian Trypanosomiasis, heart disease.

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INTRODUCTION

American trypanosomiasis is a serious disease that leads to chronic progressive heart disease in approximately 20% to 40% of infected persons. It is also known as Chagas disease, having been named after the Brazilian physician Carlos Chagas who first described it in 1909[1]. It is one of the leading causes of sudden death after coronary heart disease. Chagas disease occurs in roughly 150 species of wild and domestic animals and is transmitted to humans by the *Trypanosoma cruzi* parasite. Chagas disease exists only on the American Continent. A related disease called African trypanosomiasis, or sleeping sickness, is limited to sub-Saharan Africa.Chagas named the pathogenic parasite *Trypanosoma cruzi* and later that year as *Schizotrypanum cruzi*, both honoring Oswaldo Cruz, the noted Brazilian physician and epidemiologist who fought successfully epidemics of, smallpox and bubonic plague in Rio de Janeiro and other cities in the beginning of the 20th century. Chagas' work is unique in the history of medicine because he was the only researcher so far to describe *solely* and completely a new infectious disease: its pathogen, vector, host, clinical manifestations, and epidemiology.

CHAGAS DISEASE:-

Portuguese: *doença de Chagas*, Spanish: *enfermedad de Chagas-Mazza*, *mal de Chagas* in both languages; also called **American trypanosomiasis** is a tropical parasitic disease caused by the flagellate protozoan *Trypanosoma cruzi*. *T. cruzi* is commonly transmitted to humans and other mammals by an insect vector, the blood-sucking insects of the subfamily Triatominae (family Reduviidae) most commonly species belonging to the*Triatoma*, *Rhodnius*, and *Panstrongylus* genera.[1] The disease may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites, and from a mother to her fetus.[2].The symptoms of Chagas disease vary over the course of an infection. In the early, acute stage, symptoms are mild and usually produce no more than local swelling at the site of infection. The initial acute phase is responsive to antiparasitic treatments, with 60–90% cure rates. After 4–8 weeks, individuals with active infections enter the chronic phase of Chagas disease that is asymptomatic for 60–80% of chronically infected individuals through their lifetime. The antiparasitic treatments also appear to delay or prevent the development of disease symptoms during the chronic phase of the disease, but 20–40% of chronically infected individuals will still eventually develop life-threatening heart and digestive system disorders. The currently available antiparasitic treatments for Chagas disease are benznidazole and nifurtimox, which can cause temporary side effects in many

patients including skin disorders, brain toxicity, and digestive system irritation.[3,4,5].Chagas disease is contracted primarily in the Americas, particularly in poor, rural areas of Mexico, Central America, and South America; very rarely, the disease has originated in the Southern United States. The insects that spread the disease are known by various local names, including *vinchuca* in Argentina, Bolivia, Chile and Paraguay, *barbeiro* (the barber) in Brazil, *pito* in Colombia, *chinche* in Central America, *chipo* in Venezuela, *chupança*,*chinchorro*, and "the kissing bug". It is estimated that as many as 8 to 11 million people in Mexico, Central America, and South America have Chagas disease, most of whom do not know they are infected. Large-scale population movements from rural to urban areas of Latin America and to other regions of the world have increased the geographic distribution of Chagas disease, and cases have been noted in many countries, particularly in Europe.[4]

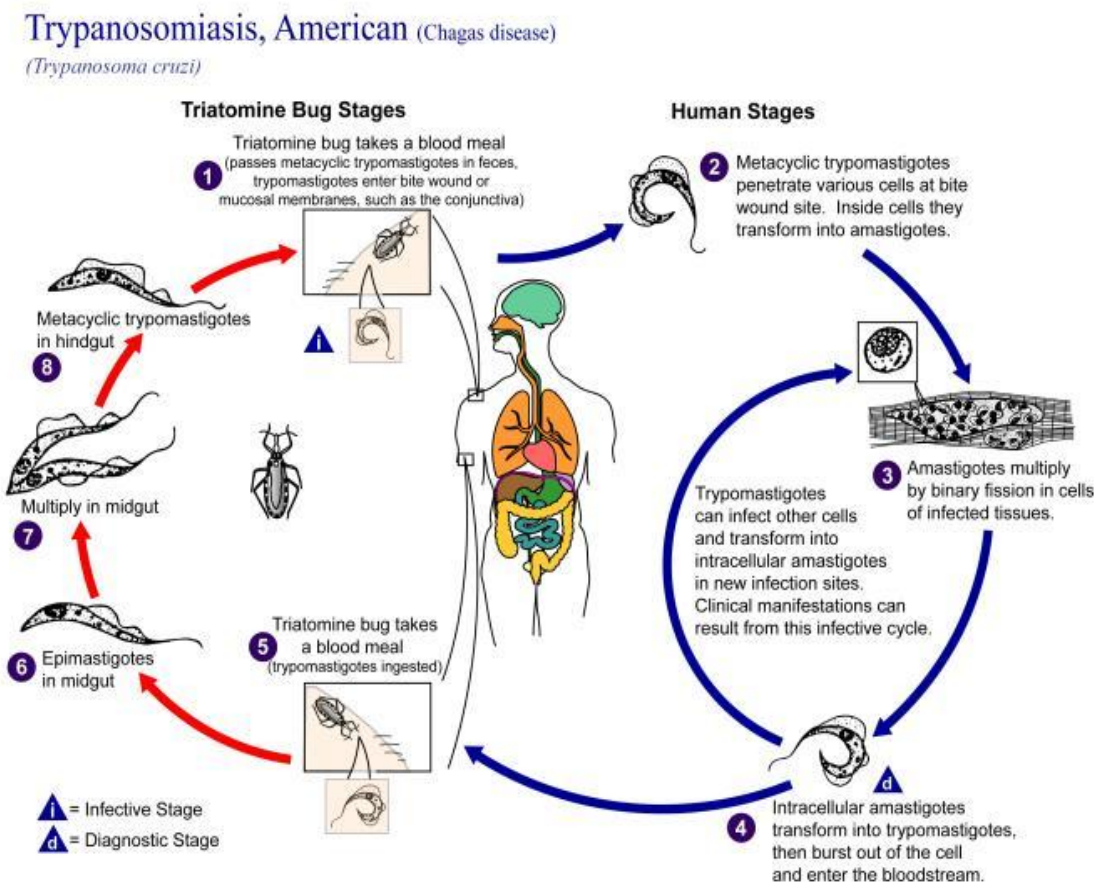

Figure 1 Life cycle and transmission of *T. cruzi*

Sign and Symptoms:-

The human disease occurs in two stages: an acute stage, which occurs shortly after an initial infection, and a chronic stage that develops over many years. The acute phase lasts for the

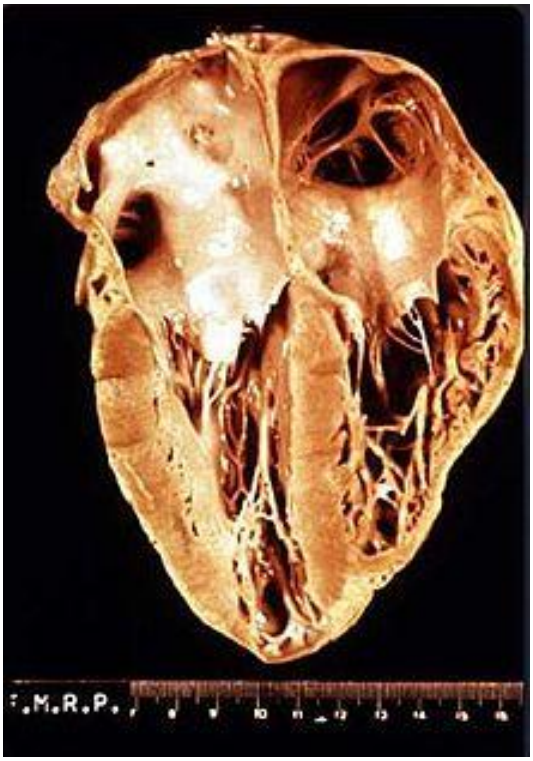

Figure 2 Gross anatomy of a heart that has been damaged by chronic Chagas disease.[6]

first few weeks or months of infection. It usually occurs unnoticed because it is symptom free or exhibits only mild symptoms that are not unique to Chagas disease. These can include fever, fatigue, body aches, headache, rash, loss of appetite, diarrhea, and vomiting. The signs on physical examination can include mild enlargement of the liver or spleen, swollen glands, and local swelling (a chagoma) where the parasite entered the body. The most recognized marker of acute Chagas disease is called Romaña's sign, which includes swelling of the eyelids on the side of the face near the bite wound or where the bug feces were deposited or accidentally rubbed into the eye. Rarely, young children, or adults may die from the acute disease due to severe inflammation/infection of the heart muscle (myocarditis) or brain (meningoen cephalitis).[6] The acute phase also can be severe in people with weakened immune systems.[1] If symptoms develop during the acute phase, they usually resolve spontaneously within 3–8 weeks in approximately 90% of individuals.[3,4] Although the symptoms resolve, even with treatment the infection persists and enters a chronic phase. Of individuals with chronic Chagas disease, 60–80% will never develop symptoms (called *indeterminate* chronic Chagas disease), while the remaining 20–40% will develop life-threatening heart and/or digestive disorders during their lifetime (called *determinate* chronic Chagas disease). In 10% of individuals the disease progresses directly from the acute form to a symptomatic clinical form of chronic Chagas disease.[3,4] The symptomatic

(determinate) chronic stage affects the nervous system, digestive system and heart. About two thirds of people with chronic symptoms have cardiac damage, including dilated cardiomyopathy, which causes heart rhythm abnormalities and may result in sudden death. About one third of patients go on to develop digestive system damage, resulting in dilation of the digestive tract (megacolon and megaesophagus), accompanied by severe weight loss.Swallowing difficulties (secondary achalasia) may be the first symptom of digestive disturbances and may lead to malnutrition.[2] Twenty to fifty percent of individuals with intestinal involvement also exhibit cardiac involvement.[2] Up to 10% of chronically infected individuals develop neuritis that results in altered tendon reflexes and sensory impairment. Isolated cases exhibit central nervous system involvement, including dementia, confusion, chronic encephalopathy and sensitivity and motor deficits.[7] The clinical manifestations of Chagas disease are due to cell death in the target tissues that occurs during the infective cycle, by sequentially inducing an inflammatory response, cellular lesions, and fibrosis. For example, intracellular amastigotes destroy the intramural neurons of the autonomic nervous system in the intestine and heart, leading to megaintestine and heart aneurysms, respectively. If left untreated, Chagas disease can be fatal, in most cases due to heart muscle damage.[2]

Transmission:-

Figure 3

Figure 4

Transmission of T. cruzi

Rhodnius prolixus is the principal vector in Colombia, Venezuela, Guatemala, Honduras and some parts of Nicaragua and El Salvador.In Chagas-endemic areas, the main mode of transmission is through an insect vector called a triatomine bug.[1] A triatomine becomes infected with *T. cruzi* by feeding on the blood of an infected person or animal. During the day, triatomines hide in crevices in the walls and roofs. The bugs emerge at night, when the inhabitants are sleeping. Because they tend to feed on people's faces, triatomine bugs are also

known as "kissing bugs." After they bite and ingest blood, they defecate on the person. Triatomines pass *T. cruzi* parasites (called trypomastigotes) in feces left near the site of the bite wound. Scratching the site of the bite causes the trypomastigotes to enter the host through the wound, or through intact mucous membranes, such as the conjunctiva. Once inside the host, the trypomastigotes invade cells, where they differentiate into intracellular amastigotes. The amastigotes multiply by binary fission and differentiate into trypomastigotes, which are then released into the bloodstream. This cycle is repeated in each newly infected cell. Replication resumes only when the parasites enter another cell or are ingested by another vector.[1] Dense vegetation (such as that of tropical rainforests) and urban habitats are not ideal for the establishment of the human transmission cycle. However, in regions where the sylvatic habitat and its fauna are thinned by economic exploitation and human habitation, such as in newly deforested areas, piassava palmculture areas, and some parts of the Amazon region, a human transmission cycle may develop as the insects search for new food sources.[8] *T. cruzi* can also be transmitted through blood transfusions. With the exception of blood derivatives (such as fractionated antibodies), all blood components are infective. The parasite remains viable at 4 °C for at least 18 days or up to 250 days when kept at room temperature. It is unclear whether *T. cruzi* can be transmitted through frozen-thawed blood components.[9].Other modes of transmission include organ transplantation, through breast milk,[10] and by accidental laboratory exposure. Chagas disease can also be spread congenitally (from a pregnant woman to her baby) through the placenta, and accounts for approximately 13% of stillborn deaths in parts of Brazil.[11] In 1991, farm workers in the state of Paraíba, Brazil, were infected by eating contaminated food; transmission has also occurred via contaminated açaí palm fruit juice and sugar cane juice.[12,13,14] A 2007 outbreak in 103 Venezuelan school children was attributed to contaminated guava juice.[15]

Diagnosis:-

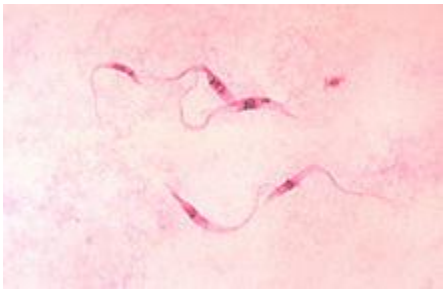

Figure 5 Photomicrograph of Giemsa-stained *Trypanosoma cruzi*

The presence of *T. cruzi* is diagnostic of Chagas disease. It can be detected by microscopic examination of fresh anticoagulated blood, or its buffy coat, for motile parasites; or by preparation of thin and thick blood smears stained with Giemsa, for direct visualization of parasites. Microscopically, *T. cruzi* can be confused with *Trypanosoma rangeli*, which is not known to be pathogenic in humans. Isolation of *T. cruzi* can occur by inoculation into mice, by culture in specialized media (for example,, NNN, LIT); and by xenodiagnosis,[16] where uninfected Reduviidae bugs are fed on the patient's blood, and their gut contents examined for parasites.[2]Various immunoassays for *T.cruzi* are available and can be used to distinguish among strains (zymodemes of *T.cruzi* with divergent pathogenicities). These tests include: detecting complement fixation, indirect hemagglutination, indirect fluorescence assays, radioimmunoassays, and ELISA. Alternatively, diagnosis and strain identification can be made using polymerase chain reaction (PCR).[2]

Prevention:-

There is currently no vaccine against Chagas disease[17]and prevention is generally focused on fighting the vector *Triatoma* by using sprays and paints containing insecticides (synthetic pyrethroids), and improving housing and sanitary conditions in rural areas.[18] For urban dwellers, spending vacations and camping out in the wilderness or sleeping at hostels or mud houses in endemic areas can be dangerous; a mosquito net is recommended. Some stepstones of vector control include:

- A yeast trap tested for monitoring infestations of certain species of triatomine bugs (*Triatoma sordida*, *Triatoma brasiliensis*, *Triatoma pseudomaculata*, and *Panstrongylus megistus*).[19]
- Promising results were gained with the treatment of vector habitats with the fungus *Beauveria bassiana*.[20]
- Targeting the symbionts of Triatominae through paratransgenesis.[21]

A number of potential vaccines are currently being tested. Vaccination with *Trypanosoma rangeli* has produced positive results in animal models.[22,23] More recently, the potential of DNA vaccines for immunotherapy of acute and chronic Chagas disease is being tested by several research groups.[24] Blood transfusion was formerly the second most common mode of transmission for Chagas disease, but the development and implementation of blood bankscreening tests has dramatically reduced this risk in the last decade. Blood donations in all endemic Latin American countries undergo Chagas screening, and testing is expanding in

countries, such as France, Spain and the United States, that have significant or growing populations of immigrants from endemic areas.[24,25] In Spain, donors are evaluated with a questionnaire to identify individuals at risk of Chagas exposure for screening tests.[25] The US FDA has approved two Chagas tests including one recently approved in April 2010, and has published guidelines that recommend testing of all donated blood and tissue products.[25,26] While these tests are not required in U.S., it is estimated that 75–90% of the blood supply is currently tested for Chagas, including all units collected by the American Red Cross which accounts for 40% of the U.S. blood supply.[26,27] The Chagas Biovigilance Network reports current incidents of Chagas positive blood products in the United States, as reported by labs using the screening test approved by the FDA in 2007.[28]

Medication:-

Antiparasitic treatment is most effective early in the course of infection, but is not limited to cases in the acute phase. Drugs of choice include azole or nitro derivatives such as benznidazole[29] ornifurtimox. Both agents are limited in their capacity to effect parasitologic cure (a complete elimination of *T. cruzi* from the body), especially in chronically infected patients, and resistance to these drugs has been reported.[30] Studies suggest that antiparasitic treatment leads to parasitological cure in about 60–85% of adults and more than 90% of infants treated in the first year of acute phase Chagas disease. Children (age 6 to 12-years) with chronic disease have a cure rate of about 60% with benznidazole. While the rate of cure declines the longer an adult has been infected with Chagas, treatment with benznidazole has been shown to slow the onset of heart disease in adults with chronic Chagas infections.[2, 4] Treatment of chronic infection in women prior to or during pregnancy does not appear to reduce the probability the disease will be passed on to the infant. Likewise, it is unclear whether prophylactic treatment of chronic infection is beneficial in persons who will undergo immune suppression.[2]

Complications:-

In the chronic stage, treatment involves managing the clinical manifestations of the disease. For example, pacemakers and medications for irregular heartbeats, such as the anti-arrhythmia drug amiodarone, may be life saving for some patients with chronic cardiac disease.[31] while surgery may be required for megaintestine. The disease cannot be cured in this phase, however. Chronic heart disease caused by Chagas disease is now a common reason for heart transplantation surgery. Until recently, however, Chagas disease was considered a contraindication for the procedure, since the heart damage could recur as the parasite was expected to seize the

opportunity provided by the immunosuppression that follows surgery.[32] It was noted that survival rates in Chagas patients could be significantly improved by using lower dosages of the immunosuppressant drug ciclosporin. Recently, direct stem cell therapy of the heart muscle using bone marrow cell transplantation has been shown to dramatically reduce risks of heart failure in Chagas patients.[33]

Epidemiology:-

Chagas disease affects 8–10 million people living in endemic Latin American countries, with an additional 300,000–400,000 living in non-endemic countries, including Spain and the United States. An estimated 41,200 new cases occur annually in endemic countries and 14,400 infants are born with congenital Chagas disease annually. About 20,000 deaths are attributed to Chagas disease each year.[2, 4] The disease is present in 18 countries on the American continents, ranging from the southern United States to northern Argentina.[1] Chagas exists in two different ecological zones. In the Southern Cone region the main vector lives in and around human homes. In Central America and Mexico the main vector species lives both inside dwellings and in uninhabited areas. In both zones Chagas occurs almost exclusively in rural areas, where triatomine breed and feed on the over 150 species from 24 families of domestic and wild mammals, as well as humans, that are the natural reservoirs of *T.cruzi*.[34]Although Triatominae bugs feed on birds, they appear to be immune against infection and therefore are not considered to be a *T. cruzi* reservoir. Even when colonies of insects are eradicated from a house and surrounding domestic animal shelters, they can re-emerge from plants or animals that are part of the ancient, sylvatic infection cycle. This is especially likely in zones with mixed open savannah, with clumps of trees interspersed by human habitation.[35] The primary wildlife reservoirsfor *Trypanosoma cruzi* in the United States include opossums, raccoons, armadillos[36] squirrels, woodrats and mice.[37] Opossums are particularly important as reservoirs because the parasite can complete its life cycle in the anal glands of the animal without having to re-enter the insect vector.[37] Recorded prevalence of the disease in opossums in the U.S. ranges from 8.3%[37] up to 37.5%.[38] Studies on raccoons in the Southeast have yielded infection rates ranging from 47%[39] to as low as 15.5%.[37] Armadillo prevalence studies have been described in Louisiana and range from a low of 1.1%[38] up to 28.8%.[40] Additionally small rodents including squirrels, mice and rats are important in the sylvatic transmission cycle because of their importance as bloodmeal sources for the insect vectors. A Texas study revealed 17.3% percent *T. cruzi* prevalence in 75 specimens representing four separate small rodent species.[41]Chronic Chagas disease remains a

major health problem in many Latin American countries, despite the effectiveness of hygienic and preventive measures, such as eliminating the transmitting insects. However, several landmarks have been achieved in the fight against Chagas disease in Latin America including a reduction by 72% of the incidence of human infection in children and young adults in the countries of the Southern Cone Initiative, and at least three countries (Uruguay, in 1997, and Chile, in 1999, and Brazil in 2006) have been certified free of vectorial and transfusional transmission.[2,42,43] In Argentina vectorial transmission has been interrupted in 13 of the 19 endemic provinces.[42] and major progress toward this goal has also been made in both Paraguay and Bolivia. Screening of donated blood, blood components, solid organ donors, as well as donors of cells, tissues and cell and tissue products for *T. cruzi* is mandated in all Chagas endemic countries and has been implemented.[44] Approximately 300,000 infected people live in the United States, which is likely the result of immigration from Latin American countries.[45] With increased population movements, the possibility of transmission by blood transfusion became more substantial in the United States. Transfusion blood and tissue products are now actively screened in the U.S., thus addressing and minimizing this risk.[46]

CHAGAS DISEASES AFFECT ON PREGNANCY:-

The interactions between malaria and pregnancy have been the subject of many investigation in the post.The placenta infected in 80% of all malaria cases in pregnancy and this may occur in absence of detectable parasites in the peripheral blood of the mother.Father more imported cases of malaria due to in adequate prophylaxis are seen with increase frequency in adults in Europe and North America pregnancy may also associated with a relapse of plasmodium vivax infection years after the initial attack.

Side effect of chagas:-

Chagas disease is an infectious disease caused by the parasite Trypanosoma cruzi. It is spread from person to person by the bite of a type of insect called a reduviid bug (also called a kissing bug) These insects are found only in the Americas, and typically people who get the disease live in poverty-stricken areas of rural Latin America.The disease has both an acute and a chronic phase. The acute phase can last several months while patients have fever, fatigue.

Trypanosomiasis:-

Trpanosomiasis is an infection by protozoal parasites of the genus Trypanosoma. Two types of African trypanosomiasis West African Trypanosomiasis and East African Trypanosomiasis infect more than 40,000 people a year in sub-Saharan Africa.

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