30% of patients develop cardiac abnormalities, 10% digestive complaints, and less than 5% of patients develop a neurologic form of disease. The aim of this work is to determiner the effect of Benznidazol treatment (5 mg/kg/day) 60 days, in patients with chronic Chagas disease.

Methods: In 53 samples of patients we were tested by enzyme linked immunoassay (ELISA Dade Behring CHAGO560DB) for IgG antibodies against TC, and indirect immunofluorescence (IFI Biocientifica SA Immunofluor Chagas NF09-60) as confirmatory tes, for IgG (Bio-Merieux 75 692) antibodies, with serial serum dilutions to determine the level of these antibodies. In addition, all PCR were performed before treatment and at the end of it. As a criterion of cure was established a significant (more than 2 degrees) in the rate of antibody after treatment.

Results: About the 53 patients studied, 37 were performed two or more determinations of antibodies before and after treatment and in 80% of them, a diminution of the levels were found. The PCR was negative after treatment in all cases. In 13 patients was carried out only antibody titer before treatment, administering it even with low rates from them, because they had organ involvement suggestive of Chagas.

Conclusion: More studies are needed to clearly establish the criteria for cure of Chagas disease.

Furthermore, because in these patients with chronic Chagas disease parasitaemia sometimes is intermittent and low have to question the result of a negative PCR.

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82.010

Population structure of *Leishmania infantum* from Morocco

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Background: Visceral leishmaniasis (VL) is endemic in northern Morocco where it is caused by *Leishmania infantum*. It predominantly affects children under 4 years with incidence of 100 cases/year. Genetic variability and population structure has been investigated for 55 strains isolated from infected dogs and humans in Morocco.

Methods: A multilocus microsatellite typing (MLMT) approach was used in which a MLM type based on size variation in 14 independent microsatellite markers was compiled for each strain. MLMT profiles of 21 European strains which belonged to zymodeme MON-1 and non-MON1 according to multilocus enzyme electrophoresis (MLEE) were included for comparison.

Results: A Bayesian model-based approach and phylogenetic analysis based on genetic distances inferred two populations of the Moroccan *L. Infantum;* population A consists of 25 strains and population B consists of 30 strains. Theses populations were significantly different from the

Gene flow was noticed between populations A and B. Five strains have shown mixed A B genotype indicating possible recombination between the two populations

Conclusion: No genetic differences were detected between parasites isolated from dogs and humans emphasizing the role of dogs as reservoir. MLMT has proven to be a powerful tool for epidemiological and population genetic investigations in *Leishmani*.

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82.011

Propolis and derivatives of megazol: *In vitro* and *in vivo* activity on *Trypanosoma cruzi*, mechanism of action and selectivity

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Background: One hundred years after its discovery, Chagas disease, caused by *Trypanosoma cruzi*, still represents an important health problem and in need of alternative drugs for the treatment of chagasic.

Methods: Ethanolic extract of Brazilian green propolis (Et-Bra) was assayed on amastigotes proliferation, trypomastigote by transmission and scanning electron microscopy and flow cytometry. Thirty two 1,3,4-thiadiazole-2-arilhyldrazones of megazol were synthesized and assayed on trypomastigotes.

Results: Et-Bra was active against amastigotes proliferation inside mammalian macrophages and induced plasma membrane damage in the infective trypomastigote forms as determined by transmission and scanning electron microscopy and flow cytometry. In non-infected mice, propolis induced no toxicity as determined by the GPT, GOT and CK plasma levels. Treatment of *T. cruzi*-infected mice (up to 300 mg Et-Bra/kg/day for 10 days) led to a significant reduction of the mortality but not of the parasitemia, did not reversed the hepatic, renal or muscular damage induced by the parasite.

The most active analogues *in vitro* -S1 to S8- were assayed *in vivo* by a single oral dose at 5 dpi, being selected S1, S2 and S3, together with megazol for subsequent *in vitro* and *in vivo* studies. In trypomastigotes, ultrastructural analysis revealed that the compounds led to alterations at kDNA, mitochondrion and flagellar membrane and rounding and torsion of the parasite's body. S1 and S2 inhibited the amastigotes proliferation inside macrophages, while in cardiac muscular cells only S1 was active. The administration of 10 consecutive doses (50 and 100 mg/kg) of S1 caused no effect on the course of infection, while S2 led to a significant decrease of the parasitemia and S3, only of the mortality. The three analogues were not toxic for the animals based on the levels of GPT, GOT and urea.

Conclusion: Our results demonstrate the promising activity on *T. cruzi*, especially S2 and S3, justifying *in vivo* assays

with longer period of treatment and the continuity of the investigation of new analogues.

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82.012

Alanine 163 in loop C of *Leishmania major* aquaglyceroporin LmAQP1 resides near the pore mouth of the channel

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Background: The *Leishmania major* aquaglyceroporin, LmAQP1, is responsible for the transport of trivalent metalloids, arsenite and antimonite. We have earlier shown that down regulation of LmAQP1 provides resistance to trivalent antimony compounds whereas upregulation of LmAQP1 in drug resistant parasites can reverse the resistance. We have implicated this transporter to volume regulation and osmotaxis, two important characteristics for successful infection. Recently we have shown that a single change in the loop C of LmAQP1 changes its substrate specificity. Beitz et al (2004) have shown that E125 in loop C of PfAQP is close to the mouth of the pore and is critical for high water permeability of PfAQP (Beitz, 2004). Loop C of PfAQP is twelve residues shorter than LmAQP1. Therefore, E125 of PfAQP lines up with A163 in the primary sequence. To confirm that A163 is near the pore mouth we have created different mutants of LmAQP1 and their transport properties were compared.

Methods: Different mutants of A163 were created using site directed mutagenesis method. Wild type and mutant LmAQP1 were transfected into wild type *L. donovani*. Metalloid sensitivity, transport and osmoregulation ability of the transfected parasites were measured. cRNA of wild type and mutated LmAQP1 were injected into *Xenopus levis* oocytes followed by the determination of metalloid, water and solute transport.

Results: Change of A163 to glutamate, glutamine or aspartate made it impermeable to water, metalloids and other solutes. However, changes to serine and threonine did not change the transport properties of the channel. Water transport through LmAQP1 is mercurial insensitive. Introducing cysteine (s) in loop C in the vicinity of A163 made the water transport through the channel mercurial sensitive.

Conclusion: We report that A163 in loop C is localized near the pore mouth of LmAQP1.

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82.013

Chagas disease: Mother to child transmission (MTCT). A single experience in a public hospital from Buenos Aires

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Background: Mother to child transmission of Chagas Diseases (ChD) rates was reported from 1 to >10%. Factors reported to increase risk include younger maternal age, human immunodeficiency virus infection, and parasite strain.

Methods: Retrospective analysis of children assisted in infectious diseases department from 2001 to 2008. Inclusion criteria was: every child born from a mother suffering of ChD with accesing a diagnostic procedures before 24 months of life and never traveled to endemics areas until finish diagnostic process. Diagnosis of ChD among mothers and children over 6 months old were performed by serology (ELISA and HAI). Diagnosis of ChD among children) 6 months was performed with parasitemia investigation.

Results: We studied 307children born from mother with ChD, 165 were $\leq$24 moths of life. Ratio man/woman 87/78. MTCT was 26/152 (17%). Diagnosis was performed by parasitemia in 20/26: the 1st parasitemia perfomed was positive in 13 cases, 2nd parasitemia was positive in 5 cases and 3rd parsitemia was positive in only a case. In six patients, ChD diagnosis was performed by serology.

Mothers were from: Argentina = 28, Bolivia = 96, Paraguay = 19 and without records = 22. Only 11/26 chagasic children were symptomatic. Most frequent symptoms were: anemia 9/11, hepatosplenomegaly 3/11, hydrops fetalis 1/11, sepsis 1/11, abnormalities in serum transaminases 1/11 and cardiac abnormalities 1/11.

Prematurity was observing in 5/26 with ChD vs 2/111 no ChD. Low birth weight was present in 5/26 (19.2%) with ChD vs 6/111(5.4%) no ChD.

Three patients born from mother with HIV infection. MTCT were 3/3 (100%) vs 23/145 (15.8%) no HIV. No children were infected with HIV. The study of newborn allowed us performed study of ChD among 97 sibblings never studied; in 11 of them ChD was diagnosed. Benzindazol was indicated in all cases of vertically acquired ChD; 9 of the were lost of follow up and 5 had adverse reactions that.

Conclusion: MTCT was higher than previously reported. Even if sample was small; it can be possible that mothers with HIV co-infection have more MTCT than no HIV. We have the opportunity to study all the members of family and bring treatment if it is necessary.

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