



Abstracts

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V. Congress of the Russian Society for Trace Elements in Medicine (RUSTEM)

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Russian Society for Trace Elements in Medicine (RUSTEM), Moscow, Russia
Trace Element Institute for UNESCO, Lyon, France
Peoples' Friendship University of Russia (RUDN University), Moscow, Russia

Abnormally low selenium status of domestic animals and humans in conditions of extremely high groundwater pollution with Se, Li, F, NO₃, B, Cd, and As

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Se content in drinking water rarely exceeds maximum permissible concentration level (MPCL, 10 µg/L) but chronic consumption of water with toxic Se levels is known to increase morbidity of several forms of cancer and neurodegenerative diseases. Nevertheless, MPCL levels are adopted for individual pollutants not taking into consideration the possibility of the effect of other toxic elements. In the southern province of Mongolia (Dorno-Govi), using ICP-MS and fluorimetric analysis of Se we have revealed for the first time abnormally low Se status of domestic animals and humans in conditions of extremely high groundwater concentration of Se, Li, F, NO₃, B, Cl, Cd, and elevated levels of As, being indicative of antagonistic relationships between Se and other contaminants. In these respect multielement analysis of human hair may become the most prospect indicator of environmental risks.

Effect of a standardized bischofite solution on the reproductive function of male rats with experimental hypomagnesaemia

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Objective: To study the effect of standardized bischofite solution (SBS) on the spermatogenesis in male rats with dietary magnesium deficiency (DMD). **Materials and methods:** Experiments were carried out on 90 male rats in 3 equal groups (1: intact control, 2: low magnesium, 3: low magnesium with SBS treatment). For modeling the DMD, rats of the groups 2 and 3 were kept on a diet without magnesium AIN-76 for 2 months. Then, the rats of group 3 were treated by SBS 0.01 mL/kg for 2 months, while groups 2 and 3 continued to receive a low-magnesium diet. Reproductive function of males with DMD, and after its correction with SBS, was evaluated at the end of the 2 and 4 months. **Results and discussion:** After 4 months in group 2 total spermatozoa (TS) was decreased by 48%, time of motility of spermatozoa (TMS) by 45% and spermatogenesis index (SI) by 11.9%, whereas the number of pathological forms increased by 81.8% compared to controls. In group 3 TS, TMS, and SI were increased 3.5-fold, 2-fold, and 12.8%, respectively. **Conclusion:** SBS promotes activation of spermatogenesis in male rats with

dietary hypomagnesaemia, being indicative of its potential effectiveness for correction of DMD.

Assessment of cobalt and iron content in immature mice following chronic CoCl₂ exposure

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The aim of the study was to assess the iron distribution in blood serum, erythrocytes (RBC), spleen, and liver in relation to Co accumulation in immature mice. Pregnant ICR mice were subjected to 125 mg/kg b.w. daily CoCl₂ × 6H₂O for 2 – 3 days before birth and during lactation. 25-day-old offspring were separated into individual cages and had free access to food and water. Tissue metal levels were assessed using inductively-coupled plasma mass-spectrometry. Chronic CoCl₂ exposure induced significant metal accumulation in RBC and blood plasma compared to the control values (tap water). Spleen and liver Co content in the exposed mice increased ~ 5-fold and 20-fold, respectively. Co concentration was

Selenium Treatment and Chagasic Cardiopathy (STCC) clinical trial: first results on selenium levels at baseline

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GM², Saraiva RM², Cardoso CSA², de Sousa AS², Mediano MFF², do Brasil
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Infection and disease: a delicate balance



Infection by *T. cruzi*

Host response

Inflammation

Specific immune response

70%

30%

homeostasy

parasite load

pathology

Form

Indeterminate

X
→
< 1-3 %
/year

Form

Cardiac/digestive

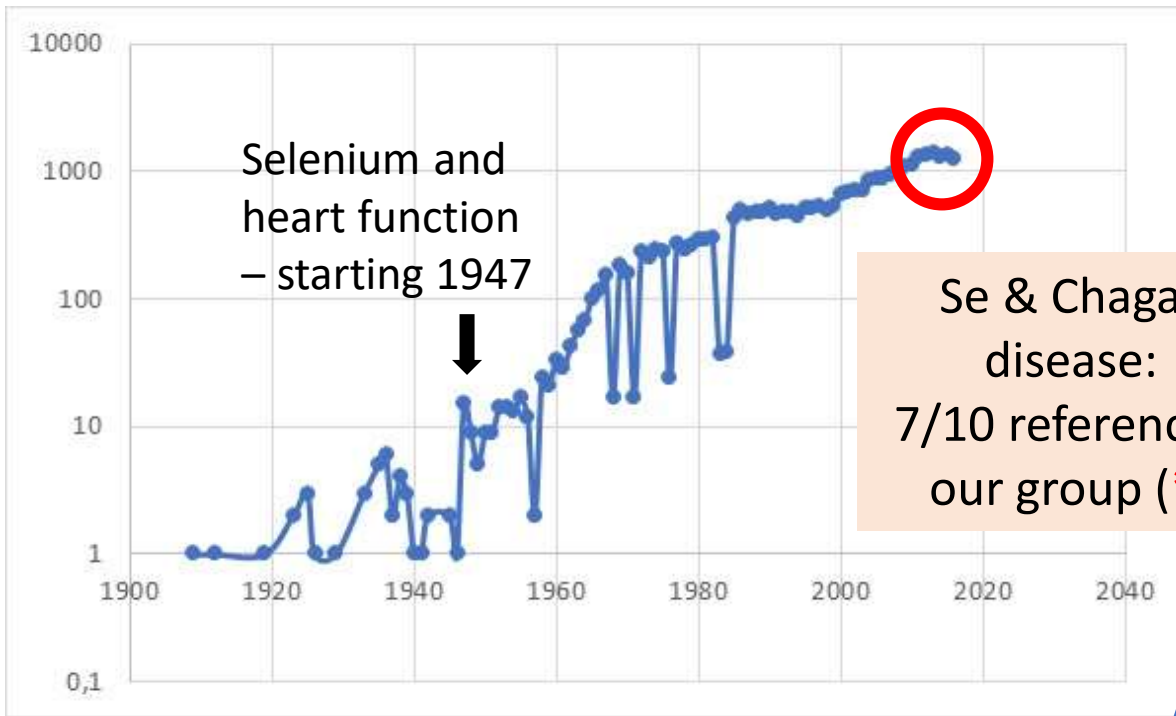
**Anti-oxidants
should be
recommended**

**1 Brazilian nut a
day → Se**

Vit E + Vit C (AO)

+ Vit B12 (Tc)

Number of references about Selenium in PubMed (1909-2017): only 10 in Chagas disease



PubMed | selenium & "chagas disease"

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Search results

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1. [Selenium Treatment and Chagasic Cardiopathy \(STCC\): study protocol for a double-blind randomized controlled trial.](#)
Avaringa Amencant do Brasil PE, Pereira de Souza A, Hassiocher-Moreno AM, Xavier SS, Lambert Passos SR, de Fátima Ramos Moreira M, Santini de Oliveira M, Sperandio da Silva GM, Magalhães Saraiva R, Santos de Aguiar Cardoso C, de Sousa AS, Mediano MF, Bonacini de Almeida Mda G, da Cruz Moreira C, Brito C, de Araujo-Jorge TC. *Trials*. 2014 Oct 8;15:335. doi: 10.1186/s13067-014-0388-2.
PMID: 25294194 Free PMC Article
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2. [Evaluating Chagas disease progression and cure through blood-derived biomarkers: a systematic review.](#)
Requena-Montero A, Lopez MC, Angheben A, Izquierdo L, Ribeiro I, Pinazo MJ, Gascon J, Muñoz J. *Expert Rev Anti Infect Ther*. 2013 Sep;11(9):971-76. doi: 10.1586/1473712013.12013.024718. Review.
PMID: 24053278
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3. [Would selenium supplementation aid in therapy for Chagas disease?](#)
Jelicks LA, de Souza AP, Araujo-Jorge TC, Tanowitz HB. *Trends Parasitol*. 2011 Mar;27(3):102-6. doi: 10.1016/j.pt.2010.12.002. Epub 2011 Jan 4.
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4. [The benefits of using selenium in the treatment of Chagas disease: prevention of right ventricle chamber dilatation and reversion of Trypanosoma cruzi-induced acute and chronic cardiomyopathy in mice.](#)
Souza AP, Jelicks LA, Tanowitz HB, Olivieri BR, Medeiros MM, Oliveira GM, Pires AR, Santos AM, Araujo-Jorge TC. *Mem Inst Oswaldo Cruz*. 2010 Sep;105(9):748-51.
PMID: 20944917 Free Article
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5. [The role of selenium in intestinal motility and morphology in a murine model of Trypanosoma cruzi infection.](#)
de Souza AP, Sieberg R, Li H, Cahill HR, Zhao D, Araujo-Jorge TC, Tanowitz HB, Jelicks LA. *Parasitol Res*. 2010 May;108(5):1295-6. doi: 10.1007/s00436-010-1794-1. Epub 2010 Feb 27.
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6. [Trace elements, innate immune response and parasitosis.](#)
Riviera MT, De Souza AP, Araujo-Jorge TC, De Castro SL, Vanderpas J. *Clin Chem Lab Med*. 2003 Aug;41(8):1020-5. Review.
PMID: 12964517
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7. [Trypanosoma cruzi: host selenium deficiency leads to higher mortality but similar parasitemia in mice.](#)
de Souza AP, Melo de Oliveira G, Nave J, Vancorpas J, Pirmex C, de Castro SL, Araujo-Jorge TC, Riviera MT. *Exp Parasitol*. 2002 Aug;101(4):193-9.
PMID: 12594265
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8. [Progressive Chagasic cardiomyopathy is associated with low selenium levels.](#)
Riviera MT, de Souza AP, Moreno AH, Xavier SS, Gomes JA, Rocha MD, Consta-Oliveira R, Nave J, Vancorpas J, Araujo-Jorge TC. *Am J Trop Med Hyg*. 2002 Jun;66(6):796-12.
PMID: 12244778
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9. [Host selenium deficiency increases the severity of chronic inflammatory myopathy in Trypanosoma cruzi-infected mice.](#)
Gomez RM, Solana ME, Levander DA, J. *Parasitol*. 2002 Jun;83(3):411-7.
PMID: 12339423
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10. [Beneficial effect of selenium supplementation during murine infection with Trypanosoma cruzi.](#)
Davis CD, Brooks L, Calisi C, Bonnett BJ, McElroy DM. *J Parasitol*. 1999 Aug;85(1):27-7.
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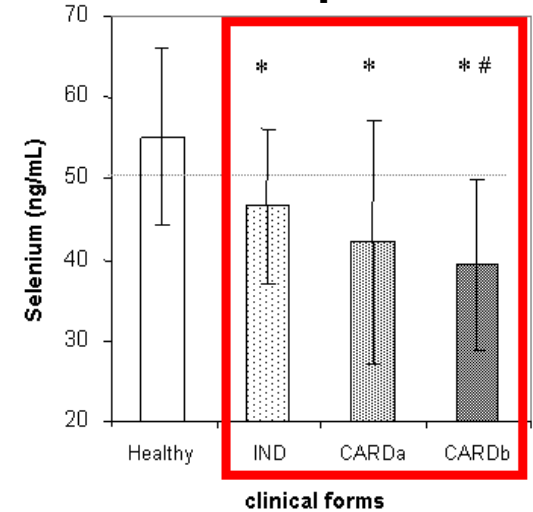
	Total number of references	first year
selenium	30,571	1909
selenium & cancer	4,759	1946
selenium & muscle	1,821	1957
selenium & heart	1,339	1947
selenium & cardiovascular	1,426	1960
selenium & chagas disease	10	1998

1998

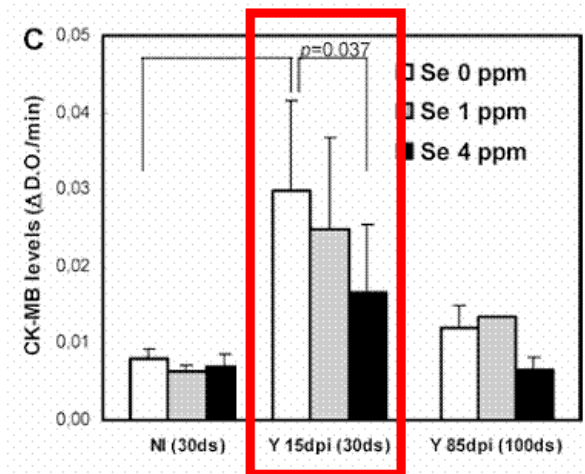
Introduction: Se and Chagas disease

- Heart disease progression occurs in 30% of patients with chronic *Trypanosoma cruzi* infection.
- There is evidence that patients with Chagas heart disease have lower Se levels than healthy individuals and patients with *T. cruzi* infection without of cardiac disease
- Supplementation with selenium (Se) in animal model of *T. cruzi* infection produced promising results.

2002 – human patients



2003 - mice



Introduction

Alvarenga Americano do Brasil et al. *Trials* 2014, **15**:388
<http://www.trialsjournal.com/content/15/1/388>



STUDY PROTOCOL

Open Access

Selenium Treatment and Chagasic Cardiopathy (STCC): study protocol for a double-blind randomized controlled trial

Pedro Emmanuel Alvarenga Americano do Brasil^{1*}, Andréa Pereira de Souza², Alejandro Marcel Hasslocher-Moreno¹, Sérgio Salles Xavier¹, Sonia Regina Lambert Passos³, Maria de Fátima Ramos Moreira⁴, Marília Santini de Oliveira⁵, Gilberto Marcelo Sperandio da Silva¹, Roberto Magalhães Saraiva¹, Claudia Santos de Aguiar Cardoso⁶, Andréa Silvestre de Sousa¹, Mauro Felipe Felix Mediano¹, Maria da Gloria Bonecini de Almeida⁷, Otacílio da Cruz Moreira⁸, Constança Britto⁸ and Tania Cremonini de Araújo-Jorge²



- The Selenium Treatment and Chagasic Cardiopathy (STCC; [Trials](#) 6;15:388, 2014; doi: 10.1186/1745-6215-15-388) trial is a superiority, double-blind, placebo-controlled, randomized clinical trial aiming to estimate the effect of Se treatment on prevention of heart disease progression in patients with chagasic cardiopathy.
- TRIAL REGISTRATION: Clinical Trials.gov ID: [NCT00875173](#) (registered 20 October 20 2008).

Eligibility criteria

- (1) a Chagas disease diagnosis confirmed by serology;
- (2) segmental, mild or moderate global left ventricular systolic dysfunction; and
- (3) age between 18 and 75 years.

The trial is still in the recruiting phase and its final conclusion will not sort out before 2020, after the complete follow up of the 130 calculated patients that will be invited to participate.

Exclusion criteria

- (1) pregnancy,
- (2) diabetes mellitus,
- (3) tobacco use,
- (4) alcohol abuse,
- (5) evidence of nonchagasic heart disease,
- (6) depression,
- (7) dysphagia with evidence of food residues in the esophagus,
- (8) dysphagia with weight loss higher than 15% of usual weight in the last four months and/or
- (9) conditions that may result in low protocol adherence

5/5/2014: Start recruiting

Protocol

Volunteers receive **100 µg of sodium selenite** once daily for 365 consecutive days compared to placebo.

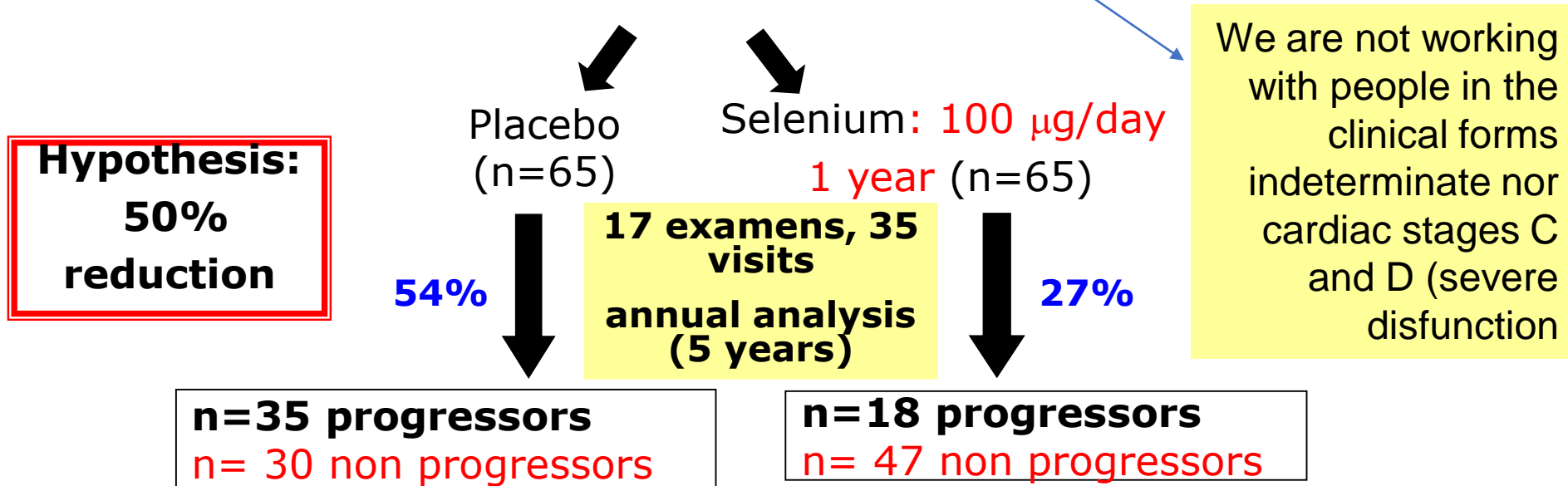
Primary outcomes to be measured during the **5 years of follow-up** includes:

- (1) the trajectories of the left ventricular ejection fraction in the follow-up period;
- (2) reduction of heart disease progression rates, with progression defined as a 10% decrease in left ventricular ejection fraction; and
- (3) rate of hospital admissions attributable to dysrhythmia, heart failure or stroke due to Chagas disease.



STCC- Selenium treatment and chagasic cardiomyopathy

Chronic chagasic patients (**n=130**)
mild or moderated disfunction (VEF $\geq 0,45$ + abnormal ECG e ECO)
randomization



Primary endpoint: 50% reduction in the progression rate from mild to moderate and from moderate or severe heart disfunction

Secondary endpoints:

- 50% reduction in mean value of VEF
- reduction in the frequency and type of ECG alterations

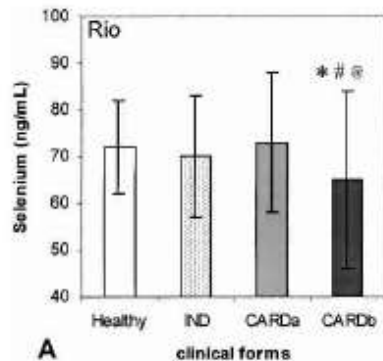
Selenium, Zinc and Copper measurements at baseline in 47 patients

Plasma baseline levels in 47 patients measured by ICP-MS

	Age	Se (mcg/L)	Se F	Se M	Zn mcg/dL	Cu mcg/dL
mean	61	88	86	90	74	99
median	61	82	82	82	73	96
minimum	34	48	48	55	57	46
maximum	74	152	152	137	99	151
percentile 25	56	71	64	78	67	88,7
percentile 75	69	99	99	105	80	115
n total	47	47	29	18	46	46

PROGRESSIVE CHAGAS' CARDIOMYOPATHY IS ASSOCIATED WITH LOW SELENIUM LEVELS

MARIA TERESA RIVERA, ANDRÉA P. DE SOUZA, ALEJANDRO HASSLOCHER M. MORENO, SERGIO S. XAVIER, JULIANA A. S. GOMES, MANOEL OTÁVIO C. ROCHA, RODRIGO CORREA-OLIVEIRA, JEAN NÈVE, JEAN VANDERPAS, AND TANIA C. ARAÚJO-JORGE



In 2002 we observed a higher % of cases with lower seleniun levels in the group of patients with moderate/severe disease (CARD b)

In 2017 the trend of the STCC clinical assay is to confirm that 10/47 patients start the study in the lower seleniun level range

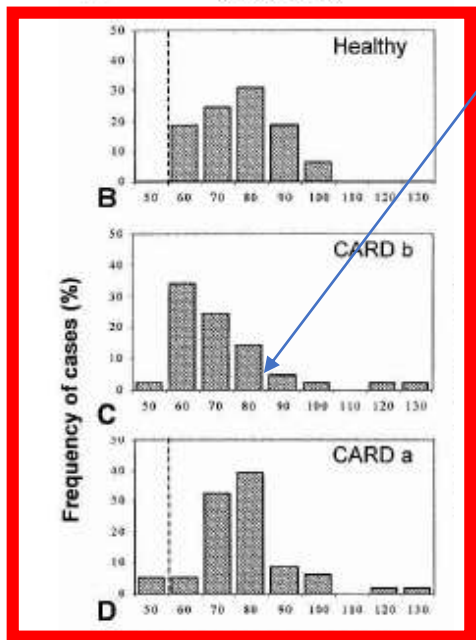
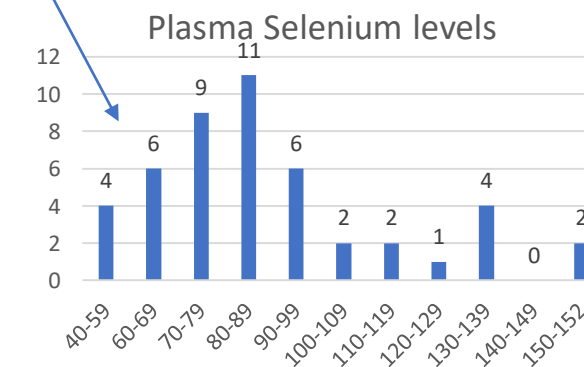
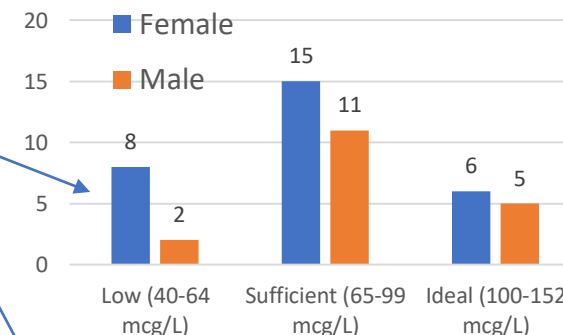
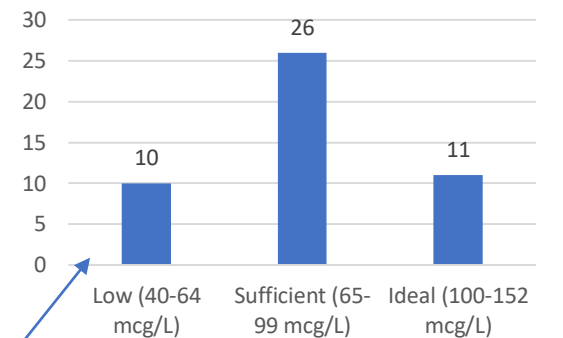


FIGURE 1. page 709. Seleniun levels (A) and frequency distribution (B–D) in chronic chagasic patients from different clinical groups living in the urban area of Rio de Janeiro. The frequency distribution curve in (C) is significantly different ($P < 0.05$) from

We are waiting the 1-year follow-up of these patients to see if there is any correlation of outcome depending on the initial range of plasma seleniun levels. The hypothesis is that in the first group there is a higher risk of pathology evolution, and that the others may not evolve or may evolve more slowly.

STCC will follow patients with slight and moderate heart dysfunction, supplemented or not with Se, to observe the pathology evolution



Se and heart Chagas disease (mice)

De Souza et al, 2010 Mem Inst Oswaldo Cruz, Rio de Janeiro, Vol. 105(6): 746-751, September 2010

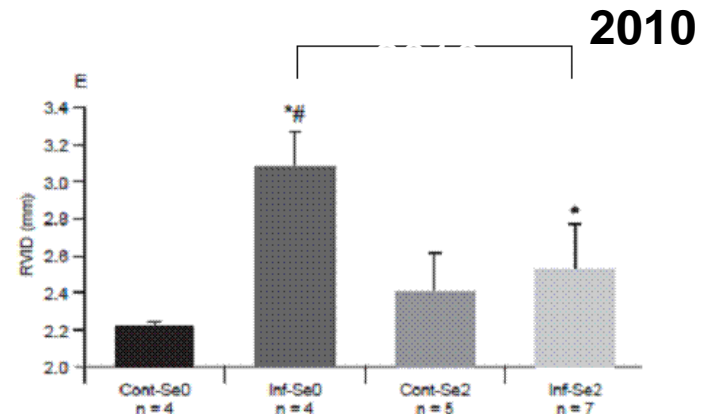
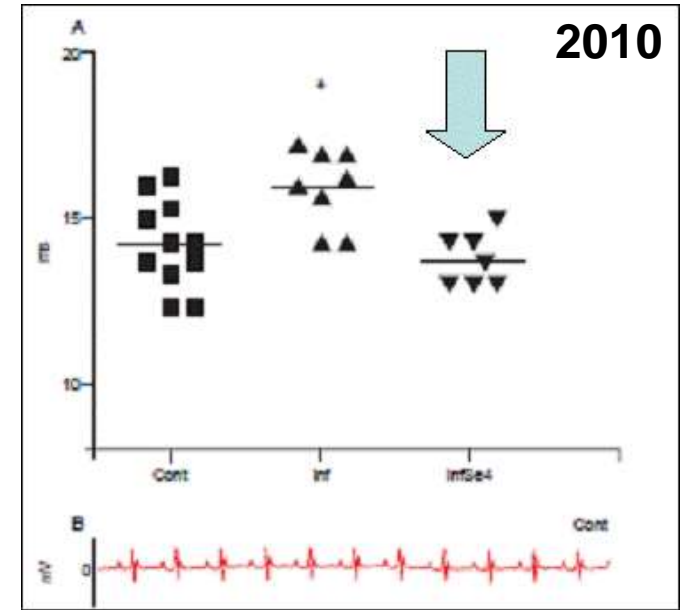
The benefits of using selenium in the treatment of Chagas disease: prevention of right ventricle chamber dilatation and reversion of *Trypanosoma cruzi*-induced acute and chronic cardiomyopathy in mice

Andréa P de Souza¹, Linda A Jelicks², Herbert B Tanowitz³, Bianca P Olivieri¹,
Monica M Medeiros¹, Gabriel M Oliveira⁴, Andrea Rodrigues Cordovil Pires⁵,
Alessandro M dos Santos¹, Tania C Araújo-Jorge^{1/*}

- ✓ Low Se levels → severity of heart disease (humans, mice)
- ✓ Deficient Se ingestion → higher death (mice)

In mice:

- ✓ Se supplementation → less lesions (mice)
- ✓ Se prevents pericarditis, arrhythmia and cardiomegaly, normalizes P wave (mice)



Perspectives

If Se treatment reduces the progression of Chagas cardiopathy, the inclusion of this micronutrient in the daily diet can improve the therapeutic regimen for this neglected tropical disease at low cost.

Acknowledgements



Patients participating on the study

Selenium Project team: 33 people – INI/ IOC/ ENSP

Support:



Ministério da Saúde



APOIO



Catalent.



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REALIZAÇÃO

