

# THE BRAZILIAN CONTRIBUTION TO THE STUDY OF NEUROCYSTICERCOSIS

## Moses and Lange's role in cerebrospinal fluid diagnosis

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**ABSTRACT** - We report the seminal contributions of both Dr. Arthur Moses (Instituto Oswaldo Cruz, Rio de Janeiro), in 1911, and Dr. Oswaldo Lange (Faculdade de Medicina da USP, São Paulo), in 1940, to the diagnosis of neurocysticercosis (NC). Moses was the first person to report an immunologically based method for the diagnosis of NC, whereas Lange reported the cerebrospinal features of NC.

**KEY WORDS:** Arthur Moses, immunological diagnosis of neurocysticercosis, Oswaldo Lange, CSF diagnosis of neurocysticercosis, cerebrospinal fluid, neurocysticercosis.

### **A contribuição brasileira para o estudo da neurocisticercose: o papel de Moses e Lange no diagnóstico líquido céfalo-raquídeo**

**RESUMO** - Descrevemos as contribuições pioneiras de Arthur Moses (Instituto Oswaldo Cruz, Rio de Janeiro) em 1911 e de Oswaldo Lange (Faculdade de Medicina da USP, São Paulo) em 1940, para o diagnóstico da neurocisticercose (NC). Moses fez a primeira descrição mundial de um método para o diagnóstico imunológico da NC e Lange fez a descrição da síndrome líquórica da NC.

**PALAVRAS-CHAVE:** Arthur Moses, diagnóstico imunológico da neurocisticercose, Oswaldo Lange, diagnóstico líquido céfalo-raquídeo da neurocisticercose, líquido cefalorraquídeo, neurocisticercose.

Current criteria used for the diagnosis of neurocysticercosis (NC) include, among others, a positive immuno-assay test (ELISA) used to detect anticysticercic antibodies in the cerebrospinal fluid (CSF)<sup>1</sup>. The cerebrospinal syndrome induced by NC has been defined by several authors as a combination of pleocytosis, demonstration of eosinophils in CSF, high protein content in the CSF and a positive immunological test in CSF<sup>2-5</sup>.

Among all the main contributions to CSF diagnosis of NC are included the works of two Brazilian researchers: Dr. Arthur Moses, from Rio de Janeiro, and Dr. Oswaldo Lange, from São Paulo<sup>3,5-8</sup>.

The aim of our study is to report how the seminal works of Drs. Moses and Lange aided in the CSF diagnosis of NC.

### **ARTHUR MOSES' CONTRIBUTION**

Dr. Arthur Alexandre Moses (Fig 1) was born in

Rio de Janeiro in 1886 and graduated as a physician in 1908. He pursued a career as researcher of the Instituto Oswaldo Cruz for many years, working in several different basic research areas of Medicine, such as histology and microbiology; as well as some research in Veterinary Medicine, including the description of a specific type of myxoma in rabbits<sup>8</sup>.

As a result of his prolific scientific output, mostly in microbiology, Dr. Moses was awarded in 1927 the golden medal of the Kummel award from the University of Hamburg in Germany. In 1932 he received another award from the German Red Cross, personally given by the president of that time<sup>8</sup>.

Moses also occupied the post of President of the Brazilian Academy of Sciences for years and died in the 23<sup>rd</sup> November 1967<sup>8</sup>.

In 1911, Moses published an article titled "Dos métodos biológicos de diagnóstico nas cisticercoses", "Biological methods for the diagnosis of cysticercosis", in

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Recebido 13 Abril 2005, recebido na forma final 17 Janeiro 2006. Aceito 8 Março 2006.

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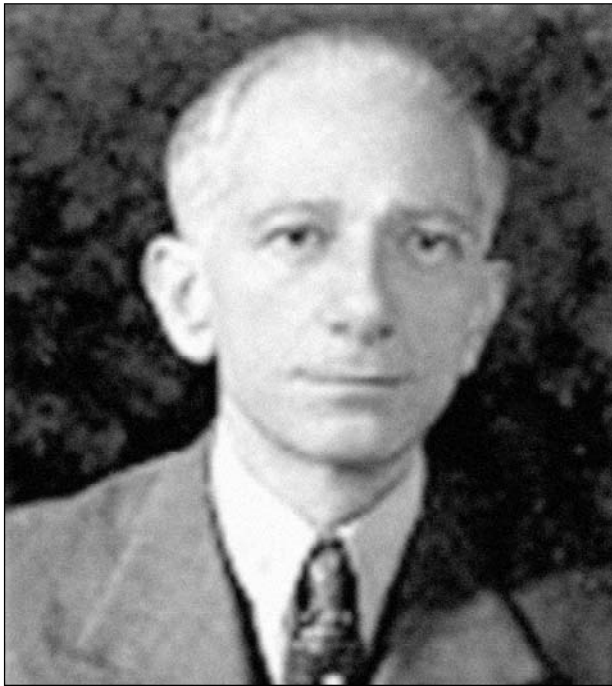


Fig 1. Dr. Arthur Moses (1886-1967).

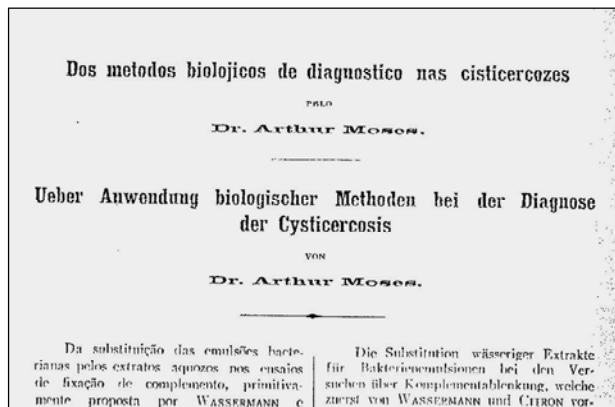


Fig 2. Moses A. *Dos metodos biologicos de diagnostico nas cisticercoses*. *Mem Inst Oswaldo Cruz*, 1991;3:322-326.

a Brazilian periodical "Memórias do Instituto Oswaldo Cruz"<sup>9</sup>. In his research he used an "aqueous extract" derived from "Cysticercus celulosae" and obtained positive results when testing it in the serum of three patients who had cutaneous cysticercosis and in CSF of another patient who had encephalic cysticercosis<sup>3,9-11</sup>. Thus, Moses' work was the first unequivocal demonstration worldwide of the existence of anticysticerc antibodies in the CSF of a patient, a diagnosis which was later confirmed through autopsy (Fig 2)<sup>3,9-11</sup>.

One should remember that Weinberg, in 1909, first published the results of his research on the use of porcine serum from pigs infected with "Cysticercus

celulosae", using the liquid material found within the vesicles as an antigen<sup>11,12</sup>. Ever since, this immunological test has been known as Weinberg's reaction, or Weinberg's test<sup>3,10-12</sup>. However, Weinberg only used the serum of infected pigs and never tested the reaction in CSF samples<sup>11,12</sup>.

If we take that into account, the first tests performed with human serum and human CSF, for the diagnosis of human cysticercosis and neurocysticercosis, respectively, were first performed by Moses in 1911<sup>9</sup>.

The immunological reaction described by Moses was then used by other researchers, in his original article on the liquoric syndrome found in NC, reports that Moses' reaction was indeed safe: "...in Brazil, on the other hand, our data demonstrates that complement fixation reaction for cysticercosis merits confidence"<sup>11</sup>. Lange also stresses in his article that Moses' own work antedated those of several foreign researchers<sup>11</sup>.

Reis and col. suggest that Arthur Moses should be honoured, and the reaction first described by him should be known as "Moses reaction", instead of "Weinberg's reaction", as it is widely known<sup>3</sup>.

Finally, the fact that Moses made published his own experience in a Brazilian periodical with low international repercussion, even though it was both published in Portuguese and in German, might have been the main reason why his discovery had so little scientific impact at the time.

#### OSWALDO LANGE'S A CONTRIBUTION

Dr. Oswaldo Lange (Fig 3) was born in São Paulo, SP, on the 28<sup>th</sup> August 1903. He graduate in Medicine at the Faculdade de Medicina (Faculty of Medicine) which would later become part of the Universidade de São Paulo (University of São Paulo) in 1927<sup>6,7</sup>. He was a member of the group of collaborators working with Dr. Enjolras Vampré, the founder of the school of Neurology in São Paulo, and for several years was the Chief of the Neurologic Clinic of Faculdade de Medicina da Universidade de São Paulo<sup>6,7</sup>. In 1938 he was awarded the title "livre docente" in Neurology, after succeeding in a written examination and in an evaluation of his curriculum vitae<sup>6,7</sup>.

Lange was among the founders of many medical societies, such as the Associação Paulista de Medicina, where he acted also as the editor of the Revista Paulista de Medicina, and the Academia Brasileira de Neurologia (Brazilian Academy of Neurology), working as a delegate for the World Federation of Neurology<sup>6,7</sup>.

Also of extreme importance is the fact that Oswaldo Lange was the founder of the official journal



Fig 3. Dr. Oswaldo Lange (1903-1986)

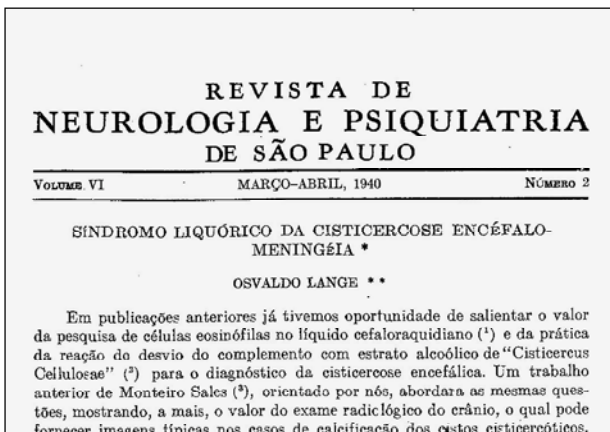


Fig 4. Lange O. O síndrome líquido da cisticercose encefalo-meningéia. Revista de Neurologia e Psiquiatria de São Paulo 1940;2:35-54.

of de Brazilian Academy of Neurology, the "Arquivos de Neuro-Psiquiatria" in 1943, working as its editor for 44 years in a row. Lange passes away on the 29<sup>th</sup> August 1986, exactly one day after he had turned 83 years-old<sup>6,7</sup>.

From very early in his career, Lange had a great interest in the study of the cerebrospinal fluid and how it could be used in clinical practice, which made him the first neurologist devoted to the study of CSF in our country. Through his academic life he published several studies on CSF findings, mostly related either to NC or neurosyphilis<sup>6</sup>.

In 1936 published his first paper on CSF abnormalities in Central Nervous System Cysticercosis and in 1940 described in minute detail the cerebrospinal fluid syndrome found in NC, including the complement-fixation test, the occurrence of pleocytosis with eosinophils and the elevated protein content (Fig 4)<sup>10,11</sup>.

After studying the CSF abnormalities in 24 cases of NC, he came to the following conclusions: "...1- high CSF pressure, elevated cell count, elevated albumin and globulin content are not sufficient for the diagnosis of encephalic cysticercosis; 2- colloidal flocculations of the parenchymatous type and a negative Wasserman reaction are indicators of probability; 3- the presence of eosinophils in the CSF is an excellent tool in the investigation of encephalic parasitosis; 4- Weinberg's reaction with total alcoholic extract of "Cysticercus cellulosa" is the only tool that gives certainty to the diagnosis"<sup>11</sup>.

Lange's studies clearly stated that despite the fact that the finding of eosinophils in the CSF is very important in supporting the obligatory for the diagnosis of NC<sup>10,11</sup>. Lange established that: "the demonstration of eosinophils in the CSF is not constant in meningoaxial cysticercosis and cannot be used as a substitute for Weinberg's reaction, which is the only test that can be considered specific amid the other CSF changes"<sup>11</sup>.

The published studies of Lange were even cited by Del Bruto, Sotelo and Román in 1998<sup>13</sup>, when writing on the use of the complement fixation test (CFT): "initially developed to determine the presence of anticysticercal antibodies in serum, Lange (1949) used the CFT in CSF with better results; the author considered that a positive CFT was part of a characteristic "CSF syndrome" of neurocysticercosis that also included the presence of eosinophils and increased protein levels"<sup>13</sup>.

## CONCLUSION

Two Brazilian researchers, Dr. Arthur Moses, in Rio de Janeiro (Instituto Oswaldo Cruz) in 1911, and Dr. Oswaldo Lange, in São Paulo (Faculdade de Medicina da Universidade de São Paulo) in 1940, contributed immensely to the cerebrospinal fluid diagnosis of neurocysticercosis. The former was the creator of the reaction used in both blood and CSF samples for the immunological diagnosis of cysticercosis, whereas the latter described in detail the CSF findings of what he termed CSF syndrome in NC.

**Acknowledgments** - The authors would like to thank Professor Antonio Spina-França for providing us with a photograph of Dr. Oswaldo Lange, as well as many important bibliographic references. We would also like to thank Dr.

Francisco M.B. Germiniani for the translation of this manuscript. Extended thanks got to the Academia Brasileira de Ciências (Brazilian Academy of Sciences) for the biographic data of Dr. Arthur Moses.

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