## **THESES**

TUBERCULOUS MENINGOENCEPHALITIS IN CHILDHOOD: CRITICAL EVALUATION OF NEW LABORATORY DIAGNOSTIC METHODS (Abstract)\*. Dissertation. São Paulo. 1996.

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Tuberculosis (TB) is caused by Mycobacterium tuberculosis an alcohol-acid-resistant bacillus described by Robert Koch in 1882. The pathology of TB is well known since long time ago but still remains current interest because of the number of infected people; its worldwide situation is considered critical. After the acquired immunodeficiency syndrome (AIDS), tuberculosis has assumed a new context and had its incidence significantly increased.

Among the consequences of tuberculosis, the most worrying and serious one is tuberculous meningoencephalitis (TBM). It may affect up to 20% of the assailed patients under 20 years old and reach a lethality rate near 50%, as it is found in Brazil. The accepted pathophysiological mechanism is the dissemination through the blood stream. The most frequent presentation form in the central nervous system is the acute inflammatory caseous meningitis. The clinical manifestation is related to the affected neurological structure and its pathophysiology. The meningeal exudate is responsible for meningeal signs, cranial nerves disturbances and hydrocephaly. Injury of the encephalic parenchyma results in lowered consciousness levels, convulsive crisis, hypothalamic and brainstem alterations. The arteritis and vascular occlusions cause focal neurological deficits and the hypersensitivity phenomena may produce cerebral edema and intracranial hypertension. It may develop to disabling sequelae or even death if not diagnosed and early treated.

Most frequent in the childhood, MTB has often the clinical and epidemiological diagnosis difficult to perform, requiring the aid of laboratorial exams. The bacteriological and chemocytological cerebrospinal fluid (CSF) evaluation presents low sensitivity. Other exams like image investigation may reveal suggestive alterations but not pathognomonic for the disease. The presence of CSF signs as compatible TBM syndrome in patients with an extraneural TB is accepted as a diagnostic criterion, even in the absence of microbiological confirmation. Therefore, the investigation of TB in other systems is critically important. Unfortunately, is large the percentage of cases not presenting classical clinical forms, epidemiology, nor the suggestive CSF syndrome.

Based upon these facts, new methods for laboratorial diagnosis in the CSF have been proposed seeking an efficient and fast etiological confirmation of TBM, making it possible the early introduction of an appropriate therapy. Among new methods evaluated, emphasis was given to those based on the detection of bacillus tracers in the CSF, on the host reaction (specific antibodies to the Mycobacterium) and for characterization of blood-CSF barrier damage.

The new exams are discussed and conclusions are as follows. The combined utilization of clinical criteria, image observations, classical CSF syndrome with the bacteriological search, the CSF adenosine-deaminase activity (ADA) determination, and the CSF antigen and specific antibodies tests, permits to establish an adequate target-population. For the new exams it is fundamental to evaluate their sensitivity and specificity. Because of its practicability, low cost and fast performance, the ADA could be associated to TBM investigation as a sorting method. Considering the currently available exams, it is not possible yet to find an ideal one which should demonstrate fast diagnosis, high sensitivity and specificity at a low cost. The most promising method is the aetiological evaluation through polymerase chain reaction (PCR).

KEY WORDS: tuberculosis, tuberculous meningoencephalitis, laboratorial diagnosis, cerebrospinal fluid.

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