# Evaluation of Adenosine Deaminase Level in Reactional and Non–Reactional Leprosy

*Thesis*
*Submitted for Partial Fulfillment*
*of Master Degree in*
*Dermatology and Venereology*

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**2010**

# تقييم مستوى إنزيم أدنوزين دى أمينيز فى مرضى الحزام الفاعلي وغير التفاعلى

توطئه مقدمة الى كلية الطب

جامعة عين شمس

للحصول على درجة الماجستير

فى الجلدية والتناسلية


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جامعة عين شمس

كلية الطب

2010

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# Abbreviation

- **ADA**: Adenosine deaminase.
- **ADP:** Adenosine diphosphate.
- **AFB**: Acid fast bacillus.
- **AIDS**:Acquired immune deficiency syndrome
- **ATL**: Acute T cell leukemia.
- **ATP**: Adenosine triphophatse.
- **APCs**: Antigen presenting cells.
- **BBL**: Borderline borderline leprosy.
- **BCG**: Bacillus Calmette-Guérin.
- **BL**: Borderline leprosy.
- **BT**: Borderline tuberculoid.
- **BI:** Bacteriological index.
- **bp**:base pairs.
- **C** : Cytosine.
- **CD:** Cluster of differentiation**.**
- **CMI***:* Cell-mediated immunity.
- **CRF:** Case report form.
- **CXCL10:** Chemokine (C-X-C motif) ligand 10**.**
- **DNA**: Deoxyribonucleic acid.
- **EC number:** Enzyme Commission number.
- **ENL:** Erythema nodosum leprosum.
- **G:** Guanine.
- **HIV:** Human immunodeficiency virus
- **HLA:** Human leucocytic antigen.
- **HTLV**-1: Human T cell virus-1.
- **IL:** Interleukin.
- **IFN:** Interferon.
- **iNOS**: inducible nitric oxide synthase .
- **ISBN:** International Standard Book Number.
- **kD:** kilodalton**.**
- **Lepromin A**: Lepromin armadillo.
- **Lepromin H**: Lepromin human.
- **L-ADA:** Lymphocyte adenosine deaminase.

- **LL:** Lepromatous leprosy.
- **Lrtl**: Low resistant tuberculoid leprosy.
- **M. leprae**: Mycobacterium leprae.
- **Mal**: Maculoanesthetic.
- **Mb**: Megabases (million of base pairs).
- **MB:** Multibacillary.
- **MDT:** Multidrug therapy.
- **MHC:** Major histocompatibility complex.
- **MI:** Morphological index.
- **MoAb**: Monoclonal antibodies.
- **mRNA**: Messenger ribonucleic acid.
- **NASBA:** Nucleic acid sequence basd amplification.
- **NAPCs:** New antigen presenting cells.
- **PB:** Paucibacillary leprosy.
- **PCR** : Polymerase chain reaction.
- **PGDF:** Platelet-derived growth factor.
- **PGL**-1: Phenolic glycolipid-1.
- **PNL**: Pure neuritic leprosy.
- **qRT –PCR :**quantitative reverse transcriptase polymerase chain reaction.
- **RL**:Reactional leprosy
- **rRNA** : ribosomal ribonucleic acid.
- **SCs:** Schwann cells**.**
- **SCID**: Severe combined immunodeficiency.
- **sLL** :subpolar lepromatous.
- **TB:** Tuberculosis**.**
- **Th:** T-helper cell.
- **TLR**: Toll-like receptor.
- **Tm**: macular tuberculoid leprosy.
- **TNF-α**: Tumor necrosis factor alpha.
- **Tt:** subpolar tuberculoid.
- **TT:** Tuberculoid leprosy.
- **WHO:** World Health Organization.

# Acknowledgments

*Thanks to God first and foremost. I feel always indebted to God, the most kind and the most merciful.*

*I would like to express my gratefulness and respect to* ***Prof. Dr. Hoda Ahmed Moneib,*** *Professor of Dermatology and Venereology, Ain Shams University, for her moral and scientific support and for giving me the honor of working under her supervision and valuable guidance.*

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# Introduction

Leprosy, or Hansen's disease, is a chronic infectious disease caused by the bacterium Mycobacterium leprae (M.Leprae) (***Sasaki et al., 2001).*** Leprosy is primarily a granulomatous disease of the peripheral nerves and mucosa of the upper respiratory tract; skin lesions are the primary external symptom ***(Stefani et al., 2009)***. Leprosy is still a significant public health problem. Disease prevalence has fallen due to introduction of multidrug therapy (MDT) (***World Health Organisation, 2010).***

Reactions are a characteristic and clinically important aspect of Hansen's disease. Fifty percent will experience reaction after the institution of MDT. In addition to antibiotic therapy, intercurrent infection, vaccination, pregnancy, vitamin A, iodides and bromide may trigger reactions. Reactions can be severe and are an important cause of permanent nerve damage in leprosy patients. Reactional state is frequently abrupt in their appearance which changes slowly. It is therefore a common reason for patients to seek consultation ***(James et al., 2006).***

There is no quick and easy method for identification of M.Leprae in clinical specimens, diagnosis of leprosy is based primarily on clinical ground. M.Leprae cannot be cultured in the laboratory ***(Clark-Curtiss et al., 1985)***. Diagnosis is often confirmed by microscopic observation of acid–fast bacilli (AFB) in fresh slit skin smears**.** Since microscopy requires an estimated 10,000 organisms/g of tissue, AFB staining is positive for most patients with multibacillary, but is frequently negative in paucibacillary cases. Serological testing is not useful for diagnosis as it does not detect most paucibacillary cases ***(Roche et al., 1993)***. A cutaneous nerve biopsy is frequently required to establish the diagnosis of pure neural

leprosy ***(Jacob and Mathai, 1988)***. So a sensitive and specific method for detection of M. leprae might simplify the diagnosis of leprosy. Recently developed molecular techniques have the potential for more sensitive detection of M.Leprae but they are expensive ***(De-Wit et al., 1993; Pham et al., 2009).***

There is a need for a method not only less expensive but also facilitates detection of the activity of microorganisms especially in reactional leprosy. Adenosine deaminase (ADA), an enzyme of purine metabolism in part regulates the lymphocyte metabolism and is also important for lymphocytic differentiation and growth ***(Fischer et al., 1976)***.

ADA is present in T-lymphocytes and varies according to cellular differentiation. Its activity appears to be necessary for an effective immune response as shown by many studies like in combined immunodeficiency disease and in typhoid fever. Besides this, increased activity of serum ADA has also been demonstrated in tubercular pleural effusion and active tuberculosis ***(Bhargava et al, 1990; Ahmed et al., 2008).***

An increased activity of serum ADA has also been demonstrated in leprosy patients. The cellular immune aberration seen in the different types of leprosy may be due to abnormal proliferation of lymphocytes in response to M. leprae ***(Suri Babu et al., 1990)***. There was also increase in serum ADA level in multibacillary leprosy patients as compared to paucibacillary leprosy patients. Furthermore, this was increased in patients of leprosy with reaction. This may be because of increased lymphoreticular activity during the reactional phase. So ADA can be applied as a marker of activity of leprosy ***(Nigam et al., 2005)***.

# AIM OF WORK

The aim of this study is to evaluate ADA as a marker of activity of leprosy in general and in lepra reaction in particular.

# Leprosy

## Synonyms:

Hansen's disease, hanseniasis, elephantiasis grecorum and names in local languages in endemic areas are different names of leprosy (***Lockwood, 2004).***

## Leprosy definition:

Leprosy is chronic granulomatous disease of the skin, mucosa of the upper respiratory tract and peripheral nerves caused by M. leprae ***(Stefani et al., 2009)***.

## Etymology:

The word leprosy is derived from the Greek lepi (λέπι), meaning scales on a fish and lepein, to peel ***(Barnhart, 1995).***

## History:

Leprosy was described in the Hindu religious book Atharva-veda. The Cambridge Encyclopedia of Human Pale pathology holds that: "The Sushruta Samhita from India describes the condition well and even offers therapeutic suggestions as early as about 600 B.C." ***(Aufderheide et al., 1998)***.

Chinese text on bamboo slip in the third century B.C., not only described the destruction of the "pillar of the nose", but also the "swelling of the eyebrows, loss of hair, absorption of nasal cartilage, difficult and hoarse respiration, as well as anesthesia. In the West, the earliest description of leprosy was made by the Roman (25 B.C. – 37 A.D.), called leprosy "elephantiasis". In the Muslim world, the Persian polymath Avicenna (980–1037 A.D.) was the first outside China to describe the destruction of the nasal septum in those suffering from leprosy ***(Mc Leod et al., 1981).***