

RAPID DIAGNOSIS OF TYPHOID FEVER BY ANTIGEN AND / OR ANTIBODY DETECTION

THESIS

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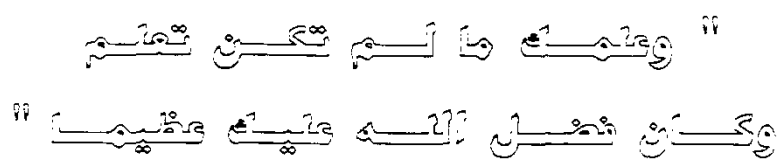
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DEDICATION

*I am Specially Greatly Indebted To
My
Parents and Brothers .
&*

Deep Thanks To My Husband .

*THIS THESIS HAS NOT BEEN SUBMITTED FOR A DEGREE
AT THIS OF ANY OTHER UNIVERSITY*

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ABBREVIATIONS

AFT	: Adult Worm Freeze-thaw antigen .
Ag	: Antigen .
AP	: Alkaline Phosphatase .
BSA	: Bovine Serum Albumin .
CIE	: Counter Immunoelectrophoresis .
COAG	: Coagglutination .
ELISA	: Enzyme-linked immunosorbent assay .
KDa	: Kilo dalton .
LPS	: Lipopolysaccharide .
MAbs	: Monoclonal antibodies .
OMPS	: Outer membrane proteins .
PBS	: Phosphate buffered saline .
PBS-T	: Phosphate buffered saline Tween .
SDS-PAGE	: Sodium dodecyl sulfate polyacrylamide gel electrophoresis.
SEA	: Soluble egg antigen.
SIgA	: Secretory IgA.
<i>S.mansoni</i>	: <i>Schistosoma mansoni</i> .
<i>S.paratyphi</i>	: <i>Salmonella paratyphi</i> .
<i>S.typhi</i>	: <i>Salmonella typhi</i> .
SWAP	: Soluble worm antigen preparation.
VBE	: Veronal buffer extract.
Vi antigen	: Virulence antigen.
XIE	: Crossed immunoelectrophoresis.

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AIM OF WORK

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Typhoid fever is diagnosed by blood culture and/or antibody estimation. The validity of Widal agglutination test in the diagnosis of typhoid is questioned in areas endemic for typhoid fever and other diseases. Cross-reacting antigens between *Salmonella typhi* and other *Enterobacteriaceae* e.g.: *Shigella sonnei*, *Escherichia coli*, *Klebsiella pneumonia*, *Neisseria meningitides* have been demonstrated. Also, it has been shown that *Salmonella typhimurium* and *Schistosoma mansoni* share antigens. The association between Schistosomiasis and Salmonellosis is common in Egypt. This prompted us to investigate the antigenic pattern of *S.typhi* (O) antigen (used in Widal test) and schistosoma antigens with the purpose of identifying shared epitopes which could influence Widal test titers, since it is the most widely used test in typhoid immunodiagnosis. Further, unshared *S.typhi* specific antigens are evaluated for their diagnostic potential.

APPROACH

The following experimental design was followed in order to achieve the study objectives:

- 1 - *S.typhi* and *S. paratyphi* antigenic preparations and antigens derived from worms and eggs of *Schistosoma mansoni* were electrophoresed. The antigenic fractions were transferred to nitrocellulose sheets, followed by blotting and cross-blotting with rabbit antisera raised against both bacterial and helminthic antigens.
- 2 - Bacterial antigens that are "shared" with *schistosome* antigens are defined as those being recognized by antisera against bacterial as well as helminthic antigens.
- 3 - Bacterial antigens which are "not shared" i.e "specific" with *schistosome* antigens are defined as those being recognized only by antisera raised against the respective bacterial antigens.
- 4 - The sensitivity was evaluated by immunoblotting assay using sera from patients with typhoid fever (positive culture), however the specificity was evaluated by using sera from patients with other bacterial infection and schistosomiasis.

INTRODUCTION

INTRODUCTION

Typhoid fever is an unsolved health problem in the world . There are approximately 12 million cases per year, and in developing countries the incidence is about 540 new cases per 100,000 inhabitants . (**Edelman; and levine, 1986**).

It is an acute systemic illness caused by infection with *Salmonella typhi* . It is characterized by prolonged fever, sustained bacteremia without endothelial or endocardial involvement, bacterial invasion and multiplication within the mononuclear phagocytic cells of the liver, spleen, lymph nodes, and peyer's patches. (**Strickland 1984**).

Paratyphoid fever is a similar pathological and clinical illness, but generally milder . It is caused by many species of salmonellae, but most commonly by *S. paratyphi* A, *S. schottmuelleri* and *S. hirschfeldii* .(**Strickland, 1984**).

Enteric fever, which includes typhoid and paratyphoid, causes more serious illness and is endemic in certain geographical regions, including all Southeast Asian countries, India, Egypt and Chile (**Macario 1986**).

S. typhi is similar to other salmonellae in that it is gram- negative, flagellated, nonencapsulated, nonsporulating and facultative anaerobic bacillus. *S. typhi* ferments glucose, reduces nitrate to nitrite, synthesizes peritrichous flagella when motile. It has a somatic (O), a flagellar (H), an envelope (K) antigens and a lipopolysaccharide macromolecular complex called endotoxin that forms the outer portion of the cell wall . The endotoxin is composed of three layers, an outer (O - oligosaccharide), a middle (R-core) , and a basal (lipid A), Also *S. typhi* is capable of developing R -plasmide-transmitted antimicrobial resistance. (**Strickland, 1984**). (as in schematic diagram).