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NEUTROPHIL PHAGOCYTIC FUNCTIONS AND SERUM OPSONIC ACTIVITY IN CHILDREN WITH NEPHROTIC SYNDROME

Thesis

Submitted to the Faculty of Medicine,

University of Alexandria,

In partial fulfillment of the requirements of the degree of,

Master of Paediatrics

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2003

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صدق الله العظيم

ACKNOWLEDGEMENT

I would like to express my deepest gratitude and sincere appreciation to **Dr. Tarek Mostafa El-Walili**, Professor of Paediatrics, for his valuable supervision, encouragement and meticulous scientific guidance.

I am deeply grateful to **Dr. Ashraf Ahmed Galal**, Assistant Professor of Paediatrics, for his patience, constructive criticism, and unlimited assistance to accomplish this work.

My great thanks to Professor **Dr. Ezzat Mohamed Hassan**, Professor of Immunology, Alexandria Medical Research Institute, for his valiable advice and active participation that allowed the accomplishment of the practical part of the work.

Also great thanks to Professor **Dr. Amina Sedki El-Halwany**, Professor of Paediatrics, who gave me continuous encouragement and valuable advice.

I wish to express my thanks to Professor **Dr. Eman Ali Ahmad Rashwan**, Professor of Immunology, Alex. Medical Research Institute for her active participation in the practical part of the work.

Finally, a special debt of gratitude and cordial appreciation to my kind **husband** for his continuous encouragement to accomplish this work.

CONTENTS

List of Abbreviations

NS	Nephrotic Syndrome
MCNS	Minimal Change Nephrotic Syndrome
PMNS	Polymorphonuclears
C	Complement
GM-CSF	Granulocyte-Macrophage Colony-Stimulating Factor.
G-CSF	Granulocyte Colony-Stimulating Factor.
H.M.P	Hexose Monophosphate Shunt.
NADPH	Nicotinamide Adenine Dinucleotide Phosphate
NBT	Nitroblue Tetrazolium
SSNS	Steroid Sensitive Nephrotic Syndrome

Introduction

Nephrotic Syndrome

Nephrotic syndrome (NS) is the clinical manifestation of a number of morphologically distinct glomerular disorders characterized by oedema, massive proteinuria, hypoproteinaemia and hyperlipidaemia[1,2,3].

Ninety percent of the nephrotic cases are primary in origin; minimal-change disease is found in approximately 85%, mesangial proliferation in 5%, and focal sclerosis in 10%. Secondary NS represents the remaining 10% of children with nephrosis, where it is mediated by some form of glomerulonephritis; memberanous and membranoproliferative being most common[2,3].

The basic abnormality in NS is proteinuria, which results from increased glomerular capillary wall permeability. The mechanism of this increased permeability in minimal change nephrotic syndrome (MCNS) is unknown, but may be related to loss of negatively charged sialoproteins within the capillary wall[3,4,5]. On the other hand, in secondary NS either antigen-antibody immune complexes are deposited on the glomerular basement membrane or the basement membrane itself is the antigen involved in the antigen antibody reaction, both mechanisms trigger a sequence of complement-mediated events which ultimately lead to damage of the basement membrane and alter its permeability[6].

In the nephrotic state, the protein loss generally exceeds 2gm / 24 hours and is composed primarily of albumin. In general oedema appears when the serum albumin level falls below 2 gm /dl [3].

In the minimal change disease, there is no evidence of structural damage to the basement membrane. The defect is in the electrostatic function of the glomerular barrier to protein filteration[7]. It is suggested that hormonal circulating factors (Lymphokines), released from T lymphocytes sensitized against glomerular antigen is the cause of loss of glomerular polyanionic barrier [8,9,10].

The large majority of children with minimal change disease are steroid responsive. They will have repeated relapses until the disease resolves itself spontaneously towards the end of the second decade of life[11,12].

Approximately 50 – 60 % of patients with mesangial proliferation will respond to corticosteriod therapy, and approximately 20 % of patients with focal sclerosis respond to prednisone or cytotoxic drugs or both[3].

Because of the potential severity of infection in nephrotic children, the problem of the selection of effective antibiotic therapy is of a vital importance[13]. Most importantly a broad

spectrum antibiotic should be started to cover both gram positive and gram negative encapsulated organisms while waiting definite culture and sensitivity results[14].

Prophylaxis against pneumococcal infection may be attempted with pneumococcal polysaccharide vaccine and with oral penicillin[15]. Parenteral hyperimmune serum globulin may occasionally be indicated in high-risk patients (infants and elderly adults). Vaccination may be best administered during remission, because immunization may not be effective if given during relapse[16], where the ability of MCNS patients to generate specific antibodies is impaired[17].

Although corticosteroid responsive NS has a good prognosis, yet it is not without complications. These include:

(1)<u>Infection:</u>

Originally, infection was a frequent cause of death in nephrotic children, and the biggest reduction in the mortality in these patients followed the introduction of antibiotics rather than any specific therapy of the NS itself. Primary peritonitis causes abdominal pain and vomiting that may be difficult to differentiate from a hypovolemic episode[18].

Viral infections are ordinarily tolerated well unless immunosuppressive agents are being given[16].