LYMPHORETICULAR REACTION IN RELATION TO OVARIAN NEOPLASMS

Thesis

Submitted for the Degree
of Ph. D. in *(Pathology)*

By

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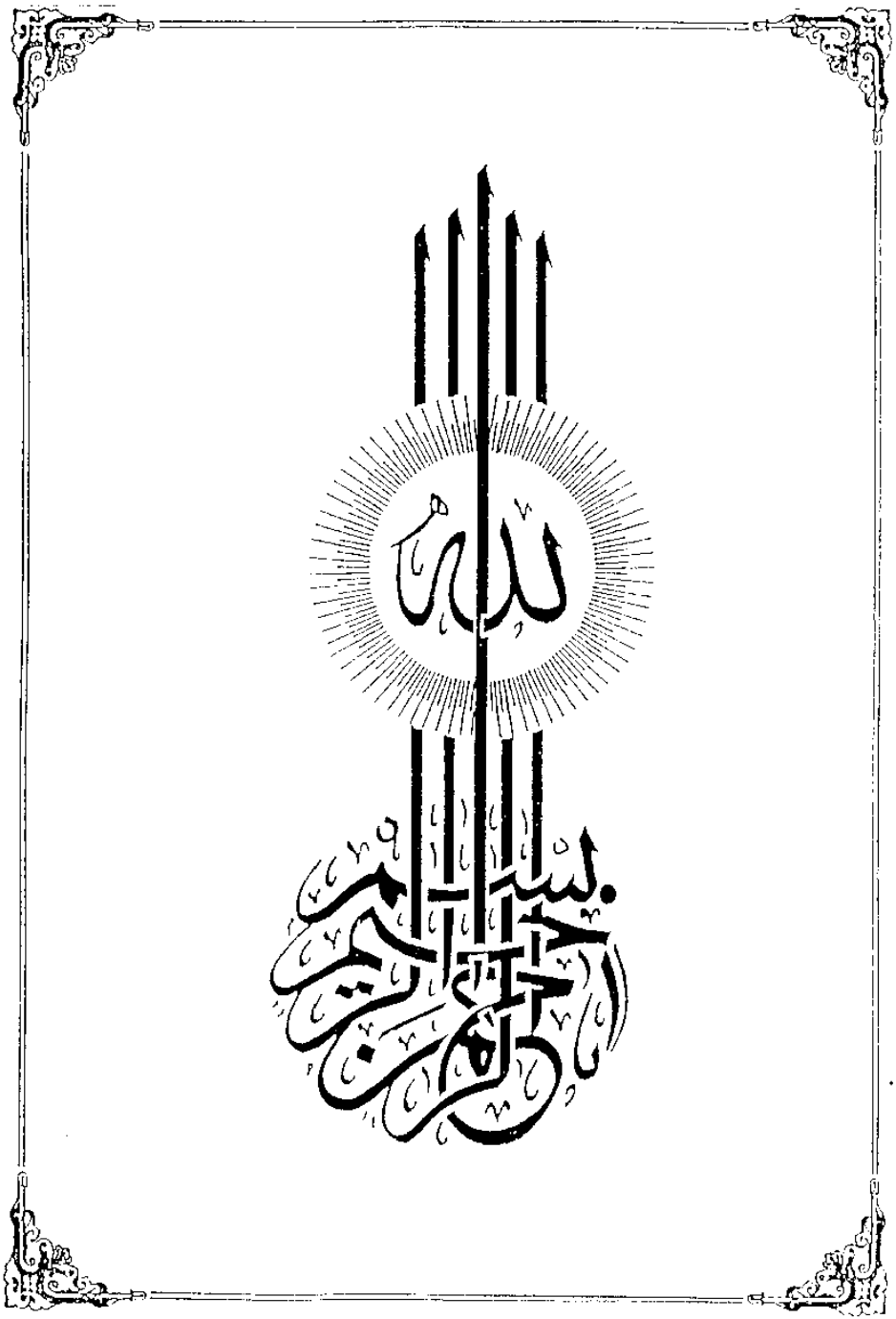
1987

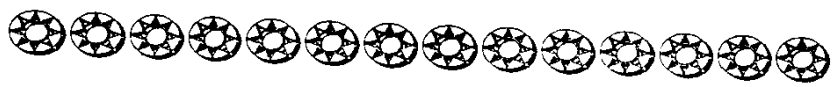
بسم الله الرحمن الرحيم

وَقُلْ رَبِّ زِدْنِي عِلْمًا



To My Parents

With Love and Affection



ACKNOWLEDGMENTS

I would like to express my profound gratitude and deep appreciation to Professor Dr. M.A. Sherif, Professor of Pathology, Faculty of Medicine, Ain Shams University, for his most valuable support particularly during my stay in England. His guidance and advice helped make my stay more productive and fruitful.

My most sincere thanks and respect are cordially presented to Professor M.B. Sammour, Professor of Obstetrics and Gynaecology, Faculty of Medicine, Ain Shams University, for his continuous help and co-operation particularly while establishing the scientific channel with England.

I am extremely grateful to Dr. M. Moore, Head of Immunology Department, Christie Hospital, Manchester, England, for his most valuable guidance, advice and encouragement. He also supplied me generously with monoclonal antibodies.

I wish to thank deeply Professor, H. Fox, Professor of Pathology Manchester University, England, for granting me the chance to do this piece of work in his Department, the use of his materials and his scientific guidance and valuable criticism.

Many thanks are also due to Dr. H. Buckley for her kind help and illuminating discussions.

I am indebted to Mrs. Linda Chauner for her limitless generosity and her technical help.

The idea of this work was first inspired by Professor Ahmed El Tawil, Professor of Pathology, Faculty of Medicine, Ain Shams University, to whom I am extremely grateful.

This work was sponsored by the Mission Department, Ministry of Higher Education and by Ain Shams University to both I am extremely thankful and to the Pathology Department, Ain Shams University for nominating me for this mission.

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According to *Old (1981)* recent progress in the field of cancer research was directed towards the topic of tumour immunology. An underlying assumption in much of the work dealing with cancer immunology is that antigenic changes recognizable by the host's immune system are an invariable accompaniment of malignant transformation.

Benjamini et al. (1982) pointed out that the immunodiagnosis of cancer may be based on two approaches:

- Identification, isolation and characterization of cancer antigens.
- Definition and assessment of cellular and humoral host's antitumour response.

Csiba et al. (1984) pointed out that the use of monoclonal antibodies to leucocytes on tissue sections allows the examination of the inflammatory response in situ. The approach also has the advantage that properties of the plasma membranes of tumour cells (e.g. expression of tumour-associated antigens or histocompatibility antigens) critical for certain types of immune interaction, may be simultaneously examined.

Moore (1984) reported that the mononuclear cell infiltration frequently seen in malignant neoplasms may have a tumour-related functional activity and imply a good prognosis. He suggested that leucocytic infiltration may be associated with the generation of an immune response to tumour-associated antigens.

Whitewell et al. (1984) found that in addition to immunocompetent cells, certain epithelia and a significant number of non lymphoid neoplasms (e.g.,

breast cancer, colon cancer and malignant neoplasms melanoma) display class II major histocompatibility complex (MHC) molecules.
Guerry et al. (1984) questioned whether this property is a requirement for the induction of lymphoproliferative responses to tumour antigens.

Ferguson et al. (1985) stated that as class II MHC antigens are implicated in the sensitization phase (afferent limb) of cell-mediated cytolysis which involves antigen recognition and presentation of effector cells, their expression by tumour cells is relevant to the recognition of these cells by the host's defensive cells.

According to *Sevelda et al. (1987)* cancer of the ovary is the third frequent carcinoma of the female genital tract and is the leading cause of death from gynaecologic malignancies. The major therapeutic limitations in ovarian carcinoma is imposed by the fact that the disease is frequently diagnosed at an advanced stage (50 - 70% are diagnosed in stage III and IV according to the FIGO classification). Likewise, post-therapeutic recurrences are frequently not recognized at a time early enough to allow the advantageous application of therapeutic procedures. Only 5 - 15% of patients live longer than five years in spite of radical surgery and cytotoxic treatment. However, marked improvement of survival by earlier treatment may be anticipated in that therapeutic success correlated strongly with tumour volume as well as with the clinical stage.

The aim of this work is to assess and compare the in situ lymphoreticular reaction in normal ovary and in the different benign and malignant ovarian neoplasms, and simultaneously examine the properties of the plasma membranes of ovarian tumour cells that may be related to the

capacity of the tumour to evoke an immune response leading to a leucocytic infiltrate.

The membrane properties are the expression of tumour associated antigens and class II MHC antigen.

A correlation will be attempted between the extent of the lymphoreticular reaction and the histologic type, grade, clinical stage and prognosis of the disease process.

By utilizing specific monoclonal antibodies (to leucocytes, major histocompatibility complex antigens and tumour-associated antigens) and sensitive immunohistochemical techniques on formaline fixed, paraffin embedded material, this work aims at providing a quantitative means of measuring the leucocyte infiltrate in ovarian or other tumours that can be applied on stored tissues.

REVIEW OF LITERATURE

THE NORMAL OVARY

A. ANATOMY *Howkins and Bourne (1978)*

Each ovary is roughly almond-shaped and measures 35 mm in length, 25 mm in width and 18 mm in thickness. The colour is pearly grey and the outer surface is slightly corrugated.

The ovaries are situated one on each side of the uterus close to the lateral wall of the lesser pelvis. Each ovary is attached to the back of the broad ligament by a thin mesentery, the mesovarium. This area is called the hilum and is the point of entry and exit for all the ovarian vessels, lymphatics and nerves.

The long axis of the ovary is vertical, its convex border is directed posteriorly, while its attachment to the mesovarium is anterior. Laterally the ovary is related to the fossa below the bifurcation of the common iliac artery and the ureter. Medially the ovary is attached to the cornu of the uterus by the ovarian ligament. The ovario-pelvic fold (infundibulo-pelvic) is the outer border of the broad ligament and contains the ovarian vessels, nerves and lymphatics.

The ovarian arteries arise from the aorta, just below the level of the renal arteries. They pass into the infundibulo-pelvic fold to send branches to the ovaries and to the outer part of the Fallopian tube; it ends by anastomosing with the terminal part of the uterine artery.

The small lymphatics of the ovarian cortex drain into large channels in the medulla and via the hilum reach the infundibulo-pelvic fold to end in the superior lumbar group of lymph nodes. There is free inter-