ANAESTHESIA AND CARCINOID TUMOURS

An Essay Submitted in Partial Fulfilment

of the Master Degree in Anaesthesia and Intensive Care

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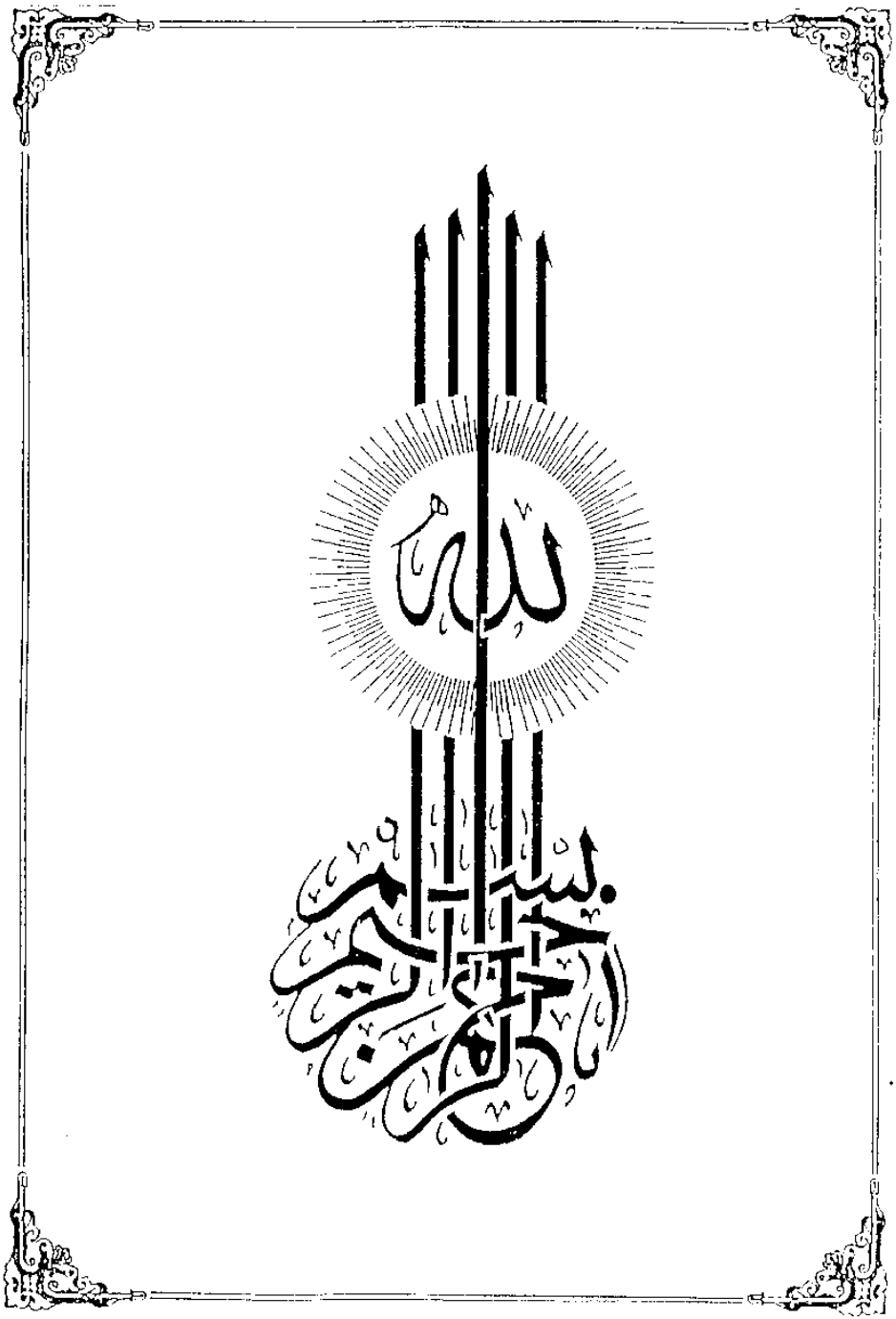
1993

ACKNOWLEDGEMENT

I would like to express my deepest gratitude to **Prof. Dr. Hussein Sabri,** Professor of Anaesthesia and Intensive Care, Faculty of medicine - Ain Shams University, under his supervision and kind advice, I had the honour to complete this work.

I am greatly indebted to **Dr. Nehal Nooh,** Assistant Professor of Anaesthesia and Intesive Care, Faculty of Medicine - Ain Shams University, for her guidance and valuable suggestions, spending quiet precious time for the completion of this work.

Many thanks are also due to **Dr. Galal Abu El Seoud,** Lecturer of Anaesthesia and Intensive Care, Faculty of Medicine - Ain Shams University, for his continuous guidance and encouragement.



CONTENTS

INTRODUCTION

Carcinoid tumours are first described by Merling in 1838 and named by Obendorfer in 1907 because they are less malignant than carcinoma. (Atkinson et al., 1993).

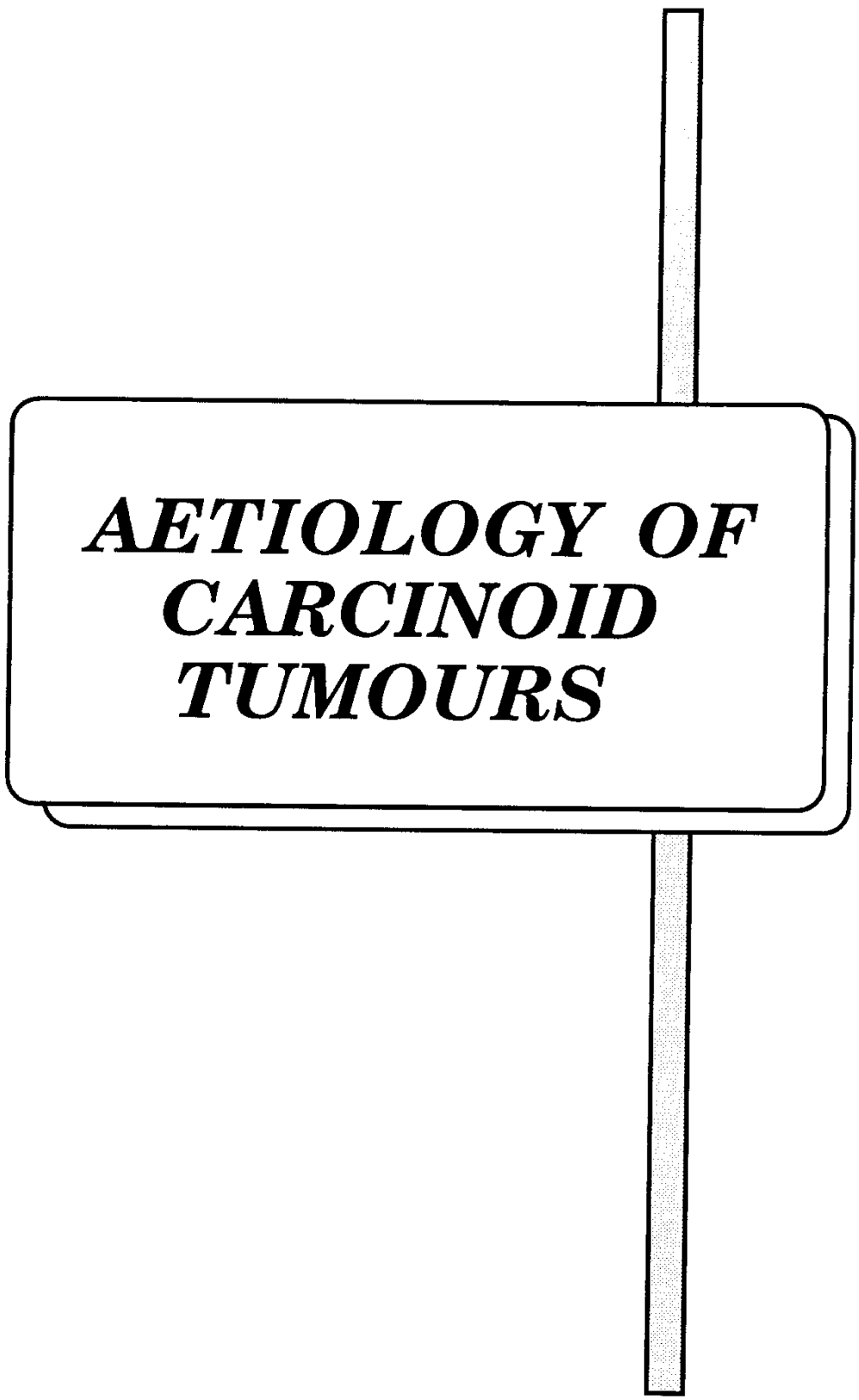
Carcinoid tumours arise from enterochromaffin cells, which embryologically migrate from the neural crest, and are scattered throughout the body but primarily reside in the submucosa of the gastrointestinal tract and the main bronchi. (Wall, 1992).

They are the most common neoplasms of the small intestine, with the highest incidence being in the appendix. The estimated incidence of carcinoid tumours is 8 per 100,000 persons. (Stoelting et al., 1988).

These tumours secrete over 20 substances with a variety of effects on vascular, bronchial, and gastrointestinal smooth muscle activity. These include serotonin, Kallikrein, prostaglandins, histamine and substance P. (Aitkenhead and Smith, 1990).

Only 5% of patients with carcinoid tumours develop carcinoid syndrome. It is this rare group of patients that is of particular interest and concern to anesthesiologists. The syndrome is caused by the release of sufficient quantities of

mediators from the tumour into the systemic circulation resulting in cutaneous flushing, diarrhea, broncho-constriction, and valvular heart disease. (Wall, 1992).



AETIOLOGY OF CARCINOID TUMOURS

Carcinoid tumours are of neuroendocrine cell origin and in the stomach arise from enterochromaffin or enterochromaffin like cells. (Rubin, 1973).

They share common cytochemical and ultrastructural characteristics with other Amine Precursor Uptake and Decarboxylation (APUD) cells, all of which secrete amines and polypeptide hormones. (Kaplan, 1979).

The APUD Concept:

This acronym APUD introduced by Pearse, 1968 refers only to a few of the many common characteristics of the APUD cells. The ability of the APUD cells to take up precursor amine, to store amines and to synthesize peptides is basic to their normal and abnormal potentiality and is probably attributed to their neural crest origin. (Friesen, 1979).

It was thought that the APUD cells arose from the neural crest, but it is now known that only some of these cells are derived from the definitive neural crest. Other APUD cells, specially those in the central nervous system, are neuroectodermal in origin. However the largest group of APUD cells, those of the gut and pancreas, are derived from

a single region of neuroendocrine programmed ectoplast.

Thus in the APUD concept the gut acts as an endocrine organ within a diffuse neuroendocrine system (Sagor, et al., 1982).

Characteristics of APUD cells:

1- APUD cells synthesize and secrete most of the hormones in the body except for the steroids. They take up amino acids and modify them, so that the hormones secreted are amino acids derivations, chiefly amines or peptides, e.g. gut endocrine cells. They can take up 5-hydroxytryptophan (5-HTP) and convert it to 5-hydroxytryptamine (5-HT or serotonin).

2- APUD cells consist of special neurons as well as endocrine cells. These nerve cells and endocrine cells share many characteristics.

Pearse and Takor, 1979 regarded all of the APUD endocrine cells of the gut as having so many activities like those of the nerve cells so they designated them as constituting part of the "diffuse neuroendocrine system".

3- APUD endocrine cells are enterochromaffin, argentaffin or argyrophil clear cells. They have a fluorogenic amine content.

4- Many of the APUD endocrine cells contain dopamine, serotonin, histamine as well as peptide hormones.

These hormones tend to be released together.

5- APUD hormone binds to its receptor, modifies messenger action leading to increase or decrease function such as proteogenesis or glycogenesis. (Williams, 1981).

Expansion of the APUD concept:

The idea which became the APUD concept was formulated in 1968 when the observed common cytochemical and ultrastructural characteristics of a small group of endocrine cells situated in different regions of the body, suggested that they share a common origin from the neuroectoderm of the neural crest. Since that time elaboration of the concept has been made and the number of cells in the series has increased from the original sex to approximately 40.

There are two principal reasons for this expansion :

First, there has been an almost explosive increase in the number of endocrine cells identifiable in the gastrointeropancreatic (GIP) system.

Second, despite earlier misgivings, it has become necessary to incorporate into the APUD series the endocrine cells of the hypothalamus and pineal gland together with the endocrine cells of the pituitary gland. These now constitute the central neuroendocrine division, leaving the remaining cells of the

original series to represent the peripheral neuroendocrine division. (Pearse and Takor,1979).

Incidence of carcinoid tumours:

Carcinoid tumours are not rare tumours, for they are found in one out of every 150 autopsies (Misiewic et al., 1966) and in one out of every 300 regular appendectomies. (Moertel et al., 1968).

Carcinoid tumours of the appendix are the most common neoplasm of that organ, occurrence rate varies from 0.36 - 0.71% of all surgically removed appendeses. (Beaton et al, 1981).

Distribution of Carcinoid Tumours:

Primary sites of gastrointestinal tract carcinoid tumours in decreasing order of frequency are: appendix, ileum, rectum, duodenum, stomach, colon, Mickel's diverticulum, biliary tract.

On occasion, carcinoid tumours arise in the bronchi, rarely they may arise from the ovaries.

Site	No.	% of total	average metastatic spread %
Appendix	1686	47	2
Jejuno-ileum	1032	29	34
Rectum	392	12	18
Duodenum	135	4	20
Stomach	93	3	23
Colon	91	3	60
Mickel's diverticulum	42	1	19
Biliary tract	10	< 1	30
Pancreas	2	< 1	-
Oesophagus	1	< 1	-
Total	3484		

(Based on Carter et al., 1982).

Sex:

The sex distribution of malignant carcinoid tumours is 1.5 : 1 females : males. (Jagar and Polk, 1977).

Age:

Average age was low for appendix, rectum, rectosigmoid. Carcinoid tumours occur in nearly all age

groups from 6 - 98 years, it showed an average age of 56 years at time of surgery. (Godwin, 1975).

Diseases associated with carcinoid tumours:

Von Recklinghausen's disease (VRD) may be associated with intestinal carcinoids particularly ampullary or peri-ampullary carcinoids (Hough et al., 1983).

VRD and carcinoids arise from a common neural crest cell line, it is supported by the association of both conditions with glioma and meningioma. It has been suggested that the linkage of neurofibromatosis, pheochromocytoma and duodenal carcinoid is a specific multiple endocrine neoplasm syndrome. (Wheeler et al., 1986).

Multiple polypoid carcinoid tumours were found in patients with achlorhydria and atrophic gastritis.

Some patients have a triad of hypergastrinemia, achlorhydria (pernicious anaemia) and carcinoid tumours. These multifocal tumours arise as a direct result of enterochromaffin like (ECL) cells hyperplasia (they are the commonest endocrine cells in the stomach, and in patients with hypochlorhydria or achlorhydria their number is increased). Gastrin is trophic to ECL cells and increased level of gastrin may produce ECL cell hyperplasia, this occurs in patients with Zollinger-Ellison syndrome (ZE) who

have increased gastrin level and increased acid secretion (Harvey et al., 1985).

Antisecretory drugs (Cimetidine - Ranitidine - Omiprazol) in therapeutic doses produce moderate increases in gastrin level, these are far from the high concentration observed in patients with ZE syndrome or atrophic gastritis who sometimes develop ECL cells hyperplasia and carcinoid tumours. The short term treatment with acid secretion inhibitors can not be judged as a risk (Bordi et al.,1987).

Hyperplasia of enterochromaffin cells in ulcerative colitis and also dysplasia of these elements as a part of pancellular dysplasia may occur, this is a possible explanation for carcinoid tumours in chronic ulcerative colitis (Dodd, 1986).

Cases of intestinal carcinoids coexisting with Crohn's disease was described by Brown et al., 1986.

Coeliac disease has been proposed to be a premalignant condition also (Cooper et al., 1980).

It is widely accepted that, the flat coeliac mucosa contains features predisposing to later development of small intestinal malignancies (Fric et al., 1963).