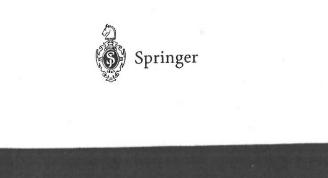
C.D. Johnson and C.W. Imrie

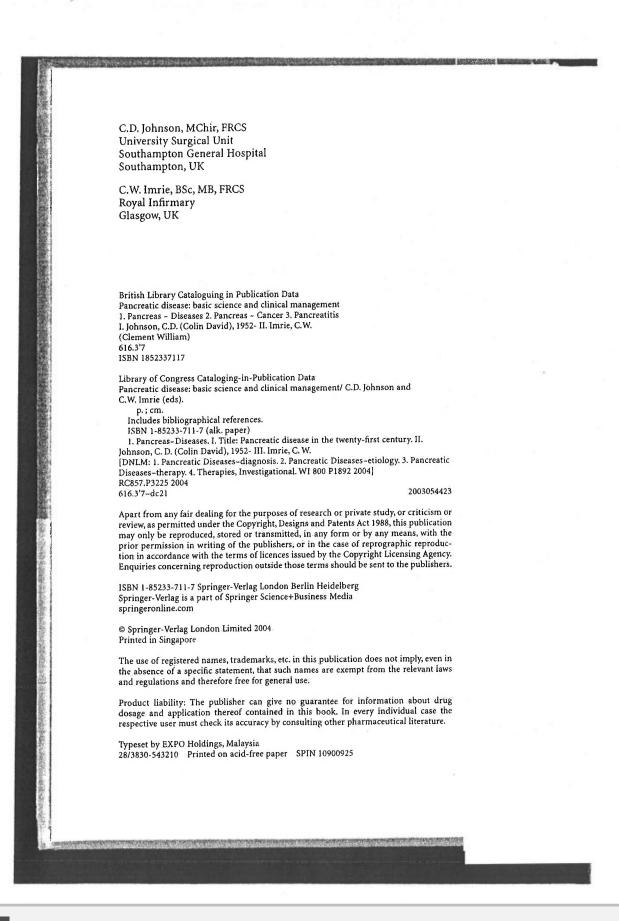
# **Pancreatic Disease**

**Basic Science and Clinical Management** 

With 82 Figures

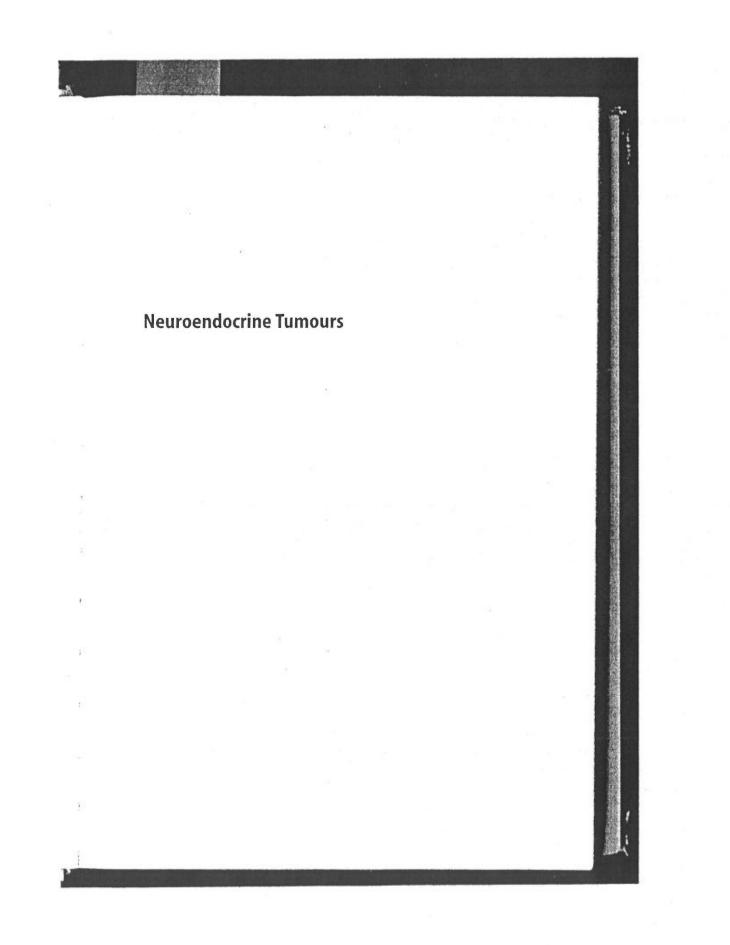


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### 4 GI Hormone Producing Tumours: Syndromes and Treatment Options

Mary McStay and Martyn E. Caplin

Neuroendocrine tumours of the pancreas (also called pancreatic endocrine tumours or islet cell tumours) may be *functioning* or *non-functioning*. Functioning tumours are those associated with a clinical syndrome that is caused by hormone release, and are named according to the hormone that they secrete (Table 4.1). Non-functioning neuroendocrine tumours of the pancreas include those that have all the histological characteristics of a neuroendocrine pancreatic tumour (NPT), but no associated clinical syndrome related to hormone hypersecretion. NPTs are rare tumours, with an incidence of less than 1/100 000 population/year. Non-functioning tumours form the biggest group (30–40%), followed by gastrinomas and insulinomas, which have approximately the same incidence. With the exception of insulinomas, the majority of NPTs are malignant.

Eight of the NPTs are well established and are included in most classifications. These are gastrinomas, insulinomas, VIPomas, glucagonomas, somatostatinomas, growth-hormone releasing factor secreting tumours (GRFomas), ACTH secreting tumours of the pancreas (ACTHomas), and 'non-functioning' tumours, which may in fact be pancreatic polypeptide-secreting tumours (PPomas). Other rarer NPTs have recently been considered as causing syndromes, including NPTs causing hypercalcaemia (producing parathyroid hormone and parathyroid hormone-related protein), NPTs secreting calcitonin and NPTs causing the carcinoid syndrome.

#### Pathophysiology and Pathology of Neuroendocrine Tumours

The histological diagnosis of neuroendocrine tumours relies first on the identification of general markers of neuroendocrine differentiation, and then cell-specific characterisation. Neuroendocrine differentiation is evaluated by immuno-histochemistry using antibodies against secretory granule proteins (chromogranin A, synaptophysin) and cytosolic proteins (neuron-specific enolase, protein gene product 9.5). The cell-specific characterization of neuroendocrine tumours requires hormone immunohistochemistry. According to the World Health Organisation (WHO) classification, neuroendocrine tumours of the gastroenteropancreatic tract are classified as well-differentiated and poorly differentiated depending on their histological and functional features.

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Table 4.1. The different types of pancreatic neuroendocrine tumours and their associated hyperfunctional syndromes

Tumour	Cell type	Predominant hormone	Major clinical symptoms	Tumour location	Percent malignant
Gastrinomas	G	Gastrin	Recurrent peptic ulcer	Pancreas 50% Duodenum 50%	90
Insulinoma	В	Insulin	Hypoglycaemia (fasting or nocturnal)	Pancreas	10
VIPoma	?	Vasoactive intestinal polypeptide (VIP)	Watery diarrhoea, hypokalaemia, achlorhydria	Pancreas 90%	60
Glucagonoma	A	Glucagon	Diabetes mellitus, necrolytic migratory erythema	Pancreas	90
Somatostatinoma	D	Somatostatin	Diabetes mellitus	Pancreas 55% Duodenum 45%	80
GRFoma	?	Growth-hormone releasing- hormone	Acromegaly	Pancreas 30% Lung 50% Jejunum 15%	60
ACTHoma	7	ACTH	Cushing's syndrome	Pancreas 90%	95
PPoma	PP/F	Pancreatic polypeptide (PP)	Hepatomegaly, abdominal pain	Pancreas 100%	80

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