MEDICAL AND SURGICAL ENDOCRINOLOGY

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Medical and Surgical Endocrinology

D. A. D. MONTGOMERY

M.B.E., M.D.(Belfast), F.R.C.P.

Physician, and Physician in charge, Metabolic Department, Royal Victoria Hospital, Belfast.

Honorary Reader in Medicine (Endocrinology), The Queen's University of Belfast.

and

R. B. WELBOURN

M.A., M.D.(Cantab.), M.D.h.c.(Karolinska), F.R.C.S., F.W.A.C.S.

Professor of Surgery, University of London.

Director, Department of Surgery,

Royal Postgraduate Medical School and Hammersmith Hospital.

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R. B. WELBOURN

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Contributors

Author Chapter 11

MARY G. McGEOWN, M.D., PH.D., F.R.C.P.ED. Honorary Reader in Nephrology, The Queen's University of Belfast

> Consultant Medical Urologist, Royal Victoria Hospital and Physician in Administrative Charge, Renal Unit, City Hospital, Belfast.

Co-authors

D.J. COWLEY, M.CH., F.R.C.S. (Part of chapter 14)
Senior Lecturer in Surgery,
University of Manchester;
Consultant Surgeon, University Hospital of South Manchester.

G. V. FOSTER, M.D., PH.D. (Chapter 10 and part of chapter 12)
Associate Professor of Physiology and Medicine,
The Johns Hopkins University School of Medicine, Baltimore.

I. D. A. JOHNSTON, M.CH., F.R.C.S. (Chapter 16)
Professor of Surgery,
University of Newcastle upon Tyne.
Consultant Surgeon,
Royal Victoria Infirmary, Newcastle.

C. U. McRAE, M.B., CH.B., F.R.C.S. (Part of chapter 6 and chapter 18)
Senior Registrar in Urology,
Christchurch Hospital, New Zealand.

R. A. SELLWOOD, CH.M., F.R.C.S. (Part of chapter 17)
Professor of Surgery,
University of Manchester.
Consultant Surgeon,
University Hospital of South Manchester.

Preface omiod aguith to some marican has

This largely new book has grown out of one entitled 'Clinical Endocrinology for Surgeons', which we published in 1963. Friends and reviewers were kind enough to persuade us that the title was wrong because it tended to prevent physicians and other clinicians, for whom it was suitable, from reading it. They also pointed out that laboratory workers and pre-clinical teachers found that it provided them with an account of clinical endocrinology based on the laboratory sciences and that candidates for examinations in the basic medical sciences used it for learning physiology and pathology. For these reasons we have changed the title and have tried to meet the needs of all these people.

Our first aim, as before, is to help all concerned with clinical endocrinology to understand, investigate and treat their patients. Anatomy, physiology and pathology are essential to understanding, and considerable clinical detail is required if patients are to be managed effectively. Our second aim is to help graduates and senior undergraduates to study for examinations. Our third aim is to present the clinical aspects of endocrinology to those not directly involved in the care of patients.

Endocrinology has advanced very rapidly in the past decade. The hypothalamus and the endocrine function of the gut have sprung to life, new hormones have been discovered, the interdependence of the nervous and endocrine systems has become much clearer, increasing numbers of hormones can be measured in the body fluids, the modes of action of hormones at the cellular level are being elucidated, and so on. Inclusion of much new material has increased the size of the book considerably. Many new tests of glandular function have been included. At the same time many old ones, which have been superseded in some specialized units, have been retained because the new ones are not generally available.

We believe firmly that all clinical medicine is one and that in endocrinology, as in other branches of medicine, physicians, surgeons, gynaecologists, radiodiagnosticians, radiotherapists, laboratory workers and others should, when required, work together for the solution of each patient's problems. We have therefore discussed the total management of patients from all points of view. We have discussed the indications for surgical operations and radiotherapy, and what may be expected of them, and have advised surgeons and radiotherapists what to do, without telling them in detail how to do it.

We have again attempted to provide a systematic account of clinical endocrinology, in which the essential unity of the endocrine system is emphasized. The arrangement is a little different and three new chapters have been added. The book is divided into six parts. Part 1 (the longest) describes the hypothalamus, the anterior pituitary and their dependent glands. Part 2 deals with calcium metabolism and the hormones which control it. Part 3 is concerned with the alimentary tract, including the islet cells of the pancreas.. Part 4 provides a description of multiple endocrine adenopathy and of the paraendocrine syndromes. Part 5 discusses some of the endocrinological aspects of general medicine and surgery, and Part 6 is a chapter concerned with miscellaneous topics.

It is impossible for a book such as this to be up to date when it is published, because the subject is moving so fast. Indeed many alterations and additions have had to be made to chapters after their revision was thought to be complete. However, we have attempted to include everything of importance that was published up to the end of 1972 and have added a few things that have appeared since.

As before, we have not used formal references in the text, except when quoting numerical data about the results of tests (references marked*), but have included a selected list of papers and books for further reading at the end of each chapter. Some additional ones have been added at the proof stage. We have quoted SI units, when they are employed commonly, and have given them in brackets when other units are still in general use. A key to the abbreviations, which

we have used for units, hormones, etc. and for other terms, is provided on pp. xiv and xv and inside the back cover. A list of equivalent British and American names of drugs, hormones, etc. is given on p. xvi. We have omitted nearly all clinical photographs to prevent the book being too expensive.

We are very grateful to many present and former colleagues for their help. Dr. Mary McGeown has again written chapter 11 and has graciously accepted our editorial amendments. Five others (Mr. Cowley, Dr. Foster, Professor Johnston, Mr. McRae and Professor Sellwood) have made such considerable contributions that we have designated them 'co-authors'. In addition, the following have helped us in various ways with individual chapters and we appreciate their generous assistance:

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- (13) Dr. K. D. Buchannan, Dr. D. R. Hadden, Mr. C. J. F. Maguire, Mr. P. Martin, Dr. J. A. Weaver;
- (14) Dr. J. Polak, Mr. J. Spencer;
- (15) Dr. J. Azzopardi, Dr. J. Polak;
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The Metabolic and Endocrine Sanotations and Endocrine Sanotation

Significance of metabolic and endocrine reZTINU

cu cubic MUU mouse uterine units g gram MV megavolt (10 ⁶ volts) h hour mv millivolts (10 ⁻³ volts) iu international unit ng nanogram (10 ⁻⁹ g) kcal kilocalorie (4·2 kJ) nm nanometre (10 ⁻⁹ m)	
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kcal kilocalorie (4·2 kD) nm nanometre (10 ⁻⁹ m)	
kg kilogram (10 ³ g) p.d. potential difference	
litre pg picogram (10 ⁻¹² g) cosmed	
m metre pH log ₁₀ hydrogen ions per l	
mCi millicurie rad radiation absorbed dose (1 rad	1=
mEq milliequivalent 0.01 joule/kg)	
mg milligram (10 ⁻³ g) s.d. standard deviation	
min minute (time) u unit	
miu milli-international units y gamma gamma	91
mm millimetre \(\lambda\) wavelength	
mm ³ cubic millimetre mCi millicurie and bus autourt?	
mmol millimole µCi microcurie microcurie	
mN millinormal μg microgram (10 ⁻⁶ g)	
mol mole µm micrometer (10 ⁻⁶ metre)	
mol. wt. molecular weight µu microunit	

HORMONES AND RELATED SUBSTANCES

			Jasmaolsvan isuxaa
ACTH	corticotrophin (adrenocortico-trophin)	HCC HCG	hydroxycholecalciferol human chorionic gonadotrophin
ADH	antidiuretic hormone	HGH	human growth hormone
CCK	cholecystokinin-pancreozymin	5-HIAA	5-hydroxyindole acetic acid
155	(CCK-PZ)	HMG	human menopausal gonadotro-
CRH	corticotrophin-releasing		phin
	hormone	HMPG	4-hydroxy-3-methoxyphenyl-
D_2	calciferol		glycol
D_3	cholecalciferol	HPG	human pituitary gonadotrophin
DCA	deoxycortone acetate	HPL	human placental lactogen
DHA	dehydroepiandrosterone	5-HT	5-hydroxytryptamine
DHCC	dihydroxycholecalciferol	5-HTP	5-hydroxytryptophan
DHT	5α-dihydrotestosterone	HVA	homovanillic acid
DIT.	diiodotyrosine	ICSH	interstitial cell-stimulating
DOC	deoxycorticosterone		The prostaglandins enomon
DOCA	deoxycorticosterone acetate	ILA	insulin-like-activity mydrod T
DOPA	dihydroxyphenylalanine	IRI	immunoreactive insulin
EPS	exophthalmos-producing	IZS	suspension of zinc insulin
	substance	LATS	long-acting thyroid stimulator
FRH	follicle-stimulating hormone-	LH	luteinizing hormone
	releasing hormone	LH/FSH-RH	luteinizing hormone/follicle
FSH	follicle-stimulating hormone		stimulating hormone-releasing
GH	growth hormone, somatotrophin		hormone
GRH	growth hormone-releasing	LPH	lipotrophin, lipolytic hormone,
	hormone		fat mobilizing agent
GR-IH	growth hormone release-inhibi-	LRH	lutenizing hormone-releasing
	ting hormone		hormone

LVP	8-lysine vasopressin	PMSG	pregnant mare's seru m
6-MAP	medroxy-progesterone		gonadotrophin
MIT	monoiodotyrosine	PRIH	prolactin release-inhibiting
MRIH	melanocyte-stimulating hor-		hormone
	mone release-inhibiting hormone	PTH	parathormone
MSH	melanocyte-stimulating hor-	SI	soluble insulin
in this book	.) names of drugs, hormones, enomed	$Imerican (U_8TA)$	triiodothyronine
NPH	neutral protamine Hagedorn	T ₄	thyroxine
	AMERICAN inlusni	TRHTISE	thyrotrophin-releasing hormone
NUSO	neutral soluble insulin	TSH	thyroid-stimulating hormone,
OGS	oxogenic steroids oxogenic steroids	tinomyem D	thyrotrophin
OHCS	hydroxycorticosteroids	Vit.DDA	vitamin D
OXOS	oxosteroids (D)	VMA lonelinia	
PBI	anatain bound inding		3-methoxy-mandelic acid
PG	prostaglandin		
10		NERAL	Dibenyline (Phenox
AFID	Amusal Fances Institute of		Dibotin (Dibotin (
AFIP	Armed Forces Institute of	I.V.P.	intravenous pyelogram
ATTT	Pathology (U.S.)	JG M. bimsxedots	juxtaglomerular
AIU	absolute louine uptake		
AMP	adenosine monophosphate	MAO	monoamine-oxidase
A-P	anterio-posterior vellovel muibo?	MEA SO SMIX	multiple endocrine adenopathy
ATP	adenosine triphosphate	Isoprene TIM	migration inhibition factor
APUD	amine, precursor uptake,	mRNA	messenger ribonucleic acid
	decarboxylase	MTA	anaplastic malignant teratoma
Au	8014	MTI	malignant intermediate teratoma
BEI	butanol extractable iodine odisM	MTT	malignant trophoblastic
BMR	basal metabolic rate graygodisM.	Metyrapone	teratoma
B.P.	British Pharmacopoeia	NPN	non-protein nitrogen
C-cells	calcitonin-secreting cells	p.	page
CA ₂	second colloid antigen	PAS	periodic acid Schiff or sodium
CAH	congenital adrenal hyperplasia	Oestradiol	aminosalicylate
CBG	corticosteroid-binding globulin	Pco ₂	partial pressure of carbon
CFT	complement fixation test	Oestrone	dioxide
C.N.S.	central nervous system	PES mercion	paraendocrine syndrome
CoA	coenzyme A	PII	plasma inorganic iodide
CPK	creatine phosphokinase	RAI	radioiodine
C.S.F.	cerebrospinal fluid biologicolox-	RDS	repiratory distress syndrome
C.V.P.	central venous pressure	RNA Model	ribonucleic acid
DBH	dopamine β-hydroxylase	RUR	
DNA	doorywihonyolojo goid	Sammelotand	seminoma
E.C.F.	extra-cellular fluid	SHBG	sex hormone-binding globulin
E.C.G.	electrocardiogram	Millione and Million	(protein)
EDTA	ethylenediamenetetraacetic acid	TBA	thyroid-binding albumin
E.E.G.	electroencephalogram T)	TBGmsxsloT	thyroid-binding globulin
E.S.R.	erythrocyte sedimentation rate	TBP	thyroid-binding protein
F.	female	TBPA	thyroid-binding pre-albumin
FFA	free fatty acid	TD	differentiated teratoma
FTI	free thyroxine index	TNM	tumour, nodes and metastases
GFR	glomerular filtration rate	114141	classification
GTT	glucose tolerance test	TRC	tanned red cell
H&E	haematoxylin and eosin	TTPR	Testicular Tumour Panel and
Hg	mercury	TITIK	Registry
HIOMT	hydroxyindole-0-methyl-	U.S.P.	United States Pharmacopoeia
HOMI	transferase		ultraviolet
I.C.F.	intra-cellular fluid	u.v. WDHA	
I.C.F. IHC		WDHA	watery diarrhoea, hypokalaemia,
inc	idiopathic hypoglycaemia of	WIIO	achlorhydria
:	childhood	WHO	World Health Organization
I.M.	intramuscularly	Y	yttrium
INH	isoniazid	Z-E	Zollinger-Ellison
1.V.	intravenous or intravenously		

Glossary of equivalent British and American (U.S.A.) names of drugs, hormones, etc used in this book

HAITING thyrotrophin-releasing hormone	neutral protamine Hagedorn TANDAMA THE AMERICAN THE AME	H9N
I nisymonity Actinophing hormone,	neutral soluble insulin	NUSO
	Dactinomycin sbiorots oinogoxo	065
d nimely Adrenaling		OHCS
-yxorbyd-4) bios oilebasmins Calciferol (D2		SOXO
bioa oilabnam-yxodfam-E Deoxycorton	e Desoxycorticosterone	
Dibenyline (Phenoxybenzamine) Dibenzyline (Phenoxybenzamine)	
Dibotin (Phenformin) DBI (Phenformin)	
metgoleve zuoneventui Dibotin SA	Armed Forces institute odr-Iad	AFIP
Dimelor (Acetohexamide	Dymelor (Acetohexamide)	ULA
de la companie de la		AMP
with a second se	Sodium levothyroxine	9-A
Isoprenalin	adenosine imphosphiorerenological	ATP
bios pielpunodia reguezaem Lignocain		APUD
analysis anaplastic malignant teratoma	e Methandrostenolone	
Methandienon Methandienon Methandienon	Methalicital blog	лA
Suzaldongon mangilan Methohexiton	Methohexital eldersative loneind	BEI
amotaret Metyrapon	e Methopyrapone silodsism iszad	BMR B.P.
negonin nietorg-nonNoradrenalin	Norepinephrine	C-cells
Muibos to Ridos bios oibonos. Norethisteron		CAs
otslyoilazonims Oestradio	Estradiol and Isase as a second	CAH
oirteo partial pressure of carbon	correcosteroid-binding globlorited Pl	CBG
abixoib Oestrone	e Estrone les nonexil lumalemoo	
omorbuya eninoobnastaq Orciprenalin	e Metaproterenol a suovien la meso	C,N.S.
abilioi oinsgroni si 17-oxogenic steroic	d 17-ketogenic steroid	AoO
emorbines syndrome 17-oxosteroid	17-ketosteroid	
bios pislounodia Phenytoin	Diphenylhydantoinagony Istingo	
Rastinon (Tolbutamide		Had
Rogitine (Phentolamine		DNA
Soluble insulin	Dogular inquisi DIM ISIMBO-SHXO	E.C.F.
(1001010)		E.C.G.
nimudla guibaid-bioryal Stilboestro		EDTA
niludolg gnibmiTolanase (Tolazamide		E.E.G.
10 thyroid-binding protein 11 thyroid-binding pre-albumin	erythrocyte sedimentation rate TB	
	free fatty acid	FFA
IM tumour, nodes and metastases		179
classification	glomerular filtration rate	GFR
C (anned red cell		GIT
PR Testicular Turnour Panel and		H & E
Registry	mercury	
S.P. United States Pharmacopoeia		TMOIH
ultraviolet DHA watery diarrhoea, hypokalaemia,	transferase u.v intra-cellular fluid Wi	I.C.F.
achlorhydria	idiopathic hypoglycaemia of	OHI
HO World Health Organization	childhood Wil	
yttrium	intramuscularly	.mli
E Zollinger-Ellison	isoniazid Z-	

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hormone		unidona agricon anomion ma org	
lipotrophin, lipolytic hormone,	LPH	growth hormone-releasing	GRH .
fat mobilizing agent		hormone	*******

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Introduction Introduction

Finally a group of endocrine glands and tissues (B) is apparently mainly independent of the nervous system. It includes the parathyroids, part of the adrenal cortex, parts of other organs

Living organisms are remarkable in that they maintain their integrity and their capacity to reproduce in a hostile world. The animal body does so by means of a highly delicate and complex organization which is controlled mainly through the nervous and endocrine systems; and these, as we shall see, are so closely related as to be almost one.

Endocrinology, although a young branch of biological science, is now approaching maturity. Most of the secretions of the endocrine tissues have been identified, many can be estimated by precise analytical methods and a large number of them have been synthesized. Much is known of the chemical processes involved in their biosynthesis, and those concerned with their biological effects are now being elucidated. The endocrine tissues must be considered as a closely integrated system which influences many of the metabolic processes of the body in health and disease. They are involved not only in the diseases which are commonly regarded as endocrine in nature but also in such common processes as growth and pregnancy, the response of the body to infection and trauma, and the development of cancers of the breast and prostate.

ANATOMY OF THE ENDOCRINE SYSTEM

No anatomical classification of the endocrine system is entirely satisfactory (fig. 1). Its constituent parts are derived from all three germ layers and in many instances (the anterior pituitary, the adrenal glands and the thyroid gland, for instance) derivatives of two different layers are combined. While some parts of the

system form distinct glands whose only functions are endocrine, others are scattered as separate cells or as clumps of cells in organs which have other important, and sometimes more important, functions.

Much of the endocrine system, however, is related developmentally, anatomically or functionally to the nervous system, and since the two are so interdependent, it seems important and convenient to base the classification on this relationship (table I).

Hypothalamus and dependent glands

The hypothalamus (AI), which is part of the brain and under the control of the higher nervous centres, is the most important part of the endocrine system. It controls directly the anterior pituitary gland (adenohypophysis) (AII) and, indirectly (via the pituitary), several other glands, namely the adrenal cortex, the gonads and the major part of the thyroid. Part of the hypothalamus (AI2) extends into the posterior pituitary (neurohypophysis) to form a single anatomical and functional unit. Nuclei within the hypothalamus, or closely related to it, (AI3) control the sympathetic nervous system, which includes the adrenal medulla.

Endocrine glands and tissues of neural crest origin

Another group of widely separated endocrine tissues (AII) is derived (or probably derived) in early fetal life from the neural crest, which is formed from the neural folds. They are thus, embryologically, derivatives of the nervous system, and share with the primitive neural crest

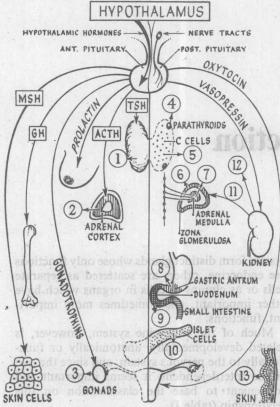


Fig. 1 The endocrine system. Glands and structures on the *left* are influenced largely by the hormones of the anterior pituitary, while those on the *right* are not.

indicates that the hormone shown controls the gland or tissue to which the arrow is directed. The pineal and the thymus are omitted, because their endocrinological roles are uncertain.

1 = thyroid hormones 5 = calcitonin
2 = cortisol and sex hormones 6 = aldosterone
3 = sex hormones 7 = catecholamines
4 = parathormone 8 = gastrin
9 = alimentary hormones
10 = insulin, glucagon
11 = renin
12 = erythropoietin

13 = vitamin D

certain structural and histochemical characteristics. Although they become separated from the central nervous system anatomically, some develop important secondary connections with it through the autonomic nerves. These tissues, unlike the glands controlled by the hypothalamus, comprise endocrine cells or clusters of cells within other organs, most of which are not primarily endocrine in nature. They include the parafollicular cells of the thyroid, the endocrine

cells of the alimentary tract and the islet cells of the pancreas. Other cells of this series, particularly some in the alimentary tract, the bronchi and the carotid body, and the melanocytes of the skin, whose characteristics suggest an endocrine function, have no known secretions. The whole of the sympathetic nervous system (already listed under AI) and possibly some of the cells of the anterior pituitary (those secreting ACTH and MSH) are also of neural crest origin.

Endocrine glands and tissues mainly independent of nervous system

Finally a group of endocrine glands and tissues (B) is apparently mainly independent of the nervous system. It includes the parathyroids, part of the adrenal cortex, parts of other organs and tissues, and the blood.

PHYSIOLOGY OF THE ENDOCRINE

through the nervous senomore systems; and

The endocrine system produces its effects by elaborating hormones. These are substances which stimulate or inhibit the function of cells, without themselves being used as sources of energy. Their actions are physiological and they are effective in very low concentrations. Most known hormones are secreted directly into the blood by specialized groups of cells and are carried to other responsive cells, where they exert their effects. In some cases the lymphatics provide an important, and occasionally the major, channel of entry into the blood. Some hormones do not follow this simple pattern. A few, such as angiotensin II, are formed from precursors in the blood, and dihydrotestosterone, an active hormone, is formed from its inactive precursor, testosterone, within androgen-responsive target cells. Vitamin D (which is a hormone by definition) has several singular features. It is synthesized in an inactive form in the skin, under the influence of sunlight, and is carried by the blood to the liver and to the kidneys, where it is converted into active derivatives. In the absence of sunlight, closely related compounds, supplied as vitamins in the diet, provide adequate substitutes.

The nervous and endocrine systems are closely related functionally as well as anatomically. Neurotransmission at synapses in the central and

Table I Classification of the endocrine system (The pineal and the thymus are omitted, because their endocrinological roles are uncertain)

V			man an down and all
Key: BLOCK CAPITALS indicate Endocrine glands or tissues.			substances such as acer
Words in <i>italics</i> indicate Hormones			dopamine and 5-bydro
indicates that hormone preceding controls hormone	e, gland or	tissue following.	se regarded as local
: indicates that gland or tissue preceding secretes hor	rmone(s) fo	ollowing.	nonal activity, mediate
A. Endocrine glands and tissues related to nervous system.	at the		gous to neurotransm
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of I. Hypothalamus and dependent glands but yishudiq	S153119	exerting their	
1. HYPOTHALAMIC NUCLEI SECRETING	TROPHIC	C HORMONES:	ocally at synapses, do s
NATURALYSIS, the adrenal medulla (via the sympa-		Target Glands	Main Hormones
TIUTIS nerves) and the alimentary tract (via the		and Tissues	typothalamus, the ne
a. Releasing hormones (RH) Hormone	es per les	defy definition as	
i. Growth hormone— $RH \longrightarrow GH$ —	\rightarrow	All tissues	urrely pervous or burn
ii. Thyrotrophin—RH → TSH —	→	THYROID	Thyroxine and
be influenced by the nervous system are the para-		(follicular cells):	
blowd siii. Corticotrophin—RH	(a) njo		Cortisol, androgens
(which secrete calcitonin) the zona glomerulosa		CORTEX (inner zones):	oestrogens
iv. Follicle-stimulating FSH —	func-	OVARY: UP dilw	Oestrogens
hormone—RH —>		Testis (tubules)	— .800
v. Luteinizing hormone—RH> LH	\rightarrow	OVARY:	Progesterone
ditalishasii Asudusa L		TESTIS (Leydig	
The secretions of most endocrine slands are		cells):	Testosterone Some
b. Inhibiting hormones (IH)			
i. Prolactin release—IH> Prolactin			Hormones vary great
ii. Melanocyte-stimulating	des fall		heir chemical structure
hormone—IH ———————————————————————————————————	>	Melanocytes	ato three categories:
2. HYPOTHALAMIC NUCLEI RELATED TO POS	STERIOR	PITUITARY (NEUR	OHYPOPHYSIS):
a. Antidiuretic hormone> 18 emeinschoom		Renal tubules	d puw apridading (r).
b. Oxytocin>		the most commen	
3. HYPOTHALAMIC (OR CLOSELY RELATED) N	NUCLEI C	Uterus and breast	ares. They include m
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