

# THE THIRD NERVOUS SYSTEM

## WHAT ARE THE FIRST 2?

### THE AUTONOMIC AND SOMATIC DIVISIONS

#### THE CHROMAFFIN SYSTEM

CHROMAFFIN CELLS/PHAEOCHROMOCYTES ARE CLASSICALLY DEFINED AS ELEMENTS DERIVED FROM NEURO-ECTODERM, INNERVATED BY PREGANGLIONIC SYMPATHETIC NERVE FIBERS CAPABLE OF SYNTHESIZING AND SECRETING CATECHOLAMINES [DOPAMINE, NORADRENALIN OR ADRENALIN].

GROUPS OF SUCH HORMONE-SECRETING CELLS **ARE ASSOCIATED** STRUCTURALLY AND FUNCTIONALLY **WITH THE SYMPATHETIC NERVOUS SYSTEM.**

THIS SYSTEM COMPRISES A LARGE NUMBER OF MASSES OF TISSUE SIMILAR IN DEVELOPMENT, STRUCTURE AND HISTOCHEMICAL REACTIONS TO THE MEDULLA OF THE SUPRARENAL/ADRENAL GLAND CALLED **CHROMAFFIN** BECAUSE OF ITS AFFINITY FOR CHROMIUM SALTS.

THE MASSES OF TISSUE ALL ORIGINATE IN INTIMATE ASSOCIATION WITH THE SYMPATHETIC NERVOUS SYSTEM AND THE CHARACTERISTIC CHROMAFFIN CELLS. THE NEURONS OF THE SYMPATHETIC GANGLIA ARE DERIVED MAINLY FROM A COMMON MOTHER CELL, THE CELL OF THE NEURAL CREST.

IT INCLUDES THE MEDULLA OF THE SUPRARENAL GLAND AND THE EXTRA-SUPRARENAL CHROMAFFIN BODIES WHICH MAY OCCUR IN ANY PART OF THE SYMPATHETIC SYSTEM, THOUGH THEY ARE MOST NUMEROUS IN THE ABDOMEN.

THE MAJORITY OF THE EXTRA-SUPRARENAL CHROMAFFIN BODIES ARE ADJACENT TO THE AORTA: THE PARA-AORTIC CHROMAFFIN BODIES.

SOME CELLS IN THE **WALL** OF THE INTESTINE CONTAIN GRANULES GIVING THE CHROMAFFIN REACTION AND ARE TERMED ENTEROCHROMAFFIN CELLS.

THE EXTRA-SUPRARENAL CHROMAFFIN BODIES ARE ENCAPSULATED STRUCTURES.

NON-ENCAPSULATED COLLECTIONS OF CHROMAFFIN CELLS MAY BE ASSOCIATED WITH ANY OF THE SYMPATHETIC GANGLIA.

THE LARGEST COLLECTIONS OF ABDOMINAL PARA-AORTIC CHROMAFFIN BODIES ARE FOUND IN THE COELIAC AND MESENTERIC PLEXUSES.

THE **CAROTID BODY** [GLOMUS CAROTICUM] IS SITUATED CLOSE TO THE BIFURCATION OF THE COMMON CAROTID ARTERY, ADJACENT TO THE CAROTID SINUS, SOMETIMES WEDGED IN BETWEEN THE ROOTS OF THE INTERNAL AND EXTERNAL CAROTIDS, OR AT A HIGHER LEVEL, SHOWS A SLIGHT CHROMAFFIN REACTION, BUT **NOT** CONSIDERED PART OF THE CHROMAFFIN SYSTEM.

THE **CORPUS COCCYGEUM** IS A SMALL VASCULAR BODY LYING IMMEDIATELY ANTERIOR TO THE TIP OF THE COCCYX IN INTIMATE RELATION WITH A BRANCH OF THE MEDIAN SACRAL ARTERY AND WITH THE **GANGLION IMPAR** OF THE SYMPATHETIC TRUNK AND A GROUP OF SMALLER BODIES OF SIMILAR STRUCTURE.

THE CORPUS **AND ITS SATELLITE BODIES** ARE ENCLOSED IN A FIBROUS CAPSULE, ENSHEATHING THEM INDIVIDUALLY, **NOT** GIVING A CHROMAFFIN REACTION OR **INCLUDED IN** THE CHROMAFFIN SYSTEM.

**ALL** CHROMAFFIN TISSUE DEVELOPS IN INTIMATE RELATION WITH THE SYMPATHETIC NERVOUS SYSTEM, THE **SYMPATHOCHROMAFFIN** TISSUE

**THIS INCLUDES** THE MEDULLA OF THE SUPRARENAL GLANDS, PARA-AORTIC BODIES, PARAGANGLIA, **CAROTID BODIES** AND SMALL MASSES OF CELLS SCATTERED IRREGULARLY AND VARIABLY AMONG THE GANGLIA OF THE PARAVERTEBRAL SYMPATHETIC CHAINS, SPLANCHNIC NERVES AND THE GREAT PREVEREBRAL AUTONOMIC PLEXUSES, AND MAY BE CLOSELY RELATED TO VARIOUS ORGANS [HEART, LIVER, KIDNEY, URETER, PROSTATE, EPIDIDYMIS, OVARY, ETC.].

ENTEROCHROMAFFIN CELLS ARE FOUND IN THE **EPITHELIAL TISSUE LINING THE GASTROINTESTINAL AND RESPIRATORY TRACTS** AND AMINE-STORING MAST CELLS FOUND IN CONNECTIVE TISSUES OF THE GUT, PANCREAS AND LIVER.

THESE HAVE ABILITY TO TAKE UP AND DECARBOXYLATE AMINO ACIDS [APUD CELLS] AND OTHER NON-CHROMAFFIN CELLS IN THE WALLS OF THE GASTROINTESTINAL AND RESPIRATORY TRACTS, PANCREAS AND OTHER ENDOCRINE GLANDS HAVE SIMILAR ULTRASTRUCTURE AND AMINO-ACID UPTAKE CHARACTERISTICS AND PARANEURONS HAVING MANY OF THE FEATURES OF CHROMAFFIN CELLS IN SYMPATHETIC GANGLIA RAISE QUESTIONS ABOUT THE ADVISABILITY OF CONTINUING TO RESTRICT THE TERM 'CHROMAFFIN SYSTEM' TO THE 'TRUE' CHROMAFFIN CELLS AND IT MAY BE MORE APPROPRIATE TO CONSIDER IT AS PART OF A **DIFFUSE NEURO-ENDOCRINE SYSTEM**.

## **THE DIFFUSE NEURO-ENDOCRINE SYSTEM**

IN 1938 STUDIES OF FEYRTER DREW ATTENTION TO THE EXISTENCE OF ISOLATED GROUPS OF HORMONE-SECRETING CELLS WHICH WERE NOT

RESTRICTED TO SPECIFIC ENDOCRINE GLANDS BUT WHICH WERE WIDELY SCATTERED THROUGHOUT THE TISSUES OF THE BODY

FEYRTER DESCRIBED THESE CELLS AS **CLEAR CELLS**/HELLE ZELLEN AND NOTED THAT THEY WERE PARTICULARLY PROMINENT IN THE GUT AND THE PANCREAS.

THEY HAVE SINCE BEEN CLASSIFIED AS TYPES OF **APUD** CELLS, **A**MINE **P**RECURSOR **U**PTAKE AND **D**ECARBOXYLATION, THEIR CHARACTERISTIC AMINE-HANDLING PROPERTIES, AND HAVE BEEN SHOWN TO MANUFACTURE STRUCTURALLY-RELATED PEPTIDES WHICH **ACT AS HORMONES** OR **NEUROTRANSMITTERS**, ALTHOUGH IN OTHERS THE MAIN SECRETION IS A SIMILARLY ACTING AMINE.

COLLECTIVELY, THE APUD CELLS COMPRISE A 'SYSTEM' **FAR MORE EXTENSIVE** THAN THAT VISUALIZED BY FEYRTER, INCLUDING, AMONG OTHERS, **CHROMAFFIN** CELLS, **SIF** CELLS, **PEPTIDE-PRODUCING CELLS** OF THE **HYPOTHALAMUS**, **PITUITARY**, **PINEAL**, **PARATHYROIDS** AND **PLACENTA**, AND THE **KULCHITSKY** CELLS OF THE **LUNG**.

SO FAR, SOME **FORTY DIFFERENT CELL TYPES** HAVE BEEN CATEGORIZED AS **THE DIFFUSE NEURO-ENDOCRINE SYSTEM**.

PEARSE PROPOSED THAT CELLS MANUFACTURING PEPTIDE HORMONES SHARED A COMMON SET OF CYTOCHEMICAL CHARACTERISTICS, THE MOST STRIKING BEING RELATED TO THE PRODUCTION OF BIOGENIC AMINES [**ADRENALIN**, **NORADRENALIN**, **DOPAMINE**, 5-HYDROXYTRYPTAMINE, ETC.] COULD BE LINKED TO THE PROCESS OF PEPTIDE HORMONE PRODUCTION IN GENERAL, FROM WHICH THE DESIGNATION 'APUD' CELL AROSE.

PEARSE SUGGESTED THAT ALL CELLS OF THE APUD SERIES ARE DERIVED FROM **NEUROENDOCRINE**-PROGRAMMED CELLS OF THE ECTOBLAST, AND OTHERS SUGGEST THAT SOME APUD CELLS, SUCH AS THE

***GASTRO-ENTERO-PANCREATIC ENDOCRINE*** CELLS MAY BE SIMILARLY PROGRAMMED BUT OF ENDODERMAL ORIGIN.

PEARSE SUGGESTED THE APUD CELLS MAY COLLECTIVELY BE CONSIDERED AS **A THIRD DIVISION OF THE NERVOUS SYSTEM** ACTING AS THIRD-LINE EFFECTORS TO SUPPORT, MODULATE OR AMPLIFY THE **ACTIONS OF NEURONS** IN THE **AUTONOMIC** AND **SOMATIC** DIVISIONS AND OF **EACH OTHER**.

THEY POSSESS ACTIVITIES WHICH ARE **SLOWER IN ONSET AND LONGER IN DURATION** THAN THOSE OF CELLS IN THE **AUTONOMIC DIVISION**, WHICH IN TURN BEAR A SIMILAR FUNCTIONAL RELATIONSHIP TO THE FASTER-ACTING NEURONS OF THE **SOMATIC DIVISION**.

THE VARIOUS SECRETIONS OF THE APUD CELLS [CELLS OF THE DIFFUSE NEURO-ENDOCRINE SYSTEM] MAY ACT UPON **CONTIGUOUS** CELLS, UPON GROUPS OF **NEARBY CELLS**, OR UPON **DISTANT CELLS** AFTER TRANSPORT IN THE BLOOD, IN THIS RESPECT BEING CONSIDERED AS **INTERMEDIATE** BETWEEN THE LOCALLY-ACTING TRANSMITTERS PRODUCED BY **NEURONS** AND THE DISTANTLY ACTING SECRETIONS OF THE **DISCRETE** ENDOCRINE GLANDS.

THE DIFFUSE NEUROENDOCRINE SYSTEM THUS **COMPLEMENTS** AND **LINKS** THE **NERVOUS AND ENDOCRINE SYSTEMS**, ALL THREE SYSTEMS **INTERACTING** TO PROVIDE A SENSITIVE MECHANISM ALLOWING FOR **HOMEOSTATIC CONTROL**.

IT HAS BEEN SUGGESTED THAT DEVIATIONS IN THE RELATIVE LEVELS OF THE SECRETIONS OF THE DIFFERENT CELL TYPES OF THE DIFFUSE NEUROENDOCRINE SYSTEM MAY RESULT IN MANY OF THE DISORDERS CURRENTLY DESCRIBED AS **PSYCHOSOMATIC** OR **FRANKLY PSYCHOTIC**, WHICH MAY LEAD TO SIGNIFICANT CLINICAL PROGRESS IN THEIR TREATMENT.

THE SUPRARENAL MEDULLA IS COMPOSED OF GROUPS AND COLUMNS OF **CHROMAFFIN CELLS** THAT SYNTHESIZE AND SECRETE NORADRENALIN AND ADRENALIN INTO VENOUS SINUSOIDS, THE RELEASE BEING UNDER PREGANGLIONIC SYMPATHETIC CONTROL.

### PARAGANGLIA

THE PARAGANGLIA ARE GENERALLY DEFINED AS **EXTRA-ADRENAL** AGGREGATIONS OF **CHROMAFFIN TISSUE** WIDELY DISTRIBUTED **ALONG AND WITHIN** THE **AUTONOMIC NERVOUS SYSTEM** ADJOINING VARIOUS **AUTONOMIC GANGLIA**.

CELLS SIMILAR TO THOSE WHICH CHARACTERIZE VARIOUS AUTONOMIC GANGLIA ARE ALSO FOUND **WITHIN** SYMPATHETIC GANGLIA WHERE THEY ARE REFERRED TO AS **SMALL, INTENSELY FLUORESCENT [SIF]** CELLS IN THE WALLS OF VARIOUS VISCERA AND IN A VARIETY OF RETROPERITONEAL AND **MEDIASTINAL** LOCATIONS.

THE INTRANEURALLY DISPOSED ACT AS **INTERNEURONS** AND THE REMAINDER ARE SOURCES OF A VARIETY OF ENDOCRINE SECRETIONS, INCLUDING A **TRYPTOPHAN-CONTAINING PROTEIN** AS WELL AS **CATECHOLAMINES**.

THIS DIFFUSE COLLECTION OF EXTRA-ADRENAL CHROMAFFIN TISSUE IS REFERRED TO AS THE **PARAGANGLION SYSTEM**.

TYPE 1 CELLS OF THE PARAGANGLIA RECEIVE A '**PREGANGLIONIC**' **SYMPATHETIC INNERVATION** LIKE THAT OF CHROMAFFIN CELLS OF THE ADRENAL MEDULLA.

PARAGANGLIA **SHOULD BE CONSIDERED AS ENDOCRINE ORGANS** WHOSE SECRETORY CELLS MANUFACTURE CATECHOLAMINES AND PROTEINS, STORED UNTIL STIMULATED TO BE RELEASED BY INTRINSIC AND EXTRINSIC FACTORS.

AS WELL AS HAVING A REMOTE ENDOCRINE EFFECT, **LOCAL PARACRINE ACTIONS** BY THESE SECRETIONS ON NEARBY CELLS OCCUR.

THE PARAGANGLIA **COLLECTIVELY COMPRISE A DIFFUSE SYSTEM** WHICH MAY ACT THROUGHOUT LIFE **AS A SOURCE OF CATECHOLAMINES** ADDITIONAL TO THOSE PROVIDED BY THE ADRENAL MEDULLA, ASSUMING A ROLE OF CONSIDERABLE METABOLIC AND CLINICAL SIGNIFICANCE.

### **PARA-AORTIC BODIES**

IN ADULTS, PARA-AORTIC BODIES ARE PRESENT AS DISCERNIBLE STRUCTURES MAINLY IN THE VICINITY OF THE COELIAC AND SUPERIOR MESENTERIC ARTERIES WHILE ONLY MICROSCOPIC COLLECTIONS OF CHROMAFFIN CELLS PERSIST IN ASSOCIATION WITH THE LOWER PARTS OF THE INTERMESENTERIC PLEXUS.

ALTHOUGH THE CHROMAFFIN CELLS OF THE SYMPATHETIC GANGLIA MAY ACT AS **INTERNEURONS**, THOSE OF THE OTHER EXTRA-ADRENAL CHROMAFFIN TISSUES ARE ENDOCRINE IN NATURE AND PROBABLY SUBSERVE THE ADRENAL MEDULLA AS SOURCES OF CATECHOLAMINES.

THERE IS ALSO ULTRASTRUCTURAL EVIDENCE THAT CHROMAFFIN CELLS ASSOCIATED WITH NODES OF THE **SOLAR PLEXUS** HAVE PROCESSES EXTENDING BEYOND THE ENSHEATHING GLIAL CELLS TOWARDS BLOOD CAPILLARIES INTO WHICH THEIR **CATECHOLAMINES** PASS.

### **CAROTID BODIES**

THESE ARE INNERVATED BY THE CAROTID BRANCHES OF THE **GLOSSOPHARYNGEAL NERVE**, INCLUDING THE CAROTID SINUS NERVE, AND BY A FINE PLEXUS CONTAINING **GLOSSOPHARYNGEAL, VAGAL** AND **SYMPATHETIC** COMPONENTS.

THEY ARE **ARTERIAL CHEMORECEPTORS** WHEN STIMULATED BY **HYPOXIA, HYPERCAPNIA** [WHEN YOU HAVE **TOO MUCH CARBON DIOXIDE (CO<sub>2</sub>)** IN YOUR BLOODSTREAM] OR **ELEVATED HYDROGEN ION CONCENTRATION IN THE BLOOD** ELICITS A REFLEX INCREASE IN THE RATE AND VOLUME OF VENTILATION THROUGH NEURAL CONNECTIONS WITH THE ARRAY OF RESPIRATORY CENTERS IN THE BRAINSTEM.

THEY HAVE TIGHTLY PACKED COLLECTIONS OF 'GLOMUS' [TYPE 1] CELLS STORING DOPAMINE, OTHER NEUROTRANSMITTERS AND THE PROTEIN 'GLOMIN', AND ARE ACCEPTED AS A VARIETY OF **CHROMAFFIN CELL, PARANEURONS** AND **DOPAMINERGIC INTERNEURONS**.

THE ABOVE IS WHY THERE IS **AN INSTANT SHOT OF ADRENALIN** AT THE SYMPATHETIC NERVE SYNAPSES FOR FLIGHT OR FLIGHT, INSTEAD OF WAITING THE AVERAGE OF 1 MINUTE FOR AVERAGE ADULT BODY CIRCULATION TO BRING IT AROUND.

**THIS IS ALSO WHY YOU CAN STIMULATE THE APPROPRIATE CHROMAFFIN/SYMPATHETIC NERVE ENDING/CONNECTION TO STOP ALLERGIC REACTIONS.**

WHAT DOES THE MEDICAL PROFESSION GIVE FOR SEVERE ALLERGIC REACTIONS?

ADRENALIN.

**WHY DOES YOUR BODY NOT REACT WITH ADRENALIN SO THE ALLERGY ISN'T SEVERE?**

**PROBLEMS AT THE NERVE SYNAPSE[S], SUCH AS SCAR TISSUE.**

CORRECT THIS BY TREATING THE APPROPRIATE SYNAPSE[S] APPROPRIATELY AND THE ALLERGIC REACTION[S] WON'T OCCUR.