Grave's Disease

The proper functioning of the human body is dependant upon the normal working of the systems of the human body. The coordination of these systems is essential for maintaining all the normal processes that take place with in the body. The endocrine system is an important system vital for leading a normal life. Any pathologic condition affecting the endocrinology of the body usually does not only produce local effects but it is a cause of many systemic disturbances affecting the efficient working of the body. This paper will particularly focus upon the pathological condition of the endocrine system known as Grave's disease. This disease condition which affects the thyroid gland produces a wide range of effects on the human body. This paper will encompass all the aspects of Grave's disease describing its causes and the body wide effects of this condition. Furthermore, for a proper understanding of the disorder it will also provide an account of the normal functioning of the gland.

Grave's disease has been given the name after the scientist Robert Graves who actually found out about this condition in 1835. This disease which is considered to be the most common reason leading towards hyperthyroidism has a genetic predisposition. That is the disease has a hereditary component associated and people within the same family have high chances of having the disease. Not only this, the disease also has a gender deviation associated with it. That is this disease is more commonly found in females than in males with the women being seven times more affected than the males. This disease occurs between the age groups of 20 and 40. According to statistics, in the United States 1.5 to 2.0 percent of the females suffer from the condition.

The gland that is affected by Grave's disease is the thyroid gland. The thyroid gland is an endocrine gland which is present in the neck. It lies in front of the trachea and immediately below the larynx. It has a normal weight of 15 to 20 grams in a normal healthy person. The thyroid gland has an outer covering of a capsule of thin connective tissue. The basic units of the thyroid gland are the thyroid follicles which are closed follicles. The follicles consist of a single layer of epithelial cells which are known as follicular cells or the principal cells. These cells which are cuboidal in shape form an outer boundary of the thyroid follicles and within them is enclosed a cavity which is known as the follicular cavity. This cavity contains colloid which is a gelatinous substance which consists of thyroglobulin. This thyroglobulin has the function of storing the thyroid hormones which are synthesized with in the gland. This function makes the thyroid gland distinct from the other glands because it is only this gland which has the capability of storing large amounts of hormones within the follicle. This stored amount is sufficient to meet the body needs up to two to three months in cases of deficiency. As the thyroid hormone is synthesized in the principal cells, they contain a large amount of mitochondria to provide for the energy requirements, ribosomes, rough endoplasmic reticulum for the synthesis of proteins and Golgi apparatus as well. The thyroid gland has a very rich blood supply and this gland is considered to have a blood supply five times more than its weight.

The basic function of the thyroid gland is the secretion of the thyroid hormones which are triiodothyronine T3 and thyroxine T4. Thyroid stimulation hormone TSH is a hormone of the anterior pituitary gland which binds to specific receptors on the thyroid gland and triggers the release of the thyroid hormones. The thyroid follicular cells have the function of the synthesis of these thyroid hormones which are stored in the colloid with in the thyroglobulin molecule and are released according to the stimulus and the needs of the body. The thyroid gland is very

important because any alterations in the functioning of the gland disturb the synthesis of the thyroid hormones which have major functions in the body. The thyroid hormones function to increase the rate of transcription in cells, hence leading to the formation of new intracellular proteins. They increase cellular metabolic activity by increasing the number and activity of the mitochondria and also increasing the transport of ions within the cells by enhancing the process of active transport. They have an effect on growth and development as well. They provide a stimulus for the metabolism of carbohydrates and lipids. These hormones increase the basal metabolic rate of the body. These functions can be a cause for the increased requirement of vitamins and can lead to a decline in body weight. This is because with active metabolism going on there is an increased demand of vitamins to carry out these processes. Thyroid hormone has a great effect on the heart and its functions. As it promotes metabolism there is increased blood demand. Hence it leads to increased blood flow and a high heart rate. This increased metabolism also provides a stimulus for increased respiration. The thyroid hormone also increases the GIT motility and stimulates the central nervous system as well. It increases the working of the muscles as well.

These functions clearly explain how important the thyroid gland is and alteration in its structure and function can greatly disturb the bodily functions. This disturbance is led to by Grave's disease as well. Grave's disease is basically an autoimmune disorder. In this disorder certain antibodies are developed in the body against the thyroid gland. Though a proper reason for the development of these antibodies has not been concluded but it is believed that due to the release of certain antigens from the thyroid cells of a person during his life results in the formation of antibodies against the gland or it may also be due to decreased activity of the protective mechanism of the T helper cells.. Another cause for this disease which has been presented by

Robert Graves as well is that the condition can be led to because of extreme stress. But this is also not a much proved cause. The antibodies which are formed are known as thyroid stimulating immunoglobulin (TSI), thyroid growth stimulating immunoglobulin (TGI) and TSH binding inhibitor immunoglobulin (TBII). The Thyroid stimulating immunoglobulin (TSI) antibodies bind to the receptors on the thyroid gland where under normal conditions TSH binds and stimulate the secretion of the thyroid hormone. The TSI antibodies have a very long lasting effect of about 12 hours as compared to the 1 hour effect of the thyroid stimulating hormone of the anterior pituitary. The TGI antibodies also function on the same TSH receptor but their function is basically the dividing of the follicular epithelial cells. The TSI antibodies prevent the binding of the TSH to its receptor on the thyroid gland. While bound to the receptor to block the effect of TSH they actually lead to the increased secretion of the thyroid hormone. But in certain instances they also suppress the activity of the thyroid gland. These antibodies account for the excessive secretion of the thyroid hormone. The thyroid hormone has an effect of negative feedback on the thyroid stimulating hormone. So irresponsive of the fact that the thyroid hormone is released in Grave's disease because of the autoimmune antibodies, there is always suppression in the secretion of thyroid stimulating hormone from the anterior pituitary because of the presence of increased thyroid hormone in the blood.

Thyroid hormone is essential for the carrying out of normal body processes. But an increase in the hormone due to the disease can have many adverse effects. The basal metabolic rate of the body can increase 60 to 100 percent more than normal and this can account for the increased sweating and decreased tolerance to heat. The increased quantities lead to an increase in the GIT motility leading to diarrhea and the increased metabolism is the cause of weight loss which may be of varying degrees. The thyroid hormone stimulates the central nervous system but increased

quantities can lead to psychological issues and nervousness. The muscles become weak because of the increased catabolism of proteins. The main clinical manifestations of Grave's disease are hyperthyroidism and there are pathologies of the eyes and skin. These are particularly known as infiltrative opthalmopathy and infiltrative dermopathy. In the case of pathology of the eyes the patient presents with exopthalmos which is the protrusion of the eyeball because of the increased activity of the sympathetic nervous system due to its overstimulation by the thyroid hormone. This effect on the eyeball is because of an autoimmune response of the T cells against the TSH receptor which is present in the preadipocyte fibroblasts in the eyes. Because of this autoimmune effect the retro orbital space becomes occupied with T cells and adipocytes, the extra ocular muscles became edematous and there is deposition of Glycosaminoglycans in the extracellular space. All of these reasons lead to the protrusion of the eyeball. Hence the patient presents with exopthalmos. This exopthalmos can be very serious as the person is unable to close his eyelids completely even during sleep. This can lead to an ulcer of the cornea and make the patient's eye susceptible to infections. Because of the protrusion the optic nerve also becomes stretched and this can greatly affect vision. A person might also suffer from blurred vision. The skin pathology particularly affects the area of the tibia bone that is the shins. The skin around the shins becomes red but it is not tender on touch.

Morphologic changes in the structure of the thyroid gland take place because of Grave's disease. Due to the hyperactivity and increased stimulation of the thyroid gland, the gland becomes enlarged. This enlargement is symmetrical and diffuse. This enlargement accounts for the increased weight of the thyroid gland which ca increase to as much as 80 grams. The follicular epithelial cells become columnar and increase in size and number both. Due to this increase in size and number, there is an enfolding of the follicular epithelium of the gland. This enfolding

can also lead to formation of papillae which protrude into the colloid which the follicular epithelial cells provide a boundary for. Apart from these findings, there are a great number of T cells found in the interstitium. Histological changes are also observed in other tissues of the body which are affected by this pathological condition. As the thyroid hormone increases the activity of the heart muscle, hypertrophy of the heart muscle is observed. This hypertrophy and increased activity provides reason for the ischemic changes in the heart. Due to increased antibodies and lymphocytes there is hyperplasia of the lymphoid tissue of the body. Swelling is observed in the muscles of the orbit and this can proceed to fibrosis at a later stage. The tissues of the eye also have a raised number of antibodies and fibrosis can also be observed there at a later stage. The skin of the shins that is affected becomes thickened and raised lymphocytes and the presence of glycosaminoglycans is also observed there.

Certain diagnostic tests can also be performed to check for Grave's disease. The presence of antibodies in the blood should be seen. The levels of the thyroid hormones should also be checked. The TSH concentration is also important to rule out the hyperthyroidism resulting from pathologies of the anterior pituitary gland. The basal metabolic rate can also be checked because it is always raised in the case of Grave's disease because of the hyperthyroidism. The disease can be treated both medically as well as by surgical procedures.

Grave's disease is a pathological condition of the thyroid gland. It not only effects the gland itself but it disrupts major physiological processed of the body. Many histological changes are seen not only in the gland but also in other tissues of the body. Grave's disease puts a person at a very high chance of developing hypothyroidism at some late stage in life because of the inflammation and destruction of the cells of the gland. Medical and surgical intervention can help a person overcome most of the symptoms associated with the disease.

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