An Up Date On The Problem
OF THYROTOXICOSIS

ESSAY SUBMITTED

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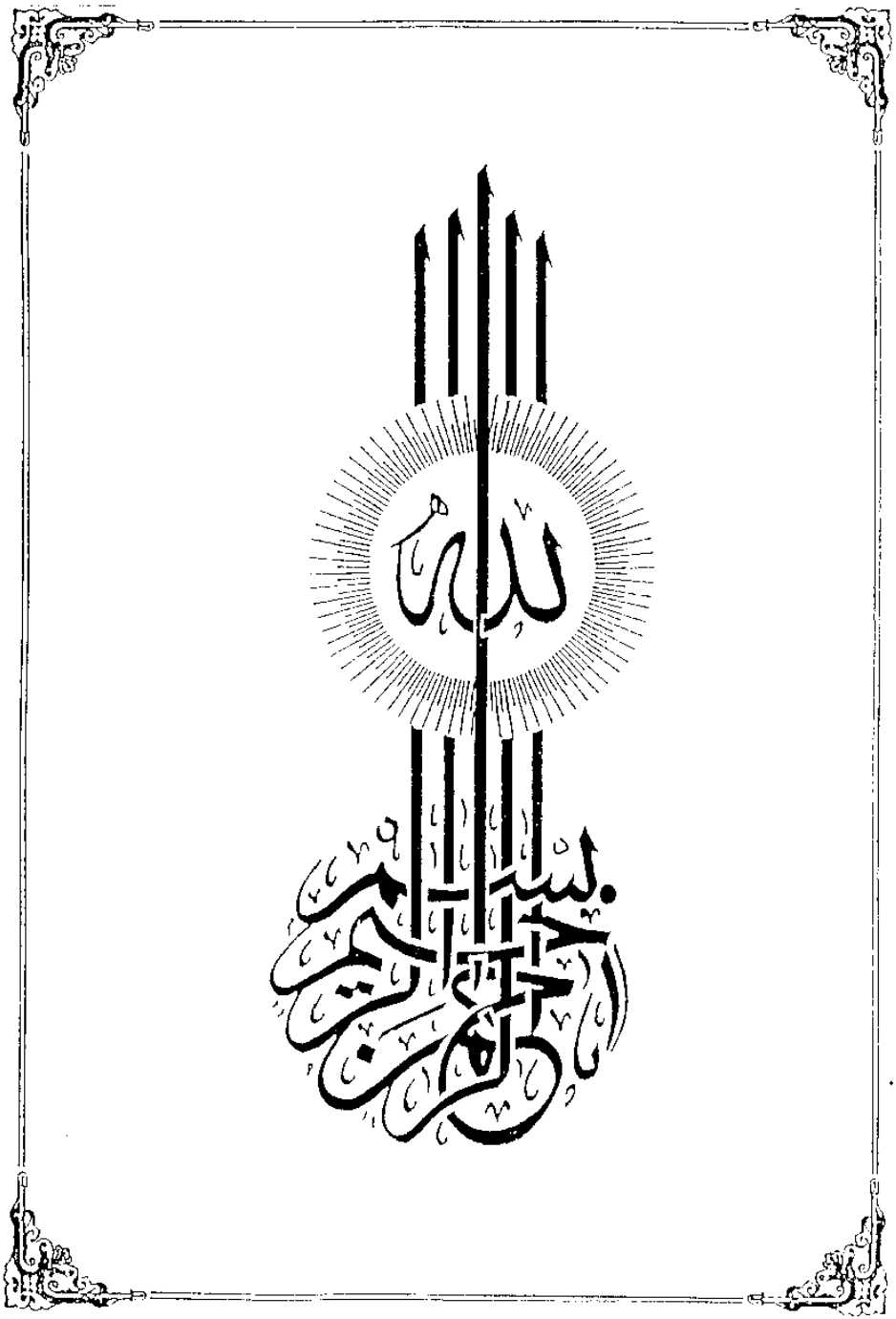

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CONTENTS

- Introduction ---------- 1
- Technetium-99m ---------- 5
- Magnetic Resonance Imaging ---------- 7
- Serum Angiotensin Convering Enzyme ---------- 10
- Tests of Thyroid Function ---------- 12
- Serological Aspect of Thyrotoxicosis -------- 18
- Clinical Manifetations of Thyrotoxicosis ----- 22
- Pituitary and or Peripheral Resistance to Thyroid Hormones ---------- 34
- High Serum Thyroxine-Binding Globulin An Important Cause of Hyperthyroxinemia ------ 36
- Transient Hyperthyroidism ---------- 37
- Investigations ---------- 38
- Differential Diagnosis ---------- 47
- Treatment ---------- 49
- Pregnancy and Thyrotoxicosis ---------- 67
- Tretment of Complicationts ---------- 71
- Prognosis ---------- 75
- Summary and Comment ---------- 77
- References ---------- 86
- Arabic Summary ----------

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INTRODUCTION

The term thyrotoxicosis denotes the complex of clinical, physiological, and biochemical findings that results when the tissues are exposed to excessive supply of the active thyroid hormone. Rather than a specific disease, thyrotoxicosis is a clinical syndrome that can originate in a variety of ways. In general, three main categories of disorder can produce the thyrotoxic state. The first, and most important category, is sustained overproduction of hormone of the thyroid gland itself. Here hyperfunction variously results from the action of an abnormal unregulated thyroid stimulator of extrapituitary origin, as in patients with Graves' disease or trophoblastic tumours; or the development of one or more areas of autonomous hyperfunction within the gland itself; or rarely due to excessive secretion of TSH associated with pituitary tumour. The second category are the thyrotoxic states associated with subacute thyroiditis and the syndrome termed: "chronic thyroiditis with spontaneously resolving thyrotoxicosis". The third category is one in which the sources of excess hormone is outside of the thyroid gland itself, as in cases due to ingestion of exogenous thyroid hormone: "thyrotoxicosis factittia", or the rare functioning metastatic thyroid carcinoma.

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Although all of the foregoing disorders are associated with thyrotoxicosis, not all are associated with hyperthyroidism, a term which denotes only those conditions in the first category described above, i.e., those with sustained hyperfunction of thyroid leads to thyrotoxicosis thus thyrotoxic state can be classified according to whether or not they are associated with hyperthyroidism. This distinction is important from both the diagnostic and therapeutic standpoints. In hyperthyroidism, hyperfunction of the thyroid is reflected in an increased Radio-active Iodine Uptake (RAIU), wheres in the nonhyperthyroid thyrotoxic states, thyroid function including RAIU is subnormal. Further, treatment of thyrotoxicosis by means intended to decrease hormone synthesis (antithyroid agents, surgery or radioiodine) is appropriate in hyperthyroidism but is inappropriate in other forms of thyrotoxicosis. (Ingbar and Woeber, 1983.)

Thyroid hormone affects cellular oxidative process in the body. Circulating thyroxine is found in thyroxine-binding globulins, and prealbumin. High levels of estrogen (eg, in pregnancy or in women taking oral contraceptives) increases the thyroxine binding globulin and thus the total level of T4. The binding can be inhibited by certain compounds, eg, high doses of aspirin,

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phenytoin, and several anesthetic agents particulary ether, The free unbound levels of circulating hormone regulate TSH release.

The peripheral metabolism of the thyroid hormone especially by the liver, and its alterations in disease states are particulary significant. Most of the circulating T3 derives from peripheral conversion of T4, which is also metabolized to a biologically inactive compound, reverse T3. In may chronic illnesses, starvation, etc, the proportion of T3 formed decreases and that of reverse T3 increases. The importance of this peripheral conversion, as well as hypothalamic-pituitary regulation altered by the adrenergic nervous system, is becoming apparent. In addition, an autoregulatory mechanism within the thyroid gland itself seems to maintain the constancy of thyroid hormone stores.

Thyroid disorders may occur with or without diffuse or nodular enlargement of the gland (goiter). A strong genetic predisposition to thyroid disease is being recognized.

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This Essay will discuss the diagnosis of many problems of the hyperfunctioning thyrotoxicosis, including Tc-99m, nuclear magnetic resonance (NMR or MR) imaging, computed tomography (CT) and the hypothesis about serum angiotensin converting enzyme (ACE). The medical means of control will be discussed in brief to give more space for the surgical aspect.

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What is technetium-99m ?

It is well known that the radiation dose to the thyroid from I-131 is considerably higher than that from Tc-99m pertechnetate or I-123. The survey that was taken from U.S.hospitals showed that over one half of thyroid scans were with Tc-99m. (Parker, 1984.)

The most commonly used tracer in clinical nuclear medicine today is technetium-99m. This radioactive isotope has a 6-hour half-life which permits ample time for manufacture of the radiopharmaceutical, its administration to the patient. and subsequent imaging, while restricting the radiation dose to which the patient is exposed to extremely low levels. Relatively inexpensive, Tc-99m is readily available to the clinical nuclear medicine laboratory through the use of a Tc-99m generator, making it feasible to have some of the procedures available on a 24-hour emergency basis. Tc-99m is used also in radiopharmaceuticals designed to localize in the liver, spleen, and gastrointestinal (GI) tract, as well as in the lungs, kidneys, bone, heart, blood, and brain.

Comment on the properties of Isotopes:

By careful selection of the physical and chemical properties of the tracer used to generate the radio-

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pharmaceutical, different physiologic processes, biochemical reactions or anatomic sites may be studied. For example, the physical size of radiolabeled colloid particles is an important factor in determining which organ will be labeled. When injected subcutaneously, a colloid with a small mean particle size (50 nm) would be more likely to localize in the lymph nodes than one with a larger particle size colloid (500 nm) that when injected intravenously, has a greater propensity for phagocytosis by the reticuloendothelial (RE) cells of the liver and spleen. By altering in the chemical properties of a radiopharmaceutical, different physiologic phenomena may be studied. A chelate with a small molecular weight tends to be excreted by the kidneys, wheres a chelate with a greater molecular weight will be excreted by the hepatocytes of the liver into the bile.

(Wilson, 1985.)

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What is NMR or MR ?

Bradley and Shelden, 1983. and Starer, 1985.

Nuclear magnetic resonance (NMR or MR) tomography is a new imaging modality capable of producing cross-sectional images like its predessor, x-ray computerized tomography. Unlike computerized tomography, it does not use ionizing radiation (x-ray), but rather safe interaction between magnetic fields, radiowaves, and atomic nuclei. Rather than dipcting tissue electron like CT, it shows hydrogen density in thin slices. The pictures are potentially more useful than those obtained by CT.

The magnetic field causes hydrogen protons to arrange themselves in an orderly fashion. The radio-frequency beam is tuned to the resonant frequency of the ratating proton and thus additional energy is given to the particle. When the radio-frequency current is interrupted, the extra energy is radiated by the proton and this radiation is used as the basis for formation of the image.

Advantages of NMR over CT:

1- The patient is not subjected to ionising radiation

2- Image reconstruction can take place in any desired plane.

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3- It is also possible, by the use of specially designed radiofrequency coils, to examine selected parts of the body, such as the spine.

4- The combination of proton density and magnetic relaxation time 1 (T1) images may provide more information in some circumstances than does CT.

Disadvantages of NMR:

The disavantages of NMR at present are the high installation and running costs and the slow rate of imaging. The latter is being overcome by apparatus able to carry out several images simultaneously while retaining spatial resolution of several millimeters.

Comparison between NMR and CT:

The strength of the NMR signal depends on the hydrogen density and on the magnetic relaxation times T1 and T2, which in turn are dependent on temperature, viscosity, and magnetic interaction. The intrinsic differences in hydrogen density, T1 and T2 between fat,muscle, blood, and bone are the major determinants of contrast in the nuclear magnetic resonance image. Since these differences are significantly greater than those of the equivalent determinant of x-ray contrast (electron density), there is much more contrast in NMR image than in its x-ray (CT) equivalent.

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Compared with CT, which distinguishes tissues on the basis of a single window-level control for x-ray attenuation, NMR tomography can provide the equivalent of the three window-level controls for hydrogen, T1 and T2. The following is a brief summary of early clinical experience with NMR imaging. Its use in the neck will be discussed with the radiological investigations.

SUMMARY:

NMR tomography is a powerful new imaging modality which produces cross-sectional images similar to those obtained by CT. Unlike CT, NMR does not utilize ionizing radiation but rather uses an apparently safe interaction between magnetic fields, radiowaves, atomic nuclei. basic principles of NMR imaging are discussed briefly.

The two magnetic relaxation times, T1 and T2 provide discrimination between tissues based on differences in fat and water content. Tumours differentiated from normal tissue on the basis of increased water content, primary due to edema and hypervascularity. Although NMR is very sensitive in the detection of these abnormalities, it is not yet able to provide a specific diagnosis. It remains to be seen whether NMR will ultimately replace CT, but it should be remembered that the latter is also undergoing rapid improvement.

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WHAT HAPPENS TO SERUM ANGIOTENSIN CONVERTING ENZYME IN THYROID DISORDERS ?

Smallridge et al, 1983.

Serum Angiotensin-Converting Enzyme (ACE) has two recognized activities:

1- It inactivates bradykinin,

2- It converts angiotensin 1 to angiotensin 11.

The ACE is localized in the vascular endothelium of several organs and also in the renal cells of the proximal tubules. In humans, this enzyme has been purified from lung and kidney. The ACE is also detectable in human serum and is presumably derived from the vascular endothelial cells. Elevated levels of serum ACE has been identified in several medical disorders. Recently, changes has been reported in hyperthyroidism. In the present study we have determined that patients with altered thyroid function have changes in serum ACE levels. In hyperthyroidism the mean level is 76 ٪ higher than in euthyroid patients and restoration of euthyroidism reverses the abnormal ACE value. The abnormality is reversible regardless of the therapy employed.

The explanation for the observed alterations in serum ACE levels in thyroid disorders is unknown.

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Yotsumoto (1982) suggested that elevated levels in hyperthyroidism might result from an increased release of the enzyme from vascular edothelial cells, as has been postulated in diabetics. Several other possibilities exist, however, since thyroid hormone may induce protein synthesis, it is possible that enzyme synthesis is enhanced. It may be that additional ACE is produced as a response to increased available substrate, as increased and decreased concentration of plasma renin activity have reported in hyperthyroid and hypothyroid patients, respectively. It is possible that teleologically this enzyme becomes elevated in hyperthyroidism not for its function as a converting enzyme, but instead for its ability to inactvate the potent vasodilator bradykinin, since hyperthyroid patients have peripheral vasodilation.

CONCLUSION

These studies indicate that the serum ACE level is highly correlated with thyroid function and interpretation of any alterations in its measurements requires knowledge of the patient's thyroid states. Additionally, ACE may prove useful as a peripheral marker or as a probe for exploring the biologic effect of thyroid hormone in human and, conceivably, might be employed clinically to help discriminate euthyroid patients from those with increased or decreased biologic effect of T4 or T3.

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