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بالرسالة صفحات
لم ترد بالأصل

STUDY OF CARBAMYLATED HEMOGLOBIN IN PATIENTS WITH END-STAGE RENAL DISEASE UNDER MAINTENANCE HEMODIALYSIS

Thesis submitted to Medical Research Institute
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Hanan Moselhi.

CONTENTS

LIST OF ABBREVIATIONS

- ACTH: Adrenocorticotropic hormone
- BMI : Body Mass Index
- BUN : Blood Urea Nitrogen
- CarHb : Carbamylated Hemoglobin
- DPG : 2,3 Diphosphoglycerate
- DW : Dry Weight
- ESRD : End Stage Renal Disease
- G : Urea Generation Rate
- HPLC : High Performance Liquid Chromatography
- Kt/V : Dose of dialysis
- LDL : Low-density Lipoproteins
- MAC : Mid Arm Circumference
- MAMC : Mid Arm Muscle Circumference
- NCDS : National Cooperative Dialysis Study
- PCRn : Normalized Protein Catabolic Rate
- tid : Interdialysis time
- TSF : Triceps Skin Fold
- UF : Ultrafiltration rate
- UKM : Urea Kinetic Modelling
- URR : Urea Reduction Ratio
- V1 : Urea distribution volume at the end of the dialysis session
- V2 : Urea distribution volume at the beginning of the next dialysis session

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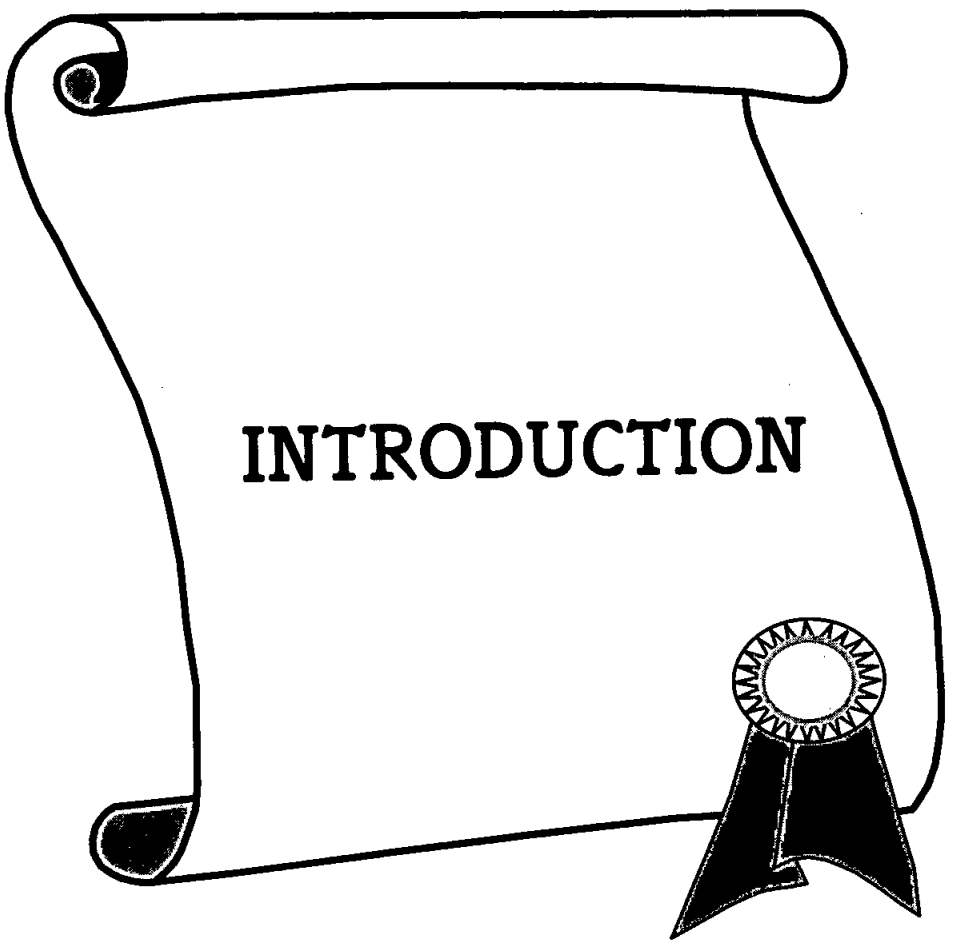
INTRODUCTION

CHAPTER I

CARBAMYLATED HEMOGLOBIN

Urea is spontaneously rearranged in plasma to form ammonium and cyanate ions (1). The protonated form of cyanate, isocyanic acid, reacts with the amino terminal group of proteins, resulting in the carbamylation of proteins (2).

When urea is retained as in renal failure along with other metabolites, carbamylation of amino acids, plasma proteins, leukocyte proteins and hemoglobin have all been shown to occur. [3-14]

In mammals carbamylation of proteins, lipids, peptides and amino acids is widespread in health [3,7,8,12,15-18] and is a natural physiological phenomenon. In the lens, gamma crystallin is carbamylated at the lysine site [19]. In lipid envelope of the red cell, the carbamylated lipids are phosphatidyl-ethanolamine and serine . The site of carbamylation of insulin, T3 and other plasma proteins is uncertain [17].

Carbamylation is a non-enzymatic, irreversible reaction. Once a protein, lipid, polypeptide or amino acid is carbamylated the concentration of the carbamylated material can only fall through two possible mechanisms- firstly, catabolism with destruction of the modified protein, lipid, peptide or amino acid, or secondly, entry of newly synthesized noncarbamylated proteins, lipids, peptides or amino acids into the compartment under study, usually but not always, the blood or plasma.. However, the concentration of carbamylated substrate can increase if there is greater exposure to urea, either by longer exposure of the proteins to the same concentration or exposure to higher urea concentrations [3,10,20].

Major plasma proteins and hemoglobin have a considerable half-life measurable in days, are demonstrably carbamylated, and the physiological consequences of carbamylation have been studied[21].

Some studies [16] have shown that plasma proteins are carbamylated in renal failure in a similar way to hemoglobin and point out that there is good reason to extrapolate from carbamylation of plasma proteins to tissue proteins which are most likely

carbamylated because of the ubiquitous presence of urea in cells. How this affects their function is at the moment unknown, but the same group has pursued this matter in the peptides insulin, triiodothyronine and ACTH [15,21,22].

Insulin was carbamylated in vivo and its immunological activity and its bioactivity were determined. The authors found that the biological activity of insulin was reduced to one fifth of that of uncarbamylated insulin. In addition, they found that immunologically carbamylated insulin was only immunoprecipitable with insulin antibodies to one third of the amount precipitable by non-carbamylated insulin [16,23].

Triiodothyronine has similarly been carbamylated in vitro, and its biological activity was determined.[23]. There is also a statistically significant decrease in the activity of the carbamylated triiodothyronine in vivo which could be remotely related to the situation in uremic man, but the majority of patients in advanced uremia do not display hypothyroidism , so the significance of carbamylation experiments in vitro or in vivo is not clear. A possible