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CONTENTS

9 MICROHETEROGENEITY OF THYROXINE-BINDING GLOBULIN (TBG) IN DIFFERENT METABOLIC STATES.+

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The interpretation of microheterogeneity of TBG demonstrated in isolated TBG from pooled human serum in analytical isoelectric focusing (IEF) is still controversial. Whereas Gershengorn et al. (1977) assumed an irreversible transition of TBG near the isoelectric point we now could demonstrate that microheterogeneity of TBG is caused by different N-acetylneuraminic acid contents. The purpose of this study was to investigate the microheterogeneity of TBG in native human sera in different metabolic states and in sera from patients with TBG deficiency.

Methods: IEF was performed on flat-bed polyacrylamide gels (PAG-plates), with a continuous pH-gradient from pH 3.5 to 5.0 and pH 4.0 - 6.5 respectively. The focussed TBG was identified by immunofixation using cellulose-acetate strips, soaked with monospecific TBG-antiserum. Immediately after IEF, strips were placed on the PAG-plates for an incubation time of two minutes. The non-precipitated proteins were removed by washing in tap-water and the strips stained with Coomassie-Blue.

Results: In agreement with the pattern of TBG isolated from pooled serum three major TBG-bands were found at pH 4.55, pH 4.45, pH 4.35 and a minor band at pH 4.25 in individual sera from normal adults. These typical patterns were also demonstrated in hypo- and hyperthyroidism as well as in genetic TBG-deficiency. Characteristic deviations from this microheterogeneity could however be demonstrated in pregnancy: during the continuous increase in TBG-concentration a further band at pH 4.15 appeared and the precipitation line at pH 4.25 became more intensive, whereas the most alkaline band at pH 4.55 faded. In contrast, liver diseases with elevated TBG-concentrations are characterised by an intensified band at pH 4.55 and diminution of the band at pH 4.25.In the sera of healthy mature newborns a comparable pattern to that of normal adults was found. In contrast, in the sera of premature infants four double bands were found in the pH area typical for normal adults This foetal TBG pattern was normalized when the sera were re-examined 6 months later.

Conclusions: Typical microheterogeneity of TBG was found in native sera of normals which was not influenced by thyroid diseases. However in states with increased glycoprotein synthesis as induced by oestrogens a more sialylated TBG, detected by an additional acid band could be demonstrated in IEF. In contrast, in liver diseases with diminished glycoprotein degradation an increase of desialylated TBG with an intensified alkaline band was found. In genetic TBG deficiency microheterogeneity of TBG was comparable to that of normals.

Gershengorn M.C. et al.: J.Biol.Chem.252 (1977) 8719-8723.

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