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ABSTRACTS FOR THE VI INTERNATIONAL SYMPOSIUM ON HUMAN PURINE AND PYRIMIDINE METABOLISM

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1 CELL CYCLE REGULATION OF RIBONUCLEOTIDE REDUCTASE M2 SUBUNIT SPECIFIC RNA IN WILD TYPE and MUTANT S49 CELLS. Daniel A. Albert, Edwardine Nodzenski, and Gloria Yim. Dept. of Medicine, The University of Chicago.

Ribonucleotide Reductase reduces all four ribonucleoside diphosphates to deoxynucleoside diphosphates and functions as the major source of decoxyribonucleotides for DNA synthesis in vivo. Ribonucleotide reductase is cell cycle regulated and most of the increased activity during S phase results from a 6 to 10 fold increase in M2 subunit activity. Hydroxyurea resistant cell lines have increased M2 activity and M2 gene amplification but normal cell cycle regulation of ribonucleotide reductase activity. We investigated M2 specific mRNA content of cell cycle specific populations using a 1487 bp long mouse M2 cDNA to probe northern dot blots of total cellular RNA from wild type, cyclic AMP dependent protein kinase deficient, and two hydroxyurea resistant cell lines one with and one without cAMP dependent protein kinase activity. Five sequential cell cycle fractions were obtained by centrifugal elutriation. Hydroxyurea resistant cell lines had greater M2 specific RNA per mg than wild type though their cell cycle regulation appeared to be largely the same. All cell types have low concentrations of M2 specific RNA in very early G1, a dramatic increase in late G1/early S, a rapid decline in later S and finally a gradual rise in G2 phase. These data suggest transcriptional regulation of M2 during the cell cycle is at least in part responsible for cell cycle variation in ribonucleotide reductase activity.

2 URATE NEPHROPATHY: A RARE BUT NOT VANISHED ENTITY

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Chronic urate nephropathy in the past decades was a frequent cause of renal failure in gouty patients but this entity has become very rare in the recent years and in many centers of hemodialysis the registries of chronic renal failure populations do not list gouty nephropathy as a cause.
Some authors even discuss the existence of gouty nephropathy (1).
In our series of 140 patients with primary gout (128 M, 12 F) including 20 patinets with late onset (over 65 years) of the disease (15 M, 5 F) we never observed renal insufficiency with serum creatinine over 1.5 mg/dl; but the urate nephropathy exist also as a rare familial form, inherited in a autosomal dominant manner and, more rarely, as an idiopathic form, without clinical evidence of gouty arthritis.
Recently we observed an idiopathic form of this disease in a male patient, 51 years old, who presented a middle renal insufficiency (serum creatinine over 2.0 mg/dl and albuminuria).
Ultrasonic kidney study and C.A.T. have shown numerous microcysts in the cortical of the kidney, but only the needle biopsy has confirmed the urate nature of the interstitial chronic nephropathy.

1- L.H. Beck Kidney Int. 30 (1986) 280-286.

3 DETERMINATION OF ALLANTOIN IN MAMMALIAN TISSUES.

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Allantoin - the key compound in purine catabolism - is determined in biological systems using the Rimini's reaction, which involves treatment with 0.1 N alkali (100°C) and formation of allantoic acid, 0.025 N HCl (100°C), and production of urea and glyoxylic acid; final determination of the latter compound as a dinitrophenylhydrazine derivative. The reaction is subject to several interferences. The purification of allantoin is also difficult and thus it cannot be analyzed after labelled precursor administration. We evaluated the allantoin content in rat tissue extracts using two procedures: (1) allantoinase treatment (instead of alkali), subsequently proceeding as described above, (2) NaOH and HCl treatment, but a final determination of urea with urease and glutamate dehydrogenase. Results were lower compared with the conventional dinitrophenylhydrazine reaction. Precipitation of allantoin with Hg-acetate (followed by ion -exchange chromatography) guarantees excellent recovery of pure allantoin from tissue extracts. This has proved to be a simple procedure for determination of true allantoin content and of its labelling with isotopes for kinetic studies in different tissues.

4 IS GOUT RELATED TO AN ALTERATION OF THE PROTEIN BINDING URIC ACID?

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The concentration of free and protein-bound urate in plasma was studied in control and gouty subjects. The uric acid bound to the plasma proteins was estimated by ultrafiltration method using Amicon's micropartition system. The total concentration of uric acid in the plasma and in the ultrafiltrate was analyzed by an enzymatic colorimetric method and the amount of uric acid binding was obtained from the difference between uric acid in plasma and in ultrafiltrate. In gouty patients the percentage of uric acid is quite the same that in control subjects, but it must be considered in relation to the higher values of uricemia; consequently, what is really increased is the free uric acid amount step by step with the increase of uricemia. So, the whole amount of free uric acid is available for the deposition in the tissue. The reduced binding capacity showed by gouty patients in comparison with healthy subjects is also confirmed by the results following to an hypoxanthine load per os, carried out in the two groups.