

قسم : الباثولوجيا - كلية الطب البيطرى - جامعة أسيوط .
رئيس القسم : أ.د / محمد الشرقى .

دراسة مورفومترية وهستياثولوجية للتغيرات التى تحدث فى كلية الفئران
البياض نتيجة انخفاض نشاط الغدة الدرقية

محمد خيرى ابراهيم

أجرى هذا البحث لدراسة تأثير انخفاض معدل نشاط الغدة الدرقية على الكلية . ولقد استخدمت مادة الميثيل ثيورايل بحقنها تحت الجلد فى حيوانات التجارب . واستخدم فى هذا البحث ٥٠ فأر أبيض قسمت الى أربع مجموعات بالإضافة الى مجموعة لم تحقن واستخدمت للمقارنة ولقد تم دراسة التغيرات الهستياثولوجية التى حدثت فى الكلية وكانت عبارة عن احتقان نسي الأوعية الدموية للكلية وتعبد فى فراغ باومان . ولقد تم دراسة التغيرات المورفومترية التى حدثت فى الكلية واستخدم لذلك قياس حجم أنوية الخلايا المبطنة للقنوات المتعرجة وكذلك قياس حجم فراغ باومان بالإضافة الى قياس حجم الكبيبات . ولقد أُنضج من الدراسة المورفومترية الآتى :

- ١- تقل أوعية الكبيبات فى الحجم نتيجة حقن مادة الميثيل ثيورايل .
- ٢- زيادة حجم أنوية الخلايا المبطنة للقنوات المتعرجة العليا فى المجموعتين الأولى والثانية .
- ٣- زيادة حجم الكبيبات فى المجموعة الأولى التى حقنت بتركيز عال .

London, 18th June 1864

My dear Mr. Stowe

I have just received your letter of the 14th inst. and am
glad to hear that you are well. I am
very much interested in the
progress of the cause, and
am glad to hear that you are
doing so much for it. I am
very much interested in the
progress of the cause, and
am glad to hear that you are
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EXPERIMENTAL STUDY OF HYPOTHYROIDISM IN RATS
1- MORPHOMETRICAL AND HISTOPATHOLOGICAL CHANGES IN THE KIDNEY
(With 2 Tables & 6 Figures)

By

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(Received at 2/9/1982)

SUMMARY

The present study was designed to investigate the effect of experimental hypothyroidism induced by subcutaneous injection of methylthiouracil (M T U) on the morphological and morphometrical changes in the kidneys of rats. Fifty rats were used in this experiment. They were divided into 4 groups A,B,C and D which were treated by S/C. injection of (M U T) at dose level 10, 0,5 0,2 0,1 mg. per Kg body weight respectively. In addition, fifth group E of 10 animals was used as control.

The morphometrical changes revealed that.

- 1- The glomerular tuft is significantly decreased by administration of antithyroid drug.
- 2- Increase in the nuclear diameter in the first two groups.
- 3- Increase in the glomerular diameter in the first group.

INTRODUCTION

The kidney plays a dominant role in maintaining the constancy of the body's internal environment by excretion of metabolic waste products and regulation of water content, salt and acid-base balance. In spite of many publications on hypothyroidism that could be found, little work was carried out on the quantitative changes in the kidney under this condition. In normal and abnormal cases, different quantitative morphometrical methods for evaluation of the functional activity of the kidney were performed, among which are histometrical studies in human glomeruli (ELJAS and HENNIG, 1967; WEHNER, 1968; KAWANO *et al.* 1969, WEHNER and OSWALD, 1978) as well as morphometrical analysis of the glomeruli of rabbit, mouse and guinea pig. (ELJAS and HANNIG, 1967). The increase in glomerular size has been found to be characteristic in cases of compensatory renal hypertrophy, glomerulonephritis as well as diabetes mellitus (VAN DAMME and KAUDSTAAL, 1976; QSTERBY, 1973).

In the present work, microscopical picture and morphometrical changes of the kidney were studied in rats under the condition of hypothyroidism induced experimentally by administration of methylthiouracil (M T U).

MATERIAL and METHODS

The materials employed in the present work included 50 male wistar rats (200 - 250 gm body weight). The experimental animals were manipulated under the same environmental conditions of 22°C room temperature and were rationed *ad libitum* and adequately supplied with tap water. The animals were regularly exposed to light for 12 hours per day. The rats were divided into 4 groups A,B,C and D, of 10 animals each. The animals were individually treated daily by S/C injection of 6-hydroxy-2-methyl-pyrimidin, Methylthiouracil (M T U) for one week at a dose level 10, 0,5,0,2 and 0.1 mg. per kg body weight for group A,B,C and D respectively. In addition, a fifth group E, of 10 animals was used as a control.

The kidneys were collected from the rats after they were sacrificed (by decapitation) and were fixed in 10% neutral buffer formalin. Paraffin sections were cut 4-5 microns thickness and were stained with haematoxylin and eosin.

The histometrical parameters employed were:

- 1- Glomerular diameter.
- 2- Capillary tuft-diameter.
- 3- Diameter of the nucleus of the epithelial cells lining proximal convoluted tubules.
- 4- Diameter of the Bowman's space.

The histological slide was projected on a screen using a "Karl Zeiss" microscope with halogen lamp to obtain a magnification of 800 fold; each kidney was represented in 5 serial sections. From each animal the diameter of 50 glomeruli, and 50 nuclei of the epithelial cells lining proximal convoluted tubules which are located centrally were measured. Statistical methods were carried out to postulate the changes given in each Test. The mean values of each measurement for different groups were statistically analysed.

RESULTS

Compared with control animals, microscopical examination of the kidney of treated groups revealed a hyperaemia of the organ especially manifested in the intertubular blood vessels which were dilated and engorged with blood with no haemorrhage. The glomerular tuft of many glomeruli were shrunken and appeared more cellular while the Bowman's space was widely dilated. The lumenae of the convoluted tubules were filled with eosinophilic homogeneous albuminous materials while the collecting tubules were dilated and empty (Fig. 1). The degree of these changes directly correlated with the dose level of administered methylthiouracil.

Data of morphometrical parameters of the kidneys in different groups are shown in table 1 and 2. Statistical analysis of these data revealed a significant difference ($P \leq 0.05$) of the average value of glomerular diameter in group A given a high dose of methylthiouracil as compared to control animals. In this group the glomerular diameter was increased (Fig. 2). No changes were recognized in the glomerular diameter of the other 3 groups. The size of the glomerular tuft significantly decreased ($P \leq 0.05$) (Fig. 3) in the three group (A,B,C.) compared with normal. The average values of the diameter of Bowman's space of all treated groups were significantly large ($P \leq 0.05$) than control animals (Fig. 4). Significant difference was determined only in the first two groups, A and B, with respect to the average diameter of the nucleus of epithelial cells lining the convoluted tubules (Fig. 5). The increase in both nuclear diameter and Bowman's space directly correlated with the dose level.

Table (1): Relative measures of glomerular diameter, capillary tuft and Bowman's space in different groups of experimental animals

Group	Glomerular diameter		Capillary Tuft		Bowmans Space	
	\bar{X}	S.D	\bar{X}	S.D	\bar{X}	S.D.
A	* 103.91	± 7.76	*** 77.42	± 6.58	*** 26.47	± 4.45
B	97.42	± 3.37	*** 76.00	± 4.41	*** 21.37	± 2.26
C	99.10	± 4.60	*** 77.97	± 4.39	*** 21.16	± 2.93
D	97.00	± 4.62	82.34	± 4.87	14.66	± 4.71
E	98.45	± 12.07	83.50	± 8.98	14.94	± 6.63

N.B. : \bar{X} = mean, S.D. = Standard deviation, * = $P \leq 0.05$,

** = $P \leq 0.01$, *** = $P \leq 0.001$

Table (2): Diameter of the nucleus of the epithelial cells lining proximal convoluted tubules

Group	\bar{X}	S D
A	7.03*	± 0.42
B	6.79	± 0.41
C	5.29	± 0.21
D	5.43	± 0.21
E K	5.41	± 0.52

N.B. : \bar{X} = mean, S.D. = Standard deviation,

* = $P \leq 0.05$, ** = $P \leq 0.01$, *** = $P \leq 0.001$

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DISCUSSION

In the present study, experimental results showed that the diameter of the glomerular tuft, which is indicative for glomerular volume, significantly decreased by administration of antithyroid drugs. These results are consistent with clinical findings in hypothyroid patients who were found to have diminished urinary output (LESLIE and STANBURY, 1975). In these patients, the renal blood and glomerular filtration rate were stated to be decreased because of decreased cardiac output (YOUNT and LITTLE, 1955; DISCALE and KIDNEY, 1971). Wide Bowman's space in the glomeruli of our experimental animals appeared to be related mainly to decrease in the size of glomerular tuft with exception of the first group only in which the diameter of the glomeruli were enlarged.

Reduction in the blood pressure of the renal arterioles under the effect of administered antithyroid drugs probably may lead to stimulation of secretion of renin by the kidney. Renin, through activation of angiotensin, stimulates aldosterone secretion from the adrenal glands leading to sodium retention by the tubules. This effect is potentiated by angiotensin which has a direct action on the tubules as well (WALTER and ISRAEL, 1979). Reabsorption of the filtered sodium is an active process associated with cellular activity. This was manifested by an increase in nuclear diameter which was statistically significant in group A and B of our experiment.

The increase in the diameter of the nuclei in the first two groups under the effect of (MTU) can be explained either by increased physiological activity of the proximal convoluted tubules i.e. hyper resorption of water and sodium and their retention in the blood and subsequently oligourea but this fact is contradictory with the other morphometrical parameter (decrease in the diameter of the glomerular tuft and increase in the process of urine reabsorption by the proximal convoluted tubules. The only probable other explanation for increase in the size of the nuclei of proximal convoluted tubules is the start of process of hyperplasia due to deficiency of thyroid Hormones and hypoactivity of the tubule similar to the hyperplasia of the target organ due to hormonal deficiency in general.

It is known that tubular reabsorption of water starts in the proximal convoluted tubules where most of the water returned to the blood stream. The reabsorption of water is the passive results of active reabsorption of much of the filtered sodium. If there is an increased amount of solute to be retained by the kidney, an increased amount of water is reabsorbed. Dilation of Bowman's space and renal tubules in the first animal groups treated with antithyroid drugs indicated, in contrast, a retardation of water reabsorption from the tubules. This decrease in the rate of reabsorption of filtered fluid may be related to an inhibitory effect of (Methylthiouracil) on the proximal convoluted tubules.

Slight difference was found in our measurements in normal rats from those of other investigators, these may be related to the applied strain. KINKMAN and STOWELL (1942) recorded that albino rats with 275 g. average body weight have a medium glomerular diameter of 142 μ while in wistar rats the glomerular diameter was 101.4 μ for animals having a body weight from 262 to 294 g.

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Kidney. Control Untreated rat. (10x10)



Fig. (1) kidney showing shrinkage of glomerular tuft with
of the bowman'S space and collecting tubules(10x10)

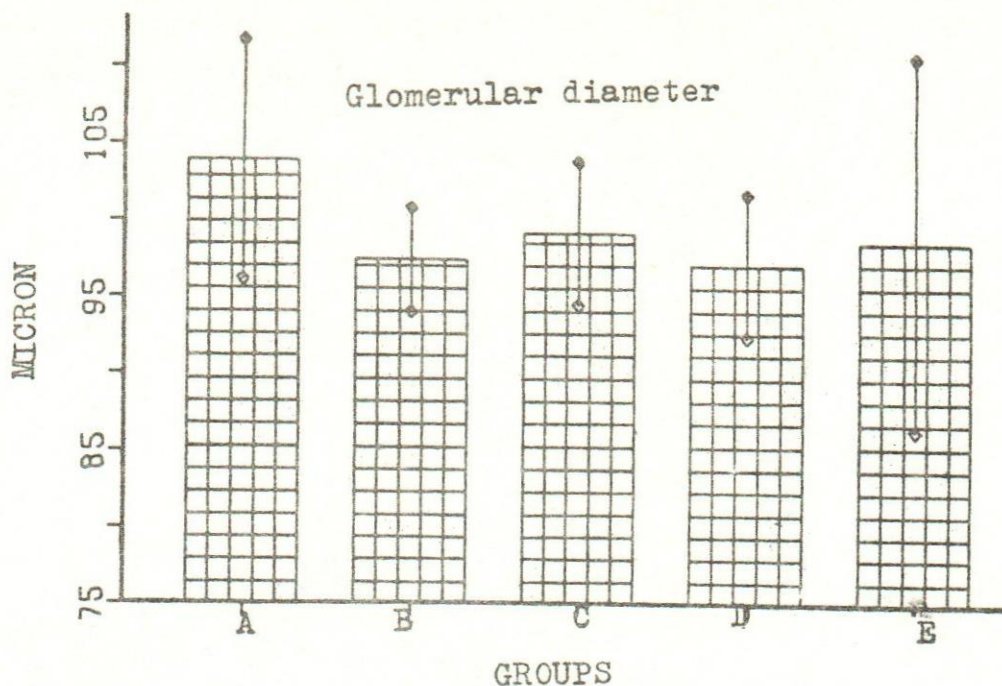


Fig.(2) A histogram showing the average diameter and standard deviation. of the glomeruli in rats under different dose level of M T U.

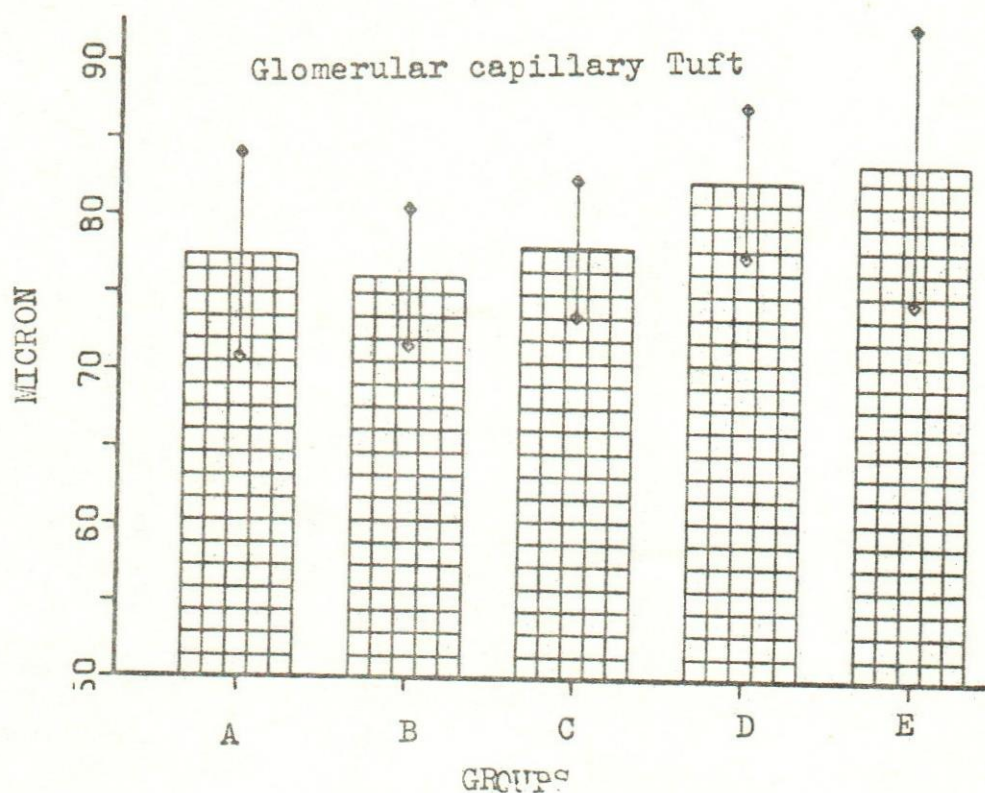
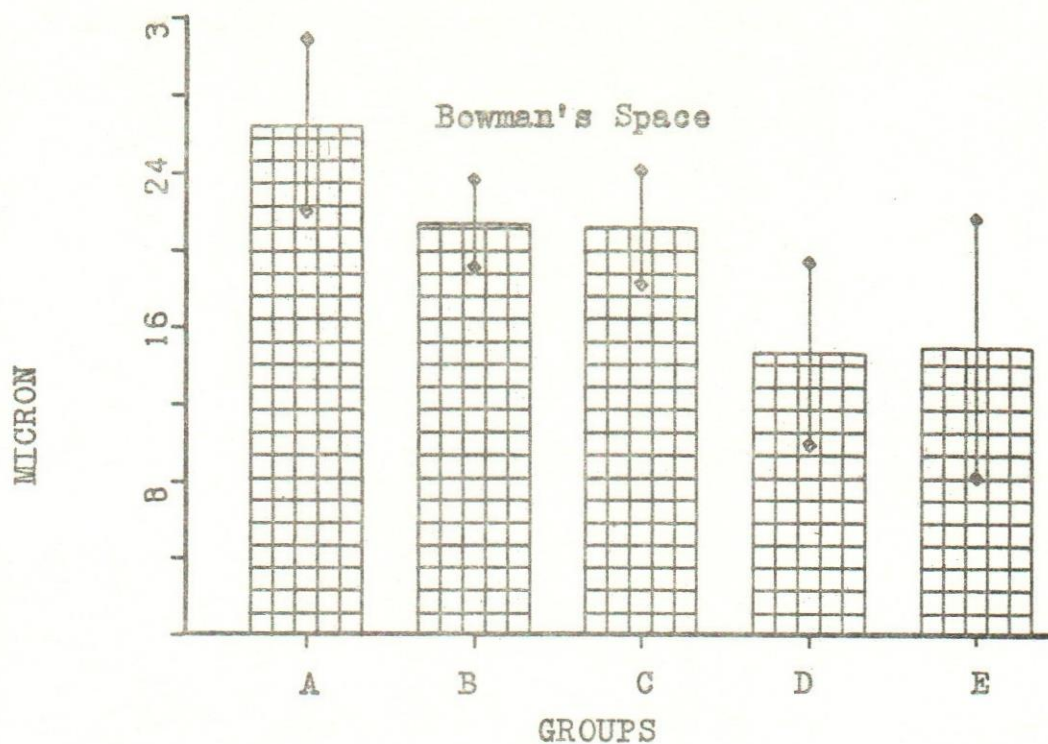
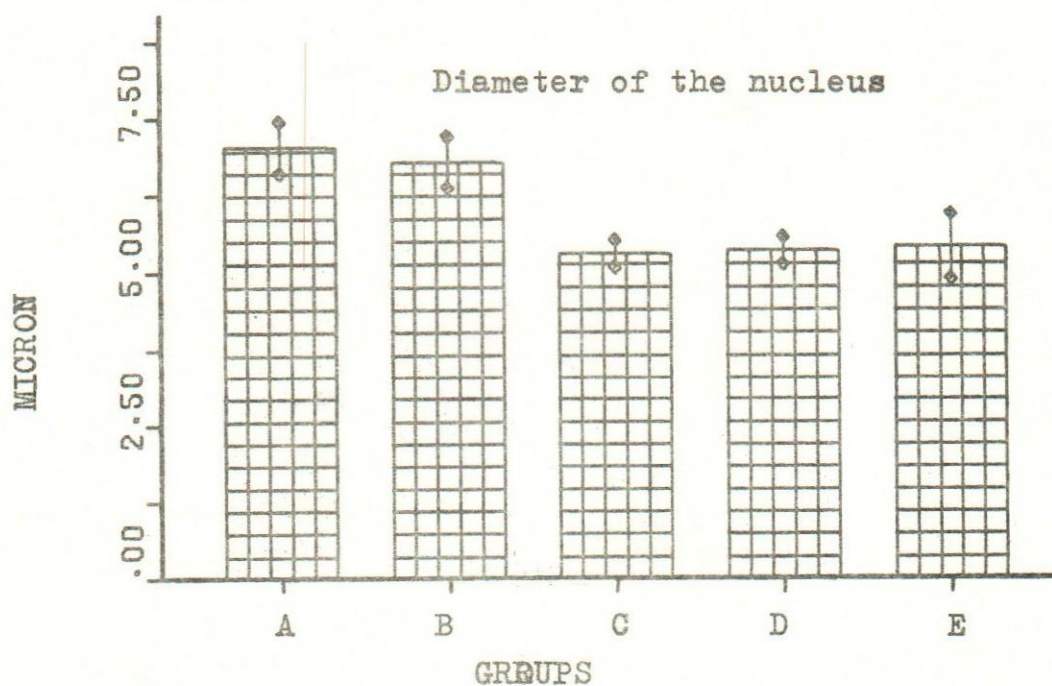


Fig.(3) A histogram showing the average diameter and standard deviation of the glomerular capillary tuft in rats under different dose level of M T U.



Fig(4) A histogram showing the average diameter and standard deviation of the Bowman's space in rats under different dose level of M T U .



Fig(5)A histogram showing the average diameter and standard deviation of the nucleus of the epithelial cells Lining proximal convoluted Tubule.

