رقم البحث (32)

HISTOLOGICAL AND HISTOCHEMICAL STUDIES ON THE METANEPHROS OF WHITE RATS

BY

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ABSTRACT

Histological and Histochemical Studies on the Metanephros of Rats' Embryos

Metanephros originates form the metanephrogenic tissue and ureteric bud. The nephrogenic tissue appears at 13 day of foetal life caudal to mesonephros as condensed mass of mesenchyme.

At 14 day of foetal life, the ureteric bud appears as elongated tubular structure within the metanephrogenic cell mass.

At 16 day of foetal life, the ureteric bud is branched toward the superficial covering epithelium, the branching process increase and takes dichotomous manner, The cell masses surround the ureteric bud branches and changed to S – shape tubules with peripheral invaginations containing mesenchymal cells and blood capillaries to from the glomerulus, The invaginated ends differentiate into parietal and visceral layers separated by corpuscular space. The collecting tubules appear surrounded by mesenchyme.

At 18 day of foetal life to birth, the primitive renal pelvis appears as dilatation in ureteric bud within the primitive renal sinus. Newly formed renal corpuscles continue to appear in sub capsular basophilic zone of cortex and the older one appears in internal acidophilic zone.

The characteristic features of the proximal and distal tubules appeared and the brush border on the epithelial lining of the proximal tubules and the macula densa appeared.

The collecting tubules appear more straight and some of them extend toward the cortex forming the medullary rays , The thin and thick ascending and descending segments of nephron and the papillary ducts and renal papilla were appeared .

At 19 day of foetal life the renal capsule appears to be covered by mesothelium with thin fibrous sub epithelial layer.

At the last day of foetal life the renal glomeruli and the parietal layer of renal corpuscle in addition to brush border of the epithelial lining of proximal tubules show positive

INTRODUCTION

Several studies have been carried out on developmental, histological and histochemical features of kidney in experimental and domestic animals such as **Al-Awdan and Kandil (1979)** in rats, **Tiedmann and Wettstein** and **El-Gharbawy (2002)** in rabbit and **Canfield (1980)** in large ruminants.

The rats is the most suitable experimental animals in field of organogenesis owing to its great similarity with other mammals, short gestation period , large number of young's in addition to its polyestrous nature.

The present study was directed to describe the organogenesis of metanephros in rats and throw the light on different histological and histochemical features of it.

MATERIAL AND METHODS

Thirty females and 10 males' white albino sexually mature rats (Rattus rattua) with average weight of 109-210 gm. were used in this study.

The females were inspected daily for detection of the best time for mating through examination of vaginal swaps **(Cohen, 1966)**. The females in estrous were transmitted to mature males along the night. Surly occurrence of mating and detection of the first day of fetal age via vaginal swap showing sperms **(Monson et. al., 1982, Al-Hamidy et. al., 1998** and **Abd El-Samie, 2004)**

After selecting the required ages of embryos, the females scarified and their abdominal cavities opened and the fetuses was taken through the uterus.

Fifty two fetus of different ages (9-21 days prenatally) were used. They were weighted then immediately fixed in the different solution including formalin 10%, bouin`s solution, zenker`s solution. The foeti of 9-15 day were situated intact however that of 16-21day only their caudal half of body were used.

The specimens were processed and embedded in paraffin and then serial sections of 5µ thick were taken, prepared and stained with H&E , Crossman's trichrome stain, Gomoris reticuline method, Aldehyde fuchsine stain , periodic acid Schiff , alcian blue and alcian blue / Period acid Schiff (AB PH 2.5 according to **Bancroft and Gamble(2002)** and **Crossman (1973)** then examined through light microscope.

RESULTS

The studies revealed that, the metanephrogenic tissue appears at 13 day of foetal life caudal to mesonephros as condensed mass of mesenchymal cells

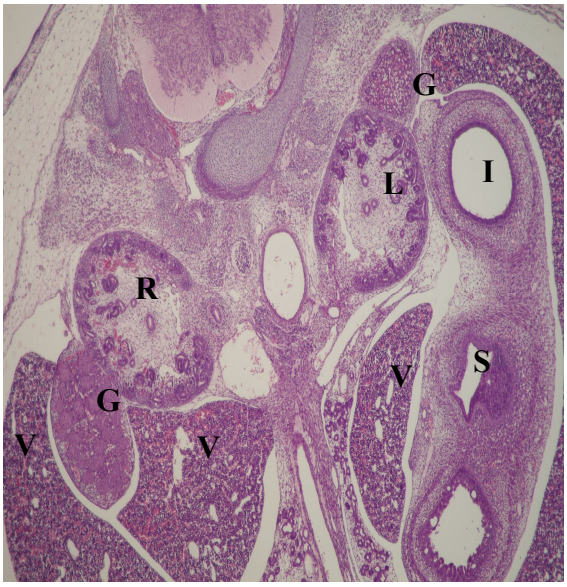
At 14 -day of foetal life, the mesonephros, became smaller with signs of atrophy and decay of its tubules while the mesospheric duct was continued. The ureteric bud appears as elongated tubular structure within the middle of the metanephrogenic cell mass. It appeared lined by single columnar cells with basophilic oval nuclei in its cranial part and cuboidal cells with spherical nuclei at its caudal segment (Figure 1).

The metanephrogenic cells appear larger and thicker and more crowded around the cranial end of the ureteric bud at day 15 of fetal life.

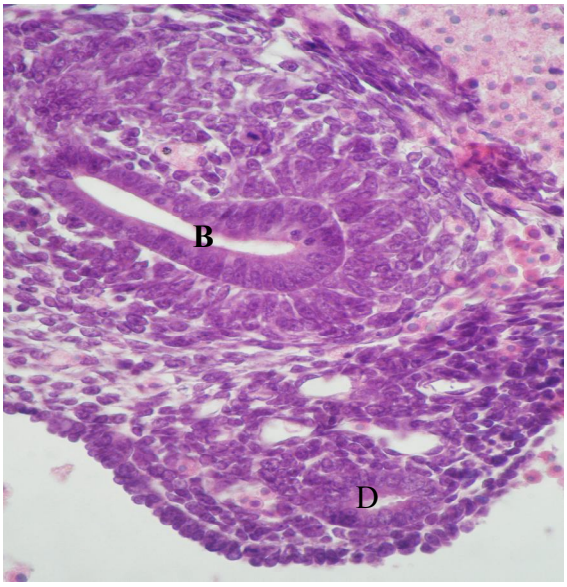
At 16 day of foetal life**,** mesonephric tubules were completely disappeared while the mesonephric duct remain giving the ureteric bud. Metanephrogenic tissue inflated and appeared as large prominent mass within the embryonic cavity. They begin to differentiate into metanephric tubules which appear in various forms on periphery of the kidney, while the mesenchymal tissue between these tubules is decreased (Figure 3&2)

The ureteric bud is branched between the metanephric tubules toward the superficial covering epithelium. The branching process increase and takes dichotomous manner.

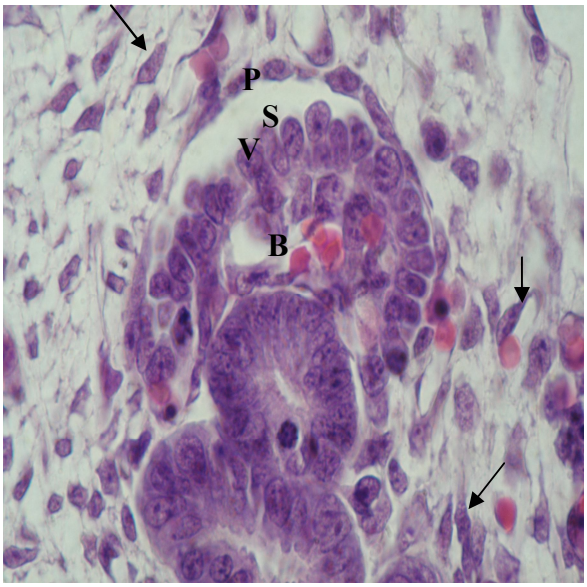
The cell masses surround the ureteric bud branches and changed to S – shape tubules with peripheral invaginations. Blood capillary with nucleated and non-nucleated red cells originated within mesenchymal tissue between these tubules (Fig 3).



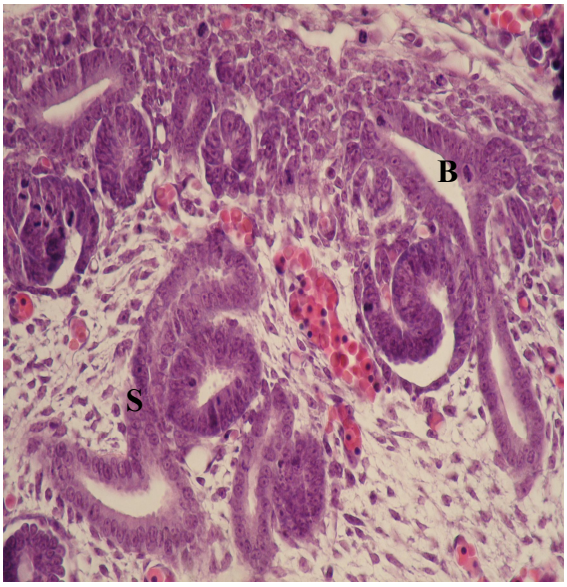
(Fig. 2) Section in16 days age rat embryo showing disappearance of mesonphros & appearance of R. Kidney (R) L. kidney (L). Note renal tubules on periphery of kidney. Gonads (G) intestine (I) stomachs(S) Liver (V) 100X. (H & E)



(Fig. 1) Section in rat embryo of 14 days age showing distorted cells and shirinked corpuscles of mesonphros, metanphrogenic duct (D). Note the onset of ureteric bud (B). 400x (H & E)



(Fig. 4) Section in rat embryo of 16 days age showing renal corpuscles formed from glomerular capillary (B) visceral layer (V) parietal layer (P) of corpuscular capsule, corpuscular space(S) Note fibroblast (Arrow) around renal corpuscle 1000X (H&E)



(Fig. 3) Section in rat embryo of 16 days age showing branching of ureteric bud (B) S- shaped tubules (S) Note crowded mesenchymal cells on periphery of kidney. 400X. (H & E)

Mesenchymal cells and blood capillaries are extended within the invaginated peripheral ends of the metanephric tubules to from the Primitive glomerulus .The invaginated ends differentiate into parietal and visceral layers separated by corpuscular space.

The renal corpuscles were formed with differentiation of surrounding mesenchymal cells intoo spindle shaped fibroblast with oval nuclei; some of them send thin cytoplasmic process (Figure 4).

Collecting tubules appeard in renal medulla surrounded by mesenchymal tissue which differentiated mostly into fibroblasts and blood capillaries containing red blood cells with and without nuclei. These tubules lined by ill-distinct bordered columnar cell with round or oval nuclei overlapped with each other's at the basal part of cells (Figure 5).

***At 17day of foetal life*,** complete disappearance of mesonphros occurred and the ureteric bud became clearer extending from primitive hilus to peripheral area of metanphros between metanephric tubules (Figure 6).

By arrival of 18 day foetal life, the ureteric buds dilated to form primordia of renal pelvis .The primitive renal sinus appear containing numerous fibroblast and blood vessels. The collecting tubules appear straighter, extended from branches of ureteric bud toward the renal cortex. Some tubules are present between growing renal corpuscles forming the medullary ray (Figure 7).

The mesodermal cells surrounding the cortex begin to differentiate into fibroblast covered by squamous cell to form the primitive renal capsule.

The outer part of the growing cortex showing numerous cell masses, renal corpuscles and elongated S-shaped tubules. Newly formed renal corpuscles continue to appear in sub capsular zone, they characterized by its smaller size with numerous dark nuclei giving basophilic appearance of the external part of the cortex .While the older corpuscles appears larger in size in inner zone of the cortex with paler nuclei giving its acidophilic appearance

The characteristics features of proximal and distal tubules appeared. The proximal tubules are lined with cubic or pyramid-shaped cells with rounded nuclei and acidophilic cytoplasm, while the distal tubules are lined with numerous low cuboidal cells. The branching

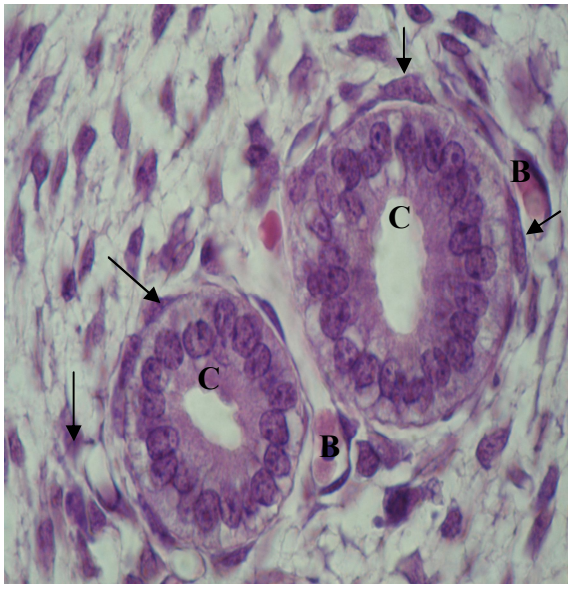
of the ureteric bud continues in dichotomous manner, these branches are lined by cuboidal epithelium with large rounded nuclei; some of them are connected with surrounding tubules (Figure 8).

***From age of 18 days until the end of fetal life*,** differentiations of proximal and distal tubules continue to appear in sub capsular zone with formation of new renal corpuscles . The collecting tubules extend from medulla toward the cortex forming medullary rays (Figure 9).

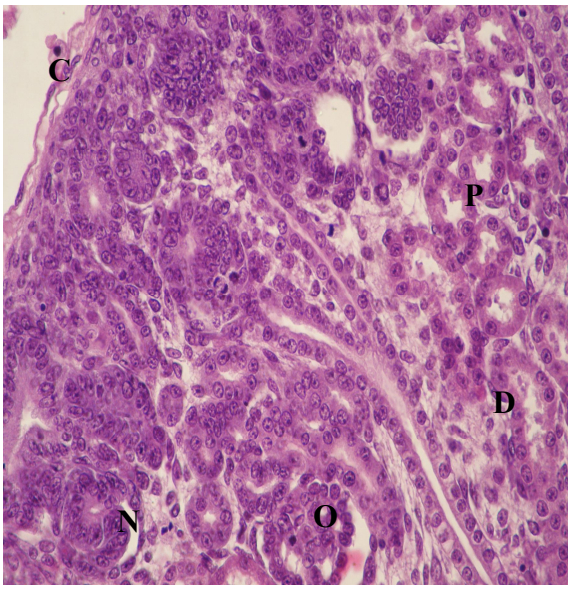
- Some renal corpuscles show signs of maturity in the inner zone of cortex where their parietal and visceral layers are clearly appear with characteristic differentiated squamous cells. Appearance of glomerular blood capillaries contain mature non-nucleated red cells .Some glomeruli present some nucleated red cells in. Macula densa begin to appear next to vascular pole in the part of distal convoluted tubules facing the renal glomerulus (Fig. 10). The capsular space is more pronounced and the cells of parietal layer of the corpuscular capsule at urinary pole of corpuscle are shifted gradually from squamous to cuboidal cells lining the beginning of the proximal convoluted tubules (Figure 11).

The thick descending and ascending segments begin to appear in medullary zone.The descending segment appear with narrow cavity lined by pyramidal cells with basophilic oval nuclei while ascending segments has wider cavity lined with pyramidal cells with large rounded nuclei, These structures are surrounded by fibroblasts and blood capillaries (Figure 12).

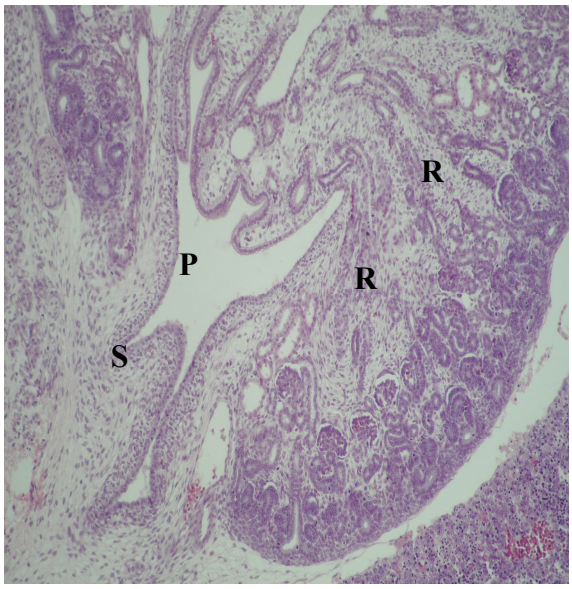
(Fig. 6) Section in rat embryo of 16 days age showing extension of ureteric bud (B) from primitive hilus (H) until the peripheral area H&E) (40X.



(Fig. 5) Section in rat embryo of 16 days age showing renal medulla contain collecting tubules (C) surrounded by *mesenchymal tissue with* fibroblast (Arrow) and blood capillary (B) 1000X (H&E).

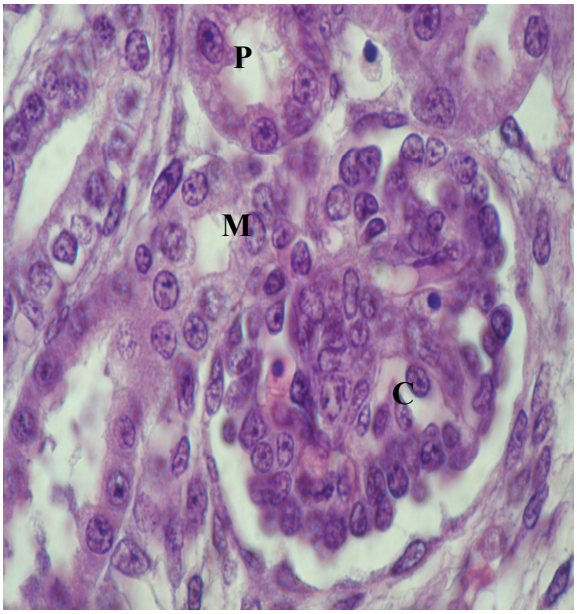


(Fig. 8) Section in rat embryo of 18 days age showing renal capsule (C) proximal tubules (P) distal tubules (d) Note branches of ureteric bud and newly formed renal corpuscles (N) and older corpuscles (o) 400X (H&E)

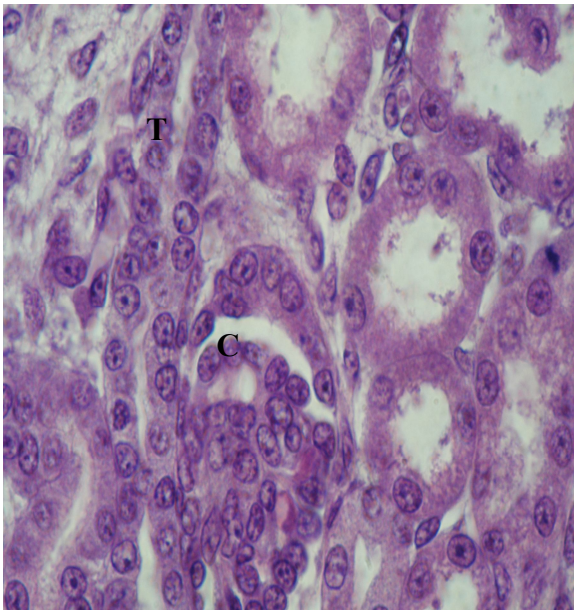


(Fig. 7) Section in rat embryo of 18 days showing dilatation of ureteric buds forming primordial renal pelvis(P) Note renal sinus (S) *collecting tubules,* extended from ureteric bud toward the renal cortex *forming the medullary ray*(R) 100X (H&E) .

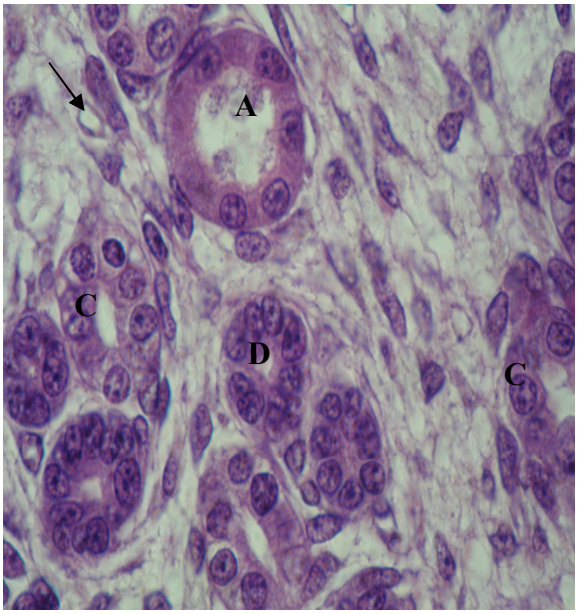
At 19 day of foetal life, the renal capsule appears to be covered by mesothelial cells with thin fibrous sub epithelial layer. The thickness of sub capsular basophilic zone is increased . The branching of the ureteric bud with formation of new tubules and corpuscles are continued. The tubules increased in number and size with continued differentiation of proximal and distal tubules (Figure 13).



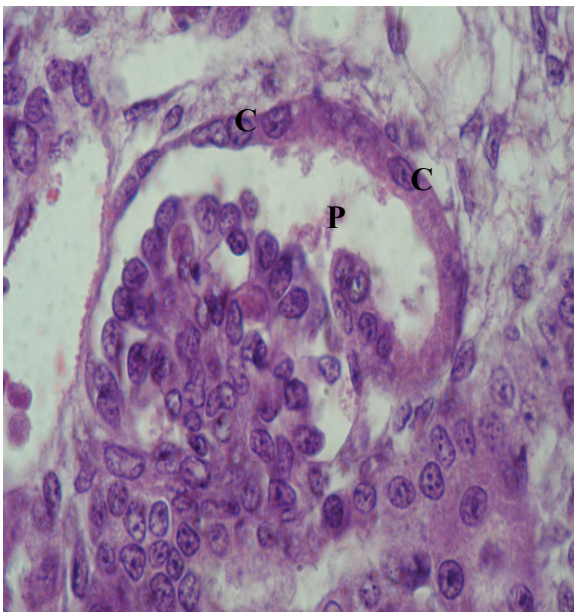
(Fig. 10) Section in rat embryo of 18 days age showing mature corpuscles (C) in inner zone of cortex. Note macula densa (M) in distal convoluted tubules facing glomerulus and proximal *tubules (P)* 1000X (H&E)



(Fig. 9) Section in rat embryo of 18 days age showing renal corpuscles (C) *collecting tubules (T)* which form *medullary ray*(R) 1000X (H&E)



(Fig. 12) Section in rat embryo of 18 days age showing thick descending (D) ascending segments (A) collecting tubules (C) and blood capillary(Arrow) 1000X (H&E)

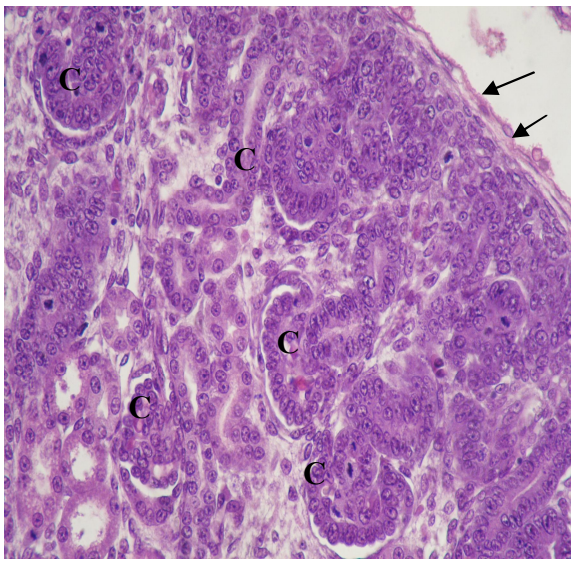


(Fig. 11) Section in rat embryo of 18 days age showing proximal convoluted tubules (P) at renal pole of corpuscle. Note shifting of lining epithelia of parietal layer of renal corpuscle from squamous to cuboidalcells (c) 1000X (H&E)

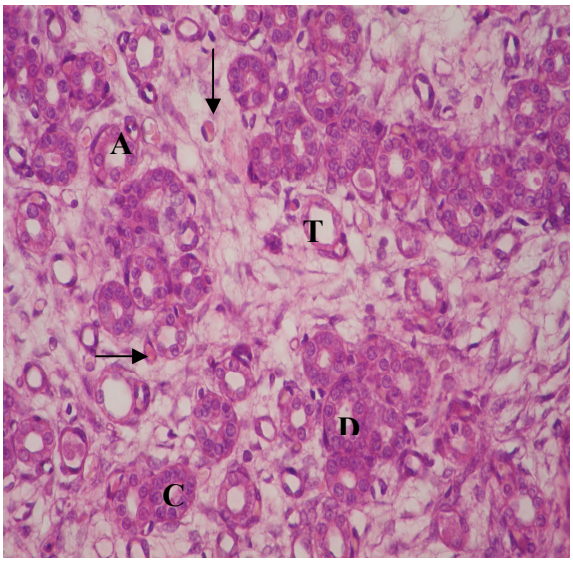
On the last day of fetal life, the renal pelvis appeared more extensive surrounded by renal sinus and blood vessels. The collecting tubules appeared straighter and extend to papillary ducts that open in the renal pelvis at the renal papilla. The medullary rays become more apparent and the cortex differentiated into outer sub capsular basophilic zone and inner acidophilic zone (Figure 14).

At the last day of foetal life the renal glomeruli and the parietal layer of renal corpuscle in addition to brush border of the epithelial lining of proximal tubules show positive PAS reaction (Figure 15).

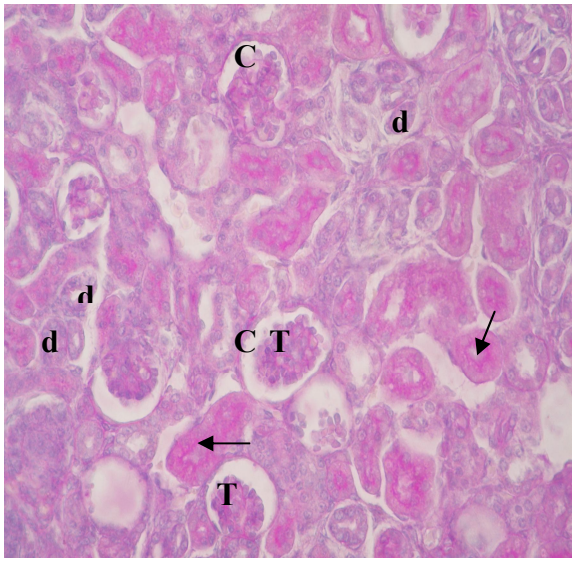
(Fig.14) Section in rat embryo of 21 days showing *collecting tubules* (C) *renal pelvis (p) renal papilla* (arrow) outer cortical basophilic zone (B) inner cortical acidophilic zone (A) 40X (H&E)



(Fig. 13) Section in rat embryo of 19 days showing mesothelium covering (Arrow) Note numerous large sized corpuscle (c) 400X (H&E)



(Fig. 16) Section in renal medulla of 21 day rat embryo showing thick descending segments (D) ascending segments (A) thin segments (T) collecting tubules(C) and blood capillary(Arrow) 400X (H&E)



(Fig.15) Section in rat embryo of 21 days showing *positive PAS reaction in brush border of proximal tubules (arrow) renal glomeruli (T) and parietal layer of renal corpuscle(C)* while distal convoluted tubules (d) show negative PAS reaction 400X (PAS)

The renal medulla appears more clearly filled with thick ascending and descending segments with collecting tubules and blood capillaries. The thin segment begins to appear (Figure 16).

DISCUSSION

The present studies revealed that, the metanephrogenic tissue appears as condensed mass of mesenchymal cells caudal to mesonephros during atrophy and decay of mesonephric tubules at 13 day foetal life. At day 14 foetal life, the ureteric bud appears as elongated tubular structure within metanephrogenic cell mass which showing great similarity with that mentioned by **AL-Awdan and Kandil (1979)** in rats and **EL-Gharbawy (2002)** in rabbit except that the first author mention onset of this tissue at 10 days fetal life and the latter said the onset of this tissue with ureteric bud at 15-day fetal life.

At 16 day fetal life, metanephrogenic tissue differentiate into metanephric tubules in various forms on periphery of kidney and S – shape tubules and blood capillaries appear which agree with that mentioned by **EL-Gharbawy (2002)** in rabbit at day 20 foetal life and **Emara (1989**) in camels at 45mm CVRL length.

In our study, the renal corpuscles appears at 15 day fetal life and differentiate into parietal and visceral layers at day 16 with clear appearance of their corpuscular space at day 18 of foetal life, however **AL-Awdan and Kandil (1979**) in the same animal asserted its appearance early at 10 day with complete maturation at 15 day fetal life. EL-**Gharbawy (2002)** in rabbit recorded onset of these corpuscles at 20 day fetal life with complete maturation at 32 day fetal life. **Azmi (1975)** in goat emphasized that these corpuscles appear at 28 day fetal life, while **Osathanondh and Potter (1963)** in human reported their first appearance at 40 day fetal life with complete maturation at 12 week fetal life.

Onset of characteristic features of proximal and distal convoluted tubules at 18 day fetal life .These features **appeared** at 25mm CVRL fetal length in rabbit **(El- Gharbawy 2002)** and at 5.5 cm CVRL fetal length in buffalo embryo **(Moustafa et.al., 1986).**

Macula densa appear next to vascular pole in part of distal convoluted tubules facing the renal glomerulus at 18 day fetal life which are similar to what was said by **Mrsevic et.al. (1978)** in rabbits at 21 day fetal life and **Soliman (1991)** in buffalo at 33cm CVRL fetal length.

The present study revealed that the thick segments could distinguish in medullary zone at 18 day fetal age, while thin segments appear at last day of fetal life which consistent with what was said by **EL-Gharbawy (2002)** in rabbit at 27 days fetal life and **Emara (1989)** in camel at 28cm CVRL fetal length.

Our study showed the onset of ureteric bud at 14 day fetal life as elongated tubular structure lined with single row of columnar to cuboidal cells Which converge with that

recorded in rats at 13 day fetal life **(AL-Awdan and Kandil, 1979)**, in rabbit at 15 day fetal life **(EL-Gharbawy, 2002)** , in pig at 7mm CVRL fetal length (**Haines and Mohiuddin, 1972**) , in buffalo at 1.2 cm CVRL fetal length **(Soliman, 1991)** and in human at 4-5 week fetal length **Carlison (1981**).

Current results showed branching of ureteric bud at 16 days fetal life which become more pronounced day 17 simulating that mentioned by **EL-Gharbawy (2002)** and **Moustafa and Enany (1985)** in rabbits and buffalo at 17 day fetal life and 4cm CVRL length respectively

In our study, the ureteric buds dilated forming primordia of renal pelvis at 18 day fetal life which occured in rabbits at 23 day fetal life **(EL-Gharbawy, 2002)** , Camel at 6cm CVRL fetal length (**Emara.1989)** , buffalo at 4cm CVRL fetal length (**Moustafa and Enany, 1985)** and in human at 1.5 cm CVRL fetal length **(Arey, 1974)**.

The correlation between branching of ureteric bud and division of cortical tissue has a great significant as it plays a major role in the evolution of the metanephros where the ureteric bud divided only after arriving to cortical tissue which is compatible with what was reported by **Moustafa and Enany (1985)** in Buffalo and **Canfield (1980)** in cows, **Emara (1989)** in camel and **Carlison (1981)** in human

The renal capsule at 18 day foetal life was appeared to be covered by mesothelial cells with thin fibrous sub epithelial layer which in agreement with that mentioned by **EL-Gharbawy (2002)** in rabbits at 25 day fetal life and **Moustafa and Enany (1985)** in Buffalo at 5.5cm CVRL fetal length.

The brush border of proximal tubules showed positive PAS reaction which consistent with that recorded by **Lesson and Baxter (1957)** and **EL-Gharbawy (2002)** in rabbit embryos, Davies **(1952)** in sheep embryo and **Ammar et. al. (1982)** in camel embryos.

Positive PAS reaction appeared in renal glomeruli and parietal layer of renal corpuscle which is compatible with that stated by **Moustafa and Enany (1985)** in buffalo. These substances represent a source of energy as mentioned by **Marinov and Lovell (1968)** in bovine embryos.

. The cells of the ureteric bud not show any reactions with PAS stain However **Canfield (1980)** in cattle embryos and **Emara (1989)** in camel embryos confirmed the presence of positive PAS reaction in the cells of this bud.

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الملخص العربي

دراسات نسيجية ونسيجية كيميائية على الكلية البعدية في أجنة الجرذان البيضاء

مصباح عبد الجواد * - سعد الغرباوي** - سامية إفكيرين ***

تنشأ الكلية البعدية من أصل مزدوج ؛ الأول هو النسيج المولد لنفرونات الكلية البعدية والذي ظهر خلف الكلية الوسطى في صورة كتلة خلوية مكونة من تجمع كثيف من الخلايا الميزودرمية عند العمر الجنيني ١٣ يوم. والثاني هو البرعم الحالبي الذي بدأ في الظهور في صورة تركيب أنبوبي متطاول عند العمر الجنيني ١٤ يوم وسط الكتلة الخلوية السابقة.

عند العمر الجنيني ١٦ يوم : يبدأ البرعم الحالبي في التفرع داخل النسيج المكون للكلية الدائمة لتصل تفرعاته أسفل الظهارة المغطية لسطح الكلية ، وبتقدم العمر الجنيني استمرت عملية تفرع البرعم الحالبي بصورة تكرارية مزدوجة وتتصل نهايات هذه التفرعات بالأنيبيبات المحيطة بها .

تبدأ الكتل الخلوية المحيطة لتفرعات البرعم الحالبي في التحول إلى أنيبيبات كلوية بدائية تأخذ أشكال مختلفة . تستطيل هذه الأنيبيبات وتلتوي على نفسها مكونة أنيبيبات على شكل حرف *S* ، يحدث انغماد داخلي بهذه الأنيبيبات ليدخله مجموعة من الخلايا الميزودرمية تتحول إلى شعيرات دموية بها كريات دموية حمراء مكونة بداية الكبيبة ، تتحول منطقة الإنغماد إلى محفظة مكونة من طبقتين ؛ طبقة حشوية ملاصقة للشعيرات الدموية وطبقة جدارية تنفصل عن الطبقة الحشوية بواسطة حيز محفظي وبذلك تكون الكبيبة والمحفظة المحيطة بها بداية الكريه الكلوية . يبدأ النخاع الكلوي في الظهور حيث ظهرت الأنيبيبات المجمعة محاطة بنسيج ميزودرمي تمايز معظمه إلى أرومات ليفية وشعيرات دموية .

عند العمر الجنيني ١٨ يوم وحتى نهاية الحياة الجنينية (٢١ يوم) : يظهر بداءه الحوض الكلوي كاتساع في البرعم الحالبي، وظهر الجيب الكلوي الأولي مليئا بالأرومات الليفية ومحتويا على العديد من الأوعية الدموية . يستمر ظهور كريات حديثة التكوين وصغيرة الحجم تتركز في الجزء الخارجي للقشرة تحت المحفظة وتتميز باصطباغ قاعدي . بينما تظهر الكريات السابقة التكوين كبيرة بالجزء الداخلي للقشرةاتجاه النخاع والتي تصبح حامضية الاصطباغ.

كما ظهرت الصفات المميزة لكل من الأنيبيب الداني والقاصي حيث ظهر القطب البولي للكرية الكلوية مقترنا ببداية الأنيبيب الداني الملفوف ؛ وظهرت الحافة الفرشاتية على الخلايا المبطنة لهذه الأنيبيبات ، كما بدأت البقعة الكثيفة في الظهور من خلايا الأنيبيب القاصي المواجه للكبيبة الكلوية بجوار قطبها الوعائي.

ظهرت الأنيبيبات المجمعة أكثر استقامة ، ويمتد بعضها باتجاه القشرة الكلوية بين الكريات والأنيبيبات الكلوية المتنامية لتكون الأشعة النخاعية . وتظهر القطع السميكة الصاعدة والهابطة .

عند العمر الجنيني ١٩ يوم : تظهر المحفظة مكونة من ظهارة مصلية تتكون من خلايا حرشفية بسيطة ذات أنويه مسطحة ويظهر تحت الظهارة طبقة ليفية رقيقة .

في اليوم الأخير من الحياة الجنينية تظهر القطع الرقيقة لعروة النفرون إضافة إلى القنوات الحليمية والحليمة البولية وكذلك تظهر الكبيبات الكلوية والطبقة الجدارية لمحفظة الكبيبة إضافة إلى الحافة الفرشاتية المبطنة لخلايا الأنيبيبات الدانية تفاعلا موجبا مع صبغة حمض شيف البير أيودي*PAS*