WILM'S TUMOUR
(NEPHRO BLASTOMA)
NEW TRENDS IN DIAGNOSIS AND MANAGEMENT OF WILM'S TUMOUR

ESSAY

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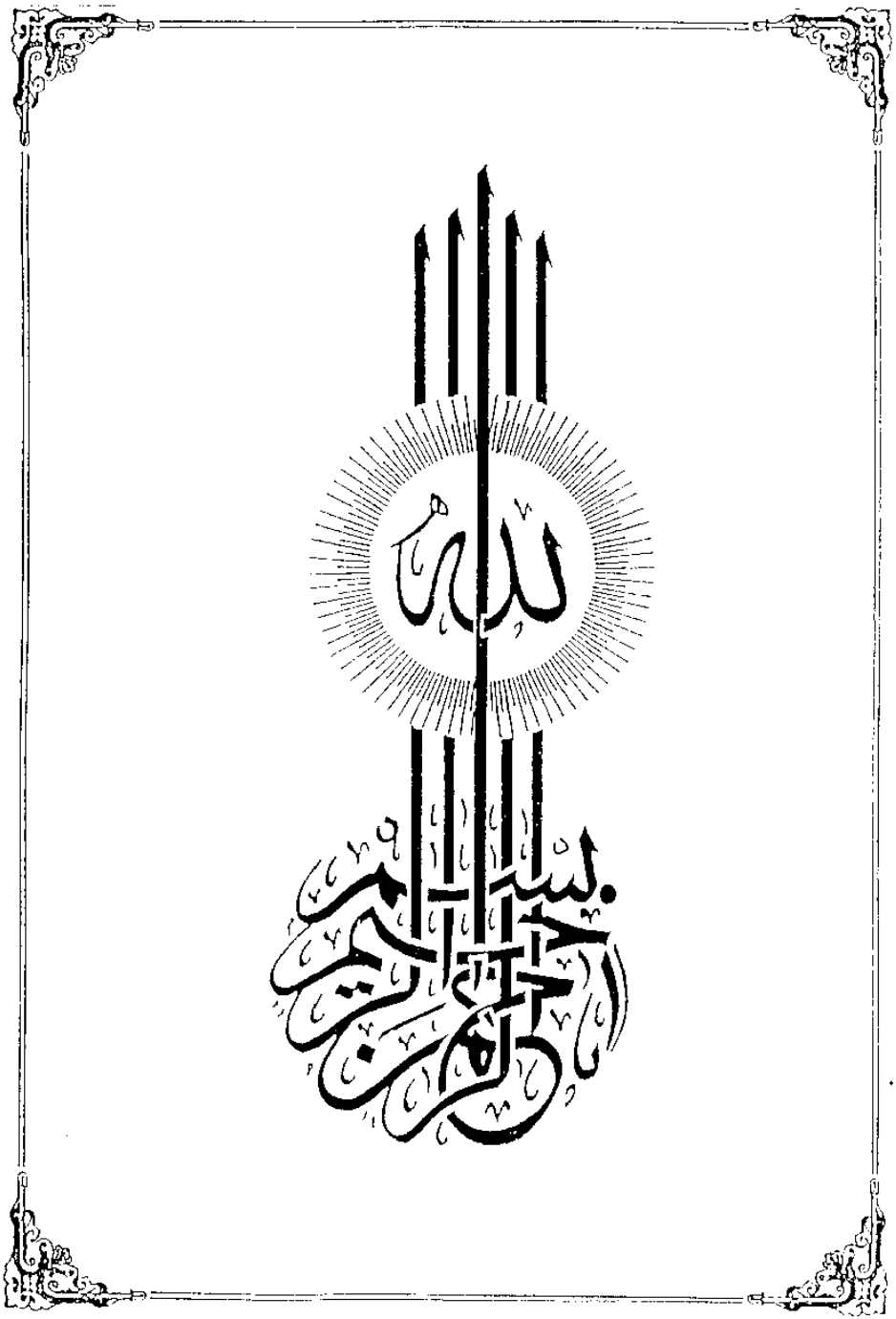

CONTENTS

EMBRYOLOGY

EMBRYOLOGY OF THE KIDNEY

The development of the urinary system appears to repeat the phases of development of lower vertebrate [Felix, 1912].

The pronephros is the first urinary tissue to appear, next the mesonephros and finally the metanephros. [Gruenwald, 1943].

Pronephros:

During the 4^{th} week of development condensed mesoderm adjacent to the midline divides into block like units called somites. The pronephros appears in the cervical region of the 10-somite embryo between the 2^{nd} to 6^{th} somites [Gruenwald, 1943]. Cells derived from the intermediate mesoderm, cluster and differantiate into pronephric tubules which are non functioning. It is believed that the duct of the pronephric tubules continues caudally as the mesonephric duct. The pronephros is not apparant by 30 days [Potter, 1972].

Mesonephros:

The mesonephric duct descends from the cervical somites to the caudal region of the embryo mediated by caudal growth of the terminus of the duct. The duct is adjacent to mesoderm intermediate between somites and the caelom. After

the duct and mesoderm appose, mesonephric tubules appear. The nephrons of the mesonephros are induced by the advancing ampulla of the mesonephric duct. During its descent, the mesonephric duct induces about forty pairs of tubules [Potter, 1972].

By 28 days the mesonephric duct has descended to contact the urogenital sinus and it later drain into the sinus. By 37 days the mesonephros are fully developed. As the mesonephros of several mammals can excrete marker dyes as phenol red [Hamilton and Mossman 1976_b] it is belived that human mesonephros can clear the plasma of unwanted metabolites. After 10 weeks of development, many mesonephric nephrons degenerates [Stephens , 1983] but some tabules become [incorporated] into the genital duct system.

Metanephros:

After the mesonephric duct reaches and drains into the urogenital sinus, the ureteral bud appears as a diverticulum from the postromedial aspect of the mesonephric duct at the point where the terminus of the duct bends to enter to cloaca.

According to Pottre [1972] the ureteric bud is veiwed to develop further in four periods:

Period one: (5th - 14th week):

The ureteric bud divide dichotomusly and the initial four to six branches contribute to the renal pelvis and the metanephrogenic blastema proliferates to remain appose to all the new ampullae of the new ureteral bud branches. The initial branch establishes the superior and inferior poles of the kidney. By seven week there are six generations of ampullae at the poles and only four generations at the midsection of the kidney and this helps to maintain the reniform shape of the kidney [Hamilton and Mossman, 1976].

After 7 weeks other three to five generations appears and contribute to the calyces, many branches appear to arise from common stem and the set resembles tubules chamber. With later growth the renal parenchyma project into this chamber as a conical papilla. The next five to seven generations create the collecting tubules. During this interval the bud branches progressively more slowly [Potter, 1972].

Period Two (15th - 22nd week):

During this period the collecting tubules at the corticomedullary junction begins centrifugal growth and lay down a family of nephrons about 4 [range from 2-8].

Period three [22nd - 36th week]:

This period forms the nephrons whose glomeruli lie in the outer half of the cortex. It induces four to six nephrons in series. About 75% of the complement of glomeruli are induced during periods two and three.

Period four [32nd - 36th week to adulthood]:

The ureteral bud ampullae caese to induce new nephrons and the collecting duct elongates, proximal tubules convolute and the loops of Henle penetrate deeper into the medulla and typical collecting duct drains nine to eleven nephrons and surface of the kidney is lobular at birth.

Morphogenesis of the nephron : The nephron develop in phases:

a) Mesenchyme is determind to become the metanephrogenic blastema. The factors responsible for this determination are unknown.

b) Metanephrogenic mesenchyme is induced by close contact with the ampulla of the ureteric bud [Lehtonen et al., 1975] and is associated with loss of components of the extra cellular matrix [collagen from the ampullae and fibronectin from the mesenchyme] the condensed cells of the metaneophrogenic blastema, first

laminate into a comma-shaped double- layered structure then swell as a vesicle.

c) The nephric vesicle segregates into the glomerulus, where the cells forming viscral layer of Bowman's capsules becomes flattened and angiogenic cells proliferate to form vascular tufts, proximal and distal tubule and loop of Henle. The factors leading to this further differentiation are also unknown. However inhibitors of DNA, RNA or protein synthesis impair the morphogenesis of tubules when applied to metanephrogenic blastema during induction but not later [Ekblam, 1981].

Ascent of the Kidney:

The renal blastema ascends from the level of upper sacral segments to upper lumbar vertebrae in the following mannar:

1. Thirty days: caudal growth of the spine causes ureteral bud to appear to ascend the pelvis from the level of the coloaca [Gruen-Wald, 1943, Friedland and DeVaries, 1975].

2. Thirty two days: the ureteric bud activly elongates cranially and dorsally to reach the umbilical artery [Friedland and DeVaries, 1975].

3. Thirty eight days: when the kidney reaches the umbilical artery, intrinsic growth and moulding of the

renal parenchyma hurdles the kidney over the umbilical arteries: First, the umbilical artery tilts the upper pole ventrally and lower pole dorsally, next, the kidney elongates and causes further cranial ascent and finally the kidney increase in its transverse diameter and rounds itself to elevate the lower pole above the umbilical artery [Boyden , 1932, Gruenwald, 1943].

4. Fifty-six days: The kidney fixes to the tissues of the peritoneum which permits axial growth of the spine to elevate the kidney to its final position [Gruenwald, 1943].

During ascent the kidney rolates 90 degrees ventromedially and it is postulates by Felix [1912] and accepted by Weyrauch [1939] to be due to excessive ventral versus dorsal branching of ureteral tree as during each generation of division two branches extend ventrally and one dorsally.

Development of renal vessels:

The renal arterial tree is derived from three groups of vascular channels that coalesce to form the imature vascular pattern for all retroperitoneal structures. The cranial group consists of two pairs which shift dorsally to form the phrenic artery. The middle group is made up of three pairs that pass laterally through the suprarenal area and becomes

adrenal artery. Finally the caudal group has four pairs that pass ventral to the renal area and becomes the main renal artery, sometimes joined by the most inferior pair of the middle group [Guggemas, 1962]. Durging migration of the Kidney and by a process of elemenation, one primitive renal arterial pair eventually becomes the dominant vessel and the completed process is dependent on final position of the Kidney [Graves, 1956].

AETIOLOGY

AETIOLOGY OF WILMS' TUMOUR

Wilms' tumour is the most common malignant neoplasm of the urinary tract in children and represent 8% of all childhood solid tumours and makes up more than 80% of genitourinary cancer below fifteen years [Young et al., 1978].

The incidence has remained relatively constant at 7.8/million children per year in U.S.A. In about 75% of cases diagnosis is made between 1-5 years of age with peak incidence between 3-4 years of age. Occasionally it occurs in adults [Orlen and Bischaff, 1970]. Familial cases are rare [1%] the male and female ratio is 0.97 to 1.0.

Bilateral involvement occurs in approximately 5% of cases and is usually present at initial diagnosis [Lampkin et al., 1985].

Wilms' tumour is believed to be the result of abnormal proliferation of metanephric blastema without normal differentiation into tubules and glomeruli and this view is supperted by :

- This was confirmed by electron-microscopy.
- Small nodules of metanephric tissue deteched from the kidney without uretral connection called beinieren, are

occasionally found at autopsy of patients suffering from this tumours [McCauley et al., 1979].

- an itravenous pyelogram of a case showed bilateral mesonephric ducts, providing evidence ofthe persistance of tissue precursors of the kidney.
- Histological evidence of the persistance of pro-meso- and metanephric elements as well as mullerian ducts were shown in 23 years old man [Tannir, 1982].

In order to explain the presence of muscles and cartilage in some cases, Wilms' and conheim postulated that wilms' tumour had to originate from the region of the middle plate or nephrotome at the time when portions of nearby myotome and sclerotome could be included [McCauley et al., 1979]. Since then it has beeen recognized that metaplasia of less primitive mesenchymal cells can occur [McCauley et al., 1979].

For extra renal Wilms' tumour:

1. The development of tumours in utero, while metanephric blastema is still present [Ledlie et al., 1970].
2. The tumour originates from differentiated cells that, under certain circumstances regain embryonic potentialities [Cell rest theory of Conheim] [McCauley et al., 1979].