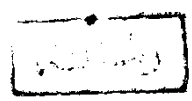
RENAL FUNCTION IN THE FIRST MONTH OF LIFE



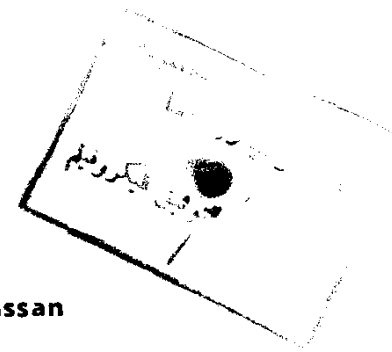
Thesis

SUBMITTED FOR PARTIAL FULFILMENT

OF THE DEGREE OF

Doctor of medicine

(PEDIATRICS)



By

Hassan Ahmed Mohamed Hassan

M.B., B.Ch., M.Sc,

AIN SHAMS UNIVERSITY

SUPERVISED BY :

Prof. Dr. Mahmoud Essawy

Prof. of Pediatrics

AIN SHAMS UNIVERSITY

Prof. Dr. Ali Khalifa Ali

Prof. of Biochemistry

From Biochemistry Department

AIN SHAMS UNIVERSITY

Dr. Farida Ahmed Farid

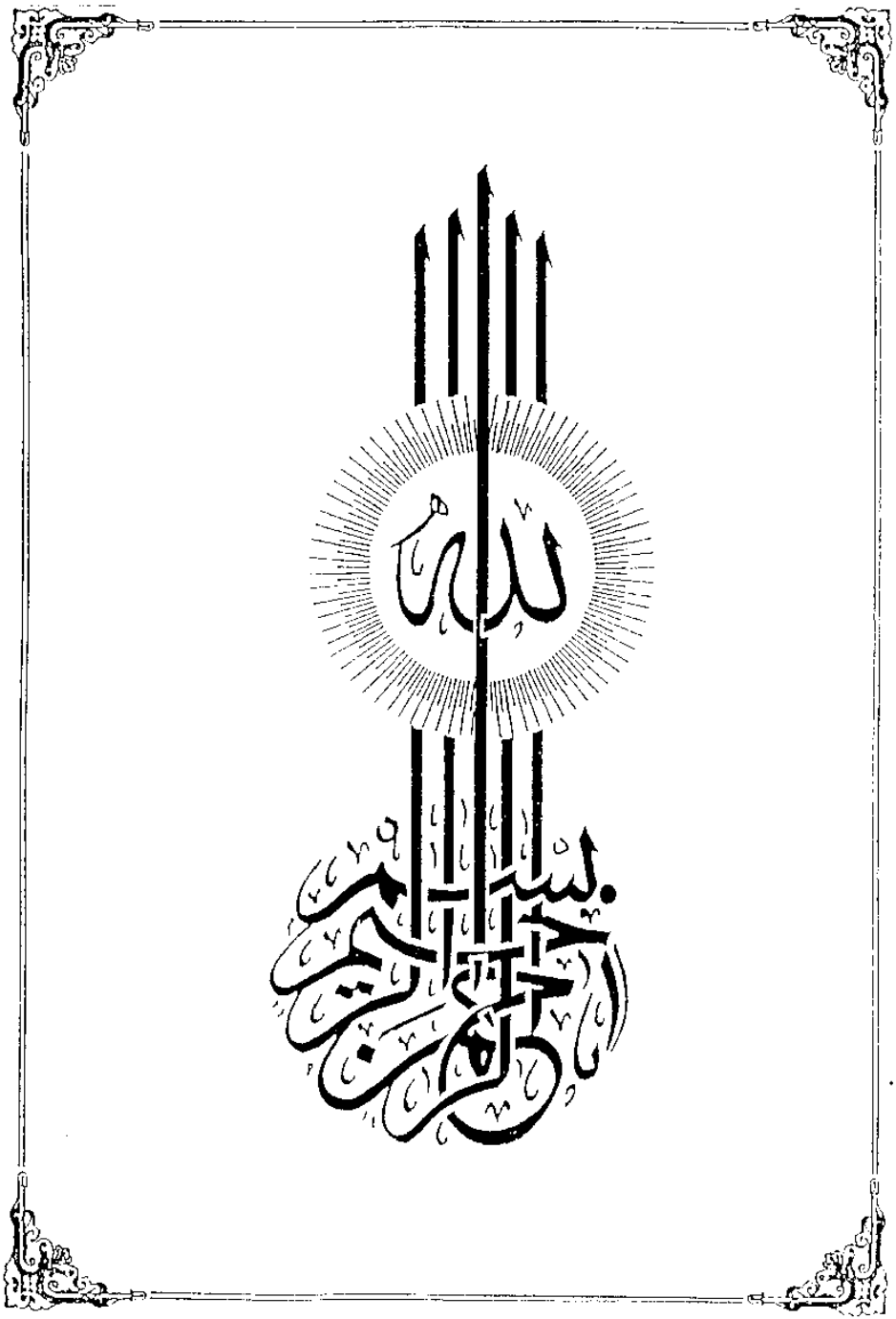
Ass. Prof of Pediatrics

AIN SHAMS UNIVERSITY

1985

C O N T E N T S

****



ACKNOWLEDGMENT

I would like to express my deep thanks and gratitude to my professor **Dr. Mahmoud Essawy,** Professor of Pediatrics, for giving me the privilage of working under his supervision, for his encouragement, his patience and fruitful guidance throughout the whole work.

I am sincerely indebted to **Dr. Farida Ahmed Farid,** Assistant professor of Pediatrics, who suggested the point of the study and gave me her great support and help, for her illuminating advice, encouragement and support throughout this work, she had revised this work and suggested many valuable remarks.

I would like to express my deep thanks and gratitude to **Dr. Ali Khalifa Ali,** Professor of Biochemistry, who had kindly helped me during the practical work, I am grateful to him for his efforts and co-operation, I am sincerely indebeted to him for his indespensible guidance and valuable suggestion.

I would like to express my thanks and gratitude to all my colleagues, the residents of pediatric department at Ahmed Maher teaching hospital who participated in some way or the other to let this work come to such a final picture.

INTRODUCTION

AND

AIM OF WORK

INTRODUCTION AND AIM OF THE WORK

Adaptation to extrauterine life is a challenge to the kidney of the newborn infants, which must respond to rapidly growing functional requirements and may have to respond to various endogenous and exogenous stresses. A normally developed kidney in a full term neonate can usually cope with most of the demands. But the external conditions may be severe enough to overcome its adaptive capacities. In the prematurely born neonate, the kidney may also have to work long before its complete maturation and adaptation will be more difficult then. The concentration of creatinine is one of the most simple and most commonly used indices of glomerular filtration rate in children and adults. It has been reported to be appreciably raised and variable during the first month of life **Stonestreet and Oh, 1978.** A laboratory test that identifies early reductions in glomerular filtration rate in the neonatal period would lead to earlier and more efficacious treatment of acute renal failure, a condition which is significantly increased in neonatal intensive care **Norman and Asadi, 1979.** In a search for such a test plasma creatinine levels were measured by a reaction kinetic principle (creatinine-kinetics) a technique which seems to minimize the interference of noncreatinine chromogens **Bartels et al., 1972.**

The estimation of glomerular filtration rate is of great importance in assessment of renal function. However the most precise methods are difficult for routine clinical use and in practice a compromise between accuracy and simplicity has to be thought. The 24-hour creatinine clearance is widely used to estimate glomerular filtration rate, but difficulties in the accurate collection of timed urine samples, particularly from neonates limits its value and even under research conditions its reproducibility is poor **Chuntler and Barratt, 1972.**

Counahan et al., 1976 reported that an accurate estimate of glomerular filtration rate could be obtained from the simple determinations of true serum creatinine and body length. So renal function can be easily followed using Counahan's formula especially in neonatal period where the occurance of renal failure will be a great problem. Therefore true serum creatinine and body length permit a rapid, simple, accurate and as precise as measuring the 24-hour creatinine clearance in preterm and term newborn infants, thus obviating the necessity for urine collection.

Our aim was to know the kidney functions through serum creatinine and creatinine clearance in full term and preterm infants during the first month of life, and to know the effect of respiratory distress and high risk pregnancy on renal functions.

REVIEW OF LITERATURE

NORMAL DEVELOPMENT OF THE KIDNEY

Defects of renal development constitute about 10 percent of all live born infants **(Kissane, 1966).**

These defects which are compatible with survival are frequently not recognized until secondary symptoms appear such as growth failure, anemia, uremia, rickets, pyelonephritis or abdominal masses. It is clear that congenital abnormalities of the urinary tract must be recognized early for optimal management and correction. These necissitate understanding of the normal development of the urinary tract. A disturbance or failure in the normal embryologic development of the kidneys may play an important role in causing delay or absence of spontaneous voiding in the immediate newborn period. In vertebrates there are three successive overlapping embryologic stages in development of the kidney: these are the pronephros, mesonephros and metanephros **(Williams, 1968).**

The two primitive kidneys, the pronephros and mesonephros, become vestigial in the human being but act as inducers of the definitive metanephric kidney. Thus, faulty development of either of the primitive kidneys may result in agenesis of the metanephros. The pronephros forms from a solid mass of cells (nephrogenic cord) on the ventrolateral border of the somites at the cervical level and causes a slight elevation

on the exterior surface of each side of the embryo at about 3 weeks of embryonic life (1.7mm stage or 8 to 9 semites). Fig. A.

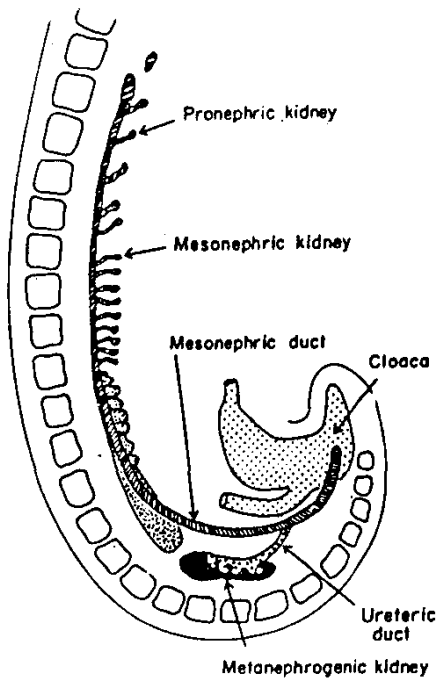


Figure A. Schematic representation of the relationships of the three embryonic kidneys in the human fetus. Note the continuity of the duct system and the interdependence of the various excretory organs (see text).

Thus, infection of the embryo or other insults at this very early period of gestation and organogenesis may be reflected in abnormal development of the definitive kidneys. Degeneration of the pronephros begins soon after formation, and no excretory function occurs.

The ureter of the pronephros forms the wolffian or mesonephric duct which induces the formation of the second kidney,

the mesonephros. It has been speculated that retention of abnormal pronephric tissue may be one cause of mediastinal cysts. **(John et al., 1971).**

The mesonephros arises more caudally than the pronephros (thirteenth to fifteenth semites, i.e first to third thoracic segments) in 23 somite embryo (4mm embryo of 31 days gestation).

This kidney also develops from the nephrogenic cord as a swelling along the posterior coelomic wall and eventually forms about 40 pairs of thin-walled tubules and glomeruli (7 to 15 pairs being functional at any one time). In man the mesonephros is functional until about the end of the fourth month, and then degenerates as the metanephric kidney begins to function. Portions of the vestigial mesonephric duct system are retained in male as the following functional tissues: ducts of the epididymis, ducts deferns, and the ejaculatory duct.

Complete degeneration of the mesonephros occurs in the female except for a branch from the mesonephric (wolffian) duct which in both sexes induces the third and definitive kidney, the metanephros.

An interesting consequence of defective mesonephric development has been described in males with mucoviscidosis (cystic fibrosis). Recognizing that males with this syndrome had azoospermia **(Denning et al., 1968).**

About the thirty-first to thirty-fourth days (4 to 5 mm stage) a branch, the ureteric bud grows from the postero-medial wall of the wollfian (mesonephric) duct near its junction with the cloaca.

The tip of the hollow bud migrates to the posterolateral wall of the embryo and the most caudal portion of the nephrogenic cord at the level of the first and second sacral segments. As maturation of the kidney proceeds, the tip migrates to its final lumbar position and rotates medially on its longitudinal axis. The cephalic migration of the kidney is probably due in part to the straightening of the fetus from its extremely curled position as an embryo. The rotation of the kidney moves the ureter from an anterior location on the surface of the kidney to the normal medial position. Abnormalities of both migration (e.g. pelvic kidney) and rotation (e.g laterally placed ureter)are among defects that may be found in man.

The ureteric bud grows into the nephrogenic cord (metanephric blastema) and branches dichotemously (the tip or ampulla divides into two portions) repeateadly. The stimulus for branching is contact with the nephrogenic cells. The initial branches form the pelvis, the third to fifth generations of branches form the major calyces, single branching between the third and sixth generations forms the minor calyces, and the seventh to eleventh generations of branches form the papillary

ducts. The development of this complex collecting system has been beatifully described and illustrated by the classic reports of Osathanondh and Potter, 1963). **Fig.B.**

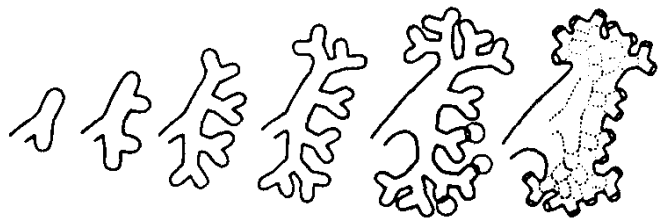


Figure B. Diagram of the development of the pelvis, calyces, and collecting system of the metanephric kidney as by a series of dichotomous branchings of the ureteral bud. (*From* Osathanondh, V., and Potter, E. L.: Arch. Pathol., 76:271-302, 1963. Reproduced with permission.)

Continued branching of the ureteric bud as it advances through the metanephric tissue is associated with nephron induction and involves 20 to 38 additional generations of branches. Some of the early nephrons induced in the medulla and the corticomedullary junctions degenerate, and it is not unusual to find "hyalinized" nephrons in the kidney of otherwise normal human embryos and newborn infants. Growth and branching of the ureteric bud, and thus nephron induction ceases in the human at 32 to 35 weeks of gestation (above 2500 gm) **Mc Crory, 1972.**

Cells of the metanephric blastema clump around the dilated tip of the ureteric bud as it advances. **Fig.C.**

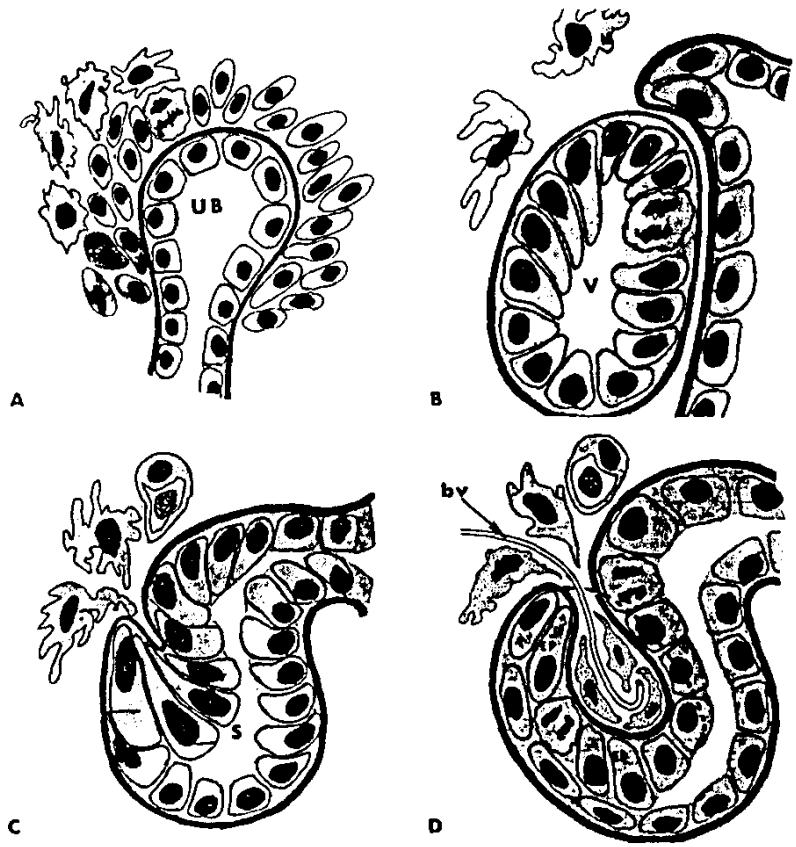


Figure C. Schematic representation of the formation of nephrons (see Fig. 4). *A*. Cells of the metanephric blastema cluster around the ureteral bud (*UB*). *B*. The cells form a hollow vesicle (*V*). *C*. The hollow vesicle elongates and indents to form an S-shaped structure. *D*. Penetration of a cleft in the S-shaped structure by a vessel (*bv*) and primitive mesenchyme, the anlage of the definitive glomerulus. (*Modified from* Jokelaenin, P.: Acta Anat., 52(Suppl 47), 1963, by permission.)

These cells form a spherical mass, which becomes a hollow vesicle, elongates to form an ovoid tube, and then twists into an S-shaped tube. The cortical (outer) end of the S-shaped structure connects with the tip of the ureteric bud, which becomes the collecting duct. The lower (toward medulla) portion of the S-shaped body ultimately forms Bowman's capsule around the glomerulus. The portion of the S attached to the ureteric bud rapidly increases in length, extends toward the

medulla, develops the typical convolutions of the distal tubule, and thins out to form Henle's loop. This stage of tubular development requires 4 to 5 weeks after formation of the nephrogenic vesicle. Subsequently, tubular development progresses to the formation of the proximal convoluted tubule through further growth and specialization of the proximal cells of the originally S-shaped tube.

Increase in length of the tubule continues to occur into young adult life, and it is primarily the increase in tubular mass which accounts for the progressive increase in kidney size and weight until about the age of 18 years. **(Fetterman et al., 1965).**

The filtering apparatus of the glomerulus is the glomerular basement membrane. The glomerular epithelial cells are primarily responsible for the formation and turnover of the basement membrane but there is some evidence that endothelial cells may also play a part. **(Striker and Smuckler, 1970).**