Prenatal causes of kidney disease

Essay

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Abstract

Patients with nephrectomy for bilateral disease, more extensive loss of renal mass (bilateral tumors), unilateral nephrectomy at a younger age, and unilateral renal agenesis show a surprisingly high incidence of glomerular sclerosis, proteinuria, hypertension, and renal insufficiency.

Key word:

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Patients with nephrectomy for bilateral disease, more extensive loss of renal mass (bilateral tumors), unilateral nephrectomy at a younger age, and unilateral renal agenesis show a surprisingly high incidence of glomerular sclerosis, proteinuria, hypertension, and renal insufficiency.

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11β-HSD-2	:	Type 2 isoform of 11-β Hydroxysteroid Dehydrogenase.
ACE	:	Angiotensin – Converting Enzyme
AT	:	Angiotensin
BSCI	:	Bumetanide N2-K-2CL Cotransports
CAKUT	:	Congenital Anomalities of the Kidney and Urinary Tract
CKD	:	Chron Kidney Disease
C-Ret	:	Retinoic acid Receptor
CYS-C	:	Cystine C
E	:	Embryonic day
ENOS	:	Endothelial Nitric Oxide Synthetase
GDNF	:	Glial cell line-Derived Neurotrophic Factor
GFR	:	Glomerular Filtration Rate
GFR α1	:	Glial Cell line-derived neutrophic Factor family receptor α1
GH	:	Growth Hormone
GLUT	:	Glucose Transporter
HPA	:	Hypothalamic Pituitary Adrenal
HTN	:	Hypertension
IGF	:	Insulin – like Growth Factor
IUGR	:	Intra Uterine Growth Restriction
LBW	:	Low Birth Weight
MAPK	:	Mitogen-Activated Protein kinase.
MET	:	Mesenchymal-to-Epithelial Transition
MM	:	Metanephrogenic Mesenchyme
MODY	:	Maturity Onset Diabetes of the Young
ND	:	Nephric Duct
NO	:	Nitric Oxide
NR	:	Nutrient Restriction

NSAIDs	:	Non Steroidal Anti Inflammatory Drugs
PG	:	Prostaglandin
RAS	:	Renin – Angiotensin System
RN	:	Reflux Nephropathy
ROS	:	Reactive Oxygen Species
SGA	:	Small for Gestational Age
TSC	:	Thiazide Sensitive – Na-K-2CL Contransport
UB	:	Ureteric Bud
UPJO	:	Uretero Pelvic Junction Obstruction
URA	:	Unilateral Renal Agenesis
VUR	:	Vesico-Ureteric Reflux

Introduction

Acute and chronic kidney disease is a leading cause of morbidity and mortality worldwide with overall mortality rates between 50 and 80%. **(Chhabra and Brayman, 2009)**

Chronic kidney disease is increasing all over the world and the major two causes are diabetes and hypertension. **(Wani *et al.*; 2004)**

It has recently been increasingly recognized that disturbed intrauterine development may impact on renal and cardiovascular risk in adult life, e.g. albuminuria and chronic kidney disease. **(Koleganova *et al.*; 2009)**

Nutritional and other environmental cues during development can permanently alter the structure, homeostatic systems, and functions of the body. This phenomenon has been referred to as 'programming'. **(Barker *et al.*; 2006)**

Fetal programming is gaining momentum as a highly documented phenomenon which links poor early growth to adult disease. **(Fernandez-Twinn and Ozanne, 2006)**

This developmental programming determines the set points of physiological and metabolic responses in adult life. **(Lau and Rogers, 2004)**

It is suggested that the fetus makes physiological adaptations in response to changes in its environment to prepare itself for postnatal life. These changes may include epigenetic modification of gene expression. **(De Boo and Harding, 2006)**

The root causes of programming link closely with maternal condition during pregnancy, and therefore the fetal environment. Suboptimal fetal environments due to poor or inadequate nutrition, infection, anemia, hypertension, inflammation, gestational diabetes or hypoxia in the mother expose the fetus to hormonal, growth factor, cytokine or adipokine cues. **(Fernandez-Twinn and Ozanne, 2006)**

Nephrogenesis per se is affected by changes in maternal nutrition and health. Additionally, renal functional changes in later life may be influenced by changes in renal tubular transporters noted early when maternal nutrition is compromised. **(Ingelfinger, 2004)**

It has been demonstrated that intrauterine growth retardation, defined as birth weight below the 10th percentile, gives rise to a reduction in nephron number. Oligonephropathy has been suggested to increase the risk for systemic and glomerular hypertension in adult life as well as enhance risk for expression of renal disease after exposure to potentially injurious renal stimuli. **(Wani *et al.*; 2004)**

Restriction of food or protein during specific windows of pregnancy leads to hypertension in adult offspring. Depending on the degree of maternal restriction, nephron number and renal function in the offspring may be reduced, and proteinuria and histological signs of renal disease are present. All of these abnormalities appear to worsen with age. **(Woods, 2007)**

Studies have shown that the risk of hypertension in adulthood can be affected by the in utero environment. It is established that hypertension is linked to compromised kidney function and that factors affecting organogenesis can increase the risk of later disease. **(Brennan *et al.*; 2006)**

Type 2 diabetes, which has dramatically increased during the last decade normally results from a combination of pancreatic beta cell dysfunction and insulin resistance. One of the most recent risk factors identified for type 2 diabetes is a sub-optimal fetal and neonatal environment. **(Reusens *et al.*; 2007)**

Aim of the Essay;

Discussion of Prenatal causes of kidney disease

Chapter I

Kidney Development

Development of the human fetal kidney runs through a series of continual and mutually dependent changes during which the kidney obtains its morphological and functional maturity. **(Vlajković *et al.*; 2006)**

Three different renal organs are formed during fetal life, the pronephros, mesonephros and metanephros. **(Aperia *et al.*; 1992)**

The first two degrade, but the latter becomes the permanent kidney . Through various complex and partly understood interactions between metanephros and the ureteric bud , nephrons start to form from day 30 of gestation in humans. **(Nigam *et al.*; 1996)**

The development of the metanephric kidney begins when the nephric duct (ND) gives rise to ureteric bud (UB) on embryonic (E) day E10.5 in mice and E28 in humans (Fig. 1). The initial events controlling UB induction are regulated by numerous transcription factors and signaling molecules that are expressed in a specific spatial and temporal patterns. **(Costantini, 2006)**

Signals from the mesenchyme induce the UB to originate from the ND, invade the mesenchyme and then branch repeatedly by a process called branching morphogenesis (Fig. 2). Initial generations of UB branches will be remodeled into the ureter and collecting system. Subsequent generations of UB branches will differentiate into collecting ducts. **(Yosypiv, 2008)**

Collecting ducts will subsequently undergo patterning to contribute importantly to the renal papilla and medulla. Each UB tip is capable of inducing the adjacent metanephrogenic mesenchyme (MM) to undergo mesenchymal-to-epithelial transition (MET) and form nephrons (from the glomerulus to the distal tubule). **(Ekblom, 1989)**

Therefore, UB branching morphogenesis is critical in determining total nephron number , proper kidney size and structure. **(Yosypiv, 2008)**

UB branching morphogenesis proceeds in concentric layers, such that newly forming nephrons are located in the outer layer, with the more mature nephron units occupying successively deeper layers. Fortunately, when growth rate is impaired during this fixed developmental window, the fetal kidney forms-not incomplete nephrons-but fewer layers of normal nephrons. **(Bagby, 2009)**