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A Short Historic View of Nephrology upto the 20th Century

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Abstract

It is easy for a non-nephrologist to become lost in the complexities of renal physiology, diagnosis, and treatment —i.e., to miss the forest for the trees. It is not unusual for one to "fall" into the loop of Henle (discovered by the 19th century German anatomist, Friedrich Gustav Jakob Henle [1809-1885] and not return after being weighed down by a seemingly skimble-scamble litany of renal sagacities. Thus, one can ask: "what is the role ("the forest") of the primary care clinician in the diagnosis and management of pediatric renal disorders ("the trees")?" What is the forest and what are the trees in this perspective? Certainly, seeking to stay current on basic principles of pediatric nephrology is important such as fluid and electrolyte physiology and management of pediatric dehydration. In this short review we summarize some of the pioneer work done in nephrology up till the 20th century.

Introduction

The study of life began with the emergence of Homo sapiens over 100,000 years ago [1]. Prior to the development of writing by the Sumerians in 3200 BCE that emerged from earlier Neolithic proto-writing, we can only guess at what ancient humans thought of the twin bean shaped organs we now call kidneys (Middle English: kednei; Scottish: nere, near; ancient Greek: nephrós) found in vertebrates. They were first discovered in animals and used as food for esurient humans; eventually cannibalistic ancient human carnivores found that human kidneys were a satisfying source of nutrition and various mystical myths arose about the pathetic fallacy power of these structures to empower, enhance, and elongate life. Rudimentary knowledge of medical conditions is traced to Mesopotamia (3100 BCE to 332 BCE) that included Sumer and the Akkadian, Babylonian, and Assyrian empires in modern-day Iraq. The word, Mesopotamia, is Greek for "land between rivers" and indeed was between the Tigris and Euphrates rivers—major waterways of both antiquity and our coeval time. Scholars who have looked at cuneiform clay tablets of this enchorial era identify references to descriptions reflective of urinary obstruction, urethritis (and urethral discharge), renal stones, and cysts [2-4]. Archaic models of a kidney have been found such as that from the 13th century BC found at an ancient temple in Kition, Cyprus; this bronze artifact has been interpreted by scholars as an example of an offering ("ex voto suscepto or from the vow made") to the temple gods by a person with kidney disease or as a teaching aid by the euhemerists or priest doctors of the temple [5].

Babylonian physicians based diagnoses on the appearance of urine (i.e., beet juice, wine, beer, paint, others) and therapy of renal or genitourinary conditions was with local remedies from indigenous plants or minerals and blowing chemicals into the urethra; also, alcohol served as an anesthetic. In the spirit of 20th century French explorer and researcher, Jacques Cousteau, these clinicians passed their understanding of renal science on to the future clinicians in Greece who ex post facto moved their tenuous knowledge of renal function forward.

"What is a scientist after all? It is a curious man looking through a keyhole, the keyhole of nature, trying to know what is going on" Jacques Cousteau: 1910-1997

Examination of Egyptian mummies reveals evidence of renal disease including renal stones and cysts. An inaugural or eoan medical enchiridion or vade mecum was the Ebers Papyrus (1550 BCE) from ancient Egypt; it recommends a remedy for fluid retention (dropsy) that involves smearing on these patients a concoction made from cooked old papyri documents in oil [2,6]. Unfortunately, there is only exiguous documentation on renal disease available to modern scholars from this time though there is some identified information about urinary retention, frequency, dysuria, and particularly red urine. Hematuria was etiologically linked, then, as now, in Egypt to schistosomiasis particularly that from infection with S. haematobium eggs implanted in the bladder wall [7]. The Egyptian "Book of the Dead (1600 BC-1240 BC) was revered by ancient Egyptians to help those in the afterlife and was an early work to link the kidney with the heart [8]. The heart and kidneys were the only organs left in the process of mummification.

"Homage to thee, O my heart! Homage to you, O my kidneys.!: (Book of the Dead-8)

Kidneys are identified five times in the Old Testament Bible and represent organs (called "reins") examined by God to pronounce judgment on humans [8]. Ancient Hebrew teaching was that the kidneys provided the heart with advice and represented inner sources of cognition and desire that were not available to humans but were tested by God [8].

…"Examine me, O Lord, and prove me; try my reins and my heart." (Psalms 26:2—1000 BC).

"…I, the Lord, search the heart; I try the reins, even to give every man according to his ways, and according to the fruit of his doings." Jeremiah [Yirmeyahu] 17:10—600 BCE

Hippocrates

Western civilization's understanding of science is traced to the Greek natural philosophers of the 6th Century BCE. Modern Western medicine traces its roots to the famous Greek physician, Hippocrates of Kos (460-370 BCE), who taught all future people of medicine to emphasize the patient and powers of observation, and not the disease itself or only rely on the leading of experience. The Hippocratic school speciously linked health and disease to four bodily humors (black bile, yellow bile, blood and phlegm). Its Corpus Hippocraticum was the beginning of modern, Western, medicine and is a link between ancient medicine and medicine of the 21st century. Hippocrates has been called the (ancient) father of clinical nephrology as his statements on the kidney (Greek: nephros) were unchallenged for over 19 centuries [5].

"Bubbles appearing on the surface of the urine indicate disease of the kidneys and a prolonged illness…..colorless urine is bad…..the sudden appearance of blood in the urine indicates that a small renal vessel has burst…" Corpus Hippocraticum [2]

The preeminent Greek philosopher and physician, Aristotle (387-322 BCE), in his text, De Partibus Animalium, wrote that the kidney was not basic for life based on his observations in animals. He described renal anatomy and wrote that urine was made at the bladder. The purpose of the kidneys, concluded this Hellenic sage, was to provide blood vessel support, but when found, they often were filled with stones, abscesses, and growths [9]. Perhaps this vacuous view of the Aristotelian kidney encouraged limited progress in understanding this organ for the next 2 millennia. However, other Greeks in the two centuries after Aristotle's death identified the prostate gland and noted the urine was actually made in the kidneys [10].

Roman physicians of the first century, often Greeks from Asia Minor (Anatolia, now present day Turkey), began to advance the ancient nescience of genitourinary medicine. Areteus of Capadocia (81-138 AD), known for his descriptions of diabetes ("melting away of flesh into urine"), also commented on anemia from renal insufficiency, renal colic, hydronephrosis, and other renal pathology [2,11]. Pedanius Dioscorides (40-90 AD) formulated the famous De Materia Medica (Latin for "on Medical Material") in about 60 AD that became the standard encyclopedic pharmacopoeia of herbs and medicines from the mid-first century until the Renaissance period. In this five volume document this Greek physician, pharmacologist, and botanist wrote about herbs to improve renal disease such as use of enemas with ptisan or mallow for renal failure [2]. Other scholars of the first century AD mixed various drug conconctions, such as the Greek physician from Crete, Andromachus the Elder (Theriaca Andromach—"Archiater"---60 AD), looking for theriacs or catholicons to cure the ailments of mankind.

Galen of Pergamos (130-201 AD), father of modern and experimental Western medicine, wrote about renal conditions and concluded that the kidneys clear blood; in his capacity as a surgeon, he showed that urine flows from the kidneys to the bladder by performing ligation of the ureters [10]. Later in this first millennium, Byzantine physicians expanded our knowledge of the renal system and the term "ureter" was first used by Oribasius (326-403); he galvanized renal physiology erudition by sagaciously suggesting that urine was absorbed from the blood circulation by the kidneys [12].

The fall of the Roman Empire in 476 AD cast the Western world into the Dark Ages (476 AD to 1000 AD) or European Middle Ages (Medieval Period-- 5th century to 15th century) with loss of much knowledge in medicine, other sciences, and the arts. Medicine, including cognizance of renal disorders, was preserved and heightened by Arab physicians of the 9th and 10th centuries including the Galen of Islam, Rhazes (865-925), a musician turned physician, and Avicenna (980-1037) whose work on describing urine foreshadowed the science of uroscopy [2]. One of Avicenna's renal advice involved urethral insertion of a louse to improve urination [2,13].

The great Jewish scholar, Moses Maimonides (Rambam 1138-1204 AD) who was a noted physician (as well as rabbi, philosopher, astronomer) expanded the understanding of urinalysis that included descriptions of red urine (later identified by the eminent 19th century English physician, Richard Bright MD as glomerulonephritis) and black urine (later identified as a sign of malaria). This scholar who was born in Cordova and carried for the sultan Saladin in Cairo, Egypt commented on the realities of being a 12th century physician: "…I have never seen anyone who urinated black urine who survived" [2,14].

Renaissance

Modern nephrology perhaps can be traced to salient scientists and paramount physicians of the Renaissance who began to unravel the mysteries of the renal and genitourinary systems in the spirit of Sir Issac Newton, standing on the shoulders of giants of the past. The founder of pathological anatomy, Morgagni (Giovanni Battista Morgagni: 1682-1771) described various renal disorders via autopsy [2,15]. Paracelsus (Theophrastus Bombastus von Hohenheim: 1493-1541), a famous and colorful physician from Switzerland, wrote about proteinuria, hematuria, gout, and edema; his prevenient work was the forerunner of using specific gravity in urinalysis [2,16]. Edema (oedema) was originally called dropsy, a word first recorded in the penultimate decade of the 13th century and later connected to renal disease in the 19th century (vida infra). The father of anatomy, Andreas Vesalius (1514-1564), born in Brussels, Belgium, illustrated renal anatomy in his seminal work, De Humani Corporis Fabrica (1543) with convincing clarity that resonates into the 21st century [2,17].

The father of microscopic anatomy, Marcello Malphighi (1628-1694), identified the glomerulus (Malpighian corpuscle) and in 1666 published his observations on the kidney (and other organs) in De viscerum structura exercitatio anatomica. He wrote about the pyramids of the renal medulla and collecting ducts as well as other microscopic aspects of the kidney; use of dye injection led him to describe glomeruli as "…hanging like apples from the blood vessels, which, swollen with the black fluid, look like a beautiful tree" [2,18].

Other anatomic scholars continued to advance the knowledge of this organ called the reins, such as the Italian Lorenzo Bellini

(1748-1795: Bellini's ducts) in his Exercitatio Anatomica de Structura Usu Renum (1662), the Russian Alexander Schumlansky (1748-1795: De Structura renum in 1782), and the Englishman William Bowman (1816-1892; The Physiological Anatomy and Physiology of Man-1857 with Robert Bentley Todd) [19], and many other sages of science and medicine.

19th century pioneers

The 19th and 20th century brought forth a salmagundi of sempiternal scholars, who, standing on the shoulders of previous giants, advanced the field of clinical nephrology to unprecedented levels. Perhaps the beginning of modern nephrology can be traced to the Richard Bright (1789-1858) who has been called the "greatest physician of his day and one of five or six great physicians of all time" [20]. He was one of the famous triumvirate of London's Guy's Hospital in the Victorian era along with Thomas Addison (1793-1860) and Thomas Hodgkin (1798-1866). Each of these three medical paragons has diseases named after them.

Richard Bright made original advances in medicine including nephrology and neurology (i.e., Jacksonian seizures, infantile seizures, syringomyelia, brain arteries, and narcolepsy, others [21]. This father of modern renal diseases concluded that the finding of albuminuria with edema meant the patient had renal disease. The first clinical mention of proteinuria was in 1697 but it was Richard Bright who, standing on the shoulders of giants, moved this observation further in 1827 [22]. This ingenious izzat established the first medical research unit at his hospital and provided a series of insightful, iatric descriptions of acute nephritis, nephrotic syndrome, uremia, small and enlarged kidneys, and a link between renal disease and enlarged ventricles of the heart perhaps an a fortiori adumbration of the ancient Hebrew link of the heart and the "reins" [23-28].

Richard Bright's studies were often post-mortem on patients with advanced renal disease and his written observations are preserved in the Gordon Museum at London's Guy's Hospital [24]. Analysis by late 20th century nephrologists revealed two had mesangiocapillary (membranoproliferative) glomerulonephritis; one had a five-year clinical history and died from chronic renal failure with uremia while the other died after 3 to 4 months with severe nephrotic syndrome [24]. Acute and chronic nephritis was called Bright's disease long after his death that may have been caused by his own eponym.

Sir Robert Christison (1797-1882)

Another early pioneer and pharos in nephrology of the 19th century was Sir Robert Christison from Edinburgh, Scotland who made seminal advances in nephrology, pharmacology, and jurisprudence [29]. He provided many contributions to the understanding of renal disease including confirming the observations of Richard Bright, expanded the understanding of uremia as well as anemia in renal failure, discerned that albuminuria and edema might be reversible in some situations, detailed microscopic studies of urine as well as the kidney, and linked some cases of acute renal failure to toxins or poisons [29,30]. He was a professor of medicine in Edinburgh for half a century and was president of the Royal College of Physicians in Edinburgh on two occasions. He remains one of the triumvirate founders of clinical nephrology of the 19th century.

Pierre Rayer (1793-1867)

The First Triumvirate of ancient Rome was Julius Caesar, Pompey (Gnaeus Pompeius Magnus) and Crassus (Marcus Licinius Crassus) in 60 BC and the Second Triumvirate was Antony (Mark Antony), Lepidus (Marcus Aemilius Lepidus), and Octavian (Gaius Julius Octavius) in 43 BC. The classic though unaffiliated triumvirate of 19th Century Nephrology the fortuitous, feracious founders of modern nephrology—were Richard Bright, Sir Robert Christison, and Pierre Rayer. Pierre-François Olive Rayer (1793-1867) was a French physician who contributed important, ingenious information to various fields, including physiology, pathological anatomy, comparative pathology, medical chemistry and parasitology [31].

Between 1837 and 1841 he published a 2,200 page, 3-volume treatise on kidney diseases: Traité des maladies des reins [31,32]. This masterpiece provided a clinical approach to renal disorders (uro-nephrology) and was translated in to German but not into English. This renowned clinical scientist represents themes often repeated in history a perspicacious paragon lost to the monolingual English-reading population because of translation failure and one often not fully understood even in his own country [33,34]. He also expatiated eloquently about skin diseases and eponyms associated with his name include Rayer's disease and Rayer's nodules (xanthomas).

Claude Bernard (1813-1878)

A sagacious scientist whose works were translated into many languages and who is acclaimed in his native country and beyond is Claude Bernard, the most distinguished French physiologist of the 19th century (and beyond!) [35]. He accomplished a gallimaufry of erudite experiments in physiology that set the stage for sound scientific methodology and is acclaimed as the father of modern physiology [36]. He emphasized blind experiments to ensure scientific objectivity and he performed now classic experiments on the pancreas' function (discovered the lipolytic function of the exocrine pancreas) as well as the glycogenic function of the liver (with improvement in knowledge of diabetes mellitus) [36-42]. He was the first to describe homeostasis or constancy of the internal environment (le milieu intérieur) and the vasomotor system. This allowed future researchers to apply these Promethean principles of perlustration to renal physiology. For example, research in the first half of the 20th century lead to the disambiguation of electrolyte content of le milieu intérieur the extracellular, intracellular, and interstitial fluid compartments of tissue elements that was unknown or confusing for eons of human life [43-45].

"The living organism does not really exist in the milieu exterieur (the atmosphere if it breathes, salt or fresh water if that is its element) but in the liquid milieu interieur formed by circulating organic liquid, which surrounds and bathes all tissue elements,…the stability of the milieu interieur is the primary condition for freedom and independence of existence; the mechanism which allows this is that which ensures in the milieu interieur the maintenance of all conditions necessary to the life of the elements." Claude Bernard [43].

Francis Delafield (1841-1915)

Contributions to clinical nephrology in the 19th century were by European scientists and clinicians. Contributions from across the Atlantic Ocean began at the end of this century with Francis Delafield (1841-1915) that foreshadowed an onslaught of American ingenuity in understanding the kidney. He graduated in 1963 from New York's

College of Physicians and Surgeons and continued his studies in London and Berlin. After returning to New York he is acknowledged as a panoptic pioneer in renal histology correlating renal symptoms with kidney histological pathology [46]. Francis Delafield developed nosological classification of Bright's disease (as it was called in his day). He was the first recognized renal expert from America and his beloved city named a hospital after him in 1948: the Francis Delafield Hospital which opened in 1950. Cardinal concepts in nephrology: the 20th Century and the accession of American nephrologists It is not beyond peradventure to note that, standing on the shoulders of giants from other lands (ancient Mesopotamia, Egypt, Greece, Rome, Arab countries, Renaissance Europe, 18th and 19th century Europe), remarkable achievements in the understanding of renal physiology and renal disease management resulted from the notable achievements of American scientists and clinicians albeit in the 20th century [47]. Some were Europeans transplanted to America and some were native born Americans. There are of course, more European clinicians of the 19th century of neoteric note such as Ségalas' and Wöhler's work on extra load of urea leading to diuresis, Ludwig's studies on urine fluctuations due to hypertension, Ustimowitsch's (with Falck and Richet) work on urinary solutes and renal flow, Cushny's work in 1900 on what was later called osmotic diuresis, Friedrich von Muller's work on what he termed "nephrosis" in 1905 (as differentiated from "nephritis"), and many more savvy scientists [48]. However, a salient summary is now presented of the American influence in the 20th century and more data will be provided in the Second Edition of this breviloquent megillah on the history of the Pediatric kidney.

No human being is constituted to know the truth, the whole truth, and nothing but the truth; and even the best of men must be content with fragments, with partial glimpses, never the full fruition- William Osler MD: 1849-1919

Thomas Addis (1881-1949)

This section of our wee, pensive synopsis begins with a Calvinist, Thomas Addis, an innovative hematologist and researcher who was born and trained in Scotland and moved his academic position in 1911 to USA's Stanford School of Medicine to direct their clinical laboratory [49]. He was recruited by Stanford's first dean of medicine, Ray Lyman Wilbur. Though known to legions of cognizant clinicians because of the Addis count of the urinary sediment, Thomas Addis' contributions to nephrology were immense and included physiology in Bright's disease, protein metabolism and renal growth (hypertrophy), and use of diet as well as rest in management of renal disorder [49-52]. He studied blood coagulation and haemophilia research that included transfusing fresh blood into a patient with hemophila to shorten the clotting time. He followed his patients throughout their life to better understand their disease and precedently pioneered the concept of contributions from nonmedical team members foreshadowing the benefaction of non-profit organizations such as the National Kidney Foundation [52].

Alfred Newton Richards (1876-1966)

Born in Stamford, New York Alfred Newton Richards was an eminent American pharmacologist involved in the discovery of the mechanism of urine formation [47,53,54]. He led a group of scientists at the University of Pennsylvania that meticulously established the physiology of renal glomerular filtration and selective tubular reabsorption. He was a president of the National Academy of Sciences and one of his many honors was to have his beloved University of Pennsylvania establish the Richards Medical Research Laboratories in his honor.

Donald Dexter Van Slyke (1883-1971)

Dubbed the 20th century iatro-chemist, Donald Dexter Van Slyke provided key concepts for scientists and clinicians in the 20th and now 21st century on cardinal concepts of acid-base balance. [55,56] This allowed clinicians to more accurately understand diabetes and nephritis with particularly reference to acidosis and alkalosis [57-63]. He published a brilliant paper on lung volume in 1918 but later published his seminal work on amino-acids and the significance of the urea clearance in renal disease from the Rockefeller Institute for Medical Research in New York [64-66]. This renowned Dutch-American biochemist, who was a graduate of the University of Michigan (as was his father), used his research at the Rockefeller Institute Hospital (1907-1948) to help develop the field of modern quantitative blood chemistry that included seminal work on the measurement of gas and electrolyte levels in tissues. He co-authored the authoritative two volume text, Quantitative Clinical Chemistry with another pioneer John P. Peters (vida infra). Among his many honors were being the first recipient of the American Medical Association's Scientific Achievement Award (1962) and the first Van Slyke Award in Clinical Chemistry (1957) by the American Association of Clinical Chemists.

"Neither the urea clearance, nor any other physiological measurement, should be asked to serve as the sole criterion to discriminate between health and disease. The clinician using such a test must evaluate the results in terms of all known causes of variation, physiological and pathological." - Donald D. Van Slyke, 1949 [66].

John P Peters (1887-1955)

John P Peters was an MD from Columbia College of Physicians and Surgeons and completed a residency in internal medicine at Cornell Medical College. He worked at the Rockefeller University Hospital with Donald D Van Slyke PhD and others in biochemistry before establishing his medical career at Yale University School of Medicine. He was a master of both bedside medicine as well as biochemistry and used these traits along with gifted writing skills to establish clarity regarding the human body's chemistry for the foundation of modern nephrology [47,67]. Research in the United States after World War I focused on diseases that disrupted homeostasis and John Peters was able to use his Yale laboratory to study renal disorders in this manner [68]. The emphasis was on improving knowledge in details of chemical make-up of blood and urine as well as how these normal states were disrupted by renal diseases as well as other disorders (i.e., liver, disease, diabetes mellitus, others) [68]. He applied prominent principles of physiology to his work including Starling's law, the Donnan effect, the Henderson-Hasselbalch equilibrium and others [67]. John Peters established the importance of the flame photometer to accurately measure sodium and potassium concentrations in small amounts of serum or urine, utilized the balance technique in clinical research, and was one of the most refulgent researchers who were able to integrate raw research data into clinical applications of patients with severe renal disease [67]. He was able to examine other researcher's data better than the original researcher and draw conclusions sometimes contrary to the original study. He was able to combine his ideas with that of others to formulate a better understanding of such issues as water balance in health and disease [69]. He wrote about various organs but the reins seemed to be his preferred one [67]. He researched and taught about disease and metabolism, electrolyte and acid- base equilibrium, nephritis, and water exchange. He co-founded the field of quantitative clinical chemistry with Donald Dexter Van Syle PhD (vida supra) [70,71]. Dr. Peters was also an advocate for responsible social reform to improve medical care for all [67,72,73]. The grateful students of this rebellious son of an Episcopal minister went on to continue with progress in nephrology in the 20th century for the benefit of mankind and they include Robert Petersdorf, Lawrence R. Freedman, Jack Orloff, Arnold S. Relman, Franklin H. Epstein, Donald Seldin, and others [67].

"A patient needs a doctor, not a committee….Doctors treat individuals, not statistical averages…If you don't examine the trees, you may get lost in the woods... the proper study of mankind is man" - John P. Peters, MD [67]

Homer W Smith (1895-1962)

Homer W Smith was an American investigator who was chair of physiology at the University of Virgina but moved to New York University in 1928 where he spent most of his illustrious career as director of the NYU Physiology laboratories. His NYU time has been called the Smithian Era of renal physiology for his monumental research clarifying glomerular filtration, tubular absorption, and secretion of solutes in renal physiology [48,74-77]. His work established the concept that the kidney worked according to principles of physiology both as a filter and also as a secretory organ. Twenty-first century clinical nephrology stems from his work and teaching on the awareness of normal and abnormal functioning of the kidney. He removed the then held belief of vitalism in renal physiology that life's processes are not subject to laws of physics and chemistry alone, i.e., life is in part self-determining. Dr. Homer W Smith spend many summers at the Mount Desert Island Biological Laboratories (Mount Desert Island, Salisbury Cove, Maine, USA) researching osteichthyes and this work led to his famous book, From Fish to Philosopher, Man and his Gods that has a foreword by Albert Einstein (1879-1955) [78]. He also authored his book on the kidney in 1951 that discussed various issues of the Pediatric kidney (pages 461-491): Renal function in infants and childhood; The fetal kidney; surface area as a basis for the comparison of renal function in infants and adults; maturation of renal function in infancy; relation of urine flow to filtration rate; urea clearance; maintenance of salt and water balance in infancy [79]. The American Society of Nephrology (founded in 1966) established the Homer W. Smith award annually starting in 1964 to an outstanding individual who significantly advances knowledge in states of normal and abnormal renal functioning.

Even then, a new branch of mythic thought had already grown strong, one not religious in nature but no less perilous to mankind exaggerated nationalism. Half a century has shown that this new adversary is so strong that it places in question man's very survival. It is too early for the present-day historian to write about this problem, but it is to be hoped that one will survive who can undertake the task at a later date. Albert Einstein in his foreword to Homer W Smith's "Man and his Gods", 1952 [78]

Pediatric Nephrology emerging from adult nephrology

Though there are many other giants who lead to current knowledge of adult nephrology, this meditative epitome now turns to consideration of the focus of this iatric issuance—the pediatric kidney. The first book on pediatrics in the Western world was published in 1544 AD by Thomas Phaer (1510-1560)—a truly assiduous Renaissance man of sagacity---physician, lawyer, poet, philosopher, and father of English paediatrics [79]. However, sustained interest in diseases of children has come over the past two centuries as attention before that was primarily, and certainly continues to be, with diseases of adults [80,81]. Prior to this medical care for children was provided by midwives, families, and family friends [80]. Research in diseases of children was often focused on infectious diseases in the 19th century with attention given to the causes and management of diphtheria, infant diarrheal illnesses, tuberculosis, streptococcal infections, and others [82]. The era of vaccinology was ushered in by Edward Jenner (1749-1823) in the waning years of the 18th century and then by Louis Pasteur (1822-1895) in the latter part of the 19th century [83]. European clinicians and researchers began a nidus of interest on renal disease in children in the penultimate decade of the 19th century with writings on bladder extrophy, renal rickets, nephritis, and Henoch's purpura [84,85]. As adult nephrology was arising in the 20th century, pediatric nephrology emanated later---analogous in the spirit of Greek mythology as depicted by the dominant Danish artist Rudoph Tegner's (1873-1950) classic sculpture of Zeus giving birth to Athena; pediatric nephrology emerged as a result of attempts to deal with fluid and electrolyte metabolism that was disrupted in diarrheal dehydration of infants and children [84-86].

Conclusion

It is easy for a non-nephrologist to become lost in the complexities of renal physiology, diagnosis, and treatmen i.e., to miss the forest for the trees. It is not unusual for one to "fall" into the loop of Henle (discovered by the 19th century German anatomist, Friedrich Gustav Jakob Henle [1809-1885]) and not return after being weighed down by a seemingly skimble-scamble litany of renal sagacities [87]! Thus, one can ask: "what is the role ("the forest") of the primary care clinician in the diagnosis and management of paediatric renal disorders ("the trees")?" What is the forest and what are the trees in this perspective? Certainly, seeking to stay current on basic principles of pediatric nephrology is important such as fluid and electrolyte physiology and management of paediatric dehydration [43].

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