URINARY TRACT ANOMALIES IN RELATION TO RECURRENT URINARY TRACT INFECTIONS IN CHILDREN

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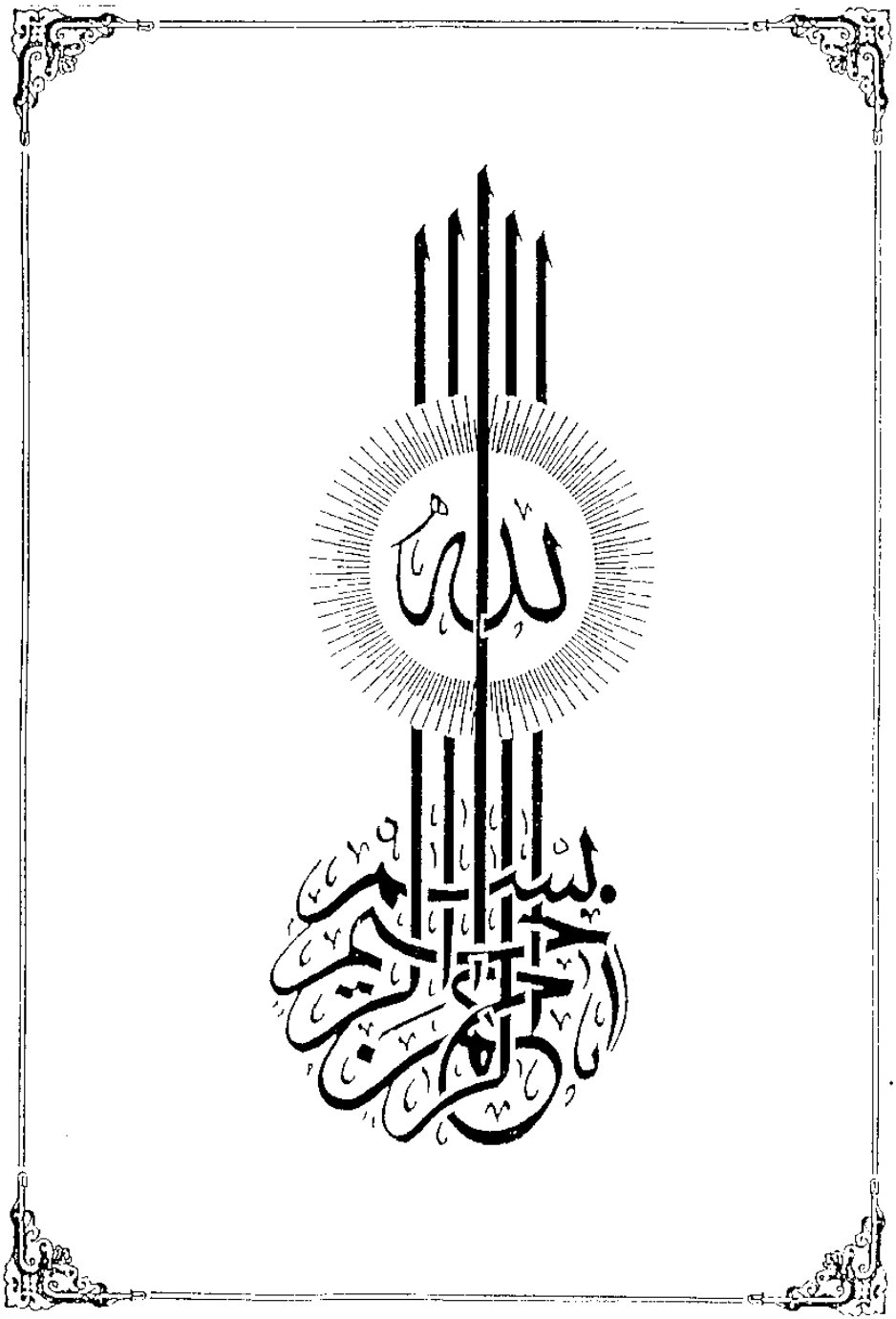

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LIST OF ABBREVIATIONS

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ABU	-	Asymptomatic Bacteriuria
APN	-	Acute Pyelonephritis
BSU	-	Bag Specimen Urine
CCSU	-	Clean Catch Specimen of Urine
CFU	-	Colony-Forming Units
CI	-	Confidence Interval
CPN	-	Chronic Pyelonephritis
CSU	-	Catheter Specimen of Urine
CT	-	Computed Tomography
DMSA	-	Dimercaptosuccinic Acid
DTPA	-	Diethylenetriamine Penta-Acetic Acid
ESRD	-	End-Stage Renal Disease
HPF	-	High Power Field
IC	-	Isotope Cystogram
IVU	-	Intravenous Urogram
LET	-	Leukocyte Esterase Test
LPS	-	Lipopolysaccharide
MCU	-	Micturating Cystourethrogram
MRI	-	Magnetic Resonance Imaging
MSU	-	Mid-Stream Specimen of Urine
OIF	-	Oil Immersion Field
pH	-	Logarithm of the reciprocal of H ion concentration
PN	-	Pyelonephritis
RCS	-	Renal Cortical Scintigraphy
RD	-	Renal Dysplasia
RNC	-	Radionuclide Cystography
RPM		Revolution Per Minute
SB	-	Significant Bacteriuria
SPA	-	Suprapubic Aspirate
SVC	-	Surface viable counts
UPJ	-	Ureteropelvic junction
US	-	Ultrasonography
UT	-	Urinary Tract
UTI	-	Urinary Tract Infection
UVJ	-	Ureterovesical Junction
VCUG	-	Voiding Cystouretherography
VUR	-	Vesicoureteric Reflux
WBC	-	White Blood Cell

INTRODUCTION

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Urinary tract infection (UTI), is a common, recurrent, and a potentially serious pediatric problem (Al-Mugeiren, 1992). Recurrence of infection is a common event when functional or anatomic abnormalities are not corrected (Kunin, 1987; Brumfitt et al, 1991).

Although the prognosis of UTIs in childhood is generally favorable (Hansson et al, 1989), any delay in management may predispose them to renal parenchymal damage, hypertension, and even renal failure (Sherbotie and Cornfeld, 1991).

UTIs are commonly misdiagnosed in children. Dysuria and passage of cloudy urine are common symptoms in children with febrile illness and do not necessarily reflect UTI. On the other hand, many children with UTIs are symptomless or have unexplained fever, vomiting or even failure to thrive; in these patients the diagnosis may be overlooked.

In this study we will aim at evaluating the lines of diagnosis and management of recurrent urinary tract infections, and we hope to reach a clear conclusion to improve the fate of the affected children.

1. HISTORICAL PERSPECTIVES

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Early views

The ninth century Arab physician Alrazi is credited by Asscher (1980) for the initial diagnosis of pyelonephritis in a Baghdad patient with a febrile illness and nectrotizing papillitis. The fact that freshly voided urine is an excellent culture media for the common bacterial pathogens of the urinary tract, has been known since the time of Pasteur (1863). Doetsch 1968 reported that Lister 1893 observed that freshly voided urine was generally sterile, a finding that was also confirmed by Sherrington (1893).

Roberts (1881) noted the presence of bacteria in the urine of patients with urinary symptoms, and a year later Wagner described focal histological changes in women with recurrent UTI. Apparently it was Roberts who introduced the term bacteria and observed that, although urine was free from bacteria, it could become contaminated with organisms at the time of voiding.

Escherich (1897) cultured bacillus coli in the urine of children with UTIs and described pyelitis as a disease of childhood. Lohlein (1917) recognized the relationship between recurrent UTI and progressive pyelonephritis with renal impairment and ESRD.

The chemotherapeutic era

Prior to the chemotherapeutic era, methamine, mandelate, cranberry juice, and ketogenic diets were prescribed to prevent and treat recurring symptomatic UTI. During the thirties, recurrent UTI and its outcome in patients were described in detail. Dodds (1931) emphasized the importance of meticulous care in obtaining urine specimens for culture, and observed that variations in techniques could account for differences in the prevalence of UTIs observed by other investigators. Longcope and Winkenwerder (1933) characterized hypertension and atrophic pyelonephritis as complications of recurrent renal infection. Weiss and Parker (1939) further clarified the entity of

pyelonephritis, including the radiographic changes, the focal nature of the pathology, and the acute interstitial inflammation and abscesses seen in renal parenchyma. They also described "pyelonephritis lenta" or silent subclinical pyelonephritis, a progressive disease predominantly in young adult women that is usually associated with hypertension and leads to ESRD.

These investigators introduced an era in which recurrent bacterial infections of the UT were assumed to put the patient at risk of chronic fatal renal disease, concluding that chronic pyelonephritis was more frequent than glomerulonephritis as a cause of ESRD.

In a follow-up study of women who presented with pyelonephritis during pregnancy, Crabtree and Reid (1940) reported the patients acquiring renal stones and the development of significant renal impairment.

Experience derived from following adult patients in the pre-antimicrobial era supported the hypothesis that progressive destruction of the renal tissue could gradually lead to sustained pathologic increase in blood pressure or renal impairment. By 1940 patients with renal infection were being treated with sulfonamides, and persistent, recurrent destructive infection became less common. Antimicrobial regiments to treat acute and asymptomatic infections and prevent recurrence were identified in a plethora of studies as each therapeutic agent was introduced in clinical practice. Generally, in patients with asymptomatic disease, the natural history of UTIs could no longer be observed. Nevertheless, the growth of bacteria on qualitative culture of the urine under optimal conditions had been accepted as an expression of UTI for many years, even though a positive culture might also be the result of contamination of the urine with organisms in the urethra at the time of collection. Even cultures of urine obtained by urethral catheterization did not exclude the possibility of contamination (Guze and Beeson, 1956). The mere demonstration of bacterial growth from a urine sample obtained by catheterization could not be accepted as a proof that the organisms were originally in the bladder cavity. The inadequacy of qualitative bacteriology

therefore led to the application of other techniques and criteria to the clinical evaluation of UTIs.

Interpretation of urine culture

Many attempts had been made in the past to distinguish between true bacteriuria and contamination. Most of these attempts did not receive widespread acceptance because the criteria for distinguishing between contamination and true bacteriuria were usually arbitrary.

Microscopic urine analysis for predicting positive urine culture has been achieved by standardizing methods and by combining results of tests for pyuria and bacteriuria in criteria for test positivity. Dukes (1928) described more accurate and reproducible urine analysis results by counting white blood cells (WBCs) in uncentrifuged urine using a haemocytometer. Marple (1941) was the first to apply the principle of quantitative bacteriology to cultures of urine. However, this concept was not widely accepted. Few innovations have had far-reaching results as the introduction by Kass in (1955) of quantitative bacteriological methods for the diagnosis of urinary infection. More precise definition of infection by such methods has led to critical appraisal, not only of diagnosis criteria but also of the incidence, natural history and significance of urinary infection. However, the presence of pyuria or bacteriuria alone on microscopic urine analysis has been found to be a poor predictor of positive urine cultures. Kass (1957) defined pyuria as at least 5 WBCs per high power field (hpf) on centrifuged urine and found it to be present in a third to half of patients with at least 10^5 Colony Forming Unit (CFU)/ml but only in 2% of those with bacterial counts less than 10^5 CFU/ml. He concluded that pyuria was of value diagnostically only when it was clearly present and that its absence should not be interpreted as absence of bacteriuria. Similar findings had been reported by other authors (Pryles and Eliot, 1965; Krober et al, 1985; Goldsmith and Campos, 1990). It was only until Sanford et al, (1956) and Kass (1957) revived this method and insured its validity by reporting systematic analysis of bacterial counts of urine that established reliable criteria for separating contamination from infection. The studies of careful quantitative

bacteriologic examination of urine provided a most important aid in diagnosis of UTI.

More precise definition of infection by such methods has led to critical reappraisal, not only of the diagnostic criteria but also of the incidence, natural history and significance of urinary infection. In addition it also provided reliable criteria for evaluating the epidemiology as well as the effects of treatment on these infections. From this in turn has stemmed such major changes in our concepts and the introduction of new powerful antibacterial drugs and their longer and more careful supervised administration. Improved diagnostic procedures have also been devised for detection of the UT abnormalities and new surgical approaches for their correction. Together these have led to more rational and effective treatment, and their longer and more carefully supervised administration.

The role of surgery

In the sense of speciality which a surgeon might reasonably set out to practice, pediatric urology has existed no more than 30 years ago. In the sense of compendium of diseases requiring surgical treatment, it goes back at least to the birth of surgery as a craft and science since lithotomy was one of the first planned operations and sufferers from stone in those days were very frequently children (Owen, 1885).

Urinary tract anomalies

Congenital valves in the posterior urethra are a cause of severe urinary obstruction in the male infant. The lesion was once regarded very rare. But now since we give proper attention to the investigation of neonatal disorders it has proved to be relatively common.

The idea of simple urethral dilatation could cure, led to a phase in which the urethral caliber aimed at exceeded the ordinary adult dimensions or was replaced either by meatotomy or by urethrotomy. Some careful controlled investigations seemed to show little advantage of any method.

The concept of bladder neck obstruction arose from the common observation of the adult that chronic retention of urine with trabeculation and diverticulae of the bladder could occur in the absence of either prostatic enlargement or stricture. Since many little girls with frequency exhibit a mildly trabeculated bladder and small volumes of urine may be found at times, bladder neck obstruction was postulated as the cause of recurrent infection (Williams, 1984).

Vesicoureteric reflux (VUR) was at first conceived to be a complication of other disorders, chiefly obstruction or neuropathy. It was not until the work of Hodson and Edwards (1960) that identified the pyelographic features of chronic pyelonephritis without dilatation and demonstrated that reflux was almost invariably associated with this process. This led to perfect an operation for reflux.

The observation that the classical picture of chronic pyelonephritis was associated not simply with VUR but with intra-renal reflux, and the work by Hodson et al (1975) and later by Ransley (1977) has clearly suggested that there are many cases in which reflux itself will be harmless whereas in others it is likely that the damage has already occurred by time symptoms first brought the child to hospital (Williams, 1984).

Imaging

Plain x-ray of the abdomen was the first to be used. Until recently, micturating (voiding) cystourethrography (VCUG) and intravenous urography (IVU) were performed in all children with UI. In an attempt to reduce the radiation exposure of these children, the techniques were modified by decreasing the number of films and by the use of rare earth screens (Segal et al, 1982). At a later stage the low radiation and radiation free alternatives of scintigraphy and ultrasonography (US), were introduced. The use of US has been advocated as part of the initial investigation of children (Leonidas et al., 1985).

Radionuclide voiding cystography is advocated for the diagnosis of VUR (Willi and Treves, 1983). Diverse diagnostic imaging techniques are now available for assessing normal and abnormal UT anatomy and function. These include intravenous urography (IVU), ultrasonography, retrograde and antegrade urography, nuclear medicine, computed tomography (CT), magnetic resonance imaging (MRI) and angiography. As imaging methods proliferates so do polices of investigating childhood UI.

Techniques using radioisotope for nuclear cystography were first reported by Winter (1959) who used several radiopharmaceuticals to evaluate VUR. Conway et al., (1972) showed that the technique could determine the presence or absence of reflux at a significantly lower radiation dose than radiographic cystography. The radioisotope techniques continue to be refined