

Outpatient Evaluation of Hematuria in Children

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Hematuria

- Common in pediatric patients
- Hematuria alone accounts for about 30% of children referred to a pediatric nephrology clinic.
- Prevalence of hematuria tends to increase with age during childhood and adolescence.

Epidemiology of Hematuria in Children

Author	Location	Age	N
Dodge 1976	Galveston	6 – 12 years	6070
Vehaskari 1979	Finland	8 – 15 years	8954
Murakami 1991	Japan	6 – 14 years	560,000

Epidemiology of Hematuria

- Prevalence of hematuria in 2 or more urine specimens
 - Higher in girls than boys throughout childhood
 - Tends to increase with age throughout childhood and adolescence
 - 0.05 to 3% of school age children

Definition of Hematuria

- Healthy individuals excrete 1-2 million RBC's/day (1500/minute)
- > 5 RBC's/ hpf on a centrifuged urine specimen
- Gross hematuria = red, brown, "coke-colored", smoky, or other color
 - Often very worrisome to parents
- Microscopic hematuria = > 5 RBC's/ hpf on urine specimen but no discoloration of urine.

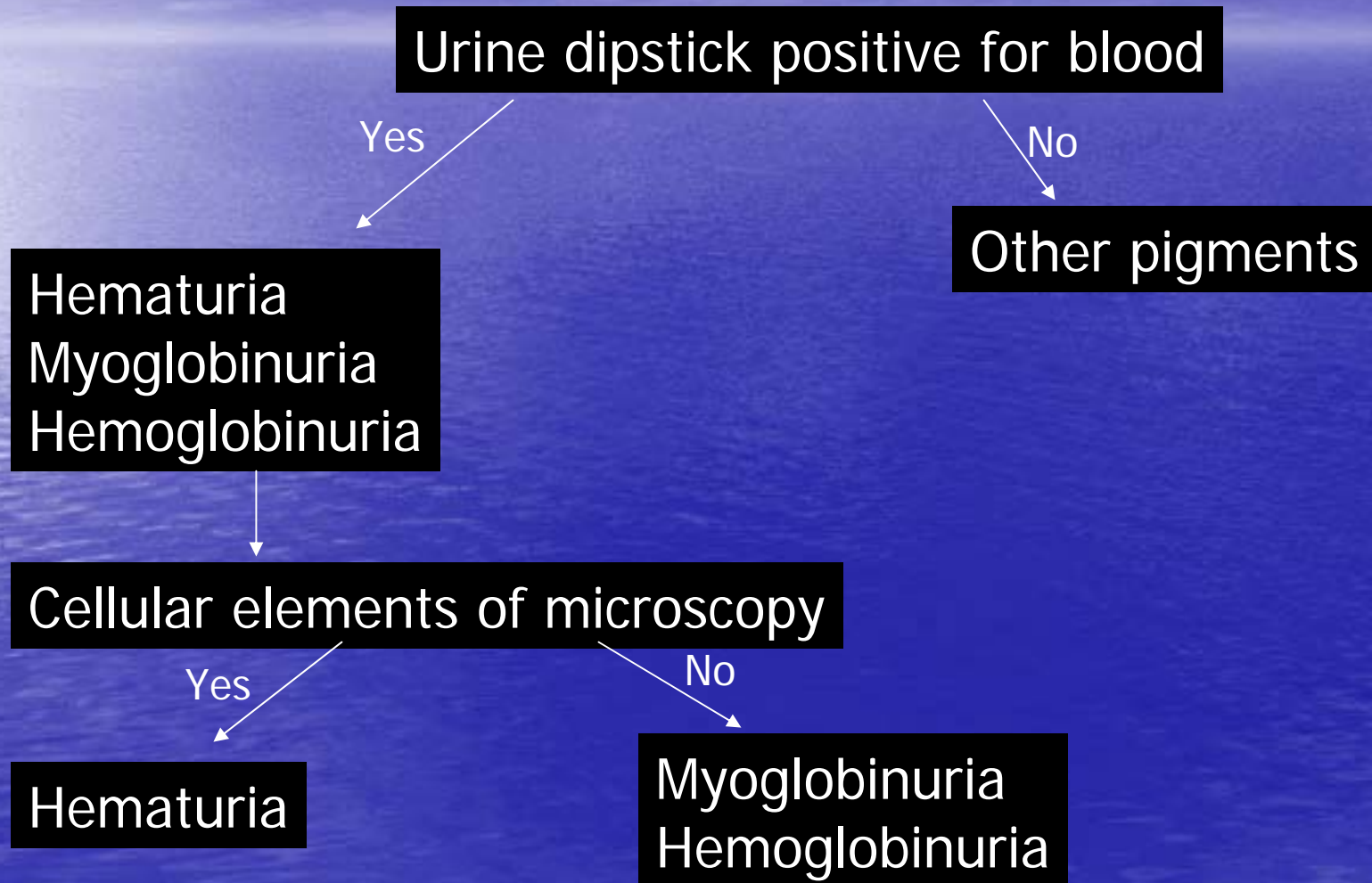
Urine dipstick for hemoglobin

- Paper strip tests
 - Orthotoluidine impregnated, buffered with peroxide
 - Hemoglobin catalyzes oxidation reaction
- Green-Blue color change in presence of hemoglobin or myoglobin
 - Hemoglobin may be free or within RBC's
 - Dipstick more sensitive for free hemoglobin than for RBC's
 - Diffuse vs. speckled
 - Detects as few as 2-5 intact RBC's
 - False + with hypochlorite or microbial peroxidase with UTI

Confirmation of Hematuria

- Microscopic examination is essential.
 - Fresh urine centrifuged in a conical tube
 - Consider phase contrast microscope
 - Glomerular hematuria:
 - Great variation in size, shape, and hemoglobin content between RBC's.
 - May also have RBC cast or heavy proteinuria
 - Nonglomerular hematuria:
 - Uniform size and shape of RBC's, no casts

Causes of Red Urine



Causes of Red Urine

- Hemoglobinuria
 - Drugs: quinine, sulfonamides
 - Chemicals: CO₂, chloroform, fava beans, naphthalene, oxalic acid, phenylhydrazine, snake venom, tin
 - Exercise, cold, intravascular hemolysis
- Myoglobinuria

Causes of Red Urine

- Discolored urine
 - Drugs: phenytoin, phenolphthalein, phenothiazides, pyridium, rifampin, chloroquine, deferoxamine
 - Foods and dyes: blackberries, beets, vegetable dyes
 - Internal pigments: bilirubin, urates (red diaper syndrome), porphyrins, metabolic errors (alcaptonuria, tyrosinosis, homogentisic acid)

Etiology of Hematuria

Glomerular

PSAGN

Lupus

IgA, HSP

MPGN

RPGN

Alport's, benign hematuria

FSGS, NIL

MGN

nephrosclerosis

Tubulointerstitial

infection

ATN

trauma

cystic kidney disease

nephrocalcinosis

nephrolithiasis

Vascular

RVT

malformations

Tumor

Upper collecting system

urolithiasis, hypercalcuria

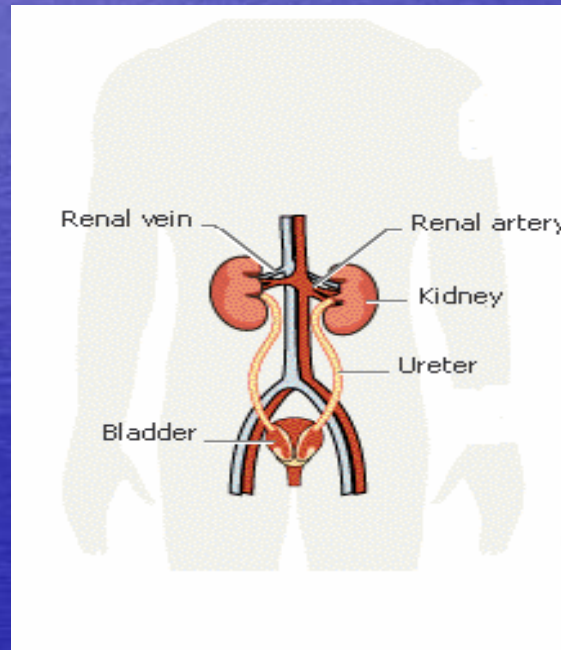
hydronephrosis

trauma

vascular malformations

papillary necrosis

infection



Lower collecting system

infection

foreign body

trauma

urolithiasis

tumor

drugs (cyclophosphamide)

Poststreptococcal Acute Glomerulonephritis: Clinical Features

- 60% of cases in children 2 to 12 years of age
- 2:1 male: female ratio
- May follow either pharyngeal or skin infection even if treated with antibiotics
- Abrupt onset of nephritic syndrome following a latent period averaging 10 days after streptococcal infection
- Clinical presentation varies from mild hematuria to severe hypertension or renal insufficiency

Poststreptococcal Acute Glomerulonephritis: Diagnosis

- Nephritic syndrome with no other systemic signs or symptoms
- Positive streptococcal antibody
- Decreased C_3

Poststreptococcal Acute Glomerulonephritis: Serologic Findings in First Week of Disease

	Test	Frequency (%)
Anti-streptococcal antibodies	ASO > 200 Todd units	60
	Antihyal > 1:512	63
	Streptozyme > 1:200	89
Immunoglobins	S IgG > 1600mg/dl	90
	S IgM > 150mg/dl	85
Other immunologic studies	RF > 1:32	44
	Decreased C ₃	89
	Cryoglobulins	73

Poststreptococcal Acute Glomerulonephritis: Clinical Course

- Gradual improvement in acute symptoms over 1 to 3 weeks
- Clinical resolution in 6 to 12 months
- Histologic resolution may take as long as 2 years
- Prognosis = excellent

IgA nephropathy

- Common presentation is gross hematuria with URI
- C3 is normal
- Confirmation is on renal biopsy – same pathology as HSP
- Treatment?
- Prognosis is related to presence of proteinuria or hypertension

Henoch-Scholein purpura

- Systemic vasculitis affecting multiple organs
 - Skin – purpuric rash in essentially all patients
 - GI – in 33% with abdominal pain, GI bleeding
 - Joints – in 66% with arthralgias and arthritis
 - Kidneys – in 50% with hematuria to more severe with long-term complications
- Clinical diagnosis
- Treatment?

Alport's syndrome

- X-linked inheritance
- Results from mutation in gene for alpha-5 chain of basement membrane collagen
- Associated with sensorineural deafness and hypertension
- Female carriers have less urinary findings and rarely develop renal failure.
- Hypertension and hematuria often develop during childhood with renal failure in teens or as young adult.

Myoglobinuria and Rhabdomyolysis

- No or few RBC's with positive urine dipstick for blood
- May present with dark urine
- Can occur with strenuous exercise in the heat especially if dehydration is present
- Can progress to ARF if not promptly treated
- Rapid diagnosis, fluid replacement, and alkalinization of the urine can improve outcome

Hypercalcuria: Definition

- Urine calcium > 4 mg/kg/d in timed urine collection
- Screening with Ur Ca/Cr ratio
 - > 0.2 in school-aged children and adults
 - > 0.6 in infants from 6 to 12 months of age
 - > 0.8 in infants < 6 months of age
 - Not completely diagnostic as calcium excretion varies with meals

Hypercalcuria: Epidemiology

- Occurs in 3-4% of healthy children
- Occurs in 27-35% of children with isolated hematuria
- In patients with hematuria, hypercalcuria is more common in:
 - Males
 - Caucasians
 - Patients with a family history of nephrolithiasis
 - Patients with gross hematuria
 - Patients with calcium oxalate crystals on urinalysis

Hypercalcuria: Prognosis

- Resolution of both microscopic and gross hematuria occurs in 70-80%
- Hypercalcuria may be episodic
- 17% of children with hypercalcuria developed nephrolithiasis over 5 year follow-up
- Treatment is probably not merited unless nephrolithiasis develops

Evaluation of Hematuria

- Literature often difficult to follow
- Goals for the Primary Care Physician
 - Recognize and confirm the presence of hematuria
 - Identify common etiologies
 - Select those patients with potentially more significant problems related to hematuria for referral

Recognition of Hematuria

- Reasons children are seen and discovered to have hematuria
 - Onset of gross hematuria
 - Onset of urinary or other symptoms with a finding of hematuria
 - Routine visit where urinalysis is required
- Most commonly discovered with dipstick + for blood

Confirmation of Hematuria

- Microscopic examination of centrifuged urine
 - ≥ 5 RBC's/hpf
- Repeat urinalysis with microscopic exam
 - ≥ 5 RBC's/hpf in three specimens collected over a few weeks period

Categories of Hematuria

- Gross hematuria
- Microscopic hematuria with clinical symptoms
- Asymptomatic microscopic hematuria (isolated)
- Asymptomatic microscopic hematuria with proteinuria

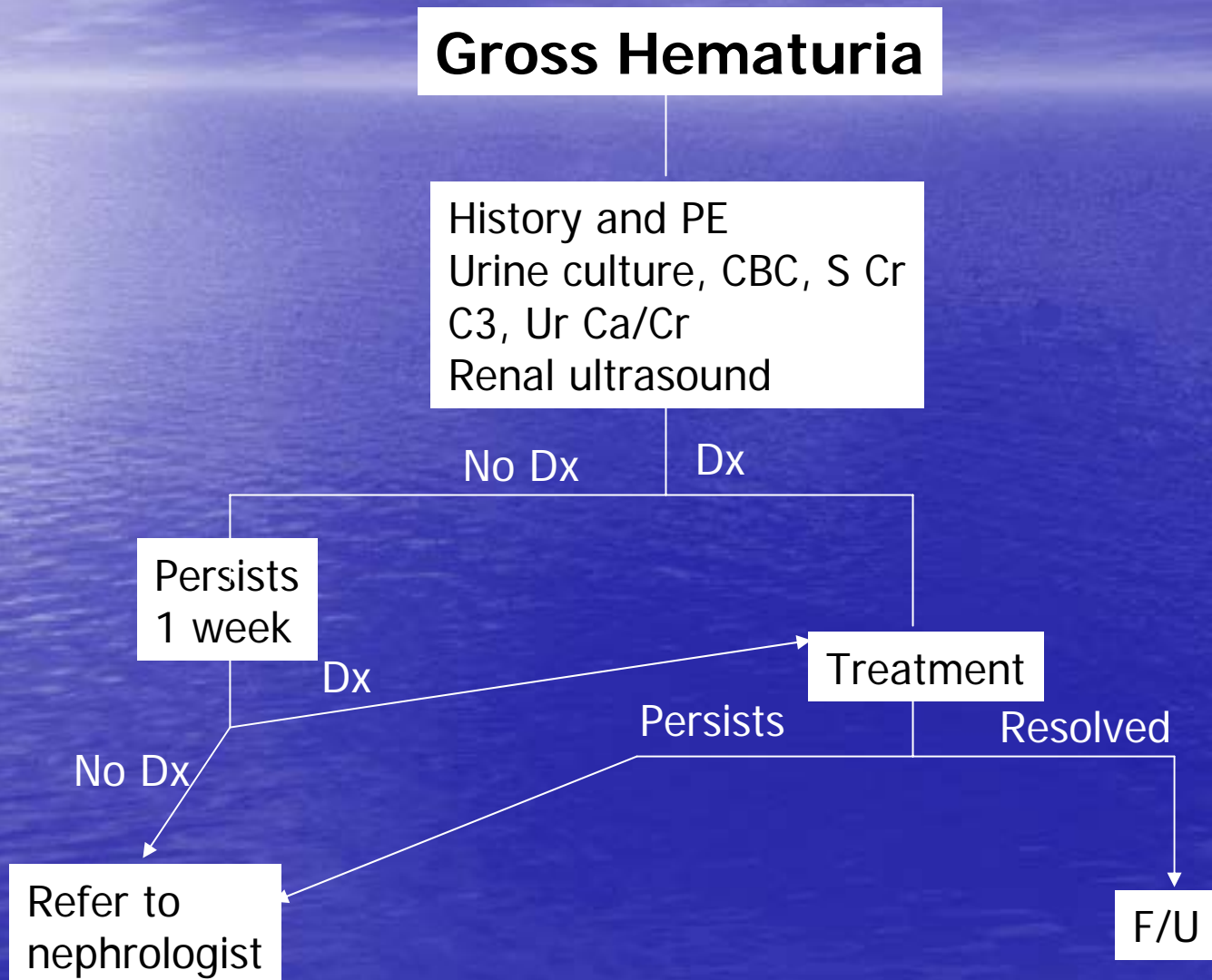
Caveat: Severity of the disease generally varies with the degree of the hematuria and with the presence of proteinuria.

Gross Hematuria

- Uncommon with prevalence of 0.13%
- 56% of these children had an easily recognizable cause

Most Common Diagnoses		Less Obvious Diagnoses	
UTI	26%	Recurrent	5%
Perineal irritation	11%	Acute nephritis	4%
Trauma	7%	UPJ	1%
Meatal ulceration	7%	? UTI	23%
Coag	4%	Unknown, other	12%
Stones	2%		

Algorithm for Gross Hematuria



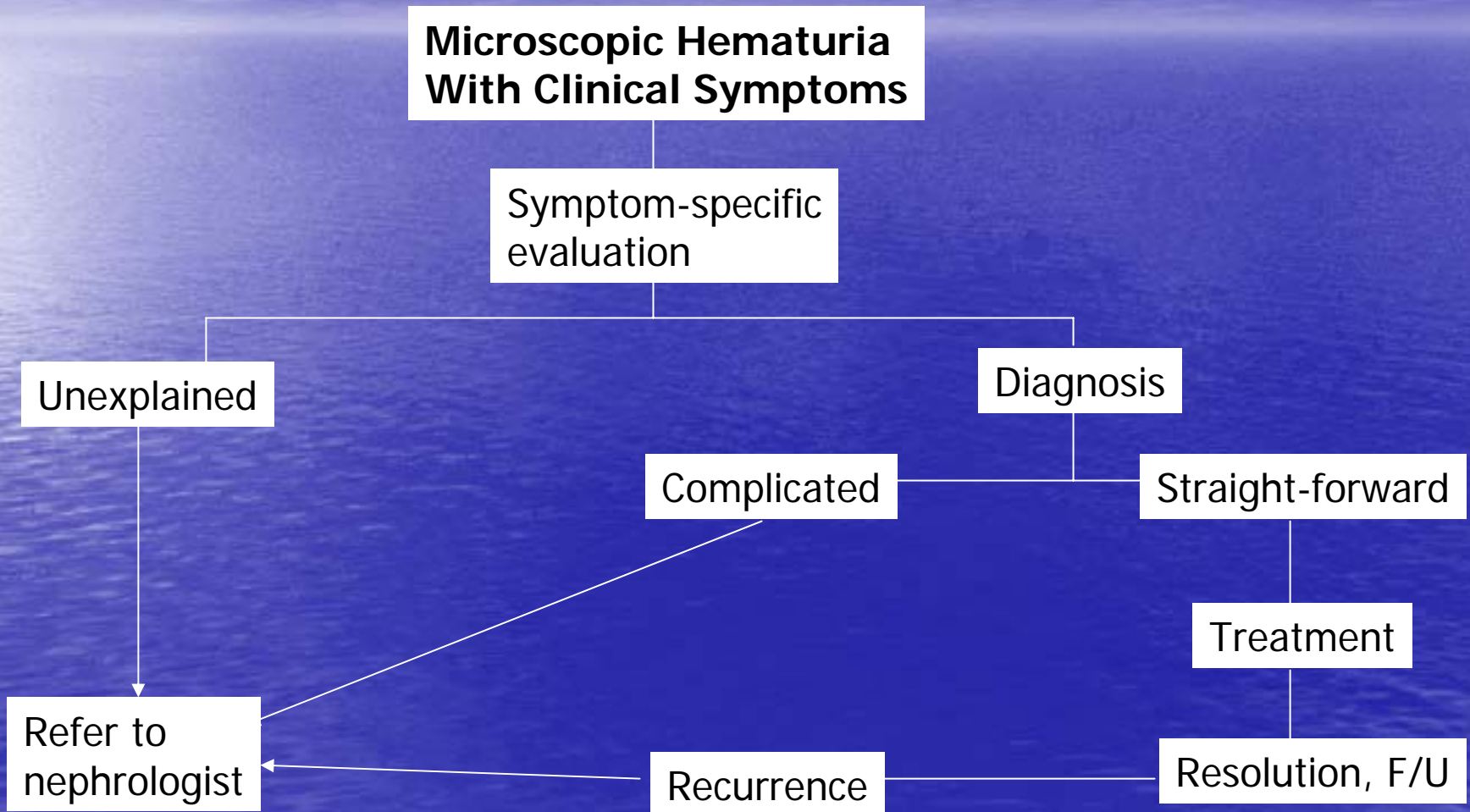
Evaluation for Microscopic Hematuria

- History and physical exam
- Define associated symptoms if present
 - General: fever, malaise, pain, HTN, edema
 - Non-urinary tract: rash, arthritis, jaundice, respiratory, GI, etc.
 - Urinary tract: dysuria, frequency, enuresis, edema, HTN
- Urinalysis for protein
- Determine category
 - Microscopic hematuria with clinical symptoms
 - Asymptomatic microscopic hematuria
 - Asymptomatic microscopic hematuria with proteinuria

Microscopic Hematuria with Clinical Symptoms

- Wide variety of etiologies in this group
 - infectious, renal, rheumatologic, immunologic, lower urinary tract disease, tumors, vascular disease, hematologic, drug-related, and others
- Probably the most difficult for the primary care physician
- Unless a clear diagnosis is readily apparent, these probably need to be referred to a nephrologist.

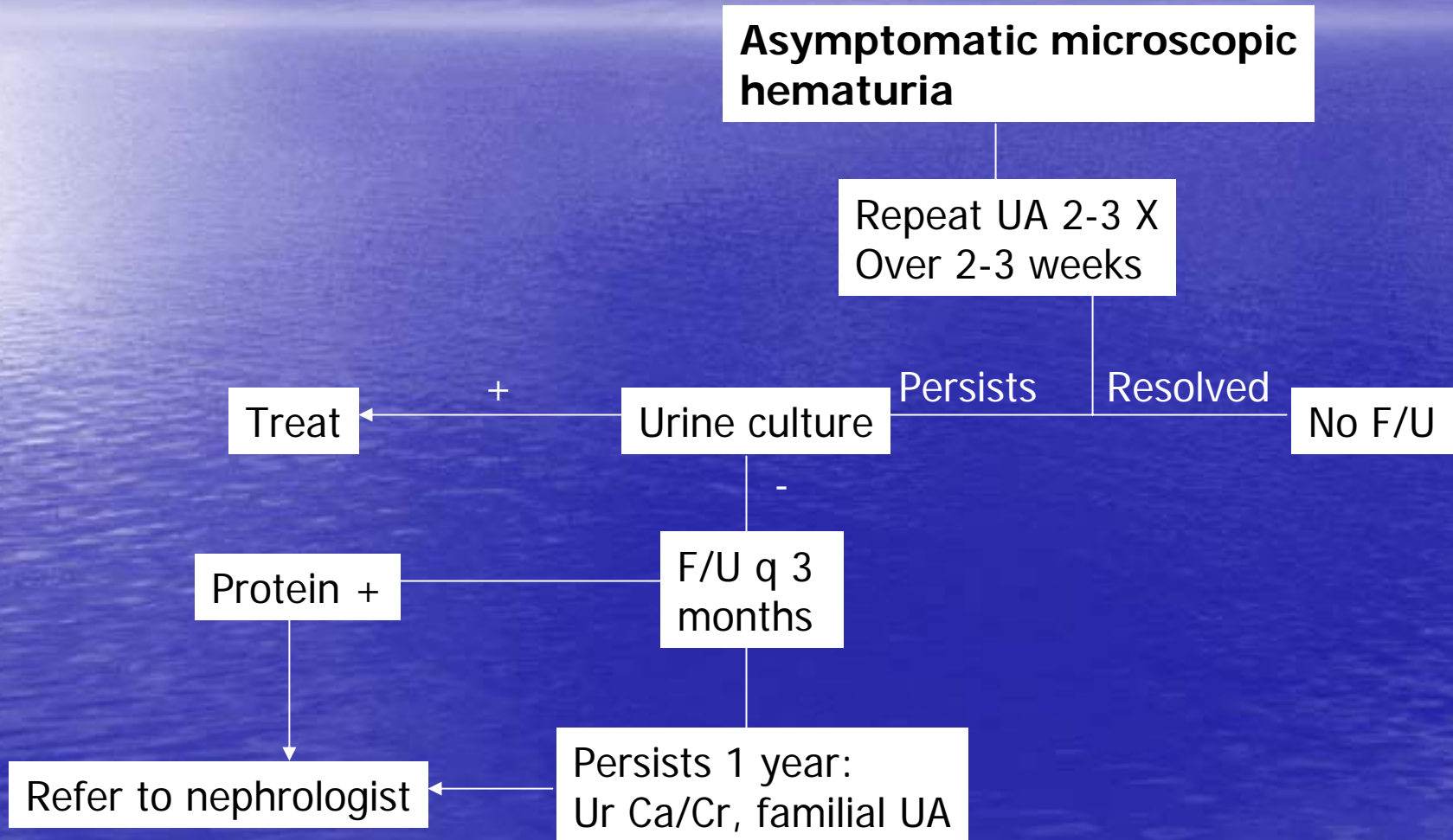
Algorithm for Microscopic Hematuria with Clinical Symptoms



Asymptomatic Microscopic Hematuria

- Common with prevalence of 0.4 to 4.1% of children depending on criteria used to define hematuria
- Indication for repeat urinalysis over the next few weeks
- No further investigation unless hematuria is persistent over these few weeks

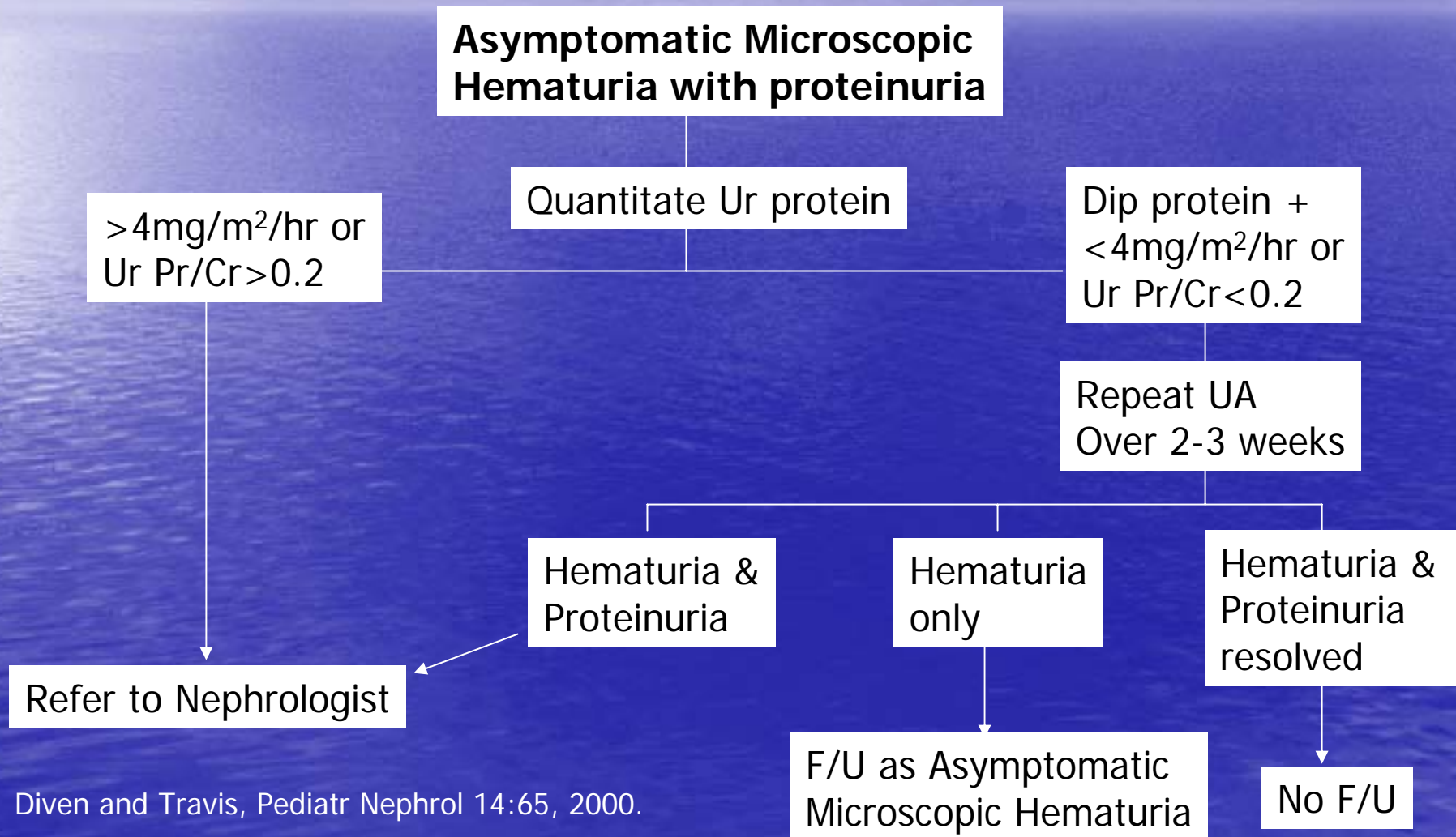
Algorithm for Asymptomatic Microscopic Hematuria



Asymptomatic Microscopic Hematuria with Proteinuria

- Uncommon with prevalence of about 0.06%
- Children with significant renal disease tend to be in this group in epidemiologic surveys
- However, spontaneous resolution may occur in as many as 50% in this category during follow-up.
- Presence of proteinuria strongly suggests glomerular origin of hematuria
- Presence of significant renal disorder is correlated with the amount of proteinuria

Algorithm for Asymptomatic Microscopic Hematuria with Proteinuria



Conclusions

- Hematuria is common in pediatric patients.
- The goals for the primary care physician are to:
 - Recognize and confirm the presence of hematuria.
 - Identify the common etiologies.
 - Select patients who need referral to pediatric nephrologist.
- A complete urinalysis is the first step in the evaluation of hematuria.