The application of urinary flow cytometry in renal diseases

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The clinical utility of urinary flow cytometer is promising, and the cumulative data on this technique is intriguing. Nevertheless, its application in certain populations such as in children, may require careful procedures to ascertain laboratory quality and optimize the balance between the required acceptable quality and the minimization of workload. Specimens from patients with nephrolithiasis who have undergone extracorporeal shock wave lithotripsy may also decrease the accuracy of the test. It is noteworthy to emphasize that all physicians and medical technologists should develop their own criteria for diagnosis or management depending on their cut-off values, patient population, their own limitation and experience in interpreting the information derived from this instrument. Moreover, further study of the comparative clinical relevance between this technique and urine specimens is the sine qua non for confirmation of its clinical utility in managing patients with renal diseases.

Key words: Urinary cell flow cytometer, Urine sediment analysis.

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Objective

To inform the application of urinary flow cytometry in renal diseases

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ชัยพร บุญเฉลิมวิเชียร, วิโรจน์ ไววานิชกิจ, กฤตยา สุธิ์โสภณ, นารา ผริตโภคี, นวพรรณ จารุรักษ์. การประยุกต์ใช้เทคโนโลยีโฟลไซโตเมตรี้ในการวินิจฉัยโรคไต. จุฬาลงกรณ์เวชสาร 2544 ต.ค; 45(10): 915 - 29

การประยุกต์ใช้หลักการของโฟลไซโตเมตรี้ในงานตรวจวิเคราะห์ปัสสาวะเป็นเทคโนโลยีที่ ยอมรับกันว่ามีศักยภาพ แต่อย่างไรก็ตามการนำไปใช้ในกลุ่มประชากรบางกลุ่ม เช่น ผู้ป่วยเด็กยังคงต้อง รอข้อมูลจากงานวิจัยเพิ่มเติม และยังจำเป็นที่จะต้องมีมาตรการที่เหมาะสมเพื่อรักษาคุณภาพของการ ตรวจวินิจฉัยของงานตรวจวิเคราะห์ปัสสาวะ การนำข้อมูลดังกล่าวไปใช้กับผู้ป่วยโรคนิ่วในไต และได้ รับการรักษาด้วย extracorporeal shock wave lithotripsy อาจจะทำให้การแบ่งประเภทของโรคไต คลาดเคลื่อน การนำข้อมูลที่ได้จากการตรวจวิเคราะห์ ดังกล่าวมาใช้ แพทย์ผู้ทำการรักษาตลอดจน เทคนิคการแพทย์ จำเป็นต้องกำหนดมาตรการตลอดจนเกณฑ์การวินิจฉัยที่เหมาะสมตามข้อจำกัด ของแต่ละสถาบัน ประสบการณ์ กลุ่มประชากรในการช่วยวินิจฉัย ตรวจติดตาม ตลอดจนประกอบ การดูแลรักษาผู้ป่วยโรคไต

An overview of clinical utility of urine sediment analysis.

There is cumulative data that urine sediment analysis may aid physicians in proper management of patients with kidney diseases. (1-3) Generally, some typical urine sediment findings are very useful for diagnostic purposes in these following entities Figure 1. (4-8)

- 1. The nephritic syndrome
- 2. The nephrotic syndrome
- 3. Urinary tract infection

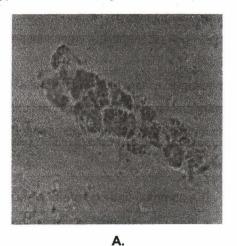
1. The nephritic syndrome (A nephritic – type urine sediment)

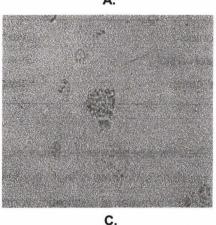
In general, the diagnostic hallmark is composed of the abrupt onset of hematuria, oliguria and hypertension in conjunction with proteinurea. (8)

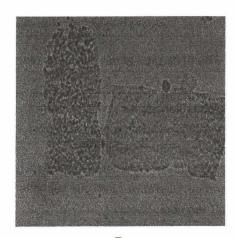
Moreover, the common findings of nephritic syndrome consist of many erythrocytes, frequent casts of varied types (e.g. waxy cast, granular cast, erythrocyte cast, etc).⁽⁷⁻⁸⁾

The presence of waxy cast may herald a sinister prognosis, indicating the onset of serious renal insufficiency. (5) Birch *et al* also classified the urinary erythrocytes into two groups depending on morphology as follows. (9-15)

- Isomorphic erythrocyte: indicating its nonglomerular origin as well as its association with urologic diseases.
- 2. Dysmorphic erythrocyte: indicating its glomerular origin as well as its association with glomerular diseases.







D.

Figure 1. A. renal eptithelial cell cast, B. board cast, C. oval fat body, D. white blood cell cast

The morphology of erythrocytes is affected by many factors; for example, the thickness of glomerular basement membrane, pH change, osmolality and pressure in the renal tubule. (16) To improve the precision of diagnosis of renal diseases based on erythrocyte dysmorphism, some authorities have used acanthocyturia as a marker for glomerular bleeding; the definition of an acanthocyte is its small size and deformation of the cell membrane with extensions of the cytoplasm. The count of acanthocytic erythrocytes must exceed 5 percent. Using these criteria the sensitivity and specificity of this classification for the diagonoses of renal diseases are improved dramatically. (17-18) However, the effective cut-off values to differentiate renal diseases from urological diseases may require further investigations. The etiologies of the nephritic syndrome are shown in Table 1. (4-8)

Table 1. The etiologies of the nephritic syndrome.

Primary glomerulonephritis

- Acute nephritic syndrome e.g. acute poststreptococcal glomerulonephritis
- Rapidly progressive glomerulonephritis e.g. membranoproliferative glomerulonephritis (MPGN), IgA nephropathy
- 3. Nephrotic syndrome e.g. minimal change disease
- 4. Asymptomatic abnormalities of the urinary sediments e.g. IgA nephropathy
- Chronic glomerulonephritis e.g. membranoproliferative glomerulonephritis

Secondary glomerulonephritis

- 1. Lupus nephritis
- 2. Henoch-Schonlein nephritis
- 3. Goodpasture's syndrome
- Other glomerulopathies associated with systemic diseases

Other conditions

- 1. Acute interstitial nephritis
- 2. Malignant hypertension

2. The nephrotic syndrome

The diagnosis of nephrotic syndrome is usually established when the total urine protein exceeds 3.5 gram per day or there is massive proteinuria as defined by total urine protein > 50mg/kg/day or > 40mg/m²/hour in children. Other features include edema, plasma albumin<25 g/L, hyperlipidemia, hypercoagulopathy and lipiduria. (19-20) The classification of the nephrotic syndrome is listed in Table 2. (21) The common findings of urine sediments in patients with nephrotic syndrome are as listed in Table 3. (2-5,20)

Table 2. The classification of nephrotic syndrome.

Minimal change nephrotic syndrome

Focal segmental glomerulosclerosis (FSGS)

Diffuse mesengial proliferative glomerulonephritis

(MesPGN)

Diffuse mesangiocapillary glomerulonephritis (MCGN) or Membranoproliferative glomerulonephritis (MPGN) Diffuse membranous glomerulonephropathy (MGN)

Table 3. The common findings of urine sediments in the patients with nephrotic syndrome.

*	
Lipid droplets	Oval fat bodies
Cholesterol crystal	Granular casts
Epithelial casts	Fatty casts

The difference between the nephrotic syndrome and the nephritic syndrome is that very few or even no erythrocytes are seen in nephrotic syndrome. (4-8,20) Despite that lipiduria is a rather good marker, the disadvantages of using this finding as an indicator

for the nephrotic syndrome are low specificity and sensitivity for diagnosis. (22) Certain situations like the polycystic kidney diseases, acute tubular necrosis, Fabry's disease, and some abnormalities of lipid metabolism can produce lipiduria without the nephrotic syndrome. (4-8,20)

3. Urinary tract infection

Diagnosis can be based on a urine culture obtained from a clean catch or a catheterized specimen: the diagnosis is established when colony counts are greater than 100,000 in a clean catch urine or in any urine culture in excess of 5,000 colonies from urine obtained from a suprapubic puncture or catheterized specimen is significant. (22) To make the diagnosis of urinary tract infection, the method of the specimen collection and the colony counts must be taken into account. (22) The common findings in urine sediment are leukocytes, white blood cells, casts, or bacteria. (22) The range of sensitivity and specificity of the presence of white blood cells for diagnosis of urinary tract infection in children is about 32-100 % and 45-98 % respectively. (23-24) When using the bacteria obtained from the microscopic examination, sensitivity and specificity are about 16-99 % and 11-100 %. (23-24) If the positive of leukocyte esterase or positive of nitrite or positive of microscopic examination is used for the diagnosis of urinary tract infection in children, the sensitivity and sensitivity will reach about 99.8 % and 70 % respectively. (23-24)

Principle of the urinary cell flow cytometer

Flow cytometry measures fluorescence and optical characteristics of single cells, including any particles such as nuclei, latex beads, or

microorganisms. (25-26) Physical properties, such as size (represented by forward angle light scatter) and internal complexity (represented by right-angle scatter) can differentiate certain cell populations. (25-26) Fluorescent dves can bind with different cellular components such as DNA or RNA. (25-26) In addition, antibodies conjugated to fluorescent dyes can bind specific proteins inside cells or on the cell membrane. (25-26) When labeled cells are passed by a light source, the fluorescent molecules are excited to a higher energy state. (25-26) When returning to their resting states, the fluorochromes will emit light energy at higher wavelengths. (25-27) Commonly used dyes include propidium iodide and fluorescein. (25-27) Cells in suspension are drawn into a stream created by a surrounding sheath of isotonic fluid that creates laminar flow, allowing the cells to pass cell by cell through an interrogation point. (25-27) At the interrogation point, a beam of monochromatic light, usually from a laser, intersects the cells. (25-27) Emitted light is given off in all directions and is collected via optics that direct the light to a series of filters and dichroic mirrors that isolate particular wavelength band. (25-27) The light signals are detected by photomultiplier tubes and digitized for computer analysis. (25-27) The result is usually displayed in a histogram or two-dimensional dot-plot format. (25-27)

The principle of flow cytometry is thus based on the analysis of the properties of the particles by irradiating a laser beam on the particles and measuring fluorescence and scattered light. (25-28) The scattered light, fluorescence, and impedance are recorded and converted into electrical signals. (25-28) Cell or particle distributions are demonstrated and analyzed in histograms and scattergrams. (25-28) The flow cytometry principle is illustrated in Figure 2.

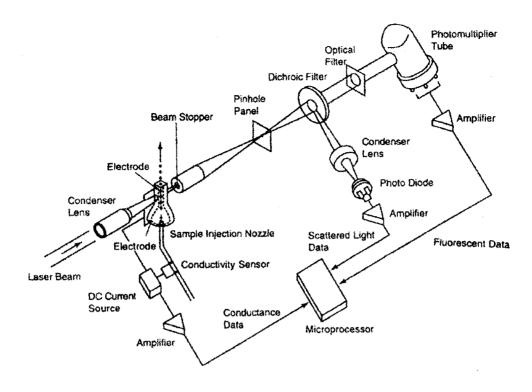


Figure 2. Principle of flow cytometry in the UF - 100

For each electrical signal, the height and width are measured. (25-28) One example of a urinary flow cytometer is the UF-100 by TOA MEDICAL ELECTRONICS, this instrument exploits fluorescence and forward light pulse measurement to produce scattergrams and impedance measurements to indicate the volume of cells Figure 3-5⁽²⁸⁾ The electric impedance is detected by using two electrodes attached to both sides of the orifice, A stable D.C. is passed through the circuit. (28-29) Whenever a urine cell passes through this orifice, the voltage will change in proportion to the impedance change due to different volume of cell. (28-29) Hyodo et al have proposed criteria to discriminate types of abnormality of red blood cells by using the Forward scatter (Fsc). (30-31) The Fsc indicates the cross-sectional area of the cells in proportion to the luminocity whereas the forward scatter pulse width (FSCW) represents the length of cells and the fluorescence length (FL) represents the amount of

membranous protein in the cell membrane and DNA or RNA in the nucleus. (28-31) Moreover, the fluorescence pulse width (FLW) reflects the length of the stained portion in the cells. When the Fsc of ch 126 and Fsc of ch 84 are used as important indicators Figure 6. the diagnosis of dysmorphic erythrocytes is made if \geq 80 % of erythrocytes have Fsc \leq ch 126 and <80 % of erythrocytes have Fsc ≥ ch 84 suggesting glomerular erythrocytes; whereas, the diagnosis of isomorphic erythrocytes is considered when > 80 % of erythrocytes have Fsc ≥ ch 84 which suggests rionglomerular red blood cells. (30-31) Furthermore, in cases where < 80% of erythrocytes have < ch 126 and < 80 % of erythrocytes have Fsc > ch 84, a mixed type of erythrocyte origin between glomerular bleeding and non-glomerular bleeding is a likely diagnosis. (30-31) The percentage of 80 % is used for the discrimination level because this criterion is generally supported. (32-33) The ranges of Fsc intensity

between 84 and 126 corresponds to a red blood cell size of 4 to 6 μ m. When the sizes of spherical latex particles were analyzed, the size of 1 μ m corresponded with Fsc intensity of 21. Thus, the urine cell flow cytometer may make routine urinalysis

more quantitative, provide additional information on erythrocyte morphology, giving scattergrams as well as histograms to help physicians gain insights in the of diagnosis and management of diseases.

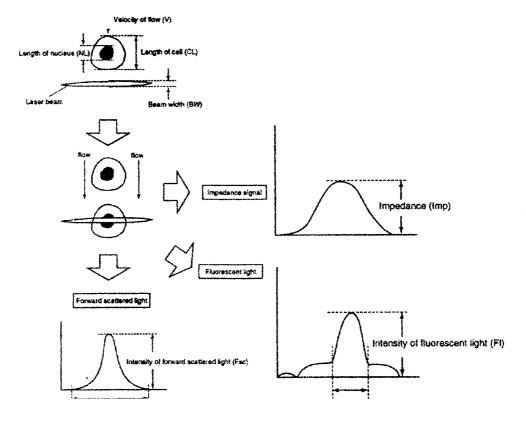


Figure 3. Demonstration about the source of parameters from UF - 100

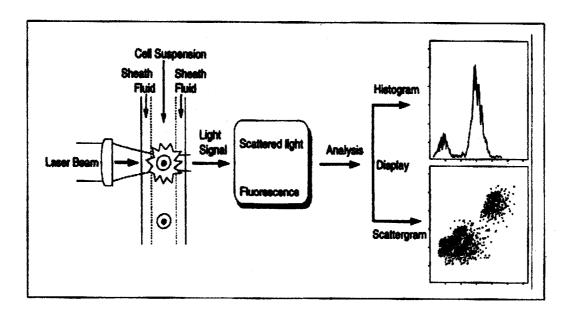


Figure 4. Demonstration of source of the parameters in UF -100

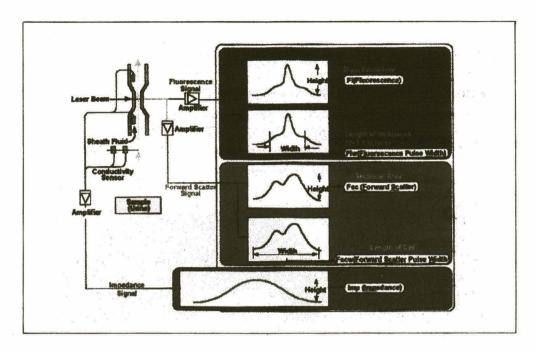


Figure 5. Demonstration of source of the parameters in UF - 100

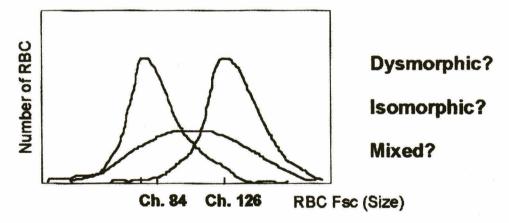


Figure 6. The Fsc as a parameter for discrimination of the origin of hematuria

The application of urinary flow cytometer in renal disease

The benefit of having the urinary flow cytometer in the laboratory comes from balancing routine laboratory work and required quality standards. In certain circumstances, like in laboratory in a medical school, or in hospitals responsible for a large number of specimens daily, automated instruments will play important role in reducing the need for unnecessary manual examination. (30-31,34) An effective screening tool is essential in cases of an unavoidable overwhelming

daily workload. (34) Irrespective of whether manual urinalysis or automated urinary flow cytometer based urinalysis is used in a laboratory, to achieve satisfactory laboratory standards, proper collection, specimen transportation, and specimen handling must still be emphasized. (35) When a new technique is used in a laboratory, formal training and appropriate evaluating and surveillance protocols should ascertain the competency of the technicians. Parallel testing may be necessary by comparison with mainstay laboratory procedures and a backup plan should be available

in case of the occurrence of discrepancy between two procedures or instruments. In most cases of urine specimens analysis performed by the urinary flow cytometer (Data obtained from using UF-100), a good correlation is obvious when compared with standardized microscopic methods. (36-37) Most cases of microhematruia seem to be isolated, and the prevalence of an abnormal renal biopsy specimen in isolated microhematuria in children without a family history was 40 %. (38) For screening purposes in this clinical setting, the urinary flow cytometer may not pose any diahnostic problems. (30-31) Another benefit of using this instrument is that the physician can obtain the extra information on red blood cell morphology easily, and the classification of the origin of red blood cells in the urine specimens may be feasible. (30-31) This classification of red blood cells may help to provide proper and prompt management of patients with hematuria or clinical manifestations of glomerulonephritis. (10-15,17,30,31,39) Some equivocal classification may be encountered in specimens obtained from patients who have undergone extracorporeal shock wave lithotripsy (ESWL) and patients with bladder cancer who have undergone transurethral resection. The findings of the test in these cases may suggest mixed-type when the above criteria are used. (30-31) When the microscopical examination applied to all cases with ESWL, this showed that it was isomorphic hematuria. (30-31) This sort of specimens had an FSC intensity ≥ 84 in more than 80 % of urinary red blood cells population and < 80 % of all red blood cells had FSC intensity < 126, or it might have fallen in the overlapped size; \geq 80 % of all red blood cells had FSC intensity < 126, and> 80 % of all red blood cells had FSC intensity > 84. (30-31)

The misclassification of red blood cells is also influenced by the storage condition of urine specimen and the physiological urinary red blood cells. (16) When bacterial counts are extremely high, this bacterial interference will affect the counts of red blood cells. (30-31) Moreover, when the red blood cells counts are extremely high, the microscopic exami-nation of urine sediment is mandatory. (30-31) According to experience with UF-100, a high number of epithelial cells will mandate the microscopic examination of urine specimens. (30-31) The drawback of using this instrument is that the specimens from newborns and very young children under three years of age seem not to be analyzed properly due to very poor storage condition before an acceptable volume is reached. (40-41) Our experience with the UF-100, raises problems about bacterial counts obtained by this instrument, since the bacterial count is expressed in cell/I which seem to be unfamiliar to most physicians. Such bacterial counts cannot be used, as are conventional criteria, for diagnosing urinary tract infection Table 4, Figure 7. (35-36) We explain these high results by three hypo-theses as follows:

- This may come from the limitation of differentiation between organism and nonspecific particles commonly found in urine which can be interpreted carefully by using the proper reference range and adjusted according to evaluation protocols in each own institute^(90-31,41)
- 2. The asymptomatic bacteriuria may contribute to such problem. The prevalence of this disease varies depending on age, sex, and certain clinical settings, thereby the significance of this interference should be considered before using this technique. (42-43)

Table 4. Data obtained from normal adult population in our laboratory based on the urinary cell flow cytometer*

Parameters	cell/μL, cell/HPF(95% coefficient interval)
red blood cell	4.64, 0.84 (2.54-6.74, 0.46-1.22)
white blood cell	7.16, 1.28 (3.77-10.54, 0.67-1.9)
epithelial cell	5.59, 1.01 (1.88-9.31, 0.34-1.68)
cast	0.14, 0.41 (0.06-0.23, 0.18-0.64)
bacteria	409.14, 73.56 (76.13-742.15, 13.70-133.59)

- * From 38 normal adults with 21 are male (55.3%). Normal population is defined as:
- Not have undergone any treatments in the previous 6 weeks for any diseases
- Absence of hypertension
- Not menstruating or pregnant
- Not taking any treatments, by physician, home remedy, over-the-counter medication for urinary tract infection

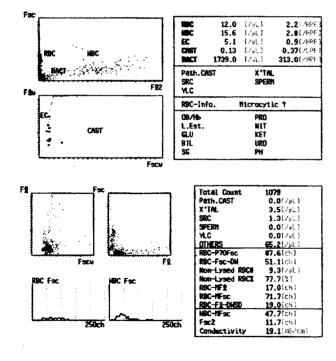


Figure 7. A normal subject without symptomatic urinary tract infection, data indicating that bacteria count by this method may be higher than conventional method.

3. Normal flora may be counted as pathologic ones, and this hypothesis can be proved by using the proper urine culture technique. (41-43)

Hence we recommend all laboratories set their own cutoff levels to suit their facility, their population, standard operating procedures, prevalence of certain diseases, and their experience. However, quantitative measurement of organisms: by using microscopic examination, has varied sensitivity, specificity, intraobserver, and inter-observer variability(23-24) Comparing the results with urine culture may be a more favorable and feasible method. (36) The instrument has a measurement range below 40,000 per 9.0 µl of urine, thereby a specimen with high concentration is outside this limit of measurement, its reliability may be decreased. (30-31) Based on our observation, markedly turbid urine specimens from our pediatric subjects such as urine containing significant amorphous materials or lipiduria, will strongly interfere with cell count by this instrument, therefore proper dilution protocols may be warranted Figure 8. Furthermore, some controversial pattern of histogram in pediatric samples obtained from previous observation by other

researchers as well as ours show two distinct population of white blood cells, the diagnostic utility of which may need further evaluations. (40)

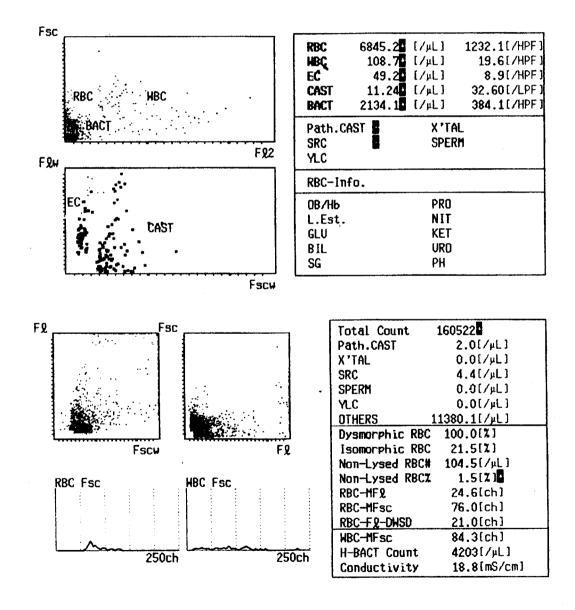


Figure 8. Specimens obtained from our subject with nephrotic syndrome, data indicating that all parameters are high, when care ful microscopic examination is done, we found that lipiduria may interfere the particle or cell counts in this clinical setting.

Summary

The clinical utility of urine flow cytometer is promising. Its application in certain population such as in children may require procedures to ascertain the laboratory quality and optimize the balance between quality and minimization of workload. It is noteworthy to emphasize that all physicians and medical technologists should develop their own criteria for diagnostic or management aspects depending on

their cut – off values, patient population, their own limitations and their experience in interpreting the information derived from this instrument such as the scattergram or the histogram. A summary of research evaluating this instrument is shown in Table 5. (30-31, 34-37) Further studies on the comparative clinical relevance between this technique and urine specimens in a large array of population with varied diseases are necessary.

Table 5. Related researches on urinary cell flow cytometer.

Research group/year of study	Details
1. Hyodo T, et <i>al.</i> / 1995	The research group indicated that flow cytometricAnalysis of urinary blood
	cells was fast, simple, Reliable method to differentiate glomerular and non-
	glomerular hematuria.(The sensitivity and sensitivity of detecting glomerular
	red blood cells were 100% and 92.54%, respectively
2. Hyodo T, et <i>al.</i> / 1999	The automated urinary flow cytometer is useful as a routine screening test for
	differentiate between glomerular and non-glomerular haematuria. A proposed
	Kitasato Univeristy Kidney Center Criteria is used to differentiate between two
	kinds of haematuria. The sensitivity and specificity of this instrument using
	these criteria in diagnosing glomerular haematuria were 90.3% and 92.5% respectively.
3. Kouri TT, et <i>al.</i> , 1999	They indicated that the urinary flow cytometer had a high correlation of white
	blood cell and red blood cell between the manual chamber counting and this
	instrument (r = 0.98, and 0.88, respectively). Identification of bacteria by this
	instrument, has a sensitivity and specificity of 55% and 90% respectively,
	compared with bacterial culture cutoff of > 10 ³ colony-form unit per milliliter
Research group/year of study	Details
4. Ben-Erza J <i>et al.</i> , 1998	They concluded that the UF-100 could perform reliable quantitative
	microscopic urinalysis. Good correlation between manual microscopic
	method and this automated urinalysis analyzer was achieved. (gamma
	statistics: 0.880-0.970)
5. Hyodo T, et <i>al.</i> , 1997	They analyzed the values of urinary red blood cells in the healthy adults by an
	automated urinary flow cytometer. Their result pointed out that the hematuria
	was e"11.0 cells /microliter and the results seemed corresponded to the repor
	of Birch et al.
6. Muranaka K., 1996	The correlation of this method with microscopy is excellent($r = 0.86$,
	agreement ratio = 97.7%). The specificity and sensitivity of the UF-100 for
	bacteria in urine is good (sensitivity = 77.8%, specificity = 90.0%).

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References

- Henry JB. Clinical Diagnosis and Management by Laboratory Methods. Philadelphia: W.B. Saunders, 1984.
- Chen KJ.Nephrology. In: Barone MA.ed. The Harriet Lane Handbook.14th ed. St. Louis: Mosby -Year Book, 1996:381 - 401
- Bensema DJ.Hematuria. In: Haist SA, Robbins JB, Gomella LG,eds. Internal Medicine on Call.
 2nd ed. Stamford: Appleton & Lange, 1997: 147 - 51
- Fenili D. The clinical relevance of urine sediment analysis. The Sysmex Urine Flow Cytometry Workshop. Hamburg: Sysmex Coparation 1997:5 - 11
- 5. สมชาย เอี่ยมอ่อง, เกื้อเกียรติ ประดิษฐ์พรศิลป์, เกรียง ตั้งสง่า. การตรวจและการแปลผลการตรวจทาง ห้องปฏิบัติการในโรคไต (Laboratory investigation and interpretation in renal diseases) ใน: สมชาย เอี่ยมอ่อง, เกรียง ตั้งสง่า, บรรณาธิการ. โรคไต กลไก พยาธิสรีรวิทยา การรักษา. กรุงเทพฯ:
- Bergstein JM. Glomerular diseases.In: Behrman RE, Kliegman RM, Arvin AM, Nelson WE,eds. Nelson Texbook of Pediatrics. 15th ed. Philadelphia: W.B. Saunders, 1996:1484 - 5
- 7. Japanese Committee for Clinical Laboratory Standards. Urine sediment analysis. JCCLS

- guideline GP1-P2. Tokyo: JCCLS 1995: 21
- 8. Brady HR, O'Meara YM, Brenner BM. The major glomerulopathies. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, eds. Harrison's Principles of Internal Medicine. New York: McGraws-Hill. 1996: 1536 1545
- 9. Birch DF, Fairley KF.Hematuria: glomerular or nonglomerular? Lancet 1979 Oct 20;2(8147): 845 - 6
- Fassett RG, Horgan B, Mathew TH. Detection of glomerular bleeding by phase-contrast microscopy. Lancet 1982i: 1432 - 4
- 11. Fasset RG, Horgan BA, Gove D, Mathew TH. Scanning electron microscopy of glomerular and non-glomerular red blood cells. Clin Nephrol 1983 Jul;20(1):11 - 6
- 12. Rizzoni G, Braggion F, Zacchello G. Evaluation of glomerular and nonglomerular hematuria by phase-contrast microscopy. J Pediatr 1983 Sep;103(3):370 - 4
- 13. Chang BS. Red cell morphology as a diagnostic aid in hematuria. JAMA 1984 Oct 5;252(13): 1747 9
- 14. Obroniecka I. Values of phase-contrast microscopy in the etiological diagnosis of hematuria in adults. Part I. Establishing individual norms for glomerular hematuria. Pol Merkuriusz Lek 1998 Nov;5(29):277 - 9
- 15. Gerc V, Schubert A, Burnier M. Differentiation between glomerular and non-glomerular erythrocyturia: what is the value of differential microhematuria diagnosis? Schweiz Rundsch Med Prax 1997 Jul 30;86 (31-32):1198 - 203
- 16. Bernard DB, Barchman MJ. Clinical and laboratory

- evaluation of altered renal function. In: Krane RJ,Siroky MB, Fitzpatrick JM, eds. Clinical Urology. Philadelphia: Lippincott, 1994:17-45
- 17. Kitamoto Y,Tomita M, Akamine M, Inoue T, Itoh J, Takamori H, Sato T. Differentiation of hematuria using a uniquely shaped red cell. Nephron 1993;64(1):32 6
- 18. Lettgen B, Wohlmuth A. Validity of G₁—cells in the differentiation between glomerular and non-glomerular hematuria in children. Pediatr Nephrol 1995 Aug;9(4):435 7
- 19. Clark AG, Barratt TM, Steroid responsive nephrotic sysndrome. In: Barratt TM, Avner ED, Harman WE, eds. Pediatric Nephrology. 4 th ed. Baltimore: William & Wilkins, 1999:731 - 47
- 20. Bergstein JM. Nephrotic syndrome. In: Behrman RE, Kliegman RM, Arvin AM, Nelson WE, eds. Nelson Textbook of Pediatrics. 15 th ed. Philadelphia: W.B.Saunders, 1996:1500
- 21. International Study of Kidney Diseases in Children. Nephrotic syndrome in children: prediction of histopathology from clinical and laboratory characteristics at time of diagnosis. Kidney I nt 1978 Feb;13(2):159 - 65
- 22. Walker RD. Vesicoureteral reflux and urinary tract infection in children. In: Gillenwater JY, Duckett JW, Grayhack JT, Howards SS,eds. Adult and Pediatric Urology. St Louis: Mosby, 1996:2259 - 95
- 23. Pezzlo M. Detection of urinary tract infection by rapid methods. Clin Microbiol Rev 1988 Jul; 1(3):268 80
- 24. Waisman Y, Zerem E, Amir L, Mimouri M. The validity of the uriscreen test for early detection of urinary tract infection in children. Pediatrics

- 1999 Oct; 104(4):e 41
- 25. Mandy FF, Bergeron M, Minkus T. Principles of flow cytometry. Transfus Sci 1995 Dec;16(4): 303 14
- 26. Brown M, Wittwer C. Flow cytometry: principles and clinical applications in hematology. *Clin Chem* 2000 Aug; 46(8 pt 2): 1221-9
- 27. Orfao A, Ruiz-Arguelles A, Lacombe F, Ault K, Basso G, Danova M. Flow cytometry: its applications in hematology. Haematologica 1995 Jan-Feb; 80(1): 69 81
- 28.Taulaniemi A. The UF-100[™]: principle and operation
 The Sysmex Urine Flow Cytometry Workshop.
 Hamburg: Sysmex Coperation, 1997: 12-7
- 29. Nakamoto H. Automated urinalysis. Sysmex J Int 1996; 6(2) 168-72 (Product of Sysmex Coperation
- 30.Hyodo T, Kumano K, Sakai T. Differential diagnosis between glomerular and non glomerular hematuria by automated urinary flow cytometry. Kitasato University Kidney Center criteria. Nephron 1999;82(4):312 23
- 31. Hyodo T, Kumano K, Haga M, Sakai T. Detection of glomerular and non glomerular red blood cells by automated urinary sediment analyzer.
 Nippon Jinzo Gakkai Shi 1995 Jan;37(1):
 35 43
- 32. Tsukahara H, Yoshimoto M, Sudo M. Determination of the site responsible for hematuria. Shoni Igaku 1990;23: 773-88 (In Japanese)
- 33. Hyodo T, Miyagawa M. Classification of hematuria using a real-time cofocal scanning laser microscope. Igaku No Ayumi 1992;162:935 (In Japanese)
- 34. Ben-Ezra J, Bork L, McPherson RA. Evaluation of

- the Sysmex UF-100 automated urinalysis analyzer. Clin Chem 1998 Jan;44(1):92 5
- 35. Hyodo T, Kumano K, Haga M, Sakai T, Fukuda M, Isami Y, Okada T. Analysis of urinary red blood cells of healthy individuals by an automated urinary flow cytometer. Nephron 1997;75(4):451-7
- 36. Kouri TT, Kahkonen U, Malminiemi K, Vuento R, Rowan RM. Evaluation of Sysmex UF-100 urine flow cytometer vs chamber counting of supravitally stained specimens and conventional bacterial cultures. Am J Clin Pathol 1999 Jul;112(1):25 35
- 37. Muranaka K. Clinical uses of the UF-100[™] for the diagnosis of urinary tract infection. Sysmex

 J Int 1996;6(1):46-50 (Product of Sysmex Coperation
- 38. Trachtman H, Weiss R, Bennett B, Greifer I. Isolated hematuria in children: indications for

- a renal biopsy. Kidney Int 1984 Jan;25(1): 94 9
- 39. Funfstuck R, Stein G. Erythrocytes in the urine: glomerulonephritis or other source of bleeding. Answer with the microscope. MMW Fortschr Med 2000 Mar 2;142(9):30 2
- 40. Herkner K. Analysis of paediatric urine samples.

 The Sysmex Uurine Fiow Cytometry

 Workshop. Hamburg: Sysmex Coperation,

 1997: 41 7
- 41. Lun A, Ziebig R, Hammer H, Otting U, Filler G, Sinha P. Reference values for neonates and children for the UF-100 urine flow cytometer.

 Clin Chem 1999 Oct; 45(10):1879 80
- 42. Raman GV, Pead L, Lee HA, Maskell R. A blind controlled trial of phase-contrast microscopy by two observers for evaluating the source of haematuria. Nephron 1986;44(4): 304 8

กิจกรรมการศึกษาต่อเนื่องสำหรับแพทย์

ท่านสามารถได้รับการรับรองอย่างเป็นทางการสำหรับกิจกรรมการศึกษาต่อเนื่องสำหรับแพทย์ กลุ่มที่ 3 ประเภทที่ 23 (ศึกษาด้วยตนเอง) โดยศูนย์การศึกษาต่อเนื่องของแพทย์ จุฬาลงกรณ์มหาวิทยาลัย ตามเกณฑ์ของศูนย์การศึกษาต่อเนื่องของแพทย์แห่งแพทยสภา (ศนพ.) จากการอ่านบทความเรื่อง "การประยุกต์ใช้เทคโนโลยีโฟลไซโตเมตรี้ในการวินิจฉัยโรคไต" โดยตอบคำถามข้างล่างนี้ พร้อมกับส่ง คำตอบที่ท่านคิดว่าถูกต้องโดยใช้แบบฟอร์มคำตอบท้ายคำถาม แล้วใส่ของพร้อมของเปล่า (ไม่ต้องติดแสตมป์) จำหน้าของถึงตัวท่าน ส่งถึง

ศ. นพ. สุทธิพร จิตต์มิตรภาพ
 บรรณาธิการจุฬาลงกรณ์เวชสาร

และประธานคณะกรรมการการศึกษาต่อเนื่อง
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
หน่วยจุฬาลงกรณ์เวชสาร
ตึกอบรมวิชาการ ชั้นล่าง

เขตปทุมวัน กทม. 10330

จุฬาลงกรณ์เวชสารขอสงวนสิทธิ์ที่จะส่งเฉลยคำตอบพร้อมหนังสือรับรองกิจกรรมการศึกษา ต่อเนื่องอย่างเป็นทางการดังกล่าวแล้วข้างต้น สำหรับท่านที่เป็นสมาชิกจุฬาลงกรณ์เวชสารเท่านั้น สำหรับ ท่านที่ยังไม่เป็นสมาชิกแต่ถ้าท่านสมัครเข้าเป็นสมาชิกจุฬาลงกรณ์เวชสารสำหรับวารสารปี 2545 (เพียง 200 บาทต่อปี) ทางจุฬาลงกรณ์เวชสารยินดีดำเนินการส่งเฉลยคำตอบพร้อมหนังสือรับรองให้ตั้งแต่ฉบับ กันยายน 2544 จนถึงฉบับเดือน ธันวาคม 2545

คำถาม - คำตอบ

- 1. ลักษณะตะกอนปัสสาวะที่มีองค์ประกอบต่อไปนี้ช่วยบ่งชี้ว่าผู้ป่วยน่าจะมีการทำงานของไตเสื่อม อย่างรุนแรง (severe renal insufficiency) ?
 - ก. granular cast
 - 1. waxy cast
 - ค. white blood cell cast
 - 1. red blood cell cast
 - ৭. hyaline cast

คำตอบ สำหรับบทความเรื่อง "การประยุกต์ใช้เทคโนโลยีโฟลไซโตเมตรี้ในการวินิจฉัยโรคไต" จุฬาลงกรณ์เวชสาร ปีที่ 45 ฉบับที่ 10 เดือนตุลาคม พ.ศ.2545





- 2. มักพบลักษณะใดต่อไปนี้ในผู้ป่วย nephrotic syndrome ?
 - n. lipiduria
 - 1. hemoglobinuria
 - ค. polyuria
 - 1. bleeding tendency
 - ৰ. severe hypotension
- 3. ขนาดของเซลที่วัดได้จากเครื่อง urine cell flow cytometer(UF-100) มีขนาด 126 ch เทียบเท่ากับ ขนาดประมาณกี่ µm ?
 - ก. 84
 - ป. 126
 - ค. 21
 - **1**. 4
 - a. 6
- 4. ข้อความต่อไปนี้ข้อใดถูกต้อง
 - ก. จะวินิจฉัย dysmorphic erythrocyte ได้เมื่อ น้อยกว่า 80 เปอร์เซ็นต์ ของเม็ดโลหิตแดงมีขนาด เล็กกว่า 126 ch และ พบว่าน้อยกว่า 80 เปอร์เซ็นต์ ของเม็ดโลหิตแดงมีขนาดใหญ่กว่า 84 ch
 - ข. จะวินิจฉัย dysmorphic erythrocyte ได้เมื่อ มากกว่าหรือเท่ากับ 80 เปอร์เซ็นต์ของเม็ดโลหิตแดง มีขนาดน้อยกว่า 126 ch และน้อยกว่า 80% ของเม็ดโลหิตแดงขนาดโตกว่า 84 ch
 - ค. จะวินิจฉัย dysmorphic erythrocyte ได้เมื่อ มากกว่า 80 เปอร์เซ็นต์ของเม็ดโลหิตแดง มีขนาดโต กว่า 84 ch
 - ง. จะวินิจฉัย non-glomerular red blood cell ได้เมื่อ มากกว่าหรือเท่ากับ 80 เบ๋อร์เซ็นต์ของเม็ด โลหิตแดง มีขนาดน้อยกว่า 126 ch และน้อยกว่า 80% ของเม็ดโลหิตแดงขนาดโตกว่า 84 ch
 - จ. จะวินิจฉัย non-glomerular red blood cell ได้เมื่อ น้อยกว่า 80 เปอร์เซ็นต์ ของเม็ดโลหิตแดงมี ขนาดเล็กกว่า 126 ch และพบว่าน้อยกว่า 80 เปอร์เซ็นต์ ของเม็ดโลหิตแดงมีขนาดใหญ่กว่า 84 ch
- 5. ข้อใดเป็นจุดประสงค์ของการบอกแหล่งกำเนิดของเม็ดโลหิตแดงในตะกอนของปัสสาวะ
 - ก. ช่วยในการวินิจฉัยแยกโรค
 - ข. ช่วยเสริมความเข้าใจเกี่ยวกับพยาธิกำเนิดของโรคไต
 - ค. ช่วยประเมินความจำเป็นของการตรวจเพิ่มเติมด้วยหัตถการที่ invasive หรือ ราคาแพง
 - ง. ช่วยลดภาระของการตรวจวินิจฉัยด้วยกล้องที่ซ้ำซ้อน
 - จ. ถูกทุกข้อ

ท่านที่ประสงค์จะได้รับเครดิตการศึกษาต่อเนื่อง (CME credit) กรุณาส่งคำตอบ

ศาสตราจารย์นายแพทย์สุทธิพร จิตต์มิตรภาพ ประธานคณะกรรมการการศึกษาต่อเนื่อง คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย หน่วยจุฬาลงกรณ์เวชสาร ตึกอบรมวิชาการ ขั้นล่าง คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย เขตปทุมวัน กทม. 10330