User Report

Effects of Introducing the Fully Automated Integrated Urine Analyzer UX-2000 and Basic Evaluation of Its Performance

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INTRODUCTION

Recent years have seen considerable advancement in automation of clinical laboratory tests. Automated analyzers used for urine analysis also have become faster, more multi-functional, and smaller in size. Such automation has enabled rapid analysis through simpler procedures. What is required of medical technologists working in such an environment is the appropriate use of the analyzers after understanding their characteristic features and the supply of high quality test data to the clinicians, by exploiting the advantageous features of the automated analyzers and manual methods.

Our hospital started to use a Sysmex fully automated integrated urine analyzer UX-2000 (hereinafter "UX-2000") from April 2011. UX-2000 is a compact device wherein a urine test strip analyzer and a urine particle analyzer are integrated. It has a cross-check function and a reflex test function also as standard features. Thus, we can expect more efficient urine analysis and improved precision of testing because of the integrated data management [1].

For the staff of our clinical laboratory it was our first experience with a urine particle analyzer that used flow cytometry (FCM) as the principle of measurement. Therefore, we conducted various investigations to achieve efficient and appropriate utilization of the UX-2000. Furthermore, we examined the cross-check function, a characteristic function of UX-2000, to arrive at the optimum settings for it. We report here how urine analysis has changed in our laboratory during the 10 months after introduction of the UX-2000.

AN OVERVIEW OF OUR HOSPITAL

The hospital has 364 beds and treats about 650 outpatients per day. About 100-130 test strip analyses are performed daily as routine urine tests and urine sediment analysis is requested in about 30-60 of these cases. Urine specimens, both of hospitalized patients and outpatients, are sent to the clinical laboratory in urine test tubes. The laboratory where the urine is analyzed works on a one-floor system with 5 medical technologists normally assigned to it. Apart from the analysis itself, the staff members receive the specimens, process them, and load them on the analyzer. Assignments are rotated as needed to carry out the work in a flexible manner. One staff member each is assigned for microscopy of blood and microscopy of urine sediments. Requests for tests are issued through the HOPE/EGMAIN GX (Fujitsu) electronic medical record system, and the medical testing management system used is Techno-TOMOROW (Techno Aska). A UX-2000 is used for day-to-day routine urine analysis. In the present study, the conventional fully automated urine (test strip) analyzer ARKRAY AX-4280 (hereinafter "AX-4280") and the Hitachi automated urinary sediment analyzer 6800 (hereinafter "H6800") were also used for comparison in evaluating the performance of UX-2000.

Testing system terminals are provided at 11 locations in the clinical laboratory and all the staff are checking the progress of processing and testing of the specimens. Apart from this, the progress of testing is displayed on a 50-inch monitor and the system is so set up that one can check the progress without touching a terminal. When a specimen is found to require microscopic examination, this can be known from the large monitor display or any terminal, and any of the technologists in the laboratory can perform the centrifuging immediately, even if he or she had not been specifically assigned the job.

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SHORTENED TURNAROUND TIME (TAT)

Patient urine specimens (n=1,836) submitted to our hospital's clinical laboratory for testing during June and July 2011 were analyzed for evaluating analyzer performance. After the test strip analysis (CHM) and urine particle analysis, the TAT of samples that did not require review (microscopy) were compared between the conventional method and UX-2000. The time from confirmed arrival of each specimen up to the reporting of its analysis results was taken as TAT. The mean values of TAT of these specimens by the different methods were used for the comparison.

The mean TAT for the conventional method was about 9.8 minutes and more than 50% of the specimens required 10 minutes or longer for the test report to be issued. The mean TAT with UX-2000 was about 5.8 minutes and 69% of the specimens required 4 to less than 7 minutes (***Fig. 1*** and ***Fig. 2***).

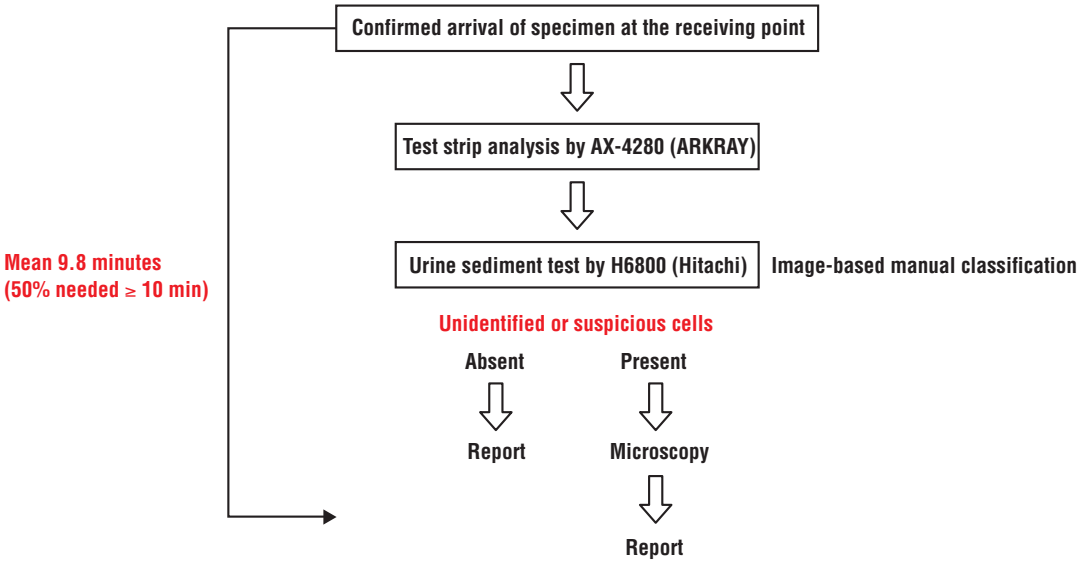

Fig. 1 *Workflow of conventional urine analysis*

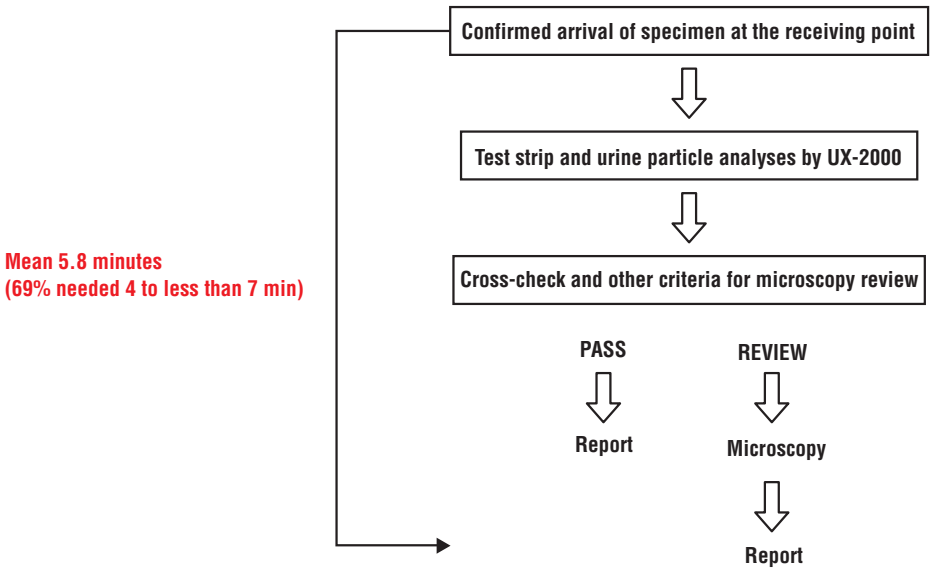

Fig. 2 *Workflow of urine analysis after introduction of UX-2000*

Earlier, after confirming the arrival of a urine specimen it was loaded on the test strip analysis equipment for measurement. If there was a request for urine sediment analysis also, the sample was then loaded on an H6800, which used image analysis for measurement. With the H6800, the medical technologist further manually reviewed the specimens one by one and microscopy was opted for depending on the results. If there were no unidentified components or suspected atypical cells, the final report was prepared without undertaking microscopy. Now, as the test strip analysis (CHM) and urine particle analysis (FCM) are integrated in UX-2000, the testing is done automatically according to the details ordered, after the specimen is set in the analyzer. This makes "sample reloading on another device" unnecessary and prevents inadvertent omission of sample loading due to "operator's error". For "specimens that do not require microscopy", i.e., those that did not meet the preset criteria for further microscopy or the cross-check criteria, the report is sent to the host computer after an average of 5.8 minutes from the arrival of the specimen in the laboratory. For about 60% of the specimens that did not require microscopy, the TAT was shortened by about 4 minutes compared to the earlier method. Furthermore, manual review also became unnecessary with UX-2000, and this enables microscopic observation with more sufficient time. This also increased the opportunity for the persons assigned microscopy work to undertake other types of analysis or processing.

SETTING CRITERIA FOR REVIEW

As mentioned earlier, the use of a FCM-based urine particle analyzer was a new experience for us. Therefore when we started using the UX-2000, the criteria for review were set taking into account values set by laboratories that use UF-1000*i* analyzers, and after seeking advice from the scientific staff of Sysmex Corporation. The initial settings were partly changed after further examination of the suitability of the criteria for use in our hospital (***Table 1*** and ***Table 2***). To be more specific, the appropriateness of the criteria for review and their effect on the review rate were evaluated for CAST and Path CAST (pathological casts), two parameters for which there are differences between laboratories in the values set for review criteria, by analyzing the results obtained with patient urine specimens (n=1,836). The appropriateness of the handling of PRO positive specimens (among entire urinalysis workflow) was also examined.

1. CAST

The review rate was examined with the review criterion for CAST set at 2.5/μL and at 5.7/μL. The results showed that 28% of the specimens that had CAST in the range 2.5/μL to 5.7/μL were designated to be reviewed by microscopy because of some other review criterion. Thus, there was no major change in the review rate when the criterion for review was set at 5.7/μL compared to 2.5/μL.

When we started using UX-2000, we had set the CAST criterion for review at 5.7/μL because it was expected that at 2.5/μL the review rate would increase by 7-8%, to about 47%. However, the present study revealed that even at 2.5/μL, the number of samples reviewed by microscopy in a day would increase only by 1 or 2. Therefore, we changed the criterion of 5.7/μL to the currently used 2.5/μL. This was considered appropriate because there was no major change in the review rate after this modification.

Table 1 *Criteria (1) for microscopy review set for UX-2000 FCM parameters*

RBC	**≥ 275.3/μL**
CAST	**≥ 2.5/μL**
SRC	**≥ 7/μL**
X' TAL	**≥ 20/μL**
YLC	**≥ 10/μL**
Path CAST	**≥ 0.5/μL**
SPERM	**≥ 10/μL**

Table 2 *Criteria (2) for microscopy review set for UX-2000*

PRO ≥ (2+) in test strip analysis
"Dysmorphic?" or "Mixed?" in RBC Information
"REVIEW" is displayed because of low-reliable results due to analytical limitations of the analyzer

2. Path CAST

When results were examined after setting the Path CAST criterion at 0.5/μL, 428 (24%) of the 1,836 specimens analyzed by FCM were assessed as requiring review because of the Path CAST result. These 428 specimens were 62% of the total of 692 that were marked for microscopy review. However, when examined under the microscope, only 20 (4.7%) out of the 428 actually had pathological casts.
It is conceivable that certain factors potentially affect the review rate. We have focused our attention on Path CAST for not only bringing down the review rate but also maintaining it at a reasonable level. As described above, 62% of the specimens sent for microscopy review had Path CAST 0.5/μL or more. Of these, only 4.7% actually showed the presence of pathological casts. Although it was possible to bring down the review rate by changing the Path CAST criterion, we concluded to maintain the current review criteria on Path CAST at 0.5/μL or more because current review rate enables us to detect some clinically important cells and components.

3. Handling of PRO (Protein) positive cases

In our laboratory, specimens with PRO (2+) or higher are considered targets for microscopy review, and urine sediment analysis is carried out. Currently we are not reviewing PRO (1+) specimens. But in practice about 60% of the PRO (1+) specimens are reviewed anyway because their FCM results satisfy some other review criterion. This method of microscopy review, i.e., not reviewing all specimens with PRO (1+) or higher but only those that meet some other criterion, contributes to efficient testing. When we consider all the 3,180 specimens for which urine sediment analysis had been ordered, the review rate would have increased by 5-6% to about 45% if all the PRO (1+) specimens were to be reviewed. As there is a certain limit for the detection sensitivity for casts in FCM, we felt that keeping PRO (2+) or higher as the review target can maintain an acceptable detection rate of casts.

4. Use of RBC Information

As with UF-1000*i*, UX-2000 also provides RBC Information. Identification of whether the red blood cells in urine are glomerular or nonglomerular provides crucial information for estimating the site of bleeding. Currently, all specimens with the red blood cells judged as "Dysmorphic?" or "Mixed?" are reviewed.

EXAMINATION FOR OPTIMIZATION OF THE CROSS-CHECK FUNCTION

Specimens that showed discrepancy in cross-check under the initial settings (***Table 3***) used in our laboratory were 17.5% of the total. Discrepancy between BLD and RBC was seen in 7.5% (66.7% of the specimens showed agreement between the FCM results and microscopy results), there was discrepancy between LEU and WBC in 5.2% (93.6% showed agreement between FCM and

Table 3 *Criteria (3) – Cross-check settings in UX-2000 for microscopy review*

BLD in CHM	FCM
(–)	≥ 5-9/HPF (≥ 25.1/μL)
(1+)	≥ 20-29/HPF (≥ 108.5/μL)
(2+)	≤ 1-4/HPF (≤ 25.0/μL)
	≥ 50-99/HPF (≥ 275.3/μL)
(3+)	≤ 20-29/HPF (≤ 164.0/μL)

LEU in CHM	FCM
(–)	≥ 8/HPF (≥ 44.5/μL)
≥ 75	≤ 55.56/μL

NIT in CHM	FCM
≥ (1+)	BACT (–) (≤ 10/μL)

microscopy results), and 6.7% of the specimens had PRO ≥(2+). Among the PRO ≥(2+) specimens, 56% were negative (0.00 - 1.49/μL, according to the setting used in our laboratory) for CAST in FCM. 52% of these did not show casts in microscopy whereas the remaining 48% showed varying number of casts.

Based on the above background, we investigated the optimal settings of the cross check function utilizing combinations of CHM and FCM parameters. We extracted specimens that showed significant discrepancy in measured values between BLD and RBC and between LEU and WBC from the 1,242 patient urine specimens tested by both CHM and FCM of UX-2000, and compared their FCM results and urine sediment analysis results. "Significant discrepancy" here means a difference of more than 1 rank between CHM qualitative results (–, 1+, ...) and theoretically corresponding FCM results converted into Rank value (i.e. <1/HPF, 1 - 4/HPF, 5 - 9/HPF ....)

This examination showed that 83 (6.7%) specimens had discrepancy between BLD and RBC, and 48 (3.9%) between LEU and WBC (***Table 4*** and ***Table 5***). When the cases where the FCM results and the urine sediment microscopy results agreed were excluded from the

Table 4 *Cross-check (BLD vs. RBC)*

: Assessed as cross-check error
: Not assessed as cross check error
: Cases where FCM results agreed with urine sediment microscopy results

Semi-quantitative Rank (RBC/μL)	Semi-quantitative Rank (mg/dL)	Qualitative Rank
	OVER	3+
300	1	
	0.5	2+
60	0.2	
	0.1	1+
20	0.06	
10	0.03	±
		–

CHM \ FCM	1	2	3	4	5	6	7	8	9
11									
10									
9									
8	1	2	2	3	2	0	7	23	
7	1	2	5	11	2	4	11	4	
6	0	3	4	8	5	3	2	0	
5	0	14	18	12	5	2	4	0	
4	4	30	23	14	0	2	0	0	
3	4	55	19	5	0	0	0	0	
2	33	123	9	4	0	0	0	0	
1	472	266	14	5	0	0	0	0	

	1	2	3	4	5	6	7	8
/HPF	<1	1-4	5-9	10-19	20-29	30-49	50-99	≧100
/μL	<5.6	<27.8	<55.6	<111.2	<166.8	<222.4	<556.0	≧556.0

Table 5 *Cross-check (LEU vs. WBC)*

Semi-quantitative Rank (WBC/μL)
500
250
75
25
–

CHM \ FCM	1	2	3	4	5	6	7	8	9
11									
10									
9									
8									
7									
6									
5	0	0	5	7	6	6	18	36	
4	0	11	6	11	5	7	16	1	
3	2	23	15	16	3	3	2	0	
2	7	40	13	10	4	1	0	0	
1	696	248	21	2	2	0	0	0	

	1	2	3	4	5	6	7	8
/HPF	<1	1-4	5-9	10-19	20-29	30-49	50-99	≧100
/μL	<5.6	<27.8	<55.6	<111.2	<166.8	<222.4	<556.0	≧556.0

discrepancy cases after comparing these two results of all the discrepant specimens, the specimens that can be defined as discrepant between BLD and RBC were 62 (5%), and those discrepant between LEU and WBC were 25 (2.0%). The agreement between FCM analysis and microscopy was high for white blood cells and there was a tendency for the test strip analysis to show falsely high values of this parameter.

After examining the agreement between BLD and RBC, and LEU and WBC, we could arrive at efficient cross-check settings that would eliminate unnecessary urine sediment analysis. It is however necessary to reexamine the settings from time to time to make them even more optimal.

It is difficult to cross-check between PRO and CAST because there appears to be no definite correlation between the two (***Table 6***). The cross-check function can be used for checking abnormal values in test strip analysis. As for cross-checking between NIT and BACT, NIT has a lower sensitivity than BACT because of its

Table 6 *Cross-check setting: Review if PRO is (2+) or higher*

: Assessed as cross-check error
: Not assessed as cross-check error
: Cases where FCM results agreed with urine sediment microscopy results

Semi-quantitative Rank (mg/dL)	Qualitative Rank
OVER	4+
600	3+
300	
200	2+
100	
70	1+
50	
30	
20	±
10	
	−

CHM

CHM \ FCM	1	2	3	4	5	6	7	8	9
11									
10	2	1	1	0	0				
9	9	14	0	0	1				
8	13	2	6	1	0				
7	15	5	10	3	0				
6	11	6	3	0	1				
5	12	7	9	0	1				
4	25	26	14	5	0				
3	60	34	24	3	2				
2	74	37	11	1	0				
1	742	41	11	0	0				

FCM

Qualitative Rank	−	±	1+	2+	3+
/LPF	<0.99	1.00-2.99	3.00-9.99	10.00-29.99	≧30.00
/μL	<0.34	0.34-1.03	1.04-3.39	3.40-10.34	≧10.35

Table 7 *Cross-check (NIT vs. BACT)*

CHM

CHM \ FCM	1	2	3	4	5	6	7	8	9
11									
10									
9									
8									
7									
6									
5									
4									
3	0	0	8	35					
2	0	2	5	3					
1	1045	95	36	12					

FCM

Qualitative Rank	/μL
2+	<100.0
1+	100.0-999.9
−	1000.0-9999.9
	≧10000.0

reaction principle. Therefore, a setting that does not detect NIT (–) but can detect false negatives for BACT (NIT(+) but BACT(–)) is desirable (***Table 7***).
The microscopy review rate in our laboratory came down to about 39% by the combined use of certain review criteria for FCM parameters and certain cross-check settings.

GENERAL COMMENTS AND DISCUSSION ON FUTURE PROSPECTS

We have achieved a major reduction in TAT by introducting the UX-2000 in our laboratory. This has allowed us to dedicate more time to the microscopic examination of abnormal samples. Even more effective review settings may become possible in the future as we make further modifications based on our experience in using the analyzer. We believe that in the future we can become even more efficient in our review process by excluding healthy specimens through the use of suitable logic. Our emphasis in setting review criteria for FCM parameters is not on just detecting abnormalities but also on not missing any abnormality. Setting of a Path CAST of 0.5/μL or more as a review target appears to be one such effective measure. A variety of settings are possible for the cross-check function in this integrated analyzer, and cross-checking can be done with even greater precision in future by choosing even more appropriate settings. Currently, the results of FCM are not included in urine sediment analysis reports. But we feel that it is necessary to consider including the results of FCM analysis also in future. We would like to comprehensively interpret the results of test strip analysis, FCM analysis and sediment analysis, and effectively use them for clinical diagnosis as pathophysiological information obtained from urine specimens.

References

1) Kobayashi H. Overview of a fully automated integrated urine analyzer UX-2000. Sysmex J. 2011; 34 (Suppl. 1): 70-75. (Japanese).