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## Screening Urine Specimen Populations for Normality Using Different Dipsticks: Evaluation of Parameters Influencing Sensitivity and Specificity

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**Summary:** The reagent test strip Combur-9 Test-RL (Boehringer Mannheim) and the 8-SG Multistix (Ames) were simultaneously evaluated as a rapid method for screening urines for normality.

Differences between the two methods are for a considerable part determined by adjustment of the lowest detection limits of the leukocyte and erythrocyte dipstick fields.

Patient populations (243 specimens presented to the routine laboratory and 230 specimens submitted for microbiological culture), sediment analysis (routine or standardized) and composition of the screening protocol strongly influence values obtained for the sensitivity, specificity and predictive values, whereas use of a different dipstick is of minor importance on the final results.

Higher sensitivity and specificity are observed when relating positive dipstick screening to positive culture than when relating positive standardized sediment to positive culture. Evaluation of dipstick method, using microscopic sediment analysis as a reference parameter appears to be very dependent on the quality of the latter, which is therefore relatively unsuitable for this purpose. Apart from standardization, additional clinically significant findings are obtained using dipstick screening.

### Introduction

Examination of urine sediments traditionally is done by microscopy. In an attempt to reduce the workload in the urine analysis laboratory, reagent test strips for the rapid screening of urine specimens have been developed. Schumann proposed the use of 8-parameter strips, without an esterase field for leukocyte detection, in order to screen urines for normality, i. e. "macroscopic urinalysis" (1). After the introduction of dipsticks with a field for leukocyte detection, urine screening attracted more attention. Many reports on the evaluation of the first leukocyte-sensitive dipstick (Cytur-test or Combur-9 dipstick, marked Chemstrip-9 in USA, from Boehringer Mannheim) have been published (2–25). Meanwhile several more strips have become available. Comparison of different

dipsticks intended to replace laborious microscopy should involve estimation of correlation of the results with those obtained by microscopy.

In the present study the influences of differences in dipstick analyses as well as in sediment microscopy (routine or standardized) and patient populations (urines presented to routine laboratory  $n = 243$ , or submitted for microbiological culture  $n = 230$ ) on the sensitivity and specificity and predictive values of methods for screening urines for normality were evaluated simultaneously. Receiver operating characteristic (ROC) curves (26) were constructed for comparison of optimal sensitivity and specificity of different dipsticks. Cut-off values in screening procedures predicting normality of urine sediments could thus be determined.

Moreover, microscopic examination and dipstick results were also compared with results obtained from microbiological cultures.

## Materials and Methods

### Routine urine specimens

A total of 243 arbitrarily chosen urine specimens presented to the routine laboratory of the De Wever Hospital in Heerlen were examined, and for all the analytical techniques the majority providing vastly overlapping populations for each method. For technical reasons a small number ( $n = 24$ ) of normal samples dropped out from the Urotron population. No attempt was made to modify or improve the routine urine collection arrangements or the routine laboratory procedure for urine analysis. Urine specimens were examined within one hour after receipt in the laboratory.

### Routine sediment microscopy

The urine specimens were analysed according to routine laboratory procedures. Approximately 10 ml urine were centrifuged for 5 min at 2000 g, whereafter urine was decanted. One drop of the sediment was placed on a slide covered with a cover slip and microscopy performed at magnification  $10 \times 10$  (casts) and  $10 \times 40$  (other elements).

### Standardized sediment microscopy

The "count-10 system" from V-Tech Inc. (American Scientific Products, USA) for standardized microscopic sediment analysis was used. Twelve ml urine were centrifuged for 5 min at 2000 g. After decantation the sediment was resuspended to a volume of 1 ml and analysed on calibrated disposable slides at  $10 \times 10$  and  $10 \times 40$  magnification.

Dipsticks were analysed by reflectometry. We compared Combur-9 strips (with Urotron RL-9, Boehringer Mannheim) and 8-SG Multistix (with Clinitek 200, Ames/Bayer). Analyses were performed according to the manufacturer's instructions. Both dipsticks contained fields to test for pH, glucose, protein, ketone bodies, esterase activity (indicates leukocytes), haemoglobin (indicates erythrocytes) and nitrite (indicates bacteria).

### Urine specimens presented for culture

A second population of urine specimens ( $n = 230$ ) presented to the microbiology laboratory for culture was examined. These urines were properly submitted in sterile containers and were analysed using the two different dipsticks. Standardized sediment microscopy and quantitative microbiological cultures were performed.

Quantitative cultures were performed using the Mast bacteriuria-test filter strips inoculated onto a Cled agar plate and incubated at 37 °C (18–24 h). Bacteria were typed with an API-series.

Significant bacteriuria was defined as  $\geq 10^4$  microorganisms per ml of one clearly predominant organism. A second microorganism was accepted when present at a concentration of  $\geq 10^5$  microorganisms per ml. Urines containing three or more microorganisms were considered to be contaminated and were excluded from investigation.

Gram staining was considered to be positive at one or more microorganisms per field.

## Results

### Chemical constituents

Results of pH, protein, glucose, nitrite (in accordance with literature (27)) and ketone body levels for 243 routine specimens, measured with two different strip readers, showed good comparison. However, the lowest detection limit for ketone levels differed significantly for the two strip readers, i. e. Clinitek 200 "trace" and Urotron  $>1$  mmol/l, resulting respectively in 7% and 21% positive specimens. The Clinitek 200 allows more extensive differentiation of pH values.

### ROC curves

Receiver Operating Characteristic (ROC) curves were constructed to evaluate and compare the usefulness of leukocyte and erythrocyte dipstick analysis as a predictive test for positive microscopic results for leukocytes or erythrocytes, both in standardized and routine sediment analyses.

ROC curves are graphical presentations of pairs of sensitivity and specificity obtained when taking different leukocyte or erythrocyte dipstick cut-off values to determine positivity of the dipstick analysis. These positive dipstick values were compared with microscopy data, taking the presence of leukocytes  $>4$  (fig. 1) or erythrocytes  $>2$  (fig. 2) or erythrocytes  $>4$  (fig. 3) per field at  $10 \times 40$  magnification as positive in the sediment, either by the standardized or the routine procedure.

The ROC curve nearest to the upper-left corner (see graphs) belongs to the more accurate procedure.

From figures 1, 2 and 3 it can be concluded that better results are obtained with standardized sediment microscopy than with the routine technique. Leukocyte analyses for the two different test strips are very comparable. The lower detection limit for the Clinitek 200 is  $15 \mu\text{l}^{-1}$  and for the Urotron  $25 \mu\text{l}^{-1}$ , which explains the somewhat higher sensitivity observed for the Clinitek 200 (point A, fig. 1) compared with the Urotron (point 1, fig. 1). The detection limit of the Urotron can be adjusted to  $15 \mu\text{l}^{-1}$ .

However, better results are obtained for the erythrocytes using the Urotron.

The lowest detection limit for the Clinitek 200 is not expressed in erythrocytes per microlitre, but as a trace, and it appears to be less sensitive than the lowest detection limit of the Urotron (10 erythrocytes per  $\mu\text{l}$ ).

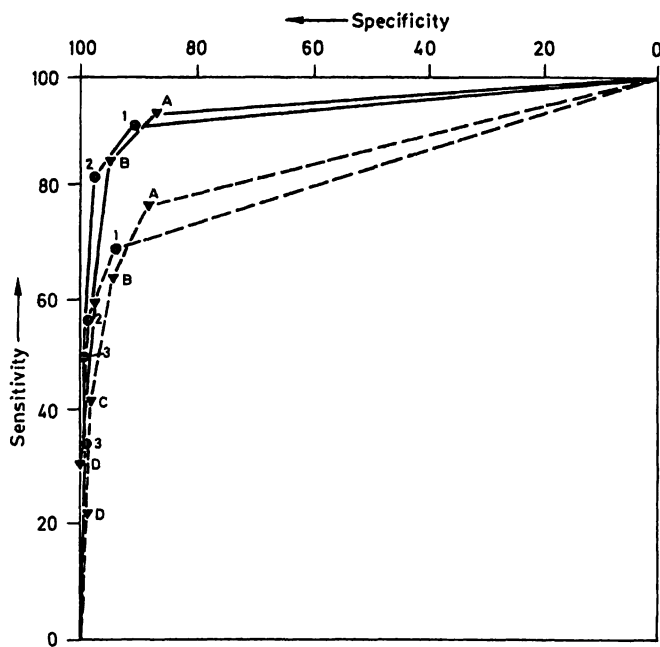


Fig. 1. Receiver Operating Characteristic curve for the leukocyte dipstick fields and routine (dashed curves) and standardized (solid curves) sediment microscopy (positive leukocytes >4). Clinitek (▼), cut-off values A ≥ 15 μl<sup>-1</sup>; B ≥ 70 μl<sup>-1</sup>; C ≥ 125 μl<sup>-1</sup>; D ≥ 500 μl<sup>-1</sup>. Urotron (●), cut-off values 1 ≥ 25 μl<sup>-1</sup>; 2 ≥ 100 μl<sup>-1</sup>; 3 ≥ 500 μl<sup>-1</sup>.

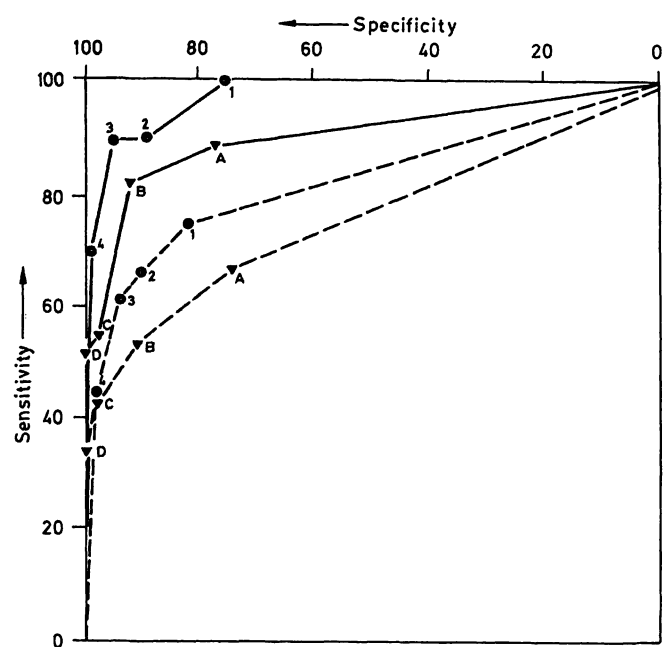


Fig. 3. Receiver Operating Characteristic curve for the erythrocyte field, see figure 2, positive microscopy erythrocytes >4.

Cut-off values for a positive dipstick, as derived from the ROC curves appear to be:

Clinitek: erythrocytes trace; leukocytes > 15 μl<sup>-1</sup>; protein ≥ 0.3 g/l

Urotron: erythrocytes > 10 μl<sup>-1</sup>; leukocytes > 25 μl<sup>-1</sup>; protein ≥ 0.3 g/l

Cut-off values for positive microscopy, both routine and standardized, were selected at erythrocytes > 2 and leukocytes > 4 at 10 × 40 magnification; casts present (other than hyaline) at 10 × 10 magnification.

Although a cut-off value for erythrocytes > 4 resulted in a higher sensitivity, erythrocytes > 2 was preferred in order to include samples with microhaematuria (28, 29).

Specimens showing only bacteriuria with all other parameters negative were considered to be either normal (computation A tabs. 1 and 2), or pathologic (computation B tables 1 and 2). These samples are possibly false positives, i. e. ambient bacteriuria.

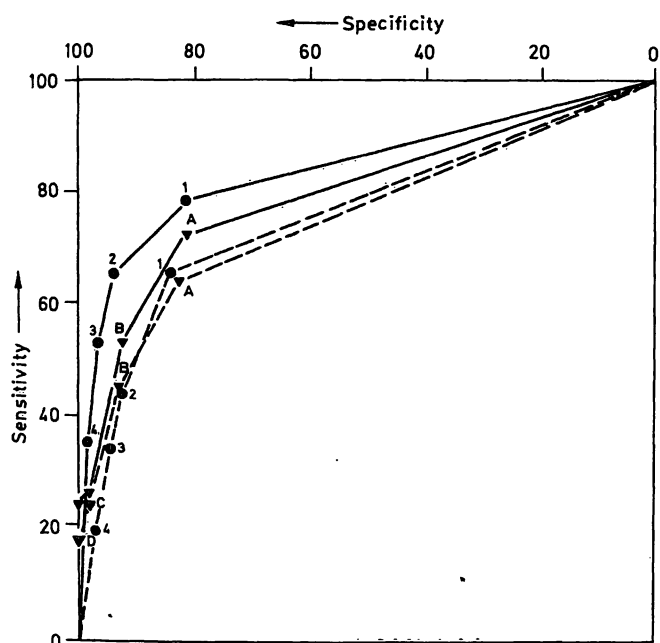


Fig. 2. Receiver Operating Characteristic curve for the erythrocyte dipstick fields and routine (dashed curves) and standardized (solid curves) sediment microscopy (positive erythrocytes >2). Clinitek (▼), cut-off values A ≥ trace; B ≥ small; C ≥ moderate; D ≥ large. Urotron (●), cut-off values 1 ≥ 10 μl<sup>-1</sup>; 2 ≥ 50 μl<sup>-1</sup>; 3 ≥ 150 μl<sup>-1</sup>; 4 ≥ 250 μl<sup>-1</sup>.

Urine specimens for routine examination

Tables 1 (standardized microscopy) and 2 (routine microscopy) present the sensitivity, specificity and predictive values for different screening protocols using the selected cut-off values for specimens presented to the routine laboratory. Slight differences between

Tab. 1. Sensitivity, specificity and predictive value (PV) for dipstick fields when related to positive standardized sediment microscopy.

	Dipstick field parameters					
	A Erythrocytes	A Leukocytes	B Erythrocytes Leukocytes	B Erythrocytes Leukocytes Protein	B Erythrocytes Leukocytes Protein Nitrite <sup>1</sup>	C Erythrocytes Leukocytes Protein Nitrite
Positive sediments (n)	51	32	53	53	53	87
Sensitivity						
Clinitek	0.73	0.94	0.94	0.95	0.95	0.74
Urotron	0.78	0.91	0.96	0.96	0.98	0.74
Specificity						
Clinitek	0.82	0.87	0.71	0.69	0.60	0.68
Urotron	0.81	0.92	0.76	0.73	0.67	0.75
PV positive						
Clinitek	0.51	0.53	0.48	0.46	0.40	0.56
Urotron	0.56	0.66	0.56	0.54	0.49	0.60
PV negative						
Clinitek	0.92	0.99	0.98	0.98	0.97	0.82
Urotron	0.93	0.98	0.98	0.99	0.99	0.81

## Parameters determining pathology:

A Single dipstick fields are related to the corresponding parameter in the sediment.

B Combined dipstick fields are related to positive sediment: erythrocytes &gt;2, leukocytes &gt;4, casts (apart from hyaline).

C Combined dipstick fields are related to extended positive sediment:

erythrocytes &gt;2, leukocytes &gt;4, casts (apart from hyaline), bacteriuria positive (includes urines with bacteria as only positive parameter, probably false positive, ambient bacteriuria).

All combined screening protocols are and/or.

Total number of samples n = 243 (Clinitek) and n = 219 (Urotron); see text.

Tab. 2. Sensitivity, specificity and predictive value (PV) for dipstick fields when related to positive routine sediment microscopy.

	Dipstick field parameters					
	A Erythrocytes	A Leukocytes	B Erythrocytes Leukocytes	B Erythrocytes Leukocytes Protein	B Erythrocytes Leukocytes Protein Nitrite	C Erythrocytes Leukocytes Protein Nitrite
Positive sediments (n)	75	53	77	77	77	95
Sensitivity						
Clinitek	0.65	0.76	0.84	0.86	0.89	0.77
Urotron	0.66	0.69	0.79	0.80	0.81	0.77
Specificity						
Clinitek	0.83	0.88	0.73	0.71	0.64	0.71
Urotron	0.84	0.94	0.77	0.74	0.68	0.76
PV positive						
Clinitek	0.63	0.63	0.59	0.58	0.53	0.63
Urotron	0.68	0.79	0.65	0.63	0.58	0.71
PV negative						
Clinitek	0.84	0.93	0.91	0.91	0.93	0.83
Urotron	0.83	0.91	0.87	0.88	0.87	0.81

Legends: see table 1.

percentage abnormality in the Clinitek versus Urotron population are due to drop-out of a number of normal samples ( $n = 24$ ) in the Urotron population. When positive microscopy includes urine specimens with mere bacteriuria a low sensitivity is observed for the routine specimens (tabs. 1 and 2 part C). Specimens for routine investigation are not collected in sterile containers, causing increased ambient bacteriuria (false positives). Bacteriuria with no other positive microscopic parameters was observed more frequently in the standardized sediment analyses ( $n = 36$ ) than in routine sediment analyses ( $n = 17$ ). A higher sensitivity and negative predictive value are observed when isolated bacteriuria is disregarded, i. e. considered to be the result of contamination. With standardized microscopy better results were obtained than with routine microscopy.

On the basis of sensitivity, specificity and predictive values of the screening protocols no differences were observed between the Clinitek and the Urotron. The more sensitive detection of leukocytes with the Clinitek and better detection of erythrocytes with the Urotron finally results in equal sensitivities for screening protocols.

In order to examine the consequences of disregarding urines with mere bacteriuria in the sediment we compared results obtained from sediment analysis with results obtained from bacteriological culture.

#### Urine specimens submitted for microbial culture

Table 3 presents the sensitivity and specificity of the dipstick fields related to positive culture. Totals of investigated populations were 230 samples (Clinitek) and 193 samples (Urotron). Positive cultures were obtained in 57 samples (Clinitek) and 56 samples (Urotron) and miscellaneous contaminations were found in 22 and 14 samples respectively. Specimen populations overlapped for 107 samples. For leukocytes a higher sensitivity was observed for the Clinitek, whereas erythrocytes were better detected with the Urotron. As the presence of leukocytes is an important parameter for the detection of infection c. q. bacteriuria, a higher sensitivity for the screening protocols is observed with the Clinitek method (lower detection limit  $15 \mu\text{l}^{-1}$ ). Again it is evident that the calculated values for sensitivity and specificity of the

Tab. 3. Sensitivity, specificity and predictive value (PV) for dipstick fields when related to either positive microbial culture or positive microscopy/sediment.

	Dipstick field parameters					
	A Erythrocytes	A Leukocytes	A Leukocytes Nitrite	A Leukocytes Protein Nitrite	A Erythrocytes Leukocytes Protein Nitrite	B Erythrocytes Leukocytes Protein Nitrite
Positive samples cul- ture (A) or sediment (B)						
Clinitek	57	57	57	57	57	110
Urotron	56	56	56	56	56	98
Sensitivity						
Clinitek	0.70	0.88	0.91	0.97	0.97	0.96
Urotron	0.79	0.71	0.79	0.82	0.89	0.88
Specificity						
Clinitek	0.62	0.68	0.68	0.55	0.42	0.57
Urotron	0.59	0.85	0.85	0.82	0.55	0.69
PV positive						
Clinitek	0.38	0.47	0.49	0.41	0.35	0.68
Urotron	0.46	0.66	0.68	0.65	0.45	0.75
PV negative						
Clinitek	0.86	0.94	0.96	0.98	0.97	0.94
Urotron	0.87	0.88	0.91	0.92	0.93	0.85

#### Parameters determining pathology:

A Positive microbial culture.

B Positive sediment microscopy: erythrocytes  $>2$ , leukocytes  $>4$ , casts (apart from hyaline) and microscopic bacteriuria.

All combined screening protocols are and/or.

Total number of samples  $n = 230$  (Clinitek) and  $n = 193$  (Urotron); see text.

dipstick fields depend mainly on the detection limits of leukocyte fields, which result in different effects in different specimen populations.

Table 3 also presents the sensitivity and specificity for the screening protocol when related to positive microscopy; this allows comparison, for this population, with the results obtained for the routine samples (tabs. 1 and 2).

Table 4 demonstrates lower sensitivities when relating sediment results to positive culture, than for dipstick results related to positive culture. This indicates that better results are obtained from the dipstick analysis than from sediment analysis.

Of the 230 urine specimens presented to the bacteriology department, 151 culture results were negative, 57 had a positive culture, and 5 of these contained two

organisms (22 contaminated samples were excluded, reducing the investigated population to 208 samples). Table 5 presents the bacteriological data. It is an important finding that in eighteen cases of positive culture no leukocytes were detected by microscopy, whereas eleven were still detected with the dipstick method (Clinitek). Although it is known that e. g. *Proteus* causes lysis of leukocytes, the esterase activity from lysed cells is still detected with the dipstick.

Tab. 5. Leukocytes in 57 urine specimens with positive microbial culture.

Isolates	Number of patients	Specimens with positive culture and no leukocytes in the sediment; positive leukocyte dipstick reaction ( )
<i>Escherichia coli</i>	25	5 (3)
<i>Streptococcus faecalis</i>	6	
<i>Proteus mirabilis</i>	10	6 (3)
<i>Klebsiella pneumoniae</i>	5	1 (1)
<i>Staphylococcus epidermidis</i>	1	1
<i>Pseudomonas aeruginosa</i>	3	1 (1)
Group B streptococcus	2	1 (1)
<i>Torulopsis glabrata</i>	2	2 (1)
<i>Klebsiella oxytoca</i>	1	
<i>Candida albicans</i>	2	
<i>Staphylococcus aureus</i>	1	
<i>Staphylococcus saprophyticus</i>	1	1 (1)
<i>Citrobacter diversus</i>	1	
<i>Enterobacter cloacae</i>	1	
<i>Lactobacillus</i> species	1	

Note: 5 specimens contained 2 organisms.

Tab. 4. Sensitivity, specificity and predictive value (PV) for standardized sediment results when related to a positive culture (n = 208, contaminated urines excluded; positive culture n = 57).

	Sediment parameter		
	Leuko-cytes >4	Leuko-cytes >4 Bacteria	Erythrocytes >2 Leukocytes >4 Casts Bacteria
Sensitivity	0.68	0.91	0.91
Specificity	0.82	0.76	0.68
PV positive	0.58	0.59	0.52
PV negative	0.87	0.96	0.95

All combined parameters are and/or.

Tab. 6 a. Literature review: evaluation of dipstick analysis vs. microscopy.

Evaluated parameters	Parameters determining pathology	Sensi-tivity	Speci-ficity	PV positive	PV negative	n	Reference
Dipstick field	Chamber counting						
Leukocytes	Leukocytes > 10 $\mu\text{l}^{-1}$	0.91	0.87	0.94	0.80	1985	(2)
Leukocytes	Leukocytes > 10 $\mu\text{l}^{-1}$	0.88	0.94	—	—	466	(5)
Leukocytes	Leukocytes > 10 $\mu\text{l}^{-1}$	0.81	0.90	0.87	0.86	706	(6)
Leukocytes	Leukocytes > 10 $\mu\text{l}^{-1}$	0.92	0.97	0.88	0.98	292	(13)
Leukocytes	Leukocytes > 25 $\mu\text{l}^{-1}$	0.87	0.81	0.70	0.93	706	(6)
Dipstick field	Sediment/Microscopy						
Leukocytes	Leukocytes > 7 ( $\times 400$ )	0.90	0.87	0.59	0.98	720	(8)
Leukocytes	Leukocytes > 4 ( $\times 400$ )	0.82	0.85	0.55	0.95	782	(18)
Leuk., Ery., Prot., Nitr., Turb.*)	Leukocytes > 5 ( $\times 400$ )	0.98	0.85	0.88	0.97	478	(13)
Erythrocytes	Erythrocytes > 3 ( $\times 400$ )	0.93	0.83	0.64	0.97	720	(8)
Erythrocytes	Erythrocytes > 2 ( $\times 400$ )	0.91	0.81	0.50	0.98	782	(18)
Leuk., Ery., Prot.*)	Leuk. > 4, ery. > 2, casts	0.92	0.71	0.58	0.95	782	(18)
Leuk., Ery., Prot., Nitr.*)	Leuk. > 4, ery. > 4, bact. > 2+, casts	0.94	0.66	0.72	0.93	469	(21)
All fields Combur-9*)	Sediment positive	0.94	0.58	—	0.96	923	(20)
Leukocytes	Bacteriuria positive	0.59	0.78	0.34	0.91	782	(18)
Leuk., Nitr.	Bacteriuria positive	0.67	0.78	0.36	0.93	782	(18)
Leuk., Ery., Prot., Nitr.	Bacteriuria positive	0.82	0.59	0.27	0.95	782	(18)

\*) Specimen negative after dipstick screening according to indicated protocol: (13) 41%; (18) 52%; (21) 51%; (20) 43%.

## Discussion

Several studies on the reliability of dipstick methods for screening urines for normality have been published (1–25). Values for sensitivity, specificity and predictive values show large variations for the different studies (table 6a, b, c). Originally dipsticks with a leukocyte field requiring 15 minutes reaction time were used (2, 5, 6, 7, 8), whereas in later studies more sensitive methods (6), requiring 1–2 minutes reaction time were used (6, 12, 13, 14, 18, 21–25).

In some of these studies, samples investigated after presentation to the routine laboratory had been collected without special precautions to ensure sterile conditions (2, 6, 8, 15, 18, 23, 24). In others, special care was taken, such as the use of sterilized containers and collection of clean voided, midstream or catheter urine (5, 7, 12, 13, 14, 22).

The main problem in evaluating dipstick screening methods is the choice of a reference parameter determining pathology. In some of the studies, dipstick

Tab. 6b. Literature review: evaluation of dipstick analysis vs. positive microbial culture.

Evaluated parameters	Parameters determining pathology	Sensitivity	Specificity	PV positive	PV negative	n	Reference
Dipstick field	Positive microbial culture						
Leukocytes (female)	> 10 <sup>4</sup> CFU/ml*)	0.62	0.72	0.43	0.84	371	(7)
Leukocytes (male)	> 10 <sup>4</sup> CFU/ml	0.91	0.83	0.55	0.98	424	(7)
Leukocytes (total population)	> 10 <sup>4</sup> CFU/ml	0.75	0.78	0.49	0.92	795	(7)
Leukocytes	> 10 <sup>5</sup> CFU/ml	0.79	0.90	0.51	0.97	291	(13)
Leukocytes	> 10 <sup>5</sup> CFU/ml	0.98	0.75	—	—	252	(22)
Leukocytes (female)	> 10 <sup>5</sup> CFU/ml	0.84	0.60	0.49	0.89	600	(14)
Leukocytes (male)	> 10 <sup>5</sup> CFU/ml	0.81	0.82	0.43	0.96	600	(14)
Leukocytes (total population)	> 10 <sup>5</sup> CFU/ml	0.83	0.68	0.48	0.92	600	(14)
Leuk., Nitr. (female)	> 10 <sup>5</sup> CFU/ml	0.92	0.59	0.51	0.94	600	(14)
Leuk., Nitr. (male)	> 10 <sup>5</sup> CFU/ml	0.81	0.82	0.43	0.96	600	(14)
Leuk., Nitr. (total population)	> 10 <sup>5</sup> CFU/ml	0.90	0.67	0.49	0.95	600	(14)
Leuk., Nitr.	> 10 <sup>5</sup> CFU/ml	0.82	0.98	0.94	0.95	484	(12)
Leuk., Nitr.	> 10 <sup>5</sup> CFU/ml	0.78	0.83	0.61	0.92	459	(21)
Leuk., Nitr.	> 10 <sup>3</sup> CFU/ml	0.68	0.86	0.70	0.85	459	(21)
Leuk., Nitr.	> 10 <sup>4</sup> CFU/ml	1.00	0.73	0.40	1.00	252	(22)
Leuk., Nitr. (in patients)	> 10 <sup>4</sup> CFU/ml	1.00	0.59	0.44	1.00	125	(22)
Leuk., Nitr. (out patients)	> 10 <sup>4</sup> CFU/ml	1.00	0.84	0.35	1.00	127	(22)
Leuk., Nitr. (female)	> 10 <sup>4</sup> CFU/ml	1.00	0.65	0.35	1.00	—	(22)
Leuk., Nitr. (male)	> 10 <sup>4</sup> CFU/ml	1.00	0.81	0.50	1.00	—	(22)
Leuk., Nitr.	> 10 <sup>4</sup> CFU/ml	0.84	0.50	0.24	0.95	903	(23)
Leuk., Ery., Prot., Nitr.	> 10 <sup>4</sup> CFU/ml	0.91	0.44	0.35	0.94	459	(21)
Leuk., Ery., Prot., Nitr.	> 10 <sup>3</sup> CFU/ml	0.87	0.46	0.44	0.90	459	(21)

\*) CFU = Colony forming unit

Tab. 6c. Literature review: evaluation of microscopy vs. positive microbial culture.

Evaluated parameters	Parameters determining pathology	Sensitivity	Specificity	PV positive	PV negative	n	Reference
Chamber counting	Positive microbial culture						
Leukocytes > 10 $\mu\text{l}^{-1}$	> 10 <sup>4</sup> CFU/ml	0.70	0.76	0.35	0.93	903	(23)
Sediment microscopy	Positive microbial culture						
Leukocytes > 6 ( $\times 440$ )	> 10 <sup>4</sup> CFU/ml	0.82	0.72	0.51	0.92	600	(14)
Leuk. > 6, Bact. > 10 ( $\times 440$ ), Yeast +	> 10 <sup>4</sup> CFU/ml	0.96	0.66	0.50	0.98	600	(14)
Gram stain	Positive microbial culture						
Gram stain	> 10 <sup>4</sup> CFU/ml	0.93	0.95	0.86	0.98	459	(21)
Gram stain (female)	> 10 <sup>4</sup> CFU/ml	0.77	0.93	0.81	0.92	371	(7)
Gram stain (male)	> 10 <sup>4</sup> CFU/ml	0.95	0.98	0.93	0.99	424	(7)
Gram stain (total)	> 10 <sup>4</sup> CFU/ml	0.85	0.96	0.86	0.96	795	(7)

screening protocols were related to standardized microscopy (4, 18, 23, 24, 25), whereas in others routine procedures were used (8, 13). From the present study it appears that performance of microscopy and choice of cut-off values greatly influences the values for sensitivity and specificity. Microscopic examination has its own inaccuracies, making it less suitable as a reference parameter. Long standing of urine specimens and presence of e. g. *Proteus* may result in lysis of leukocytes.

*Kierkegaard* et al. demonstrated that 35% of the samples positive for leukocytes immediately after voidance were negative after three hours (30).

Lysed cells can only be detected by dipstick and not by sediment analysis. The quality of the specimen should also be considered. Bacterial contamination can greatly influence the final results. Evaluation of the reliability of dipstick screening methods for samples presented to the routine laboratory is especially difficult because reference to pathology is only possible by comparison to positive microscopy, which as mentioned above has its own drawbacks. For samples presented to the bacteriology department for investigation of infection, the reference parameter is a positive culture, making better evaluation of dipstick screening possible.

The population under investigation also greatly influences the results. *Perry* et al. (7) observed that the leukocyte esterase activity of urine in a male population is an excellent screening technique for significant bacteriuria, comparable with the *Gram* stain. It should, however, be used with caution when evaluating midstream specimens collected from females where leukocytes may arise from vaginal secretions; this results in a lower specificity (false positives) (7) as shown in other studies (14, 22). Collection of non-contaminated clean-catch midstream urine remains a persistent problem particularly for female patients.

## References

- Schumann, G. B. & Greenberg, N. F. (1979) *Am. J. Clin. Pathol.* 71, 452-456.
- Kooperative Studie an elf Zentren (1979) *Dtsch. Med. Wochenschr.* 104, 1236-1240.
- Kutter, K. (1980) *Dtsch. Med. Wochenschr.* 105, 1246-1249.
- Gillenwater, J. I. (1981) *J. Urol.* 125, 383-384.
- Kusumi, R. K., Grover, P. G. & Kunin C. M. (1981) *J. Amer. Med. Ass.* 245, 1653-1655.
- Kooperative Studie an acht Zentren (1982) *Dtsch. Med. Wochenschr.* 107, 853-857.
- Perry, J. L., Matthews, J. S. & Weesner, D. E. (1982) *J. Clin. Microbiol.* 15, 852-854.
- Bonard, C., Weber, E., Koller, P. U., Willamowski, K. D. & Bachmann, F. (1982) *Dtsch. Med. Wochenschr.* 107, 249-251.
- Benham, L. & O'Kell, R. T. (1982) *Clin. Chem.* 28, 1722.
- Gelbart, S. M., Chen, W. T. & Reid, R. (1983) *Clin. Chem.* 29, 997-999.
- Schaller, G. (1983) *Clin. Chem.* 29, 1692-1693.
- Smalley, D. L. & Dittmann, A. N. (1983) *J. Clin. Microbiol.* 18, 1256-1257.
- Highlights of an international symposium London (1983) Medicine publishing foundation. Oxford.
- Loo, S. Y. T., Scottolini, A. G., Luangphinit, S., Adam, A. L., Jacobs, L. D. & Mariani, A. J. (1984) *Am. J. Clin. Pathol.* 81, 634-642.

Among the many differences in the reports perhaps the one of the greatest practical importance is the comparability of the prevalence of disease. Tests have often been assessed in a population of more or less healthy patients, bearing no resemblance to the prevalence of disease that exists in the group of patients for whom the test is intended. From the present study it appears that results obtained for the routine population can not be extrapolated to samples presented for culture, originating from a population under justified suspicion of infections of the urinary tract.

## Conclusions

By using dipsticks in screening urines for normality it is possible to reduce the workload associated with sediment microscopy. This is especially true for urine samples to be investigated for urinary tract infection.

The presence of leukocytes or leukocyte remnants can be detected with dipsticks sensitive to esterase activity. This type of screening should also include nitrite and protein. Negativity justifies the decision to omit culture for bacteria, because no additional information can be expected.

In order to reduce microscopy of urine samples submitted for routine investigation, the dipstick analysis must include screening for erythrocytes, leukocytes, protein and nitrite. The assessment of cut-off values in the routine screening procedure for urine samples is dependent on the population to be investigated and the inherent sensitivity of the test.

Evaluation of dipstick methods by comparison with sediment microscopy can only be performed with caution, because additional potentially significant findings of the dipstick such as occult haematuria and leukocyturia, are not evaluated as such (28, 29, 30, 31).



15. Valenstein, P. N. & Koepke, J. A. (1984) *Am. J. Clin. Pathol.* **82**, 444–448.
16. Bartlett, R. C. & Kaczmarczyk, L. A. (1984) *Am. J. Clin. Pathol.* **82**, 713–716.
17. Hafner, J., Hermann, R., Hefti, M. & Binswanger, U. (1984) *Schweiz. Med. Wochenschr.* **114**, 1883–1886.
18. Modder, C. P. (1984) *Tijdschr. Ned. Ver. Klin. Chem.* **9**, 209–213.
19. Punt, J. M. H. M. (1984) *Tijdschr. Ned. Ver. Klin. Chem.* **9**, 214–220.
20. Chu, S. Y., Macleod, J. E. & Aterman, K. (1984) *Clin. Biochem.* **17**, 249–252.
21. Sewell, D. L., Burt, S. P., Gabbert, N. J. & Bumgardner, M. (1985) *Am. J. Clin. Pathol.* **83**, 740–743.
22. Oneson, R. & Groschel, D. H. M. (1985) *Am. J. Clin. Pathol.* **83**, 84–87.
23. Wilkins, E. G. L., Ratcliffe, J. G. & Roberts, C. (1985) *J. Clin. Pathol.* **38**, 1342–1345.
24. Loo, S. Y. T., Scottolini, A. G., Luangphinit, S. & Adam, A. L. (1986) *Am. J. Clin. Pathol.* **85**, 479–484.
25. Morrison M. C. & Gifford, L. (1986) *Am. J. Clin. Pathol.* **85**, 590–594.
26. Sackett, D. L., Haynes, R. B. & Tugwell, P. (1985) *Clinical epidemiology*, Little Brown Company, Boston/Toronto.
27. James, G. P., Paul, K. L. & Fuller, J. B. (1978) *Am. J. Clin. Pathol.* **70**, 671–678.
28. Ritchie, C. D., Bevan, E. A. & Collier, St. J. (1986) *Br. Med. J.* **292**, 681–683.
29. Bullock, N. (1986) *Br. Med. J.* **292**, 645.
30. Kierkegaard, H., Feldt-Rasmussen, U., Horder, M., Andersen, H. J. & Jorgensen, P. J. (1980) *Scand. J. Clin. Lab. Invest.* **40**, 259–261.

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