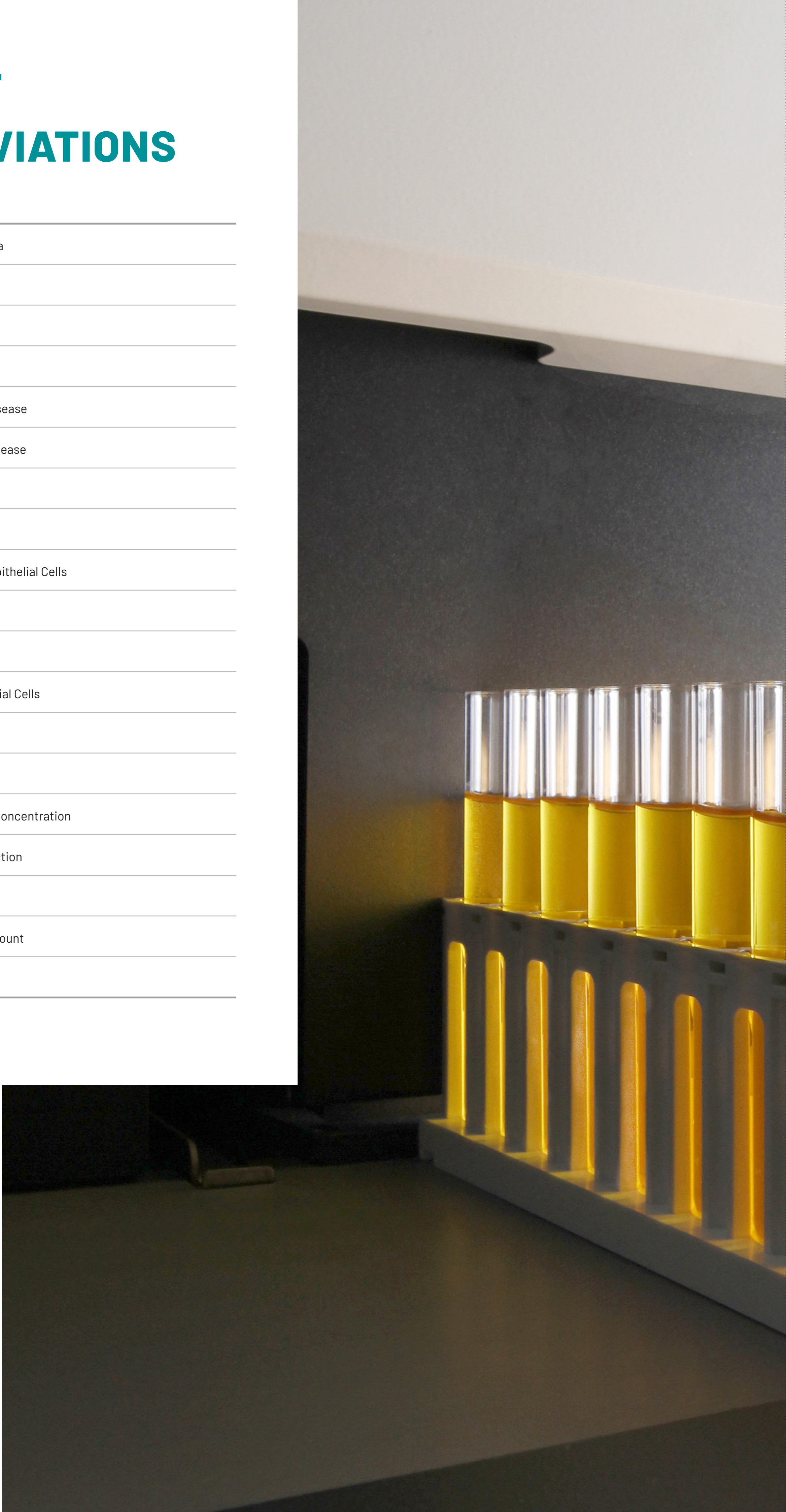
REAL WORLD EXPERIENCE OF FULLY AUTOMATED URINALYSIS

01 LIST OF ABBREVIATIONS

BACC	Cocci-like Bacteria
BACR	Rod-like Bacteria
CaOX	Calcium Oxalate
CAST	Casts
CKD	Chronic Kidney Disease
CVD	Cardiovascular Disease
HYA	Hyaline Cast
MUC	Mucus
NSE	Non-Squamous Epithelial Cells
RBC	Red Blood Cell
SPRM	Sperm
SQEP	Squamous Epithelial Cells
TRIP	Triple Phosphate
UA	Uric Acid
UUN	Urinary Nitrogen Concentration
UTI	Urinary Tract Infection
WBC	White Blood Cell
WBCC	White Blood Cell Count
YST	Yeast



02 EXECUTIVE SUMMARY

Urinalysis is one of the most frequently performed clinical investigations. It's used to screen for, diagnose, and monitor a wide variety of renal, urological and metabolic conditions. Manual urinalysis involves visual examination, dipstick test, and microscopy of the urinary sediment. Manual urinalysis is time- and labour-intensive, requires specific expertise and is prone to analytical errors. Automatic urine analysers are now commonplace in larger laboratories.

The Laura XL (Erba Mannheim) is a fully automated urine analyser, combining urine strip reading with digital microscopy, aimed at mid-sized laboratories. It uses the gravity sedimentation technique for automatic microscopy, producing clear, high-resolution digital images reducing the need for additional manual microscopy. 125-160 tests per hour can be performed, and just 0.9 mL of urine is needed for full analysis. The Laura XL features active humidity protection and automatic programmed maintenance. There are 3 operating modes (chemistry only, sediment only, and hybrid), 10 chemistry parameters, 16 automated sediment categories, another 16 manual sediment categories, and 4 customised sediment categories. The Laura XL is compact, powerful, fast and economical.

The Laura XL analyser is being used in the large CITILAB laboratory in Moscow. Staff felt that it increased their productivity and so conducted a comparison with another fully automated urine analyser, which uses flow cytometry for sediment examination. The number of urine samples which required additional manual microscopic examination was evaluated for each analyser.

For the flow cytometry analyser, 18.6% of samples required additional microscopic examination compared to 1.7% for the Laura XL. This amounted to 57.7 ± 11.2 samples per work shift for the flow cytometry analyser, compared to just 5.1 ± 2.0 samples for the Laura XL ($p<0.0001$).

The difference can be explained by one of the key features of the Laura XL. When pathological or atypical elements appear on the Laura XL screen, the operator can check the accuracy of the automatic identification and, if necessary, make changes.

Modern fully automated urine analysers, such as the Laura XL, make it possible to avoid many of the errors characteristic of visual and semi-automated examinations, since sampling, chemical and microscopic analysis, as well as the issuance of results occur automatically in compliance with specified criteria.

03 CLINICAL UTILITY

Urinalysis is one of the most frequently performed clinical investigations carried out in both inpatient and outpatient settings, due to its high information content and accessibility. Its importance in diagnosis has been understood throughout history. In fact, Sumerian and Babylonian physicians dating back to 4,000 BC recorded their assessment of urine on clay tablets.[1]

Today, urinalysis is used to screen for, diagnose and monitor numerous renal, urological and metabolic disorders. Chronic Kidney Disease (CKD) is a global health burden, with a prevalence of around 13%.[2] CKD is regarded as both an accelerator of cardiovascular disease (CVD) risk, and an independent risk factor for CVD events. Decreased renal function is a predictor of hospitalisation, cognitive dysfunction and poor quality of life.2 With increasing global awareness of, and importance placed on CKD, the role of urinalysis in screening, diagnosing and monitoring of the condition remains paramount.

Urinalysis also has a vital role in diabetes management. Glycosuria is often the first finding in both type 1 and type 2 diabetes, with the presence of ketones pointing to the development of diabetic ketoacidosis. In established diabetes, urinary microalbumin is routinely tested for, as a marker of associated kidney damage.

Several urological malignancies, including bladder cancer, can be revealed by the presence of blood and abnormal cells in the urine. After treatment, routine urine cytology is common to detect recurrence.

Urinary tract infections (UTIs) are extremely common worldwide, especially in women. Urinalysis to detect the presence of leukocytes and nitrites is diagnostic, while microscopy to identify the bacteria guides treatment. Treatment usually commences based on these findings while urine culture results may be awaited.

Urinary specific gravity yields valuable insight into a patient's hydration status and the ability of the kidneys to concentrate urine – important in a number of conditions such as adrenal insufficiency, diabetes insipidus and the syndrome of inappropriate antidiuretic hormone. Urinary pH is useful in the diagnosis of renal tubular acidosis, UTIs and renal calculi.[3]

Haematuria, detected on dipstick tests, indicates the presence of either red blood cells, myoglobin or haemoglobin in the urine. Microscopic examination distinguishes haematuria from other conditions. Haematuria has a wide differential diagnosis including glomerulonephritis, tumours, calculi and infections.[3] Like haematuria, the presence of protein in the urine has many causes. Urinalysis alerts clinicians to the proteinuria, allowing further investigations to take place.

Urinalysis also has a role to play in the evaluation of liver function. Detection of bilirubin suggests possible liver dysfunction or biliary obstruction. High levels of urobilinogen in the urine points to haemolysis or hepatocellular disease, while low levels may result from bile duct obstruction.[3]

Microscopic examination of urine is a crucial part of urinalysis, and aids in the diagnosis of a variety of diseases. The identification of cells such as erythrocytes and epithelial cells can be useful in the diagnosis of renal disease. Examination of casts in the urinary sediment can help to localise disease.

04 MANUAL URINALYSIS

The urinalysis strategy recommended by the European Urinalysis Guidelines[4] is a two-step process:

Step 1: Visual examination and dipstick test

Step 2: If there is erythrocyturia, leukocyturia, bacteriuria or proteinuria, urine samples are subjected to further analysis by microscopy

As the dipstick test has poor sensitivity and negative predictive value, screening by this method alone carries the risk of missing infections and other diseases.[5]

Until recently, the most widely accepted urinalysis methodology was microscopic urine sediment analysis. There are different manual methods for urine sediment examination. Counting can be done in a standardised or a non-standardised way; counting can be done from a sample under a coverslip or in a chamber, and from centrifuged or uncentrifuged samples. Other potential variables in manual urine microscopy include the speed of centrifugation, the time of centrifugation, the amount of urine remaining in the tube for resuspension, and whether the urine is stained.[6]

Manual urine microscopy is both time- and labour-intensive, and requires specific expertise which may not be available at all times of day. Both manual dipstick testing and manual microscopy are also associated with extensive analytical errors.[7]

Main errors associated with manual and semi-automated urine dipstick testing

- At the moment the strip is being immersed into the urine reservoir, all reaction sections of the strip are simultaneously wetted. This often leads to cross-carry and distortion of results.
- Analysis on test strips determines the parameters of urine sediment (leukocytes, red blood cells, bacteria) indirectly, that is, not the cells themselves are determined, but biochemical parameters.
- Limitations specific to strip technologies.

Main errors associated with manual microscopy of urine sediment

- Lack of standardisation for all stages of analysis
- Lack of quality control methods
- Lack of reference ranges
- Lack of a reference method for urine microscopy to provide correct identification of particles and accurate quantification[6]
- Several steps in manual microscopy, such as centrifugation, decantation, and resuspension can lead to cellular lysis and loss[7]

Over the past 25 years, technological advancement has led to the development of automatic urine sediment analysers for high-volume laboratories. The demand for automation was fuelled by concerns over standardisation, inaccuracy, and the time and labour needed for manual microscopy. Progress in computer technology and informatics now allows automated microscopy based on pattern recognition.

05 LAURA XL

The Laura XL is a fully automated urine analyser, combining urine strip reading with digital microscopy. Launched in 2019, it forms part of Erba Mannheim's Vertex range of diagnostics, aimed at mid-sized to large laboratories. The two-module integrated station consists of one module which performs analysis of the chemical parameters of urine on diagnostic test strips using reflective photometry; and one module performs urinary sediment examination using automated microscopy technology in a format compatible with manual microscopy.

The Laura XL offers the following key benefits:

⊕ 3 operating modes

- Chemistry only
- Sediment only
- Hybrid

⊕ Fully automated processing of the urine samples: automated homogenisation, dispensing onto strip, sedimentation and result evaluation

⊕ Workflow optimisation

- Up to 160 tests per hour in chemistry only mode
- Up to 125 tests per hour in sediment only and hybrid modes

⊕ Gravity sedimentation is a gentle technique meaning less damage to fragile elements like casts, and a lower risk of RBC lysis. Gravity sedimentation also results in cost savings compared to centrifugation and measurement in flow techniques, as it removes the need for expensive disposable cuvettes

⊕ Active humidity protection of diagnostic strips. Some diagnostic pads, such as nitrites, blood and leukocytes, are very sensitive to humidity which can cause false positive results. Unlike most analysers which have passive humidity protection like silica gel bags, the Laura XL has two desiccators working in parallel, blowing dry air into the strip feeder, maintaining humidity 40% lower than ambient humidity

Just 0.9 mL of urine needed for full analysis. The efficient fluidics system means far fewer samples will be rejected due to low volume, causing delayed treatment as samples are re-collected. This is particularly helpful in paediatric and neonatal samples

Automatic programmed maintenance saves time and labour, and ensures the analyser is always fully calibrated and ready for analysis

10 chemistry parameters

- Specific gravity, Leukocytes, Nitrites, pH, Protein, Glucose, Ketones, Urobilinogen, Bilirubin, Blood
- Plus sample colour and clarity

16 automated sediment categories

- WBC, WBCC, RBC, SQEP, NSE, HYA, CAST, Crystals (CaOX, TRIP, UA) BACR, BACC, YST, MUC, SPRM, UUN

16 manual sediment categories for additional manual re-evaluation

4 customised sediment categories

User friendly and simple graphical user interface utilises large icons and an intuitive software structure. The GUI guides the user through many of the procedures

Full LIS connectivity streamlines data processing and reporting

Small footprint frees up valuable workspace. The Laura XL measures just 943 x 675 mm

The Laura XL has been specifically designed to solve the problems faced by many mid-sized laboratories facing increasing demands for urinalysis. Full automation allows for workflow optimisation, and clear high-resolution digital images reduce the need for additional manual evaluation by visual microscopy. Use of re-usable cuvettes, allowed for by the gravity sedimentation technique, contribute to the economical operation of the Laura XL. Powerful, high performance analytics are blended with ease of use and a compact design.

125 - 160 tests/h

10 chemistry parameters

18 automated sediment categories

20 manual categories

06 THE RUSSIAN EXPERIENCE

Three Laura XL automated urine analysers operate in the CITILAB laboratory in Moscow, a large lab with a high throughput. According to anecdotal user assessment, the Laura XL significantly increased the productivity of the laboratory staff. To quantify this assessment, a comparison was made between the Laura XL (Erba Mannheim) and another automatic urine analyser which uses the flow cytometry technique for sediment examination. During the study, the number of urine samples which required additional manual microscopic examination was evaluated.

When using the flowing cytometry analyser, on average, staff were required to manually examine every fifth urine sample (18.6% of all samples). However while using the Laura XL, only every 50th sample required manual examination (1.7% of all samples). In absolute terms, this amounted 57.7 ± 11.2 samples per work shift for the flow cytometry analyser, compared to just 5.1 ± 2.0 samples for the Laura XL ($p<0.0001$).

The number of samples that needed manual microscopic analysis of urinary sediment when using the station with flow cytometry technology was around 10 times higher than the number of manual urinary sediment studies using one of the Laura XL stations. This fact can be explained by one of the key features of the Laura XL. When pathological or atypical elements appear on the Laura XL screen, the operator can check the accuracy of the automatic identification and, if necessary, make changes.

To date, no automatic analysers of urine sediment entirely avoid the need for additional microscopic examination for 100% of urine samples. However, analysers based on automatic microscopy technology can significantly reduce repetitions, reduce labour requirements and reduce financial costs for laboratories.

07 CONCLUSION

Modern fully automated urine analysers, such as the Laura XL, make it possible to avoid many of the errors characteristic of manual and semi-automated examinations, since sampling, chemical and microscopic analysis, as well as the issuance of results occur automatically in compliance with specified criteria. These systems not only level the human factor, making it possible to standardise the results, but also significantly increase laboratory productivity. With greater emphasis on the early detection of conditions such as chronic kidney disease and diabetic nephropathy fuelling the relentlessly high demand for urinalysis, fully automated systems are no longer the luxury of large laboratories, but are becoming a necessity in many mid-sized labs worldwide.

08 REFERENCES

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