Laboratory Results Assessment by the Laboratory Physician and Clinical Chemist

Befundung von Laborergebnissen durch den Laborarzt und Klinischen Chemiker

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Summary: Laboratory results assessment by the laboratory physician and the clinical chemist can support the clinician in his decision-making process. This is effective in cases where the laboratory physician knows the hypothesized diagnosis. However, the main support of the laboratory physician and clinical chemist in the decision-making process is not patient oriented and is only of indirect nature. This support consists of the education of clinicians in the following: which tests to order and how to interpret the results, to consciously consider alternative tests or even specific laboratory tests to solve certain problems, to reduce reliance on intuition by developing simplified test strategies to promote rational decision-making taking into account the sensitivity, specificity, and predictive values of a test and the prevalence of disease.

Keywords: laboratory results; assessment; laboratory physician; clinical chemist.

Zusammenfassung: Die Beurteilung von Laborergebnissen durch den Laborarzt und Klinischen Chemiker kann für den Kliniker in den Entscheidungsprozessen der Diagnosefindung nützlich sein. Das ist besonders effektiv in Fällen wo der Laborarzt die Vermutungsdiagnose kennt. Die wesentliche Hilfe des Laborarztes und Klinischen Chemikers ist jedoch indirekter Natur und nicht patientenbezogen. Sie besteht in der konstanten Schulung des Klinikers in folgenden Belangen: den zur klinischen Fragestellung adäquaten Test anzufordern und richtig zu interpretieren, in der Auswahl alternativer oder spezifischerer Labortests bei bestimmten klinischen Fragestellungen, den Kliniker zu überzeugen, sich nicht zu sehr auf die Intuition zu verlassen, sondern zur Entscheidungsfindung einfache Teststrategien gemeinsam zu entwickeln unter der Kenntnis von Krankheitsprävalenzen sowie der Sensitivität und Spezifität einer Laboruntersuchung.

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Schlüsselwörter: Laborergebnisse; Befundung; Laborarzt; Klinischer Chemiker.

The use of clinical laboratory tests by physicians has a significant effect on the quality of patient care as well as on total health-care costs. However, a laboratory test should only be ordered if its result will influence the choice of therapy or patient management. It should impact the prognosis or quality of life in a wide context [1]. Today, clinical routines are far from this ideal, a fact that can be improved if the laboratory physician and the clinical chemist are actively involved in the decision-making process of the treating physician.

As shown in Figure 1, laboratory tests are used to make medical decisions. In approaching a case, the

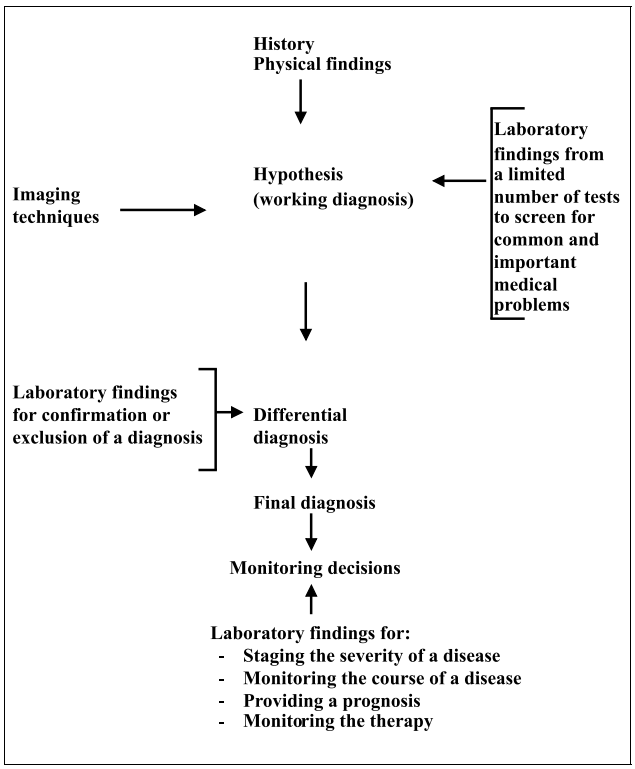

Figure 1 Framework for laboratory testing in medical decision making.

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Table 1 Approaches of the clinical chemist to support the physician in decision-making processes

Development of decision-oriented laboratory testing programs
Education of the clinician in approaching a diagnosis using laboratory tests
Development of recommendations for rational decision making in special clinical scenarios
Assessement of laboratory findings with high laboratory diagnostic disease probability

clinician makes a series of inferences, based on patient history and physical findings about the patient's condition and, using a screening panel of laboratory tests, proceeds towards a working diagnosis. Along with some alternatives, such as imaging techniques and using follow-up laboratory tests, he confirms or excludes a disease in question and generates a differential diagnosis [2].

Young clinicians often create a possibilistic differential diagnosis, that is a listing of all the possible causes of the patient complaint. Experienced clinicians create a different kind of differential diagnosis, based on a combination of the following experiences [3]:
- probabilistic (considering first those disorders that are more likely),
- prognostic (considering first those disorders that are more serious if missed),
- pragmatic (considering first those disorders most responsive to treatment).

The clinician then refines the diagnostic hypotheses, often with the use of further laboratory tests. In doing so, he reduces the inherent uncertainty so that the most appropriate diagnosis will be the final diagnosis.

How can the laboratory physician support the clinician in decision-making processes? The laboratory physician has a direct influence in medical decisions by the assessment of laboratory findings only in a small percentage of cases. However, he can indirectly influence the assessment of laboratory results by educating the clinician in decision-oriented laboratory testing. Approaches of the laboratory physician to support the clinician are shown in Table 1.

Development of decision-oriented laboratory testing programs

An important issue in the decision-making processes of the clinician is the structural layout of the laboratory request form. In many laboratories, a long list of individual tests together with multitest panels are offered like a restaurant menu to the physician. Sometimes these panels are created by the manufacturers and have no clinically related basis [2]. The use of panels is not inappropriate, however their content is important. The content of a panel must follow clinical diagnostic reasoning, which proceeds from effect to cause, that is from symptoms, signs, and laboratory data to cause. The content of a laboratory panel should not follow pathogenic reasoning which proceeds from cause to effect, that is from cause to symptoms and laboratory findings. The differences between the diagnostic and the pathogenic reasoning in the development of a diagnostic profile for the case finding in icteric patients is shown in Table 2.

Table 2 Examples for the formation of laboratory test panels according to clinical diagnostic and pathogenic reasoning in the icteric patient

Clinical diagnostic reasoning	Pathogenic reasoning
– Bilirubin, total, conjugated, unconjugated	– Hepatotropic viral antigens and antibodies
– ALT, AST	– Pancreatic cancer, e. g. CA 19–9
– ALP, LD – Haptoglobin – Reticulocyte count	– Autoimmune hemolysis, e. g. autoantibodies, complement

Contents of the laboratory request form should concentrate on the following items [2]:
- Panels for the identification of common diagnostic problems: By concentrating on these problems, the issue of inappropriate test utilization from an endless number of tests, which confuse the clinician, to a finite list of medical decisions can be managed.
- Decision-oriented panels and tests to solve problems in differential diagnostics and in patients with mono symptomatic disorders: Decision-oriented laboratory testing encourages the physician to use the right test and eliminates unnecessary ones.
- For a given screening or decision-making situation, tests with high pre-test probability should be listed on the request form. If the disease in question is a kidney disorder, the panel serum creatinine, blood and albumin in urine has the highest test probability to diagnose most of the renal diseases.

The laboratory request form should also convey information to the laboratory physician and the clinical chemist which help the laboratory to make test interpretation. Important items are [2]:
- the health-care facility (e. g. hematologic/oncologic, gastro-enterologic, or obstetric unit) from which a test or test panel was ordered because this limits the number of possible diseases in question.
- gender and age of the patient can give further diagnostic information for the interpretation of laboratory test results.

Individualized request forms should be used for special health-care facilities or special specimens. They can re-

Table 3 Examples of decision-oriented laboratory testing

Decision	Laboratory testing
Anemia	Complete blood count (CBC)
Hyperthyreoidism	TSH
Myocardial infarction	Troponin
Inflammation	CBC with differential, CRP
Acute abdominal pain	CBC with differential, lipase, ALT, glucose, creatinine, electrolytes, C-reactive protein (CRP), urinalysis, Watson-Schwartz test, hCG
Coma	Glucose, ketone bodies, urea, ammonia, osmolarity, electrolytes, Ca, FT4, alcohol, drugs
Acute liver disease	ALT, AST, GGT, ALP, bilirubin
Cholestasis	ALT, ALP, bilirubin
Chronic liver disease	AST, ChE, Elektrophorese

duce the number of tests ordered for special health-care situations.

The presentation of decision-oriented tests and test panels on the request form is very important. Decision-oriented laboratory testing represents an effective way to encourage physicians to use the right test and eliminate unnecessary ones. A further advantage of decision-oriented testing programs is that they enhance serially linked, test-dependent decisions. Rational decision-making programs have to use simplified strategies take into account probabilities and values of outcomes. In decision-oriented laboratory test programs, the laboratory physician has to combine his experience about the likelihood of pathological laboratory findings in a disease with the prevalence of this disease in a clinic. Examples for decision-oriented tests and test panels are shown Table 3.

Education of the clinician

Laboratory results assessment of common laboratory tests is mainly a task of the clinician. The interpretation of special laboratory findings should be made by the laboratory physician. For rational decision making using results of common laboratory tests, the clinician must be educated from the laboratory physician in the concept of probability. Probability is an expression of likelihood and thus represents an opinion of the relative frequency with which a laboratory finding is likely to occur in a disease. This education should include the following items [4]:

– pre-test probability,
– threshold probability,
– interpreting of test characteristics and evaluating test performance.

Pre-test probability

Normally a clinician estimates pre-test probability based on personal experience or on the experience of colleagues and the literature. In this way, he transforms experiences with a laboratory test into quantitative expression of probability. The clinician may turn to the laboratory physician for assistance in estimating the pre-test probability of diseases. The laboratory physician should evaluate the prevalence of diseases and calculate the pre-test probability of diseases in particular medical units of the hospital. For example, in the gastro-enterological clinic of Krankenhaus Nordwest, the prevalence of liver diseases is 18 %. The diagnostic sensitivity reported in the literature for the panel ALT, GGT, and CHE for liver diseases is 94 %. However 55 % of all the patients in this clinic have at least one pathologic test of the panel, indicating a pre-test probability of liver disease of 0.3.

Threshold probability

Clinicians must be educated by the laboratory physician in setting the threshold probability of a laboratory test. At a special threshold value of a test, the clinician has to decide whether to treat the disease in question. The treatment threshold probability is defined as the probability of disease at which the clinician is indifferent between giving treatment and withholding treatment. Likewise, the treatment threshold probability is generally low when treatment has high benefit in diseased and low risk for non-diseased patients. The laboratory physician has to inform the clinician about the threshold probabilities of important tests. For example, a gastroenterologist evaluating a patient with acute abdominal pain and suggesting an acute pancreatitis using ultrasonography would need to be as certain as possible that the patient has elevated lipase activity before recommending to withhold surgical treatment. He has to be educated that for the turbidimetric test, used in the laboratory, the upper reference value is 200 U/l, however, the cut-off level for acute pancreatitis is 600 U/l.

Interpreting test characteristics

The clinician has to know how much a positive test discriminates diseased from non-diseased patients. He has to be educated by the laboratory physician about the post-test likelihood of disease of the gold standard test and the index test. Laboratory tests with high diagnostic sensitivity and specificity are gold standards. The gold standard test is the test used as a surrogate marker for disease. The index test is the test whose characteristics are in question. For example, the immunoblot is the

gold standard test for the diagnosis of HIV infection, the immunoassay with a lower diagnostic specificity is used as index test.

Recommendations for laboratory test assessment

Clinical laboratory recommendations should outline optimal care for patients in a given clinical scenario. They represent a teaching tool for improving informed decision-making by physicians. Recommendations address the grey area between the knowledge and experience of the clinician and the laboratory physician regarding the use and assessment of laboratory tests. The main argument for recommendations is the evidence of a wide practice pattern variation in using laboratory tests. Practice variation usually indicates uncertainty in the use and assessment of laboratory tests.

Recommendations are useful [4]:

- when strong diagnostic evidence of a laboratory test exists for a clinical condition,
- in high-prevalence conditions because high-prevalence conditions have a greater impact on hospital expenditure,
- if disease outcomes or costly treatment regimens can benefit,
- in situations where variation in the use of laboratory tests by clinicians usually indicates uncertainty either in the diagnosis or in monitoring the treatment of a condition,
- if potentially fatal disease requires precise laboratory testing and monitoring of treatment.

Recommendations are useless in the following situations:

- if the variation in the use of laboratory tests in a decision-making process by the clinician is the result of controversy in the literature,
- if there is no evidence for a laboratory test in a decision-making process,
- if good evidence is not available regarding the clinical question.

Recommendations should concentrate on a special situation and not aim to address all aspects of patient care. Recommendations should be made for physicians:

- in primary-care medicine, because inappropriate requests of laboratory tests and inappropriate decisions are more frequent in primary-care medicine than in routine diagnostics,
- in clinics with traditionally low experience in the assessment of laboratory results, e. g. surgeons, orthopedics,
- in specialty-care units. However the laboratory physician must be cautious. In specialty-care medicine, cookbook medicine is very common because physicians have taken years of additional training to gain expertise in the management of their patients, who are often atypical.

It is important that the laboratory physician develops these recommendations with the input from specialists and opinion leaders of the hospital or scientific associations and under the aspects of evidence-based medicine [5].

Assessment of laboratory results by the laboratory physician and clinical chemist

The assessment of laboratory findings should follow two rules.

1. The assessment of laboratory results should not be performed for tests where well known reference ranges exist nor in standard decision-making processes which can easily be practiced by the clinician. Exceptions are situations in patient management where clinical decision levels are included. Decision levels refer to threshold values above or below which a particular management action is recommended. For example, the reference range for potassium is 3.6 to 4.8 mmol/l. The decision level above which hyperkalemic coma can occur is 6.2 mmol/l. It would be inappropriate to assign the cause of a patients coma to hyperkalemia if the concentration is 5.9 mmol/l.
2. The assessment of laboratory results must rely on scientific papers and on textbooks. The assessment should be focused on the clinical scenario of the patient and must have a positive effect on:
   - case finding,
   - treatment intervention,
   - or lead to a change in patient management.

An important precondition is that the laboratory physician knows the disease in question of the patient. The discrimination between diseased and non-diseased patients should only be made in processes where a panel of index tests can be assessed or in a situation where a gold standard test was used.

In the laboratory department of the Krankenhaus Nordwest the main field in the assessment of laboratory results is the active involvement in case finding. The laboratory physicians have an agreement with the clinicians to do extended laboratory testing in cases of special laboratory findings.

- In testing for thyroid diseases, we determine prolactin in situations where FT4 is normal and TSH is increased. TSH, like cortisol, prolactin and growth hormone is a stress hormone. The combination of increased TSH and normal FT4 in our hospital mainly results from transient TSH increase in acutely stressed patients. In this situation, TSH and prolactin concentrations are elevated.
- In patients with ferritin concentrations in the range of 15 to 99 µg/l, CRP is determined, and if higher than 5 mg/l, the concentration of the soluble transferrin receptor is measured in addition. If the value of the sTfR is increased, we make the assessment “iron deficiency”.

– In cases of normocytic, normochromic anemia we have a special program for evaluation of the cause of the anemia.

In conclusion, the laboratory physician and the clinical chemist can play numerous roles in the assessment of laboratory results. They are not the stake holders in patient care but have an important diagnostic perspective to contribute. They are well qualified to evaluate the medical literature for strong evidence-based assessment of laboratory results. Although laboratory physicians and clinical chemists have no or only second-hand information for a given clinical scenario or disease, they can support the clinical input of the clinician, support the streamlining of the case-finding process, and can help to save costs.

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