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Recommendations for the frequency of ordering laboratory testing

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Abstract: Laboratory testing is crucial for the successful medical treatment of many patients. Laboratory tests should neither be ordered too infrequently nor too frequently (in the form of repeat testing). These recommendations summarize the intervals for repeat testing based on studies, pathophysiology and consensus, in regard to both the time intervals between two tests and the additional criteria for the repeat testing. These recommendations are complemented by general principles for the indication and testing frequency of laboratory testing.

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Introduction

The central objective of health care is the prevention of premature death and suffering, and the restoration of functional health. Information on further action to be taken is derived from diagnostics by way of medical laboratory tests. These data, however, are only clinically useful for the patient if clinical action can be derived from them. In general, laboratory tests result in therapies being started, ended or modified; in individual cases, the pathophysiology of an illness is examined more closely through laboratory diagnostics.

In addition to the clinical and scientific aspects of the consequences of diagnostics, psychological aspects must also be taken into account when determining the indication of laboratory tests. Thus, waiting for the findings and the failure to perform a test can trigger anxiety and stress in patients [1]. The results of a test and/or the fact that a test is done can lead to social stigmatization (e.g., in connection with HIV tests). However the findings from laboratory tests can also contribute to improved lifestyle habits, such as when it comes to smoking or physical activity. In some cases, if a hereditary disease, which would show symptoms only in the distant future (e.g., Huntington's disease), can be ruled out by laboratory testing, this can have a liberating effect for the patient.

As with drug treatment or surgical intervention, the use of laboratory tests must also be evaluated in terms of the clinical benefit. Such an evaluation is generally complex, because most laboratory tests are used to rule out illnesses. Thus, the benefit of laboratory tests is always indirect, i.e., the treating physician must always take additional action to achieve therapeutic success. Such action may involve starting patients with positive

test results on immediate treatment or sending patients with negative test results for further diagnostic tests with different methods, such as imaging. When evaluating the benefit of laboratory diagnostics, there must also be a distinction between a direct, patient-relevant benefit (i.e., a direct link to the suspected illness) and the controlling merely of surrogate parameters [2].

Particularly in differential diagnostics, the evaluation of the benefit depends on the incidence of the illness in the population, because this strongly affects the positive and/or negative predictive value of a test procedure [3]. Furthermore, an evaluation of the benefit must not only look at the direct benefit to the patient, but also the (economic) benefit for the community.

The validity of the laboratory findings figures in all benefit considerations. The validity is determined by the uncertainty of the analysis itself, the day-to-day variability in terms of circadian rhythms, and also by food intake, physical activity, medication and the differences between various test assays [4]. An example of the latter is the difference in determining cardiac peptides or creatinine between the POCT format and conventional laboratory equipment [5, 6] and/or in determining tumor markers with test systems from different manufacturers [7].

The evaluation of the validity of medical laboratory findings is highly complex. Many quantitative parameters – e.g., in enzymology – can be measured highly standardized and with the highest degree of precision. For other parameters (e.g., clotting factors and tumor markers), however, the result of the measurement is often very much dependent on the assay used. In the case of semi-quantitative results (e.g., in autoimmune serology, infectious serology), the evaluation of findings in the gray area may be linked to poor reproducibility. Thus, results obtained via highly standardized test methods on a specific test platform can generally be transferred also to other platforms in terms of the validity. However this transferability to other test platforms must be questioned when it comes to poorly standardized tests.

Factors influencing the frequency of repeat testing

If the half-life of the analyte in vivo as well as the performance of the test (such as the day-to-day variation coefficient, detection limit and/or lower of limit of quantification) are known, minimum periods can be defined that, if not reached, do not give rise to the expectation of changes to the measured values, which means that a repeat measurement will not yield any additional information. Typical examples for this are the Hb_{A1c} analysis [8], the determination of troponins with the acute coronary syndrome [9] or the PSA test after surgery to remove a tumor and/or an organ [10]. This assumes that an additional condition did not affect the half-life of the analyte in this particular patient. Common causes of such changed half-life times include the development of renal insufficiency in connection with renally eliminated substances, enzyme induction through specific drugs in connection with TDM or volume changes in the case of bleeding, the administration of infusion solutions or erythrocyte concentrates. Special conditions apply to repeat frequencies of laboratory tests for special issues. Thus, the determination of Hb_{A1c} in pregnant patients should be carried out monthly, as well as for patients with poorly controlled diabetes mellitus or after changes in diabetic treatment [11].

In addition to the known analytical parameters of laboratory tests – i.e., deviation in the measurement from the 'true value' – one must also take into account pre-analysis and, if necessary, post-analysis. Some factors of pre-analysis, such as circadian rhythms [12] or food intake [13], are known and are therefore controllable, in theory at least. In contrast to the situation of analysis, with its highly developed quality management system in the laboratory, serious errors in pre-analysis and post-analysis are not rare [14], nor can they be fully controlled: the biggest source of major errors is by far the misidentification of patients. This happens almost always at the time a sample is taken at the doctor's office, a clinic or hospital ward or when the findings are assigned to a patient record (typically by slipping the findings in the wrong patient record). According to a large number of studies, serious pre-analytical errors occur in approx. 0.1%–0.5% of all samples submtitted for testing [15–18], i.e., an almost daily occurrence at every major medical facility.

Another important source of pre-analytical errors is the submission of unsuitable test material – particularly due to artificial hemolysis, wrong collection containers, insufficient sample volumes and/or incorrect mixing ratios regarding the anticoagulant. The submission of unsuitable material is a much more common source of errors than the misidentification of patients. However the evaluation of the consequences of such pre-analytical errors for the analytical findings is problematic: for example, in the case of low hemolysis, the use of LDH may still be possible to rule out hemolytic anemia, but the sample would be inappropriate for follow-ups with a known diagnosis. The marking of the findings in the event of a problem in the measured value caused by icterus, lipemia and hemolysis (if the measured value deviates

from the 'true value' by more than 10%/15%/20%) is arbitrary and not always helpful in assessments: thus, when looking at the total error, a deviation of 10% may be irrelevant (e.g., in the triglyceride analysis), but it may also be crucial to the diagnostics (e.g., in the analysis of creatinine) [19, 20]. The evaluation of 'unsuitable test material', therefore, is highly uncertain even in combination with automated analyses of serum indices [21]. Problems due to in vitro hemolysis, the most common cause of unsuitable test material, should therefore always be eliminated through timely repeat analyses using materials obtained and transported correctly [22]. This can be done easily if it is not an emergency situation.

Avoiding repeat testing

The number of laboratory tests should be optimized to ensure the responsible use of existing resources in medical treatment. Avoiding multiple analyses of an analyte, among other issues, is one way to achieve this goal. Many public health efforts – e.g., the obligation to hand over the findings or the networking of inpatient and outpatient care – are designed to reduce the number of repeat tests. However, the patients' active desire to have certain repeat tests done has a significant influence on the frequency of requests [23]. On the other hand, an excessive reduction in the frequency of tests also carries the risk of overlooking changes in the health of the patients or making wrong medical decisions due to a laboratory result that does not apply (e.g., in the case of the misidentification of patients).

However the focus on avoiding laboratory tests does reveal that the decision not to repeat laboratory tests (and the resulting potential damage to the patients and/or society) is much more common than overly frequent requests. A meta-analysis of studies conducted between 1997 and 2012 (at least in those carried out outside of Germany) found that the rate of forgone, necessary laboratory tests was twice that of requests made with excessive frequency [24].

The numbers available on the frequency of avoidable repeat tests vary greatly. An Israeli study identified 19% of tests as avoidable [25], while a Dutch study found only 0.56% to be avoidable, in accordance with a cost reduction of only 0.33% [26]. The share of redundant requests is very small particularly for high-volume and cost-efficient tests. Requests for repeat testing are much more common for rare tests. However, the data available on what is a meaningful time span between repeat tests for such rare tests are inadequate [24].

The optimal use of medical laboratory tests is influenced by a multitude of factors. Apart from specifications on optimal frequency (i.e., frequency and time interval of repeat tests), key factors include the use of stepwise diagnostics and/or diagnostic paths [27, 28], avoidance of obsolete tests [29], the replacement of historically grown profiles with current profiles [30], and the timely use of innovations.

Principles for the repetition of medical laboratory tests

The repetition of medical laboratory tests is necessary in certain circumstances and, given specific constellations, may even be mandatory under the law. Examples of this are the determination of the blood group from several blood samples and the blood count before and after a transfusion to document the therapeutic success [29], the confirmation of a positive HIV finding from a second blood sample [31], the detection of bacteria in the urine of pregnant patients [32] or, if necessary, the repetition of a genetic test after 10 years, because findings have to be deleted after 10 years under the German Genetic Diagnostics Act [33]. Similar to blood grouping and HIV tests, a repeat of other laboratory tests may also be indicated where the laboratory test may have serious consequences for the patient. This may be the case, e.g., if the medical laboratory test cannot be confirmed by other diagnostic methods (such as other laboratory or clinical methods, through imaging), if the result is unexpected in light of the clinical picture (e.g., also with pre-operative screening), if there are unexplained fluctuations in the TDM, and also if there is a lack of clarity in the allocation of patients to sample material ("misidentification of patients"). Even if the findings of the laboratory test necessitate further testing with increased invasiveness and a significant risk to the patient (which is also true of some invasive diagnostics) or treatment with serious side effects (e.g., pathogen detection in connection with osteomyelitis or endocarditis), confirmation of the laboratory findings from a second sample may be useful.

As for drugs that require therapeutic drug monitoring (TDM), control measurements should generally be taken at the start of the drug treatment, after changes to the dose of the drug or any co-medication, as well as in cases of suspected changes to the pharmacokinetics, such as due to changes in the liver, kidney or heart functions [34]. As a rule, the determination of drug concentrations makes sense only in the steady state, which is reached after 4–5

Table 1 Recommended minimum time intervals for the repetition of some medical laboratory tests.

			References
HbA_{1c}	3 months in patients with diabetes mellitus undergoing insulin therapy, 6 months in patients with diabetes mellitus without insulin therapy, no specifications for use in the diagnosis of diabetes mellitus outside of pregnancy.		
Note:	Amended intervals in patients receiving transfusions or in the case of hemolysis [8, 11].		
Ferritin	2 months		[38]
Vitamin B12	2 months in case of suspected vitamin B_{12} deficiency Parenteral substitution requires repeat testing only at very long intervals. For enteral substitution, normalization of vitamin B_{12} is regularly achieved in the serum; analysis may be useful for compliance monitoring.		[38]
ANA	4 weeks, only if clinical picture changes and in connection with previous negative findings; serial measurements for standard activity determination are not recommended		[39–41]
ENA	4 weeks, only with conspicuous ANA		[40, 41]
dsDNA	6–12 weeks with active, 6–12 weeks with inactive Lupus erythematosus. This requires a conspicuous ANA.		[40, 41]
Note regarding requirements of autoimmune serology: the request is indicated only for corresponding clinical suspicion. Follow-ups are not generally advisable. The time intervals indicated refer to patients for whom a negative finding has been obtained and for whom, due to a change in the clinical picture, further clarification is needed.			
RF	4 weeks, except for Sjögren's syndrome		[40, 42]
AMA	4 weeks		[40]
ASMA	4 weeks		[40]
Parietal cell AB	4 weeks		[40]
IgG, IgA, IgM	4 weeks, to determine the CSF/serum ratio, if necessary more frequently		[40]
AFP	12 weeks		[40]
CEA	12 weeks		[40]
CA15.3	12 weeks		[40]
PSA	12 weeks		[40]
Note: To estimate the residual tissue after tumor removal, a repeated determination of tumor markers (such as ß-HCG and AFP in connection with testicular carcinoma) is recommended at weekly intervals [7, 43].			
Urine albumin/g creatinine	2x, in discrepant cases, 3x analysis on 2 and/or 3 non-consecutive days necessary (to exclude renal involvement with diabetes mellitus)		[44]
Creatinine	1 day (after application of X-ray contrast media) – 6 months as checkup for diabetic patients		[44–46]
Infectious serology (depending on the immune status of the patient and/or the presumptive stage of the disease)[a]			
	Patients		
	Seropositive	Seronegative	
HBs-Ag	180 days	7 days	
Note: In case of isolated positive result of HBs-Ag ELISA, after 30 days test for HBV-DNA, as well as in case of suspected escape mutants [47].			
Hbs-Ab, Hbc-Ab, Hbc-IgM Ab, Hbe-Ag, HBe-Ab	180 days	25 days	[48–50]
HCV-Ab	180 days	25 days	[51]
HCV-RNA	60 days	7 days	[51]
HIV-Ab	–	28 days	[31]

[a]A follow-up regarding a continuing clinical problem – especially in the early phase of infection – may be necessary at intervals of several days, with an individual assessment especially of IgM/IgA antibodies.

elimination half-lives. This means that repeat measurements are indicated already after 1 day for drugs with a short half-life (t 1/2), such as cyclosporine (t 1/2 approx. 6 h), while it would be only after 6–7 days for drugs with a long half-life, such as digoxin (t 1/2 approx. 36 h). Immediately after the start of treatment, frequent concentration controls (and/or activity determination) may be necessary in consideration of the t 1/2 until the therapeutic range has been reached, especially for drugs with varying inter-individual kinetics and narrow therapeutic

Criteria for the existence of MGUS
- Clonal plasma cells in the bone marrow: <10%
- Monoclonal protein in the serum: <30 g/L
- Absence of organ damage (anemia, hypercalcemia, renal failure, osteolysis)

Risk of progression in case of MGUS

The most important risk factor for progression is an M-protein >25 g/L as a 50% risk of transition to a multiple myeloma after 20 years. Other (additive) risk factors are an abnormal ratio of free kappa and lambda light chains in the serum and non-IgG MGUS [53]

Laboratory diagnostics sequence

Basic diagnostics:

Full blood count; in the serum, sodium, potassium, calcium, creatinine, total protein, albumin, IgA, IgG, IgM, free kappa and lambda light chains; in the urine, protein; possibly bone marrow cytology and histology

Follow-up:

For low-risk patients with MGUS: control of the parameters listed under basic diagnostics only after onset of clinical symptoms.

For high-risk patients with MGUS: control of the parameters listed under basic diagnostics every 6–24 months.

After initial diagnosis of multiple myeloma and in the further course: control of the parameters listed under basic diagnostics every 3–6 months [54, 55].

Figure 1 Laboratory diagnostics in the context of the initial diagnosis and the follow-up of patients with MGUS.
Monoclonal gammopathy of undetermined significance (MGUS) is defined by the laboratory evidence of complete or incomplete, monoclonal immunoglobulins in the serum of patients without clinical symptoms [56].

index, for example, in the case of vitamin K antagonists [35]. Repeat tests, however, are generally needed only rarely for well-controlled and stable patients who undergo maintenance treatment. Thus, the recommendation calls for controls every 3–6 months for psychotropic drugs [36], or every 1–3 months for immunosuppressants with an uncomplicated clinical course [37].

Examples of repeat frequencies for laboratory tests

Table 1 shows examples of recommendations regarding the frequency and/or minimum time intervals of repeat tests. These are usually based on international or only local consensus opinions. Quite often, minimum time intervals can be defined only for certain diagnoses and/or patient groups. Most of the recommendations mentioned for time intervals also apply to outpatients seen by a family physician: in contrast to inpatients, the influence of further factors is of little significance in their case. In the event of missing data, test frequencies for other parameters may be derived from known parameters, taking into account formation kinetics and specific analytical performance data. Thus, for example, the recommendation for determining cystatin C corresponds to the recommendation for the determination of creatinine [52]. As an example of recommended test frequencies in connection with a complex illness, Figure 1 shows the time intervals for control tests on patients with a monoclonal gammopathy of undetermined significance (MGUS).

Further development of the recommendations

The data situation for determining the optimal frequencies for the repetition of laboratory tests is currently highly unsatisfactory. Generally applicable and widely accepted test intervals have been mentioned only for few tests in the literature. These test intervals, as a rule, apply only to selected groups of patients, as shown in Figure 1. It is therefore necessary to work out further diagnostics and treatment guidelines with the input of laboratory physicians. While the guidelines available so far do recommend regular laboratory tests, the test intervals mentioned therein are usually not sufficiently grounded in science, i.e., scientific, medical laboratory concepts for defining such intervals have not been taken into account adequately thus far.

In the practical implementation of time intervals for controlling requests, IT systems are used on a regular basis. Frequently, the time intervals are set in such a way that premature requests are suppressed. It must therefore be ensured that the test can be requested more often as well in justified individual cases in order to avoid disadvantaging patients (what is known as “e-iatrogenesis”) [57]. Rather than suppressing a request automatically, it would make more sense if the IT system, when processing a request, were to give an indication that the desired test had been requested prior to the expiry of the proposed test interval. This would then allow the requesting physician to decide actively whether the request should be carried out or be canceled.

The general use of time intervals for request control can be recommended only for few analytes at this time [38]. By contrast, when using diagnostic pathways, the concept of given test intervals is extremely useful and also technically feasible [28]. The major advantage of diagnostic pathways is that the control of requests can be realized not only on the basis of a known diagnosis, but also on the basis of new findings obtained over the course of the pathway, which makes it possible to adjust it gradually.

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References

1. Rang M. The Ulysses syndrome. Can Med Assoc J 1972;106:122–3.
2. Ciani O, Buyse M, Garside R, Pavey T, Stein K, Sterne JA, et al. Comparison of treatment effect sizes associated with surrogate and final patient relevant outcomes in randomised controlled trials: meta-epidemiological study. Br Med J 2013;346:f457.
3. Houben PH, Winkens RA, van der Weijden T, Vossen RC, Naus AJ, Grol RP. Reasons for ordering laboratory tests and relationship with frequency of abnormal results. Scand J Prim Health Care 2010;28:18–23.
4. Plebani M. Evaluating laboratory diagnostic tests and translational research. Clin Chem Lab Med 2010;48:983–8.
5. Mueller C, Scholer A, Laule-Kilian K, Martina B, Schindler C, Buser P, et al. Use of B-type natriuretic peptide in the evaluation and management of acute dyspnea. N Engl J Med 2004;350:647–54.
6. Straseski JA, Lyon ME, Clarke W, Dubois JA, Phelan LA, Lyon AW. Investigating interferences of a whole-blood point-of-care creatinine analyzer: comparison to plasma enzymatic and definitive creatinine methods in an acute-care setting. Clin Chem 2011;57:1566–73.
7. Passerini R, Cassatella MC, Boveri S, Salvatici M, Radice D, Zorzino L, et al. The pitfalls of CA19-9: routine testing and comparison of two automated immunoassays in a reference oncology center. Am J Clin Pathol 2012;138:281–7.
8. Driskell OJ, Holland D, Hanna FW, Jones PW, Pemberton RJ, Tran M, et al. Inappropriate requesting of glycated hemoglobin (Hb A1c) is widespread: assessment of prevalence, impact of national guidance, and practice-to-practice variability. Clin Chem 2012;58:906–15.
9. Cullen L, Mueller C, Parsonage WA, Wildi K, Greenslade JH, Twerenbold R, et al. Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. J Am Coll Cardiol 2013;62:1242–9.
10. Gregorakis AK, Stefanakis S, Malovrouvas D, Petraki K, Gourgiotis D, Scorilas A. Total and free PSA kinetics in patients without prostate cancer undergoing radical cystoprostatectomy. Prostate 2008;68:759–65.
11. Loh TP, Tan KM, Saw S, Sethi SK. Glycated haemoglobin: what is the diagnostic yield at shortened testing intervals? Diabetes Res Clin Pract 2011;94:e40–2.
12. Oosterhuis WP. Gross overestimation of total allowable error based on biological variation. Clin Chem 2011;57:1334–6.
13. Orth M, Luley C. Circadian rhythms of lipoproteins. Clin Chem 1995;41:326–7.
14. Hawkins R. Managing the pre- and post-analytical phases of the total testing process. Ann Lab Med 2012;32:5–16.
15. Wiwanitkit V. Types and frequency of preanalytical mistakes in the first Thai ISO 9002:1994 certified clinical laboratory, a 6 – month monitoring. BMC Clin Pathol 2001;1:5.
16. Plebani M, Carraro P. Mistakes in a stat laboratory: types and frequency. Clin Chem 1997;43:1348–51.
17. Carraro P, Zago T, Plebani M. Exploring the initial steps of the testing process: frequency and nature of pre-preanalytic errors. Clin Chem 2012;58:638–42.
18. Grecu DS, Vlad DC, Dumitrascu V. Quality Indicators in the Preanalytical Phase of Testing in a Stat Laboratory. Lab Med 2014;45:74–81.
19. Pieroni L, Delanaye P, Boutten A, Bargnoux AS, Rozet E, Delatour V, et al. A multicentric evaluation of IDMS-traceable creatinine enzymatic assays. Clin Chim Acta 2011;412:2070–5.
20. Fraser CG, Petersen PH. Desirable standards for laboratory tests if they are to fulfill medical needs. Clin Chem 1993;39:1447–53; discussion 53–5.
21. Tamimi W, Martin-Ballesteros J, Brearton S, Alenzi FQ, Hasanato R. Evaluation of biological specimen acceptability in a complex clinical laboratory before and after implementing automated grading serum indices. Br J Biomed Sci 2012;69:103–7.
22. Lippi G, Blanckaert N, Bonini P, Green S, Kitchen S, Palicka V, et al. Haemolysis: an overview of the leading cause of unsuitable specimens in clinical laboratories. Clin Chem Lab Med 2008;46:764–72.
23. McDonald IG, Daly J, Jelinek VM, Panetta F, Gutman JM. Opening Pandora's box: the unpredictability of reassurance by a normal test result. Br Med J 1996;313:329–32.
24. Zhi M, Ding EL, Theisen-Toupal J, Whelan J, Arnaout R. The landscape of inappropriate laboratory testing: a 15-year meta-analysis. PLoS One 2013;8:e78962.
25. Calderon-Margalit R, Mor-Yosef S, Mayer M, Adler B, Shapira SC. An administrative intervention to improve the utilization of laboratory tests within a university hospital. Int J Qual Health Care 2005;17:243–8.
26. Janssens PM, Wasser G. Managing laboratory test ordering through test frequency filtering. Clin Chem Lab Med 2013;51:1207–15.
27. Aufenanger J, Schernikau E, Wieland E. Die zukünftige Rolle des Krankenhauslabors/The future role of laboratory medicine in hospitals. J Lab Med 2011;34:271–6.

28. Aufenanger J. Do diagnostic pathways contribute to economic improvement of a hospital? Considerations from the perspective of laboratory medicine. J Lab Med 2011;35:285–9.
29. Wang TY, Serletti JM, Cuker A, McGrath J, Low DW, Kovach SJ, et al. Free tissue transfer in the hypercoagulable patient: a review of 58 flaps. Plast Reconstr Surg 2012;129:443–53.
30. Neilson EG, Johnson KB, Rosenbloom ST, Dupont WD, Talbert D, Giuse DA, et al. The impact of peer management on test-ordering behavior. Ann Intern Med 2004;141:196–204.
31. WHO. Delivering HIV test results and messages for re-testing and counselling in adults. Geneva 2010:31.
32. Kouri TT, Gant VA, Fogazzi GB, Hofmann W, Hallander HO, Guder WG. Towards European urinalysis guidelines. Introduction of a project under European Confederation of Laboratory Medicine. Clin Chim Acta 2000;297:305–11.
33. Orth M, Rost I, Hoffmann GF, Klein H-G. Praktische Umsetzung des Gendiagnostikgesetzes (GenDG) in der Laboratoriumsmedizin, dem humangenetischen Laboratorium und der humangenetischen Beratung. J Lab Med 2011;35:243–53.
34. Warner A, Privitera M, Bates D. Standards of laboratory practice: antiepileptic drug monitoring. National Academy of Clinical Biochemistry. Clin Chem 1998;44:1085–95.
35. Zhu Y, Shennan M, Reynolds KK, Johnson NA, Herrnberger MR, Valdes R, Jr., et al. Estimation of warfarin maintenance dose based on VKORC1 (-1639 G>A) and CYP2C9 genotypes. Clin Chem 2007;53:1199–205.
36. Rentsch KM. Update zum Therapeutic Drug Monitoring und zu pharmakogenetischen Untersuchungen zur Optimierung der Therapie mit Psychopharmaka. J Lab Med 2014;38:63–74.
37. Oellerich M, Armstrong VW, Kahan B, Shaw L, Holt DW, Yatscoff R, et al. Lake Louise Consensus Conference on cyclosporin monitoring in organ transplantation: report of the consensus panel. Ther Drug Monit 1995;17:642–54.
38. Sharma A, Salzmann M. The effect of automated test rejection on repeat requesting. J Clin Pathol 2007;60:954–5.
39. Abeles AM, Abeles M. The clinical utility of a positive antinuclear antibody test result. Am J Med 2013;126:342–8.
40. Kwok J, Jones B. Unnecessary repeat requesting of tests: an audit in a government hospital immunology laboratory. J Clin Pathol 2005;58:457–62.
41. Man A, Shojania K, Phoon C, Pal J, de Badyn MH, Pi D, et al. An evaluation of autoimmune antibody testing patterns in a Canadian health region and an evaluation of a laboratory algorithm aimed at reducing unnecessary testing. Clin Rheumatol 2013;32:601–8.
42. Nielsen SF, Bojesen SE, Schnohr P, Nordestgaard BG. Elevated rheumatoid factor and long term risk of rheumatoid arthritis: a prospective cohort study. Br Med J 2012;345:e5244.
43. Diamandis EP, Hoffman BR, Sturgeon CM. National academy of clinical biochemistry laboratory medicine practice guidelines for the use of tumor markers. Clin Chem 2008;54:1935–9.
44. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), (AWMF) AdWMF. Nationale Versorgungsleitlinie Nierenerkrankungen bei Diabetes im Erwachsenenalter 2013; (1). Available at: http://www.diabetes.versorgungsleitlinien.de. Accessed on Jun 14 2014.
45. Abujudeh HH, Gee MS, Kaewlai R. In emergency situations, should serum creatinine be checked in all patients before performing second contrast CT examinations within 24 hours? J Am Coll Radiol 2009;6:268–73.
46. Morcos SK, Thomsen HS, Webb JA. Contrast-media-induced nephrotoxicity: a consensus report. Contrast Media Safety Committee, European Society of Urogenital Radiology (ESUR). Eur Radiol 1999;9:1602–13.
47. Purdy MA. Hepatitis B virus S gene escape mutants. Asian J Transfus Sci 2007;1:62–70.
48. Buster EH, Flink HJ, Cakaloglu Y, Simon K, Trojan J, Tabak F, et al. Sustained HBeAg and HBsAg loss after long-term follow-up of HBeAg-positive patients treated with peginterferon alpha-2b. Gastroenterology 2008;135:459–67.
49. Harris KR, Dighe AS. Laboratory testing for viral hepatitis. Am J Clin Pathol 2002;118 Suppl:S18–25.
50. Cornberg M, Protzer U, Petersen J, Wedemeyer H, Berg T, Jilg W, et al. Aktualisierung der S3-Leitlinie zur Prophylaxe, Diagnostik und Therapie der Hepatitis-B-Virusinfektion. Z Gastroenterol 2011;49:871–930.
51. Sarrazin C, Berg T, Ross RS, Schirmacher P, Wedemeyer H, Neumann U, et al. Update der S 3-Leitlinie Prophylaxe, Diagnostik und Therapie der Hepatitis-C-Virus(HCV)-Infektion. Z Gastroenterol 2010;48:289–351.
52. Premaratne E, MacIsaac RJ, Finch S, Panagiotopoulos S, Ekinci E, Jerums G. Serial measurements of cystatin C are more accurate than creatinine-based methods in detecting declining renal function in type 1 diabetes. Diabetes Care 2008;31:971–3.
53. Kyle RA, Durie BG, Rajkumar SV, Landgren O, Blade J, Merlini G, et al. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. Leukemia 2010;24:1121–7.
54. Dispenzieri A, Kyle R, Merlini G, Miguel JS, Ludwig H, Hajek R, et al. International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders. Leukemia 2009;23:215–24.
55. Bianchi G, Kyle RA, Colby CL, Larson DR, Kumar S, Katzmann JA, et al. Impact of optimal follow-up of monoclonal gammopathy of undetermined significance on early diagnosis and prevention of myeloma-related complications. Blood 2010;116:2019–25; quiz 197.
56. International Myeloma Working G. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. Br J Haematol 2003;121:749–57.
57. Weiner JP, Kfuri T, Chan K, Fowles JB. "e-Iatrogenesis": the most critical unintended consequence of CPOE and other HIT. J Am Med Inform Assoc 2007;14:387–8.

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