Utilization Management in the Routine Hematology Laboratory

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Introduction

The hematology laboratory traditionally performs testing for blood and fluid cell counts, coagulation, and often urinalysis. Many hematology laboratories have been consolidated with chemistry to form centralized core laboratories. The modern hematology laboratory has undergone a major and continued transition to increasing automation over the past 50 years. Though nearing a state of total automation, there are still a select number of highly manual and skilled tasks to be performed in the hematology laboratory, especially those pertaining to microscopy. Thus, there is a divide in the hematology laboratory menu characterized by some of the most automated tests (e.g., hemoglobin/hematocrit) and the least automated tests (e.g., manual microscopic review of leukocyte differential).

This dichotomy has a significant effect on the approach to utilization management as the hematology laboratory shares features in common with other highly automated components of the core laboratory, especially chemistry, but also more manual sections of the laboratory such as special coagulation testing. Optimizing utilization of the automated and manual components of hematology testing requires distinct approaches. As such, this chapter is divided into two sections to address the management of each component separately. Key examples of utilization management in hematology are shown in Table 10.1. Utilization management in the special coagulation laboratory is discussed in more detail in the chapter by Van Cott.

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Utilization Management of Automated Testing

Automated complete blood count (CBC) tests comprise a significant fraction of the total requests received in the clinical laboratories. This includes CBC tests on both inpatients and outpatients. Although performed in high volume, routine hematology testing has not been as high a profile a target for utilization management as some other categories of testing. Advances in automation, which lowers the unit cost of the tests, have compensated in part for the increasing volume of requests. The complete blood count is a relatively inexpensive automated test; thus, as long as volume does not exceed the capacity of the instruments, the savings achieved by eliminating these tests is limited to the marginal variable cost of the tests (reagents and consumables) [1].

There are, however, a number of other reasons to optimize utilization of routine hematology tests. It is estimated that as much as 30 % of test requests are of questionable indication or are unnecessary [2, 3]. This phenomenon is especially true in the hematology laboratory. For example, an estimated 56 % of patients 18 years or older receive a complete blood count at their annual general medical examination, a practice deemed unnecessary in most cases [4]. This practice has been categorized as a top five "useless" activity in general medical practice and accounts for a projected 33 million in wasted costs per year in the United States alone [4]. Among other practices, this contributes to the estimated six billion dollars in unnecessary tests and procedures performed in the United States each year [5]. Even at a low unit cost, such practices are clearly wasteful. Additionally, the instrumentation for routine hematology testing takes up valuable real estate in the core laboratory and unnecessarily clutters patient charts providing further evidence for the need to reduce unnecessary routine hematology testing [6].

In addition to the wasted costs for the health system, unnecessary hematology testing has a negative impact on patients and the way they experience care. Pain associated

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Table 10.1 Utilization management strategies for the routine hematology laboratory

Placing limits on daily orders
Discouraging preoperative orders in healthy patients
Banning obsolete laboratory tests
Institute rules for flagging abnormal CBCs to reduce manual microscopic review rates
Institute rules for flagging abnormal urinalysis findings for manual review
Use automated morphological analysis tools to improve efficiency of manual microscopic review

with phlebotomy, increased risk for hospital acquired anemia, and increased risk of transfusion due to repeated blood draws are all associated with unnecessary hematology orders [6–9]. False-positive or clinically insignificant aberrant results invariably drive additional downstream costs including follow-up testing and unnecessary diagnostic evaluations. These downstream costs also create an unpleasant experience for patients, albeit the true scope of these costs is difficult to quantify and has been poorly documented in the literature.

The key to optimizing appropriate utilization of automated hematology testing is to manage test requests prior to specimen receipt in the laboratory [1, 3]. In doing so the in-laboratory costs are eliminated, as are the costs of specimen collection and transport. Canceling such tests after they have been received in the laboratory produces proportionately less in savings and does nothing to eliminate unnecessary phlebotomy or iatrogenic anemia. Potentially divertible orders comprise four main categories—unnecessary outpatient tests, orders for daily testing on inpatients, preoperative orders, and outmoded tests (1). There is good evidence for undertaking utilization initiatives in each of these cases. Eliminating these tests can be accomplished using a variety of strategies including physician education, establishing practice guidelines, and implantation of alerts or hard stops in a provider order entry system. These strategies have been described in detail in the introductpry chapter of this book.

Daily Orders on Inpatients

Daily orders, those orders set to recur over multiple days or until discontinued, present a major opportunity for utilization management in the hematology laboratory. Daily orders impact the hematology laboratory significantly, as CBCs and coagulation tests are some of the most frequent daily orders [7]. In academic medical centers, house staff may place daily orders for routine tests on all of their patients to save time, obviating the need to consider on each day what tests are actually needed for their patients. However, they may not review the results daily or remember to discontinue orders when they are no longer needed. The most common tests that are typically ordered "daily until discontinued" are the CBC, basic metabolic panel, and calcium/magnesium/phosphate.

A number of decision support strategies have been applied to reduce the use of daily laboratory testing with marked reductions in test usage. Some well-studied interventions for impacting daily order rates include physician education and the collaborative establishment of laboratory test guidelines and formularies with clinical services [2, 3, 10–14]. These strategies are often coupled with initiatives to change the test ordering culture toward mindful ordering of laboratory tests on a daily basis, emphasizing those which will impact the patients trajectory of care, instead of a "set it and forget it" model [7, 13, 15]. Education alone often has a fleeting effect on reducing daily orders [14]. Building hard stops or alerts into an order entry system is much more effective. An important part of any educational initiative regarding test order behavior is provider auditing and feedback (physician profiling) as this increases the durability of the response (Fig. 10.1) [2, 3, 16–18].

For institutions where eliminating daily orders may not be achievable, the simple act of restricting order frequency to once daily in patients who are not actively bleeding can have significant effects on hematology test volumes [1, 14, 19]. Interruptive alerts where providers must call the laboratory to override duplicate orders within a given day (hard stops) have been shown to be more effective than soft stops, or order message alerts, at reducing duplicate orders [5]. However, simple activities that make test ordering more cumbersome through prompts, alerts, or test unbundling have been shown to be effective deterrents against frequent orders [5, 11]. Displaying fee data is another gentle but moderately effective technique for bending the order volume curve [20, 21].

Some institutions have established mechanisms to eliminate daily orders using provider order entry systems to block or eliminate the option to prospectively order tests on a daily basis [14, 22]. At many institutions with policies limiting daily orders, the intensive care unit is a special exception. In critically ill unstable patients, daily laboratory tests may be appropriate [10, 13, 23]. However, which tests should be ordered daily or more frequently depends on the patient. It has previously been demonstrated that practice guidelines concerning daily orders in an intensive care unit can significantly reduce daily orders without impacting morbidity, mortality, or length of stay [13, 22].

Guidelines are emerging that support significantly limiting daily orders. The American Association of Blood Banks and the Critical Care Societies Collaborative advocate against daily lab orders through the American Board of Internal Medicine Foundation's Choosing Wisely campaign [24]. Putting these guidelines into practice requires a significant culture change among physicians, especially house staff in academic medical centers. However, consensus is starting to emerge for the need to reduce daily laboratory test orders, and this has significant implications for hematology test volumes.

Fig. 10.1 Electronic decision support pop-up message discouraging routine daily orders

Preoperative Orders

The routine use of preoperative laboratory screening tests directly paralleled the development of automated hematology instruments in the 1960s [25]. At that time it was believed that having more laboratory data on patients would improve patient safety and outcomes [25]. However, in many cases, especially those involving presumptively healthy routine surgery patients, the opposite is true.

It is estimated that 18 billion dollars is spent annually on preoperative testing in the United States [26, 27]. The CBC and routine coagulation testing are among the most frequently ordered preoperative tests. The majority of patients undergoing outpatient surgery, even those with no indication for testing, receive some preoperative laboratory testing [26, 28–30]. Eighty percent of preoperative laboratory tests are ordered by surgeons [26]. When abnormal test results are discovered, they change patient management in only a small minority of cases [28]. The implied goal of preoperative testing is to identify abnormalities that could affect anesthesia or surgical outcomes [26, 27]. It is then reasonable to ask should physicians perform preoperative laboratory screening if the results are not used to change management.

Nonselective preoperative testing invariably leads to many borderline and false-positive results [25]. For screening tests to be beneficial, the prevalence of a disease needs to be at least 1–5 % [31]. In practice the rate of abnormal hematology tests in low-risk surgical patients does not meet this threshold. For example, a retrospective study of low-risk, outpatient, surgical candidates demonstrated a rate of anemia (≤9 mg/dL hemoglobin) of 0.8 %. A prevalence rate of <1 % is not sufficient to yield significant screening benefit and is more likely to produce false-positive results than reveal true disease [26].

Approximately 60 % of surgical procedures performed in North America are outpatient procedures, those lasting less than 2 h with low rates of complications [26, 27]. These procedures are by definition low risk and have pretest probabilities of disease which do not warrant screening [27]. Studies of preoperative testing in cerebral angiography, tonsillectomy/adenoidectomy, pediatric and adult neurosurgery, and plastic surgery have further confirmed this conclusion [29, 32–37]. For this reason a number of institutions have developed guidelines for preoperative testing.

The realization of the low value of screening preoperative tests led the American Society of Anesthesiologists (ASA) to recommend against preoperative laboratory screening tests in most patients, advocating instead for selective screening based on a patient's medical history [38, 39]. This recommendation was put forth in 2002 and reaffirmed by the group in 2012 [38, 39]. In addition to the ASA, the American Society of Clinical Pathology and the Society of Thoracic Surgeons have supported the proposal in the recent Choosing Wisely campaign [24].

There are a number of cases in which preoperative laboratory testing may be indicated. Common indications include patients who are at increased risk of complications due to a personal history of anemia/bleeding/bruising; are on anticoagulation; have liver disease, metastatic tumors; or are expected to experience blood loss greater than 500 mL [26, 27, 40]. When selective criteria are applied to preoperative laboratory testing, the rate of test abnormalities increases to approximately 30 %, a sufficient pretest probability to warrant their use [27].

Though there is a clear consensus that preoperative laboratory screening is unnecessary in most patients and guidelines have been issued, no study has been done to date on the

effectiveness of utilization management strategies to encourage/enforce these guidelines. To the extent that routine hematology tests are among the most common preoperative tests, this is an area that should be a focus of utilization management activities.

Unnecessary/Obsolete Tests

Reducing the utilization of outmoded tests in the clinical laboratory is challenging as order practices can be entrenched, especially in more senior staff [2]. There are two tests in the hematology laboratory that consensus has determined to be outmoded, iron-binding capacity (IBC) and bleeding time [1, 19, 41, 42]. Guidelines and policy changes regarding the ordering of iron-binding capacity, recommending ferritin as a first-line test followed by discontinuation of the IBC order, have been shown to be effective [43]. Restricting IBC test ordering to specific provider groups has also been shown to be an effective strategy [19]. There is no published literature on interventions for reducing bleeding time orders. However, this is widely considered to be an obsolete test that should be removed from test menus [1, 24, 42]. In our institution, we discontinued the bleeding time test over 15 years ago. This was accomplished by working collaboratively with the leadership in cardiac surgery to develop an evidence-based presentation to surgical specialties that had previously utilized the test.

Those tests which are near obsolescence and thus overutilized are another category of tests amenable to utilization management initiatives. One such example in the hematology laboratory is the assessment of serum folate in patients with anemia. Folate is required for the synthesis and maintenance of deoxyribonucleic acids (DNA), and folate deficiency is a known cause of megaloblastic, macrocytic anemia [44, 45].

While a historically important cause of macrocytic anemia, the prevalence of folate deficiency has decreased substantially in many countries with the implementation of mandatory folic acid food fortification [44, 46]. For example, mandatory folic acid fortification of flour in the United States in the 1990s resulted in decrease in the prevalence of folate deficiency from an estimated 3–16 % to approximately 0.5 % [46]. Despite this reduction in prevalence, recommendations for folate testing have remained in clinical algorithms for the workup of anemia [46]. This despite substantial evidence of low yield in a variety of patients [41, 46]. For example, a search of 2014 folate test data for inpatients and outpatients at the Massachusetts General Hospital revealed only one folate-deficient patient and four patients with borderline folate deficiency among more than 11,000 ordered folate tests. It has also been shown that folate is frequently repeated, even in cases where it is determined to be in the normal range [47]. Given its low yield in folic acid-fortified populations, utilization management strategies to decrease folate testing should be considered. Reduction in folate assessment by as much as 60 % has previously been shown through an electronic test order unbundling strategy [48].

Utilization Management of Manual Testing

The most labor-intensive tasks in the hematology laboratory involve the microscopic review of pathologic elements in the blood, body fluids, and urine. Manual review is costly in terms of both time and money [49]. Unnecessary manual review increases the workload of technologists, thereby decreasing productivity [50]. Despite being the gold standard for blood differential analysis, manual review also suffers from high inter- and intra-observer variation [51]. Automated analyzers play an important role in screening fluids for pathologic elements meriting review [52]. There are significant utilization management gains to be realized by decreasing the numbers of specimens requiring manual review through the use of instrument flagging criteria. The biggest challenge in implementing flagging criteria is ensuring that the reduction of manual review does not result in the laboratory missing significant clinical findings [50]. This is especially challenging in tertiary care medical centers where the pretest probability of disease and therefore the rates of abnormal findings are high [50].

Rules for Decreasing Hematology Review

Significant advancements have been made in automated hematology analyzers allowing for both high throughputs while maintaining consistent analytical performance [50]. However, up until the most recent generation of analyzers, instrument flagging resulted in around 30 % of CBC differentials requiring manual review [51]. Of these approximately half required a full manual differential, while the other half were released upon review, indicating a high rate of false-positive flagging [50, 51].

The Clinical Laboratory Standards Institute (CLSI) and the International Society for Laboratory Hematology (ISLH) have established criteria for the verification of flagging claims supplied by manufacturers and recommended flagging criteria [53–55]. The ISLH recommends manual review when the following are identified by an automated instrument: any blasts, >1 % immature granulocytes, >5 % atypical lymphocytes, or at least 1 % nucleated red blood cells [53].

Instruments vary in their flagging accuracy for each of these criteria [49]. The newest automated hematology instruments have made significant gains in reducing false-positive flags, including those generated by monocytes miscategorized as blasts, a common issue with older analyzers [50, 56]. These advancements have driven manual review rates to as low as 9 % in some institutions [56]. Individual rule sets should be validated by each laboratory due to the variation in the prevalence of disease in different populations (Fig. 10.2) [55].

Manual reviews can also be reduced by intervening with the clinician at the time the test is ordered. Many patients

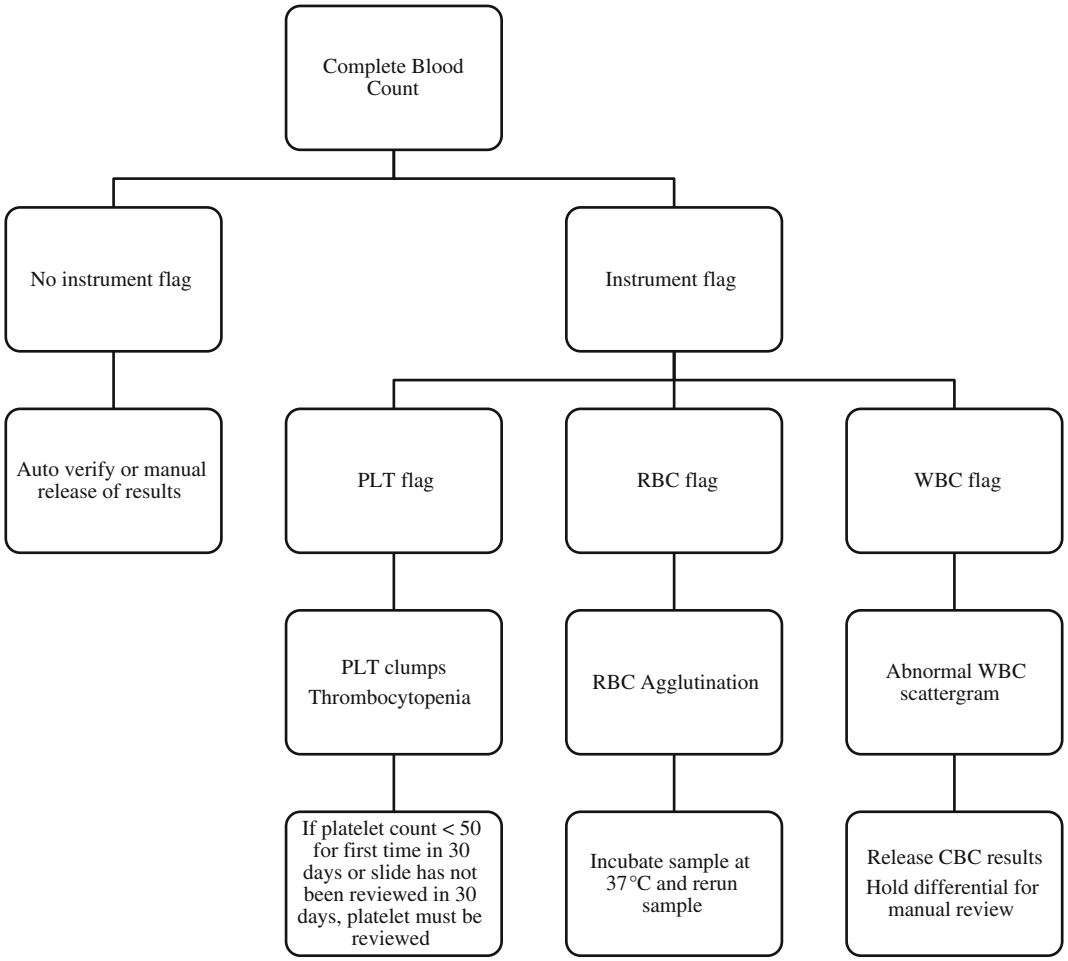

Fig. 10.2 Simplified sample flow chart of instrument flagging criteria used at the Massachusetts General Hospital. *CBC* complete blood count, *PLT* platelet, *RBC* red blood cell, *WBC* white blood cell

have known but relatively stable abnormalities on their CBC that do not need to be rereviewed when repetitive blood counts are requested over relatively short time periods (e.g., hours or days). Providing clinicians with an option to order "CBC with auto diff" only followed by an effort at physician education may reduce the number of unnecessary manual differentials. Also, in some cases, the clinician orders a CBC when all they really need is a hemoglobin, hematocrit, or platelet count. Providing an option for selective ordering will facilitate this effort and eliminate repetitive manual reviews in patients being monitored for potentially clinically significant bleeding.

In cases where manual microscopic review is required, the emergence of automated slide maker-stainers and blood smear analysis by imaging technology have significantly decreased costs associated with technologist labor. These systems rapidly scan slides and then sort cellular findings by cell class, allowing for rapid review and release of results by technologists (Fig. 10.3). Previous studies have shown increases in speed, efficiency, and turnaround time for manual differentials with the use of automated morphological analysis with result review [51, 57]. These systems provide added benefits in terms of the ability to easily review the previous work, identify small numbers of abnormal cells which may be missed by technologists, and decrease interobserver variability [57]. As such, they provide improvements in quality and safety of care in addition to reducing technologist labor.

Rules for Decreasing Urinalysis Review

Though not strictly a hematology test, urinalysis often falls under the purview of the hematology laboratory. Urinalysis consists of dipstick chemical analysis and visual microscopy in a subset of cases [58]. It is an analogous system to the process of automated hematology testing with reflex to manual microscopy in the case of screening abnormalities. Like automated hematology, urinalysis is a high volume test, with high labor costs associated with manual review [58, 59].

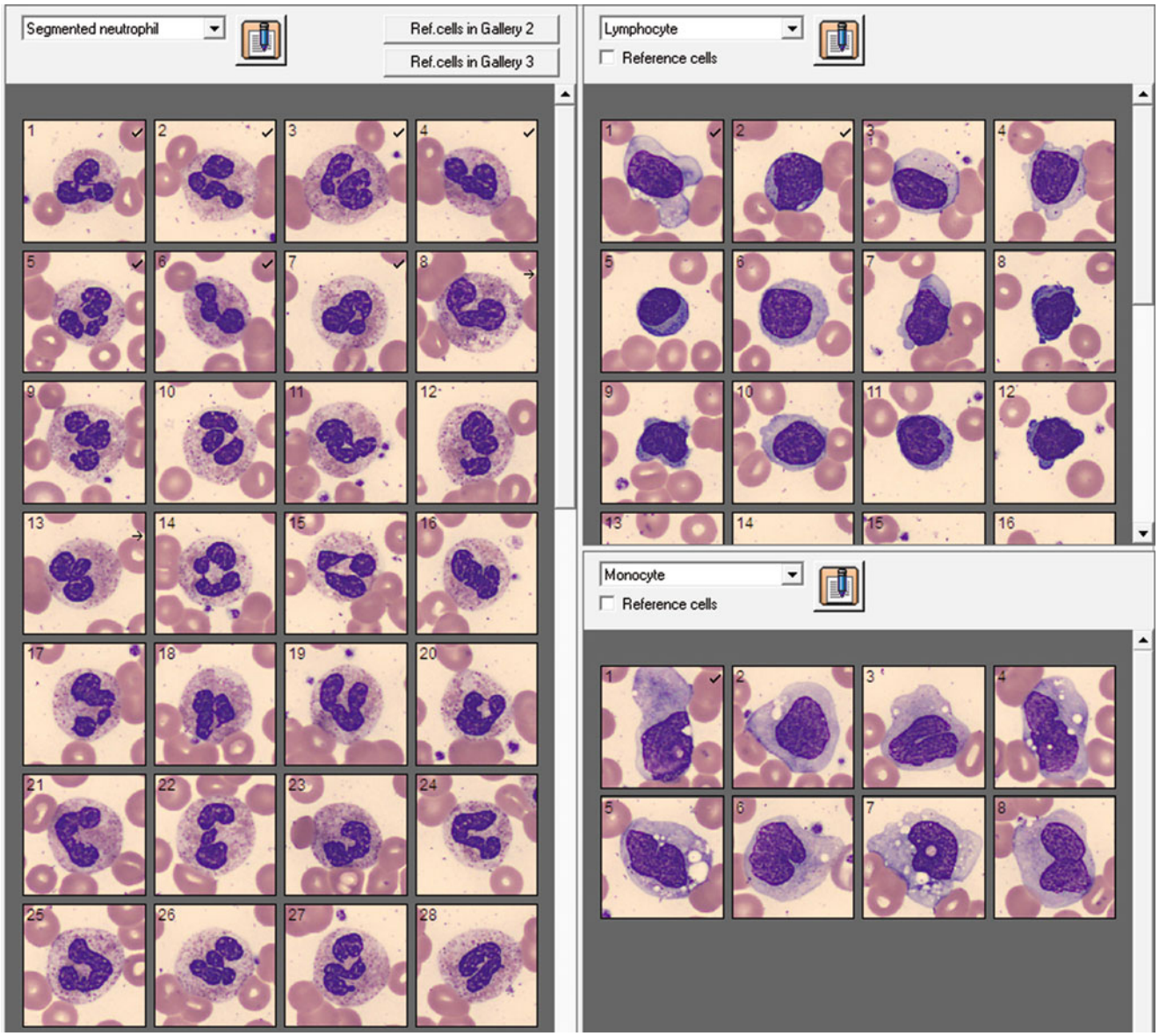

Fig. 10.3 Screen shot of an automated complete blood count image-based morphological analysis platform

Like automated hematology, modern urinalysis platforms also offer decision support software for the entry of flagging rules [59]. Examples of urinalysis flags include the presence of red blood cells, white blood cells, hyaline casts, bacteria, and epithelial cells [59]. As with hematology flags, urinalysis flags need to be validated in each individual laboratory [59, 60]. Optimization of flagging protocols can result in review rates of 40–55 % with false-negative rates in the 2–5 % range [59, 60].

One of the largest opportunities for utilization management in urinalysis is the workup of urinary tract infections (UTI). As many as 80 % of urinalyses will ultimately be determined to be culture negative [61]. Of the positive results, contamination occurs in approximately 30 % of cases [62]. Much recent work has focused on the optimization of urinalysis to rule out UTI [62–64]. Deferring some of these culture workups will result in significant savings for both the hematology and microbiology laboratories (see chapter on utilization management in microbiology). It would also prevent patients from needless antibiotic exposure while awaiting culture results, a process which takes at least 18 h but can often take 24–48 h [64]. Screening algorithms have been developed that achieve negative predictive values of approximately 90 % [63, 64]. This has generally been considered not sufficiently high for use in all patients, particularly those with the potential for a complicated UTI, but may be suitable for those under close clinical supervision or who are asymptomatic or have possible uncomplicated UTI, the most common clinical situation [63, 64].

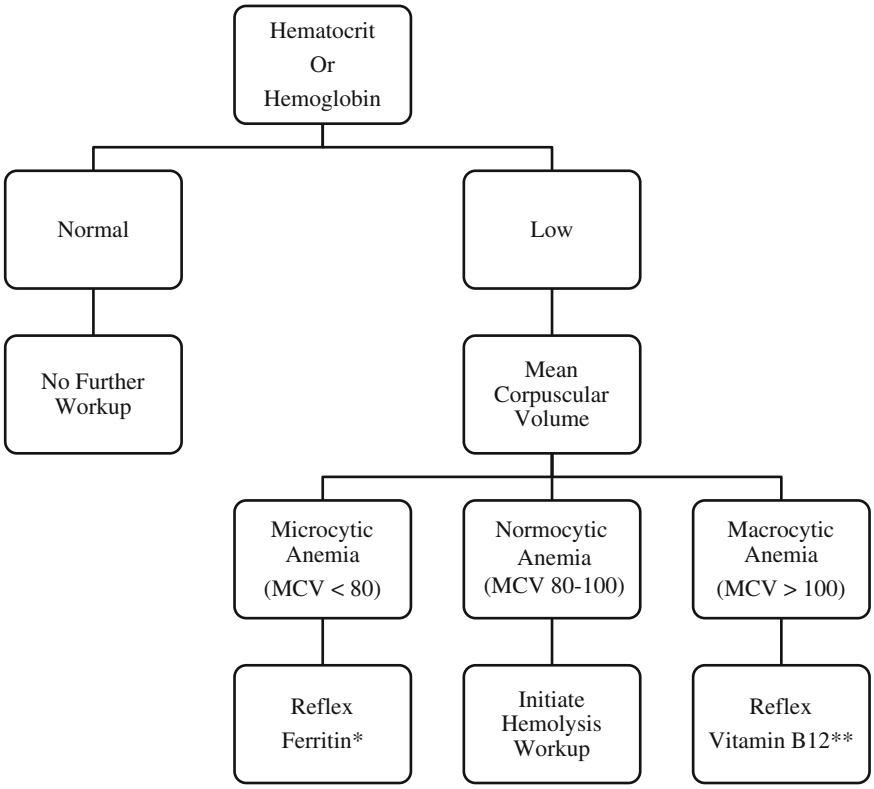

Fig. 10.4 Sample algorithm for anemia workup based on laboratory-driven parameters. Algorithms such as this could be easily automated in the hematology laboratory to increase the efficiency of laboratory anemia evaluations. *MCV* mean corpuscular volume. *Many published algorithms include total iron-binding capacity (TIBC) and iron (Fe). **Many published algorithms include folate testing

Current systems are limited in their ability to accurately identify some pathologic elements including renal tubular epithelial cells, transitional epithelial cells, lipids, and some casts [58]. As such, automated urinalysis alone is not a sufficient screening mechanism for patients with suspected kidney injury though it may be suitable for use in asymptomatic patients [65]. Concordance for other cellular elements including red and white blood cells is quite good [65, 66]. Technologies for automated urinalysis technology are quickly maturing, but further development will be required for these devices to be sufficiently analytically proficient to have a substantial impact on culture rates and some types of manual review.

Utilization Management of Routine Specialized Tests: The Anemia Algorithm

The automation and consolidation of hematology platforms with chemistry instruments on automated track lines are providing new opportunities for utilization management through the use of automated diagnostic reflex algorithms. One notable example is the routine laboratory workup of anemia. The evaluation of anemia is based in large part on laboratory results including hematocrit and mean corpuscular volume, and this directs the need for subsequent tests.

Multiple algorithms have been proposed for the evaluation of anemia in both adults and children [67–70]. However, historically the decision of which tests to order for the evaluation of anemia and when to order them has been left to individual physicians [71]. This results in significant variation in practice and the ordering of unnecessary batteries of tests [71].

In recent years, proposals have emerged to automate the laboratory workup of anemia using diagnostic reflex protocols based on laboratory results [71, 72]. Using such algorithms, the results of preliminary CBC data are used to drive further laboratory evaluation while eliminating tests that are unnecessary as shown in Fig. 10.4. For example, patients with a microcytic anemia may subsequently be tested for ferritin, while those with a macrocytic anemia might be preferentially tested for vitamin B12 deficiency. Without an algorithm, physicians often end up ordering all possible tests up front.

Prior to the automation and consolidation of core laboratory test platforms, reflex algorithms such as the anemia algorithm would not have been operationally practical as different tests were often performed on separate instruments. Finding and reloading specimens on multiple instruments would have required significant manual labor. In the modern consolidated hematology laboratory, reflex algorithms can be implemented through instrument-level rule sets, and subsequent add-on testing can occur automatically. As such, automated reflex algorithms for anemia assessment are likely to enter the clinical workflow in the coming years.

Future Technologies Impacting Utilization in the Hematology Laboratory

The last decade has seen the introduction of new image analysis technologies for the automation of morphological analysis in the hematology laboratory [51]. While currently used to improve the efficiency of manual microscopic review of hematology smears, research is underway which suggests that these systems may be capable of autonomously classifying more pathologic elements than previously recognized [73, 74]. Similar image analysis technologies are also available for urinalysis. These advances among others will no doubt continue the trend toward total automation in the hematology laboratory. When achieved, total automation will help to solve some of the utilization management issues associated with manual labor-intensive tests, by significantly reducing the unit cost of these tests. Savings can therefore be achieved by two different approaches: eliminating unnecessary tests altogether or decreasing the unit cost of the tests that are performed, or both.

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