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ORIGINAL ARTICLE

Clinical Utility of Ordered Pathology Blood Smear Reviews - an Overused Resource?

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SUMMARY

Background: **Blood smear reviews by pathologists (BSR) are ordered frequently at our institution, take time to evaluate, and result in a written report. Minimal research has been done regarding the amount of novel data reported and its clinical utility.**
Methods: **Detailed chart review was performed on BSR orders from January 1, 2015 to March 31, 2015 to assess reasons for smear review, if results were mentioned in the chart, if laboratory-driven reviews were already performed, and if novel, clinically influential data was reported. The trends in ordering was also evaluated.**
Results: **A total of 277 reviews were performed and were most commonly ordered to evaluate the presence of malignancy (43%), hemolysis (18%), and anemia (16%). For 130 of the 277 specimens, laboratory-driven smear review was already performed. The BSR smear review findings were not mentioned in the patient chart in 52% of cases. The report provided novel data in 187 cases (68%) which mainly were minor findings such as low levels of red blood cell abnormalities. The novel data appeared to influence clinical decision making in only 3 cases (1%).**
Conclusions: **Although novel data are often reported, only rarely does it appear to be clinically significant and the information frequently overlaps with information already provided by laboratory-initiated smear reviews. Discussion with, and education of, clinical staff may increase appropriate utilization.**
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INTRODUCTION

Review of peripheral blood smears are frequently performed in laboratories and regarded as a critical diagnostic tool in the workup of many conditions, and written guidelines for evaluation and enumeration of abnormal cells have been developed [1]. Blood smear reviews may be performed as a result of an abnormality in the peripheral blood which falls out of a laboratory-defined parameter and generates a laboratory-driven manual smear review [1,2]. Alternatively, blood smear review

by a pathologist (BSR) may be directly requested by clinicians.

At our institution, a state academic medical center, BSRs may be ordered by providers if a reason for review is provided in a free text field in the computerized provider order entry system. A BSR may be requested in the face of normal peripheral blood counts.

Performance of the BSR entails making an additional blood smear slide from the original EDTA tube used for the complete blood count (CBC) analysis. EDTA tubes are held for up to two days. The BSR may be placed as either an order accompanying a CBC order or as an add-on to a previously resulted CBC order. The slides for BSR are stored for at least two years. The clinical laboratory performs ongoing competency assessment for pathologists who perform BSR. The clinical laboratory also performs routine quality control for CBC and associated smear reviews.

When a BSR is ordered, clinical notes and laboratory data are reviewed in addition to a review of the peripheral blood morphology. A written report is issued (Figure 1). Approximately 15 minutes of pathologist time is involved in the analysis and write up for a BSR, including review of clinical history. Little data is available in the current literature regarding the clinical impact, cost, and relevance of information reported in BSRs [3].

Ideally, performance of BSR can increase recognition of hematologic abnormalities that may be missed by automated technology and laboratory-driven manual smear reviews. This may result in better patient outcomes by more accurate diagnosis or more timely elimination of confounding diagnoses. Providers who order BSR may thus potentially benefit from manual review of the smear in combination with the hematopathologist's analysis of the patient history and presenting symptoms. Alternatively, BSRs may instead have low impact on clinical outcome if they provide information that is mostly redundant with existing clinical and laboratory data or are ordered in cases with no hematologic abnormalities. Given modern-day automated technology used in peripheral blood count analysis, we analyzed whether BSRs provide novel and additional clinically influential data.

MATERIALS AND METHODS

The data described in this manuscript was collected as part of a retrospective study approved by the University of Iowa Institutional Review Board (protocol # 201506812). BSR orders performed from January 1, 2002 to May 31, 2015 at the University of Iowa Hospitals and Clinics were extracted from the electronic medical record (n = 6,489) (Epic, Epic Systems Inc., Madison, WI, USA) using the Reporting Workbench functionality described in our previous publications [4,5]. Data extracted from the medical record included: patient name, date of birth, gender, ordering provider, location of patient at time of order (specific inpatient unit or clinic name), order date, result time, and result date. While a more limited three month period was analyzed in detail as described below, the entire dataset from January 2002 to May 2015 was used to assess broad trends in BSR ordering.

Ordering patterns and distribution were analyzed for the entire data set. A period of three months within 2015 (January 1, 2015 through March 31, 2015; n = 277) was selected for detailed review of charts. Chart review was performed to evaluate the reason for smear review (anemia, rule out hemolysis, rule out malignancy, thrombocytopenia, infection/immunodeficiency, and other), if the results were mentioned in the chart (free text review of results vs. copy and pasted results) and if novel data was reported in the BSR result. Inpatient charts were reviewed from day of order to three days after order date. Outpatient charts were reviewed for three subsequent visits after the order date. Assessment of "novel data" was determined by reviewing laboratory results up to three days prior to BSR order.

Following data collection, clinical scenarios in conjunction with the BSR results were reviewed with a hematopathologist (N.R.) to determine if BSR results appeared to influence clinical decision making. Results considered clinically influential were those which led to a diagnosis of a novel disease or process or those which resulted in a change in therapy. Minor changes in semi-quantitation of hematologic parameters were not deemed clinically influential nor were findings explained by previously known conditions (e.g., anisopoikilocytosis in neonates and patients with liver disease or toxic granulation of neutrophils in septic patients).

RESULTS

A total of 6,489 BSRs were performed between January 1, 2002 and May 31, 2015 (Figure 2). As shown in Figure 2A, the numbers of BSRs per year have increased relatively steadily and are currently approximately 1,000 per year. Figure 2B shows the breakdown of orders sorted by patient age (adult or pediatric, with pediatric defined as less than 18 years old at time of order) and location (inpatient or outpatient, with emergency treatment center defined as outpatient). The distribution of orders between adult and pediatric outpatient and inpatient locations are similar across the last four years.

A total of 277 BSRs were ordered in the three month time period of detailed review (January 1, 2015 to March 31, 2015). During the same time period, 62,142 CBC and differentials were performed of which 16,049 (24%) were reviewed as a result of a laboratory-initiated smear review. One hundred thirty of the 277 BSRs performed had already been reviewed by the same mechanism. Of the 277 BSRs, 187 (68%) reported novel data not previously described in the patient chart. Novel data reported was most frequently red blood cell morphology (48%, 135/277) followed by white blood cell morpholo-

Table 1. Cases in which the BSR report appeared to influence clinical decision making.

Case	Reason for order	Novel data reported	Clinical action/impact
1	72-year-old female with history of refractory anemia with excess blasts-2 status post allogeneic stem cell transplant, now with concern for hemolytic anemia	3+ schistocytes	Confirmation of clinical suspicion of hemolytic anemia
2	6-year-old female in long term follow up for neuroblastoma and family history of spherocytosis. Currently low haptoglobin	1-2+ spherocytes	Subsequently diagnosed with hereditary spherocytosis
3	57-year-old female with fatigue/weakness, history of pancreatic neuroendocrine tumor. Rule out carcinoma	Monotonous population of small lymphocytes	Subsequently diagnosed with chronic lymphocytic leukemia

Table 2. Reasons for BSR orders and percentage of total order volume in the three-month period of detailed chart review.

Reason for BSR	Percentage of total order volume
Evaluate presence of malignancy	43%
Evaluate for presence of hemolysis	18%
Anemia	16%
Evaluate for infection/immunodeficiency	10%
Thrombocytopenia	7%
Other reasons (one occurrence each):	6%
Patient with history of spherocytes in blood	
Patient with hereditary spherocytosis	
Assess for Hermansky-Pudlak or Chediak-Higashi syndromes	
Patient with global developmental delay	
Patient with bilateral acrocyanosis of upper limbs	
Patient with sickle cell crisis	
Patient with concern for venous pool and chilblains	
Assess platelet morphology	
Patient with Evan's syndrome	
Patient with cerebellar ataxia	
Patient with hereditary spherocytosis	
Patient with maternal history of hereditary spherocytosis	
Patient with trisomy 21	
Assess for acanthocytes, suspicion for neuroacanthocytosis	
Assess for evidence of asplenia	
Evaluate for resolution of basophilic stippling and hypersegmented neutrophils seen on previous smear	
Evaluate for sickle cell disease or other causes for cell dysmorphology	

gy (32%, 88/277) and platelet morphology (14%, 39/277). Sixty-one percent (84/135) of novel red blood cell morphology was reporting "mild", "rare", "occasional" or "1+" of a red cell morphology (polychromasia, ovalocytes, target cells, burr cells, spherocytes, schistocytes, tear drop cells). Seventy-seven percent (68/88) of the novel white blood cell morphology was remarking on the presence of toxic and/or left-shifted neutrophils or reactive-appearing lymphocytes. Sixty-nine percent (27/35) of the novel platelet morphology was noting the presence of "occasional" or "few" large and giant platelet forms. Of these, the novel data provided in the BSR appeared to influence clinical decision making in only cases (1%) (Table 1).

BSR was most frequently ordered to evaluate for the presence of malignancy (43%, 117/277), followed by hemolysis (18%, 50/277), anemia (16%, 45/277), infection/immunodeficiency (10%, 28/277), thrombocytopenia (7%, 20/277), and other (6%, 17/277) (Table 2). The smear review findings were described in the chart in 77 cases (28%), copied directly into the chart in 33 cases (12%) and both described and copied in 22 cases (8%). The BSR results were unmentioned in the chart in 52% of cases.

Clinical History:

Review of the peripheral blood smear reveals normochromic normocytic erythrocytes without significant anisopoikilocytosis. The white blood cells appear normal in number, distribution and morphology. A normal number of platelets without morphologic abnormalities is observed.

Impression:
-Normal peripheral smear

Figure 1. Example of BSR report.

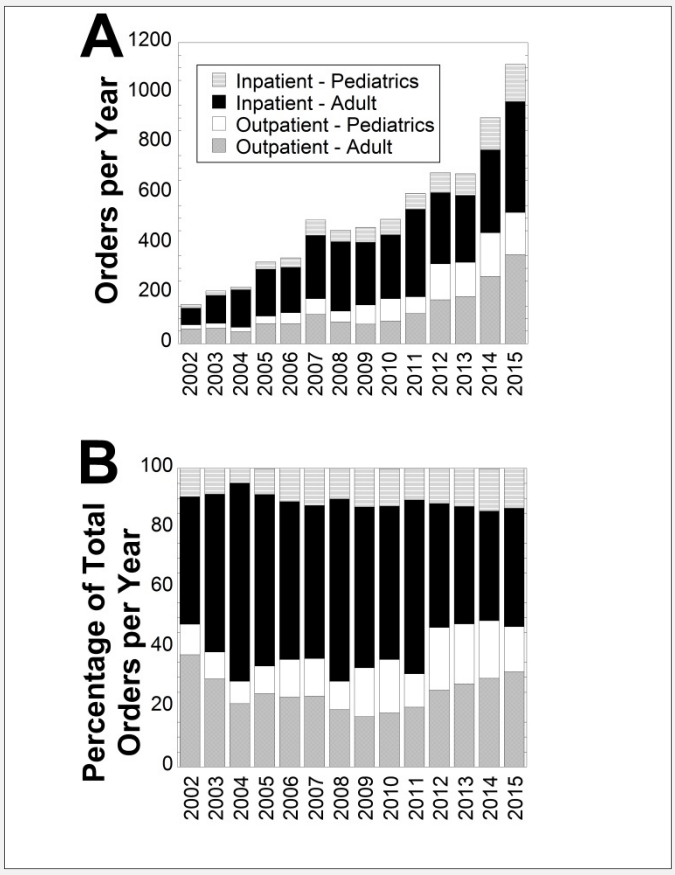

Figure 2. Ordering patterns of BSRs from 2002 to 2015.

(A) Overall orders broken down into adult vs. pediatric (with pediatric defined as less than 18 years old at time of order) and inpatient vs. outpatient as the location at time of ordering (emergency treatment center was classified as outpatient for this study). The totals in 2015 are an estimate based on the first five months of the year. (B) Breakdown of BSR orders using the same classifications as in (A) but with each of the four categories represented as percent of total for the each calendar year.

DISCUSSION

In this study, we attempted to determine if BSRs provided clinically impactful information and data not previously reported in the patient chart. Our findings suggest that most novel data reported in the BSRs did not appear to meaningfully impact clinical practice. The low rate of results which appeared to change clinical decision making (1%) is similar to that in a previous study which found that additional clinically helpful data was reported in only 4% of cases when comparing laboratory technologist review and physician review [2]. Another study demonstrated that smear review by physicians in the setting of anemia did not improve diagnostic accuracy nor did it reduce the number of ordered tests for anemia work-up [6].

Over half of the BSR report results were never explicitly mentioned in the patient chart by clinicians. While it may be reassuring to the clinicians that the laboratory is not overlooking significant abnormalities, BSR review seems to add additional costs without clearly impacting decision making. Additional education of physicians regarding the low rate of missed information by the automated instrument coupled with laboratory-initiated smear reviews may be helpful in assuring them that evaluation by the pathologist may not be needed. A further factor is that BSR adds extra charges to the patient hospital bill. At our institution during the retrospective time period of our detailed chart review, the patient charge for a BSR was $83 USD. Depending on patient insurance and location of encounter (e.g., inpatient versus outpatient), performance of BSR can result in additional out-of-pocket expenses for the patient. This is especially a factor in the outpatient setting for patients in the United States who have high co-pays and/or deductibles for clinical laboratory services.

Previous research regarding BSRs has mostly been done regarding those which are lab generated in response to an abnormality in a laboratory-defined parameter. The laboratory-driven smear review was shown to provide clinically useful results in 85% of cases in one study. This practice is currently done at our institution and provides quality assurance, additional interpretation, and a major part of residency training in hematopathology [3,6]. Our data suggests clinician-ordered BSRs provide novel and clinically useful data at a rate much lower than laboratory-initiated smear reviews.

A limitation of this study is the relatively short time period over which data was chart reviewed in detail. The several months of data analyzed may not capture changes in ordering practices that might be seen if a longer time period were assessed. However, examination of broader BSR ordering patterns over an approximately 13 year period showed that ordering trends were very similar across the last four years of retrospective analysis. In addition, as these specimens were ordered from many clinicians in both inpatient and outpatient settings, we could only infer clinical impact from chart review and evaluation of further ordering practice.

Much can be ascertained from laboratory values and a significant portion of the BSR report is based on automated results (MCV, MCH, RDW, WBC count, hemoglobin, etc.). The current-day automated methods are generally reproducible, objective, and accurate [6-8]. In a previous study, the addition of historical data resulted in a laboratory never missing a case of leukemia [9]. Of the BSRs ordered to evaluate the presence of malignancy in our institution, 9 (3% of all BSRs) reported findings suggestive of a new diagnosis or relapse of acute leukemia. However, in all of these cases, the presence of blasts had already triggered a laboratory-initiated smear review by a pathologist. The results of the laboratory-initiated smear review were reported in the chart prior to the BSR result in all cases. The automated results, coupled with laboratory-defined parameters to generate mandatory peripheral smear reviews by laboratory professionals and pathologists, are robust.

In an era of encouraging cost-effective medicine, education of clinicians to the value of data provided without the additional expense of a pathologist review may be helpful. A previous study evaluated the use of synoptic reports in this setting and found their use decreased the time pathologists spent in this endeavor [10]. This can be coupled with efforts to improve display of results in the electronic medical record.

Given the low rate (1%) of clinically influential results and seldom mention of the BSR results in the patient chart, further education of clinicians of the utility of BSRs is warranted. Facilitation of a better understanding of appropriate situations for blood smear review may increase the clinical utility as well as education into utilizing the information already provided via laboratory-driven smear reviews.

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None.

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None.

Declaration of Interest:
The authors all have no interests to disclose.

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