The incidence of duplicate genetic testing

Douglas L. Riegert-Johnson, MD[1], Daniela Macaya, MQC[2], Timothy W. Hefferon, PhD[3], and Lisa A. Boardman, MD[1]

Purpose: Duplicate genetic testing (DGT) should give the same results as the initial genetic test. Therefore, DGT is indicated only in the rare instances where the initial results require confirmation. The objective of this study was to determine the incidence of DGT by reviewing *TPMT, HFE*, and *CYP450 2D6* polymorphism testing performed in our institution's laboratories in 2006. A secondary objective was to determine the savings in charges that resulted from a system in place to limit *HFE* DGT. **Methods:** A retrospective records review at an academic medical center. **Results:** The percentage of patients having the same genetic test more than once in 2006 was 3.3% (253/7710) for *TPMT*, 0.3% for *HFE* (24/7851), and 0.9% (4/433) for *CYP450 2D6* testing. Retail laboratory charges for the DGT identified in 2006 were $76,728. To estimate the incidence of DGT over a longer period of time than 2006, an all-time records review was performed on a subset of internal patients and found the all-time incidence of DGT for *TPMT, HFE,* and *CYP450 2D6* testing to be 6.9%, 1.9%, and 0.9%, respectively. No case of DGT with an appropriate indication for duplicate testing was found. A system in place to decrease *HFE* DGT is estimated to have saved $77,479 in charges for 2006 (95% CI, $35,512–184,015). **Conclusions:** Indicated DGT is rare and decreasing DGT could result in significant savings. Institutions should consider implementing a systems-based process to limit DGT. ***Genet Med* 2008:10(2):114–116.**

Key Words: *genetic testing, molecular diagnostic techniques, duplicate genetic testing, laboratory techniques and procedures, inappropriate laboratory utilization*

Most genetic testing uses DNA extracted from peripheral blood lymphocytes. DNA extracted from these cells rarely changes during a person's lifetime, and a duplicate genetic test should give the same the results as the initial test. Therefore, duplicate genetic testing (DGT) is indicated only in the rare circumstances where the initial results require confirmation. Examples of appropriate indications for DGT include concern for switching of samples or when genetic testing results are unexpected and require confirmation.

This is the first study of the incidence of DGT, specifically the incidence of duplicate *HFE*, *TPMT*, and *CYP450 2D6* polymorphism genetic testing. Mutations in the *HFE* gene are associated with the iron overload disorder hemochromatosis.[1] The *TPMT* gene codes for the thiopurine *S*-methyl transferase enzyme, which is involved in metabolizing the immunosuppressant drug azathioprine. Clinicians use *TPMT* testing to identify patients who are poor metabolizers of azathioprine metabolites and are at high risk developing aziothioprine-related side effects.[2] *CYP450 2D6* polymorphisms can predict a patient's response to therapy and the possibility of adverse reactions from antidepressants and other drugs metabolized by the *CYP450 2D6* drug metabolism enzyme.[3]

We reviewed all *HFE* testing and the majority of *TPMT* and internally referred *CYP450 2D6* testing performed in Mayo Clinic laboratories in 2006 to determine the percentage of patients who had the same genetic test performed more than once in 2006. In addition, to determine the incidence of DGT over a longer period of time, we performed an all-time records review on a subset of consecutive patients from inside our institution that had *HFE*, *TPMT*, or *CYP450 2D6* testing in 2006.

To investigate whether the type of medical practice (academic vs. community) was associated with an increased incidence of DGT, we compared the incidence of DGT for *HFE* and *TPMT* testing in internal and external referral groups. The internal sample cohort consisted of patients seen in our institution's academic medical center practice, while the external sample cohort represented an admixture of samples referred from both academic and community-based practices.

During the time this study was performed, the laboratory performing *HFE* testing had a system in place to limit *HFE* DGT. This report also includes the performance of this system and recommendations for the management of DGT.

MATERIALS AND METHODS

Databases of all *HFE* testing, 84% of *TPMT* testing (8000/9537), and 49% of internally referred *CYP450 2D6* testing

From the [1]Mayo Clinic College of Medicine, Division of Gastroenterology, Rochester, Minnesota; [2]University of Costa Rica, Department of Medical Genetics, San Jose, Costa Rica; and [3]National Institutes of Health, National Human Genome Research Institute, Bethesda, Maryland.

Douglas L. Riegert-Johnson, MD, Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, 200 Second Street SW, Rochester, MN 55905. E-mail: riegertjohnson.douglas@mayo.edu.

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(437/884) performed in 2006 by Mayo Clinic laboratories were reviewed for DGT. In addition, consecutive series of patients from inside our institution who had *HFE*, *TPMT*, or *CYP450 2D6* testing in 2006 underwent further all-time records review for DGT.

HFE, *TPMT*, and *CYP450 2D6* testing was performed in three separate laboratories. *HFE* testing comprised testing for the *C282Y*, H63D, and S65C mutations using Lightcycler® technology. *TPMT* testing was performed using enzymatic end point or liquid chromatography-tandem mass spectrometry. *CYP450 2D6* polymorphism testing was performed using allele-specific primer extension or bead hybridization with fluorescence detection. The Mayo Clinic Institutional Review Board approved this study.

RESULTS

Duplicate genetic testing

The percentage of patients having *HFE*, *TPMT*, and *CYP450 2D6* testing in 2006 who had a duplicate test in 2006 is shown in Table 1.

The most commonly cited reasons for DGT by laboratory personnel and ordering clinicians were lack of time to adequately review records for previous testing, difficulty in accessing records of previous testing, and lack of understanding by the ordering clinician that DGT will give the same results as the initial test.

There was no significant difference in DGT between the internal or external referral cohorts for *TPMT* and *HFE* testing (*TPMT* $P = 0.13$, *HFE* $P = 0.15$, two-tailed P value using Fisher's exact test). We had expected to find a higher rate of DGT in the external referral cohort, as it included samples referred from community practice where physicians were hypothesized to be less adept at genetic testing.

A higher percentage of patients having *TPMT* testing had duplicate testing than patients having *HFE* or *CYP450 2D6* testing. Many patients had *TPMT* testing three or more times (Table 2). A possible explanation for this may be that a *TPMT* test is automatically ordered as part of routine laboratory orders for some physicians subspecializing in autoimmune diseases.

Table 1
Percentage of patients having duplicate *HFE*, *TPMT*, and *CYP450 2D6* polymorphism genetic testing

		Percentage of patients with DGT (patients with DGT/patients in group)	
Test	Cohort	In 2006 only	At anytime in the past[a]
TPMT	All	3.3% (253/7710)	—
	Internal	2.5% (25/996)	6.9% (17/246)
	External	3.4% (228/6714)	—
HFE	All	0.3% (24/7851)	—
	Internal	0.6% (4/681)	1.9% (4/207)
	External	0.3% (20/7170)	—
CYP2D6	Internal	0.9% (4/433)	0.9% (4/433)

[a]Incidence of DGT at anytime in the past determined for consecutive series of internal patients only.

Table 2
Distribution of number of *TPMT* tests per patient in 2006

Number of *TPMT* tests per patient	Cohort (number of patients)	
	Internal	External
1	971	6486
2	23	211
3	2	11
4	—	1
5	—	3
6	—	1
11	—	1

TPMT, thiopurine *S*-methyl transferase.

As expected, the all-time records review found a higher rate of DGT than analysis of the 2006 calendar year data alone. Of the 246 patients who had *TPMT* testing in 2006 included in the all-time records review, 10 had two or more tests in 2006 alone and seven additional patients had one test in 2006 and one or more additional tests at some time earlier than 2006. The all-time DGT rate most probably reflects the true incidence of DGT, but we were only able to determine the all-time rate for internal samples.

For internal patients having DGT, records were reviewed for an appropriate indication for repeating genetic testing. In no case was there documentation of an appropriate indication for DGT. From this, we conclude that appropriately indicated DGT is rare.

System to limit duplicate HFE testing

At the time of this study (2006), the laboratory performing *HFE* testing had a system in place to limit *HFE* DGT. During sample accession a technician identified requests for duplicate *HFE* testing through a computerized search of laboratory records. Duplicate tests continued through standard *HFE* test processing, while an attempt was made to contact the referring physician. Testing was canceled if the referring physician could be contacted and cancellation confirmed before *HFE* test completion.

In the consecutive series of 207 internal patients referred for *HFE* testing, five of nine duplicate test requests were canceled using this protocol. For 2006, this system saved an estimated $77,479 charges for duplicate *HFE* testing (95% CI, $35,512–184,015). This estimation was calculated by multiplying the percentage of canceled test requests per patient tested (2.4%; 95% CI, 1.1%–5.7%, Wilson procedure) by the total number of patients being tested in 2006 (7851) and the charge for *HFE* testing.

Laboratory charges associated with DGT

Laboratory charges for DGT identified in the 2006 data set were $76,728. This was calculated using 2006 retail test charges (*HFE* $411.20, *TPMT* $289.10, *CYP450 2D6* $236.30). As we did not review 16% of *TPMT* tests and 46% of *CYP450 2D6* tests or include DGT occurring outside of the 2006 calendar year data, the true charges associated with DGT in 2006 is higher than our estimate. This estimate also does not include the estimated $77,479 in savings from the system preventing *HFE* DGT.

DISCUSSION

We found that DGT accounts for a small but measurable percentage of total testing volume for the studied tests. Our results should be generalizable to genetic testing in both academic and community medical practices. These results should also be generalizable to other high volume genetic tests such as Factor V Leiden, *PT*20210G->A, and cystic fibrosis mutation panel testing.

A body of literature has been published on inappropriate laboratory utilization, and DGT could be classified under this heading. A systematic review of clinical laboratory audits found 5% to 50% of laboratory testing could be classified as inappropriate.[4] In the only published study of the appropriateness of a genetic test, 17% of *APC* tests for familial adenomatous polyposis were found to be requested for inappropriate indications.[5] The only previous report of DGT was included in a study of genetic testing in liver transplant patients where seven duplicate genetic tests were identified in a cohort of 215 patients.[6]

We predict the incidence and costs associated with DGT will grow as the use of genetic testing continues to increase. In addition to limiting unnecessary testing and costs, another reason to limit DGT is that it is a potential source of medical errors. Clinicians may wait to implement needed treatment until the results of the genetic testing they ordered are available, when in fact the results are already available.

Limiting DGT at the laboratory level, as done by the *HFE* laboratory in this study, has several drawbacks. Even if the test is cancelled in the laboratory the costs of obtaining the sample, shipping, and the system to cancel the DGT remain. Although a laboratory-based system to eliminate DGT may decrease laboratory charges to the client, the cost of implementing such a system is borne by the laboratory. Also, any single laboratory-based system limiting DGT does not prevent DGT through sample submission to a different laboratory. For these reasons, our recommended approach to DGT would be a systems-based approach to limit DGT at the time of test ordering. Ideally, a computerized test order entry system would be able to query laboratory databases and alert the ordering clinician to possible DGT. To our knowledge, such a system is not in operation anywhere. Another more feasible intervention would be increasing the accessibility of previous genetic testing results to ordering clinicians through existing medical records systems.

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