Elimination of 72-Hour Quantitative Fecal Fat Testing by Restriction, Laboratory Consultation, and Evaluation of Specimen Weight and Fat Globules

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Guest: Dr. Lawrence de Koning is a clinical biochemist with Alberta Public Laboratories at Alberta Children's Hospital, and associate professor with the University of Calgary.

Randye Kaye: Hello, and welcome to this edition of "JALM Talk," from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

The gold standard for identification of fat malabsorption has conventionally been 72h fecal fat analysis. Despite its long use, fecal fat analysis poses both preanalytical and analytical challenges for both the patient and the laboratory. Implementing changes to well-established tests can be difficult in healthcare systems. "Elimination of 72-Hour Quantitative Fecal Fat Testing by Restriction, Laboratory Consultation, and Evaluation of Specimen Weight and Fat Globules" was published in the November 2018 issue of *The Journal of Applied Laboratory Medicine*. The study details intervention efforts to reduce unnecessary quantitative fecal fat analysis and the use of historical data to support specimen weight and fat globules as alternatives for evaluation of malabsorption.

The corresponding author is Dr. Lawrence de Koning. Dr. de Koning is a clinical biochemist with Alberta Public Laboratories at Alberta Children's Hospital, and associate professor with the University of Calgary. His clinical focus is on acute and chronic health conditions in children, as well as laboratory test utilization and quality improvement.

Welcome Dr. de Koning. First question, your paper describes eliminating ordering for the 72 quantitative fecal fat test. Can you tell us more about this test and what it's used for?

Dr. de Koning: Yes, certainly. So, the 72-hour quantitative fecal fat test, it was developed by JH Van de Kamer in 1948. It's a classic test of clinical chemistry. It was designed to measure the quantity of fat including free fatty acids, fatty acid soaps, and neutral fat in the 72-hour collection of stool. The main purpose of this test is to identify fat malabsorption and fat maldigestion.

The procedure is quite amazing in the amount of manual work that's involved. Basically, it starts with a sample of stool and the undigested triglycerides and fatty acids contained in that specimen of stool, which is collected over 72 hours, are saponified in ethanolic potassium hydroxide and then fatty acid soaps along with the existing stool soaps are protonated to fatty acids in acid and extracted into ether, and the ether layer is then evaporated and reconstituted in ethanol, and then finally there is a titration step of sodium hydroxide in the presence of a pH indicator.

The results from the test are reported in millimoles of fatty acids excreted per day and they are extracted from the subsample that's tested to the average specimen weight of stool collected per day. Daily fat excretion can also be reported as a percentage of daily fat intake, and that's the second way of reporting the results for this test.

The test requires adult patients to go on a 100-gram per day high fat diet for five days, the last three days of which stool collection is done. And in children, the high fat diet is not required but dietary fat intake is measured by a diary and the parents are involved, and percent fat excretion is more likely to be reported in these patients.

Randye Kaye: All right, thank you. Well, it sounds very thorough. So, why is running this test problematic for clinical labs?

Dr. de Koning: Well, the test is entirely manual. It deals with large quantities of stool, it deals with large quantities of corrosive and flammable materials. In our lab and probably other labs like ours, it takes one technologist an entire shift to report on only nine patient results. So, from a safety and cost effectiveness perspective, it's less than ideal.

From the pre-analytic side of testing, patients also have variable compliance for the high fat diet, and we frequently would receive incomplete stool collections like a 48-hour, even a 24-hour collection, both of which cast doubt on the reliability of the result that we report. Specimens are also susceptible to anolyte consumption by bacteria in the specimen and the specimens can actually explode due to gas buildup. They are collected in paint cans, so they're sealed and so gases can exert a fair amount of pressure on the walls and lid of the specimen if they're kept at room temperature for any significant amount of time.

From the analytical side, the test is also fairly imprecise. We could expect 20% run to run variation, and this is largely due to the manual aspects of the test. The test also suffers from a lack of a proficiency testing scheme which forces us and other labs to bank our own specimens and test them repeatedly over successive months as a way of

tracking performance. And from a post-analytic perspective, we rarely had fat intake supplied with the specimen to calculate percent excretion which would have been far more valuable than simply measuring excretion itself, which actually was our usual way of reporting.

So, due to these problems plus the significant patient burden and availability of testing alternatives, the test has been obsolete probably since the early 2000s, but it's persisted due to ingrained clinical practices.

Randye Kaye: Wow, those are quite a lot of concerns. So, why did you set out to achieve with your study?

Dr. Koning: Well, we first sought to identify who was ordering the test, why it was being ordered, and then also to direct physicians to better tests. Ultimately, we want to provide simple alternatives when specimens arrive at their lab. We actually can't control the ordering of the specimens from the community because they were ordered via paper requisition and as you may know, labs have no control of whether a physician office submits a specimen with a paper requisition or not. We can only cancel the specimen once it has arrived or do something different with it.

Randye Kaye: Oh, okay. So, then what were the results of your efforts and what did it lead to?

Dr. Koning: Well, back in 2014, we began this initiative and we started by reviewing the utilization of this test. We discovered that nearly 70% of our tests per year were being ordered on adult patients. So, this was immediately inappropriate to us because we know that this test is primarily intended to confirm the presence of fat malabsorption or maldigestion in children. And the reason it's targeted for children is because gastroenterologists want to remediate poor growth due to fat malnutrition, which can be identified by this test.

So, together with the regional leads of gastroenterology in our province, we implemented a change that all orders on adult patients must receive approval by myself in order to be tested. I am the clinical biochemist for the laboratory that runs this test for a large region in the province of Alberta. And so, we required physicians to contact me so we could discuss whether the test was necessary, given the abundance of other simpler or more specific test such as fat globule microscopy or fecal elastase, or simply monitoring the patient clinically after dietary change.

So, this change in practice was announced by a regional memo with a very wide distribution. After this change was made, our workload decreased by nearly 80%. The remarkable thing was that few physicians actually called me.

So, for the first year of this project, I called them, and I did that meticulously on every order that we received. What I found through consultation was that the test was almost never regarded to be necessary given the availability of alternatives, which was surprising.

What's also interesting during this initial period was that the number of pediatric orders that we receive also dropped, probably as a biproduct of the educational or interventions of this intervention. At the same time, we performed a retrospective data analysis of all of our fecal fat results that were present in our lab information system. In doing so, we identified that actually the weight of the 72-hour specimen was a pretty good predictor of whether that specimen turned out to be abnormal by our original quantitative fecal fat test.

We use a metric called area under the curve. We do receive our operating characteristic analysis in these types of scenarios, and we found that it was between 0.75 and 0.79, which actually indicates that the weight of the specimen alone is good predictor of abnormality. And so, in coordination with the Adult and Pediatric Gastroenterology Divisions in the area of our province, we identified weight cut points that had 80% specificity for abnormal fat excretion by the original quantitative test. We chose cut points with the high specificity because the test is primarily being used for confirming, not screening, fat malabsorption as well as fat maldigestion. We also found in a separate research that is conducted by members of my lab, that a quantitative test for fat globules, a microscopic test for the presence of fat globules in the stool specimen, further improve the accuracy of this evaluation. So, we implemented on July 12 of this year, the fecal weight evaluation and the fat globule test as a replacement panel for the quantitative test, and what we ended up doing is reporting the results of the weight evaluation in a comment in place of where the original quantitative results would be.

Now, unfortunately, we couldn't affect the ordering of this test. As I mentioned, we can't control whether physician offices submits specimens with a manual requisition, so we couldn't help the patients who had to go to this horrible high fat diet and collection of stool for 72 hours, but our workload post go-live has remained very low which suggests that our message has gotten out and that we have effectively changed clinical practice.

Randye Kaye: Wow! Those are remarkable results. Do you have any advice for other labs interested in eliminating this test?

Dr. de Koning: I would say start by performing a utilization review. Speak to specialists who understand this test and who have

ordered it in the past, and it's amazing what you'll find out and what you can accomplish if you gradually provide education on best practices, which is in this case not to perform the quantitative test in almost every scenario, and to seek alternatives.

Randye Kaye: Thank you so much. This has been fascinating. Thank you for joining us today.

Dr. de Koning: You're welcome. Thank you.

Randye Kaye: That was Dr. Lawrence de Koning, Associate Professor in the Department of Pathology and Laboratory Medicine at the University of Calgary, talking about "Elimination of 72-Hour Quantitative Fecal Fat Testing by Restriction, Laboratory Consultation, and Evaluation of Specimen Weight and Fat Globules" from the November 2018 issue of JALM. Thanks for tuning in to this episode of "JALM Talk." See you next time, and don't forget to submit something for us to talk about.