Chemistry Profiles in "Wellness Programs": Test Selection and Participant Outcomes

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Insurers, employers, and individuals create demands for laboratory testing in "wellness programs." Tests chosen to identify cases deserving intervention included routine automated chemical tests plus high-density lipoprotein cholesterol, ferritin, and thyroid tests. Participants' unwarranted concerns were addressed with a personalized reporting schema. We tested 1338 individuals, identified 224 (16.7%) with significant abnormalities, and made phone contact follow-up with 193 (86%) of these six to 14 months later. Cholesterol results suggesting increased risk of heart disease were frequent, and were not studied. Interventions were initiated in 55 of the 193 followup cases (49 by physician and six by participants), including prescription of iron or thyroid hormone, counseling on dietary or alcohol intake, and repeat testing. For 58, there was medical advice without intervention; abnormal results were ignored by 79. Noteworthy participant anxiety was manifested in two of the 193 cases, both of whom were treated with iron. We conclude that 4% of the original 1338 participants potentially benefited from intervention. Ferritin and thyroid tests initiated 33 (61%) of these 55 specific therapeutic interventions.

Public interest has created a significant demand for wellness programs. Employers have shown that such programs generate a significant financial benefit (1). Many health-insurance companies encourage wellness programs and will reduce group premiums if a wellness program is instituted.

The laboratory is a portion of a complete wellness program. Fitness and blood-pressure testing plus health-history questionnaires are usually included. We have studied the laboratory component of wellness programs.

We have used a laboratory test profile that is goal oriented and is expected to find cases of disease that are reasonably frequent and have well-defined intervention schema. We report here which test results are most frequently abnormal and which tests are most likely to yield therapeutic intervention.

Laboratory testing of wellness participants can have many different outcomes. Some participants experience significant anxiety if there is inadequate participant education regarding the significance of laboratory-detected abnormalities. Both unwarranted anxiety and a false sense of security have been observed among participants given inadequate participant education. We have studied the frequency of anxiety and the frequency of therapeutic intervention after performing our laboratory component of wellness programs.

Materials and Methods

All wellness programs included in this study were initiated by third parties. All participation was voluntary. In all, samples from 1338 participants were analyzed. Of these, 1106 (82.8%) were employed health-insurance enrollees, 116 (8.7%) were from a hospital health fair, and 114 (8.5%) were from a housing project for retirees.

The tests included in the laboratory component were as follows: cholesterol, triglycerides, high-density lipoprotein cholesterol, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyltransferase, alkaline phosphatase, total bilirubin, total protein, albumin, creatinine, blood urea nitrogen, uric acid, phosphorus, calcium, sodium, potassium, glucose (usually not fasting), effective thyroxin ratio (ETR), and serum ferritin. For automated tests we used an "Astra" discrete analyzer (Beckman Instruments, Brea, CA).

The effective thyroxin ratio was determined as previously described (2), with reagents from Mallinckrodt, Inc., St. Louis, MO. Normal results were 0.89 to 1.13. If the effective thyroxin ratio was ≤0.92, we also measured thyrotropin (TSH), with reagents from Hybritech, San Diego, CA. If the effective thyroxin ratio was ≥1.13, we measured triiodothyronine by radioimmunoassay (Clinical Assays, Cambridge, MA).

For the high-density lipoprotein measurements we used "AGent" (Abbott Laboratories, North Chicago, IL) reagents and the Mg-phosphotungstate precipitation method (Sigma Chemical Co., St. Louis, MO). Ferritin was measured with Abbott's "Ferrizyme."

All results were returned to participants with an educational letter (see Appendix A). Cholesterol results suggesting risks of heart disease were highly prevalent; they were fully discussed in this letter (Appendix A) and not studied further by us.

Other results were judged to be significantly abnormal by the criteria in Table 1. The general letter to participants whose results met these criteria included result-specific addenda, presented in Appendix B. Wellness coordinators discussed results with participants.

Six to 14 months after testing, we obtained permission from each wellness program coordinator to contact the

<table>
<thead>
<tr>
<th>Test</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Serum ferritin</td>
<td>≤12 µg/L indicates little or no iron stores</td>
</tr>
<tr>
<td>Serum glucose</td>
<td>≥1600 mg/L (≥88.8 mmol/L) suggests further evaluation needed</td>
</tr>
<tr>
<td>Thyroxin*</td>
<td>ETR &lt;0.92 and TSH &gt;10</td>
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<tr>
<td></td>
<td>ETR &gt;1.12 and triiodothyronine &gt;2000 ng/L (3.1 nmol/L)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≥5000 mg/L (≥5.6 mmol/L) suggests further evaluation needed</td>
</tr>
<tr>
<td>Liver enzymes</td>
<td>Multiple tests greater than twice upper reference limits</td>
</tr>
<tr>
<td>Potassium</td>
<td>≤3.1 mmol/L</td>
</tr>
<tr>
<td>Renal tests</td>
<td>Abnormal creatinine &gt;20 mg/L (177 mmol/L) with any confirmatory abnormality of urea nitrogen, uric acid, and phosphorus</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Primary letter discusses NIH consensus values, addenda are sent only for very high results</td>
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</tbody>
</table>

*See Materials and Methods section.

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participants whose results had been abnormal enough to generate report addenda. Phone numbers were provided by the wellness coordinator and phone interviews were conducted by two of us (D.S.A., J.K.S.). Attempts were made to contact every participant having a result that met a criterion for an addendum. The phone interviews were identified as being voluntary and included some open-ended questions and some specific questions (see Appendix C). Repeat wellness testing was initiated in several groups of participants, and those data from participants with previous addenda were also reviewed.

Results

Table 2 lists the frequency of abnormal results observed among the 1338 participants. Serum cholesterol concentrations were distributed similarly to the distribution seen in previous population studies and not studied further. Serum ferritin <12 µg/L was found in 9.9% of the participants, most frequently in women. Serum glucose exceeded 1600 mg/L (8.88 mmol/L) in 39 (2.9%) of individuals. Significant abnormalities in triglycerides, liver enzymes, thyroid function, and other tests were observed in a small percentage of the participants. The total number of addenda sent was 224 (16.7%).

Repeated attempts were made to communicate with all 224 participants who had received addenda, and 193 (86%) were in fact contacted, 28 men, 165 women. Employed insured individuals accounted for 83% of the total participants; they also accounted for 80% (154/193) of the phone contacts. Among phone contacts, the average age of the 28 employed men was 45.5 years; of the 126 employed women, 41.5 years; of the health fair participants, 61.1 years; and of the 24 elderly housing residents, 74 years. Because a large proportion of abnormalities noted involved serum ferritin in females, these constituted a similar large percentage of the phone contacts.

Results of the phone interview are also shown in Table 2. Laboratory abnormalities were ignored by 79 (41%) of those interviewed. A health professional was consulted in 113 (59%) cases, but 58 of these then received no treatment. Only two individuals reported substantial anxiety over their results; both contacted a health professional and had therapy instituted. In all, 49 were treated by a physician and six instituted iron therapy themselves. The most frequent physician-ordered intervention was prescription of ferrous sulfate (25; 22 for women, three for men) or thyroid hormone (n = 3) replacement. In several cases, additional laboratory testing of liver function (n = 5) was ordered. Glucose and lipid abnormalities (n = 9 and 6, respectively) were most frequently treated by dietary intervention.

Among those who ignored the initial test results, 12 were in participant groups initiating repeat wellness testing about one year later. In all 12, the initial abnormality persisted: one with a low value for thyroxin and a high value for thyrotropin, seven with ferritin <12 µg/L, two with high glucose, one with abnormal liver enzymes, and one with high triglycerides.

Discussion

Screening cholesterol concentrations may provide significant benefit (3). Cholesterol values placing participants at increased risk of atherosclerosis (4, 5) were observed with the expected frequency (6) and therefore were discussed in the primary educational letter (Appendix A), but they were not studied further. The wellness-program coordinators used materials from the American Heart Association to stress the benefits of dietary intervention to lower cholesterol.

The most significant difference in this wellness program is the inclusion of serum ferritin and a thyroid function test with automatic follow-up testing. These tests have added significantly to the case-finding (7) effectiveness. Case-finding tests identify individuals deserving intervention and therefore must have nearly zero false positives. Case-finding tests do not find every case, but every case identified is a true positive. In contrast, screening tests attempt to find all cases, frequently having false positives requiring additional evaluation to identify the true positives before intervention. Ferritin is a more satisfactory case-finding test for iron deficiency than is serum iron (8). Effective thyroxin ratio is not altered by the common aberrations of thyroxin binding globulin and is therefore a better case-finding test than total thyroxin (9).

Results of ferritin and thyroid tests were abnormal in 10.8% of participants and accounted for 61% of cases with a therapeutic intervention. These interventions were specific and were for a new diagnosis, in contrast to chronic incurable conditions found by the more usual automated chemistry profiles (10–12).

Our test profile also included the routine chemistry tests because they are expected by the participants, inexpensive, and automated. After the fixed costs of sampling, accessioning, programming the analyzer, and reporting are incurred, the incremental cost of each automated analysis by the same analyzer is very small. The redundancy provided by multiple liver or renal-function tests increases confidence that each individual test is a true positive. Gamma-gluta-
myltransferase is frequently the only biochemical clue to ingestion of an enzyme-inducing drug or ethanol, and therefore it is an important part of the test panel. If a gamma-glutamyltransferase abnormality is accompanied by an abnormal aspartate aminotransferase or alanine aminotransferase, the redundant but confirmatory data add to the importance of the abnormal gamma-glutamyltransferase.

Results of routine automated chemistry tests were abnormal in 5.9% of participants and accounted for 39% of the physician interventions. These interventions were usually additional testing, dietary counseling, or alteration of therapy for a previously known disease.

Therapeutic intervention was initiated in 4.1% of participants. Clinical and economic outcome was not objectively assessed in our study. However, we speculate that the 2% of participants who received specific therapy for hypothyroidism or iron deficiency may have experienced therapeutic benefit, enhanced work performance, and a decreased need for future medical consultations.

Reporting laboratory results to untrained wellness participants can be associated with significant anxiety. Before the reporting schema shown in Appendices A and B were put into use, wellness participants called the laboratory reporting unhappiness and anxiety about their abnormal results. Many were not eager to incur the expense of a physician's office visit to understand the significance of their results. By obviating these negative participant responses and negative public relations for the wellness program provider, we think this reporting schema enhances the positive aspects of the laboratory portion of the wellness program.

Our findings are similar to other studies of ambulatory "well" individuals, showing a high prevalence of iron deficiency among women, about 1% with occult hypothyroidism, and about 6% with abnormal routine chemistry results (13-21). Benefit from discovery of these abnormal results is difficult to estimate, but the 2% treated with iron or thyroid probably benefited. We think the choice of wellness profile tests should reflect "case-finding" goals and therefore include tests with excellent predictive value for iron deficiency and thyroid disease.

Assessment of wellness is a vigorous activity and the laboratory is an expected portion of that process. The laboratory should endeavor to provide effective case-finding profiles. The laboratory is obligated to assure that the results are appropriately interpreted and that appropriate follow-up action is suggested. Thyroid function tests and serum ferritin are excellent examples of case-finding tests that should be included on wellness program profiles.

References
8. Witte DL. Laboratory tests to confirm or exclude iron deficiency. Lab Med 1986;16:671-5.

APPENDIX A

Dear Participant:

has provided the laboratory portion of your Wellness Screening Program. Your results have been reviewed by a laboratory physician and significant abnormalities will be indicated by an asterisk to this letter. You should contact your physician to correlate these laboratory abnormalities with portions of your health history and physical examination. The laboratory is rarely the sole diagnostic factor.

A "well" person will frequently have one or two circled laboratory tests in a large profile. This is because there are differences between people. These circled results usually represent an unusual variation from the normal and should be of no concern to the participant. Frequently, these mild variations are explained by diet, medications, exercise, or other personal habits. If you have a few circled results that are very close to the "normal" percentiles, it should be of little concern and you can mention them to your physician at your next routine visit.

Next, we would like to say a few words about each of the laboratory tests.

1. TSH (Thyroid Stimulating Hormone): This is a test of thyroid function. The thyroid gland is a major controller in the body's metabolism.
2. Ferritin: Serum ferritin is an indirect measurement of your body's iron stores. Iron is important for the production of red blood cells and prevention of anemia.
3. Cholesterol: High cholesterol is a known heart disease risk factor. The average cholesterol among Americans is too high, and associated with a high incidence of heart disease. Other equally important risk factors are SMOKE, hypertension, and family history of heart disease.

Your result needs to be interpreted in relationship to age. Cholesterol tends to be higher as you age. The National Institute of Health has provided guidelines for interpreting cholesterol results (see table). These guidelines are based on data from individuals age 20-50.

If you are over 50 and have not had prior heart disease but have a cholesterol above 200, you could discuss this with your physician on your next visit.

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High Density Lipoprotein (HDL): Some of the cholesterol in blood is associated with a specific protein called "high density lipoprotein (HDL)": Individuals with more than average high density lipoprotein cholesterol seem to have a lesser risk of coronary heart disease. Average risk is associated with an HDL value in the 40's. High HDL cholesterol results are associated with lower risk.

4. Triglycerides: Triglycerides are fats. They will be elevated in blood after a meal. The National Institutes of Health has indicated that triglycerides are not an independent risk factor of coronary heart disease unless there is also an elevation of cholesterol (see above). Elevations of triglycerides are also associated with alcohol intake or obesity.

5. Enzymes as Indicators of Liver Disease: LDH, GGT, SPT, GGT, and ALP are enzymes which reflect liver function. A mild abnormality of only one or two of these should be of little concern, especially if the elevation is minimal. GGT is frequently elevated in patients who take certain medications, or drink alcohol in more than moderate amounts.

6. Total Protein and Albumin: Total protein and albumin are measures of protein metabolism. They also reflect general nutritional status.

7. Bilirubin: Bilirubin is a normal breakdown product from hemoglobin in red blood cells. Minor abnormalities occasionally occur following an overnight fast in some individuals.

8. Creatinine, BUN, and Urine Acid: These three tests reflect kidney function. Mild abnormalities of BUN may be observed in normal people who have an unusually large intake of high protein foods. Urine acid is also influenced by certain kinds of foods and drugs and may be elevated in some patients with gout.

9. Sodium and Potassium: These are important for normal functioning of most cells in the body. Therefore, the body uses many mechanisms to ensure that their concentrations in blood remain closely regulated. These Na & K are usually abnormal only under relatively significant physiologic derangements. Most people have been controlled by physicians to watch their intake of sodium or potassium. The presence of normal sodium or potassium values in the blood does not indicate you should ignore the advice of your physician.

10. Calcium and Phosphorus: Calcium and phosphorus are important for bone formation. The body tries very hard to regulate the concentration of these in the blood. The presence of normal values for calcium does not exclude the risk of osteoporosis. If you have been advised to regulate your calcium intake, the presence of a normal value for serum calcium does not indicate any change should be made in that program.

11. Glucose: Glucose is a measure of the sugar that circulates in the blood. The most usual condition found by measuring serum glucose is diabetes mellitus which is associated with a high concentration. The level of sugar in the blood is also strongly affected by a recent meal.

We hope this brief explanation has helped you to understand your laboratory results. Again, laboratory results that we feel need to be correlated with other pertinent health history have been indicated in an addendum. If you have an addendum, we would suggest that you take your results to your physician so that this correlation can take place.

Sincerely,

Your Wellness Representative Wellness Medical Director Laboratory Director

APPENDIX B

Dear ___

This is an addendum to the enclosed general information.

ADDITION FOR HYPOTHYROID

Your laboratory results strongly suggest hypothyroidism. This diagnosis is frequently difficult to make because a patient's symptoms and findings are nonspecific and occur gradually over a long time period. We suggest you contact your physician regarding these findings.

THYROID ADDENDUM

Your laboratory results suggest the possibility of a mild thyroid abnormality. This diagnosis is frequently difficult to make because a patient's symptoms and findings are nonspecific and occur gradually over a long time period. We suggest you discuss these results with your physician on your next visit.

ADDITION FOR HYPOGLYCEMIA

Your laboratory results suggest the possibility of a mild hypoglycemia abnormality. This diagnosis is frequently difficult to make because a patient's symptoms and findings are nonspecific and occur gradually over a long time period. We suggest you discuss these results with your physician on your next visit.

ADDITION FOR POSTMENOPAUSAL FEMALE

Your serum ferritin value (which is less than 12 ng/mL) strongly suggests low iron stores. This is a frequent finding among females during their menstrual and childbearing years. This laboratory abnormality should be evaluated with your dietary, menstrual, and reproductive history by your physician. If you are postmenopausal, this finding may have greater significance, and we suggest you correlate these results with your physician.

ADDITION FOR MALE

Your serum ferritin value (which is less than 12 ng/mL) strongly suggests low iron stores. This could be a very significant finding and should be evaluated by your physician and correlated with your dietary and blood loss history.

GLUCOSE ADDENDUM

Your glucose value was elevated beyond what is usually expected even following a meal. This suggests your body responds abnormally to your foods. You should see your physician about this abnormality.

ADDENDUM FOR SEX HORMONES

Your results have several abnormalities which are associated with altered liver function. These tests alone are not the complete diagnosis. We suggest you see your physician to correlate these results with your health history and physical exam.

ADDENDUM FOR HIGH CHOLESTEROL

Your cholesterol value is significantly above both the expected and ideal range for an individual your age. As you know, a high cholesterol is associated with health risks. You should see your physician about this Abnormality.

ADDENDUM FOR TRIGLYCERIDES OVER 500

Your triglyceride value is over 500 mg/dL. It could be a normal response to a meal that was high in fats. If you did not eat 1-2 hours before your blood was drawn, you should see your physician about this abnormality.

ELECTROLYTES ADDENDUM

Abnormal electrolytes are most frequently associated with drug therapy for hypertension. They are also associated with some rare causes of hypertension. We suggest you contact your physician to correlate these laboratory results with your history and blood pressure. Do not alter any medication orders without consulting your physician.

ADDENDUM FOR ABNORMAL KIDNEY FUNCTION TESTS

Your results have several abnormalities which are associated with an altered kidney function. These tests alone are not the complete diagnosis. We suggest you see your physician to correlate these results with your health history and physical exam.

ADDENDUM FOR ABNORMAL GGT/CPK

Your GGT value was considerably higher than usual. GGT can come from many body organs. We performed additional and repeat tests to help understand your value. You had a high level of another enzyme, CPK, which strongly suggests the GGT in your sample came from muscle. Has your recent exercise been above your usual habits? You may want to discuss these results with your physician on your next routine visit.

APPENDIX C

FOLLOW-UP CONTACT OF PARTICIPANTS WITH ABNORMALITIES

1. Are you (name) ___?
2. Did you participate in (organization) wellness program in (month)? ___
3. Do you remember your report on the addendum? ___
4. Did you worry about your lab results? (Categorized by interviewer)
   a) no worry
   b) little worry
   c) very worried
   d) angry or upset
5. Did you contact a medical professional about your results?
   a) contacted an M.D. immediately/ later
   b) contacted M.D. by phone
   c) visited M.D.'s office
   d) called office nurse
   e) discussed results with RN, MT, etc.
6. What did the M.D. (RN, MT) etc do or say?
   a) no action, reassured no concern indicated
   b) ordered additional laboratory tests
   c) ordered other diagnostic tests (x-rays, etc)
   d) obtained history/physical or routine office visit
   e) therapy prescribed
   f) other
7. Was a specific diagnosis indicated to you? What was it?
8. Was therapy prescribed for that diagnosis?
9. Was this a new diagnosis? A progression of a known diagnosis?