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Lardinois' Bakers Dozen
Important Things You Need to Know About Yourself

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Brief Summary

Personalized medicine is a medical model that separates people into different groups-with medical decisions, practices, interventions and/or products being tailored to the individual patient based on their predicted response or risk of disease **[1]**. Outlined below are 13 important tests/interventions that should be done in all people to assure that the medical decisions are tailored to their specific needs.

Abbreviations: ALP: Alkaline Phosphatase, HPP: Hypophosphatasia, TNSALP: Tissue-Nonspecific Alkaline Phosphatase, XLH: X-Linked Hypophosphatemia, TC/HDL-C: Total Cholesterol/High Density Lipoprotein Cholesterol, TIBC: Iron/Total Iron Binding Capacity, HFE: Human Factors Engineering, GHF: Glomerular Hyperfiltration, CKD: Chronic Kidney Disease, UACR: Urine Albumin-To-Creatinine Ratio, IR: Insulin Resistance, OGTT: Oral Glucose Tolerance Test, FVL: Factor V Leiden, Lp: Lipoprotein, LDL: Low-Density Lipoprotein, Apo: Apolipoprotein, Hp: Haptoglobin, AZ: Alzheimer, Hcy: Homocysteine, MESA: Multi-Ethnic Study Of Atherosclerosis, NHANES: National Health And Nutrition Examination Survey

Short Report:

1. Alkaline phosphatase (ALP):

A LOW ALP is the hallmark of Hypophosphatasia (HPP), due to the loss of function of Tissue-Nonspecific Alkaline Phosphatase (TNSALP) **[2]**. While an elevated ALP attracts the attention of most health care provider, a low value does not. Whenever the ALP is LOW the patient must be assessed for HPP. Critical the ALP reported is age-adjusted. Half the cases of HHP are not diagnosed until adulthood.

2. Serum phosphate:

A LOW serum phosphate is the hallmark of X-Linked Hypophosphatemia (XLH). Gain in function mutations of Phosphate Regulating Endopeptidase Homolog X-linked (FLEX) causes hypophosphatemia **[3]**. Serum phosphate is no longer included in laboratory panels, so it is critical that each patient gets a serum phosphate measurement. A LOW value mandates a work-up for XLH. Many patients with XLH are not diagnosed until adulthood.

3. Total Cholesterol/High Density Lipoprotein cholesterol ratio (TC/HDL-C) ratio: For decades, the focus of dyslipidemia therapy has been on the LDL-C. Overwhelming data now show that the TC/HDL-C ratio is superior to LDL-C in predicting outcomes. Insurance underwriting carriers are using the TC/HDL-C ratio as the "gold standard" to determine

an individual's heart health **[4]**. The medical profession may need to consider aligning to this strategy.

4. Iron/Total Iron Binding Capacity (TIBC) Saturation:

Hereditary hemochromatosis is an autosomal recessive disorder that results from a mutated hemochromatosis (HFE [human factors engineering]) protein. The HFE C282Y mutation arose in Europe 6,000 years ago, coinciding with the arrival of the Neolithic agricultural revolution **[5]**. Anyone with an Iron/TIBC saturated greater than 50% should be evaluated for hemochromatosis.

5. 25-OH Vitamin D [25(OH)D]:

There are dose-response trends across all 25(OH)D quintiles showing curvilinear inverse associations for all-cause mortality and cardiovascular mortality. This is especially striking when the 25(OH)D level is less than 10 **[6]**. Low vitamin D levels are also associated with a higher risk of type 2 diabetes mellitus **[7]**.

6. Glomerular Hyperfiltration (GHF):

Chronic kidney disease (CKD) is a major public health problem. GHF is observed in patients with hypertension, type 1, and type 2 diabetes, and is also seen in patients with insulin resistance. GHF is hypothesized to be a precursor of intraglomerular hypertension leading to albuminuria. Persistent hyperfiltration is an independent risk factor for accelerated renal function loss and development or progression of nephropathy. An eGFR of >120 ml/min/1.73 m2 has the same cardiovascular mortality risk as an eGFR of 45 ml/min/1.73 m2 **[8]**.

7. Urine albumin-to-creatinine ratio (UACR):

An elevated urinary albumin excretion (albuminuria) is a marker of endothelial dysfunction that symbolizes the kidney's way to translate the existence of systemic vascular dysfunction. It is an independent risk factor for progression of heart disease, stroke, and CKD in people with diabetes or hypertension, the general population, and those with established heart disease even at levels well below current guidelines **[8]**.

8. Insulin Resistance:

Insulin Resistance (IR) is the Holy Grail for many chronic medical conditions. These include hypertension, dyslipidemia, heart failure, NAFLD/NASH, chronic kidney disease, albuminuria, Alzheimer's, polycystic ovarian syndrome, certain cancers, and COVID-19. Many markers are used to assess the risk of IR including fasting glucose and A1c. However, to know if there is pancreatic dysfunction and risk of IR, the b-cell must be challenged. The Gold Standard for diagnosing IR is the euglycemic clamp but is labor intensive and not practical in a real-world setting. A glucose challenge is a suitable alternative to assess to assessing IR and correlates well with the euglycemic clamp. A 2-hour Oral Glucose Tolerance Test (OGTT, 75 grams) should be performed on every non-diabetes patient. If the one-hour value is over 125 mg/dL or the two-hour value is over 120 mg/dL there is a remarkably high probability the patient has IR **[9]**.

9. Factor V Leiden (FVL):

FVL mutation is the most common prothrombotic genetic defect. It was named from Leiden, Netherlands where it was discovered. Between 3 and 8 percent of people with European ancestry carry one copy of the factor V Leiden mutation in each cell, and about 1 in 5,000 people have two copies of the mutation **[10]**. People with FVL thrombophilia have a higher-than-average risk of developing deep venous thrombosis and pulmonary embolism. The risk can increase in woman with FVL taking birth control pills.

10. Lipoprotein-a [Lp(a)]:

LP(a) is a low-density lipoprotein (LDL) particle with an added apolipoprotein(a) (apo[a]) attached to the apolipoprotein(b) (apo[b]) component of the LDL particle via a disulfide bridge. The structure of Lp(a) is highly heterogeneous secondary to many different apo(a) isoforms within the population. Values > 30 mg/dL threshold may indicate increased risk of atherosclerosis, heart attack, or stroke and warrants further investigation **[11]**.

11. Haptoglobin Genotype:

Haptoglobin (Hp) is an acute phase α-glycoprotein synthesized primarily by the liver in response to inflammatory cytokines. There are 3 Hp polymorphism in humans: 1-1, 1-2, and 2-2. A recent meta-analysis showed that the incidence of CV events in DM patients with the Hp 2-2 genotype was significantly increased as compared to non-Hp 2-2 patients. Among patients with the Hp 2-2 genotype, administration of vitamin E was associated with lower rates of CV events. Vitamin E offers a low cost means of reducing

CV events in DM patients with Hp 2-2 **[12]**.

12. Apolipoprotein E (ApoE):

Is a multifunctional protein that plays a key role in the metabolism of cholesterol and triglycerides. Three APOE alleles are dominantly inherited. The most common allele is ε3/ε3 (64%); 1% ε2/ε2; 10% ε2/ε3; 2% ε2/ε4; 18% ε3/ε4; and 5% ε4/ε4. The odd ratio of getting Alzheimer (AZ) is 3.2X higher with one copy of and ε4 14.9X greater with two copies of ε4.

In addition to the differences in AZ risk, ε4 carriers have a higher risk of CVD, response to lipid therapy, and response to medical nutrition therapy compared to non- ε4 carriers. HMG-CoA reductase inhibitors are less effective in reducing cholesterol levels in APO E4 individuals (as compared to Apo E2). Patients with ε4 achieve a much greater reduction in LDL-C with a low-fat diet. Another crucial factor is that patients with ε4 see a worsening of their lipid profile and enhanced risk of AD with alcohol consumption **[13-15]**.

13. Homocysteine (Hcy):

The mechanism by which Hcy exerts atherosclerosis effects are now being elucidated. The hypothesis is that elevated Hcy level promotes oxidant injury to the vascular endothelium, impairs endothelium-dependent relaxation, and alters the coagulant properties of blood. Hcy level (>15 umol/l) significantly predicted CVD in the Multi-Ethnic Study of Atherosclerosis (MESA) trial and CVD in the National Health and Nutrition Examination Survey (NHANES) III, after adjustments for traditional risk factors **[16]**. Any individual with an Hcy >15 umol/l should be evaluated for atherosclerosis. Whether lowering Hcy reduces vascular events remain unclear.

Conclusion

Personalized medicine is an evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health.

References

1. Vogenberg FR, Barash CI, and Pursel M. (2010) Personalized medicine: part 1: evolution and develop-ment into theranostics. P T. 35: 560-576.
2. Bianchi ML. (2015) Hypophosphatasia: an overview of the disease and its treatment. Osteoporos Int. 26: 2743-2757.
3. Chesher D, Oddy M, Darbar U, et al. (2018) Outcome of adult patients with X-linked hypophosphatemia caused by PHEX gene mutations. J Inherit Metab Dis. 41: 865-876.
4. Udell B. (2020) The lowdown on high cholesterol and life insurance. Accuqoute.
5. Ulvik RJ. (2016) Hereditary haemochromatosis through 150 years. Tidsskr Nor Laegeforen. 136: 2017-2021.
6. Schöttker B, Jorde R, Peasey A, et al. (2014) Vitamin D and mortality: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States. BMJ. 348: g3656.
7. Pittas AG, Jorde R, Kawahara T, and Dawson-Hughes B. (2020) Vitamin D Supplementation for Prevention of Type 2 Diabetes Mellitus: To D or Not to D? J Clin Endocrinol Metab. 105: 3721-3733.
8. Lardinois CK. (2017) Hyperfiltration and Albuminuria-A Deadly Combination. US Endocrinology. 13: 12-13.
9. Abdul-Ghani M, Stern MP, Lyssenko V, et al. (2010) Minimal contribution of fasting hyperglycemia to the incidence of type 2 diabetes in subjects with normal 2-h plasma glucose. Diabetes Care. 33: 557-561.
10. Kujovich JL. (2011) Factor V Leiden thrombophilia. Genet Med. 13: 1-16.
11. Miksenas H, Januzzi JL, and Natarajan P. (2021) Lipoprotein(a) and Cardiovascular Diseases. JAMA. 326: 352-353.
12. Asleh R, Briasoulis A, Berinstein E, et al. (2018) Meta-analysis of the association of the haptoglobin genotype with cardiovascular outcomes and the pharmacogenomic interactions with vitamin E supplementation. Pharmgenomics Pers Med. 11: 71-82.
13. Berkowitz CL, Mosconi L, Rahman A, et al. (2018) Clinical Application of APOE in Alzheimer's Prevention: A Precision Medicine Approach. J Prev Alzheimers Dis. 5: 245-252.
14. Slayday RE, Gustavson DE, Elman JR, et al. (2021) Interaction between Alcohol Consumption and Apolipo-

protein E (ApoE) Genotype with Cognition in Middle-Aged Men. J Int Neuropsychol Soc. 27: 56-68.

15. Corella D, Tucker K, Lahoz C, et al. (2001) Alcohol drinking determines the effect of the APOE locus on LDL-cholesterol concentrations in men: the Framingham Offspring Study. Am J Clin Nutr. 73: 736-745.
16. Veeranna V, Zalawayiya S, Niraj A, et al. (2011) Homocysteine and reclassification of cardiovascular disease risk. J Am Coll Cardiol. 58: 1025-1023.