Testing

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Testing

- Testing during perimenopause is not great as hormones are all over the place so can treat by "symptoms"
- Debate over testing before or only once on BHRT
- And within several months to check levels
- Or when they are feeling really great
- Or not responding
- Must track thyroid as giving ERT can lower thyroid signaling = this is critical
- Track post prandial insulin as high insulin can occupy sex steroid hormones and become "competitive inhibitor"
- Track cortisol as when high (or low) can occupy sex steroid hormones and become "competitive inhibitor"

Always must also run blood

- SHBG
- FSH
- RBCs like zinc
- Hormone ranges are not ideal they are norms
- There is a debate if they reflect tissue levels or not
- If run serum for hormones: estrone lower that estradiol, progesterone over 4 ng/dL,
- Total and Free T

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Testing

- 24 hour urine
- Blood
- Dried urine
- Saliva

Symptoms of Hormone Deficiencies Women

Women: Common Symptoms	Estrogen	Progesterone	Thyroid	Glucocorticoids	DHEA	Testosterone	GrowthHormone	Melatonin	Oxytocin
Hot flashes	1	√							
Night sweats	✓	✓		✓					
Headaches	✓	✓					1	1	1
Hair loss	✓		1		1	✓			
Poor sleep	1	✓		✓			1	✓	
Anxiety	✓	✓	1	1	1	✓			1
Depression	√	✓	1	1	1	✓	4	✓	1
Stress	1	4	4	✓	1	✓	1	✓	✓
Low libido	1	✓	4	4	1	✓			✓
Memory lapse	✓		1	✓		✓			
Sugar cravings		4		4	4	4			
Weight gain	1	4	4	✓	1	✓	1	✓	✓
Increased facial hair/acne	1				4	1			

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Symptoms of Hormone Deficiency Males

Men: Common Symptoms								Melatonin	
Poor stamina			4	✓.	1	✓	✓		
Decreased muscle mass/strength					1	✓	✓		
Neck/back pain						4			
Low libido									
Decreased erections		✓		4	1	1			4
Sugar cravings			4				4		
Weight gain	4		1	✓	1	✓	✓	1	
Stress			1	✓	1	✓	1	1	1
Apathy/burned out feeling			4	4	4	4	4		1
Anxiety		✓	1	✓	1	✓			✓
Depression		✓	1	✓	1	✓	✓		1
Poor Cognition	4		1	✓	1	✓	1		
Memory lapse	1		1	1	1	✓	1		

Urine Hormone Testing

- The beauty of the hormone test through urine is that we get the metabolites.
- Measuring urine hormone metabolites reveals how the patient is breaking down their hormones. The breakdown metabolites of
 estrogen for example can give us insight into the patient's ability to detoxify her/his estrogens to decrease risk of estrogendependent cancers.
- · Some estrogen metabolites have been shown to increase the risk for breast and prostate cancer in women and men, respectively.
- Urine biomarkers of risk in the molecular etiology of breast cancer. Breast Cancer; Basic & Clinical Research 3, 1-8 (2009).
- This study validates the finding that women with breast cancer or at high risk for the disease have significantly higher levels of
 depurinating estrogen-DNA adducts in their urine than healthy, normal-risk women. These data predict that depurinating
 estrogen-DNA adducts could become biomarkers for early detection of breast cancer risk and be used in prevention strategies.
- Estrogens can initiate cancer by reacting with DNA. Specific metabolites of endogenous estrogens, the catechol estrogen-3,4-quinones, react with DNA to form depurinating estrogen-DNA adducts. Loss of these adducts leaves apurinic sites in the DNA, generating mutations that can lead to the initiation of cancer.
- Novel biomarkers for risk of prostate cancer. Results from a case-control study. Prostate 69,41-48 (2009).
- This study showed that men with prostate cancer have significantly higher levels of depurinating estrogen-DNA adducts in their urine compared with healthy men. These data suggest that depurinating estrogen-DNA adducts could serve as potential biomarkers to predict risk for prostate cancer.
- <u>Clin Transl Med</u>. 2016; 5: 12. Depurinating estrogen-DNA adducts, generators of cancer initiation: their minimization leads to cancer prevention

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Urine Reflects Tissue Levels

- An important aspect of the link between estrogen and breast cancer is whether urinary estrogen levels are representative of the intratissue levels of bioavailable estrogens.
- (2010) in "Comparison of estrogens and estrogen metabolites in human breast tissue and urine" PMID: 20678202 have shown in particular that urinary 2/16 ratio is a good approximation of the ratio observed in breast tissue.

FDA: 24-hr urine reflects blood

- We made repeated measurements of serum concentrations of estrone (E1), estradiol (E2), estriol (E3), estetrol (E4), daidzein (DDZ), genistein (GEN) and bisphenol A (BPA) in 30 pregnant women using ultra-performance liquid chromatography coupled with tandem mass spectrometry detection (UPLC-MS/MS) and electrospray ionization (ESI).
- Serum E1, E2, and E3 concentrations varied significantly (coefficients of variation 9-10%) with broad ranges across the cohort: 1.61-85.1 nM, 9.09-69.7 nM, and 1.5-36.3 nM respectively.
- The 24-h urinary elimination profiles of endogenous estrogens were each strongly correlated with their corresponding serum concentrations (Pearson's Correlation Coefficients of 0.83 (E1), 0.84 (E2) and 0.94 (E3)).
- Food Chem Toxicol. 2018 Mar 13. pii: S0278-6915(18)30166-2. doi: 10.1016/j.fct.2018.03.017. Comparative estrogenicity of endogenous, environmental and dietary estrogens in pregnant women I: Serum levels, variability and the basis for urinary biomonitoring of serum estrogenicity.

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If on BHRT or HRT

- Must only test blood 4 hours later
- Do not take thyroid that morning

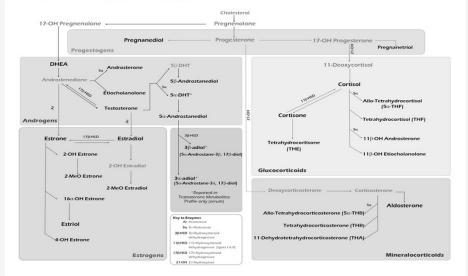
2 MEO

- 2-methoxyestradiol: considered as potential therapeutic agents due to their antitumor activity via induction of apoptosis and inhibition of angiogenesis.
- It also shows methylation capabilities as the catechol estrogens have to be methylated to make 2 MEO.
- 2-Methoxyestradiol: an endogenous antiangiogenic and antiproliferative drug candidate. Cancer Metastasis Rev. 19:173–179. [PMID: 11191057]
- The physiological estrogen metabolite 2-methoxyestradiol reduces tumor growth and induces apoptosis in human solid tumors. J Cancer Res Clin Oncol. 127:405–410. [PMID: 11469676]
- 2-Methoxyestradiol inhibits proliferation and induces apoptosis independently of estrogen receptors alpha and beta. Cancer Res. 62:3691–3697. [PMID: 12097276]
- . (1999). Potent antitumor activity of 2- methoxyestradiol in human pancreatic cancer cell lines. Clin Cancer Res. 5:493–499. [PMID: 10100698]

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Hormone Pathways



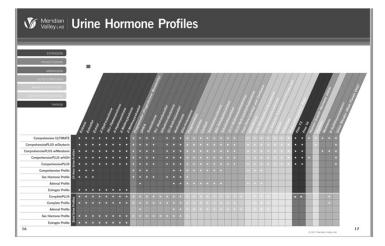
24 urine labs that collect all day long – Meridian and Rhein

- Mineralocorticoids when low may suggest a more chronic adrenal insufficiency more than looking at the glucocorticoids alone.
- Meridian Valley Lab was the first lab in the USA to offer urine hormone testing to help doctors use Bio-identical Hormone Replacement Therapy safely and effectively.
- MVL participates in proficiency testing services with the College of American Pathologists and the American Association of Bioanalysts. Meridian Valley Lab is CLIA Certified.
- https://rheinlabs.com/

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Diverse Tests



Urine Testing

- Urine hormone testing uses advanced LC-MS/MS and GC-MS/MS technology, the most sensitive and advanced hormone testing available today.
- It measures important metabolites not available in serum or saliva testing, providing a clearer picture of hormone balance and function.
- Metabolites that increase risk for cancers, osteoporosis, and other serious conditions, as well as protective metabolites, are measured. This allows greater safety in prescribing hormone therapy or herbal therapy.

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- Urine hormone testing also allows for a full-day perspective on hormone production important because some hormones are produced primarily at late at night, early in the morning, or in pulses throughout the day.
- A single blood draw or saliva sample cannot account for this variability.
- Though many top hormone doctors do only use serum, so you have to know there are many ways to test and treat and none of them deal with hormones locally produced (intracrinology).
- Urinne testing measures free and conjugated hormones, providing a true measure of bioavailable hormones.
- Serum testing is excellent for peptide hormones such as Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), Insulin-like Growth Factor-1 (IGF-1, and some thyroid hormones. Serum testing is used for Testosterone Metabolites profile.

Most complete

- Comprehensive ULTIMATE
- 24-Hour Urine Hormone Testing
- Code: 4100
- The Comprehensive ULTIMATE is the most complete urine hormone panel.
- This panel measures estrogens and clinically relevant estrogen metabolites, which allow for assessment of cancer risk factors and detoxification pathways. Pregnanediol assays progesterone activity in the body. DHEA, testosterone and their metabolites provide a detailed assessment of androgen function. Cortisol, cortisone, aldosterone and their metabolites provide an industry-leading evaluation of adrenal health. Urinary free T3 and free T4 provide a sensitive gauge of thyroid hormone status. The ComprehensivePlus panel also calculates 5a Reductase and 11β-Hydroxysteroid Dehydrogenase II enzyme activity. 5a Reductase is an important enzyme that governs androgen metabolism and is associated with insulin resistance and other conditions. 11β-HSD determines the balance between cortisol and cortisone. hGH, Oxytocin, and Melatonin are also measured.

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Follow up Dried Urine Hormone

- CompletePLUS
- Dried Urine Hormone Testing
- Code: 4990
- The CompletePLUS provides a broad and in-depth evaluation of hormone balance, function and circadian cortisol pattern.
- This panel measures estrogens and clinically relevant estrogen metabolites, which allow for assessment of cancer risk factors and detoxification pathways. Pregnanediol assays progesterone activity in the body. DHEA, testosterone and their metabolites provide a detailed assessment of androgen function. Cortisol, cortisone, and their metabolites, combined with 4-point cortisol and cortisone curves, provide an industry-leading evaluation of adrenal health.
- I use this as a follow-up of the ultimate 24-hour urine collection test.

Progesterone Metabolites

- Progesterone Metabolites Profile
- Serum / Bloodspot
- · Code: 4988 / 4989
- The role of progesterone in protecting vs. increasing breast cancer risk is not clear cut but has largely been attributed to the use of synthetic progestins.
- Recent in vitro research using normal and breast cancer cell lines suggest that there is a
 definable difference in progesterone metabolism in situ between these cell lines.
- This difference may be an important risk factor for the development and progression of breast cancer.
- Progesterone metabolites in breast cancer. Endocrine-Related Cancer (2006) 13 717–738.
 John P Wiebe Department of Biology, Hormonal Regulatory Mechanisms Laboratory, University of Western Ontario, London, Ontario, Canada N6A 5B7

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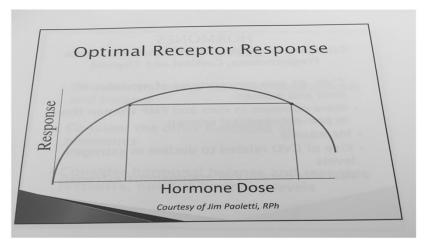
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Goldilocks Principle Rules

Hormones Are More About Balance Between Each Other & Between Receptors Than Blood, Urine or Saliva Levels



Too much not good, too little not good



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Bioidentical Versus Synthetic

Bioidentical

- Progesterone
- Estradiol
- Estriol
- Testosterone
- Pregnenolone
- DHEA
- Not FDA approved

- Progesterone Substitutes: Progestins (tamp down ER beta) MPA medroxy progesterone acette, norethindrone Acetate (OC'Ps) Norgestryl (OCP's)
- Estrogen Substitutes:
- (Conjugated Equine Estrogens CEE/Premarin)
- Ethinyl Estradiol (OCP's)
- · Not metabolized as bioidentical hormones
- Different end actions in different women
- FDA approved
- Replenish

Organic Acids

- Xanthurenic (XANA) and Kynurenic Acid (KYNA) are metabolites on the Kynurenine Pathway of tryptophan metabolism.
- These are part of the 24-hr urine test to help with the clinical management of estrogen detoxification.
- Studies indicate that individuals with low-activity catechol-Omethyltransferase (COMT) may require additional B6, B12 and folate to detoxify pro-carcinogenic estrogen metabolites.
- While high levels of Xanthurenic and Kynurenic Acid are commonly associated with mild or subclinical B6 deficiency and/or inflammation, the vitamin B2 requirement for XANA synthesis is seldom discussed or acknowledged in other laboratory reports.

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High levels

- Insulin resistance and diabetes
- • High levels of XANA may form complexes that block insulin receptors and, over time, destroy pancreatic cells.
- Cancer risk
- KYNA, and to a lesser extent, XANA both bind to and activate the aryl hydrocarbon receptor (AhR). Activation of the AhR either by environmental toxins (dioxin, etc.) or XANA and KYNA can induce cell damage and carcinogenesis.

Cardiovascular function

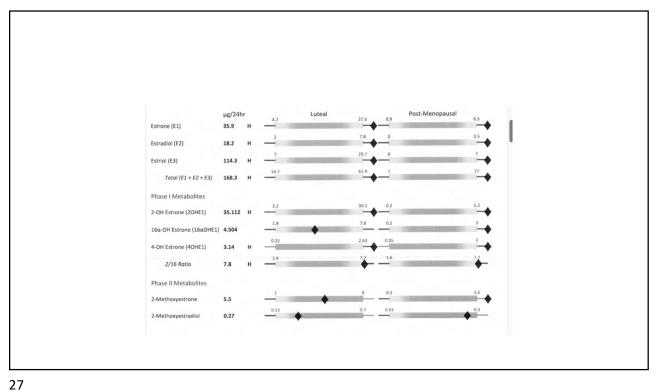
- Higher XANA levels are associated with cardiovascular disease.
- Chronic inflammation may increase the amount of circulating tryptophan metabolized outside of the liver.
- Peripheral metabolism of tryptophan in leucocytes, endothelial cells, macrophages and vascular smooth muscle cells increase risk factors for atherosclerosis in those with elevated LDL-cholesterol, BMI, or triglycerides, particularly in younger women

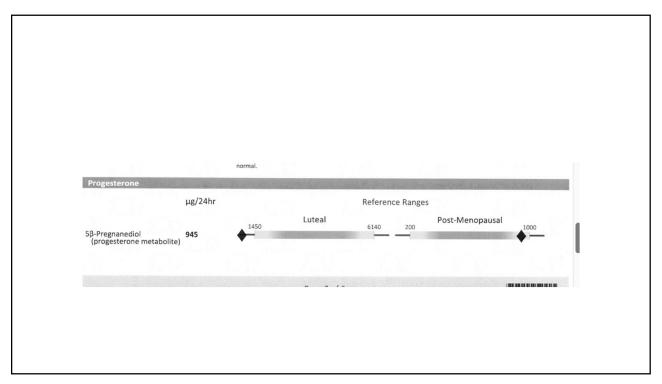
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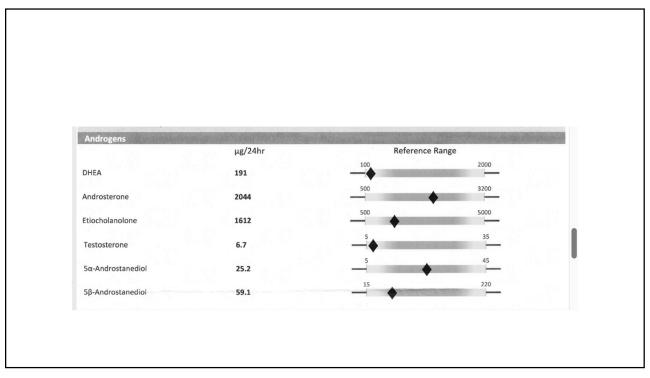
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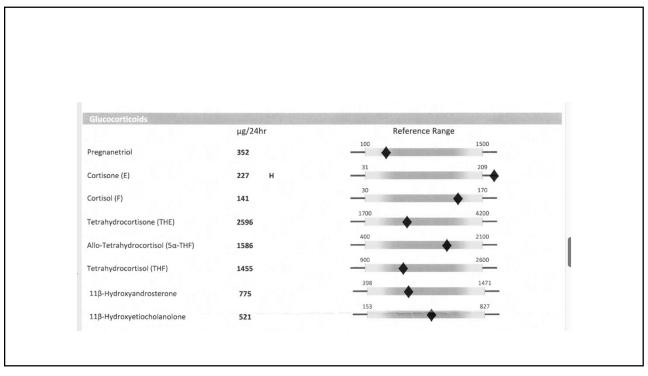
Autoimmunity + Inflammation

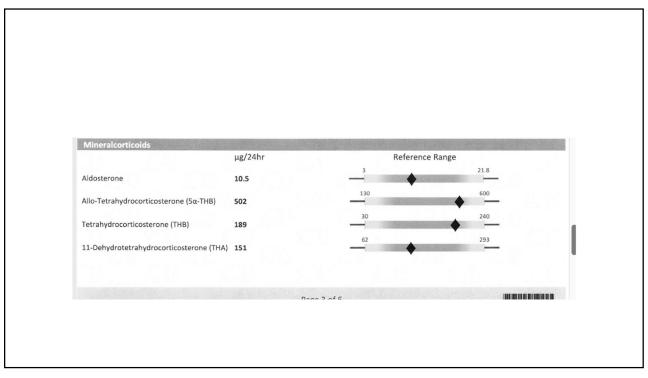
- KYNA levels modulate the production of IL-6 and increased levels of IL-6 are associated with rheumatoid arthritis (RA), systemic-onset juvenile chronic arthritis (JCA), osteoporosis, and psoriasis.
- IL- 10 lowers IL-6. Estrogen lowers IL-6. Oxytocin lowers II-6. Specific L. reuterii (BioGaia) ups II-10 and lowers II-6.
- The Kynurenine Pathway metabolizes excess tryptophan and controls hepatic heme synthesis and tryptophan availability for serotonin synthesis. The Kynurenic Pathway also produces immune-regulatory and neuroactive metabolites, nicotinic acid (vitamin B3), and oxidized nicotinamide adenine dinucleotide (NAD+).
- During homeostasis, the primary site of Kynurenic Pathway activity is the liver, where all of the enzymes to metabolize tryptophan into NAD+ are found, and account for 90% of tryptophan metabolism.
- During chronic inflammation, the extra-hepatic metabolism of tryptophan increases, and B6 levels decrease.
 Pro-inflammatory cytokines, combined with lower B6 levels, shift the Kynurenic pathway to produce more Xanthurenic and Kynurenic Acid (see diagram).
- Conversely, low levels of both Xanthurenic and Kynurenic Acid may indicate a tryptophan deficiency, a liver disorder, or a very rarely, severe B6 deficiency.

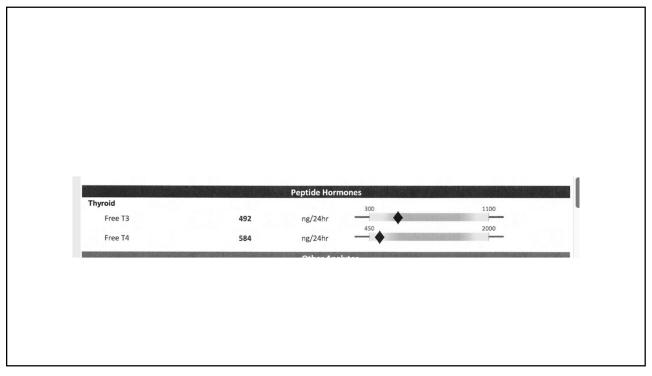


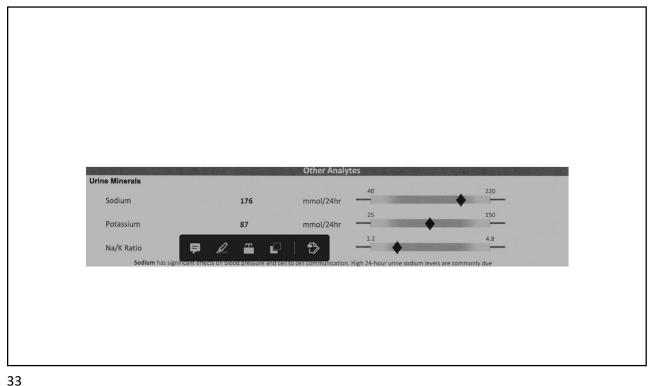


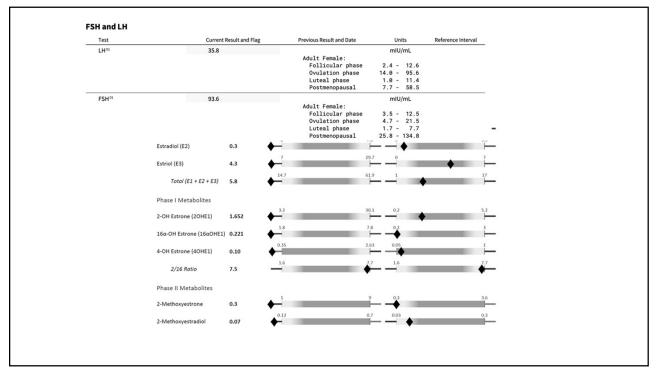


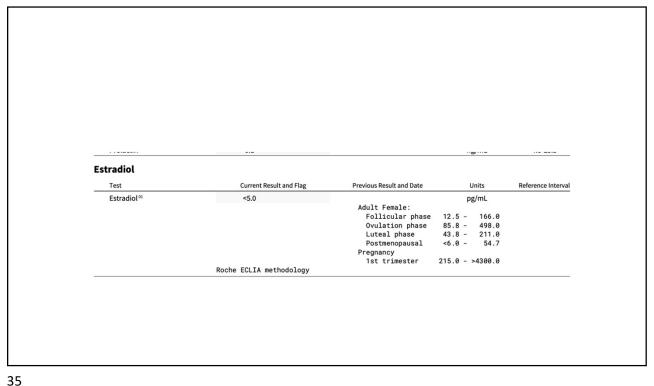


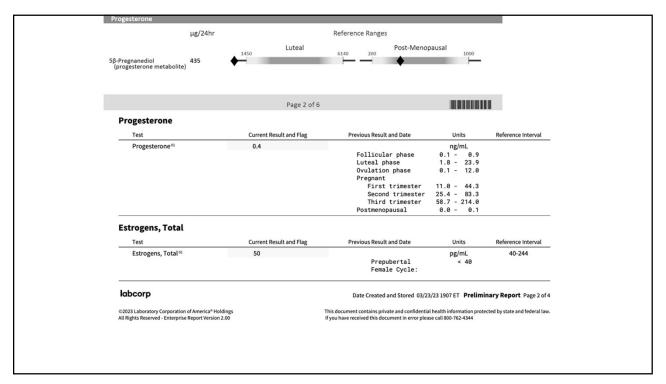












li.						
	Sex Horm Binding Glob, S	Serum				
	Sex Horm Binding Glob, S		olt and Flag	Previous Result and Date	Units	Reference Interval
	Test Sex Horm Binding Glob, Sex Horm Binding Glob, Serum ⁰¹	Current Resu	lt and Flag High	Previous Result and Date	Units nmol/L	Reference Interval
	Test Sex Horm Binding Glob,	Current Resu		Previous Result and Date		
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