

# Interpreting and Applying Lab Results for Improved Diabetes Control

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October 17, 2007

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## Objectives

- Increase knowledge of lab values as they relate to diagnosis of and care of Diabetes Mellitus.
- Learn more about "new" lab markers that may help educators better assess a person's level of blood glucose control.
- Provide a succinct guide to lab results without having to search through many resources

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## DIAGNOSIS



- Blood Glucose
- Ketones
- pH
- DKA vs Nonketotic Hyperosmolar Syndrome

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## Plasma vs. Whole Blood Glucose

- ADA recommends blood glucose values be based on plasma
- Virtually all new meters report plasma values
- Glucose is more concentrated in plasma by 10-15%



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### Diagnosing Diabetes: Blood Glucose



Normal	Impaired Fasting Glucose (IFG)	Impaired Glucose Tolerance (IGT)	Diabetes Mellitus
FPG < 100 mg/dL	FPG 100-126 mg/dL		FPG >126 mg/dL
2 hr OGTT < 140 mg/dL		OGTT 140-200 mg/dL	OGTT > 200 mg/dL or casual plasma glucose > 200 mg/dL with symptoms of DM

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## Serum and Urine Ketones

- Assessed in a Nitroprusside reaction
  - 75% to 90% B-hydroxybutyrate, Acetoacetate, Acetone
  - If B-hydroxybutyrate is main ketone, nitroprusside reaction doesn't pick up, so test can come back weakly ketotic; new test to just look at that ketone, so as to get more accurate results
- Byproduct of fat metabolism
- Test if:
  - BG consistently >300 mg/dL (if pregnant, > 200 mg/dL)
  - Acutely ill
  - Hyperglycemic with nausea, vomiting, abdominal pain, fever or "fruity breath"



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## Arterial blood gas: pH

- pH <7.3 indicates DKA; typically this is a high anion gap metabolic acidosis
- pH 7.2-7.3 mild DKA



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## Further Diagnosing DKA

- Hyperamylasemia
  - an excess of the pancreatic enzyme amylase in the blood
- Mg and Phos can be normal, elevated or reduced
- Leukocytosis
  - most often due to infections or inflammatory processes
- Hypertriglyceridemia



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## Diagnosing DKA vs. Nonketotic Hyperosmolar Syndrome

Finding	DKA	Nonketotic Hyperosmolar Syndrome
Plasma glucose	> 250 mg/dL	>600 mg/dL
Plasma osmolality [(2 x Na + K)] + (plasma glucose/18)	< 330 mOsm/kg	> 330 mOsm/kg
Ketones Urine Blood	> +3 + at > 1:2 dilution	- or small amounts - or small amounts
Serum bicarbonate	< 15 mEq/L	> 20 mEq/L
pH	< 7.3	> 7.3
Potassium	Appears normal (5.5 mmol/L), but with actual deficit	
Sodium	Hyponatremia	Hypnatremia
BUN	< 25 mg/dL	> 30 mg/dL

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## Diagnosing Gestational DM

- If BG >140 mg/dL, diagnosis confirmed with 100 g OGTT indicating any two of the following:

- Fasting >95 mg/dL
- 1 hour >180 mg/dL
- 2 hour >155 mg/dL
- 3 hour >140 mg/dL



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## Fructosamine

- Glycated serum Protein (GSP)
- Reflects BG values over preceding 7-10 days
- May be useful for monitoring women during pregnancy
- 1 hour pp blood sugars may be just as good/better

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## Fructosamine Values

- Diabetes Care 2003;26:163-167  
*Discordance Between HbA1c and Fructosamine*
- HbA1c values better assess risk for complications than do Fructosamine values

Glucose (mg/dl)	Fructosamine (umol)
90	212.5
180	325
300	475

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## Once She's Been Diagnosed...



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## Goals, post diagnosis

	Normal	Goal	Pregnancy
Premeal glucose (mg/dL)	<110	<110 ACE (90-130 ADA)	60-90
Postprandial (mg/dL)	<130	<140 ACE (<180 ADA)	<110 1 hr pp
Bedtime glucose (mg/dL)	<120	100-140	100-120
Hb A1c (%)	<6	<6.5 ACE (<7.0 ADA)	
LDL cholesterol (mg/dL)	<130	<100	<100
HDL cholesterol (mg/dL)	>40	>40 (>60 protective)	>40 (>60 protective)
Fasting triglycerides (mg/dL)	<150	<150	<150
Blood pressure (mm Hg)	<140/90	<130/85 (125/75 <small>w/kidney dx</small> )	<130/85

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## Assessing Glycemic Control

- A1c
  - Averages last 90 days
  - Heavily weighted last 30 days
  - May not show extreme glucose excursions (glucose variability)
- A1c plus GV may be more reliable predictor than A1c alone
  - Diabetic Microvascular Complications Today May/June 2005 36-40



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## HbA1c

- Are some pts rapid glycosylators and some slow glycosylators?
- More rapid glycosylation leads to increased speed of complications, AGE
- Accumulation of AGEs, whose formation is closely linked to oxidative stress, and resultant endothelial dysfunction may start early in the course of type 1 diabetes
- Risk of vascular complications may be present at an early age and best possible glycemic control should be emphasized from diagnosis

■ *Pediatric Research* 54:419-424 (2003)

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## Glycomark



- FDA-approved blood test for intermediate-term monitoring of glycemic control
- measures circulating levels of 1,5-anhydroglucitol (1,5-AG), a sugar similar to glucose, in serum or plasma
- monitors mealtime spikes over 2 days to 2 weeks in a single blood test
- Provides complementary information to A1C, to help manage transient glycemic excursions (postprandial hyperglycemia)

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## Glycomark

- GlycoMark values decrease when serum glucose levels increase (hyperglycemia)
- Upon return of better glycemic control, 1,5-AG increases at a constant rate of 0.3 ug/ml
- Consistent recovery rate in 1,5-AG levels provides a rapid indication of the patient's response to treatment.
- GlycoMark reflects more recent glycemic status (1-2 weeks) and measures mealtime spikes
- may also be used in situations where the A1C test cannot be measured or may not be useful (e.g., hemolytic anemias)

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## Normal Values of Glycomark (ug/mL)

- Normal >14
- Well Controlled (10-13.9)
- Moderately Controlled (6-9.9)
- Poorly Controlled (2-5.9)
- Very Poorly Controlled (<1.9)



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## Clinical Studies related to GlycoMark

- The 1,5AG test has been available in Japan since 1991
- Several published studies confirming the clinical utility of 1,5AG
- A major clinical study was conducted at University of North Carolina and University of Rochester. The study found that 1,5-AG reflects postprandial hyperglycemia to a greater extent than A1C and fructosamine. Postprandial hyperglycemia may exist in patients with modest A1Cs, and 1,5-AG may be used as a complementary marker to A1C for determining overall diabetes control

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## Lipid Levels by Risk for Adults

Risk	LDL*	HDL*	Triglycerides*
High	≥ 130	< 40	≥ 400
Borderline	100-129	40-59	150-399
Low	< 100	≥ 60 † ≥ 70 ‡	< 150

\*mg/dl

2005 ADA Clinical Practice Recommendations

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## Determining Heart Disease Risk

- Non-HDL cholesterol
  - Adult Treatment Panel (ATP) III guidelines rec. checking if TG >200, but LDL in normal range: the greater the non-HDL cholesterol, the greater the risk for HD
- TG to HDL ratio
- If TG 150 and HDL 40, ratio is 3.8, goal is to have a ratio of <3.8



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## Dyslipidemia Interventions

<i>Dyslipidemia</i>	<i>Intervention</i>
Elevated LDL	HMG-CoA-reductase Inhibitor; Statins
Decreased HDL	Weight loss Physical activity Smoking Cessation Glycemic Control
Elevated Triglycerides	Glycemic Control Decrease alcohol intake

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## Looking to the future...a new "Lab Value"?

- Visceral Fat produces:
  - Signaling Hormones
    - (Leptin, Resistin, PAI-1, Glucocorticoids, MMP)
  - Inflammatory Cytokines
  - ADIPONECTIN
    - secreted by fat cells
    - helps regulate energy metabolism
    - low levels are predictive of future development of DM & metabolic syndrome

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# Hypertension



	SBP		DBP
Normal	< 120	and	< 80
Prehypertension	120-139	or	80-89
Hypertension – Stage 1	140-159	or	90-99
Stage 2	≥ 160	or	≥ 100

JNC 7 classification (May, 2003)

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# Hypertension Management

- <130/80 mm Hg
- Weight loss 10 lbs
- Reduce sodium intake to 2400 mg/day
- Aerobic physical activity
- Limit saturated fat and cholesterol
- Adequate potassium intake
- No smoking



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# C-Reactive Protein (CRP)



- Always elevated with DM
- Marker of inflammation
- Statins and aspirin decrease CRP
- hs-CRP measures from 10-1000 mg/dL, may be another measure of heart disease

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## Diagnosing Celiac Disease

- Small bowel endoscopy with biopsy is still considered the gold standard for diagnosis
- Serologic tests are useful first screening tools, tests must be done while the patient is on a gluten-containing diet
- The anti-gliadin antibody (AGA) serological test is often used but it is not as sensitive and specific as the EMA and tTG antibody tests
- IgA anti-gliadin antibody, IgG anti-gliadin antibody, anti-endomysial (EMA) and tissue transglutaminase (tTG), as well as the Serum IgA to test whether the patient is IgA deficient
- Endoscopy samples may miss active patches of the disease in the specific samples that are drawn. Therefore, multiple samples (8-20 total) are recommended from both the first and second portion of the small intestine
- Presence of Celiacs is 20x higher in Type 1 DM than in the general population

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## Pernicious Anemia

- Pernicious anemia (PA) is an autoimmune disorder that causes neurological changes, including dementia, and a condition of anemia related to vitamin B12 deficiency
- Diagnosed by increased MCV (mean corpuscular volume) of the red blood cell, usually higher than 108 fL
- Vitamin B12 is an essential nutrient derived from dietary animal protein such as meat, poultry, fish, cheese, eggs and fortified cereals
- Vitamin B12 is absorbed in the gastrointestinal track
- Pernicious anemia (PA) is an autoimmune condition of anemia caused by a deficiency of vitamin B12

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## Microalbuminuria

- Urinary excretion of albumin below the detection capability of the urine dipstick, but above the upper limit of normal for healthy individuals
- Earliest clinically recognizable indicator of nephropathy, if detected early, it is reversible
- Can be caused by congestive heart failure, UTI, exercise, pregnancy, fevers, inflammatory disorders
- Annual screening after 5 yrs with type 1, annual screening for type 2 from diagnosis
  - 75% will already have microalbuminuria and 25% will have overt diabetic nephropathy at diagnosis
- If a urine dipstick test results in positive protein, pt has overt diabetic nephropathy
  - the test will only detect >300 mg/day of albumin, however 30-300 mg/day is abnormal
- To assess microalbuminuria, use an albumin to creatinine ratio from a first void urine specimen, or 24 hour urine test

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## Nephropathy



- Microalbuminuria
  - <30 mg/g creatinine = healthy kidney
  - 30-299 mg/g creatinine = microalbuminuria
  - >300 mg/g creatinine = clinical albuminuria, overt diabetic nephropathy
- If a pt has microalbuminuria, there is inflammation in the small vessels, which is an indicator of HD risk factors

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## Microalbuminuria

	Female	Male
Normal (mg/mmol)	<2.8	<2.0
Microalbuminuria	2.8-28	2.0-20
DM nephropathy	>28	>20

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## Kidney Disease

- To determine whether a pt has kidney dz, NKF recommends testing:
  - Blood pressure
  - Urine test for albumin
    - Albumin to creatinine ratio
      - <30 mg/g is normal
      - If this tests indicates concern:
        - 24 hour urine protein sample
  - Estimated GFR
    - Best indicator of kidney function



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## Creatinine Clearance

- GFR (glomerular filtration rate) "The rate at which plasma is filtered through glomeruli"
  - Normal Values:
    - Male 115-125 mL/minute
    - Female 90-100 mL/min
    - Young Adults 120-130 mL/min (decreases with age)
    - GFR below 60 for longer than 3 months is chronic kidney disease per the National Kidney Foundation; 60-89 mL/min indicates early kidney disease
- A 24 hour urine measures creatinine
- Normal 24 hr creatinine excretion values:
  - Male: 20-25 mg/kg creatinine/day
  - Female 15-20 mg/kg creatinine/day
- Serum creatinine
  - substance formed from creatine phosphate
  - primarily stored in muscle, formed at a fairly constant rate
  - production is related directly to muscle mass
  - normal is 0.8-1.2 mg/dL (slightly lower in women)
  - increase reflects renal disease, because creatinine and GFR are inversely related; from 1-2 indicates 50% loss of function, 2-4 indicates 25% of function remains

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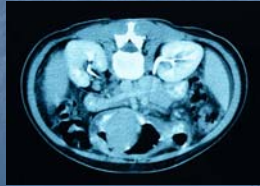
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## Measuring Creatinine Clearance

- $\frac{\text{urine creatinine (mg/dL)} \times \text{urine volume (mL)}}{\text{plasma creatinine (mg/dL)}}$
- divide answer by 1440 (number of min. in day) to get mL/minute)




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## Measuring GFR in a 30 year old person

Creatinine	0.8	2.0	2.3	2.3	0.8	2.0	2.3	2.3
Sex	F	F	F	F	M	M	M	M
Race	W	W	W	AA	W	W	W	AA
GFR mL/min	90	31	26	32	121	42	36	43

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## Cockcroft-Gault Equation

- Can use serum creatinine to estimate creatinine clearance:
- creatinine clearance =  $[(140 - \text{age}) \times \text{wt (kg)}] / (72 \times \text{serum creatinine (mg/dL)})$ ; MULTIPLY by .85 for women
- MDRD (modification of Diet in Renal Disease) equation
- [www.kidney.org/professionals/kdoqi/gfr\\_calculator.cfm](http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm)

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## Using Cockcroft-Gault Calculation on a 30 year old person

Creatinine	0.8	2.0	2.3	0.8	2.0	2.3
Sex	F	F	F	M	M	M
Weight lbs	135	135	135	170	170	170
Ccs/min	98.6	39.4	34.3	146.1	58.4	50.3

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## C-Peptide



- Connecting peptide; when proinsulin is split, it yields alpha and beta chains of active insulin and a third polypeptide chain, the connecting, or C-peptide
- Used as a measure of endogenous insulin production
- Can also be used to help assess if high blood glucose is due to reduced insulin production or to reduced glucose intake by the cells
- Type 1 diabetics produce little or none
- Type 2 can be reduced or normal
- Concentrations of c-peptide in non-diabetics are 0.5-3.0 ng/ml

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## Islet Cell antibodies (ICA's)

- Presence of ICA's indicate an autoimmune process that can lead to beta cell destruction resulting in type 1 DM
- lack of *HLA-DQ* protective genotypes was a feature of patients with slow-progressing type 1 diabetes

■ *HLA-DQ* Genotypes in Classic Type 1 Diabetes and in Latent Autoimmune Diabetes of the Adult. *Am J Epidemiol* 2002; 156:787-796

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## % of Diabetes Patients Achieving ADA Risk Factor Goals

Risk Factor	Goal	% at Goal
HgA1c %	< 7	26.7%
LDL mg/dL	< 100	35.5%
Blood Pressure mm Hg	< 130/85	26.7%
BMI kg/m <sup>2</sup>	< 25	17%

3.2% of patients met the combined ADA goal for BP, LDL, and A1c

*Diabetes Care* 25:718-723, 2002<sup>44</sup>

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## Wisdom from Albert Einstein (a man with diabetes!)

If A = success, then the formula is

$$A = X + Y + Z$$

Where X = work, Y = play, Z = keep your mouth shut



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