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B-type Natriuretic Peptide (BNP): A New Tool in the Diagnosis of Congestive Heart Failure

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Congestive heart failure (CHF) is the most common cause of hospitalization among patients age 65 and older and is the fourth leading cause of hospitalization in the US. Health care expenditures for the diagnosis of CHF exceed $38 billion per year. Coronary artery disease is a major etiology of CHF, and rates of coronary artery disease among Native Americans are rising and now surpass rates among the general US population. As the population ages, rates of CHF also rise, in part due to increased rates of hypertension and diastolic heart failure among the elderly. Rising rates and high costs underscore the importance of accurate diagnosis, prevention, and treatment.

Advances in medical, surgical, and mechanical therapies have improved symptoms and survival for heart failure patients. Our armentarium has expanded to include medications with well-proven capabilities to increase survival, improve left ventricular function, and alleviate symptoms. Angiotensin converting enzyme inhibitors (ACEI) and beta-adrenergic blockers increase survival and improve left ventricular function; spironolactone has also been found to improve survival in those with severe heart failure. Other diuretics and digoxin reduce symptoms and decrease rates of hospitalization. Those intolerant of ACEI benefit from therapy with angiotensin receptor blockers. However, the appropriate treatment hinges on the accurate identification and diagnosis of patients with heart failure.

Unfortunately, the accurate diagnosis of CHF is often difficult. The most common presenting symptoms include dyspnea on exertion, orthopnea, cough, paroxysmal nocturnal dyspnea, and edema. In the absence of edema, the diagnosis may be missed; pulmonary disease, such as interstitial lung disease or pneumonia, may masquerade as CHF, or CHF may be misdiagnosed as lung disease. Although patients with heart failure generally report weight gain from fluid overload, they may, on occasion, have weight loss from anorexia and cachexia.

Compensatory increase in cardiac filling pressures may minimize findings such as rales or fluid build-up on X-ray. Jugular venous pulsation may be difficult to assess in patients with thick necks. Some patients with significant fluid overload may develop hepatic congestion and abdominal edema, which is more difficult to diagnose than is lower extremity edema. Rales may be mistaken for interstitial disease or pneumonia, gallops may be difficult to appreciate, and pulsus alternans may not be present or appreciated. On the other hand, many symptoms are nonspecific and may be from other etiologies — for instance lower extremity edema may be from venous insufficiency or hypoalbuminemia. Two dimensional and Doppler echocardiography, essential in assessing left ventricular (LV) systolic and diastolic function, may not be available at rural IHS sites or may be available only at certain times, thereby limiting its utility in the acute care setting.

A serum assay that could accurately and inexpensively detect and differentiate CHF from other causes of dyspnea would be helpful in identifying patients with heart failure. Such an assay has been developed for B-type natriuretic pep-

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tide (BNP), and this simple blood test is likely to have an important role in the diagnosis of CHF in the near future. This article reviews some of the pathophysiology of CHF and BNP, as well as the data supporting the use of this marker for the diagnosis of heart failure.

What is BNP?

The natriuretic peptides are polypeptide molecules that share a 17 amino acid ring structure in common. A-type natriuretic peptide was described first and its major storage site includes the cardiac atrial and ventricular myocardium. BNP is stored primarily in ventricular myocardium. Unlike ANP, BNP is not contained in intracellular storage granules but is synthesized and released rapidly in response to increases in ventricular volume, pressure, and wall stress. The hemodynamic hallmark of left ventricular failure, whether due to systolic or diastolic dysfunction, is the development of an elevated left ventricular end diastolic pressure (increased pulmonary capillary wedge pressure at pulmonary artery catheterization), which triggers the transcription and release of BNP.

Left ventricular systolic dysfunction leads to activation of numerous compensatory responses, including activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system, as well as release of ANP and BNP. Initially, these compensatory mechanisms work to improve cardiac output and maintain intravascular volume and hemodynamic integrity. Over time, however, activation of the renin-angiotensin-aldosterone system and increased sympathetic tone become detrimental, resulting in fluid retention, vasoconstriction, receptor modulation, cellular apoptosis (cell death), and ventricular remodeling. ANP and BNP are naturally occurring antagonists to volume overload, enhancing natriuresis (salt and fluid loss) through their effects on glomerular filtration and renal perfusion, as well as through direct inhibition of renin and aldosterone secretion. In addition, these natriuretic peptides vasodilate the pulmonary and systemic circulations and improve afterload.

BNP levels rise with age. BNP levels in women without heart failure tend to be minimally higher than age-matched male counterparts. Elevations in right heart pressures or right ventricular dysfunction from pulmonary hypertension, valvular disease, or pulmonary disease cause elevations in BNP. Patients who are volume-overloaded for a variety of reasons, including renal failure, cirrhosis with ascites, primary aldosteronism, or Cushing's syndrome, develop elevated BNP. Interestingly, patients with renal failure have significant drops in levels of BNP once their volume overload is addressed with the initiation of hemodialysis.

Diagnostic Utility of the BNP Assay

An ideal serum marker in CHF would possess a number of key characteristics. It would be present in proportion to the severity of the condition and would have prognostic utility based on the degree of elevation. The marker would be absent or quite low in conditions other than CHF, and would not be elevated in other clinical scenarios that mimic heart failure (pulmonary processes or other causes of volume overload). Ideally, the assay could be performed at a local laboratory or at the bedside and at very low cost. The currently available BNP assay appears to meet many of these needs.

BNP levels correlate well with the severity of CHF as indicated by the patient's NYHA (New York Heart Association) classification of symptoms. While there is some overlap of BNP values between the NYHA classes, in general, BNP levels track the severity of symptoms. In addition, elevated BNP is an independent marker of increased mortality in heart failure populations. Numerous studies document decreases in BNP levels after the institution of heart failure therapy; titration of drug therapy (i.e., ACE inhibitors) guided by decreases in BNP levels may provide greater improvements in hemodynamics and exercise capacity than empiric therapy. Indeed, the use of BNP values in screening those at high risk of heart failure has also been proposed.

In patients referred for echocardiography to evaluate LV function, many of whom were asymptomatic, BNP levels correlated with the degree of dysfunction. Patients with normal LV function had significantly lower BNP levels (29.5 pg/ml) than patients with either pure diastolic dysfunction (391 pg/ml), pure systolic dysfunction (567 pg/ml), or both systolic and diastolic dysfunction (1077 pg/ml).

Perhaps most important for IHS patients and practitioners, BNP has been studied for its utility in differentiating dyspnea due to CHF from other causes in emergency departments and urgent care settings. Maisel and colleagues studied 1586 patients presenting to emergency departments with acute dyspnea and measured BNP levels. 47% of these patients were eventually diagnosed with CHF, 4% had dyspnea due to non-cardiac causes but had a history of LV dysfunction, and 49% did not have CHF. In these groups, the mean levels of BNP were 675 pg/ml in those with CHF, 346 pg/ml in those with LV dysfunction and <110 pg/ml in those without CHF. Although some overlap was present between these groups, BNP level was the single best clinical predictor of a final diagnosis of CHF in this study.

BNP has also been studied in patients with acute coronary syndromes for its prognostic value in patients with unstable angina, and ST elevation and non-ST elevation myocardial infarction (MI). Increasing levels of BNP early after presentation identified a group with increased mortality both at 30 days and at 10-month follow-up. These findings were consistent for both men and women and for those with MI or unstable angina. Using a cutoff value of 80 pg/ml, patients with elevated BNP levels were more likely to suffer death, recurrent MI, or CHF at both 30 days and 10 months.

The FDA approved level of BNP used to distinguish CHF from other causes of dyspnea is 100 pg/ml. This value was

chosen as it provided high specificity for separating all classes of CHF from normals. Very low levels (<80 pg/ml) of BNP have a sensitivity of 98% and a specificity of 92% for excluding the diagnosis of CHF.

Use of the BNP Assay in IHS Facilities and Cost Issues

At this time, the BNP assay is being utilized for diagnosis of CHF at only a small percentage of IHS sites nationally. Others facilities in the southwest have expressed interest due to the increasing burden of cardiovascular disease (CVD), the limited availability of echocardiography locally, and the distance involved for patient travel to cardiology consultation. A limited number of federal facilities outside the IHS also are beginning to utilize the assay.

A single manufacturer (Biosite Diagnostics, San Diego) currently produces the point-of-care, commercially available BNP assay. The costs that follow below are not necessarily the prices which individual IHS facilities would pay, but are provided as a reference for those facilities interested in possibly utilizing the assay. The device for analyzing BNP (Triage Meterplus) has the advantage of performing other commonly performed tests including cardiac serum markers (CK-MB, troponin-I and myoglobin) as well as a 9-test panel for urine drug screening. Thus, its use may obviate the need for other equipment in a given laboratory or enhance that lab's diagnostic abilities beyond the BNP assay. The cost for the analyzer is about $4,750 ($4,250 for a federal facility). Triage BNP tests run $29.00 ($25.40 federal) per test. BNP controls and calibration verifiers represent additional necessary expenses.

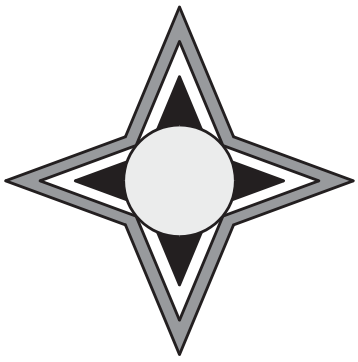
The diagnostic utility of the BNP assay continues to evolve over time and may in the future become a vital tool in the armamentarium of CHF and acute MI diagnosis. In addition, BNP levels will likely become even more important in CVD prognosis and a valuable tool for treatment of heart failure. The ideal facilities for the BNP assay at this time would be those with significantly limited availability of echocardiography and cardiovascular specialist consultation. BNP levels may also prove to be helpful in assessing the adequacy of volume removal among dialysis patients, since it rises in volume overloaded states. In patients with clearly normal BNP levels in the clinical setting of dyspnea, it appears that CHF can be effectively ruled out with a high degree of sensitivity and specificity. The savings engendered by accurately diagnosing CHF and avoiding inappropriate transfers makes the $25-$29 expense for the BNP assay appear to be a cost-effective option.

Summary

1. B-type Natriuretic Peptide (BNP) is a serum marker for congestive heart failure.
2. BNP has demonstrated utility in the differentiation of dyspnea due to congestive heart failure from dyspnea due to other causes (pulmonary disease).
3. BNP may be significantly elevated in other volume overload states such as chronic renal failure, end-stage liver disease with ascites, and pulmonary conditions resulting in right heart failure.
4. A low level of BNP (< 80 pg/ml) rules out CHF with a high degree of sensitivity and specificity. Intermediate values are less helpful and may require cardiovascular consultation with echocardiography for proper evaluation.
5. Depending upon geographic considerations and patient mix, the BNP assay may be a useful and cost-effective addition to IHS laboratories if referrals for distant consultation and echocardiography can be avoided. □

Suggested Reading:

1. Utility of B-natriuretic peptide as a rapid, point of use card test for screening patients undergoing echocardiography to determine left ventricular dysfunction. Maisel AS et al. *American Heart Journal.* 2001;141(3):367-374.
2. Rapid measurement of B-type natriuretic peptide in the diagnosis of heart failure. Maisel AS, et al. *New England Journal of Medicine*. 2002;347(3):161-67.
3. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. De Lemos JA, et al. *New England Journal of Medicine*. 2001;345(14):1014-21.
4. Comparative value of Doppler echocardiography and B-type natriuretic peptide assay in the etiologic diagnosis of acute dyspnea. Logeart D. et al. *Journal of the American College of Cardiology.* 2002;40(10):1794-1800.



Bone Disease in Chronic Kidney Disease

This article is the eighth of a series about chronic kidney disease and its management based on the new National Kidney Foundation guidelines. If you missed previous articles in this series, please log onto the IHS website. Archived issues are found at the Clinical Support Center's web page.

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Metabolic bone disease starts early in chronic kidney disease (CKD), as early as stages 2 and 3 (GFR<60 mL/min/1.73m^2). Several factors are involved. These include phosphorus, calcium, active vitamin D, and parathyroid hormone (PTH). As GFR declines, less phosphorus is excreted and less calcium is absorbed. Phosphate retention may directly interfere with the kidney's ability to activate vitamin D. Decreased active vitamin D impairs intestinal calcium absorption. This relative hypocalcemia results in higher levels of PTH. PTH maintains serum calcium levels by enhancing tubular calcium resorption as well as resorption of calcium from the bones and increases phosphorus excretion by reducing tubular resorption. High levels of PTH also increase skeletal resistance to calcium.

- The serum level of phosphorus is maintained within the normal range until the GFR falls below 20 - 25 mL/min. At that time, severely damaged kidneys can no longer respond to the higher levels of PTH.
- The serum level of calcium is generally maintained despite reduced intestinal absorption, due mainly to increased calcium resorption from the bones and in the tubules.
- The serum level of active vitamin D is generally lower at stage 4 (GFR 15- 29 mL/min).
- Elevated levels of intact PTH may be seen when the GFR falls below 60 mL/min.

This cycle continues even when the patient receives renal replacement therapy (dialysis). Serum levels of phosphorus, calcium, iPTH, and active vitamin D remain important across the CKD spectrum. Active vitamin D supplements are now available and are useful in treating vitamin D deficiency/insufficiency, and help to lower iPTH and potentially control these imbalances. Both oral and injectible supplements are available. Keep in mind, however, that active vitamin D is involved in both calcium and phosphorus absorption. Vitamin D supplements can help lower iPTH but serum phosphorus and serum calcium levels may be elevated due to improved absorption. New guidelines provide a path to follow for monitoring and treating this complicated metabolic disease process.

Phosphorus can be controlled by restricting high phosphorus foods. Refer patients to a registered dietitian for guidance. Most patients will require phosphate binding medication as well. Commonly used calcium-based binders include calcium carbonate and calcium acetate. Avoid use of calcium citrate as citrate increases aluminum absorption. New evidence suggests that the total amount of elemental calcium should not exceed 2000 mg/day. Since damaged kidneys cannot excrete the excess calcium, the potential exists for soft tissue calcification; so limiting total elementary calcium will reduce this risk of soft tissue calcification (see more below about calcium and phosphorus product). A new noncalcium-based phosphorus binder/resin (sevalamer HCl) reduces LDL levels as well as serum phosphorus. The old aluminum-based binders are used as a last resort and only temporarily when serum phosphorus > 7.0 mg/dL for patients on dialysis.

There is limited but rather compelling evidence that the product of serum calcium x serum phosphorus should not exceed 55. When this product is higher than 55, the risk for soft tissue calcification increases — in nonvisceral tissue (periarticular and vascular calcification), visceral organs (skeletal and myocardial muscle), and in the skin (itching due to cutaneous calcification). The itching in particular causes the most immediate discomfort for patients. Use of phosphate binders can help this appreciably over time.

The pending K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in CKD provide a framework for monitoring serum phosphorus, calcium, PTH, and 25-hydroxyvitamin D. **The guideline suggests measuring serum calcium, phosphorus, and intact parathyroid hormone (iPTH) when GFR falls below 60 mL/min.**

Table 1. Recommendations for monitoring calcium, phosphorus, and iPTH

CKD Stage	GFR range (mL/min/1.73 m^2)	Measure Ca and P	Measure iPTH	Target iPTH levels
3	30 - 59	Every 12 mos.	Every 12 mos.	35-70 pg/mL
4	15 - 29	Every 3 mos.	Every 3 mos.	70-110 pg/mL
5	< 15 or dialysis	Every month	Every 3 mos.	150-300 pg/mL

In CKD stages 3 and 4, serum phosphorus should be maintained between 2.7 - 4.6 mg/dL.

- Restrict dietary phosphorus to 800 - 1000 mg/day (adjusted for protein) if serum phosphorus levels are

higher than those listed OR when iPTH levels are higher than target iPTH levels.
- Monitor serum phosphorus every 3 months when dietary phosphorus is restricted.
- If serum phosphorus is not maintained by dietary restriction OR if iPTH is not controlled to target levels, calcium-based phosphate binders should be prescribed.

Corrected total calcium should be maintained within the "normal range" of the lab used. Corrected total calcium in hypoalbuminemic patients can be calculated by using the following formula:

Corrected total calcium (mg/dL) = total calcium (mg/dL) + 0.8 x (4 - serum albumin (g/dL))

- Total elemental calcium (calcium from the diet and calcium-based binders) should not exceed 2000 mg/day.
- **Serum Ca x P should be < 55**; control serum phosphorus first (binders and P restriction).
- If corrected total calcium is below normal laboratory range (< 8.4 mg/dL) AND patient has clinical signs of hypocalcemia (paresthesia, Chvostek's and Trousseau's signs, bronchospasm, laryngospasm, tetanus and/or seizures) OR iPTH is above target range for CKD stage, treat with calcium salts or vitamin D supplements.

Vitamin D Supplements

Measure serum 25-hydroxyvitamin D "25(OH) D" when iPTH is above target range for CKD stage (see Table 1). If serum 25-hydroxyvitamin D is < 30 ng/mL, start supplementing with active vitamin D.

Table 2. Recommendations for Vitamin D supplementation (if low 25(OH)D)

25 (OH)D ng/dL	Vitamin D_2	Duration	Measure corrected total Ca and P
< 5 (Severe D deficiency)	ORAL: 50,000 IU/wk x 12 wks, then monthly INJECTABLE: 50,000 IU as single intramuscular injection	6 months then recheck 25(OH)D Recheck 25(OH)D at 6 months	Every 3 months
5 - 15 (Mild D deficiency)	ORAL: 50,000 IU/wk x 4 wks, then monthly	6 months then recheck 25(OH)D	Every 3 months
16 - 30 (insufficiency)	ORAL: 50,000 IU/month		Every 3 months

- Discontinue vitamin D therapy if corrected calcium exceeds 10.2 mg/dL.
- Add or increase phosphate binder if serum phosphorus exceeds 4.6 mg/dL. If high phosphorus continues, discontinue vitamin D therapy.
- Once vitamin D level acceptable, continue supplementation with multivitamin that has vitamin D and reassess 25(OH)D annually.

If serum 25-hydroxyvitamin D is > 30 ng/mL and iPTH is elevated, an active oral Vitamin D sterol should be started. The starting dose of calcitriol is 0.25mcg/day. Following initiation of calcitriol therapy, calcium and phosphorus should be monitored monthly and iPTH measured every three months. If iPTH falls below target, calcium exceeds 9.5 mg/dl, or phosphorus exceeds 4.6 mg/dl, calcitriol should be held until the levels again fall within the threshold level. Calcitriol should then be restarted at half the previous dose.

Bone metabolism in chronic kidney disease is an intellectual and clinical challenge. Although many providers may wish to avoid dealing with this problem, management of calcium, phosphorus, and parathyroid hormone is essential to maintain the health of our patients with chronic kidney disease.

Password and Encryption for PDAs

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As stated in the previous *Provider* article (Volume 28, Number 3, March 2003), PDAs containing patient-related data are easy targets for theft and, because of their size, are easily lost or misplaced. The Health Information Portability and Accountability Act (HIPAA) regulations require that each provider take reasonable steps to maintain security and privacy of all protected health information (PHI).

This article will provide a description along with website references for several of the password-protected and encrypted programs available in the marketplace.

Most Palm-based PDAs provide an internal operating system with basic password protection for access to the handheld and the records it contains. The newer versions of the Palm PDA also include automatic device locking capabilities, new encryption services, and password "hinting" for unlocking sensitive data. Other creative mechanisms are also being explored, such as using a stylus to draw an object, pushing a specific combination of buttons, picture pin, or quick pin authentication, or using a unique identifying code. The objective of these new features is to make it easier for the user but more difficult for others to breach.

Password protection provides the beginning, elementary steps in protecting data, but it may not be enough. Therefore, layers of protection using encryption may be needed as a tool for greater protection.

To be really secure providers need a program of strong encryption and a password that is a phrase of a minimum of several words. The security of encrypted data depends on two things:

- The amount of data ambiguity in the password
- The amount of data ambiguity lost in the encryption method

Data ambiguity mean "How many possible passwords can there be?" As the length of your password goes up, the data ambiguity goes up.

Encryption generally takes one of four forms:

- Encryption of private records
- Encryption of the entire memo pad
- Organization and encryption of the user's passwords
- Encryption of databases and descriptions

The following provides a list of the various products available in the marketplace.

Password Protection

OnlyMe (www.tranzoa.com) automatically locks the Palm Pilot whenever the device is turned off. No one can read the information on the PDA. However, the PDA owner can easily, through one quick gesture of the stylus or finger, turn the device on in the state in which you left it.

LockMe! periodically locks your handheld at a specified time. It can be set to autolock once a day, hourly, or in between; can hide all private records; and can lock right after the system is reset. LockMe! provides enhanced password protection, but not encryption.

SignOn (www.cic.com) is the first signature solution to capture, verify, and encrypt your own personal signature or a memorable hand-signed word. To unlock the device, the PDA owner simply signs in.

Password And Encryption

PDASecure (www.trustdigital.com) includes both password protection and multiple levels of data encryption for Palm, Microsoft PC, and Windows CE devices. PDASecure can control who can access your data with a wireless device, and with encryption renders the device useless if stolen or compromised.

Encryption

Products such as *Secret Point Sec* or *Point Safe* encrypt only their own proprietary applications (such as the address book), leaving data in other applications on the handheld unsecured. In addition, many encryption products currently available in the marketplace require users to manually encrypt the data or follow a scripted procedure when shutting down the device. The problem with these methods is that the hurried users often forget or neglect to take these extra steps, and the data ends up being stored unencrypted. On the other hand, other products available in the marketplace will automatically decrypt and encrypt as the individual opens and closes a file. An example of the latter (discussed below) is *MovianCrypt.*

MemoSafe (www.deepnettech.com) provides easy to use memo security. All encrypted memo headings are displayed with a lock symbol. A password is needed for each memo session.

TealLock (www.teallock.com) is a secure, automatic, more customized locking program. It includes serial and infrared lockout; data encryption; optional data-destruction; custom locking for screen, text, and images; and graffiti shortcuts. *TealLock* also enables the user to hide private records immediately when the device is turned off or after a specified period of time.

MovianCrypt (www.certicom.com/moviancrypt) integrates a password-based, login system that encrypts all databases as they are stored and decrypts data as they are accessed. In addition, *MovianCrypt* provides an option to disable encryption on a per-application basis, which can be a plus for

the user but a negative for protecting sensitive information. This application conforms to government security standards.

PDADefense (www.pdadefense.com) offers a comprehensive multi-layered level of security. PDA Defense is an application that will delete all data and applications residing on your PDA if unauthorized attempts are made to access your device. Therefore, without the correct password, the user cannot use infrared and/or HotSync ports to transfer data.

SecureDigital is a highly secure memory card system that provides the ability to manually write-protect data.

JawZ Datagator automatically encrypts data when the Palm is shut down or goes to sleep.

PocketLock uses a password to protect individual files or entire folders using a powerful encryption technology.

JotLoc enables the user to draw a "passpic" instead of entering a password. All one needs to do is draw or "jot" a secret gesture in one pen stroke to give you instant access to the PDA.

As a cautionary note, remember that encryption takes a lot of memory, which many PDA devices don't have.

Password Keepers

CrypBox (www.crypbox.com) can be used for protecting your collection of passwords, PIN numbers, logins, or account numbers.

MaxSecret provides a secure place to store private information like credit cards, PIN numbers, passwords, and login Identification numbers. Besides *CrypBox* and *MaxSecret* the following applications also allow you to collect, store, and manage your many logins, often with one master password: *Gatekeeper, PalmPassword, Password Store, MasterKey Store, and 4Tnox. Web Confidential*, another password manager, also lets you encrypt your password files.

Antivirus

Most handhelds have built in safeguards to protect user data on many levels. However, handhelds based on Windows CE can be exposed to viruses that currently attach to the Windows configuration.

Infrared beaming, for the low end PDAs, is less vulnerable to viruses because it requires a close physical proximity. Both parties are aware of the beaming and must tap on the screen to accept all incoming beams. In addition, Palm OS devices have a built-in sleep mode that will not allow the acceptance of an incoming infrared beam. Finally, Palm devices are not susceptible to viruses for Windows platforms.

There are several antivirus programs available for handheld devices.

InoculateIt by Computer Associates *(www.ca.com)* offers virus detection for Palm OS devices.

Palm Scanner by Symantec *(www.symantec.com)* scans Palm files looking for signature viruses, Trojan Horses, and worms.

Virus Scan Wireless by Network Associates *(www.networkassociates.com)* scans files during synchronization.

F-Secure (www.f-secure.com) targets "phage" code (a virus that overwrites executables but does not harm databases). The symptom of a phage is that the screen goes blank when running an application.

PC-cillin provides automatic real-time scanning to prevent viruses that enter the device from any point of entry – synching, beaming, Internet, e-mail, etc. The real-time launching activates immediately when the device is activated.

Backup Protection

Besides listing your contact information in the owner field (as a reference if lost) and synchronizing your PDA, other supplemental backup applications are available. *BackUpBuddy*, *BackUpPro* and *JackBack* are software backup tools for backing up all applications and data on Palm-based devises. Some of these tools require memory sticks or Compact Flash cards, like Clie or Visor.

Regardless, data are data, and even with all these precautions, the PDA can still be stolen or lost. As an added protection, PDAs can be covered under your homeowner's insurance, probably with a high deductible cost, or they can be covered at a lower deductible through *PalmsLostorStolen.com*.

Summary

Providers need to have at least password protection for opening their PDA and, in addition, a time out feature. Also, as a second level, providers need to "hide" or "mask" all patient data. As stated in the previous *Provider* article, HIPAA is not concerned if someone gets access to calendars or eProcrates data, but is concerned with accessible patient data. Hidden patient data provides at least another layer of security, only accessible by another password. Wireless transmissions, especially with the newer and broader transmission devices, are definitely more vulnerable; therefore, providers need to proceed cautiously in this direction.

The Future Of PDA Protection And Security

With the increased use of PDAs and the continued vulnerability to loss or theft, what other measures are being explored by the vendors to further secure private and confidential patient data? Many solutions are being explored such as using *smart cards* (a credit card that includes identifying information and encryption), *biometrics* (includes fingerprints, iris images, or handwriting), *motion detection* (where users program a series of movements of the PDA such as lifting the left corner one inch and then placing it back down again), and *secure digital and multimedia cards (where* the user carries secure credentials in a small removable card the size of a postage stamp).

Companies are struggling to find ways to protect the increasing amount of sensitive information finding its way onto handheld devices. Providers need to have more and more access to clinical data as they tend to their patients; clinics and facilities want to be protected from risk and from fines; and, finally, patients want to be assured that their confidential clinical information is secure. All of these issues are leading the handheld industry to develop more secure devices for storing data.

Finally, if all else fails, there is always PDASaver by Kensington *(www.kensington.com)*. PDASaver uses a galvanized steel cable and a lock to secure the handheld to the desktop. However, if your intent is to be mobile, there is also the Palm neck strap from Force Technology *(www.force.com)*.

The New, Improved Perinatology Corner

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Last year the *IHS Provider* introduced the Perinatology Corner (PNC), and since then, many providers have taken advantage of its great attributes. The PNC modules are online, case based continuing education modules for family physicians, obstetricians and gynecologists, advanced practice nurses, midwives, and nurses who care for pregnant women.

The PNC modules are the result of collaboration between George Gilson, MD, and Neil Murphy, MD. The clinical content is provided primarily by Dr. Gilson, who is a Maternal Fetal Medicine specialist at Alaska Native Medical Center. The web based materials, patient education materials, paper based materials, and clinical content are coordinated by Dr. Murphy, OB/GYN IHS Chief Clinical Consultant.

The new PNC modules also include collaboration with various Indian Health subject matter experts. The Diabetes in Pregnancy module included in this issue was produced with the help of N. Burton Attico, MD, Maternal Health Consultant, Phoenix Indian Medical Center, who has recently retired after more than 40 years of service.

The PNC modules have just been made even better. Four new modules have now been released, and two additional modules are on the way. These modules are great sources of continuing education credit for physicians and nurses, but can also be used as clinical "best practice" resources, with all the web surfing and reference research already done for you and incorporated into the text as links.

You can find the main PNC menu at *http://www.ihs.gov/MedicalPrograms/MCH/M/MCHpericrnr.asp*

The PNC modules are:

- Case based
- Free CEU or CME credit
- ACOG/IHS Reference Text links (a.k.a. Denver Postgraduate Course Text)
- Best Practice material from ACOG, AHRQ, USPSTF, March of Dimes, National Guidelines Clearinghouse, PubMed, American Diabetes Association, and patient education resources
- Linked to online clinical material, as well as IHS proprietary online material for Indian Health, tribal and urban (ITU) users (e.g., Cochrane, UpToDate)
- Linked to paper based reference citations (e.g., Williams, Gabbe)

The NEW modules now have the following improvements:

- Recommendations are graded by strength of evidence
- References are graded by USPSTF system
- Instant references; hyperlinks for references are embedded in the text, and these links utilize PubMed abstracts or full text article when available
- American Indian/Alaska Native-specific references provided
- Expanded clinical content
- Expanded Implications for Practice from Cochrane Library
- Increased CME/CEU credits
- Frequently asked questions
- Improved Posttest

Recent Modules

Diabetes in Pregnancy, Part 1: Screening and diagnosis *http://www.ihs.gov/MedicalPrograms/MCH/M/DP01.asp#top*

Diabetes in Pregnancy, Part 2: Management and postpartum *http://www.ihs.gov/MedicalPrograms/MCH/M/DP21.asp#top*

Group B Streptococcal disease in the perinatal period *http://www.ihs.gov/MedicalPrograms/MCH/M/DP41.asp#top.*

Post term pregnancy and induction of labor *http://www.ihs.gov/MedicalPrograms/MCH/M/DP61.asp#top.*

The Process is Simple

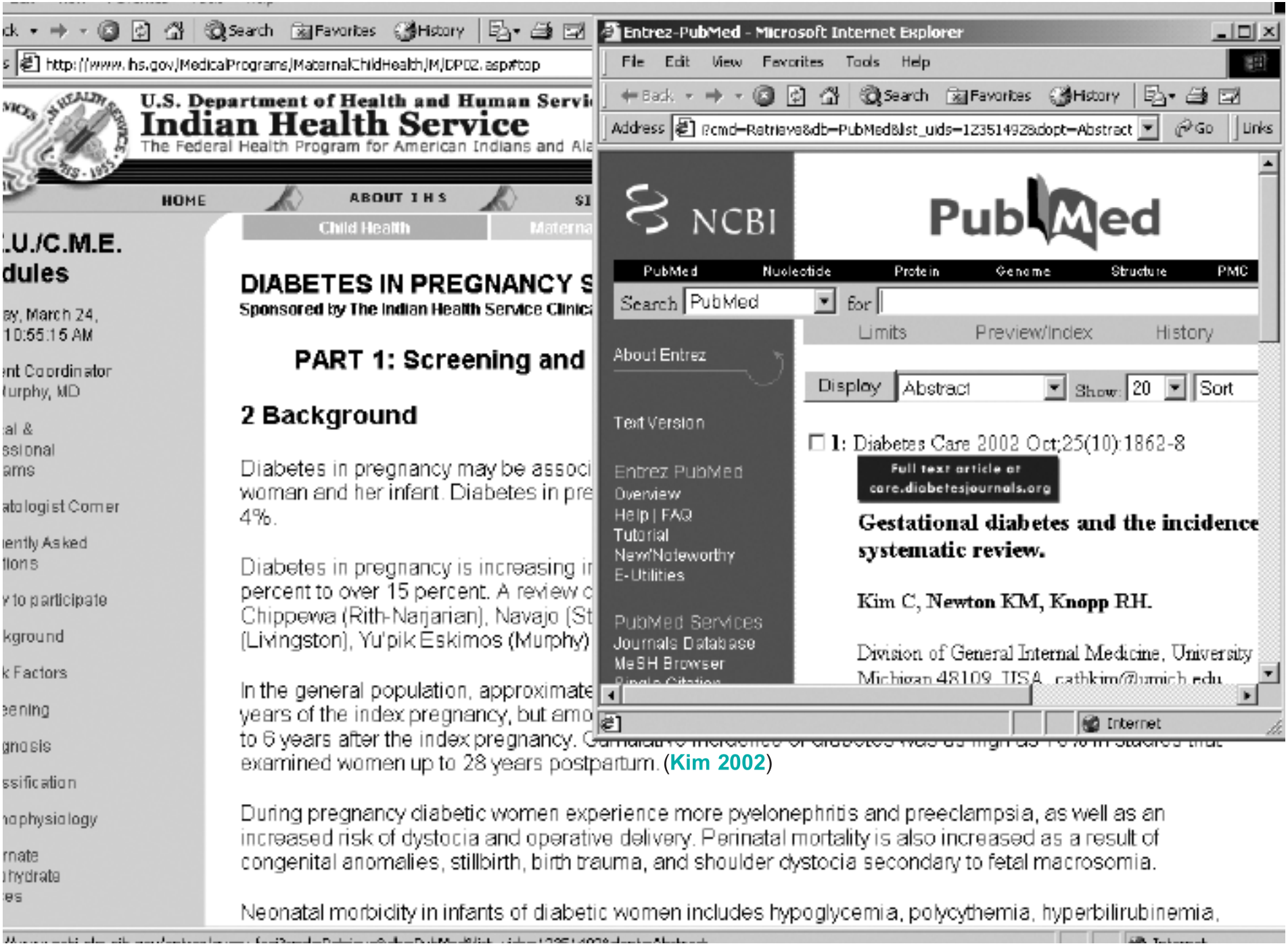
1. Read the materials provided, which include:
   - Objectives
   - Case-based scenarios
   - Background material
   - Links to on-line references
   - Paper-based references
2. Complete the Posttest, developed around case-based scenarios, and the evaluation.
3. Get feedback from Neil Murphy, MD, and George Gilson, MD.
4. Receive physician or nursing credit per module (the IHS Clinical Support Center is the accredited sponsor). Actual credits per module are noted on Perinatologist Corner main page

You can go directly to the Perinatology Corner main page at: *http://www.ihs.gov/MedicalPrograms/MCH/M/MCHpericrnr.asp*

If you prefer to navigate to this site, these CME offerings are available through the IHS website, *http://www.ihs.gov*. The Maternal Child Health webpage can be found on the Medical Programs page: *http://www.ihs.gov/MedicalPrograms/Medical_index.asp.*

You will find a link to the Perinatology Corner on the Maternal Child Health main page at: *http://www.ihs.gov/MedicalPrograms/MCH/MC.asp*, which has many other great resources.

Category 1 CME credit is awarded by the IHS Clinical Support Center after completion of each case-based clinical module. The process can be completed on-line, or the questions can be downloaded and faxed to Neil Murphy, MD at (907) 729-3172. The answer sheet can also be mailed to Neil Murphy, MD at 4320 Diplomacy Drive, PCC-WH, Anchorage, AK 99508. If you have any questions, feel free to contact Dr. Murphy at (907) 729-3154 (voice-mail available); or e-mail him at *nmurphy@anmc.org* or Dr. Gilson at *gjgilson@anmc.org*. □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1: Diabetes Care 2002 Oct;25(10):1862-8
Full text article at care.diabetesjournals.org
Gestational diabetes and the incidence
systematic review.
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PART 1: Screening and
2 Background
Diabetes in pregnancy may be associ
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examined women up to 28 years postpartum. (Kim 2002)
During pregnancy diabetic women experience more pyelonephritis and preeclampsia, as well as an increased risk of dystocia and operative delivery. Perinatal mortality is also increased as a result of congenital anomalies, stillbirth, birth trauma, and shoulder dystocia secondary to fetal macrosomia.
Neonatal morbidity in infants of diabetic women includes hypoglycemia, polycythemia, hyperbilirubinemia,

Diabetes In Pregnancy, Part 1: Screening And Diagnosis

Editor's Note: This is the first of a two-part series on Diabetes in Pregnancy. This module will concentrate on Screening and Diagnosis; it is also available online at: http://www.ihs.gov/MedicalPrograms/MCH/M/DP01.asp#top. The posttest at the end of this module can be found at: http://www.ihs.gov/MedicalPrograms/MCH/M/DP14.cfm#top. The upcoming module, which will appear in a subsequent issue of The IHS Provider*, will concentrate on Management and Postpartum care. Please note the online version has hundreds of hyperlinks to references, abstracts, and full text articles that are not included in this hard copy for space considerations. The links that were not removed in this paper version are shown as references in parentheses, but would be "clickable" hot links in the online article that would bring you to the source material. For example, the screen capture on page 87 illustrates how, by clicking on the hot link for "Kim 2002," the participant is taken to the source material for this citation.*

George J. Gilson, MD, Maternal Fetal Medicine, Alaska Native Medical Center, Anchorage, Alaska; Neil J. Murphy, MD, OB/GYN Chief Clinical Consultant, IHS, Southcentral Foundation, Women's Health Service, Alaska Native Medical Center, Anchorage, Alaska; and Burton Attico, MD, former Maternal Child Health Coordinator, Phoenix Indian Medical Center, Phoenix, Arizona

How to Participate

This module has been produced in accordance with ACCME standards and is intended for the use of physicians, midwives, advance practice nurses, and nurses. It has been field tested and found to take approximately two hours to complete. For more details about how to participate in this CEU/CME program, see the Perinatologist Corner page, described elsewhere in this issue. Also please see the information about Goals, Sponsorship and Credit, and Disclosure, below.

Goal

The student will understand the maternal and fetal consequences of, methods and limitations of screening for, and diagnosis and management of diabetes in pregnancy.

Objectives

The objectives for this module are as follows: The participant will understand

- the maternal and fetal consequences of diabetes in pregnancy.
- the methods and limitations of screening for diabetes in pregnancy.
- the management of diabetes in pregnancy.

Case Scenario

SK is a 38-year old G8P7006 who presents for prenatal care at 24 weeks gestation by her dates. Her obstetric history is significant for three prior infants who weighed over 9 pounds. Her last pregnancy resulted in the vaginal delivery of a 10 pound 8 ounce stillborn. The patient relates that, after a difficult labor, the baby's head came out, but the rest of the baby's body couldn't come out.

Background

Diabetes in pregnancy may be associated with significant morbidity and mortality for both the pregnant woman and her infant. In the general population diabetes in pregnancy has a prevalence of about 4%. The condition is increasing in AI/AN populations; rates range from 3.5 percent to over 15 percent. A review of the literature using PubMed reveals 28 articles on Alaska Coastal Indians (Murphy), Chippewa (Rith-Narjarian), Navajo (Straus, Steinhart, Sugarman), Pima (Pettitt), Tohono O'odham (Livingston), Yu'pik Eskimos (Murphy), and Zuni (Benjamin). In the general population, approximately 40% of women will go on to develop overt type 2 diabetes within 15 years of the index pregnancy, but among AI/AN women, over half will develop overt diabetes in as little as 4 to 6 years after the index pregnancy. The cumulative incidence of diabetes has been shown to be as high as 70% in studies that examined women up to 28 years postpartum (see Kim 2002).

During pregnancy, diabetic women experience more pyelonephritis and preeclampsia, as well as an increased risk of dystocia and operative delivery. Perinatal mortality is also increased as a result of congenital anomalies, stillbirth, birth trauma, and shoulder dystocia secondary to fetal macrosomia.

Neonatal morbidity in infants of diabetic women includes hypoglycemia, polycythemia, hyperbilirubinemia, hypocalcemia, hypertrophic cardiomyopathy, and respiratory distress. Maternal hyperglycemia is also linked to long-term obesity and diabetes in their offspring. For more information on this and other issues in this module, please also see the Diabetes in Pregnancy Guidelines.

Risk Factors

The woman in our case study has several risk factors for developing diabetes during pregnancy. She has a history of:

- macrosomic infants over 4000g (8 lbs. 14 oz.)
- prior term intrauterine fetal demise

- AI/AI ethnicity
- age over 35 years

Other risk factors, still unknown in this case, include:
- family history of first degree relatives with diabetes
- gestational diabetes in a previous pregnancy
- overweight
- prepregnancy weight ≥110 % of ideal body weight
- prepregnancy BMI ≥ 27
- prior infant with a birth defect or congenital anomaly
- habitual abortion (≥ 3 consecutive SAB)
- ethnic background: African American, Asian, Hispanic, Pacific Islander
- unexplained polyhydramnios in the current pregnancy
- persistent glycosuria in the current pregnancy

Screening for gestational diabetes (GDM) may be carried out on the basis of risk factors, but that strategy will still miss approximately half of women with GDM. Whether or not that is significant will be discussed later. However, in the AI/AN population, which has such a high prevalence of the disorder, universal screening is appropriate. Likewise, many patients in our population may have undiagnosed preexisting Type 2 diabetes, and these patients are definitely at higher risk from a perinatal standpoint.

Screening

Case Continued . . .. Mrs. K's initial exam reveals a weight of 187 pounds (85 kg) and a height of 60 inches (152 cm). She is normotensive and there is no evidence of retinopathy. Her fundal height is 26 cm and fetal heart tones are normal. Her routine prenatal lab work is unremarkable. Her serum creatinine is 0.7 mg/dL and she has no proteinuria. A 1-hour post-50 g glucose screen test (GST) returns with a plasma glucose of 186 mg/dL.

Screening should be differentiated from *diagnostic testing*. *Screening* tests are examinations that are relatively simple or easy to administer, and should have few false negatives. Diagnosis of the condition is not made solely from a *screening test*. A *screening test* defines which patients need additional definitive *diagnostic testing*. A *diagnostic test* is a definitive examination from which an actual diagnosis can be made.

For purposes of this module we will use the term glucose screen test (GST) for the screening test, and oral glucose tolerance test (OGTT) for the diagnostic test. Patients with known pregestational diabetes do not need glucose challenge testing during pregnancy. A management plan can be made for them directly. High-risk patients such as our case patient should be screened at their initial visit. Most patients who have abnormal glucose tolerance testing in the early trimester are probably undiagnosed pregestational diabetics.

If early pregnancy screening is negative in high-risk patients, the GST should be repeated at 24-28 weeks. This timeframe has been chosen because it is thought to represent the time when the diabetogenic hormonal alterations of pregnancy are maximally operative, but still provides sufficient opportunity to implement interventions that may be beneficial as regards fetal growth.

Some have also suggested rescreening those with risk factors at 32 weeks with a GST, thereby increasing the yield of the diagnosis of GDM. Screening with a GST may be repeated at 32 weeks, especially if there was one abnormal value on 3-hour 100g OGTT on prior diagnostic testing during this pregnancy (see Neiger et al).

Screening is accomplished with an unprepped (fasting not necessary) 50g glucose screening test (GST), followed by a venous (not finger-stick) glucose 1 hour later. Values ≥140 mg/dL are considered positive. Sensitivity of the GST is increased if a value of 130 mg/dL is used as the threshold, but of course more false positives result, and opinions remain divided as to the utility of the lower cut-off.

What About Screening Glucose Levels of > 185 mg/dL or > 200 mg/dL?

Landy et al suggested that a 3-hour 100 g oral glucose tolerance test (OGTT) was not necessary if the 1-hour 50-g glucose screening test (GST) was over 185 mg/dL. Upon further review, and considering the work of Atilano et al and Shivvers et al, it appears that a 50 g GST result ≥200 mg/dL is not diagnostic of gestational diabetes. Nearly one of five such women had a normal 3-hour OGTT. Overdiagnosis of gestational diabetes may lead to unnecessary pregnancy surveillance and intervention in that pregnancy and thereafter.

Naylor et al found that the diagnosis of GDM alone is associated with an inexplicable elevated risk of cesarean delivery with no improvement in outcome. In addition, there will be a series of unnecessary blood tests and subsequent major interventions — both short term and long term. It is better to actually perform a 3-hr OGTT, rather than misdiagnosing of 1-2 out of 5 patients.

Some providers were concerned that they might iatrogenically push these women over into diabetic ketoacidosis (DKA) with a 100-gm load test. This possibility was not verified in a PubMed literature search. That is not surprising, considering that an OGTT represents only part of one of the many soft drinks that many patients drink several times a day. DKA is a rare event, confined primarily to women known to have Type 2 DM. The only DKA found in GDM patients was in those GDM patients given bursts of steroids or ritodrine, who developed DKA while on tocolysis, not during diagnostic testing.

A viable alternative in Native Americans, in accordance with a 1993 ACOG subcommittee recommendation, is to perform one-step diagnostic testing. In tribes with a high prevalence of diabetes, one can use a 3-hour 100 g OGTT as a one step screening/diagnostic method. Pettitt et al (1994) in a small study in the Pima successfully used a one-step 2-hour 75 g OGTT using WHO criteria.

Should We Screen for GDM At All?

Having said all that, the Society of Obstetricians and Gynaecologists of Canada (SOGC) reports that some have made valid arguments not to screen for GDM until a definitive randomized trial shows that screening actually improves patient outcomes. The SOGC Clinical Practice Guidelines, No. 121, November 2002 (Berger et al) provide an excellent discussion of what evidence is available, or for the most part lacking, to correlate milder degrees of glucose intolerance and patient outcomes. This confirmed the previous Canadian SOGC analysis that suggested that guidelines for screening are currently based on consensus, rather than good evidence (Meltzer et al).

The USPSTF found no well-conducted, randomized, controlled trial that provides direct evidence for the health benefits of screening for GDM. The evidence is unclear regarding the optimal screening and reference diagnostic test for GDM. The impact of hyperglycemia on adverse maternal and neonatal health outcomes is probably continuous. Although insulin therapy decreases the incidence of fetal macrosomia for those women with more severe degrees of hyperglycemia, the magnitude of any effect on maternal and neonatal health outcomes is not clear. The evidence is insufficient to determine the magnitude of health benefit for any treatment among the large number of women with GDM at milder degrees of hyperglycemia. The USPSTF found limited evidence regarding the potential adverse effects of screening for GDM (USPSTF 2003).

The USPSTF was unable to determine the extent to which screening has an important impact on maternal and neonatal health outcomes because of the lack of high-quality evidence concerning critical issues. A randomized, controlled trial of screening is necessary to answer the many remaining questions (USPSTF 2003). There is one such trial underway, the Hyperglycemia and Adverse Outcomes (HAPO) study. This large (n = 25,000), prospective study on GDM worldwide will examine outcomes in relation to a 75 gram OGTT and will be ready in 2003. Funded by the US National Institutes of Health, the HAPO study will involve 16 centers, three continents, and 25,000 unselected pregnant patients who will undergo a 75 gram OGTT at 28 weeks gestation. Only women who fulfill the WHO criteria for diabetes will be treated, so all lesser degrees of hyperglycemia can be correlated with short-term variables of pregnancy outcome. Follow-up studies will allow the examination of medium term and long term effects of maternal hyperglycemia on the future health of the mother and her child. Only after this study will the threshold of maternal blood glucose concentration that carries no added risk to pregnancy be known.

Until the HAPO study is reported no significant attempt should be made to rewrite existing screening methods (Dornhorst et al). At this time American Indian and Alaska Native women should be considered to be at high risk for GDM and should be screened as outlined in the Diabetes in Pregnancy Guidelines.

Diagnosis

In the two-step method, if a patient has a positive GST, the next step is to order the diagnostic test, which is the 100 g 3-hour OGTT. This must be administered in the fasting state, and venous blood should be used. Patients should eat their regular diet for several days prior to testing, as trying to restrict carbohydrates may result in a false positive test due to insulin down-regulation.

The National Diabetes Data Group (NDDG) have the largest data to recommend their use (See Figure 1).

Figure 1. NDDG diagnostic values for 100 g OGTT

NDDG 100 gram cut-offs data are:

Fasting	< 105 Plasma glucose level (mg/dL)
1-hour	< 190 Plasma glucose level (mg/dL)
2-hour	< 165 Plasma glucose level (mg/dL)
3-hour	< 145 Plasma glucose level (mg/dL)

The diagnosis of GDM is made if the patient has met or exceeded two values. Patients with only one abnormal value, especially the two-hour plasma glucose level, have also been shown to have an excess of perinatal morbidity, especially macrosomia, and these patients have been designated as having "carbohydrate intolerance of pregnancy," and may benefit from intervention, e.g., medical nutrition therapy (Tallarigo et al). Kim et al found that one elevated glucose tolerance test value after one hour using NDDG criteria increased adverse maternal and perinatal outcomes. Screening with a GST may be repeated at 32 weeks, especially if there was one abnormal value on any previous OGTT during this pregnancy (Neiger et al). Multiple sets of diagnostic criteria exist and are discussed in the online version of this module. The newer, lower, criteria of Carpenter and Coustan have been suggested by the ADA, but no data from clinical trials have determined which are superior, and cost-effectiveness studies favor the NDDG criteria.

If all this seems cumbersome to you, you're not alone. The World Health Organization (WHO) tried to unite criteria both in pregnancy and outside of pregnancy. The WHO uses a 2-hour OGTT with a 75 g glucose load, followed by a fasting and 2-hour glucose. A 2-hour glucose > 140 mg/dL meets the criteria for Impaired Glucose Tolerance, but it is treated the same as GDM. The one-step test would seem to simplify things considerably, but has not yet been adopted widely in the US yet (Pettitt et al 1994). Other diagnostic criteria are discussed in the online version of this module.

Classification

Case Continued . . .. Mrs. K's 3-hour glucose tolerance test showed:

FBS108	mg/dL
1 hour	198 mg/dL
2 hour	229 mg/dL
3 hour	129 mg/dL

How is diabetes in pregnancy classified? The largest cat-

egory of diabetes in pregnancy is gestational diabetes mellitus (GDM). Such women cannot be demonstrated to be diabetic when they are not pregnant and their glucose intolerance is usually rapidly reversed postpartum. Most such women are able to achieve good glucose control with medical nutrition therapy alone and are referred to as "class A-1."

If women with GDM are not able to establish euglycemia with diet, they are designated as "class A-2" and require pharmacotherapy. GDM may be considered to represent a patient "failing the metabolic stress test of pregnancy," the pathophysiology of which will be discussed below.

Women with pregestational diabetes usually have Type 2 diabetes, and, as noted above, not all may have been diagnosed prior to their being seen for the current pregnancy. They are sometimes referred to as being "class B" diabetics.

Juvenile-onset, Type 1 diabetes, is distinctly uncommon among our patients, and not a lot of time will be devoted to discussing it here. It is a much more challenging disorder to control during pregnancy, and both maternal and neonatal morbidity and mortality are significantly higher. Depending on the length of time these women have had their disease, and what target organ damage they might manifest, they may also be assigned a White Classification "C, D, F, R, etc." See White Classification link, *http://www.ihs.gov/MedicalPrograms/MCH/M/WC01.asp.*

There is another entity currently being recognized more frequently, called "maturity-onset diabetes of youth" (MODY), an autosomal dominant disorder relatively common in Native Americans and Hispanics, usually diagnosed in late childhood or early adolescence, which has a clinical course typical of Type 2, not Type 1, diabetes. Most of these young women will have a strong family history and most, but not all, will probably have been diagnosed prior to pregnancy.

Pathophysiology

By any criteria, it would appear that Mrs. K has GDM. Might she be a pregestational diabetic? Her having an elevated fasting blood sugar makes this more likely, as does her clinical picture, and, if we had obtained these values in the first trimester, we probably could have diagnosed her as such. Now, however, we will have to see how she responds to medical nutrition therapy, and, to definitively confirm the diagnosis, will need to test her postpartum; more on that later. At present her working diagnosis is, "GDM, class A-1," gestational diabetes, hopefully amenable to diet control.

What are the physiologic mechanisms that occur during pregnancy that allow women with a diabetic diathesis to manifest themselves? Thinking of the changes as fostering "survival of the species" is helpful in understanding what we consider a "disorder." The high quantities of estriol, progesterone, cortisol, and human placental lactogen (also known as chorionic somatomammotropin) produced by the placenta in late pregnancy result in a state of "facilitated anabolism."

That is to say, when feeding occurs, glucose excursions rise to values considerably above those seen in non-pregnant individuals. Glucose crosses the placenta by facilitated diffusion once its threshold is met. A large amount of substrate (glucose) is therefore enabled to siphon across to the fetus so it will have a "surfeit of substrate" to be used for growth. This mechanism is so efficient that subsequently, relative hypoglycemia will ensue in the mother if she does not eat well.

Thus, according to the hypothesis, "accelerated starvation" actually occurs during fasting. In order to keep glucose levels high so that this substrate can be utilized for fetal aims, the hormonal milieu of late pregnancy produces a state of relative insulin resistance in the maternal tissues. This is thought to be a post-receptor "defect," which has implications for therapy. We'll discuss this again later, as well.

Insulin levels are actually significantly higher postprandially in pregnant women compared to non-pregnant subjects. In keeping with the "accelerated starvation" hypothesis, the hyperinsulinemia and insulin resistance results in lipolyis, which produces free fatty acids and ketones for fetal consumption, and enhances hepatic gluconeogenesis.

These mechanisms allow fetal survival from whatever maternal intake is available, even at her nutritional expense. When a genetic diabetic diathesis exists in the mother, however, all these mechanisms are exaggerated, and the fetus itself may experience hyperglycemia. In response, this will then result in fetal hyperinsulinemia. Since insulin is a growth factor, the fetus will develop increased muscle mass, increased adipose deposition, increased hepatic glycogen storage, and, so the theory goes, macrosomia.

The increased osmotic load presented to the fetal kidney by the high glucose will result in fetal polyuria, and possibly, the development of polyhydramnios.

Alternate Carbohydrate Sources

Alternate screening strategies, like using Jelly Beans or a standard 600 kcal meal as the "carbo load" are well tolerated, but significantly less sensitive. On the other hand, Polycose, a polymer of d-glucose, is both better tolerated and more effective.

Boyd et al used 18 Jelly Beans consumed within two minutes. That was approximately 2 ounces of Brach and Brock Jelly Beans, at 150 per pound. Lamar et al used 28 Jelly Beans (Brach No. 110 Jelly Beans). As with the use of other complex carbohydrates in solid form, Jelly Beans have a different uptake than liquid sources of simple carbohydrates.

Coustan et al (1987) evaluated plasma glucose level determined one hour after the ingestion of a standard 600 kcal mixed nutrient breakfast (breakfast tolerance test). The mean +2 SD for the breakfast tolerance test was 120 mg/dl. If this were used as the threshold for a screening test, 75% of cases of gestational diabetes would be identified (sensitivity), while 94% of normal pregnant women would be excluded (specificity).

Murphy et al (1994) found that Polycose, a polymer of d-glucose, mixed with club soda and unsweetened Kool-aid was well tolerated, and was similar to glucose in sensitivity and specificity. Polycose was an inexpensive alternative for GDM

screening. Additional tips on recipes for Alternative Options for Screening are found in the online version.

Venous Versus Capillary and Plasma Versus Whole Blood Samples

The following section is only meant for those of you who used to go for 'extra credit' in high school.

Have you ever been confused about the differences in glucose results between venous, whole blood, plasma, and serum, or between venous and capillary (fingerstick) samples?

Whole blood versus plasma or serum

The glucose concentration measure in plasma or serum of a given specimen is approximately 14-15% higher than the concentration in the same sample before separation of the cells (whole blood).

This may be more than you want to know, but . . . the reason for this discrepancy is that 35-45% of the volume of whole blood (depending on the hematocrit) is composed of red blood cells. Approximately 35% of the red blood cell is hemoglobin, and glucose is not distributed in this part of the cell. Therefore, for example, glucose is excluded from about 15% of a blood sample with a hematocrit of 43% (0.35 x 43 = approximately 15%). In other words, only 85% of the volume of blood used for the assay contains glucose, but the results are expressed for the entire volume. Thus, values obtained with whole blood are approximately 15% lower than with plasma or serum, in which glucose is distributed throughout the entire volume.

One further wrinkle is that the original GDM studies by Dr. O'Sullivan utilized the Somogyi-Nelson whole blood technique. An enzymatic process analyzes most glucose samples now. These enzymatically-derived values have been shown to be about 5mg/dL lower than the Somogyi-Nelson values because the enzymatically derived values exclude reducing sugars.

Sample site (Fingerstick or Venous)

Arterial glucose levels are higher than venous concentrations because the peripheral tissues have not yet had the opportunity to extract the glucose. Capillary blood contains a mixture of arterial and venous blood and is often obtained for sampling from the pads of the fingers. If these areas are warmed or stimulated in order to increase blood flow, the arterial contribution to the sample is enhanced (Davidson).

In the fasting state, peripheral tissues (with the exception of red blood cells in the brain) do not use glucose to a large extent; hence there is little difference between capillary and venous samples.

After a glucose challenge, depending on the amount of glucose administered and the timing of the sample, there are appreciable differences between capillary and venous samples. As would be expected, the more glucose given and the earlier the interval at which the sample is obtained, the greater the difference. For example, one hour after the ingestion of 100g of glucose, capillary values are 30-40mg/100ml higher than venous levels. On average, arterial glucose is 7% greater than venous glucose.

Reflectance and Electrochemical Photometers

As technology has advanced, the manufacturers have taken all the above into consideration. For example, Accu-Chek(tm) is calibrated to deliver plasma-like results. Murphy et al (1994) found a reflectance photometer to be both accurate and precise in a single operator situation. On the other hand, one must consider both the accuracy and the precision of reflectance photometers among individuals with a wide variety of skill levels.

At this time reflectance photometers are helpful in monitoring the clinical care of a GDM patient, but they are not felt to display enough accuracy and precision in a wide variety of settings to be recommended for diagnosis or screening for GDM. Most of the present home meters are electrochemical, rather than reflectance type.

The Bottom Line

If you are using a reflectance photometer with fingerstick samples to monitor your GDM patient, then check with the manufacturer's specifications to see to what kind of sample the device is calibrated to produce (e.g., Accu-Chek is calibrated to deliver plasma-like results).

IHS and Other Online Resources

If you are a member of the IHS or tribal wide-area network (WAN), the resources described in this section of the online version of this module are available to you. If you are not a member, some of these resources may not be available, but many additional resources are listed that are available to everyone.

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Posttest

Case 1: Ms. MW. MW is a 36 y/o G4P3 who presents for prenatal care at 13 weeks gestation. All of her previous infants have weighed over 9 pounds. She was diagnosed with GDM during her last pregnancy and did not require insulin. You

obtain a 50 g glucose screen test (GST) at her first visit and the value is 206 mg/dL.

Question 1. Please choose the best single answer for Case 1

a) Ms. MW's diagnosis at this time is gestational diabetes mellitus, class A-1.
b) Ms. MW's diagnosis at this time is gestational diabetes mellitus, class A-2 .
c) Ms. MW's diagnosis at this time is pre-gestational diabetes mellitus (class B).
d) Ms. MW's diagnosis at this time is carbohydrate intolerance of pregnancy.
e) Ms. MW's diagnosis at this time is unknown, pending her 3-hour GTT.

Case 2: Ms. EJ. EJ is an 18 y/o G2P1 at 26 weeks gestation. Her first baby weighed 9 pounds 4 ounces. Her screening 1-hour GST value was 154 mg/dL. Her 3-hour GTT gives the following results (in mg/dL): fasting: 94, 1-hour: 169, 2-hour: 191, 3-hour: 123.

Question 2: Please choose the best single answer for Case 2

a) Ms. J has a 3-hour GTT with one value outside the normal range by the NDDG criteria (2-hour >165 mg/dL). Her perinatal risks may include neonatal hypoglycemia.
b) Ms. J has a 3-hour GTT with one value outside the normal range by the NDDG criteria (2-hour >165 mg/dL). Her perinatal risks may include fetal macrosomia.
c) Ms. J has a 3-hour GTT with one value outside the normal range by the NDDG criteria (2-hour >165 mg/dL). Her perinatal risks may include maturity onset diabetes of youth.
d) Ms. J has a 3-hour GTT with one value outside the normal range by the NDDG criteria (2-hour >165 mg/dL). No additional risks are anticipated.

Case 3: Ms. ES. ES is a 28 y/o G3P2 who has been diagnosed with GDM at 26 weeks gestation. She was begun on a diet but it has been hard for her to keep her postprandial sugars in range. At 32 weeks an ultrasound reports that the estimated weight of her fetus (EFW) is > 90th percentile and that the fetal abdominal circumference (AC) is also > 90th percentile. Her AFI is 22.6. No fetal anatomic abnormalities are detected.

Question 3: Please choose the best single answer for Case 3
In women with GDM, excessive fetal growth is thought to be the result of:

a) fetal hyperinsulinemia
b) fetal hyperaminoacidemia
c) fetal hypoglycemia
d) placental glucose hyperutilization

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