University of New Mexico Health Sciences Center

PRIME Net CME on Acanthosis Nigricans

Part I of this tutorial is a review of Acanthosis Nigricans with photo demonstrations. Part II provides information on obesity and diabetes and is included merely for your interest. Although only Part I is required for study participation, clinicians who complete both Parts I and II will receive one hour of Continuing Medical Education credit.

Image Gallery (please click on the 7 photos available to view examples of AN):







Part I

What is Acanthosis Nigricans?

Acanthosis Nigricans (AN) literally means thick, coarse, and dark. It is a brown, velvety, sometimes verrucous (wart-like) discoloration of the skin affecting the collar area of the neck, the axillae, the inner surface of the thighs, the elbows and knuckles, and the skin folds of the abdomen. In fair-skinned individuals, the pigment changes are not always prominent. The back of the neck is the most commonly and most severely affected area. Of those with AN, 93%-99% have it on the back of the neck.

What is the importance of AN?

Once thought to be rare, AN is now known to be common, particularly among minority populations. Among middle school students in New Mexico, the prevalence of AN is about 40% in Native Americans and 20% in Hispanics. A high prevalence of AN has also been observed in African-American adolescents (30-40%) and adults (50%), and in Asian adolescents (25%). AN is more prevalent in obese persons (50-75%), and in women with polycystic ovary syndrome. AN is independently associated with hyperinsulinemia and insulin resistance. AN appears to be an important risk factor for type 2 diabetes.

What is the association between AN and hyperinsulinemia?

Insulin stimulates the receptor for Insulin-like growth factor-1 (IGF-1) on the surface of epithelial cells. Hyperinsulinemia leads to increased cell division in characteristic skin areas in predisposed persons. The effects of this process are most notable in groups with high concentrations of epithelial IGF-1 such as African Americans, Hispanics, Asians, and Native Americans. In one study, the positive predictive value for hyperinsulinemia was 39.4% for AN alone, compared with 34.1% for obesity alone. When AN and obesity were used in combination, the positive predictive value of the screening increased to 47.2%.

What is the association between AN and type 2 diabetes?

In some populations, a high percentage of persons known to have diabetes (60-75%) also have AN. In one study, obese women with AN were 3-4 times as likely to have type 2 diabetes and 1.5 times as likely to have a pre-diabetic level of impaired glucose tolerance. Although AN is a marker for hyperinsulinemia, it has not yet been prospectively proven to predict the subsequent development of diabetes. Likely reasons are 1) most studies have focused on children and adolescents, who have a low prevalence of type 2 diabetes, and 2) studies have not yet followed subjects longitudinally for the development of diabetes. Nonetheless, many researchers find the indirect evidence linking AN and diabetes compelling. AN is independently associated with hyperinsulinemia, which is a condition known to predict the development of type 2 diabetes. Moreover, certain populations with a high prevalence of diabetes also have a high prevalence of AN.

Should AN be used to screen for those at risk for type 2 diabetes?

Because of its high prevalence of AN, Texas implemented the first statewide school-based screening program for AN in 1999. Mukhtar and colleagues reported a high prevalence of Acanthosis Nigricans and an association with hyperinsulinemia in New Mexico adolescents (see Further Reading for details). Despite this, the CDC has advised against school-based screening of adolescents for AN, Reasons cited included 1) the desire to avoid stigmatization of children with AN, and 2) interventions to treat those with AN do not differ from recommendations for the general population , i.e. increased physical activity and, for those who are obese, weight loss. Office-based screening was not addressed, and no other published guidelines exist regarding AN.

Some experts advocate office-based screening, believing that a visible marker for a preventable disorder will not be stigmatizing when identified in the privacy of a clinician's office. Such identification may well motivate needed life-style changes. The predictive power of AN for hyperinsulinemia is quite strong. In the New Mexico adolescent study, subjects with AN were four times more likely to have hyperinsulinemia than those without AN. Parental history of diabetes, in contrast, did not predict hyperinsulinemia.

Finally, there is growing evidence that hyperinsulinemia may be independently associated with other cardiac risk factors such as hypertension and dyslipidemias, thereby increasing the utility of identifying AN.

How difficult is AN to diagnose?

AN is a unique skin condition not usually confused with other lesions. Nevertheless, contact dermatitis, tinea corporus, or drug eruptions may occasionally look similar to AN.

What testing should be done for patients with Acanthosis Nigricans (AN)?

There are no official guidelines to recommend particular tests for patients found to have AN. Fasting plasma glucose (FPG) is not an effective screen for hyperinsulinemia or glucose intolerance. FPG usually remains below 100 mg/dL for years after an individual has developed postprandial glucose intolerance and compensatory hyperinsulinemia. A fasting insulin level is the best test for detecting fasting hyperinsulinemia, but it may remain normal in the presence of significant glucose intolerance.

The two-hour oral glucose (75 g) tolerance test (OGTT) is the best test for early detection of postprandial hyperglycemia. Abnormal OGTT results include isolated one-hour hyperglycemia (>140 mg/dL) with normal two-hour glucose, pre-diabetes (two-hour glucose 140-199 mg/dL), and diabetes (two-hour glucose of 200 mg/dL or higher). Glycosylated hemoglobin A1c is not a sensitive test for detecting early glucose intolerance or pre-diabetes; it is often in the borderline range of 5.7-6.4 in patients with these conditions, as well as in patients with early mild type 2 diabetes.

What treatment is indicated for patients with Acanthosis Nigricans (AN)?

Patients with Acanthosis Nigricans should be persistently counseled regarding the benefits of healthier eating (less sweets and white starchy foods), daily exercise, and weight control. Individuals with AN who maintain these therapeutic lifestyle changes usually can reduce their hyperinsulinemia. Reduction in hyperinsulinemia, in turn, tends to reduce the size and prominence of the AN skin lesions.

Patients who are unable to make or sustain lifestyle changes, or who have persistent glucose intolerance, are candidates for medical therapy with

metformin. Metformin has demonstrated good efficacy for reducing hyperinsulinemia, glucose intolerance, and AN lesion size and prominence.

Image Gallery (please click on the 7 photos available to view examples of AN):







Part II

1. What are the accepted definitions of obesity in children and adults?

For children 2-20 years old, overweight is defined by the CDC as a BMI-for-age and -gender equal to or greater than the 95th percentile. The terms overweight and obesity are used interchangeably in the pediatric literature.

Adults with a body mass index (BMI) of 25-29.9 are considered overweight by the CDC, while individuals with a BMI of 30 or more are considered obese.

2. How is body mass index (BMI) determined?

Body Mass Index (BMI) is a number calculated from a person's weight and height. BMI is a reliable indicator of body fatness for most people. BMI does not measure body fat directly, but research has shown that BMI correlates to direct measures of body fat, such as underwater weighing. BMI is a good alternative to direct measures of body fat. BMI is an inexpensive and easy-to-perform method of screening for weight categories that tend to lead to health problems. Very muscular persons (weight lifters, serious athletes) do not have as much body fat as their BMI would suggest. Such persons may have a BMI that usually indicates obesity (30 or higher) but a healthily low percentage of body fat.

Body mass index can be calculated as follows:

$$\textbf{BMI} = [\textbf{Weight in kilograms} \div (\textbf{height in centimeters})^2] \times 10{,}000$$

The Centers for Disease Control and Prevention has created a web-based calculator to assist clinicians in determining patients' BMI. See the following link: BMI page.

To calculate adult BMI, see this CDC Calculator.

To calculate child and teen BMI, see this CDC Calculator

For additional information about BMI and other useful CDC websites:

- **BMI for Adults:** Information about BMI and interpreting this number for adults
- **BMI for Children and Teens:** Information about BMI and interpreting the BMI percentile for children and teens

- **Nutrition and Weight Resources:** Links to additional resources for BMI

PDF Documents

- BMI growth curves for boys 2-20 years *
- BMI growth curves for girls 2-20 years *
- BMI table for adults from the CDC

The above PDF files can be viewed in the free Acrobat Reader (download the reader here) available from Adobe.com

3. What are the trends for diabetes in the PRIME NET state sites and in the U.S., overall?

Data from the CDC's Behavioral Risk Factor Surveillance System survey in 2005 showed that 7.3% of U. S. adults responded positively to the question: "Have you ever been told by a doctor that you have diabetes?" The median percentage for those answering yes to this question by race/ethnicity is shown in the table below:

Prevalence of Diabetes (%) Nationwide (States and DC)		
RACE/ETHNICITY	**% in 2005**	**% in 2000**
White	6.8	5.7
Black	11.4	10.3
Hispanic	6.6	5.0
Other	7.2	5.0
Multiracial	8.3	NA
Overall	7.3	6.8

The following 2005 data (2000 is included parenthetically) reveal the racial and ethnic distribution of the prevalence of diabetes in the states in which a Prime-Net network is located. In New Mexico (2005), 7.3% of participants responded positively to the question, "Have you ever been told by a doctor that you have diabetes," up from 6.5% in 2000. This figure contrasts with an overall prevalence of diabetes in 2005 for Colorado of 4.8%, for California of 7.1%, for Texas of 7.9%, and for Georgia of 8.3%. In the eight southeastern states which comprise the SERCN (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee), the range for the overall prevalence of diabetes in 2005 was from 8.3% in Georgia (6.8% in 2000) to 10.3% in South Carolina (7.1% in 2000).

Prevalence of Diabetes in 2005 and 2000 (in parentheses) by Race/Ethnicity for State Sites of Practice Based Research Networks Which Comprise PRIME-NET				
Race Ethnicity	**NM**	**TX**	**CO**	**GA**
White	6.6 (4.6)	7.4 (5.7)	4.7 (5.1)	7.3 (5.6)
Black	11.8 (NA)	13.1 (9.0)	7.4 (NA)	10.9 (10.3)
Hispanic	7.3 (8.0)	8.1 (6.4)	5.2 (3.9)	10.3 (4.8)
Other	11.6 (9.5)	4.4 (7.8)	1.1 (NA)	6.4 (5.3)
Multiracial	8.0 (NA)	11.5 (NA)	4.5 (NA)	6.6 (NA)
Overall	7.3 (6.5)	7.9 (6.2)	4.8 (5.1)	8.3 (6.8)

These data may underestimate the true prevalence of diabetes since many diabetics are not diagnosed. The incidence of Type II Diabetes increased in four of the five PRIME-NET states from 2000 to 2005 and is increasing in the U.S., overall, and worldwide; this trend is likely to continue.

Physical inactivity and obesity are the main non-genetic determinants of Type II Diabetes. Recent studies have shown that Type II Diabetes is preventable through life style modification, especially changes to diet, exercise, and body weight.

Quiz and Evaluation

To complete this CME activity, proceed to the Assessment and Evaluation page.