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OBJECTIVES FOR PART II: AUTONOMIC NEUROPATHIES

After reading this article, you will be able to:

1) Identify the common autonomic neuropathies associated with diabetes mellitus.

2) List the modes of assessment for autonomic neuropathies.

3) List signs and symptoms associated with each of the following autonomic neuropathies: (a) genitourinary, (b) gastrointestinal, (c) cardiovascular.

(4) Discuss principles of management for persons with autonomic neuropathy.

Diabetic Peripheral Neuropathy Part II: Autonomic Neuropathies

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Diabetic autonomic neuropathies (DAN) are clinical syndromes resulting from impairments of the autonomic nervous system in patients with diabetes mellitus. Since the autonomic nervous system innervates most body organs, any or all of those organs may be affected by DAN. A high index of suspicion is the best diagnostic tool. Proper management, with patient and family education in its center, improves the quality of life of persons with DAN. Undiagnosed and ignored, DAN could cause severe disability and even death.

Diabetic autonomic neuropathies (DAN), like distal symmetrical neuropathies, can occur in all classes of diabetes. The longer the duration of the disease, the greater the likelihood that autonomic neuropathy will occur.[1,2] Autonomic neuropathies in diabetes may affect a single organ, but more often they are widespread (Table 1). They can be easily overlooked until more dramatic symptoms such as gastroparesis and impotence develop. Symptoms of DAN may be absent or intermittent and some, such as frequent urinary tract infections (in neurogenic bladder), may seem unrelated to diabetes. However, appropriate documenting can aid in correctly identifying the etiology of the abnormality. Autonomic neuropathies may become severe enough to cause serious disability or even death. As in the case of distal symmetrical neuropathy, diagnosis of DAN is made by exclusion of other perhaps more treatable causes. DAN can even affect the ability to maintain blood glucose in an acceptable range.

In the following paper, we shall discuss the manifestation of DAN in the more commonly involved organ systems and present possible therapeutic approaches.

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Table 1. Diabetic Autonomic Neuropathies

Classification	Symptoms and Signs
Genitourinary	
Neurogenic bladder	Diminished urinary frequency Incomplete or difficult bladder emptying Frequent urinary tract infections Bladder residual volume >150 mL
Sexual dysfunction	In males: Retrograde ejaculation Impotence In females: Diminished vaginal lubrication Decreased frequency of orgasm
Gastrointestinal	
Gastroparesis	Early satiety Postprandial fullness Postprandial hypoglycemia
Intestinal	Nocturnal diarrhea Fecal incontinence
Cardiovascular	Postural hypotension Cardiac denervation syndrome (painless MI, sudden death) Fixed heart rate
Impaired insulin counterregulation	Unawareness of hypoglycemia Brittle diabetes

Bladder Dysfunction

In its early stages, DAN may cause blunted sensation of the need to void, resulting in infrequent urination. Later, difficult bladder emptying, dribbling, and overflow incontinence may occur. An important point to remember is that neurogenic bladder and infrequent voiding may be misinterpreted by both patient and health care provider as reduced polyuria, an indication of improved glycemic control.[1,3] Bladder insensitivity can only be documented by a cystometrogram.

Assessment of later complications of bladder dysfunction may be made by measuring postvoiding residual urine volume by ultrasound or transurethral catheterization. A postvoiding residual volume greater than 150 mL is consistent with the diagnosis of bladder dysfunction. In older men, a coexisting prostatic hypertrophy must be ruled out by a manual rectal examination.

Untreated, neurogenic bladder dysfunction almost always leads to frequent urinary tract infections (UTI) that may interfere with diabetic control and, in serious cases, be life threatening. Frequent UTI may lead to worsening of renal function. Indeed, repeated UTIs (two or more per year) should alert the health care provider to the possibility of bladder dysfunction.

Treatment of neurogenic bladder should include vigorous treatment of UTIs with specific antibiotic, regular scheduling of urination every two to three hours during waking hours, and cholinergic stimulating drugs.[4]

Diabetes educators who have frequent and regular contact with their patients can help in early discovery of neurogenic bladder. In addition, diabetes educators can help the patient understand the importance of following a regimen of regular urine voiding. Careful assessment and instruction will help patients detect their UTIs earlier as well. In elderly patients with DAN, urinary tract infection may be present without its classic symptoms (eg, suprapubic discomfort, urinary frequency, urgency, and fever). The only manifestation may be mild to moderate change in mental status. Family members must develop a high index of suspicion and promptly report the possibility of UTI. The importance of patient and health care professional education in early detection and treatment of this problem cannot be overemphasized.

Sexual Dysfunction

As many as 50% of diabetic men and 35% of diabetic women have sexual problems due to neuropathy.

In rare cases, the sexual dysfunction may include male retrograde ejaculation with a normal libido, normal erection, and normal orgasm. Diagnosis can be made by recovering live and mobile sperm in the postcoital urine.

The more common and more disturbing sexual dysfunction in men with diabetes is impotence. One should be cautious not to assume that erectile dysfunction in a diabetic man is always due to autonomic neuropathy. Indeed, more treatable or curable conditions (eg, drug induced, hormonal deficiency) must be considered (Fig 1). It is equally important to distinguish between psychogenic and organic erectile dysfunction. In most cases, a careful history can make this distinction. Whereas psychogenic impotence is relatively abrupt in onset and may be partner-specific, organic impotence is gradual in onset and always partner nonspecific. Early morning erection is present in psychogenic impotence and characteristically absent in organic impotence. Neurogenic impotence may be shown by testing for nocturnal penile tumescence (NPT) and rigidity. In addition, the patient should have normal serum testosterone, prolactin, and penile blood pressure. Some patients with neurogenic erectile dysfunction may benefit from implantation of a penile prosthesis, but a careful discussion of pros and cons of this procedure with patient and his wife is imperative.[4,5]

Other methods for the treatment of impotence include vasodilators, injection of papaverine plus phentolamine into the penis, and mechanical low-pressure devices. These latter methods are relatively new and require more clinical experience before they are recommended for widespread use.

In women, sexual dysfunction manifests as difficulty in attaining vaginal lubrication during stimulation and reduction in the frequency or absence of orgasm.[1,4] For these patients, use of estrogen vaginal cream or water-based vaginal lubricants during intercourse may be of help.

Frank and tactful discussion of sexual problems and logical and sensible explanation by the diabetes educator go a long way toward relieving the individual's anxieties about sexual dysfunctions. This approach will ultimately assist the patient and the physician in reaching a more acceptable therapeutic decision.[6]

Gastrointestinal Neuropathy

Virtually every part of the gastrointestinal (GI) system has autonomic innervation. Therefore, DAN can produce a correspondingly broad spectrum of GI symptoms. Although delayed gastric emptying (gastroparesis) is usually asymptomatic, it may be associated with anorexia, early satiety, a sense of fullness and bloating, and nausea after meals. Radionuclide studies can document the presence of delayed solid-phase gastric emptying. This condition can increase the pa-

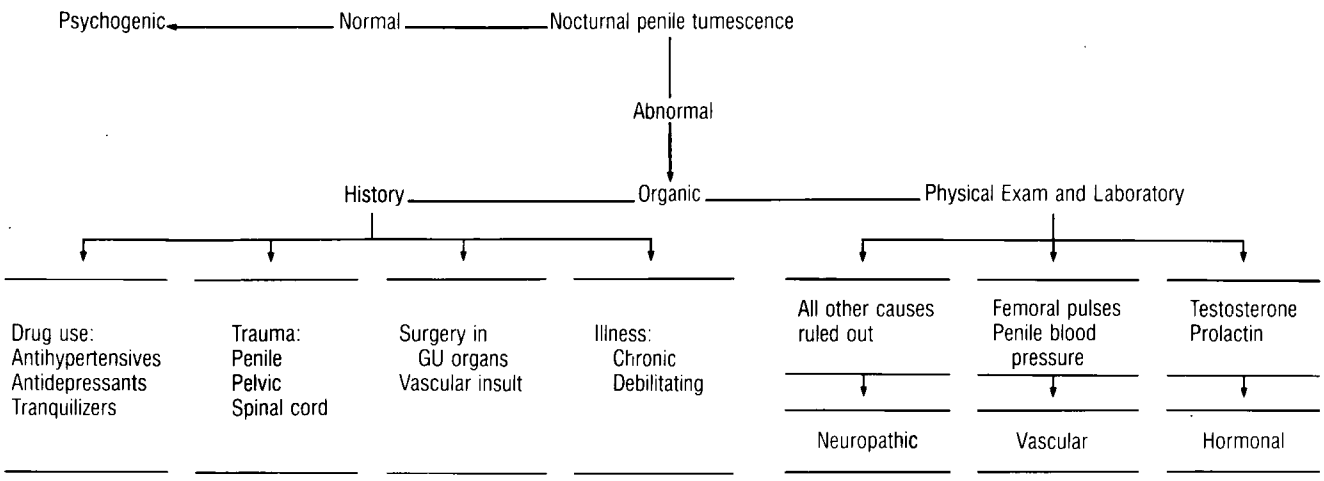

Fig 1. *Algorithmic approach to impotence.*

tient's susceptibility to postmeal hypoglycemia since the food is retained in the stomach. High-residue and high-fiber foods should be avoided.[1,4] A dose of 10-20 mg of metoclopramide before meals and at bedtime is usually effective. In severe cases, the drug should be given parenterally for the first two to three days to allow emptying and digestion of consumed food.[7] Subsequently, metoclopramide should be given orally.

Decreased small intestinal motility may lead to bacterial overgrowth and diarrhea. Cramps and pains are commonly absent. Diarrhea can also occur from hypermotility and without bacterial overgrowth. Alternatively, diarrhea may result from pancreatic insufficiency or bile salt malabsorption.

Diarrhea may be nocturnal, intermittent at first, and associated with fecal incontinence. Diagnosis is one of exclusion. When other causes have been ruled out, a radiologic study showing a disordered motility pattern, with segmentation and puddling of barium in the small intestine, suggests that the problem is neuropathic.[4] Metoclopramide, bile salt sequestrants, and broad spectrum antibiotics have all been helpful in some cases of diarrhea. But, in the more severe cases, administering 1-2 tablets of diphenoxylate hydrochloride with atropine sulfate three to four times daily may be necessary.

Patients with gastroparesis must, therefore, be taught to eat smaller and more frequent (five times daily) meals. Softer and more liquid foods should be encouraged, and solid foods must be avoided.

Cardiovascular Neuropathy

One common manifestation of cardiovascular neuropathy is a fixed pulse rate of 86-100 beats per minute unresponsive to stress, exercise, or tilting, indicating cardiac denervation.

DAN can also cause orthostatic hypotension, diagnosed when blood pressure falls at least 10/20 mm Hg from recumbency, while the patient experiences lightheadedness and dizziness. Diabetic individuals may not develop the tachycardia that usually accompanies orthostatic hypotension. Symptomatic individuals may respond to elastic stockings, mineralocorticoids (fludrocortisone acetate 0.1-0.3 mg/day), vasoconstrictors, and atrial pacing.[4,8] The most serious aspect of cardiovascular autonomic neuropathy is development of cardiac denervation syndrome in which the patient may suffer myocardial infarction without experiencing any pain. Indeed, one-third of diabetic patients who sustain an acute myocardial infarction experience no pain.[4,9] Following a myocardial infarction, these patients are at increased risk of premature sudden death, which may be caused by serious cardiac arrhythmias. Obviously, these patients are not candidates for an intensive regimen (due to risk of hypoglycemia, which may cause cardiac arrhythmias), rigorous exercise program, or even cardiac exercise testing.

Educators should help patients with cardiovascular neuropathy to understand and cope with their clinical condition. Patients must be instructed to avoid sudden changes of position, especially from recumbency to upright. This will reduce the likelihood of patients with postural hypotension becoming dizzy and falling. Finally, individuals with cardiac denervation must be cautioned against heavy exercise or straining.

Impaired Glucose Counterregulation

The maintenance of blood glucose levels during periods of food deprivation or increased insulin action depends on the integrity of glucagon secretion and the adrenergic nervous system. Patients with DAN may not only have a defective adrenergic nervous system but may also suffer from (1) defective glucagon secretion and (2) "hypoglycemia unawareness," in which typical adrenergic warning signs of impending neuroglucopenia (hunger, tachycardia, diaphoresis, etc) are absent. It should be emphasized that every patient with long-standing type I diabetes who is being considered for intensive insulin therapy should be tested for the integrity of his glucose counterregulatory mechanism. Absence of glucagon and epinephrine response to hypoglycemia induced by a standard dose of insulin is a contraindication for rigorous and tight glucose control. Importance of food intake in relation to insulin kinetics (short, intermediate, or long-acting) and the time of insulin injections must be stressed.

Sudomotor Dysfunction

Sudomotor dysfunction is commonly manifested by anhidrosis in the lower extremities with a compensatory hyperhidrosis on the trunk and face. Patients may complain of heat intolerance and excessive sweating on the face and body. The treatment is avoidance of intense heat exposure to prevent heat stroke and hyperthermia.

Clinical Assessment and Management of Autonomic Neuropathy

System	Mode of Assessment	Mode of Management
Bladder dysfunction	History of frequent urinary tract infection History of decreased urinary frequency	Investigation of causative bacteria and vigorous antibiotic therapy Scheduled bladder emptying q 2-3 hours Cystostomy Patient education
Sexual dysfunction	Documentation of lack of erection on awakening Documentation of nocturnal penile tumescence (NPT) using postage stamp or snap gauge History of dyspareunia and decreased lubrication	Penile prosthesis Other erection-inducing devices Estrogen vaginal creams for female patients Patient education
GI dysfunction	Brittle diabetes, postmeal hypoglycemia Early satiety or bloated feeling after meals Diarrhea, nocturnal incontinence	Small frequent soft-to-liquid diet Use of metochlopramide for gastroparesis Stool softener for constipation Diphenoxylate Hcl with atropine sulfate for diarrhea Patient education
Sudomotor dysfunction	Evidence of anhidrosis in the lower extremities associated with excessive sweating in the trunk.	Avoidance of intense heat Appropriate skin and foot care Patient education
Cardiovascular neuropathy	Evidence of postural dizziness Supine and uprgitht blood pressure Supine, upright, and postambulatory pulse History of documented myocardial infarction without experiencing chest pain	Fluid repletion, elastic stockings, mineralocorticoids Avoidance of intense exercise Avoidance of hypoglycemia Patient education
Adrenal medullary dysfunction	Lack of classical hypoglycemia symptoms at appropriate times	Less rigid glycemic control Frequent monitoring Patient education

Summary

Diabetic autonomic neuropathy is the name given to a variety of clinical syndromes, insidious in onset and varied in their clinical presentation. Diagnosis is made by excluding other more treatable causes. When fully manifested, DANs can lead to severe disability or even death. Treatment is primarily supportive and aimed at avoidance of inciting factors. Intensive glycemic control is contraindicated in the majority of persons with DAN. Patient education and patient involvement in the management of DAN are essential if there is to be any chance for preventing further complications.

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References

1. Pfeifer MA, Greene DA. Diabetic neuropathy. In: Current concepts. Kalamazoo, Michigan: The Upjohn Company, November 1985.

2. Pirart J. Diabetes mellitus and its degenerative complications: a prospective study of 4400 patients observed between 1947-1973. Diabetes Care 1978;1:168.

3. Bradly WW. Diagnosis of urinary bladder dysfunction in diabetes mellitus. Ann Intern Med 1980;92:323.

4. Greene DA, Pfeifer MA. Diabetic neuropathy. In: Olefsky JM, Sherwin RS, eds. Contemporary issues in endocrinology and metabolism: new concepts in the treatment and complications of diabetes mellitus. New York: Churchill Livingstone, 1984:223.

5. Karacan L. Diagnosis of erectile impotence in diabetes mellitus. An objective and specific method. Ann Intern Med 1980;92:334.

6. Manley G. Diabetes and sexual health. Diabetes Educ 1986;12:366.

7. Schade RR, Dugas MD, Lrotosky D. Metal: effect of metoclopramide on gastric liquid emptying in patients with diabetic gastroparesis. Dig Dis Sci 1985;30:10.

8. Thomas JD, Schriger A, Fedley RD, et al. Orthostatic hypotension. Mayo Clin Proc 1981;56:117.

9. Ewing DJ, Campbell IW, Clarke BF. Assessment of cardiovascular effects in diabetic autonomic neuropathy and prognostic implications. Ann Intern Med 1980;92:308.