

FROM ACADEMIC GUIDELINES TO CLINICAL CARE
(Part II)

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HYPOGLYCEMIA

This is most common complication associated with diabetes management, and the development of hypoglycemia is an ever present possibility in all patients treated with insulin or OHAs.

Hypoglycemic should be avoided, or at least recognised in the very early stages, so that prompt corrective action can avert any serious consequences.

HIGH RISK PATIENTS

- 1) Patients at greater risk from hypoglycemic sequelae:
- 2) Those who have difficulty in perceiving hypoglycemic symptoms;
- 3) Those who do not spontaneously recover from hypoglycemia;
- 4) The elderly, as well as, infants and young children;
- 5) Patients with angina pectoris, TIA's, renal and hepatic dysfunction, etc.;
- 6) Patients with erratic eating habits and timings;
- 7) Patients whose work may call for sporadic, sudden and vigorous activity.

CLASSICAL SIGNS & SYMPTOMS OF HYPOGLYCEMIA

Sympathoadrenal (a)	Neuroglycopenic (b)
Weakness	Headache
Sweating	Hypothermia
Tachycardia	Visual Disturbances
Palpitations	Mental dullness
Tremor	Confusion
Nervousness	Amnesia
Irritability	Seizures
Tingling	Coma
	Hunger

a) caused by increased activity of the sympathoadrenergic system; may be triggered by a very rapid fall in blood glucose levels

b) caused by action on the central nervous system; requires a level of blood glucose well in the hypoglycemic range

UNCOMMON Symptoms

Patients need NOT show all these classical signs and symptoms of hypoglycemia. This is especially true of the elderly and the children. Thus, diagnosis may have to be based on clinical suspicion; if available, capillary blood glucose measurement using finger prick test should aid diagnosis; in its absence, clinical improvement with glucose administration aids diagnosis.

For a short list of some common hypoglycemic signs and symptoms seen in the elderly and the in children see Appendix 8a

NOCTURNAL HYPOGLYCEMIA

It is very important to rule out hypoglycemic reaction occurring during sleep. These may not be severe enough to cause convulsions or coma. The patient may complain that they experience night sweats, has recurring vivid dreams or nightmares, has early morning headaches which disappear after he takes his breakfast.

Such complaints must be investigated to rule out nocturnal hypoglycemia.

IF IN DOUBT, TREAT AS HYPOGLYCEMIA UNTIL PROVEN OTHERWISE

PSEUDO-HYPOGLYCEMIA?

Some patients may manifest sympathoadrenal signs and symptoms, even if the blood glucose is not actually in the “hypoglycemic” range. It is often seen with a very rapid drop in the blood glucose level.

ABSENCE OF SYMPATHOADRENAL SIGNS AND SYMPTOMS

Patients may manifest neuroglycopenic signs and symptoms in the absence of sympathoadrenal reactions under certain conditions:

ABSENCE OF SYMPATHOADRENAL SIGNS AND SYMPTOMS

- 1) If the blood glucose level fall very slowly;
- 2) Diabetics with significant neuropathic involvement;
- 3) Certain drugs such as beta blockers may mask the sympathoadrenal manifestations;
- 4) Some elderly diabetics.

NON-CLASSICAL SIGNS AND SYMPTOMS

Many diabetics exhibit signs and symptoms which are truly hypoglycemia reactions although they may not fall into the “classical” manifestations.

Patients who become excessively quiet, or conversely, very boisterous, show a lack of interest in normal activities, throw uncalled for temper tantrums, become morose, ambitionless, complain of feeling faint, complain of perioral paraesthesias, etc. may all be manifesting hypoglycemia.

In simple terms,

ANY DIABETIC UNDERGOING TREATMENT WHO SHOWS A BEHAVIOUR PATTERN WHICH IS NOT IN KEEPING WITH HIS NORMAL BEHAVIOUR, SHOULD HAVE THE PRESENCE OF HYPOGLYCEMIA RULED OUT.

COMMON PRECIPITATING FACTORS FOR HYPOGLYCEMIA

It would be worthwhile to understand the most common precipitating factors for hypoglycemia are and thus, try and avoid these episodes.

COMMON PRECIPITATING FACTORS FOR HYPOGLYCEMIA

- 1) delayed or missed meals;
- 2) unexpected calorie intake reduction;
- 3) sudden, undue, vigorous activity;
- 4) errors in dosage and/or timing;
- 5) renal and hepatic dysfunction;
- 6) defective counter-regulation;

- 7) interaction with other drugs;
- 8) subtle hypothyroidism and/or adrenal insufficiency.

MANAGEMENT

The management of hypoglycemia in a patient is fairly simple when the diagnosis is done at an early stage. All that one may have to do is to have a meal, snack or even a beverage with some easily absorbed carbohydrates. In an emergency, one could also take some simple sugars or a drink with simple sugars.

It is very important that after patients have taken simple sugars and become better, they must take a meal having complex carbohydrates. This will be slowly absorbed and help in keeping the blood glucose levels even after the rapid effect of the simple sugars has worn off, especially when the hypoglycemia causing agent is still present in the body.

If the patient is unconscious or cannot take anything orally, inject 50 - 100 c.c. of 25% glucose i.v. Once consciousness is regained, treat as above.

If i.v. is not feasible, 0.5 to 1 mg of glucagon i.m./s.c. can be given. Initially inject 0.5mg and if there is no change in the condition, the other 0.5mg can be injected. Rationale for this is that in some patients glucagons can cause nausea and vomiting and would prevent oral intake by the patient even if consciousness returns.

Glucagon is effective in treating hypoglycemia only if sufficient liver glycogen present, therefore glucagon has virtually no effects on patients in states of starvation, adrenal insufficiency, or chronic hypoglycemia. Once consciousness is regained, treat as above.

For a more detailed discussion on the use of Glucagon in the management of hypoglycemia, see Appendix 8b

Section 9

NEUROPATHY

Commonest complication associated with diabetes.

Clinical Classification of DIABETIC NEUROPATHY

Somatic Neuropathy

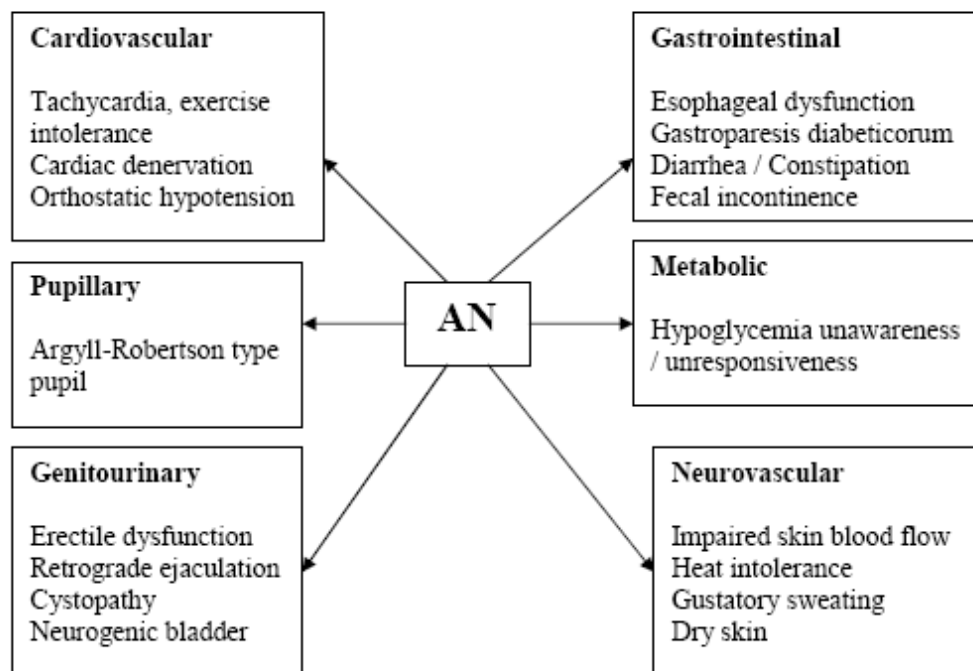
GRADUAL ONSET	
<u>Type</u>	<u>Signs and Symptoms</u>
Distal symmetrical polyneuropathy	<p>Chronic symmetrical symptoms affecting peripheral nerves with the longest nerves usually affected first; Sensory and motor functions affected in varying degrees, but may be predominantly sensory. Often associated with autonomic dysfunction;</p> <p>Signs and symptoms varies commonly presents with tingling or numbness (with or without pain) pain usually bilateral beginning in the feet, spreading proximally in stocking like fashion; Later the upper extremities develop similar manifestations and progress upwards in a glove like manner; Loss of balance, especially with the eyes closed, and painless injuries due to loss of sensation are common.</p>
ACUTE ONSET	
<u>Type</u>	<u>Signs and Symptoms</u>
Painful symmetric polyneuropathy	As above but with an acute onset and associated with significant burning, stabbing, crushing, aching, or cramplike symptoms, with increased severity at night;
Mononeuropathy and	An individual nerve can be affected, such as the peroneal nerve, resulting in footdrop, median

<p>Mononeuropathy multiplex</p>	<p>neuropathy of the wrist, ulnar neuropathy of the elbow</p> <p>Symptoms usually comprise pain, tingling, numbness and wasting and weakness;</p> <p>This might be in the form of solitary nerve involvement or in combination—mononeuropathy or mononeuropathy multiplex.</p>
<p>Cranial mononeuropathy</p>	<p>CN III, IV, and VI disease manifests as acute headache or eye pain followed by diplopia developing over a few hours; Muscle weakness is typically in the distribution of a single nerve, and pupillary light reflexes are usually spared.</p> <p>Facial neuropathy (CN VII) manifests as acute or subacute facial weakness (taste is not normally involved) and can be recurrent or bilateral.</p>
<p>Diabetic radiculoplexopathy Also known as Proximal motor neuropathy (amyotrophy)</p>	<p>Starts as sudden, severe, unilateral pain usually in the lower back, hips, and thighs and may occur in the shoulder/neck;</p> <p>Weakness and atrophy usually develop over a brief time. Reflexes in the affected limb may be depressed. Numbness and paresthesias may occur;</p> <p>Accompanied with depression and significant loss of appetite with significant weight loss in more than 50% of the patients;</p> <p>Usually seen on older people;</p>
<p>Diabetic radiculopathy and Diabetic polyradiculopathy</p>	<p>Burning, stabbing, boring, belt-like, or deep aching pain in the territory of a nerve root; usually begins unilaterally, may become bilateral. Numbness is most prominent in distal distribution of nerve roots. Skin hypersensitivity may occur;</p> <p>Weakness presents in the distribution of the affected nerve root;</p> <p>Coexisting diabetic distal symmetrical polyneuropathy often is present;</p>

	Single or more commonly multiple spinal roots are involved
Diabetic neuropathic cachexia	<p>Presents with severe weight loss usually in older subjects often not diagnosed as having diabetes;</p> <p>Followed by severe pain and signs and symptoms of autonomic neuropathy;</p> <p>Muscle weakness is rare;</p>

Autonomic Neuropathy (AN)

Clinical Manifestations of Autonomic Neuropathy (AN)



DIAGNOSIS

Screening

A) Careful History.

... Questions related to the sensory (tingling, numbness, anaesthesia, parasthesias, inco-ordination), motor (wasting, weakness, nocturnal muscle cramps) and autonomic (gastrointestinal and bladder symptoms, sexual dysfunction, postural light-headedness) nervous systems, etc.

B) Tests for Peripheral Sensation.

... Check for touch, pain (pinprick) and vibration thresholds (calibrated tuning fork).

Although tests like nerve conduction studies and EMG can be done, in clinical terms, the most simple test known as the Monofilament test. This allows a very simple but clinically important study of the sensation in the feet which, if often and correctly done can help in avoiding the most dreaded of complications such as foot injuries and infections.

For a note on the use of the Monofilament Test see appendix 9a

C) Motor Involvement.

... Check for muscle weakness and wasting.

D) Reflexes

E) Detecting Autonomic Neuropathy;

Simple clinical tests for Detecting autonomic neuropathy			
Tests for autonomic neuropathy		Normal response	Abnormal response
Resting heart rate			>100/minute
Heart rate response to standing	Measure R-R interval at beats 15 and 30 after the patient stands		A 30:15 ratio of less than 1.03 is abnormal
Systolic blood pressure changes on standing	Measure systolic blood pressure lying down then standing.	Decrease < 10 mm Hg	Decrease > 30 mm Hg
Heart rate response to deep breathing	Measure heart rate response to deep	Increase rate > 15 beats /min	Increase < 10 beats /min

	breathing		
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Differential Diagnosis

Diabetic neuropathy has a plethora of presentations that must be differentiated from other disorders that may have similar features such as alcoholic neuropathy, B12 deficiency etc.

As many as 10-20 % of people with diabetes may have an alternative cause for the neuropathy. If motor deficit or proprioceptive involvement predominates, it is important to consider nondiabetic causes of neuropathy

For a partial list of common conditions in the differential diagnosis of diabetic peripheral neuropathy, see Appendix 9b

MANAGEMENT

Somatic Neuropathy

Glycemic Control

Tight and stable glycemic control is probably the only treatment approach that may provide symptomatic relief and slow the progression of the diabetic neuropathy. Fluctuations of in the blood glucose levels can aggravate and induce neuropathic pain rather than the level of hyperglycemia. Some suggest that the stability rather than the actual level of glycemic control may be more important in relieving neuropathic pain.

MANAGEMENT

Specific Therapy

Control of the Hyperglycemia

Whilst this may not always ensure that diabetic neuropathy will not occur or progress, there is adequate evidence to show that optimal management of the blood glucose levels is of significant importance. More over there is some evidence that as much as the plasma glucose levels, wide fluctuations in these levels is also very detrimental to the nerves.

Aldose reductase inhibitors, α -Lipoic acid, γ -Linolenic acid have been used with varying results, especially the last two. Aldose reductase inhibitors did not live up to their supposed potential to treat diabetic neuropathy. Injections of B1, B6, and B12 are routinely used by many doctors when faced with a patient with diabetic neuropathy. Unless there is manifest evidence of the deficiency of these vitamins in the patient, the injections would be of use only as a placebo.

Painful Neuropathy

One of the most difficult conditions to manage in patients with diabetic peripheral neuropathy is the painful neuropathies. At the same time, many newer drugs are now available which do tend to improve our ability to give relief in such cases, provided that they are used with care.

Commonly used drugs to treat painful neuropathy

Commonly used drugs to treat painful neuropathy		
Category	Drugs	Side Effects
Tricyclic Antidepressants	Nortriptyline, start at 10-25 mg at bedtime and titrate every 3-4 days to maximum of 75-150 mg/day	Side effects common to all tricyclic antidepressants include dry mouth, drowsiness, dizziness, constipation, urinary retention, blurred vision, confusion, disorientation, increased appetite, tachycardia
	Amitriptyline, start at 10-25 mg at bedtime and titrate every 3-4 days to maximum of 75-150 mg/day	
Anticonvulsants	Carbamazepine, 400 mg <i>po tid</i>	Requires titration; side effects include ataxia, dizziness, somnolence, dyspepsia, nausea, vomiting, blurred vision, confusion, weakness, fatigue, nystagmus, aplastic anemia
	Gabapentin, Usual starting dose is 300mg at bedtime and can be titrated upwards every week to a maximum of 1800-3000mg/day in three divided doses depending on the tolerability and efficacy. Elderly patients should start at much lower	Requires titration; side effects include ataxia, diplopia, blurred vision, tremors, dyspepsia, nausea, vomiting, constipation, fatigue, leukopenia

	doses.	
	Pregabalin, Dosing can begin at 150mg/day in divided doses and may be increased to 300/day within a week depending on the tolerability and efficacy. Dose should be reduced in patients with renal dysfunction;	Requires titration; side effects similar to gabapentin but relatively better tolerated;
	Lamotrigine, start at 50mg/day increase by 100mg biweekly till 200-600mg.day is reached depending on the tolerability and efficacy	Requires titration; side effects include ataxia, dizziness, somnolence, diplopia, blurred vision, nystagmus, headache, dyspepsia, nausea, vomiting, constipation, fatigue, rash, impaired memory
Nonopioid analgesics	Tramadol, start at 50mg daily and titrate upwards by 50mg weekly till a dose of 200-400mg is reached depending on the tolerability and efficacy	Nausea, constipation, somnolence, headache, dry mouth, seizures, confusion, tremors, anorexia, urinary retention
Opioids	Oxycodone, start with 20mg every 12 hours and increase gradually by 10mg/ week till 40-160/ day in divided doses is reached depending on the tolerability and efficacy	Dizziness, somnolence, diplopia, headache, dyspepsia, nausea, vomiting, constipation, dry mouth, sweating, low blood pressure
Local therapy	5% lidocaine patch applied to painful areas; apply for 12 hours, off for 12 hours, upto 3-4 patches maximum at a time	Localised erythema, burning, swelling
	Isosorbide dinitrate spray.	

Pharmacologic treatment of autonomic neuropathy

	Drug	Dosage	Common Side effects
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Orthostatic hypotension	9 alpha flouro hydrocortisone, mineralocorticoid	0.5-2 mg/day	Congestive heart failure, hypertension
	Clonidine, alpha ₂ adrenergic agonist	0,1-0,5 mg, at bedtime	Hypotension, sedation, dry mouth
Gastroparesis diabeticorum	Metoclopramide, D ₂ - receptor antagonist	5-20 mg 30-60 minutes before meals and at bedtime	Galactorrhea, extrapyramidal symptoms drowsiness, restlessness, diarrhea, weakness
	Domperidon, D ₂ -receptor antagonist	10-20 mg, 30-60 min before meal and bedtime	Galactorrhea
	Erythromycin, motilin receptor agonist	250 mg, 30 minutes before meals	Abdominal cramp, nausea, diarrhoea, rash
	Levosulpidide, D ₂ -receptor antagonist	25 mg, 3 times/day	Galactorrhea
Diabetic diarrhea	Metronidazole, broad spectrum antibiotics	250 mg, 3 times/day, minimum 3 weeks	Orthostatic hypotension
	Clonidine, alpha 2 adrenergic agonist	0.1 mg, 2-3 times/day	Hypotension, sedation, dry mouth
	Cholestyramine, bile acid sequestrant	4 g, 1-6 times/day	
	Loperamide, opiate-receptor agonist	2 mg, four times/day	Toxic megacolon
Cystopathy	Bethanechol, acetylcholine receptor agonist	10 mg, 4 times/day	
	Doxazosin, alpha ₁ adrenergic antagonist	1-2 mg, 2-3 times/day	Hypotension, headache, palpitation

<p>Erectile dysfunction</p>	<p>Sildenafil 25-100mg Tadalafil 5-20mg Vardenafil 2.5-20mg</p> <p>GMP type-5 phosphodiesterase inhibitor</p>	<p>Lowest possible dose</p> <p>Patients over the age of 65 years, or those with significant liver disease or renal dysfunction and those who are taking CYP3A4 inhibitors (eg, indinavir, erythromycin, ketoconazole) should begin treatment at lower doses.</p>	<p>Nitrates in any form are contraindicated. Caution should also be used with other antihypertensive agents in order to avoid hypotension. Patients taking alpha blockers should avoid vardenafil and tadalafil. Lower dosages of sildenafil (25 mg) are preferable if these two types of drugs have to be combined. Headache, flushing, nasal congestion, dyspepsia, musculoskeletal pain, blurred vision;</p>
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Section 10

FOOT PROBLEMS

Foot ulcers and other foot problems are one of the commonest causes of morbidity, significant disability, and, even mortality, amongst patients with diabetes.

Foot problems in persons with diabetes are usually the result of three primary factors: neuropathy, poor circulation, and decreased resistance to infection. Also, foot deformities and trauma play major roles in causing ulcerations and infections in the presence of neuropathy or poor circulation.

Prevention

The frequency and the severity of foot problems can be decreased with adequate foot evaluation and, as importantly, patient education about foot care.

All patients at the time of diagnosis and annually, must undergo a comprehensive foot evaluation which includes a complete vascular, neurological, musculoskeletal, skin and soft tissue examination.

This comprehensive evaluation does not necessarily involve the use of sophisticated, complex and costly equipment; some patients may require more sophisticated evaluation.

Patients at high, or increasing, risk may require more frequent evaluations and proactive management.

Patients with HIGH RISK
a) patients who walk barefoot.
b) patients with diabetic neuropathy.
c) patients with significant peripheral vascular disease.
d) patients who smoke or use tobacco in any form.
e) those with a foot deformity such as claw toes and hallux valgus.
f) diabetics with a history of previous ulcers or foot infections.
g) patients with abnormal gait.
h) those with significant skin and nail infections or deformities.
i) blind/partially sighted persons.
j) elderly patients ; especially those living alone,
k) diabetics with chronic renal failure;

1) patients with a high alcohol intake.

Importantly,

The prognosis for the second limb is poor in those who have had an amputation of the contra lateral limb.
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SCREEN TESTS FOR DIABETIC FOOT PROBLEMS

A *comprehensive foot exam* assesses skin, circulation, and sensation. The test can be done during a routine clinic visit

Inspection

For evidence of dry, or excessively moist, skin, hair and nail abnormalities corns, calluses and infection

For presence of deformities, heel spurs, flat arches, etc.

Signs and Symptoms of Sensory Neuropathy

To assess protective sensation or feeling in the foot, a nylon monofilament should be done. Those who cannot sense pressure from the monofilament have lost protective sensation and are at risk for developing foot sores that may not heal properly. Other tests include checking reflexes and assessing vibration perception.

For a note on the use of the Monofilament Test see appendix 9a

If necessary, the following tests should be considered :

- A) Nerve Conduction, and
- B) EMG studies.

Vascular

- a) Inquire for symptoms of intermittent claudication;
- b) Palpation of pedal pulses; if foot pulses are absent examine proximal pulses (popliteal and femoral);
- c) Take the ankle-brachial pressure index; can give a fairly good idea of the severity of the peripheral leg arteries, if interpreted correctly;

Interpreting the ankle-brachial pressure index

Rigid or calcified vessels or both	>1.2	Risk of vascular foot ulcer very high
Normal (or calcified)	0.9 - 1.2	Risk of vascular foot ulcer is small, if vessels not calcified
Definite vascular disease	0.6 - 0.9	Risk of vascular ulcer moderate and depends on other risk factors
Severe vascular disease	Less than 0.6	Risk of vascular foot ulcer very high

Note: Vascular calcification is common so spuriously high readings can be obtained. This must be taken into account when the pressure index reading is evaluated.

If necessary, the following tests should be considered :

- A) Doppler studies for blood flow.
- B) Arteriography.

All these investigations may not be necessary in every patient and the range of investigations should be individualised.

Clinical presentations

Clinical features of neuropathic and ischaemic foot

The clinical picture would usually be mixed depending on the presence and severity of the nerve involvement along with the presence and degree of peripheral vascular dysfunction.

<u>Neuropathic</u>	<u>Ischaemic (neuroischaemic)</u>
Warm with intact pulses	Pulseless, not warm
Diminished sensation	Usually diminished sensation

Ulceration, usually on tips of toes and plantar surfaces under metatarsal heads	Ulceration, often on margins of foot, tips of toes, heels
Sepsis	Sepsis
Local necrosis	Necrosis or gangrene
Oedema	Critical ischaemia, foot pink, painful, pulseless, and often cold
Charcot's joints	

Whilst nerve involvement and the peripheral vascular disease predispose to foot problems, there is usually seen a “trigger” or precipitating factor. This can be trauma, or infection or both.

Precipitating causes of foot ulceration and infection

Friction in ill fitting or new shoes
 Untreated callus
 Self treated callus
 Foot injuries (for example, unnoticed trauma in shoes or when walking barefoot)
 Burns (for example, excessively hot bath, hot water bottle, hot radiators, hot sand on holiday)
 Corn plaster
 Nail infections (paronychia)
 Heel friction in patients confined to bed
 Foot deformities (callus, clawed toes, bunions, pes cavus, hallux rigidus, hammer toe, Charcot's foot, deformities from previous trauma or surgery, nail deformities, oedema)

Management of a Foot Infection / Ulcer

Prevention is the best management, but in spite of the best efforts, foot infections and ulcers do occur. If treated early and optimally, many feet can still be salvaged.

Infection

Foot infections MUST be treated at the earliest.

The clinical diagnosis of infection usually consists of three aspects.

(1) Systemic signs of fever and leukocytosis.

(2) Classic signs of inflammation around the ulcer (eg, heat, redness, edema, and pain); and

(3) Presence of purulent discharge from the ulcer;

It should be realized that due to the presence of varying degrees of nerve and arterial involvement, one may not see these “classic” signs. Pain and tenderness may be absent because of neuropathy. The response to injury in skin includes a local vasodilation mediated by sensory nerve fibers, which are impaired in diabetic neuropathy. Intact tissue responds to bacterial infection by increasing blood flow >20-fold in the area around the infection. However, erythema or redness may be absent in the diabetic foot because of the inability of the foot to increase its blood supply in response to infection. Furthermore, it is now established that up to 50% of patients with deep foot infections will not have leukocytosis or fever. Thus, one cannot wait for the classical signs before initiating management in all patients.

Principles of treatment

Treating Cellulitis

Empiric Antibiotic therapy

Most of the foot infections are caused by multibacterial involvement. Thus, empiric treatment should cover Gram-negative aerobic as well as aerobic organisms. The antibiotic chosen should be bactericidal as opposed to bacteriostatic. In general, bacteriostatic antibiotics require an intact immune system to function properly. The latter is often compromised in a person with diabetes.

Selected empirical antibiotic regimens for mild and non-limb-threatening infections	
Oral agents	Topical agents
• Cephalexin	• Silver sulfadiazine
• Cefdinir	• Silver powder, gels
• Amoxicillin-clavulanate	• Mafenide acetate
• Clindamycin	• Ciprofloxacin drops
• Dicloxacillin	• Mupirocin
• Ciprofloxacin, levofloxacin	• Gentamicin

• Trimethoprim-sulfamethoxazole	• Bacitracin
• Linezolid	• Cadexomer iodine

Aminoglycosides should not be used in combination therapy, if possible. In diabetes patients, who may have some degree of underlying nephropathy, the potential toxic effects of these agents is a prime concern, especially since less toxic alternatives are available. In addition, aminoglycosides are inactivated in an acidic environment, such as that found in abscess cavities. They have minimal penetration into bone, thus making them a poor choice for patients with osteomyelitis.

Later, the antibiotic choice would depend on the culture and sensitivity reports.

A patient who presents with mild infection should be closely monitored and if healing does not take place or the conditions worsens, it would be much better to refer the patient to people specializing in managing such problems.

Any person presenting with more serious infections or an abscess or ulcer should immediately be referred to others well versed in this management without wasting precious time.

Most Common Reasons For Non-Healing Ulcers

- 1) Failure to Non-Weight Bear
- 2) Unappreciated Depth of Wound
- 3) Osteomyelitis
- 4) Vascular Compromise
- 5) Noncompliance
- 6) Poor Diabetic Control

Education

All patients must be educated about the “Do’s and Don’ts of foot care.

Section 11

DIABETIC KIDNEY DISEASE

Diabetic kidney disease is a major cause of morbidity and premature death, in diabetic patients.

It is a multistage condition that requires many years before becoming clinically overt.

An estimated 5% to 15% of DM 2 cases also progress through the five stages of diabetic nephropathy (DN), but the timeline is not as clear. Some patients advance through the stages very quickly.

For a chart on the five stages associated with diabetic nephropathy and the albumin excretion, GFR and BP at each stage see Appendix 11a

Risk factors for the development of diabetic nephropathy are:

Hyperglycaemia
Raised blood pressure
Baseline urinary albumin excretion
Increasing age
Duration of diabetes
Presence of retinopathy
Smoking
Genetic factors
Raised cholesterol and triglyceride levels
Male sex
Raised serum homocysteine levels.

MICROALBUMINURIA

Incipient nephropathy is the stage of microalbuminuria;

Albumin excretion can be estimated through the following methods:

- 1) 24 hour urine collection.
- 2) Timed collection, say over a period of four hours.

3) Spot urinary sample

The results are analysed as follows:

	24 hour collection	Timed collection	Spot collection
	mg / 24 hours	ug / min	ug/mg Creatinine
Normal	< 30	< 20	< 30
Microalbuminuria	30 – 300	20 – 200	30 – 300
MacroAlbuminuria	> 300	> 200	> 300

Urinary albumin excretion (UAE) has a marked intra-individual day to day variation which may be up to 50% thus, in patients with an increase in the urinary albumin excretion rate, or a persistent proteinuria, the UAE should be measured in sterile urine on 3 different intervals over a 4-6 month period;

Albumin to creatinine ratio >30mg/g in an untimed urine specimen is a good predictor of the development of overt nephropathy during an 8 year followup period

Other condition which lead to an increase in UAE should be ruled out; more than 30% patients with raised UAE and/or persistent proteinuria may have an extra renal cause;

For a partial list of common “non diabetic” causes of raised urinary albumin excretion see Appendix 11b

INCIPIENT DIABETIC NEPHROPATHY (DIABETIC MICRO ALBUMINURIA) SHOULD ONLY BE DIAGNOSED WHEN SEEN TO BE PRESENT ON REPEAT TESTING AND WHEN OTHER CAUSES OF RAISED URINARY ALBUMIN HAVE BEEN EXCLUDED.

If tests for microalbuminuria are negative, RETEST regularly.

MANAGEMENT strategies for microalbuminuria

- 1) Meticulous glycemc control.
- 2) Exclude other causes for microalbuminuria
- 3) Meticulous control of blood pressure and dyslipidemias, if present.
- 4) Avoid dehydration.
- 5) Prompt diagnosis and meticulous management of urinary tract infections.

6) Use of ACE inhibitors (ACEIs) even in normotensive patients. Angiotensin Receptor Blockers (ARBs) used alone or in combination with ACEIs seem to be a better alternative, but more studies are necessary before this recommendation can be made as routine therapy.

MANAGEMENT strategies in clinical nephropathy

- 1) meticulous glycemic control.
- 2) tight control of blood pressure, with the aim to maintain the BP as close to 120/80 as possible, although this needs to be individualised i.e., older patients may have more leeway;
- 3) cessation of smoking.
- 4) salt restriction.
- 5) protein restriction (0.4-0.6mg/kg/day).
- 6) treat associated lipid disorders.
- 7) check for urinary tract infection; exclude other causes for renal dysfunction.
- 8) avoid dehydration.
- 9) caution against use of drugs which harm renal function and radio graphic dyes; this should always be done in any diabetic, but all the more in patients with clinical nephropathy.

End Stage Renal Disease

Renal replacement therapy (dialysis and / or renal transplant) is the treatment for end stage renal disease (ESRD).

Section 12

DIABETIC RETINOPATHY

Sight threatening eye disease is a serious complication of diabetes and can often be present without visual symptoms. Early detection and appropriate management can greatly reduce risk of visual loss.

Ophthalmologic examination schedule

All T2DM patients must have a baseline visual examination at the time of diagnosis and yearly thereafter. The presence of retinal changes would merit more frequent examination schedules.

Similarly, in women with known T2DM who are planning pregnancy should have a preconception check and then during the first trimester. Women found to have diabetes during pregnancy (GDM) should also have a visual examination as soon as the diagnosis is made. The schedule thereafter would depend on the physician discretion dependent on the findings at the baseline examination.

BASELINE VISUAL EXAMINATION MUST include :

- a) History of visual symptoms.
- b) Measurement of visual acuity and intraocular pressure : refractive errors should always be corrected after a period of stable control ; cataract and glaucoma (with special focus on open angle glaucoma) are more common in diabetics and should be actively looked for.
- c) Ophthalmoscopic examination through dilated pupils.

This examination should be carried out by a person skilled in diagnosing diabetic eye involvement.

Patients at special risk, and those who show the presence of abnormalities, may require more frequent checkups; these patients should be seen along with a specialist.

PATIENTS AT SPECIAL RISK include:

- a) women who are planning a pregnancy, must have a detailed eye examination
- b) all pregnant women must have a detailed eye examination for the presence of retinopathy at the time of diagnosis and then as frequently as warranted.

- c) patients with unexplained visual symptoms deterioration in visual acuity increased intraocular pressure any retinal abnormalities any other ocular abnormality that threatens vision.
- d) patients with preproliferative retinopathy (multiple cotton wool spots, multiple intraretinal hemorrhages, intraretinal microvascular abnormalities venous beading.)
- e) patients with proliferative retinopathy (retinal neovascularisation, preretinal or vitreous hemorrhage, fibrosis, traction retinal detachment.)
- f) macular oedema (hard lipid exudates and/or retinal thickening in side the temporal vascular arcades).
- g) presence of microalbuminuria, hypertension and smoking.

Stages of Retinopathy

- a) Mild, nonproliferative retinopathy characterized by increased vascular permeability;
- b) Moderate and severe nonproliferative diabetic retinopathy (NPDR), characterized by vascular closure;
- c) Proliferative diabetic retinopathy (PDR), characterized by the growth of new blood vessels on the retina and posterior surface of the vitreous.

Macular edema, characterized by retinal thickening from leaky blood vessels, can develop at all stages of retinopathy.

For a more detailed chart showing the morphological and functional changes at various stages of diabetic retinopathy, see Appendix 12 a

Factors affecting progression of retinopathy

- a) Duration of diabetes;
- b) Uncontrolled glycemia;
- c) Proteinuria;
- d) High blood pressure;
- e) Dyslipidemia;
- f) Pregnancy and puberty;

Clinical Approach

Signs and Symptoms

There are usually no symptoms in the early stages of diabetic retinopathy. Vision may not change until the disease becomes severe. This is why regular examinations for people with diabetes are so important. But it may not be feasible to carry out a retinal

examination at every visit. Thus, one should tell the patient to look out for signs and symptoms which may herald a serious problem and they should be told that they should seek medical attention urgently.

- a) vision becomes blurry;
- b) trouble reading signs or books;
- c) see double;
- d) one or both of the eyes hurt;
- e) the eyes get red and stay that way;
- f) feel pressure in your eye;
- g) see spots or floaters;
- h) straight lines do not look straight;
- i) can't see things at the side as one used to;

MACULOPATHY

Macular involvement in diabetic retinopathy is an emergency, and unless diagnosed in the very early stages and managed adequately, it can lead to significant visual loss (central vision loss).

It is recommended that all patients use an Amsler's Recording Chart which allows early detection of maculopathy.

For details on the Amsler Recording Chart and its utility see Appendix 12 b

The Amsler's chart is very useful for early detection of macular problems and thus is very important as this may be an early sign of macular problems and lead to a loss of central vision.

It will NOT detect proliferative diabetic retinopathy, most preproliferative changes and other types of damage that may threaten vision, nor is it useful for detecting any of the early changes.

A normal Amsler grid test does not rule out the presence of retinopathy that can threaten vision and thus, cannot replace regular fundus examinations

MANAGEMENT strategies for Diabetic Retinopathy

lifestyle	30-60 minutes exercise a day, moderate alcohol consumption only, avoid obesity if possible, balanced diet including 5 portions of vegetables or fruit a day, with the minimal of animal or 'hard' vegetable fats, and very low salt.
blood pressure	130/80 or less 125/75 or less if protein in urine present
HbA1c	6.5% or less with very few or preferably no hypos. If hypos develop, see expert advice. ACE inhibitors or AT11 unless young/pregnant/very low blood pressure/poorly tolerated
cholesterol	<4.66mmol/l, and statins recommended for most adult patients
Smoking	smoking 20 a day triples retinopathy (passive smoking: room-mates inhale at least 25%)

There are no known specific drugs which have been proven to be of help in reducing the progression of retionopathy, although some recent studies have shown that RAAS blocade may help in retarding the progression of diabetic retinopathy.

Laser photocoagulation therapy is effective in reducing the risk of further visual loss and is generally useful in preventing blindness in diabetics with high risk proliferative retinopathy and macular oedema. There is some evidence that early treatment with laser photocoagulation, without waiting for the development of severe changes, may lead to a better prognosis in preventing vision loss.

Vitrectomy may is the mode of treatment in patients with traction retinal detachment or vitreous hemorrhage.

Appendix 8

Appendix 8a

Features of hypoglycaemia in children and the elderly

	Children	Elderly
<i>Autonomic</i>	Hunger	Sweating

	Children	Elderly
	Trembling Pallor	Shaking Pounding heart Anxiety
<i>Neuroglycopenic</i>	Dizziness Poor concentration Drowsiness Weakness	Weakness Drowsiness Poor concentration Dizziness Confusion Lightheadedness
<i>Behavioural</i>	Tearful Confused Tired Irritable Aggressive	
<i>Neurological</i>		Unsteady Poor coordination Double vision Blurred vision Slurred speech

Appendix 8b

Using Glucagon in the management of hypoglycemia.

General Instructions for Use:

The diluent is provided for use only in the preparation of glucagon for [parenteral](#) injection and for no other use.

Glucagon should not be used at concentrations greater than 1 mg/ mL (1 unit/ mL).

Reconstituted glucagon should be used immediately. Discard any unused portion.

Reconstituted glucagon solutions should be used only if they are clear and of a water-like consistency.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Directions for Treatment of Severe Hypoglycemia:

Severe hypoglycemia should be treated initially with intravenous glucose, if possible.

If parenteral glucose can not be used, dissolve the lyophilized glucagon using the accompanying diluting solution and use immediately.

For adults and for pediatric patients weighing more than 44 lb (20 kg), give 1 mg (1 unit) by subcutaneous, intramuscular, or intravenous injection.

For pediatric patients weighing less than 44 lb (20 kg), give 0.5 mg (0.5 unit) or a dose equivalent to 20- 30 $\mu\text{g}/\text{kg}$.

Discard any unused portion.

An unconscious patient will usually awaken within 15 minutes following the glucagon injection. If the response is delayed, there is no contraindication to the administration of an additional dose of glucagon; however, in view of the deleterious effects of cerebral hypoglycemia, emergency aid should be sought so that parenteral glucose can be given. After the patient responds, supplemental carbohydrate should be given to restore liver glycogen and to prevent secondary hypoglycemia.

Appendix 9

Appendix 9a

Sensation threshold screening using a 10 gram monofilament (also known as Semmes-Weinstein monofilament).

How to Use the Monofilament

- Get the patient comfortable and relaxed.
- Show the patient the filament and touch his or her hand with it to show that it doesn't hurt.
- Ask the patient to say "yes" when he or she feels the filament on the foot. Don't ask, "Do you feel that?"
- Hold the filament perpendicular to the skin and use a smooth motion; touch until the filament bends, then lift off. Don't jab or bounce around.
- Touch designated parts of the feet randomly so the patient can't guess where the next point will be. Most critical are the great toe and the ball of the foot.
- If the patient doesn't say "yes" when you touch a particular spot, go to another site and come back to that one later.
- Keep the filament in its plastic case at all times when not in use. It can be cleaned with sodium hypochlorite 1:10 solution.



Consider feet to be "at risk" if patient cannot feel the 10gm monofilament at any of the sites marked.

Appendix 9b

Partial list of common conditions and drugs in the differential diagnosis of diabetic peripheral neuropathy

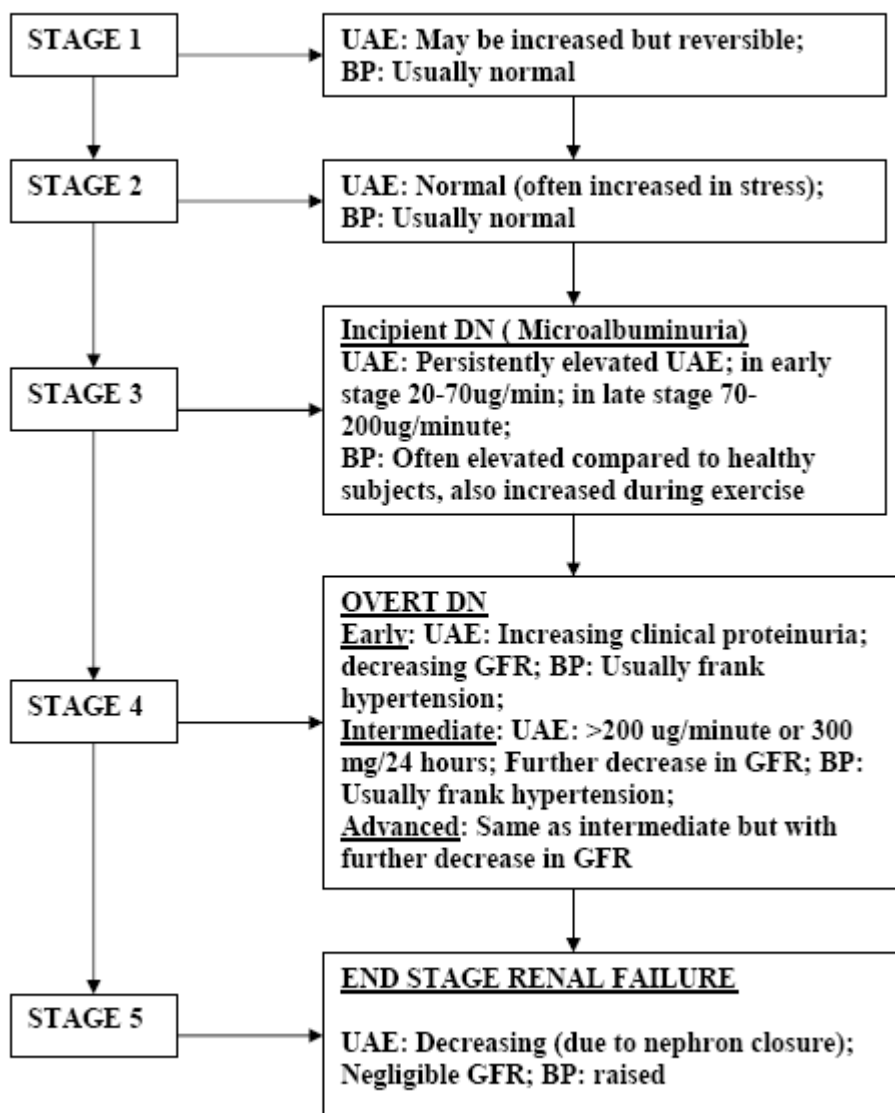
Amyloidosis
Arsenic poisoning
B12 deficiency
Cancer (paraneoplastic syndromes)
Carpal tunnel and other entrapment syndromes
Chacot Marie Tooth disease
Guillian Barre Syndrome
Heavy metal poisoning
Herpes Zoster
HIV/AIDS-related neuropathies
Leprosy
Myaesthesia gravis
Peripheral vascular disease
Sarcoidosis
Vasculitic polyneuropathy

Drug related: Alcohol, amiadirone, colchicines, dapsone, hydralazine, isoniazid, metronidazole, nitrofurantoin, phenytoin, pyridoxine, statins, sulfasalazine;

Appendix 11

Appendix 11a

Stages of Diabetic Nephropathy



POINTERS TO A “NON DIABETIC” CAUSE OF RAISED UAE

- 1) a more rapid decrease in the GFR than is expected.
- 2) sudden development of nephrotic syndrome.
- 3) absence of retinopathy.
- 4) presence of hematuria ; although red cell casts have been described in some patients.
- 5) renal bruit.
- 6) absent pedal pulses.
- 7) disproportionately high serum potassium.
- 8) sudden deterioration in renal function after starting Ace inhibitors.
- 9) presence of cardiac failure, and the use of drugs, like diuretics, in its management.
- 10) testing after heavy exercise.
- 11) testing during acute illness.
- 12) high protein intake.
- 13) decompensation of metabolic control, including recent ketosis.

Appendix 12

Appendix 12 a

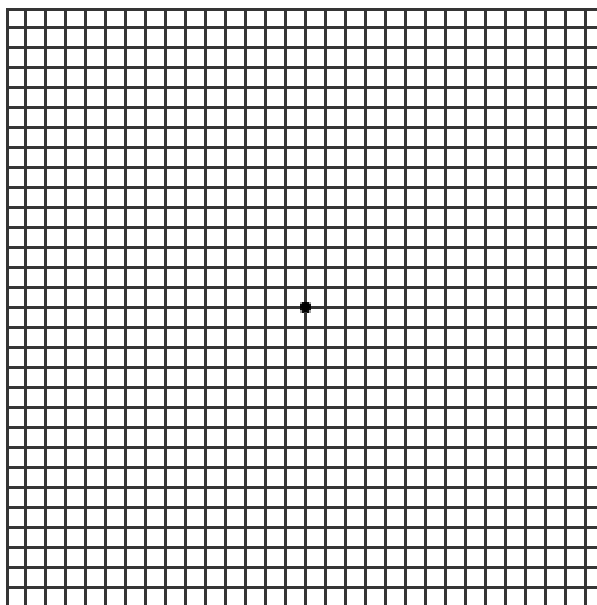
Stages of Diabetic Retinopathy

Stage	Physical Changes	Functional Changes
<p><u>Nonproliferative</u></p> <p>Moderately severe to very severe non-proliferative diabetic retinopathy is also known as pre-proliferative diabetic retinopathy.</p>	<p>Mild</p> <p>Stage of microaneurisms (bulging vessels) tiny retinal blood vessels. These changes are visible only in an eye exam, when the pupils are dilated.</p> <p>Moderate</p> <p>Some blood vessels that nourish the retina are blocked. Small bleeds may occur on the surface of the retina.</p> <p>Severe</p>	<p>Most individuals perceive no vision changes.</p> <p>Macular edema, if present, should be considered a medical sight threatening emergency.</p>

	<p>As more vessels are blocked, parts of the retina are deprived of blood supply and set the stage of new blood vessels to be formed to supply these parts.</p> <p>If vessels begin to leak, the leaking fluid and lipid may collect in the macula, a condition called "macular edema."</p> <p>Macular edema can occur at any stage of diabetic retinopathy and should be considered a medical emergency.</p>	
<p>Proliferative</p>	<p>Areas with blocked vessels show the growth of thin walled and fragile new vessels which take an abnormal course across the retina. (neovascularisation)</p> <p>These vessels can break and bleed into the vitreous, preventing light from reaching the retina.</p> <p>Scar tissue may also form near the retina, detaching it from the back of the eye and resulting in blindness.</p> <p>Fluid in the vitreous and/or macular edema may also be present.</p>	<p>Spotty or cloudy vision, double vision, reduced vision, dark or floating spots.</p> <p>In late stages, severe vision loss may occur leading to “legal” blindness in the affected eye(s).</p> <p>Macular edema, if present, should be considered a medical sight threatening emergency.</p>

Appendix 12 b

AMSLER RECORDING CHART



- 1. Look at the square (grid).***
- 2. Wear your reading glasses (if you use one) and cover one eye.***
- 3. Focus on the center dot for one full minute.***
- 4. While looking directly at the center, be sure that all the lines are straight and clear, and all the small squares are the same size.***
- 5. Repeat the test in the other eye.***
- 6. If any lines or squares appear distorted, wavy, blurred, discolored, or otherwise abnormal, call your eye doctor right away.***
- 7. In healthy eyes the lines are straight.***

The Amsler's chart is very useful for early detection of macular problems and thus is very important as this may be an early sign of macular problems and lead to a loss of central vision! But one must know its limitations. The Amsler grid will NOT detect proliferative diabetic retinopathy, most preproliferative changes and other types of damage that may threaten vision, nor is it useful for detecting any of the early changes. Remember: a normal Amsler grid test does not rule out the presence of retinopathy that can threaten your vision. It cannot replace routine eye exams. Only regular eye exams can do this.