*Bahrain Medical Bulletin, Vol. 30, No.3, September 2008*

***Family Physician Corner***

# How to Diagnose Leg Edema

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Bilateral leg edema (pedal edema) frequently presents a challenge for the primary care physician. As the cause is often multifactorial. It is difficult to make a straightforward diagnosis without having to investigate the condition comprehensively. In this review article, I present a stepwise approach to find the etiology of the edema so that it can be treated accordingly.

Edema is defined as the accumulation of fluid in the interstitial tissue. It commonly affects the lower limbs as part of peripheral edema. The usual cause of edema is an imbalance between the forces controlling fluid exchange leading to an alteration in capillary hemodynamics favoring the retention of sodium and water by the kidneys and the accumulation of fluid in the interstitium[1].

## Types of Edema

Leg edema can be classified into two major categories: venous edema and lymphedema. Venous edema is an excess of capillary filtration that cannot be accommodated by a normal lymphatic system, this lead to the accumulation of low-viscosity, protein-poor interstitial fluid. Lymphedema results from lymphatic dysfunction leading to the accumulation of protein-rich interstitial fluid within the skin and subcutaneous tissue[2].

## Causes of Leg Edema

One of the commonest causes of bilateral leg edema in primary care setting is venous insufficiency (Table 1). It is characterized by long standing pitting edema, sometimes brown due to hemosiderin skin pigmentations. In advanced cases, it can cause dermatitis and ulceration. It is frequently encountered in obese patients and those having varicose veins. It is worth to mention a common variant of venous insufficiency which is called "Dependent edema" in patients who suffered stroke or severe neurological conditions confining them to a chair for long periods.

Another cause is congestive heart failure in which patients have other symptoms like dyspnea and fatigue. Pulmonary hypertension commonly results from sleep apnea, is under-recognized as a cause of edema[3]. It can be diagnosed by echocardiography.

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**Table 1: Common Causes of Leg Edema (Modified from Up-To-Date, 2008)**

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|---|
| **Increased capillary hydraulic pressure** |
| A. Increased plasma volume due to renal Na+ retention |
| 1. Heart failure, including cor pulmonale |
| 2. Primary renal sodium retention |
| a. Renal disease, including the nephrotic syndrome |
| b. Drugs |
| c. Refeeding edema |
| d. Early hepatic cirrhosis |
| 3. Pregnancy and premenstrual edema |
| B. Venous obstruction |
| 1. Cirrhosis or hepatic venous obstruction |
| 2. Acute pulmonary edema |
| 3. Local venous obstruction |
| C. Decreased arteriolar resistance |
| 1. Calcium channel blockers |
| 2. Idiopathic edema |
| **Hypoalbuminemia** |
| A. Protein loss |
| 1. Nephrotic syndrome |
| 2. Protein-losing enteropathy |
| B. Reduced albumin synthesis |
| 1. Liver disease |
| 2. Malnutrition |
| **Increased capillary permeability** |
| |
| A. Burns |
| B. Trauma |
| C. Inflammation or sepsis |
| D. Allergic reactions, including certain forms of angioedema |
| E. Adult respiratory distress syndrome |
| F. Diabetes mellitus |
| G. Interleukin-2 therapy |
| H. Malignant ascites |
| **Lymphatic obstruction or increased interstitial oncotic pressure** |
| A. Postmastectomy |
| B. Nodal enlargement due to malignancy |
| C. Hypothyroidism<br>D. Malignant ascites |
| **Iatrogenic** |
| Due to multiple mechanisms |

There are many drugs known to cause edema [Table 2] Calcium channel blockers and non-steroidal anti-inflammatory drugs (NSAIDS) are the commonest[4]. Up to 5% of patients on NSAID might develop edema[2].

**Table 2: Drugs Known to Cause Leg Edema (from Ely JW, 2006 with Modification)**

| **Antihypertensive drugs** |
|---|
| Calcium channel blockers (Nifedipine) |
| Beta blockers |
| Clonidine |
| Hydralazine |
| Minoxidil |
| Methyldopa |
| **Hormones** |
| Corticosteroids |
| Estrogen |
| Progesterone |
| Testosterone |
| **Other** |
| Non-steroidal anti-inflammatory drugs |
| Pioglitazone, Rosiglitazone |
| Monoamine oxidase inhibitors |

**Idiopathic Edema**

Idiopathic edema is an interesting condition in which there is weight gain (>1.4Kg) due to edema that is not clearly related to menstrual cycle. It is also called cyclical edema, periodic edema, fluid retention syndrome and orthostatic edema[2,4]. It manifests itself as swelling of the hands, legs, or face, or abdominal bloating, which may be real, or perceived by the patient[4].

**Lymphedema**

It can be divided into primary and secondary. Primary can be congenital, lymphedema praecox or lymphedema tarda (Table 3).

**Table 3: Types of Lymphedema (Compiled with Information from Ely JW, 2006)**

| **Primary: Rare** | **Secondary: More common** |
|---|---|

<table>
<tr>
<td>Congenital:<br><br>• present at birth or appear by age 2 years<br>• There is a familial form of congenital lymphedema which is inherited as an autosomal dominant disorder (Milroy disease)</td>
<td rowspan="3">Secondary to:<br><br>• Tumors<br><br>(e.g., lymphoma, prostate cancer, ovarian cancer)<br><br>• Surgery involving lymphatics<br><br>• Radiation therapy<br><br>• Infection (bacterial infection or filariasis)</td>
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<tr>
<td>Lymphedema praecox:<br><br>• The commonest form of primary lymphedema<br>• Onset between age 2 and 35<br>• Female to male ratio 10:1<br>• Usually unilateral and is limited to the foot and calf in most patients<br>• The familial form of lymphedema praecox is an autosomal dominant disorder (Meige disease)</td>
</tr>
<tr>
<td>Lymphedema tarda<br><br>• Presents after age 35</td>
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**Deep Venous Thrombosis**

DVT usually presents as an acute painful swelling with or without discoloration. However, this not always the case, the symptoms and signs might be very subtle. Therefore, it is important not to rely solely on the clinical presentation.

**Obesity**

Obesity on its own will not cause leg edema but it can indirectly increase the risk of chronic venous insufficiency, lymphedema, idiopathic edema, and obstructive sleep apnea[2].

**Pregnancy**

It occurs because of an increased venous pressure from the enlarging uterus near term.

**Clinical Approach**

## History Taking

History taking is the key element in making the diagnosis. The following questions need to be asked:

- The onset and duration of edema. If the onset is less than 72 hours (acute) deep venous thrombosis (DVT), need to be ruled out. Nevertheless, this cutoff time is controversial and is not based on clinical evidence[2].
- Is the edema painful? DVT and reflex sympathetic dystrophy are usually painful.
- Is the patient on any medications? Many commonly used drugs can cause leg edema such as Calcium channel blockers, prednisone, and anti-inflammatory drugs. (See table 2).
- Is there history of any medical illnesses, such as, heart disease, pulmonary disease, renal disease, liver disease?
- Any history of malignancies? Specially pelvic and abdominal, history of radiation.
- Relieving factors, such as, sleeping at night might reduce venous edema but not lymphedema.
- Is there loud snoring or apnea noted by the sleep partner, daytime somnolence? These are indicatives of the presence of sleep apnea which can cause pulmonary hypertension manifested as leg edema.

## Physical Examination

### The Following Points Need to be Assessed:

### General:

- General appearance: Obesity can be associated with venous insufficiency as well as sleep apnea, particularly if the neck circumference exceeds 17 inches. Cyanosis is a feature of late heart diseases and jaundice in liver disease.
- Vital signs: BP, pulse and respiratory rate.
- Note where the edema is located and whether it is unilateral or bilateral. Local causes usually cause unilateral edema while bilateral edema usually results from systemic causes such as, heart or renal disease. It can also be generalized in the later cases.
- Chest and cardiovascular examination to look for signs of heart diseases specifically look for elevated jugular venous pressure and lung crackles.
- Abdominal examination: look for signs of liver disease (Jaundice, spider hemangiomas and ascites), palpate for abdominal or pelvic tumors.

### Specific:

- Test for edema tenderness, if positive it could be a sign of DVT.
- Check for pitting: if positive, think of DVT, venous insufficiency, and early lymphedema. If negative (non-pitting), think of myxedema and advanced fibrotic lymphedema.
- Look for varicose veins as an indication of venous insufficiency.
- Look for "Kaposi-Stemmer sign" which is the inability to pinch a fold of skin on the dorsum of the foot at the base of the second toe. It is a sign of lymphedema[5].

- Look for skin changes such as, a warty texture (hyperkeratosis) with papillomatosis and brownish discoloration in chronic lymphedema.

**Investigations**

The commonest cause of bilateral leg edema is venous insufficiency. It affects 25% to 30% of the general population[3]. Nevertheless we shouldn't presume that the patient have it before considering some laboratory investigations to rule out other serious diseases.

**Laboratory Investigations and Imaging Studies**

**Basic Investigations:**

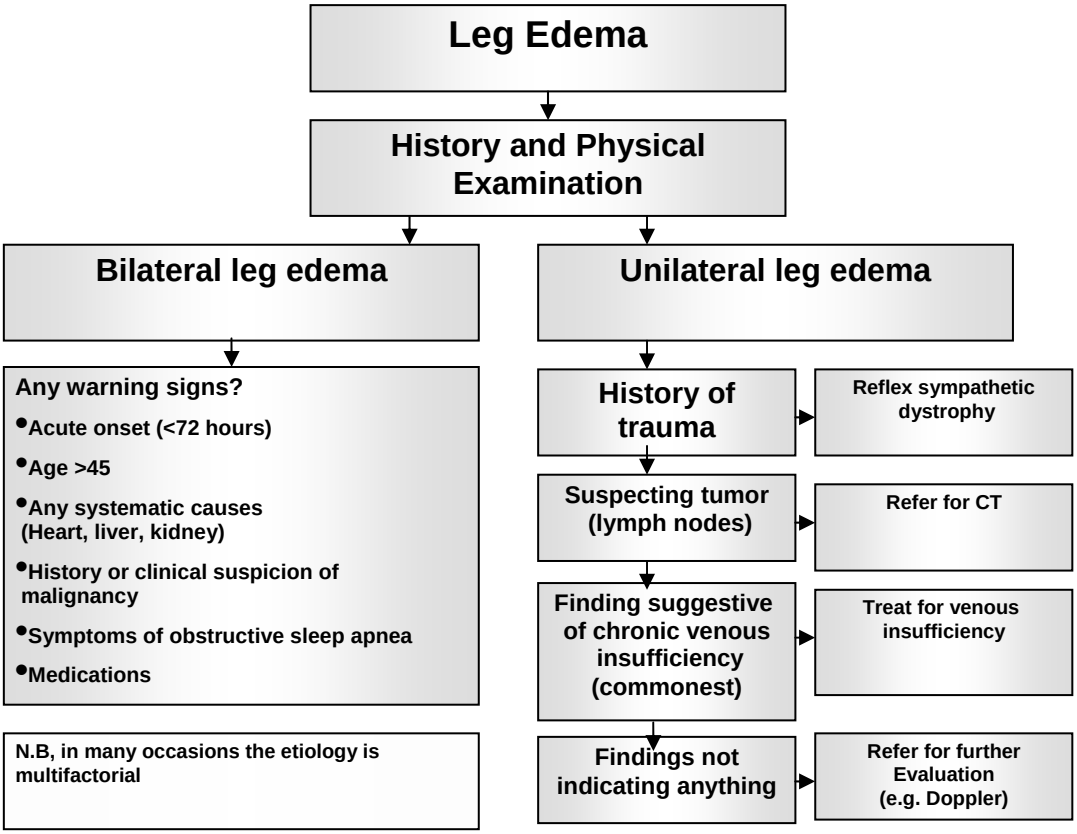
Complete blood count, urinalysis, electrolytes, creatinine, blood sugar, thyroid-stimulating hormone, and albumin are needed. Further tests are considered depending on the clinical presentation:

- If the patient's condition is suggestive of cardiac disease, request an electrocardiogram (ECG), echocardiogram, and chest radiograph. If the patient also suffer from dyspnea a brain natriuretic peptide (BNP) should be measured to help detecting heart failure with a sensitivity of 90%[4].
- If idiopathic edema is suspected in young women based on history and physical examination and there is no reason to suspect another cause, there are further tests to confirm the diagnosis such as, morning and evening weights (a difference of more than 0.7kg is suggestive)[2].
- Patients with acute edema a D-dimer test can be performed to rule out DVT.
- If nephrotic syndrome is suspected serum lipids should be measured along with the basic laboratory studies mentioned earlier.

**Further Investigations**

If the patient is 45 years or older and we still don't know the etiology of the edema, an echocardiogram should be requested to rule out pulmonary hypertension[5]. To distinguish between lymphedema from venous edema lymphoscintigraphy helps in determining the cause of lymphedema. It is performed by injecting a radioactive tracer into the first web space and monitoring lymphatic flow with a gamma camera though it is rarely performed[2,3]. Duplex ultrasound scanning can also be used to confirm DVT[3]. The clinical approach can be summarized in chart 1.

**Chart 1: An Algorithm Summarizing the Clinical Approach to Diagnose Leg Edema (Redrawn with Modification from Ely JW, 2006)**




## CONCLUSION

**Although leg edema is a common condition, we should not rely solely on clinical judgment. The approach to diagnose the etiology of leg edema should be based on clear guidelines.**

## REFERENCES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