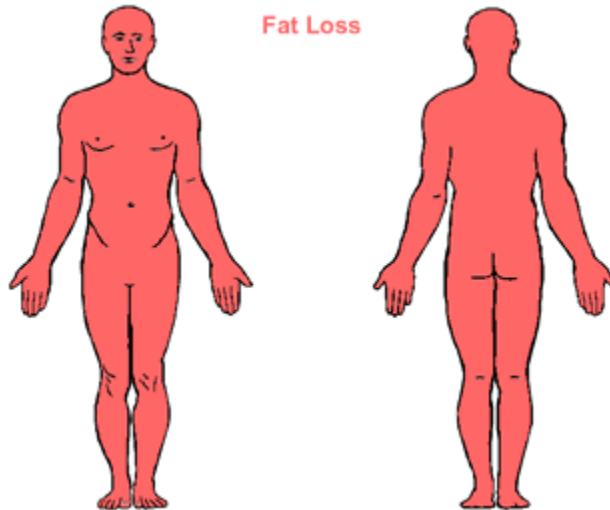


## Acquired: Generalized Lipodystrophy (AGL; Lawrence Syndrome)



This is a rare disease characterized by generalized disappearance of fat occurring during childhood and adolescence. A total of about 80 cases have been reported. Patients have normal body fat at birth thus distinguishing them from patients with congenital generalized lipodystrophy. Females are affected approximately 3 times more often than males. AGL could be due to panniculitis (inflammation in the fat) or autoimmune diseases, however, in several cases no causative factor could be identified.

The onset of AGL may also occur following infections such as varicella, measles, pertussis, diphtheria, pneumonia, osteomyelitis, parotitis, infectious mononucleosis, and hepatitis. Usually, the onset of lipodystrophy is gradual over months to years. Eventually generalized and near complete loss of fat may occur in some patients resulting in muscular appearance and prominent superficial veins (veins under the skin). There is loss of fat from the palms and soles also, while retroorbital and bone marrow fat are preserved. The degree of loss of intraabdominal fat varies. Affected children may have a voracious appetite. Dark velvety pigmentation (acanthosis nigricans) may occur in the axilla and neck, umbilicus, nipples and occasionally hands and feet. Increased linear growth may be seen in the children. Excess body hair, enlargement of genitalia (clitoromegaly) and occasional ovarian cysts (enlarged ovaries) may be seen in the females. Enlargement of liver and spleen is frequently seen. Cirrhosis has been reported in about one fifth of the patients as a late sequela of hepatic steatosis or autoimmune hepatitis.

The patients commonly have moderately severe elevation of blood lipids. Diabetes occurs usually after the onset of lipodystrophy. Diabetes is often difficult to control despite requiring large doses of injectable insulin. Most patients have low serum levels of leptin and adiponectin. Patients with AGL may also develop other autoimmune disorders like vitiligo (light-colored spots on skin), sicca syndrome, rheumatoid arthritis, dermatomyositis, thyroiditis and chronic active hepatitis. The precise mechanism involved in loss of body fat in this disorder however remains unknown but it is likely that autoimmune mechanisms (body defense mechanisms acting against body fat) are involved. Recently, it has been suggested that fat loss occurs due to adipocyte apoptosis mediated by CD95 receptor activation.

**There are 3 types of AGL:**

- **Panniculitis variety (type 1):**The patient presents with painful and inflamed subcutaneous nodules or maculopapular lesions. Upon healing, depressed scars remain but the overlying skin is normal. New nodules appear and there is progression of subcutaneous fat loss.
- **Autoimmune disease variety (type 2):**  
In this variety, the patients have past or present evidence of autoimmune diseases.
- **Idiopathic variety (type 3):**  
This is the most common variety. The etiological factor of this variety is not known.

## References

- Ziegler LH: Lipodystrophies: report of seven cases. *Brain* 1928; 51:145-167.
- Lawrence RD : Lipodystrophy and hepatomegaly with diabetes, lipemia, and other metabolic disturbances. *Lancet* 1946; 1:724-731
- [Golden JP, Charles MA, Arquilla ER, et al](#): Insulin resistance in total lipodystrophy: evidence for a pre-receptor defect in insulin action. *Metabolism* 1985; 34:330-335.
- [Stacpoole PW, Alig J, Kilgore LL, et al](#): Lipodystrophic Diabetes Mellitus. Investigations of lipoprotein metabolism and the effects of omega-3 fatty acid administration in two patients. *Metabolism* 1988; 37:944-951.
- [Klein S, Jahoor F, Wolfe RR, Stuart CA](#): Generalized lipodystrophy: In vivo evidence for hypermetabolism and insulin-resistant lipid, glucose and aminoacid kinetics. *Metabolism* 1992; 41: 893-896.
- [Seip M, Trygstad O](#): Generalized lipodystrophy, congenital and acquired (lipoatrophy). *Acta Paediatr* 1996; Suppl 413:2-28.
- [Misra A, Garg A](#). Clinical features and metabolic derangements in acquired generalized lipodystrophy: case reports and review of the literature. *Medicine* 2003; 82:129-146.
- Garg A. Acquired Generalized Lipodystrophy. In: *The NORD Guide to Rare Disorders* . Lippincott, Williams & Wilkins. Philadelphia , PA. pp 320-321, 2003.
- [Bjornstad PG, Foerster A, Ihlen H](#). Cardiac findings in generalized lipodystrophy. *Acta Paediatr Suppl*. 1996 Jun;413:39-43.
- [Westvik J](#). Radiological features in generalized lipodystrophy. *Acta Paediatr Suppl*. 1996 Jun;413:44-51.
- [Garg A](#). Lipodystrophies. *Am J Med*. 2000 Feb;108(2):143-52. Review.
- [Hague WA, Shimomura I, Matsuzawa Y, Garg A](#). Serum adiponectin and leptin levels in patients with lipodystrophies. *J Clin Endocrinol Metab*. 2002 May;87(5):2395.
- [Simha V, Zerwekh JE, Sakhaee K, Garg A](#). Effect of subcutaneous leptin replacement therapy on bone metabolism in patients with generalized lipodystrophy. *J Clin Endocrinol Metab*. 2002 Nov;87(11):4942-5.
- [Simha V, Szczepaniak LS, Wagner AJ, DePaoli AM, Garg A](#). Effect of leptin replacement on intrahepatic and intramyocellular lipid content in patients with generalized lipodystrophy. *Diabetes Care*. 2003 Jan;26(1):30-5.
- [Moran SA, Patten N, Young JR, Cochran E, Sebring N, Reynolds J, Premkumar A, DePaoli AM, Skarulis MC, Oral EA, Gorden P](#). Changes in body composition in patients with severe lipodystrophy after leptin replacement therapy. *Metabolism*. 2004 Apr;53(4):513-9.
- [Javor ED, Moran SA, Young JR, Cochran EK, DePaoli AM, Oral EA, Turman MA, Blackett PR, Savage DB, O'Rahilly S, Balow JE, Gorden P](#). Proteinuric nephropathy in acquired and congenital generalized lipodystrophy: baseline characteristics and course during recombinant leptin therapy. *J Clin Endocrinol Metab*. 2004 Jul;89(7):3199-207.
- [Hou JW, Huang SF](#). Recurrent panniculitis associated with generalized lipodystrophy and growth hormone deficiency. *J Formos Med Assoc*. 2005 Jul;104(7):518-21.
- [Pope E, Janson A, Khambalia A, Feldman B](#). Childhood acquired lipodystrophy: a retrospective study. *J Am Acad Dermatol*. 2006 Dec;55(6):947-50.

- [Park JY, Chong AY, Cochran EK, Kleiner DE, Haller MJ, Schatz DA, Gorden P.](#) Type 1 Diabetes Associated with Acquired Generalized Lipodystrophy and Insulin Resistance: The Effect of Long-Term Leptin Therapy. *J Clin Endocrinol Metab.* 2007 Oct 16.