Centre Hospitalier Universitaire et Régionale de Grenoble (CHURG)
[1] Service de Biophysique et Médecine Nucléaire (PR M. COMET)
[2] Service d'Angiologie (PR A. FRANCO)

Does medical treatment of lymphedema act by increasing lymph flow?

A. FRANÇOIS[1], C. RICHAUD[2], J. Y. BOUCHET[2], A. FRANCO[2] and M. COMET[1]

Edema of the lower limbs can result from an increase in the flow of fluid from capillary filtration or from a decrease in lymph flow. In the latter case, the edema ist caused by accumulation of proteins in the interstitial fluid, a condition known as lymphedema. To reduce lymphedema, CLODIUS [1] has proposed a combination of manual lymph drainage, elastic compression, and elevation of the limbs during rest periods. This therapy has been shown to be clinically effective, leading to a decrease in lymphedema, but its mechanism of action has not been studied with respect to lymph flow. Lymphoscintigraphy is an atraumatic technique that allows qualitative evaluation of lymph flow in the lower limbs [2, 16]. We have applied it to patients with chronic edema of the lower limbs. The objectives of the present study were to evaluate the influence on lymph flow of: (i) manual lymph drainage, and (ii) an 8-day treatment.

Methods

Selection of patients

The patients all had chronic edema of the lower limbs whose clinical signs primarily indicated lymphedema. Twenty-five subjects were included in the study, but 7 were subsequently excluded because they did not satisfy the lymphoscintigraphic criteria for lymphedema [2]. The eighteen remaining patients were divided into two groups: 11 with unilateral edeme (group G1, 1 man and 10 women) and 7 with bilateral edema (group G2, 1 man and 6 women). The patients in group G1 were 15 to 78 years of age (48.2±22.5) and those in group G2 were 18 to 73 years of age (52.6±21.6). It should be mentioned that 3 patients, 2 of which were in group G1, had a family history of lower limb edema. The personal histories were essentially of two types: venous disturbances (varicosity or phlebitis homolateral with edema) in 6 patients, i.e. 4 out of the 11 in group G1 and 2 out of the 7 in group G2, and surgical history in the inferior pelvis (4 hysterectomies, 2 bilateral inguinal hernias, 1 ovary cancer) in 6 patients, i.e. 1 out of the 11 in group G1 and 5 out of the 7 in group G2. In the latter case, the distribution differed significantly between G1 und G2 ($p < 0.05$).

Therapeutic methods

The treatment of lymphedema was based on a combination of manual lymph drainage, double compression bandaging (an elastic band over a non-elastic cotton band), mobilization exercises done under compression, and 30° elevation of the lower limbs during rest periods. Manual lymph drainage, according to LEDUC [9], begins with lymph node stimulation in the groin, corresponding to inflow maneuvers in the regions not infiltrated. Resorption maneuvers are then applied to the infiltrated regions: these amount to gentle static pressure, like blotting, applied with slow rhythm from the groin distally along the limb.

Exploration method

Isotopic lymphography was carried out with antimony trisulfide (Sb_2S_3) labeled with technetium 99m (^{99m}Tc). The injection consisted of 75 MBq of activity diluted in 0.5 ml of solvent. The size of the colloïdal particles ranged from 3 to 30 nm. The patients first walked for 15 min. They were then placed in the dorsal decubitus and the tracer was injected subcutaneously at 3 sites per limb: the fist and last interdigital spaces and the lateral retromalleolar region. The detector was an NaI bar (CGR scanni-camera) which scanned their entire length of both lower limbs, allowing a bilateral study of radioactivity. The scanning began at the feet, just after the injections, and took 40 min to reach the inguinal region. The criterion for inclusion in the study was an absence of perceptible inguinal node activity on the scintrigrams. The migration of colloïd in the lymphatic system is a reflection of lymph flow. During phlebedemas, the lymph flow is increased and the colloïd reaches the inguinal nodes rapidly, whereas during lymphedemas, lymph flow is decreased or absent and the inguinal nodes are not visible 40 min after tracer injection [2]. The speed at which the tracer rises is thus an expression of lymph flow. Based on the lymphoscintigraphic results, the patients' limbs were classified into 3 groups: H (Healthy) for healthy limbs contralateral to edematous limbs, N+ (Node+) for edematous limbs showing an increase in lymph flow after manual lymph drainage, and N– (Node–) for edematous limbs showing no increase in lymph flow after manual drainage.

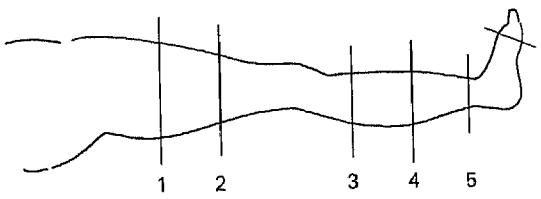

Fig. 1: Levels at which limb circumferences were measured.

Thigh – 1 = T + 15: 15 cm above the base of the patella
2 = T + 10: 10 cm above the base of the patella
Calf – 3 = C – 10: 10 cm below the apex of the patella
4 = C – 15: 15 cm below the apex of the patella
Ankle – 5 = ANK
Transmetatarsus: 6 = TM

Protocol

The patients were hospitalized for 8 days. The first lymphoscintigraphy was carried out on the first day (D1), to obtain the initial scintigram (A1). The circumferences of the limbs were then measured at different levels (Fig. 1). The 6 measurements were averaged to determine the mean circumference of each limb. Manual drainage was carried out for 20 min in each limb, after which another scan was performed without further injection, giving the second scintigram (A2) of the first lymphoscintigraphy. During the subsequent days of the week, manual drainage was applied exclusively to the edematous limbs. Healthy limbs are without bandage or elevation but lying at rest on bed. On the eighth day (D8), the patients underwent the second lymphoscintigraphy, following the same sequence, i.e. walking, injection, first scan (B1), measurements, manual drainage of both limbs, second scan (B2).

Results

Measurements

We calculated the mean limb circumference in each group. In group G1, the mean circumference of the healthy limbs was 33.5 cm (SD = 4.2 cm) and that of the edematous limbs was 37.6 cm (SD = 5.7 cm). In group G2, the mean limb circumference was 37.0 cm (SD = 1.3 cm). The edematous limbs showed the same mean circumference regardless of whether the edema was uni- or bilateral. After manual lymph drainage, the decreases in mean circumferences ranged from 0.75 to 6.8 cm (mean 2.6 ± 1.9 cm) for the edematous limbs of group G1, from 0 to 1.75 cm (0.6 ± 0.5 cm) for the healthy limbs of group G1, and from 0 to 2.8 cm (1.3 ± 0.9 cm) for the limbs of group G2. These variations differed significantly from 0 in each group, even in the case of healthy limbs. The circumferences of the edematous limbs of group G1 decreased more than those of group G2 ($p < 0.01$).

Lymphoscintigraphy

The objective lymphoscintigraphic criterion led to the exclusion of 7 patients who had clinical lymphedema, but whose initial scintigrams (A1) immediately showed one or more inguinal nodes. In the 11 patients of group G1, the inguinal nodes of the healthy limbs contralateral to the edematous limbs were still visible after manual drainage. Seven of the edematous limbs showed no visible nodes on scintigrams A1/A2 or B1/B2 after drainage on days D1 and D8 (Fig. 2a), 2 of

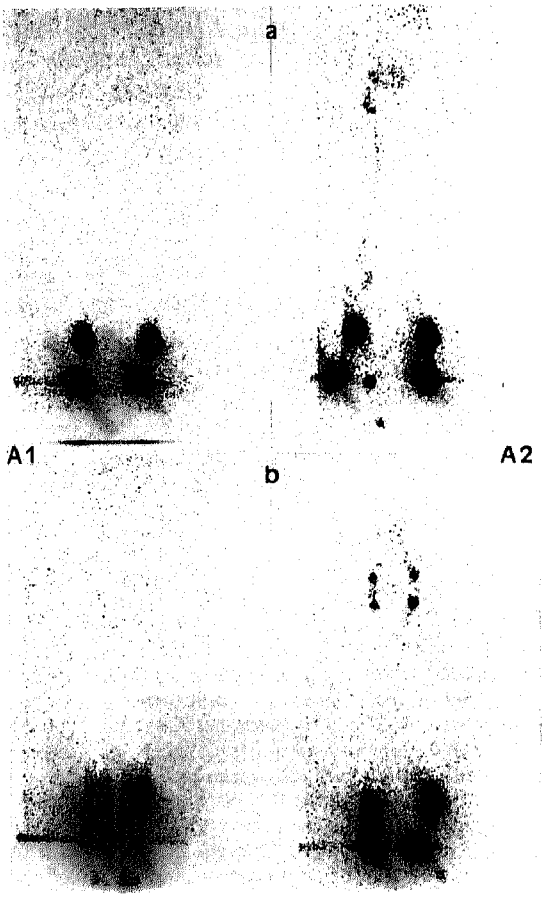

Fig. 2:

A1 = scintigram before manual drainage on D1 (anterior view)
A2 = scintigram after manual drainage on D8 (anterior view)
a: patient in group N–; left unilateral lymphedema
b: patient in group N+; bilateral lymphedema

the limbs had visible nodes on A2 and B2 after drainage, and 2 of the limbs showed no inguinal nodes on A2, but they were clearly visible on B2. The limbs of group G2 all showed the same lymphoscintigraphic behaviour, i.e. after manual drainage, one or more inguinal nodes were visible bilaterally on scintigrams A2 and B2 on days D1 and D8 (Fig. 2b). Altogether, 11 limbs were classified in group H, 16 in group N+ (2 from G1 and 14 from G2), and 9 in group N- (9 from G1 and 0 from G2).

The mean decrease in the mean limb circumferences in the different groups (N+, N-, H) was close to that observed in groups G1 and G2 (Table I). The mean decrease in mean limb circumference was significantly greater in group N- than in group N+ ($p < 0.02$). Comparing the mean limb circumferences on D1, it can be seen that the limbs of group N+ were smaller than those of group N-, but the limbs in N+ and N- reached the same mean circumference on D8 (Fig. 3). Regardless of the level of measurement, the decrease in circumferences between D1 and D8 was constant within each group (Fig. 4).

Table I: Decreases in mean limb circumferences between days D1 and D8.

Group	Number	Decrease in mean limb circumference between D1 and D8
N+	16	1.3±0.9 cm
N-	9	2.9±2.0 cm
H	11	0.6±0.5 cm

Discussion

As proposed by CLODIUS et al. [1], current treatment of lymphedemas relies on a combination of techniques essentially comprising manual lymph drainage, elastic compression, and rest with limbs elevated. The objective of the present study

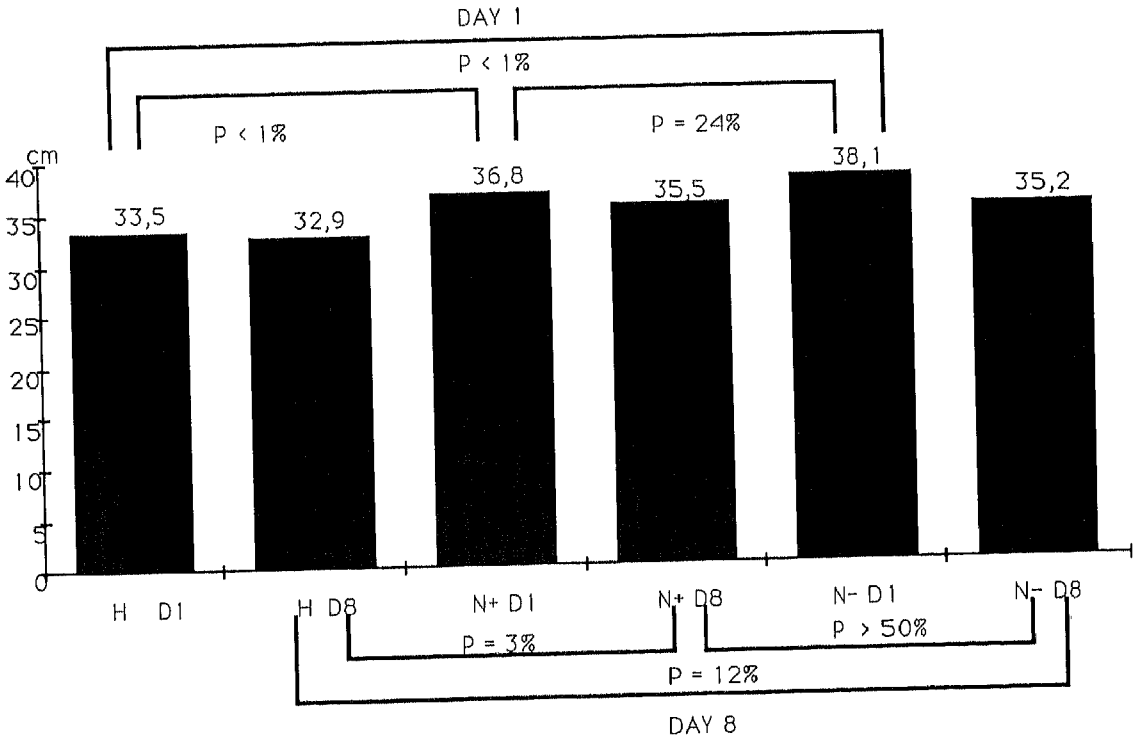

Fig. 3: Decreases in mean limb circumferences in each group (H = Healthy, N+ = Node +, N- = Node -) during manual drainage therapy.

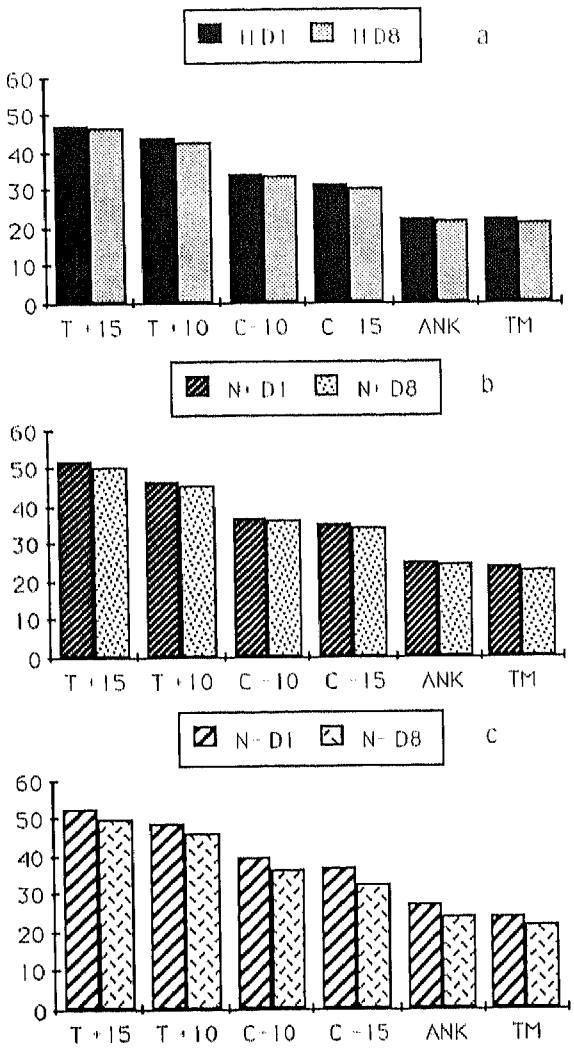

Fig. 4: Variation of the decreases in mean limb circumferences (a = Healthy; b = Node +; c = Node –) at the different levels of measurement.

was to objectify the efficacy of this treatment and the effect of manual drainage on lymph flow in patients with chronic clinical lymphedema confirmed by lymphoscintigraphy. The protocol was applied for one week, as proposed by STILLWELL [15] and not for 5 weeks, as proposed by CLODIUS [1]. The need for a simple exploration technique to evaluate lymph flow in a manner that was reproducible and not very invasive led us to choose lymphoscintigraphy. Conventional lymphoangiography is not suitable for studying lymph flow since it requires injecting the contrasting product with pressure into a lymphatic. Furthermore, it has been said to aggravate some edemas [10]. On the other hand, it visualizes anatomic anomalies found in certain lymphedemas [3, 7]. The «blue test», apart from its aesthetic drawbacks, can cause a local or, more rarely, general allergic reaction. Moreover, the test provides no information on the anatomy of the lymphatics. Analysis of the clearance of ^{198}Au colloïd injected subcutaneously in the feet was proposed in 1964 for evaluating lymph flow [13]. This colloïd has gradually been replaced by others (rhenium sulfide or antimony trisulfide) labeled with technetium 99m (^{99m}Tc) [2, 4, 5, 16]. These tracers can be used to explore both lymph flow and large morphological anomalies of the lymph vessels [2]. The three injection sites technique is a reliable method to visualize deep and superficial collectors and also the cutaneous pathways [2, 4]. The lymph flow increase is conspicious in patients with postthrombotic venous alteration and the lymph flow decrease is evedent in patients with anatomical lymphatic disease. The population of our study was similar to that of GOUGH [3]. The sex ratio (F/M) was 89%, which shows the large asymmetry in the distribution of lymphedemas in these populations. Three patients had a family history of edema (17%) but the diagnosis of lymphedema could not be verified in the family members concerned. This percentage is identical to that reported by KINMONTH [7]. The clinical results of therapy were clear, showing a significant decrease in the mean limb circumferences between D1 and D8. There was an even greater decrease in the circumferences of the more edematous limbs. However, this decrease appeared to be limited, since the circumferences never returned to the values of the healthy limbs. These results are in agreement with those of CLODIUS [1] who reported that the proposed therapy did not allow a return to the latent state of the disease. A definitive cure of edema would primarily require etiological treatment. The decrease in the circumferences of the healthy limbs can clearly be attributed to rest, since these limbs received no treatment apart from the manual drainages on D1 and D8 between scans A1/A2 and B1/B2. The decrease was slight but significant. It could also betray a slight prior increase in the circumferences, corresponding to the latent state of the disease in limbs contralateral to edematous

limbs. These limbs free of a manifest edema are not exactly healthy limbs because some bilateral lymph flow modifications are found in patients with unilateral lymphedema [2, 16]. Lymphoscintigraphy revealed an increase in lymph flow immediately after manual drainage in several patients. As shown by OLSZEWSKI [11], external manual drainage of the foot increases lymph flow by raising the frequency of the peristaltic waves of the lymph vessels, not by action on lymphatic pressure. In the human, spontaneous rhythmic contractions of the lymph vessels are the major factor of lymph flow in the limbs. The appearance of a contractile wave after massage of the lymphatics suggests that the wave is myogenic [11, 12]. In our study, nodes were visualized on scintigram A2 followed manual drainage. The lymph flow of the patients in group N+ was increased by certain stimuli such as manual drainage. Hence, the cause of the lymphedema could be a functional anomaly of lymphatic contraction. The lymph flow of the patients in group N- did not increase after manual drainage, which suggests an organic lymphatic anomaly, such as those observed in lymphangiography [7], or else a severe functional disturbance of lymphatic contraction. The effect of manual drainage on lymphatic contraction was immediate, and stopped as soon as the stimulus was removed. This can be compared to the results of JACOBSON [6] in a study of changes in lymph flow in resting and exercising muscles in the rat. Furthermore, in the normal subject, walking increases lymph flow by a factor of 15 compared to the value at rest. A shown by OLSZEWSKI [12], lymph flow only occurs in conjunction with pulsating waves: when the waves are stopped, lymph flow also stops. There was no sign of persistence in the increase of lymph flow after a week of daily manual drainge, contrary to what appears to be provided by surgical treatment [8, 14], i.e. scintigrams A1 and B1 can be superimposed. The patients of group N- showed no increase in lymph flow after manual drainage, but these were the cases that showed the greatest decrease in edema. Consequently, this decrease must have been due to a mechanism other than stimulation of lymph flow. Other hypotheses can be proposed, such as an increase in fluid resorption by the capillaries.

Conclusion

Based on the present study, we propose a classification of lymphedemas into 2 groups according to the lymphoscintigraphic results after manual drainage.

• *lymphedemas due to functional anomalies.* Lymph flow is increased by manual drainage. These are usually bilateral edemas that are short- or long-term consequences of surgery in the inferior pelvis.

• *lymphedemas due to structural anomalies.* Lymph flow cannot be increased. These are usually spontaneous unilateral edemas while lymphatic modifications are more often bilateral.

The clinical results of therapy were independent of those of lymphoscintigraphy, since the patients of group N- showed the greatest clinical improvement.

Summary

The lymphatic origin of chronic edema of the lower limbs was identified by lymphoscintigraphic exploration. Patients underwent therapy involving 8 days of manual lymph drainage combined with elevation of the limbs during rest periods and double compression bandaging. Manual drainage increased lymph flow in 16 limbs, implying that the edema resulted from a functional lymphatic anomaly. In contrast, manual drainage did not increase lymph flow in 9 limbs, suggesting a structural anomaly of the lymphatics. Hence, the same clinical picture corresponded to two different lymphatic anomalies, distinguished by lymphoscintigraphy. However, the therapeutic results were independent of the lymphoscintigraphic results. Increased lymph flow is therefore not the only explanation for the decrease in edema during therapy.

Zusammenfassung

18 Patienten, bei denen ein chronisches Ödem der unteren Extremitäten vorlag, wurden lymphszintigraphisch untersucht und die lymphatische Ursache des Ödems abgeklärt. Die in Gruppen eingeteilten Fälle erhielten alle 8 Tage lang manuelle Lymphdrainage, eine Kompression mit 2 verschiedenen Binden und Hochlagerung der Beine während der Ruhe. Der manuelle Drainage-Effekt wurde lymphszintigraphisch kontrolliert. Der Lymphfluss wurde dadurch bei 16 Extremitäten erhöht, was auf eine funktionelle lymphatische Abflussstörung zurückgeführt wird. Bei 9 Extremitäten erfolgte durch die manuelle Drainage kein erhöhter Lymphfluss, was auf eine strukturelle Anomalie der Lymphbahnen hinweist. Dies zeigt, dass das selbe klinische Bild durch zwei unterschiedliche lymphatische Erkrankungen verursacht werden kann, die sich durch Lymphszintigraphie unterscheiden lassen. Die thera-

peutischen Ergebnisse waren aber unabhängig von der lymphszintigraphischen Form. Ein erhöhter Lymphfluss stellt daher nicht die einzige Erklärung für den Rückgang des Lymphödems unter der obigen Therapie dar.

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Dr A. François, Service de Biophysique et Médecine Nucléaire, CHURG – BP 217X, F-38043 Grenoble Cedex