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ALTERATIONS OF UNTREATED LYMPHEDEMA AND ITS GRADES OVER TIME

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ABSTRACT

Lymphedema is assumed to increase in amount and Grade with time. This work verifies that assumption, and may be helpful in persuading patients to undergo treatment and provides prognosis for likelihood of future disability. Before-treatment volumes of lymphedema/normal, Grades and durations are compared in 231 postmastectomy arm, 74 primary leg, and 103 secondary leg lymphedemas. These were the first, consecutive, unilateral lymphedemas to receive treatment at 25 clinics whose therapists we had trained.

Amounts of lymphedema increased with time, as did Grades. Arms increased more rapidly (p=0.01) than secondary or primary legs, which did not differ from each other (linear regressions: 1.8 (0.34), 0.63 (0.20) and 0.68 (0.38) %/year, respectively). The Grades of primary lymphedemas increased more slowly than those of either secondary arms (p=0.02) or secondary legs (p=0.003), which did not differ from each other (regressions: 0.010 (0.0048), 0.038 (0.0063) and 0.032 (0.0048) Grades/year, respectively). Increase of lymphedema with Grade was less for secondary legs than for primary legs (p=0.004) or arms (p=0.009), which did not differ significantly (regressions: 9.9 (3.5), 35 (8.7) and 25 (3.4) %/Grade, respectively). Thus, arms increased more rapidly in size than primary or secondary legs; primary legs remained in each Grade longer — and got larger in them — than did secondary legs. This relative lack of fibrosis in primary lymphedema permitted greater amounts of edema and accorded well with histopathological studies. The increases described with duration were not caused simply by patient aging. Whereas both duration and the age at the onset of lymphedema were significant for the arms, only duration was significant for the legs. Even in the arms duration was much more important than age.

It is commonly assumed that lymphedema increases with time and worsens in Grade. However data supporting these assumptions are remarkably few. Patients treated with placebos during clinical trials from six months to over two years support such an increase over time (1), but numbers have been small and most patients had filaritic lymphedema of the legs.

The incidence of lymphedema has been estimated a few times (2-3), but not its size. Nor has the incidence been compared with the duration or Grade of the disease. Yet it would be helpful if data were available showing the alterations likely to occur with passage of time in untreated lymphedema. These would be of considerable benefit in counseling patients.

A series of 618 limbs represent the first — consecutive — limbs treated with Complex Physical Therapy (C.P.T.) by therapists whom we have trained in Australia, the U.S.A. and New Zealand (4). Only those with unilateral lymphedema were studied here

TABLE I
Ages and Durations of the Lymphedemas, by Cause and Grade

	No	Males	Age Mean	Age SD	Duration Mean	Duration SD
POST-MASTECTOMY ARMS						
Grade 1.1	20	0	50.8	8.9	1.2	1.9
1.2	45	0	53.3	14.3	2.1	3.3
1.3	36	0	56.5	14.2	2.6	3.2
2.1	33	0	56.0	10.2	5.7	5.3
2.2	81	0	56.8	13.5	5.1	4.7
2.3	16	0	63.5	8.8	8.2	8.9
PRIMARY LEGS						
connatal						
Grade 1	6	1	18.6	20.6	18.6	20.6
2	12	5	21.8	13.1	21.5	12.7
praecox						
Grade 1	6	1	36.0	18.4	13.1	13.0
2	28	3	40.9	12.2	22.3	12.8
3	4	0	58.8	6.6	32.0	6.7
tarda						
Grade 1	6	0	57.3	10.3	9.0	8.3
2	9	0	60.3	12.6	8.0	6.2
3	3	2	66.3	20.6	22.7	23.7
SECONDARY LEGS						
Surgery &/or Radiotherapy for malignancies						
Grade 1	18	3	49.4	17.8	2.6	2.9
2	34	8	50.0	11.9	7.3	9.0
3	4	3	44.3	12.0	17.8	16.5
Accidental Trauma						
Grade 1	9	3	44.3	17.9	0.8	0.9
2	10	6	50.3	10.4	6.2	5.4
3	1	0	47.0	–	4.0	–
Other Surgery (abdominal 7, arthroscopy 3, vein stripping 2)						
Grade 1	5	1	49.8	12.8	2.0	1.4
2	6	1	55.2	13.6	9.6	11.4
3	1	0	37.0	–	22.0	–
Other Causes (infection 10, filariasis 3, chronic venous insufficiency 1, snake bite 1)						
Grade 1	3	1	51.0	4.0	4.1	2.9
2	10	2	49.8	13.2	12.8	6.7
3	2	2	63.0	2.8	25.0	7.1

(231 arms and 177 legs), so that the volume of the affected limb could be compared with the contralateral (normal) limb (5). Only their initial measurements were considered, before treatment.

This report therefore provides a sample of untreated lymphedema, without active malignancy, in Western communities. It also represents a sample of the major types of lymphedema after varying periods of time, so that their natural progression could be assessed.

METHODS

In most patients, a physician made the diagnosis of lymphedema using clinical criteria, but some patients underwent conventional lymphangiography or lymphoscintigraphy. The diagnosis was confirmed by therapists, who have been trained in the differential diagnosis of swelling of the limb. Each patient was included, except for four who only had 3 or 4 days of treatment (usual is 3-5 weeks). Considerable effort was made to ensure that no patient was omitted — including transcribing the data of about half of them directly from all the records of the clinic (4). The only rejection criterion was active malignancy. It is emphasized that the study, therefore, represents a consecutive, unselected, series of patients. Apart from the exceptions described later, they represent a sample of an untreated lymphedema population.

Cause, Grade and duration of the lymphedemas is shown in *Table 1*. The Grades are as defined by the *International Society for Lymphology* (6), *viz.*: Grade 1 — no or minimal fibrosis, edema pits on pressure and reduces with limb elevation; Grade 2 — substantial fibrosis clinically, edema does not pit, and does not reduce with limb elevation; Grade 3 — Grade 2 plus elephantine (trophic) changes. We divided each of these Grades into: mild, moderate and severe; i.e. Grades: 1.1, 1.2, 1.3, 2.1, etc. A Grade represents the average over the whole of the affected limb; i.e. a limb which has a small part Grade 2.2 but is mostly 1.2 was recorded as 1.3. Lymphedema of the arms occurred only in women; that of the legs was in both sexes, but because gender made no significant differences in the findings, the sexes were combined in reporting the data.

Only patients with unilateral lymphedema were studied. Circumferences were measured of both limbs, at the mid-hand or foot, at the wrist or ankle, and then at consecutive 10 cm intervals from the finger tips or heel. Measurements were continued proximally as far as possible. Volumes, were estimated from a series of circumferences using the sum of truncated cones (5). The equation with least errors (eqn. "4" in ref. 5) was used: i.e.:

volume of lymphedematous limb/volume of "normal" limb = *L/N*.

Data were analyzed using multiple correlation coefficients and linear regressions. Significances of differences between them were tested using Fisher's z-transforms and two-tailed t-tests.

RESULTS

The individual data for the amount *versus* duration of lymphedema are shown in *Fig. 1*. Whereas the main Grades are indicated, these are better seen when plotted against duration *(Fig. 2)*. The Tables give more details.

Variations of Grade, Amounts of Lymphedema and Duration

Lymphedema/normal and duration did not differ significantly among some of the sub-Grades *(Table 2)*; accordingly, they were combined. As expected, the higher Grades had significantly more edema, and the patient often had lymphedema for a significantly longer duration.

There were no significant differences between the amounts of lymphedema, for any Grade, between the primary and the

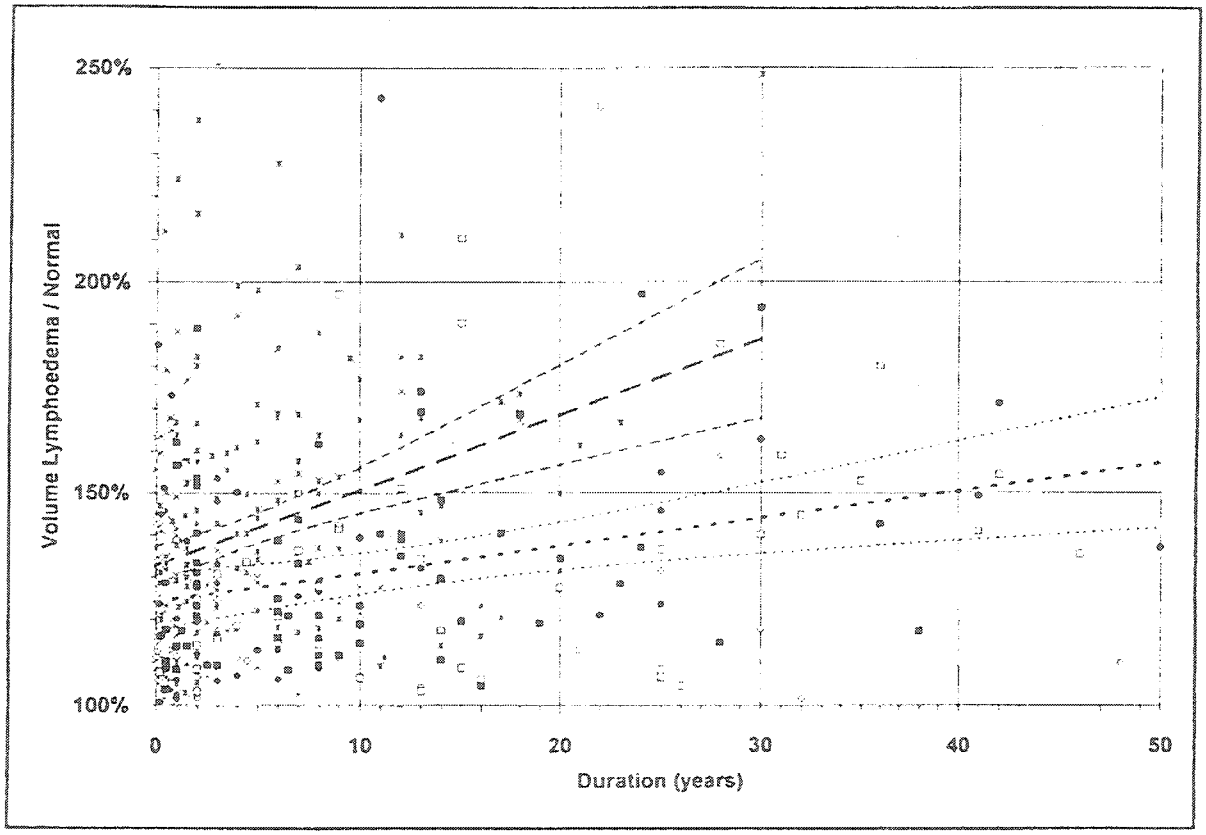

*Fig. 1. A scatter-diagram of all the values of volume of lymphedema/normal plotted against the duration of lymphedema. The major Grades and the arms, primary and secondary legs are distinguished: X arms Grade 1, *arms Grade 2, ◇ primary legs Grade 1, ◆ secondary legs Grade 1, ❑ primary legs Grade 2, ■ secondary legs Grade 1, ● primary and secondary legs Grade 3, – – – arm regression line, - - - combined leg regression line. (Regression for the arms stops at 30 years since this was their longest duration). The 95% confidence limits of the mean are shown for each line. Many points overlap each other at the lower left.*

secondary lymphedemas of the legs. However, there was a notable and significant difference between the duration of these two leg groups for Grades 1 and 2, but not for 3. Primary lymphedemas remained as Grades 1 and 2 much longer than the secondary ones — in the arm or the leg *(Fig. 2, Table 2)*.

Correlations of Amount of Lymphedema versus Duration and Grade

Table 3 shows the multiple correlation coefficients between the volumes of lymphedematous limbs/normal, the Grades, and the Durations. Whereas none of these was close to 1, almost all were highly significant because of the large numbers. Of the differences between them, only one was significant, namely between primary and secondary legs for Grade *versus* Duration ($p=0.001$).

Regressions of Amount of Lymphedema, Grade and Duration

Each linear regression coefficient for the amount of lymphedema *versus* its duration was highly significant *(Table 4, Fig. 1)* — apart from the primary legs (which had relatively small numbers). The findings

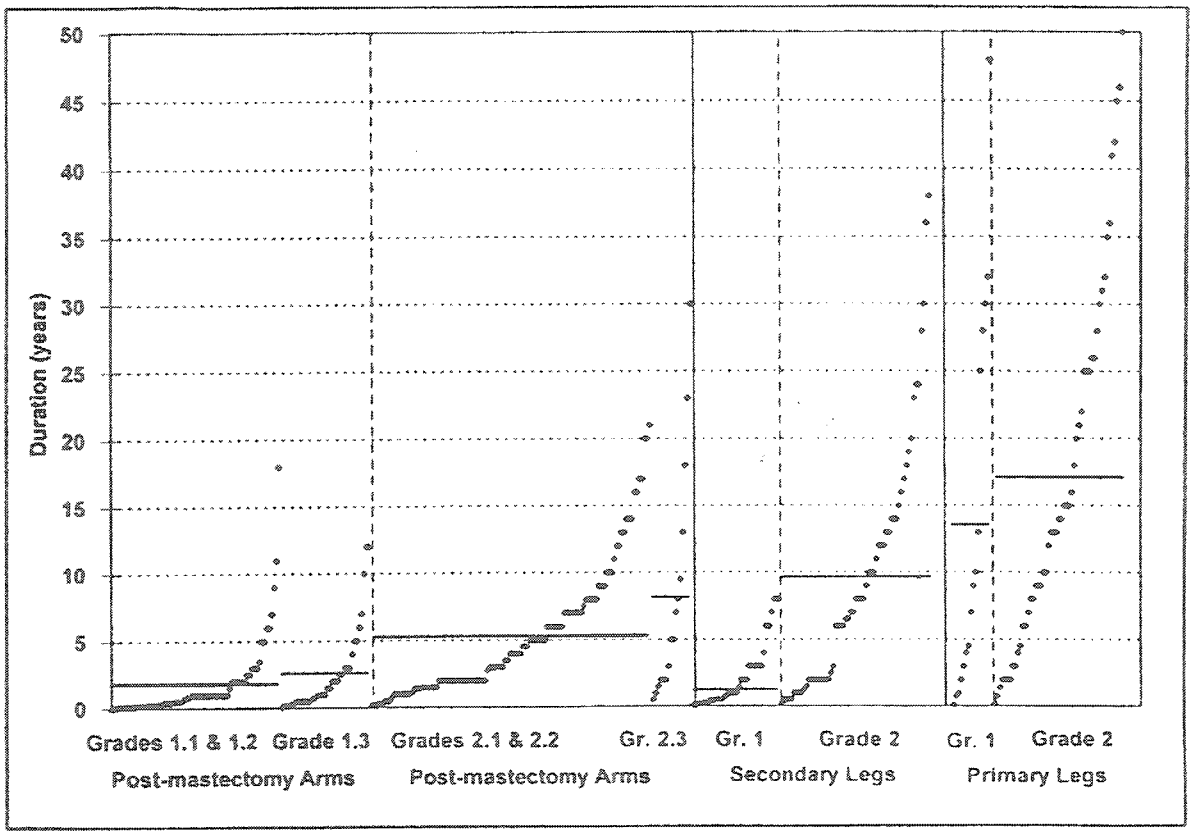

Fig. 2. The individual values for the duration of the lymphedema are plotted in their various Grades. The sub-Grades are combined when they were not significantly different. Grade 3 is omitted since it was not present in the arms and it did not differ significantly for the legs. The means are indicated by straight lines. Note that the durations for both Grades 1 and 2 are much greater for primary legs than for the secondary legs or the arms — which did not differ significantly from each other.

showed that lymphedema increased with time. There were no significant differences between the primary and secondary legs (p values >0.9) so they were combined. Differences between the arms and the combined legs were significant for both the intercepts at zero time (p=0.036) and the slopes (p=0.012). Thus, arm lymphedema was greater than leg lymphedema at each time period and it increased about three times more rapidly.

Linear regressions of Grade *versus* duration were each significant *(Table 4)*. Thus Grade of lymphedema increases with time. There were no significant differences between arms and secondary legs (p=0.6), but those between primary and secondary legs were significantly different (intercept: p=0.011; slope: p=0.003), as were those between primary legs and arms (intercept: p=0.0005; slope: p=0.017). It was noteworthy that the Grades of the primary legs increased about a third as rapidly as those of the arms and the secondary legs *(Fig. 2)*.

All linear regressions of amount of lymphedema *versus* Grade were highly significant *(Table 4)*. The differences between arms and secondary legs were not significant for the intercept (p=0.1), but were for the slope (p=0.009). Those between arms and

TABLE 2
Grade versus Amount of Lymphedema and Duration

	No.	Lymphedema Normal Mean	S.E.	p–value *cfed. next Row*	Duration (years) Mean	S.E.	p–value *cfed. next Row*
Arms							
Grade 1.1 & 1.2	67	122%	1.85%	10^{-8}	1.82	0.36	0.2
Grade 1.3	36	146%	4.15%	0.6	2.60	0.53	0.002
Grade 2.1 & 2.2	112	143%	2.61%	10^{-5}	5.30	0.46	0.05
Grade 2.3	16	177%	8.36%		8.16	2.18	
Legs, Secondary							
Grade 1	35	124%	3.56%	0.09	1.24	0.04	10^{-7}
Grade 2	60	132%	2.91%	0.2	9.63	1.18	10^{-5}
Grade 3	8	143%	6.26%		27.50	5.75	
Legs, Primary							
Grade 1	16	119%	3.98%	0.09	13.58	3.61	0.4
Grade 2	51	133%	4.41%	0.004	17.11	1.89	0.9
Grade 3	7	188%	39.6%		17.57	3.97	

There were no significant differences between some sub–Grades and they accordingly were combined. Arms Grades 1.1 & 1.2 had p–values of 10^{-7} when compared with Grades 2.1 & 2.2 for both lymphedema/normal and duration; Arms Grade 1.3 *versus* 2.3 had p = 10^{-3} for both. There were no significant differences between Primary and Secondary Legs for any Grade for Lymphedema/Normal, but the differences between them for the Durations had p–values of 10^{-6}, 0.001 and 0.2 – for Grades 1, 2 and 3, respectively.

primary legs were significant for the intercept (p=0.027), but not for the slope (p=0.18). Differences between the primary and secondary legs were significant (intercept: p=0.006; slope: p=0.004). In primary lymphedema the amount of edema increased some three times, compared with the secondary legs, for each increment in Grade. Thus, primary lymphedema seemingly had less fibrosis for a given amount of lymphedema.

The Effect of Age

It is possible that an increase in the amount of lymphedema with greater duration was simply because tissues stretch more readily as patients age. If so, then the older the patient when lymphedema started, then the greater should be the rate of increase. But this finding was not so, as shown by multiple regressions of lymphedema/normal *versus* duration and the age at which lymphedema first commenced *(Table 5)*. Whereas lymphedema was significantly increased in the arm if the patient was older when it commenced (p=10^{-5}), this was not true in either the primary or the secondary legs (p=0.3). However even in the arms, the effect

TABLE 3
Multiple Correlation Coefficients of Initial Lymphedema/Normal, Grade and Duration

	No.	Duration	p–value	Grade	p–value
Arms and Legs Combined					
Lymphedema/Normal	408	0.117	$4x10^{-4}$	0.296	10^{-9}
Grade		0.414	10^{-15}		
Arms Alone					
Lymphedema/Normal	231	0.311	10^{-6}	0.352	10^{-7}
Grade		0.372	10^{-7}		
All Legs					
Lymphedema/Normal	177	0.246	$9x10^{-4}$	0.318	10^{-5}
Grade		0.397	10^{-7}		
Legs, Secondary					
Lymphedema/Normal	103	0.300	0.003	0.253	0.013
Grade		0.578	10^{-7}		
Legs, Primary					
Lymphedema/Normal	74	0.208	0.08	0.398	0.001
Grade		0.148	0.2		

There are were no significant differences between the various correlation coefficients except for Grade and Duration for Primary versus Secondary Legs (p–value = 0.001).

of age was only one third as much as that of duration ($p=10^{-4}$). Even greater differences were found in the legs, although that for the primary legs was not significant because of the greater Standard Error. Some of these patients had lymphedema while very young; others did not.

Regression Lines

Using the data, the regression equations for the mean values were:

L/N for arms = 99.9% + 2.06% x duration (yrs) + 0.61% x age-at-start (yrs)

L/N for secondary legs = 124.5% + 0.633% x duration (yrs)

L/N for primary legs = 123.7% + 0.684% x duration (yrs)

(The "age-at-start of lymphedema" is not included in the last two because this factor made no significant difference.)

For more details, see Appendix at end of article.

DISCUSSION

TABLE 4
Linear Regressions, Lymphedema versus Duration versus Grade

LYMPHEDEMA/NORMAL VERSUS DURATION

Limbs	*No.*	*F–for Regression*	*p–value for F*	*Value at yr=0*	*SE*	*Slope (%/year)*	*SE (%/year)*
Arms/Legs Combined	408	13.1	10^{-4}	132.3%	1.89%	0.560%	0.115%
Arms	231	24.4	10^{-6}	132.6%	2.31%	1.80%	0.364%
Legs Combined	177	11.2	10^{-3}	124.2%	3.36%	0.658%	0.197%
Legs, Secondary	103	9.96	0.002	124.5%	2.71%	0.633%	0.201%
Legs, Primary	74	3.21	0.077	123.7%	8.05%	0.684%	0.381%

GRADE VERSUS DURATION

Limbs	*No.*	*F–for Regression*	*p–value for F*	*Value at yr=0*	*SE*	*Slope (Gr./year)*	*SE (Gr./year)*
Arms/Legs Combined	408	91.0	10^{-19}	Gr. 1.80	Gr. 0.031	0.0244	0.00256
Arms	231	35.9	10^{-8}	Gr. 1.73	Gr. 0.040	0.0378	0.00630
Legs Combined	177	39.6	10^{-9}	Gr. 1.87	Gr. 0.056	0.0206	0.00328
Legs, Secondary	103	43.8	10^{-9}	Gr. 1.76	Gr. 0.065	0.0317	0.00479
Legs, Primary	74	4.59	0.036	Gr. 2.06	Gr. 0.102	0.0103	0.00482

LYMPHEDEMA/NORMAL VERSUS GRADE

Limbs	*No.*	*F–for Regression*	*p–value for F*	*Value at yr=0*	*SE*	*Slope (%/Grade)*	*SE (%/Grade)*
Arms/Legs Combined	408	56.6	10^{-13}	123.7%	5.35%	19.5%	2.60%
Arms	231	53.3	10^{-12}	126.3%	6.57%	24.6%	3.36%
Legs Combined	177	22.8	10^{-6}	117.1%	8.83%	19.3%	4.03%
Legs, Secondary	103	8.01	0.006	123.0%	7.44%	9.93%	3.51%
Legs, Primary	74	16.2	10^{-4}	104.1%	19.8%	34.9%	8.67%

TABLE 5
Multiple Linear Regressions: Lymphedema *versus* Duration *and* Age at Start of Lymphedema

Limbs	No.	F–for Regression	p–val. for F	Intercept Value at yr=0	Intercept SE	*Slope for* Duration Slope (%/yr.)	*Slope for* Duration SE (%/yr.)	*Slope for* Age at Start Lymphedema Slope (%/yr.)	*Slope for* Age at Start Lymphedema SE (%/yr.)
Arms Legs Combined	408	20.2	10^{-9}	107.6%	5.15%	1.07%	0.18%	0.48%	0.09%
Significance of differences from 0: p values:						10^{-8}		10^{-7}	
Significance of difference between Duration and Age at Start of Lymphedema:						0.003			
Arms	231	23.2	10^{-9}	99.9%	7.66%	2.06%	0.35%	0.61%	0.14%
Significance of differences from 0: p values:						10^{-8}		10^{-5}	
Significance of difference between Duration and Age at Start of Lymphedema:						10^{-4}			
Legs, Combined	177	6.48	0.002	116.1%	7.13%	0.83%	0.24%	0.18%	0.14%
Significance of differences from 0: p values:						10^{-4}		0.2	
Significance of difference between Duration and Age at Start of Lymphedema:						0.02			
Legs, Secondary	103	5.47	0.006	116.8%	8.24%	0.76%	0.24%	0.16%	0.16%
Significance of differences from 0: p values:						0.002		0.3	
Significance of difference between Duration and Age at Start of Lymphedema:						0.04			
Legs, Primary	74	2.07	0.13	115.2%	12.0%	0.86%	0.42%	0.26%	0.27%
Significance of differences from 0: p values:						0.046		0.3	
Significance of difference between Duration and Age at Start of Lymphedema:						0.2			

Adequacy of Sample

This report concerns the first 408 unilateral lymphedemas who received more than a few days of treatment at the various clinics. They are considered as a representative sample of lymphedema in the general population, and of the alterations in each kind over time. However there are several sampling problems which should be considered.

The first is that only unilateral lymphedema limbs were used; accordingly, 210 patients with bilateral limb lymphedema (from 618 in the whole series) had to be excluded. Yet often the "normal" contralateral limb in "unilateral" lymphedema is in fact mildly lymphedematous, as is often shown by a reduction in its swelling during C.P.T. (5)— especially in primary lymphedema but even in secondary (e.g. postmastectomy). Whereas the use of a contralateral "normal" limb is desirable (5), the slight error it entails should not be ignored. Accordingly, the present values for lymphedema/normal are probably slightly low, especially with a longer duration.

Second, these patients are simply the ones who entered the clinic. It is possible that there are many other patients with only minor amounts of lymphedema, who did not think treatment was worth the bother. After all, C.P.T. is expensive in both time and money. It is also possible that minor lymphedemas may not be correctly diagnosed and, if diagnosed, health workers and patients are less likely to pursue relatively obscure treatments (C.P.T. and benzopyrones) which are only just becoming known. Hence this series is somewhat biased against patients with minor lymphedema.

Third, the measurements are those before patient treatment, i.e. with untreated patients. However, the term "untreated" must be understood in context. Many patients with lymphedema endure many "treatments"—including inadequate non-operative measures (6,7), diuretic drugs and ineffective operations. Some of these patients had received such treatments. However in each instance, such treatment had failed — otherwise the patient would not have come for C.P.T. As a result, our findings exclude patients treated by other therapy that was effective. But how often such other therapy is effective is unclear (6,7). For the purposes of this article, it is enough to note that such therapy, at least in these patients, had already failed. Conceivably, such alternative therapy succeeded to a modest extent and that therefore the amount of lymphedema in truly untreated patients would be even worse than we report.

Whereas these theoretical possibilities may be valid points, they tend to cancel one another. The present series is therefore a relatively unbiased sample of those less-than-trivial, poorly-treated or untreated, lymphedema patients in Western populations who do not have an active malignancy. The present data, in that sense, are not ideal and fall short of what could be achieved by prospective studies of untreated patients over many years. Nonetheless, it is not practical or ethical to deny treatment, nor is it desirable to wait 30 to 50 years for such data. The series is presented recognizing that although not ideal, none better is available. It provides a factual basis for previous assumptions about patients with lymphedema.

Comparisons with Previous Data

Patients treated with a placebo in a number of trials have been followed for six months to more than two years (1). These periods are much shorter than the duration provided here. The alterations during the previous observation periods were expressed as percentages of the initial volumes (5).

For the present data, if one uses the value at year = 0 for the initial lymphedema, the present slopes yield differences / initial volumes of: 1.36% (0.276%) for the arms, 0.53% (0.159%) for the combined legs, 0.51% (0.161%) for the secondary legs and 0.55% (0.310%) for the primary legs. The Standard Errors (in parentheses) were obtained using large number theory (8). These values are considerably less than that given for similar patients (1): 15.8% (16.1%) for 57 arms, 4.56% (12.7%) for 35 legs. They are, however, not significantly different because the Standard Errors of the previous groups were large — probably because of fewer numbers of patients, because they were combined from different trials, and because of the use of water-displacement volumetry. The latter technique often measures only a part of the swollen limb, although usually its most edematous part (5). When interpreting the present data it should be recognized that the whole limb was measured. Thus the amount of edema was often "diluted" by including non-edematous portions of the swollen limb.

What the Present Data Signify

With time, the amount of lymphedema increases and patients progress from a lower Grade to a higher Grade of lymphedema. Even primary lymphedema progresses in Grade, although more slowly than secondary. These increases in amounts of edema and in

Grade of lymphedema, which have long been assumed, have now been verified. Numerical estimates are now possible of the probable outcome of a lymphedematous limb over subsequent years.

Postmastectomy lymphedema increases in size at about three times the rate of either primary or secondary lymphedema of the leg. Yet the arm takes about the same time to reach each Grade as does a secondary leg. By contrast, the time taken to reach each Grade by a primary leg is about three times longer.

The corollary of the findings is also shown. Thus, for primary lymphedema of the leg, each Grade not only took longer to develop but had a greater amount of lymphedema/normal than the same Grade of secondary lymphedema of the leg. Thus, primary lymphedema of the leg is probably less fibrotic, for a given amount of edema, than is secondary lymphedema. This presumed lesser amount of interstitial fibrosis permits more edema to form (9). It accords with histopathological differences between primary and secondary lymphedema (R. Cluzan, M.D., personal communication, 1982): primary lymphedema had far less fibrosis and much more lipid than secondary. Why these findings should be so is conjectural. Perhaps greater lymphatic transport remaining in primary lymphedema renders the accumulated proteins in the tissues less stagnant, with therefore a lesser tendency to chronic inflammation and fibrosis (2).

The Use of this Data

These data only show means; an individual may vary considerably from the average and may not conform to the slope of the regression lines. It seems likely that a patient with, for instance, half the mean lymphedema (for type and Grade) at 10 years would still have about half the mean at 30 years; however this is still a supposition. Only following untreated patients for many years could substantiate such a presumption.

The present data, nonetheless, confirm that untreated lymphedema increases in both size and Grade over many years, and provide a reasonable mean amount for these values. They can therefore be provided for patients to indicate the likely course of limb lymphedema if left untreated, and thereby persuade them to undergo treatment and to be compliant with therapy. How successful the various treatments are in altering this anticipated course is not yet available. Reliable long-term data are still lacking for treatments which show good results over one or two years, because these treatments have not been carried out long enough for such data to be available.

Another use for the data is a medico-legal one. Lymphedema has become the subject of claims for compensation, from trauma or iatrogenic injury, and these provide guidelines from which to estimate the likely course of limb lymphedema.

Finally, both private and governmental health regulations, as well as the judiciary, need such data so that the human cost of not treating lymphedema can be compared with the financial costs of treatment. Whereas the ultimate long-term results of the optimal treatment is as yet unknown, at least the one- and two-year benefits are documented. If, as appears likely, these benefits continue or even increase, the disability from neglecting or leaving lymphedema untreated makes the cost of such treatment small by comparison.

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APPENDIX

The various linear regressions of the amount of edema against Duration all have large and significant intercepts for when Duration=0. This finding suggests that the edema increases rapidly at first and then thereafter only slowly. This observation is also supported by taking the intercept at Duration=0 as equal to the normal limb (100%). Then, the 82 arms with a duration of less than 1 year increased by 40.6% of normal (S.E. 4.89%); from 1 to 5 years, 89 arms increased by 12.4% (1.07%) per year; from 5 to 30 years, 60 arms increased by 4.22% (0.356%). The p value for the differences of these slopes between the 0-1 and 1-5 year intervals and between 1-5 and 5-30 year intervals was 10^{-8}. For the entire 0-30 years, the 231 arms increased by 5.08% (0.381%) of normal per year.

Similarly taking the intercept equal to the normal limb, the 32 legs (primary plus secondary) with a duration of less than 1 year increased by 27.5% (S.E. 6.93%); from 1 to 5 years this increase was 8.40% (1.27%) per year for 39 legs; from 5 to 50 years it was 1.59% (0.180% per year for 106 legs. The p-values for the differences between the first and second and the second and third of these slopes were 0.004 and 10^{-13}, respectively. For the entire 0 to 50 years, the 177 legs increased by 1.64% (0.161%) per year

Logarithmic equations, L/N=A+B ln(Duration), can be used to represent all values. For the arms, for 0 to 30 years, A=136.1%, and B=5.75%. For all legs, for 0 to 50 years, A=123.2% and B=5.19%. However, the two sets of linear regression lines given earlier (with their intercepts free to vary or with their intercepts=100%) are almost as informative and are much easier to apply. Nonetheless, it should be recognized that lymphedema increases rapidly at first and that most linear regressions only represent lymphedema after several years have elapsed. This phenomenon is probably explained by an initial rapid stretching of the skin and interstitial tissues with edema fluid followed by a more gradual increase once the initial interstitial compliance is completely utilized or overcome. Thereafter, the tissues gradually expand because of matrix remodeling.