Conclusion. From the data at hand it would seem that the highly unsaturated fatty acids of cod liver oil can be used by fat deficient rats for growth, but that their scaly skin is cured only by linolic and linolenic acids, which, apparently are lacking in cod liver oil.

It may prove possible to isolate a fat which will cure the skin without producing growth, as indicated by Sinclair's experience.

The fat deficiency may therefore resolve itself into 2 factors. It so happens that linolic and linolenic acids seem to relieve both growth and skin abnormalities. The relative values of several fatty acids in the prevention of the above symptoms as well as kidney degeneration is being included in our present studies.

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Individual Variation in Serum Calcium in Normal Men and Women.*

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Since the work of Bell[1] many investigators have studied the blood calcium level in relation to menstruation. The results of these investigations have been contradictory. Watchorn[2], Close and Osman[3], Allen and Goldthorpe[4], Spiegler[5], and others have concluded that there is very little or no change in the blood calcium in relation to the menstrual cycle. Sharlit et al[6] and Matters[7] report a premenstrual rise in blood calcium and a menstrual fall in the calcium level. Okey et al[8] state that "while the changes in the concentration of serum calcium at any phase of the monthly cycle are not outstanding, there is some tendency to frequency of low values for

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1 Bell, Blair W., *Proc. Royal Soc. Med.*, 1908, **1**, 291.

2 Watchorn, Elsie, *Brit. J. Exp. Path.*, 1926, **7**, 120.

3 Close, H. G., and Osman, A. A., *Biochem. J.*, 1928, **22**, 1544.

4 Allen, E., and Goldthorpe, H. C., *Am. J. Obs. and Gyn.*, 1929, **17**, 789.

5 Spiegler, R., *Arch. Gyn.*, 1930, **143**, 201.

6 Sharlit, H., Corscaden, J. A., and Lyle, W. G., *Arch. Int. Med.*, 1927, **39**, 780.

7 Matters, R. F., *Australian J. Exp. Biol. and Med. Sc.*, Part 2, 1929, **6**, 119.

8 Okey, R., Stewart, J. M., and Greenwood, M. L., *J. Biol. Chem.*, 1930, **87**, 91.

calcium a few days previous to the onset of menstruation and to frequency of higher values from the 8th to the 15th days following the onset of menstrual bleeding."

With the exception of the work of Okey et al[8], these findings have been based upon either the study of very small groups of individuals or upon blood calcium determinations taken not more than 3 or 4 times during a menstrual cycle.

Experimental work done on lower animals shows that the blood calcium level is definitely affected by the reproductive system. Riddle and Reinhart[9] found a tremendous increase in calcium in the blood of birds prior to ovulation. Mirvish and Bosman[10] have produced a decrease of 2 to 3 mg. in the plasma calcium in both rabbits and human beings by injecting ovarian follicular and corpus luteum extracts.

The present study was undertaken in an effort to determine standards of blood calcium in relation to the menstrual cycle in women with normal menstrual periods in order that we might have some basis for comparison in a study being made on a group of women with dysmenorrhea. As a control the blood calcium levels and variations in a group of men were studied.

Serum calcium determinations were made in duplicate on 14 women and 11 men 3 times a week for 4 consecutive weeks. Determinations were made on 3 of the 14 women for a period of 8 weeks, giving a total of 17 weekly readings on women. In a few instances, more than 3 determinations were made in one week and in an occasional instance only 2 were made. In each case, the blood was drawn between 8:30 and 9:30 A.M. The subjects were all healthy individuals. No attempt was made to determine the type of diet the individual was eating. The determinations were all made during the months of November and December, 1930, and January, February, and March, 1931.

The determinations of serum calcium were made by one of us (E. M. G.) using the Clark-Collip[11] modification of the Kramer-Tisdall[12] method. A total of 132 readings were made on the group of men and 157 on the group of women.

Tables I and II present the range in the amount of serum calcium and the mean of the 12 serum calcium determinations for each individual in the group of men and women respectively.

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[9] Riddle, O., and Reinhart, W. H., *Am. J. Physiol.*, 1926, **76**, 660.

[10] Mirvish, L., and Bosman, L. P., *Quar. J. Exp. Physiol.*, 1927, **18**, 11, 19.

[11] Clark, E. P., and Collip, J. B., *J. Biol. Chem.*, 1925, **63**, 461.

[12] Kramer, B., and Tisdall, F. F., *J. Biol. Chem.*, 1921, **47**, 475.

TABLE I.
Serum Calcium Variations in a Group of 11 Men.
Tri-weekly determinations for 4 weeks. Of 12 determinations.

Case No.	Age	Low	High	Mean	P. E.	S. D.
1	36	9.69	11.01	10.39	±0.0703	0.361
2	28	10.08	11.67	10.95	±0.0547	0.281
3	28	9.80	10.54	10.15	±0.0355	0.1824
4	31	9.77	11.23	10.29	±0.0773	0.3968
5	32	9.89	10.38	10.14	±0.0327	0.1679
6	38	9.85	10.68	10.24	±0.0434	0.2137
7	25	9.99	10.90	10.45	±0.0527	0.2592
8	27	10.32	11.05	10.69	±0.0592	0.3039
9	43	9.75	10.31	10.00	±0.0332	0.1634
10	39	9.85	10.66	10.17	±0.0661	0.3392
11	24	10.03	10.74	10.24	±0.0461	0.2051
Means	31.91	9.91	10.83	10.31		0.2612
		Range .92				±0.0532

TABLE II.
Serum Calcium Variations in a Group of 17 Women.
Tri-weekly determinations for 4 weeks. Of 12 determinations.

Case No.	Age	Low	High	Mean	P. E.	S. D.
1	40	9.34	10.43	9.91	±0.0838	0.3929
2	22	9.68	10.43	10.10	±0.0520	0.2441
3	25	9.53	11.14	10.08	±0.0868	0.4261
4	27	9.30	10.25	9.70	±0.0655	0.3072
5	24	9.28	10.39	9.75	±0.0794	0.3532
6	23	9.39	10.35	9.91	±0.0582	0.2860
7	28	9.52	10.31	9.93	±0.0466	0.2289
8	30	9.54	10.31	9.90	±0.0463	0.2170
9	29	9.74	10.55	10.15	±0.0568	0.2664
10	35	9.44	10.35	9.88	±0.0607	0.2701
*11 (7)	28	9.29	10.74	10.12	±0.1093	0.4570
*12 (3)	25	9.35	11.25	10.53	±0.1167	0.5193
*13 (10)	35	9.41	10.62	10.01	±0.0948	0.3712
14	24	9.00	10.86	10.00	±0.1292	0.5405
15	23	9.80	11.19	10.31	±0.0893	0.3974
16	34	9.57	10.59	10.03	±0.0936	0.3914
17	21	9.37	10.33	9.96	±0.0882	0.3220
Means	27.82	9.44	10.59	10.01		0.3523
		Range 1.15				±0.0576

*Duplicate cases.

The mean age of the men was 31.91 years and that of the women was 27.82 years.

The mean serum calcium for the entire group of men was 10.31 mg. and for the group of women 10.01 mg. The average calcium level for the women was 0.30±0.0282 mg. lower than the level for the men, a difference that is of definite significance. Although it is generally stated that there is little variation in the blood calcium

level between the sexes, in these groups the men showed a consistently higher level of serum calcium than the women.

The variability or range of calcium level is distinctly greater for the women than for the men, the mean range for the women being 1.15 mg. and for the men 0.92 mg. Nine of the 17 women show a range of more than 1 mg. while only 3 of the 11 men show such a range. This greater variation in calcium levels in women was also observed by Okey.[8]

TABLE III.
Calcium Level in Relation to Menstrual Cycle.

Week	Mean mg. Calcium	P. E.	S. D.	Difference of Means
Rest	10.05	±0.0419	0.3349	0.07±0.0640
Pre-Menstrual	10.12	±0.0484	0.4485	0.19±0.0616
Menstrual	9.93	±0.0388	0.3905	0.04±0.0591
Post-Menstrual	9.97	±0.0447	0.4090	

In order to compare the calcium levels at various phases in the menstrual cycle, the cycle was divided into 4 weekly periods hereafter designated as the rest period, the pre-menstrual period, the menstrual period and the post-menstrual period. The menstrual period included the calcium determinations made on the first day of the period and during the following week. Because of the daily variation in calcium levels, the mean readings for each week of these menstrual phases were computed as it was believed they would give better data for comparison.

Table III presents the mean serum calcium level for each period in the menstrual cycle. The highest calcium level is 10.12±0.0484 mg. in the pre-menstrual period and the lowest of 9.93±0.0388 mg. in the menstrual week. The difference of 0.19±0.0616 mg. is probably significant. It is to be noted also that the mean calcium levels for each week of the menstrual cycle, if plotted, would form a fairly regular curve.

TABLE IV.
Mean Serum Calcium Values for Men in Chronological Order.

	Mean Calcium	P. E.	S. D.	Difference of Means
First Week	10.16	0.0301	0.2961	0.13±0.0481
Second Week	10.29	0.0380	0.3471	0.01±0.0509
Third Week	10.30	0.0368	0.3140	0.25±0.0648
Fourth Week	10.55	0.0532	0.4322	0.39±0.060

Table IV presents the mean serum calcium for each week of the 4 weeks chronologically for men. The variation in serum calcium

from week to week is greater than that for women arranged according to the menstrual cycle. With the men there is found to be a definite upward trend from week to week. This was not found in women when the weekly mean calcium values were computed on a chronological basis disregarding the menstrual cycle. However, the fact that with the men there is this definite increase from week to week and the fact that it is recognized that there is a seasonal variation in blood calcium make us consider the possibility that normal chronological variations may affect the values given in Table III although in the data we have, this effect is not evident.

Since the lowest weekly mean of serum calcium in women occurred during the menstrual week and since there was no comparable biological week in the men, it was decided to tabulate the weekly

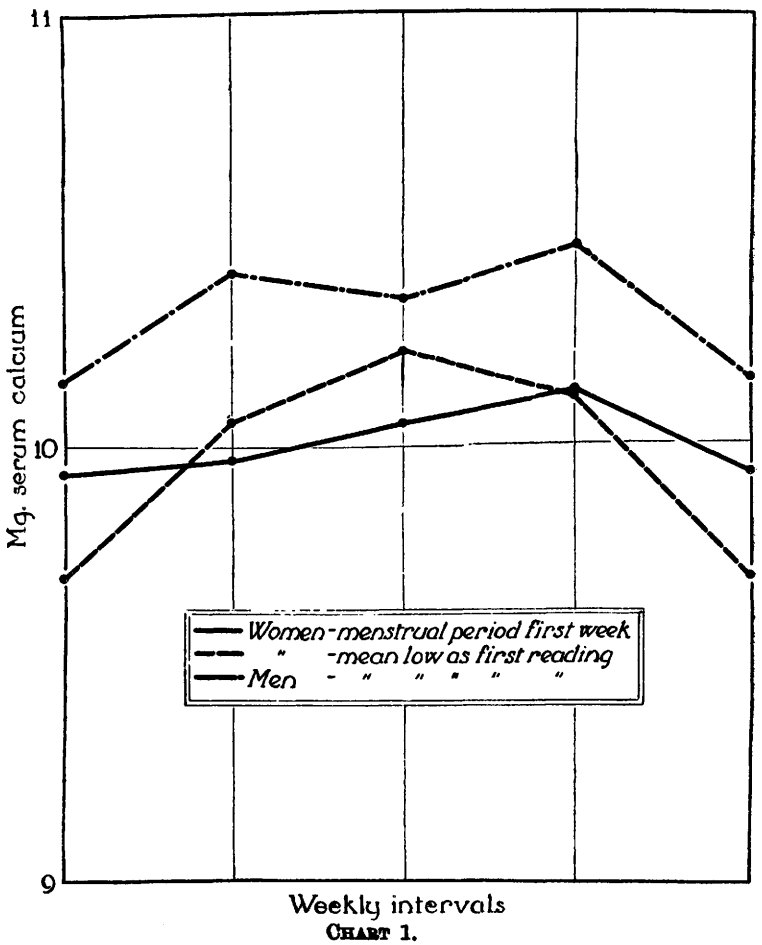

CHART 1.

mean calcium values for each individual in the 2 groups, putting the lowest mean weekly value as the first reading and the following 3 weekly mean values in sequence. We felt this method would give a better method for comparison of the men and women. These data are presented in Tables V and VI.

This treatment of the data further substantiates the finding previously given that the serum calcium level in men is higher than in women, since in each, the mean value for men is higher than that for women.

Table VI shows that in 12 of the 17 individual weekly mean calcium readings, the lowest value occurs in the menstrual or post-menstrual week. In 5 of the 17 cases the highest value occurs in the pre-menstrual week.

The mean serum calcium values for the entire group of men (Table V) starting with the low week shows an irregular variation from week to week. With the women (Table VI) it is seen that the weekly variation assumes the same type of regular curve as when the values for women were grouped according to the menstrual week. This is shown graphically in Chart I.

From this evidence it seems probable that women show a cyclic variation in blood calcium while men do not. It is appreciated, however, that it will be necessary to carry a group of women through more than one menstrual cycle before this supposition can be proved.

Summary. From a determination of serum calcium on 17 women and 11 men at tri-weekly periods for 4 weeks, the following is found:

1. The serum calcium level for women is definitely lower than

TABLE V.
Serum Calcium Variations in Men. Comparison of Weekly Averages.

Case No.	Low	Second	Third	Fourth
1	10.21	10.24	10.79	10.33
2	10.51	10.99	10.79	11.20
3	10.07	10.25	10.15	10.14
4	9.94	10.28	10.16	10.78
5	9.94	10.22	10.35	10.07
6	10.12	10.28	10.20	10.31
7	10.27	10.66	10.28	10.59
8	10.53	10.85	10.57	10.82
9	9.90	9.95	10.10	10.08
10	10.01	10.47	10.11	10.08
11	10.07	10.20	10.23	10.55
Means	10.14	10.40	10.34	10.45

TABLE VI.
Serum Calcium Variations in Women. Comparison of Weekly Averages.

Case No.	Low	Second	Third	Fourth
1	9.50*	9.61	10.29	10.28
2	10.00	10.29	10.04*	10.10
3	9.60	10.03	10.43*	9.97
4	9.32	9.78*	9.88	9.89
5	9.49*	9.66	9.61	10.37
6	9.51*	10.03	10.17	9.97
7	9.75	10.15	9.94	9.80*
8	9.81*	9.84	10.05	9.98
9	9.95	10.17	10.50	10.10*
10	9.72	9.80	10.02	10.06*
11	9.84	10.04	10.99	10.11*
12	9.97	10.28	10.96	10.68
13	9.74	10.62	10.19	9.80*
14	9.55	9.79*	10.47	10.56
15	10.04*	10.75	10.50	10.12
16	9.76*	10.35	9.92	10.09
17	9.37	9.99	10.24*	9.94
Means	9.70	10.07	10.22	10.11

*Menstrual week.

for men. 2. There is a greater daily variation in the serum calcium for women than for men as well as a greater absolute range in calcium levels. 3. There is a tendency for the serum calcium to be highest in the pre-menstrual period and lowest in the menstrual period. This is evident in the mean serum calcium values for each week in the menstrual cycle. The fact that in 12 of 17 individuals, the lowest weekly mean serum calcium occurred in the menstrual or post-menstrual period further substantiates the finding that there is a fall in blood calcium following menstruation. 4. In women there seems to be a regular cyclic curve of blood calcium level which is not present in men.

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Variations in Plasma Phosphatase, P., Ca., and Glucose Following Administration of Glucose and Calcium Glycerophosphate.

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In the course of studies on the calcium and phosphorus metabolism of children suffering from various disorders, it was observed that the level of plasma phosphatase tended to be lower than normal