CALCIUM METABOLISM STUDIES ON THE NATURE AND ROLE OF THE ACTIVATORS: RESEARCHES ON FUNDAMENTALS FOR THE PREVENTION OF DENTAL DISEASE*

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PROBABLY no subject which has engaged the interest of the dental profession of today or of any other period promises so much help to humanity as does the newer knowledge of calcium metabolism. That proper calcium utilization is important because of its effect on resistance and susceptibility to infection as well as for tooth and bone formation will be part of the evidence presented in this paper.

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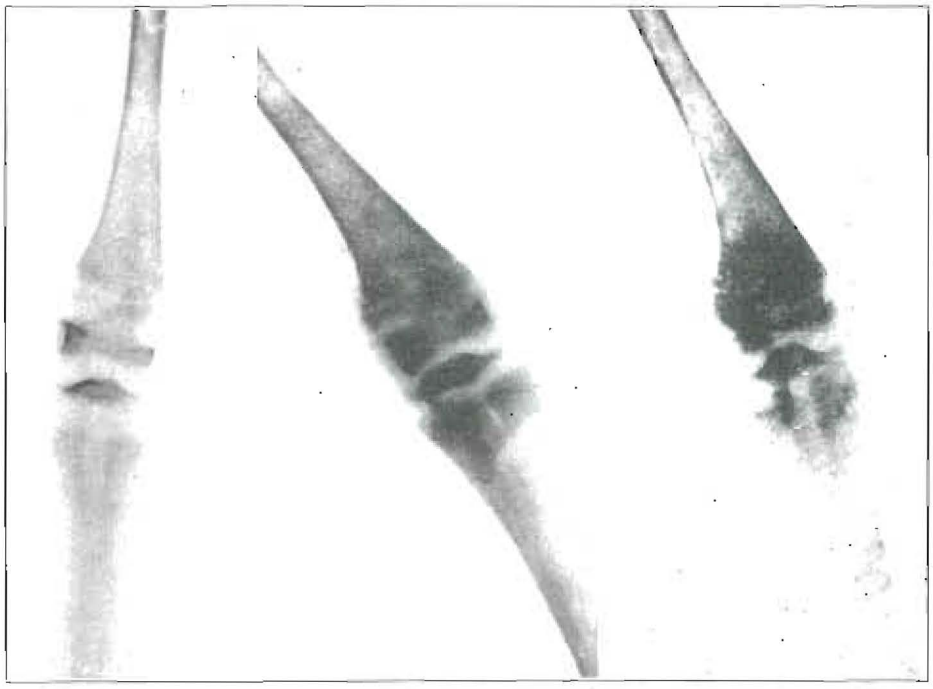
The data available clearly indicate that calcium anabolism and katabolism are dependent in part on chemical substances which must be present in the system and which are derived chiefly from the direct and indirect effects of radiant energy on plant and animal tissue. These substances are usually spoken of as vitamins. They have many characteristics, as they relate to constructive and destructive calcium metabolism, which have led me to think of them and speak of them as activators. I have accordingly spent much effort in recent

years in the study of the nature of the activators for calcium metaholism.

In a paper read before this Association in November, 1924,[1] I reported that when blood was withdrawn from an animal and the serum exposed to radiant energy from the sun or other source of ultraviolet light, and the serum so treated was injected intravenously into the same animal, there was a marked rise in the calcium, which was evident in two hours. I showed further that while an exposure of fifteen minutes raised the blood calcium, one of sixty minutes depressed it. I further showed that the serum that was capable of doing this was capable of making a photographic impression on a sensitive plate. Those studies also reported that many other substances were found to be affected—olive oil but slightly, cod-liver oil very actively, by this treatment. I also reported treatment of cases with oil specially exposed to radiant energy.



A B C

Fig. 1.—Progressive calcification in knee of a chicken in which leg weakness had been produced by a deficiency diet and lack of sunshine, treated with cod-liver oil topically and internally as indicated. *A*, deficiency diet plus sunshine through Cleveland smoke. *B*, twenty days later, after cod-liver oil had been rubbed on the leg. *C*, six days later, with cod-liver oil added to diet.

1. Price, W. A.: Fundamentals Suggested by Recent Researches for Diagnosis, Prognosis and Treatment of Dental Focal Infections, J. A. D. A., 12:641 (June) 1925.

In a paper read before this Association in Louisville in September, 1925,[2] I presented data on the rôle of parathyroids in calcium metabolism and on the relation of direct sunlight, screened sunlight, cod-liver oil, cod-liver oil activated, cholesterol, raw and activated, parathyroid extract and ultraviolet radiation to the development of several large groups of chicks, including many data on blood calcium studies. A significant new observation was that the rubbing of raw and activated cod liver oil (by "activated" I mean exposed to radiant energy) on the chicks both restored growth and healed rickets-like lesions of the bones. Even more striking in this connection and of great significance was the evidence that, whereas the lymph has ordinarily a calcium level approximately half that of the blood and prohably all or nearly all diffusible calcium, the topical application of raw and activated cod-liver oil not only raised the level of the blood caleium but also raised the local level of the lymph calcium to approximately four times that of normal lymph or twice that of blood of the same animal, instead of half. Since radiant energy applied to the cod-liver oil made it possible for oil so treated to have a distinctly greater effect than raw cod-liver oil, it seemed evident that the oil was the carrier of a force produced by tbe radiant energy.

In a paper read before the National Academy of Sciences in Washington, April, 1926,[3] I presented data showing that there was a progressive increase in the capacity of cod-liver oil to receive and transfer radiant energy with progressive exposure through a limited range, as evidenced both by animal experimentation and by physical and by chemical tests, and, further, that the disturbances expressing themselves in part as dental caries, especially in childhood and pregnancy, were directly related and in a marked degree subject to control or marked improvement by treatment with raw and activated cod-liver oil, with and without calcium lactate, as conditions indicated. A negative calcium balance (by which I mean here serum $Ca \times P = 28$ less than 40) indieating the stress of pregnancy, was shown to be changed from minus 28 to minus 7 in a few weeks.

The importance of preventing avoidable obstructions to radiant energy was supported by data in a paper read before the Second Chemical Equipment and Process Engineering Exposition in Cleveland, May, 1926.[4] Chickens on deficieney diets were not able to get enough energy through the Cleveland smoke to maintain calcium metabolism and went down with leg weakness and serious bone and tissue disturbances. It was found possible to put some of them back on their feet either by rubbing with raw or activated cod-liver oil or by exposure to radiant energy from an artificial source, or by feeding it to them.

2. Price, W. A.: Newer Knowledge of Calcium Metabolism in Health and Disease, with Special Consideration of Calcification and Decalcificarion Processes, Including Focal Infection Phenomena, J. A. D. A., 13:1865 (Dec.) 1926.

3. Price, W. A.: Calcium Metabolism Studies. (a) Raising of Serum Calcium by Topical Applications of Raw and Activated Cod Liver Oil. (b) Disturbances Associated with the Active Dental Caries of Childhood and Pregnancy, Am. J. Dis. Child., 33:78-95 (Jan.) 1927.

4. Price, W. A.: Relation of Light to Life and Health, Indus. Eng. Chem., 18:679 (July) 1926.

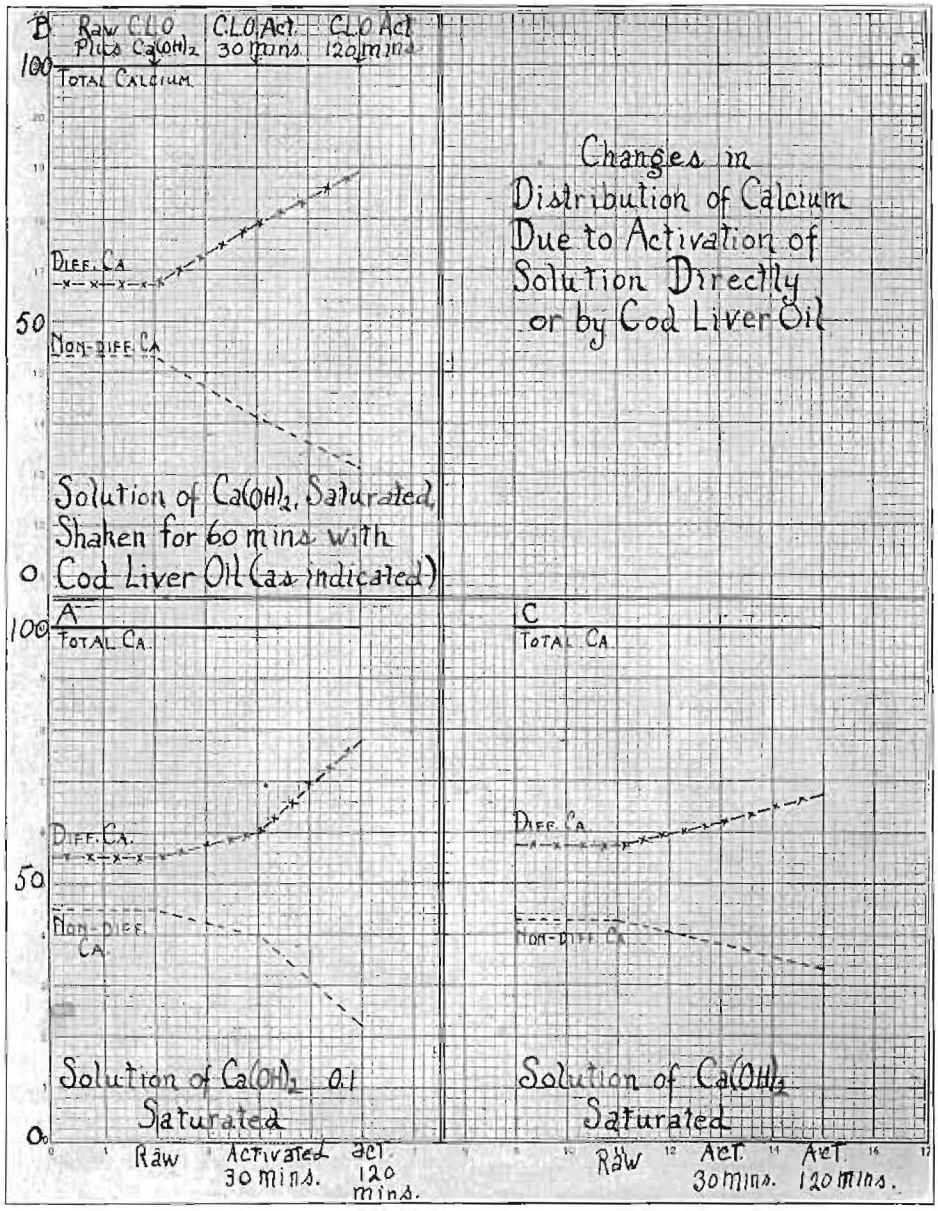


Fig. 2.—Effect of activation on diffusibility of calcium in calcium hydrate.

The changes produced in the knee joint of a chicken treated as indicated when it had gone down are shown in Figure 1. Note the marked effect of topical applications of cod-liver oil as well as from feeding it, and in a relatively short time.

Extensive studies have been made on the distribution of calcium in the blood

and of the nature of the bond between calcium and proteins. These were reported in an extended communication read before the Seventh International Dental Congress at Philadelphia, in August, 1926.[5] Three principal calcium factors were studied, namely, total, diffusible and nondiffusible. The data presented indicated that not only the level of total calcium, but also its distribution as diffusible and nondiffusible could be greatly influenced in a few hours by many procedures, among which were the administration of calcium lactate doses. A great irregularity or inconstancy was found in different samples of cholesterol. In the same paper, I reported studies on milk as a source of activators. A special study that was reported in that communication included the repeated blood and milk chemical analyses of a group of sixteen cows, extending over a period of eight and one-half months. The milk of cows under treatment by different methods produced quite different effects on different groups of chicks maintained on a similar deficient diet. The total milk calcium, which

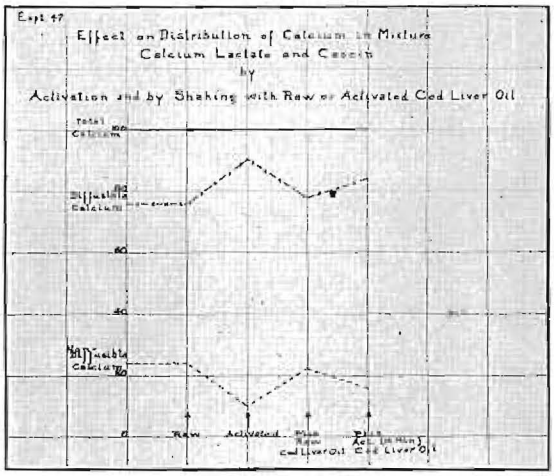


Fig. 3.—Effect of activation on diffusibility of calcium in calcium lactate and casein solution.

alone, cod-liver oil alone, cholesterol alone and combinations of these substances. The remarkable fact that the diffusible and nondiffusible calcium levels could be made to cross each other five times in a few hours was demonstrated. The effect of administering cholesterol that had been activated was shown to be very marked, and therefore made possible treatment with very small

5. Price, W. A.: Calcium, Its Activation, Utilization and Metabolism, J. A. D. A., 14: 729 (April) 1928.

normally showed a progressive decline, was in several instances caused to increase, notwithstanding the double load of lactation and gestation.

For several years, I have made blood chemical analyses a part of my diagnostic procedure in the study of the relation of dental infection to systemic disturbance. These analyses now total more than 1,500 and include many phases of calcium and phosphorus in cells, serum and plasma. Much evidence has been accumulating which indicates that such fac-

tors as total calcium may be misleading. The importance of the activators and the need of detailed information regarding them have been emphasized by each new step in these researches, both clinical and biochemical.

An importanr advance in the study of this problem seems to have been the use of biochemical reactions in test tubes as well as by the much less rapid procedure of animal reactions. Just as the administration of cod-liver oil or cholesterol or its topical application will shift the diffusibility of the calcium of the blood and two hours. Note the progressive increase in diffusible calcium. The first one saturated, *B,* was shaken with cod-liver oil that had been activated thirty minutes and two hours. Note the marked increase in the diffusibility of the calcium as a result of the activation of the cod-liver oil. The second one, series *A,* is one-tenth saturated and otherwise like tbe upper series. Note the greater influence on the diffusible calcium with this amount of dilution. It is significant that the effect is the same from treating milk as when treating a mixture of cal-

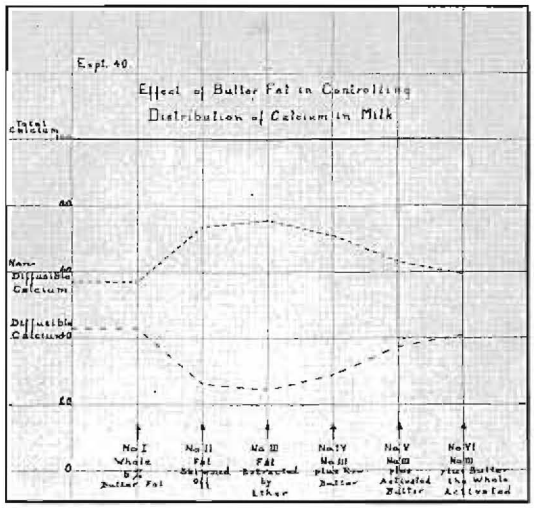


Fig. 4.—Influence of butter fat on the diffusibility of the calcium in milk.

of an animal, it has been shown by these researches that they can produce this same shift when applied to the serum of the animal in a test tube, or similarly to many organic and inorganic solutions.

A typical illustration will be found in Figure 2, which shows the effect on the distribution of calcium in three solutions of calcium hydrate by activation directly and by being shaken with cod-liver oil. The last one, *C,* shows a saturated solution, activated directly for thirty minutes cium lactate and casein wirh each direct radiation, raw cod-liver oil and activated cod-liver oil and that raw cod-liver oil acts differently from activated. This effect on calcium lactate and casein is shown in Figure 3. The cod-liver oil does not appreciably combine with the mixture, and no loss can be detected in its weight. In the figures, the dash and cross lines represent diffusible calcium; the series of dashes, nondiffusible calcium, and the solid line, the total cal-

cium. Note that the activation increases the diffusibility, raw cod-liver oil decreases it and activated cod-liver oil sends it up again.

The equilibrium ratio between diffusible and nondiffusible calcium at the beginning is shown at 76 per cent and 24 per cent. Exposing the mixture to ultraviolet radiation increased the diffusible calcium to 90 per cent and reduced the nondiffusible to 10 per cent. Shaking with raw cod-liver oil reduced the diffusible calcium to 78 per cent and increased the nondiffusible to 22 per cent. Shaking with activated cod-liver oil having fifteen minutes' activation increased the diffusible calcium to 84 per cent and reduced the nondiffusible to 16 per cent. Many biologic substances besides milk products and serum have been so studied, and it has been found that, in general, the same effect is produced on the distribution of the calcium, and indeed it now seems abundantly demonstrated that these effects are usually produced in animals and individuals by treatment such as exposure to ultraviolet radiation or the administration of raw or activated cod-liver oil; i. e., raw cod liver oil usually decreases diffusibility, while activated cod-liver oil and irradiation increase it. From my large series of blood chemical studies with regard to calcium levels, I find that normally there seems to be about 5 per cent more diffusible than nondiffusible calcium; that is, with a total serum calcium of 10 mg., a little more than five should be diffusible and a little less than five nondiffusible. A variation of 2 or 3 mg. in either direction seems usually to express itself with distinct physical disturbances. Evidence that I have accumulated in support of this observation will be published elsewhere.

Fig. 5.—Specially constructed spectrograph for studying the influence of different bands of the spectrum in biologic reactions.

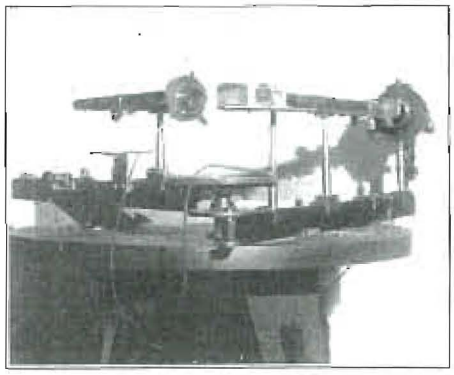


Fig. 6.—Spectroscope with complete optical system of fluorite, nsing three prisms in train.

Since one of the principal sources of activators for calcium metabolism is to be found in the dairy products, extended studies have been made of milk and milk products. Some of the activators with which we are chiefly concerned are carried in the butter fat and are well demonstrated by the data given in Figure 4. In the whole milk, the diffusible calcium is at 44 and the nondiffusible calcium at 56. After skimming, the diffusible lowered to 26, with the nondiffusible at 74. When the remaining fat was extracted with ether, the diffusible calcium lowered

a little, to 24. On the addition of raw butter, the diffusible increased to 30. Adding activated butter raised it to 38, and on activating the mixture after adding raw butter, the diffusible calcium increased to 41. While these accessory food factors have been chiefly studied by animal experimentation, evidence has been presented by Carr and Pierce[6] and by Yoder[7] that chemical tests of vitamins A and D have distinct value and eral others, the need for the exposure of the cow giving the milk to a proper amount and form of radiant energy. I have been able to shift my own diffusible calcium and nondiffusible calcium through considerable range, this depending on whether I took raw or activated cod-liver oil, and easily too far.

Little consideration has been given regarding the amount of ultraviolet light from different parts of the spectrum

TABLE 1.—MARKED VARIATIONS IN DIFFUSIBILITY OF CALCIUM OF SERUM OF PATIENTS

Case*	Total Serum Calcium	Cell Calcium	Diffusible Calcium	Non-diffusible Calcium	Inorganic Phosphorus	Calcium Balance
Group I 1504	9.96	1.68	7.32	2.64	2.99	− 10.20
1448	11.25	2.43	6.33	4.82	3.72	+ 1.66
Group II 1425	11.06	2.17	7.61	3.45	2.04	− 17.40
1409	11.23	....	8.03	3.20	2.73	− 9.40
1460	12.54	2.96	8.20	4.34	3.72	+ 6.40
1407	11.34	0.86	8.27	3.07	3.60	+ 0.70
1399	11.25	2.01	8.66	2.59	2.16	− 15.70
Group III 1452	10.49	1.36	3.80	6.69	3.89	+ 0.80
1473	11.16	3.31	3.42	7.74	3.06	− 5.90
1471	12.41	2.95	4.37	8.04	3.86	+ 7.90
1470	10.55	3.01	3.83	6.72	3.43	− 3.80
1404	11.50	1.40	3.41	8.09	1.91	− 18.00

*The serum Ca × P reading from Group I, 1504, through Group III, 1404, was: 29.80; 41.66; 22.60; 30.60; 46.40; 40.70; 24.30; 40.80; 34.10; 47.90; 36.20, and 22.00, respectively.

are parallel to the much more time-consuming method of animal tests. The researches, previously referred to, on the cows indicate, as do the studies of sev- needed or the influence on the diffusibility of the calcium produced by different bands. There is considerable difference in the diffusibility of the blood calcium of individuals studied for the possible relation of dental infections to their disturbed health, as shown in Table 1. The high diffusible calcium of the two in the first group is probably due in part to their having been treated with ultra-

6. Carr, F. H., and Price, E. A.: Determination of Vitamin A from Color Reactions Attributed to Vitamin A, Bioehem. J., 20:497, 1926.

7. Yoder, L.: Relation Between Peroxidation and Antiraehitic Vitamin, J. Biol. Chem., 70:297 (Oct.) 1926.

violet rays from a quartz mercury arc lamp. The second group is composed of cases of high diffusible calcium in which such treatment had not been given, and it would clearly be contraindicated with them. The third group of five have low diffusible calcium, and some means is needed for bringing a more nearly normal equilibrium between diffusible and nondiffusible factors. There is need for the elimination of harmful influences, while the helpful forces of the ultra-

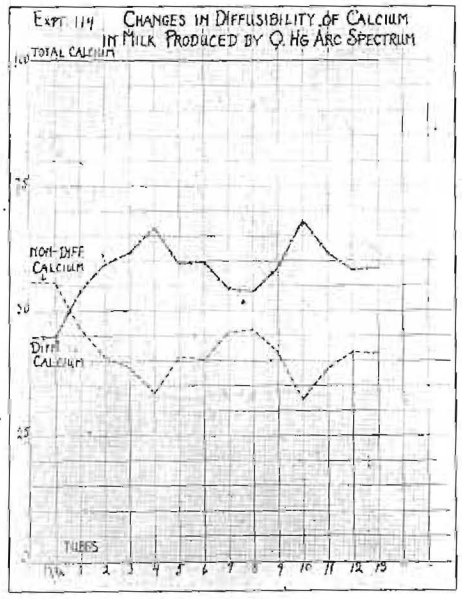


Fig. 7.—Effect of different bands of the spectrum on the diffusibility of calcium in milk. Tubes with lower numbers in infrared, tubes with higher numbers in far ultraviolet.

violet sources of light are retained. To accomplish this, a first requisite is a knowledge of the influence of the different parts of the spectrum in the matter of influencing helpfully calcium metabolism factors. Practically all of the observations that have been reported have included the full range of ultra-violet radiation and, as far as I know, no data are available to date showing the specific effect of the different spectral bands with regard to such factors as diffusibility of calcium, vitamins A and D, inorganic phosphorus and others directly related to calcium metabolism.

In order to accomplish this, I have had constructed a spectrograph, especially designed for testing the effects of the different bands in various of the biologic reactions. For this, I have used

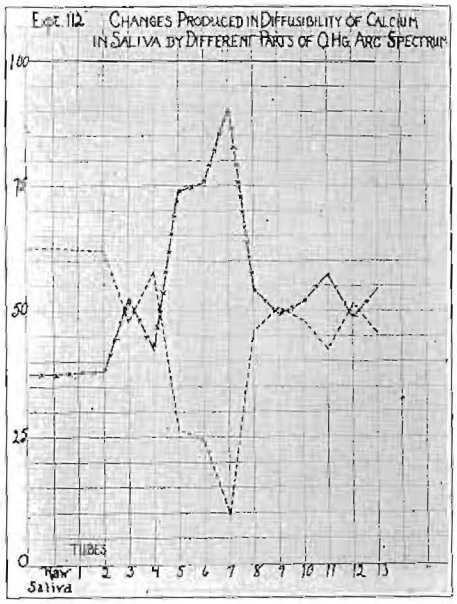


Fig. 8.—Extreme sensitiveness of saliva to change in diffusibility of calcium with different bands of the spectrum.

an all fluorite optical system, with three prisms in train. Of course, glass cannot be used because it does not transmit far into the ultraviolet. Quartz can be used, but it has distinct disadvantages as compared with fluorite. This instrument has also been constructed to record on a clock-driven film spectrums from various sources, such as the sky and artifi-

cial sources, and is provided with attachments for exposing various chemicals in quartz containers to various bands of the spectrum. A great number of new data have come out of this research, indicating that there has been much misapprehension regarding the uniformity of the influence of the different parts of the spectrum from any source which extends into the ultraviolet. Figure 5 shows the instrument as arranged for biospectographic work, and Figure 6, as a spectroscope.

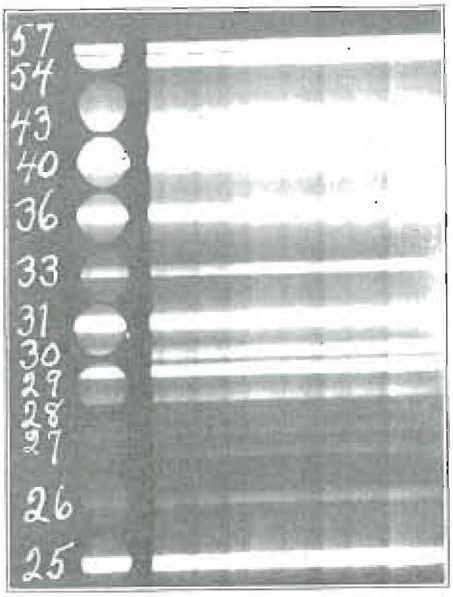


Fig. 9.—The registration of spectral lines in relation to the quartz containers.

An illustration of the striking difference in the photochemical effect of different lines is shown in Figure 7. In this, it will be seen that there is a marked difference in the diffusibility of calcium, depending on the band in the spectrum which is acting on the chemical in question. It is even more strikingly illustrated in Figure 8, which shows the changes produced in the diffusibility of calcium of saliva by exposure to different parts of the mercury arc spectrum. The method of recording the relation of the spectral lines with quartz tubes is shown in Figure 9. It is significant that these chemical actions appear at a considerable distance into the infrared and extend into the ultraviolet beyond the range of sensibility to the panchromatic photographic plate used for this record. These strong lines range from 5,790 to 2,537 angstrom units.

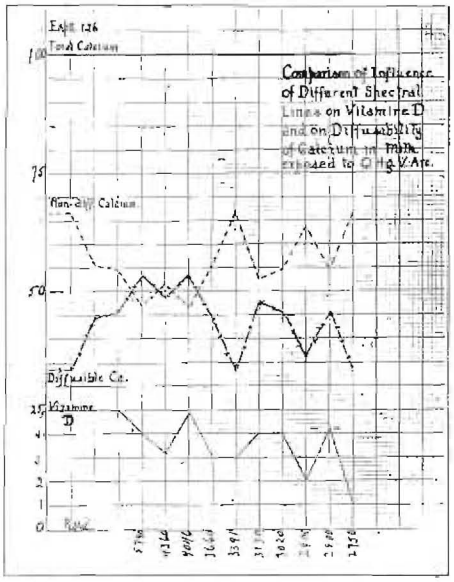


Fig. 10.—Destructive effect of extended exposure to different bands of the spectrum. Destruction of vitamin D follows somewhat the effect on diffusibility of calcium.

A comparison of the influence of different spectral lines on vitamin D and on the diffusibility of calcium in fresh milk, when it is exposed to the quartz mercury-vapor arc, is shown in Figure 10, in which it will be seen not only that there is a great difference, but also that there is, as has been shown in preceding

illustrations, an actual reversal of direction of change. Vitamin D in the milk is apparently destroyed by the short wave lengths in this experiment. Note that the D curve follows in general the diffusibility curve of the calcium. This and many other data in these studies suggest a close relationship that cannot readily be accidental, as though the diffusibility of the calcium may be related to the amount of vitamin D present.

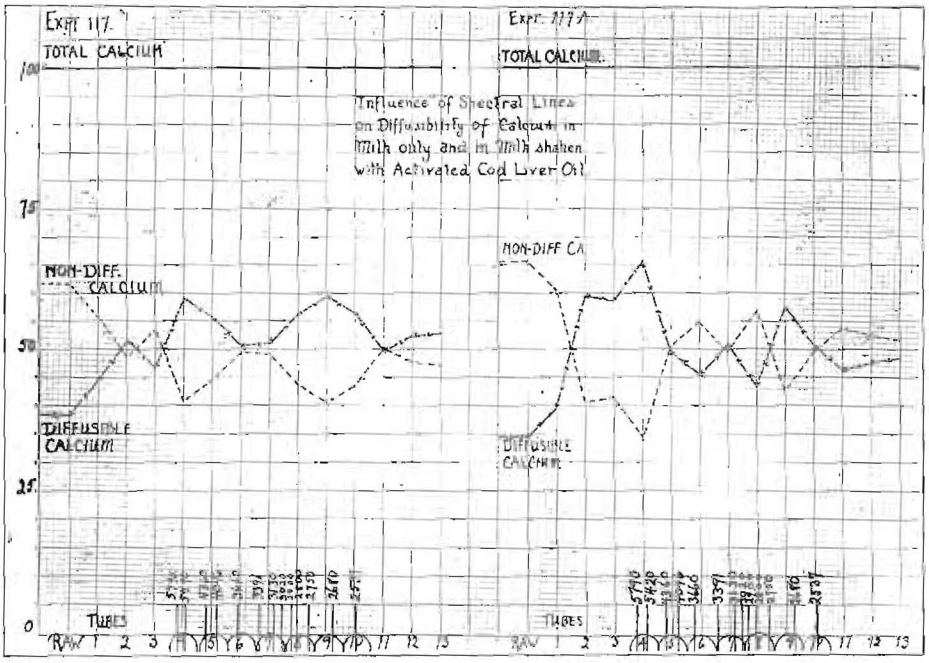


Fig. 11.—Comparison of the effect of various bands of the spectrum whether applied directly to the milk or applied to cod-liver oil, and shaken with milk.

I have previously shown that the diffusibility of calcium in various mediums can be influenced similarly by direct ultraviolet radiation of the mediums and by shaking it with cod-liver oil that had been exposed to ultraviolet radiation. In Figure 11 will be seen the remarkable similarity of the effect of particular bands in the spectrum when applied to milk and to milk shaken with cod-liver oil which has been activated by the various bands of the spectrum of the same source of radiant energy. While the graphs do not completely resemble each other, the effects produced by particular spectral bands are remarkably similar and both show many reversals.

Since only that radiation which is absorbed can produce chemical change, we have by this law a means for studying various substances with regard to both the nature of the changes and the bands of the spectrum which produce them. Figure 12 shows a comparison of the absorption spectrums of two cod-liver oils and of two butters which show marked differences, particularly of the absorption bands 3660A, 3391, 3020-2900. Normal rabbit's blood absorbs completely

bands 4046 and 3391 and partially bands 4360, 3660 and 3130, and all beyond. After activation by ultraviolet radiation, it absorbs completely 3130 and now a new line appears with band 4046 and less absorption of band 4360. This is a position of marked change in the diffusibility of calcium shown in several preceding figures and will be discussed further later.

While many workers have reported results of experimentations with concentrates made from cod-liver oil and other substances, one of the most important

I have been interested to compare the action of this chemical with the foregoing data. In Figure 13 will be seen the influence of different spectral bands on vitamins A and D in cod-liver oil and ergosterol, separately and together. By following the key, the various graphs can be followed. Judged by the chemical tests for vitamins A and D, there is no effect as production of A in ergosterol alone, but some as D. When it is combined with cod-liver oil, there is a marked increase in both A and D over either alone, it having more effect on D

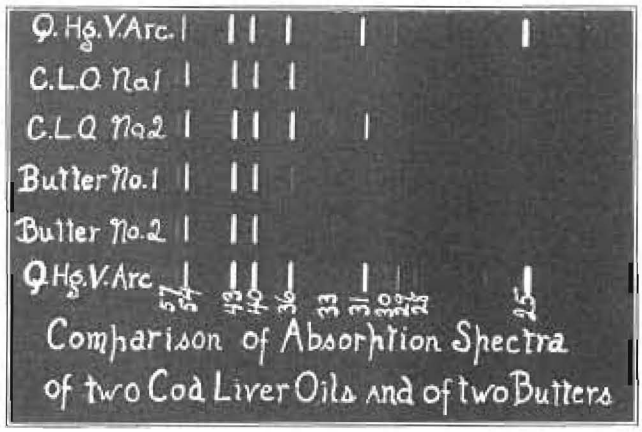


Fig. 12.—Difference in the spectrums of different cod-liver oils and butters.

advances has been made by Rosenheim and Webster.[8] Their evidence seems to identify a sterol known as ergosterol with vitamin D. This substance has been shown to prevent rickets in rats in dosages of one ten thousandth milligram, and to have an absorption for ultraviolet 2,000 times as great as cholesterol for the same bands of the spectrum.

than on A. Here, again, we have a marked difference shown in the effects produced by different bands of the spectrum as regards increasing or decreasing the amount of both A and D vitamins. It is important to note that cod-liver oil alone showed a marked increase in D in quartz tubes bathed in bands 4360 and 3660A.

As a further study of its effect as compared with that of other activators, ergosterol was injected intravenously by dissolving about 1 mg. directly in 1 c.c.

8. Rosenheim, D., and Webster, T. A.: Photochemical Production of Vitamin D from Ergosterol, Lancet, 2:622 (Sept. 17) 1927.

of a rabbit's serum and noting the changes in both the levels of certain chemical constituents and the spectrums of the blood. Figure 14, *A* and *B*, shows the latter, and in *A* also, for comparison, the effect on the serum of activating it before injection, which removed band 3130 and added band 4046. Thirty minutes after injection of this small quantity of ergosterol (less than 1 mg.), blood was taken for testing, and again in two hours and sixteen hours. In both the half-hour and two-hour samples, new bands appeared at about 5100 and 3391. Sixteen hours after injection of the ergosterol, the serum had the same spectrum bands as before the treatment. The chemical changes in the blood accompanying the procedure, shown graphically in Figure 15, reveal a marked drop in total serum calcium and in diffusible calcium and a slow return toward normal. The rabbit was large, 3,670 gm., and the amount of blood drawn, or the effect of doing so, probably did not enter largely into the result.

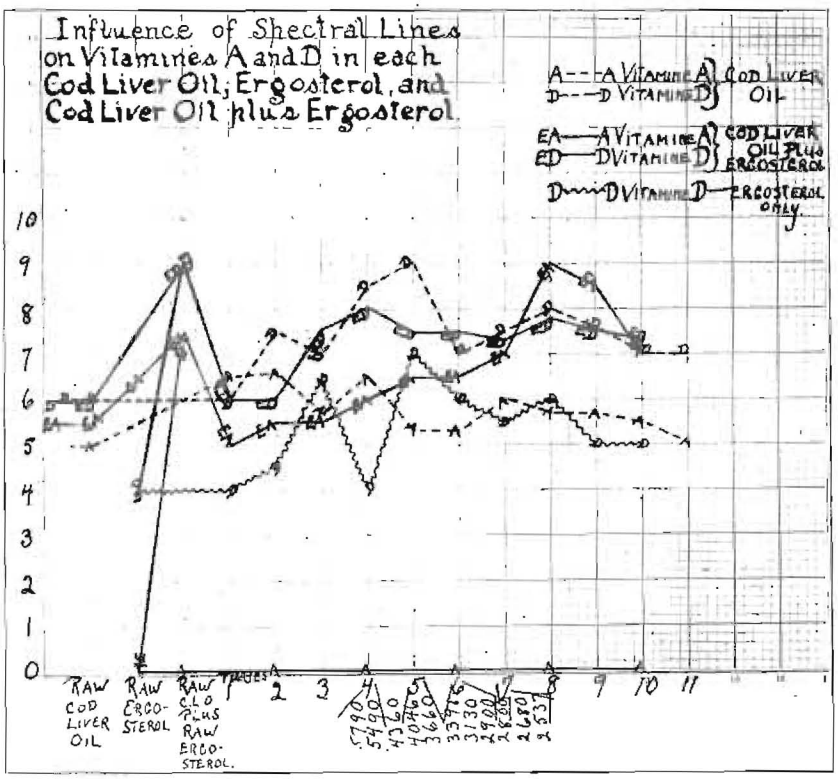


Fig. 13.—Comparison of the influence of different bands of the spectrum on vitamins A and D in cod-liver oil and ergosterol, separately and together.

Since, as indicated by the preceding data, the effect of activation on ergosterol is chiefly shown when it is in contact with such substances as milk or blood, the foregoing test was repeated

forty hours after the first test, with the following results. The total calcium fell only about 0.4 mg. instead of 2.0 mg. in the preceding test, when the ergosterol and the blood serum, in which it was injected intravenously, were not activated; and whereas, in the former, the diffusible calcium fell from 6.8 to 5.2 mg., in this case it was raised from 5.8 to 7.3 mg., with a corresponding decrease in the nondiffusible calcium from 8.1 to 5.1. This, it will be noted, is a reversal of preponderance, which was carried through the two-hour period, and, at the end of sixteen hours, had not come back to the ratio at the beginning of the test. The total calcium remained nearly constant, and marked changes

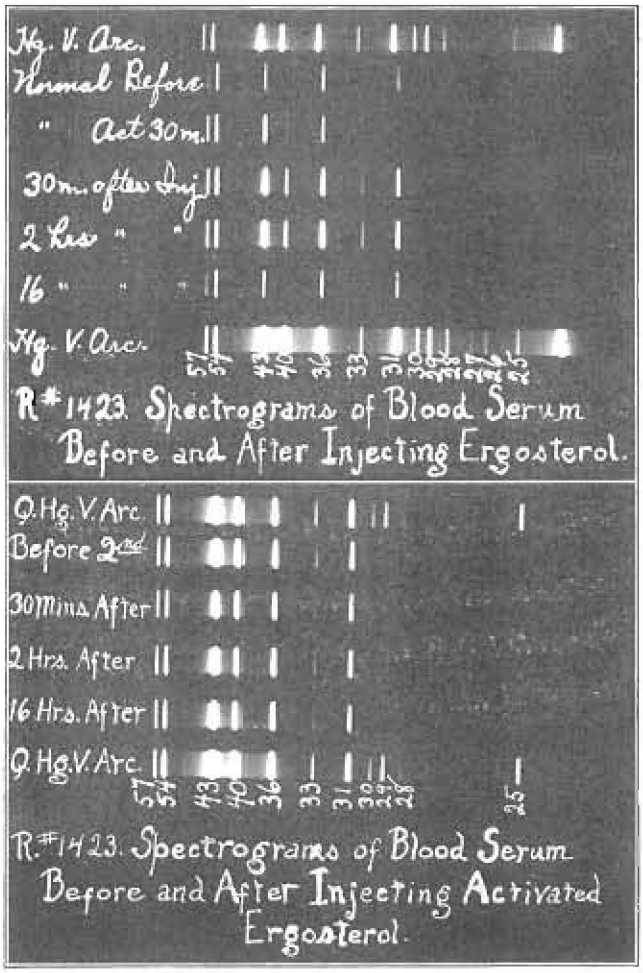


Fig. 14.—Comparison of the blood spectrums in successive periods after the injection; above, of raw and, below, of activated ergosterol.

occurred in the ratio of diffusible and nondiffusible calcium.

This is strikingly illustrated in the graph showing these two series, Figure 15 *B*. Even more striking is the change in the spectrographic record. (Figure 14 *A* and *B*.) In the first place, the blood has changed so that the normal

nearly complete of 3130, with complete absorption beyond. A further marked difference is that, after the treatment, the blood remained the same as before the treatment. A comparison of the effect of activating the serum alone will be given in a more detailed report. A comparison of these blood changes as they

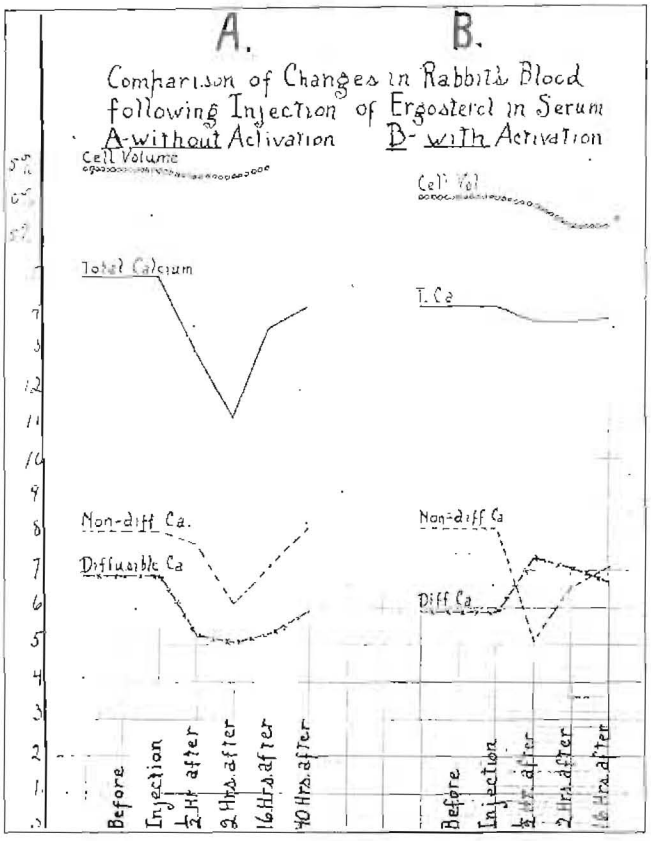


Fig. 15.—Blood chemical changes associated with the spectral changes of previous figure.

(before the second treatment) has practically no absorption from 3130 toward the longer rays and complete absorption beyond, including 2537; whereas, before the first treatment, there was complete absorption of bands 4046 and 3391 and

occurred in these two experiments is shown graphically in a comparison of *A* and *B*. (Fig. 15.) The application of these new data is being made to practical cases by recording spectral conditions before and after operations for the

removal of focal infection and treatment.

The effect on the absorption of bands of the spectrum when ergosterol is added to serum is shown in Figure 16, in which raw serum is shown to have a different absorption of the spectrum from that of activated serum. The more concentrated solution of ergosterol absorbs practically all bands except a small part of 5400 and 4300. The addition of a very small amount of ergosterol to serum changes quite markedly the absorption distribution and makes it, in some samples, like that of normal serum when

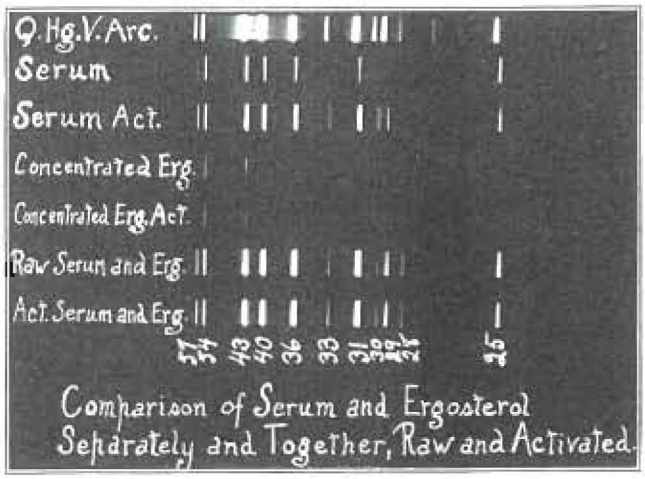


Fig. 16.—Spectrograms of serum and ergosterol alone and together, raw and activated.

activated, which it has here. The presence of the ergosterol seems to satisfy certain elements in the serum so that they do not now absorb the radiant energy. It is quite important to observe that, while the range of absorption is not extended by the presence of the ergosterol, the intensity of the absorption is not so great as when it was absent; that is, the lines are stronger. The serum seems to be satisfied, or, in a sense, in equilibrium, as far as the radiant energy of these particular bands is concerned. The length of the period of radiation was not great enough to destroy the ergosterol or vitamin D.

In this connection, it is important to note the succeeding effects on the blood of an animal when it is exposed to ultraviolet radiation for an extended period of time, four hours and forty-five minutes, which are graphically shown in Figure 17. The cell volume was reduced from 35 to 15 per cent in a period of two days. The total calcium increased nearly 2 mg. and was maintained at the high level during the period of irradiation, but dropped in the first twenty-four hours to nearly 1 mg. below its starting point, and during the next twenty-four hours, came back to a level about 1 mg. above its starting point. Practically all this increase was in diffusible calcium, as will be seen from that line, the nondiffusible ending at a lower total level and the diffusible at a level about 2 mg. higher than at the beginning of the test. The effect on the inor-

ganic phosphorus was a progressive depression during the period of irradiation, both plasma phosphorus and cell inorganic phosphorus returning to about their original level two days after the treatment.

I have previously reported[9] the ten-

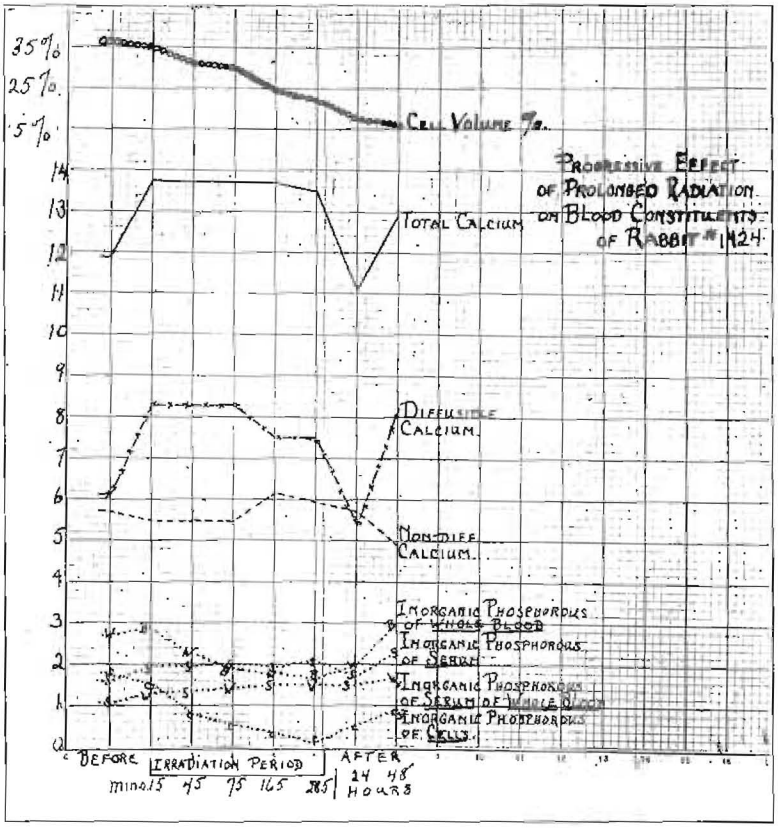


Fig. 17.—Changes in blood calcium and phosphorus factors produced by exposing a rabbit with hair clipped from the back to full quartz mercury vapor arc with blood determinations made as indicated.

dency to leukopenia lasting several days after a mild leukocytosis lasting only a few hours, as a result of exposure to ultraviolet radiation. This was accompanied by a marked decrease in polymorphonuclears and increase in small lymphocytes. Others have reported similar findings. These data seem to indicate strongly that our problem is not primarily one of exposing individuals to ultraviolet radiant energy as it may come from such artificial sources as the quartz will be helpful, and to determine the mercury arc or carbon arc, but that the radiation must be limited to that which greatest need of the individual, it is im-

9. Price, W. A.: Dental Infections Oral and Systemic, Cleveland: The Penton Press Co., Vol. I, chap. 27, 1923.

portant to know, in the light of information at present available, the diffusibility of the blood, since the full spectrum of the mercury vapor arc and carbon arc tend to increase the diffusible factor unduly. This stresses the need for filters for such artificial sources of ultraviolet radiation and for a removal from our dwellings, where feasible, of the glass filters of the type that we now employ.

Figure 18 shows the transmission of various glasses. The top and bottom show the transmission of quartz unobstructed. The second, "Corex," transmits to and including the strong band 2537, though it absorbs part of it and some to 3660. "Vitaglass" begins absorbing strongly at 2800. It only transmits a part of the radiations at 2900 and 3000. "Quartzlite" transmits very little beyond 3100 and only part of 3100 and 3300 bands. Window glass transmits only to about 3600. All of these glass substitutes have a great advantage over ordinary glass. However, practically all absorb some of the radiation that is desirable. Our atmosphere does not permit radiant energy to pass quite to 2900, and much less than this at times, even at most of the time in some locations. Our bodies were not intended to receive the extreme ultraviolet radiation and it is probable that most, if not all, people would be better not to have radiation much, if any, beyond 2900, though considerable is needed from 2900 to 3300. It is my opinion, based on these data, that a filter should be used for such artificial sources of radiant energy as quartz mercury arc and carbon arcs to limit the radiation to approximately that from the sun until further researches, particularly along spectral lines, shall reveal the bands that should be indicated for correcting special abnormal conditions.

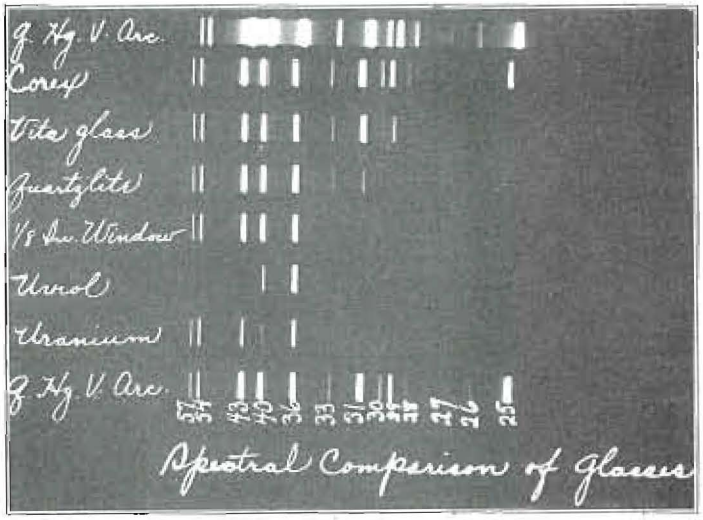


Fig. 18.—Ranges of transparency to ultraviolet rays of several glasses. The first three are available as substitutes for window glass. The sun spectrum goes to about 2950 and substitutes should transmit freely to that band.

which I believe will soon be achieved.

We have not realized how rapidly haze or humidity reduces the ultraviolet end of the spectrum. Figure 19 shows sections from films from my clock-driven attachment which makes spectrums at regular periods as desired; in the film shown, every five minutes. *1* shows the apparently clear sky, with variations due to drifting moisture or clouds. *2* shows the effect of haze, the sky still looking quite bright. *3* shows the effect of light clouds. Note that the loss begins at the ultraviolet end of the spectrum. Applying these data to practical utilization, where the diffusible calcium is too high, avoid ultraviolet radiation of the shorter wave lengths and do not give activated cod-liver oil. My researches indicate that administration of raw cod-liver oil tends to raise the nondiffusible calcium and depress the diffusible calcium and that administration of activated cod-liver oil and exposure to radiant energy to 2800 tend to raise the diffusible calcium. Some of the bands beyond 2900 have distinctly harmful effects.

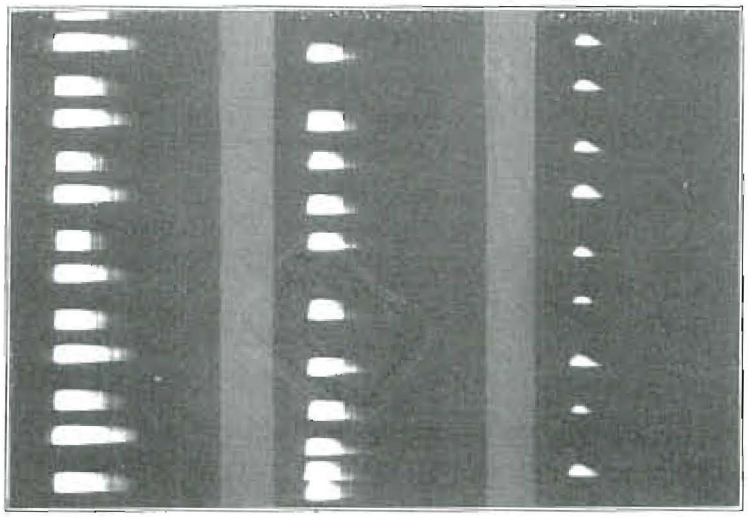


Fig. 19.—Specimen of spectrums made of sky at five-minute intervals by the recording attachmeut, which shows the effect of water vapor in absorbing chiefly the ultraviolet rays. This demonstrates the depressing effect of overcast cloudy or smoky sky. *1*, clear sky. *2*, beginuing haze. *3*, light cloud.

In a previous communication,[1] I have shown that exposure of cod-liver oil to irradiation from the sun or an artificial source changes it so that there is increased fogging of a photographic plate placed over it, not hy radiation heing given off from the surface of the oil but rather by the production of a gas, probably hydrogen dioxid, and, further, that the increase in this oxidizing agent is about proportional to the time of irradiation. I have also shown previously that oil so treated had an enhanced capacity for producing biologic reaction. If ergosterol or a similar substance is the active agent in butter fats and animal oils which increases calcification processes, and if the photographic fogging is related to these properties, it might be expected that adding ergosterol to cod-liver oil would enhance this factor. This

TABLE 2.—BLOOD CHEMICAL STUDIES OF INDIVIDUALS WITH OVERLOAD OR PHYSICAL DISTURBANCE*

	Total Serum Calcium	Cell Calcium	Diffusible Calcium	Nondiffusible Calcium	Sol. for Ca. Serum Plasma	Serum Inorganic Phosphorus	Calcium Balance	Polymorphonuclears: Small Lymphocytes
Case 1436: Xerostomia and arthritis (severe).	9.53	0.98	3.64	5.89	5. ..	1.45	−26.2	61/31
Sixteen months later—marked improvement	9.59	1.57	4.47	5.12	10 30	5.93	+16.82	55/30
Case 1772: Pregnancy, fourth month.....	10.68	2.65	7.67	3.01	7 17	3.14	− 6.4	71/22
Sixth month—lassitude, treatment commenced.....	10.01	2.15	5.40	4.61	10 42	2.08	− 19 2	73/19
Eighth month—marked improvement	11.16	1.01	5.82	5.34	6 28	3.66	+ 0.80	79/17
Case 1736: Polyneuritis (bedridden).....	11.73	0.13	8.23	3.50	7 22	2.72	− 8.00	62/23
Two months later—improvement.....	10.06	2.15	6.50	3.56	6 19	3.14	− 8.42	33/56
After six months—marked improvement	10.65	2.62	5.85	4.80	10 35	3.16	− 6.30	74/13
Case 1546: Arthritis.	10.41	.....	3.75	6.62	..	3.78	+ 2.2	52/39
Five days later—improvement.....	10.52	.....	4.21	6.33	.. ..	3.26	− 9.3	56/33
Two years later—improvement.....	10.01	3.03	6.78	3.22	10 13	3.92	− 0.80	54/34
Case 1695: Dizziness, hypertension.....	10.5	0.10	3.20	7.30	8. ..	2.74	− 11.1	48/45
Three months later—improvement.....	10.2	1.40	2.30	7.90	6. ..	3.34	− 5.0	40/41
Nine months later—marked improvement	10.93	1.50	6.28	4.65	7 23	4.48	+ 9.0	44/38
Case 1710: Ununited fracture.....	11.05	1.10	5.29	5.76	9 30	3.12	− 5.50	59/32
Three months later, preparing for operation.....	10.48	.....	5.92	4.56	8 ..	3.25	− 5.40	.....
After fourth month—operation.....	11.64	3.39	4.43	7.21	6 19	3.10	− 3.92	64/25
After fifth month—complete union.....	11.32	3.35	5.42	5.90	8 16	3.60	0.75	60/31

*Marked changes in blood calcium levels associated with improvement following treatment.

has been tested, and the results are shown in Figure 20. It is clearly seen that, in every step from a comparison of raw cod-liver oil and raw cod-liver oil containing a trace of raw ergosterol to

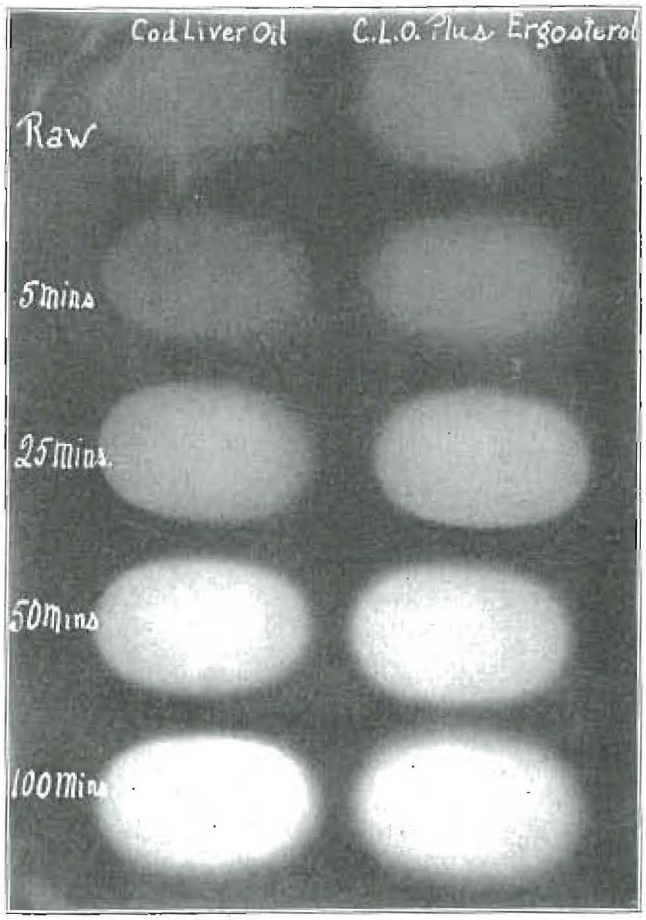


Fig. 20.—Greater fogging effect of cod-liver oil containing a very small quantity of ergosterol than of cod-liver oil alone as a result of exposure to the ultraviolet rays for varying periods of time.

activation of this combination for various periods up to 100 minutes, there is marked increase in fogging of the photographic plate, as was to be anticipated from the association of this phenomenon with other factors previously associated and reported. We are now testing the relation of these phenomena to various vitamins, particularly A, C and D, separately and combined.

For several years, I have been treating disturbed calcium metabolism both on experimental animals and in practice by the use of activators, and it is of interest here to note some of the clinical

results in the light of the blood chemical studies and in the light of the new experimental data being presented here. A little more than 1,500 blood chemical studies have been made on patients, most of them affected with degenerative disease in some organ or tissue, which, in the light of the newer knowledge, may be related directly or indirectly to focal infections, such as dental.

A large number of animal studies have also been made to throw light on these processes. In Table 2 will be seen a series of blood chemical studies on six patients. Note particularly the shift toward normal of the level of equilibrium between diffusible and nondiffusible calcium, also the changes in cell calcium, inorganic phosphorus and calcium balance. These have been given by about a 5 gm. capsule of cod-liver oil with each meal, which has been raw or activated in accordance with the balance between diffusible and nondiffusible calcium, and have had calcium lactate with it or not, in accordance with the evidence of wastage of calcium, as shown by the urine calcium and the study in every case by roentgenograms of the texture of the bone with regard to tendency to general calcification or decalcification. The cod-liver oil has been activated, as previously reported, by exposure to sunshine (not from an artificial source), from one to fifteen minutes, according to the time of the year and the patient's apparent need as indicated by the faulty equilibrium between diffusible and nondiffusible calcium. Space does not permit of an extended analysis of the clinical history. The first patient could walk only with great difficulty, owing to polyarthritis, associated with xerostomia (dry mouth), which, according to the literature, is expected to be progressive and is nearly always fatal. The patient can now produce from 10 to 20 c.c. of saliva in about half an hour and can walk without even a cane. She has received activated cod-liver oil, size No. 0 capsule (about 0.5 c.c.) and one 5-grain tablet of calcium lactate with each meal.

The second patient received mixed capsules, part raw and part activated cod-liver oil, and one 5-grain calcium lactate tablet. These patients have all also received an ample supply of vitamin C and iron from citrus fruits, vegetables and salads.

Note the great change in these two cases in calcium balance. Most patients apparently do not need calcium lactate. The last case is particularly significant. An ununited fracture of four years' duration with a history of one unsuccessful operation has had a perfect healing with an operation performed after preparing him for it. The clinical aspect will be reported in detail in the near future. These cases are presented here as illustrations both of the procedure and of the effects.

SUMMARY

Data have been presented which I interpret as follows: 1. Calcium in milk, blood and many biologic fluids, which exists partly as diffusible and partly as nondiffusible, can readily be treated so as to change the percentages of diffusible and nondiffusible, by several means, including irradiation or shaking with raw cod-liver oil and with activated cod-liver oil.

2. The effect of activation of the cod-liver oil changes it so that, whereas raw cod-liver oil in several fluids reported lowers the diffusibility of the calcium, activated cod-liver oil increases the diffusibility; which is also the effect of direct irradiation of the same fluid with the same irradiation.

3. The administration of raw and activated cod-liver oil produces, in general, the same effect in blood serum as by shaking the fluids together.

4. The effects of different parts of the spectrum have been shown to be different for certain various lengths of rays.

5. These characteristic differences are produced both by irradiation with different bands and by shaking the fluids presented with cod-liver oil which was irradiated with these same bands.

6. The irradiation of vitamin D in milk when different parts of the spectrum are used separately, with regard to the shift in diffusibility of calcium, has a general similarity; which suggests a direct association. A study of the effects of irradiation of fluids compared both with the effects of administration of the sterol egosterol, separately and in association, gives evidence of its being similar in effect to, if not directly associated with, the diffusibility phenomena presented.

7. Results of the use of the spectrograph for the study of blood serum and other body fluids indicate its great value in both research and diagnosis.

8. These data are related to the practical problems of obtaining the required amount and kind of irradiation by the use of suitable substitutes for glass.

9. The relation of these phenomena to some of life's problems seems to indicate that herein is an important step forward both in the understanding of bone and tooth formation and disease and the means for the forming of better hard tissues and the prevention of subsequent disease in these tissues.

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