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BULLETIN 78

NEW FUNDAMENTALS FOR THE TREATMENT AND PREVENTION OF DENTAL DISEASE BASED ON CALCIUM UTILIZATION AND DISTURBANCE, WITH SPECIAL CONSIDERATION OF FACTORS DETERMINING WHEN AN INFECTED TOOTH BECOMES A LIABILITY*

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CLEVELAND, OHIO

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NEW FUNDAMENTALS FOR THE TREATMENT AND PREVENTION OF DENTAL DISEASE BASED ON CALCIUM UTILIZATION AND DISTURBANCE, WITH SPECIAL CONSIDERATION OF FACTORS DETERMINING WHEN AN INFECTED TOOTH BECOMES A LIABILITY*

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THE emphasis in preventive medicine is passing from repair to prevention and the next great forward movement in dental science will doubtless be effective preventive procedure combined with much more effective treatment. My studies on the relation of dental disease to systemic health, together with the relation of general health to dental disease, have continually led in the direction of the obtaining of much additional knowledge regarding the proeesses by which the hard structures of the body are built up and taken down in health and disease, and on the rôle of calcium in determining the functional level of all organs and tissues.

The data which I have presented[1] indicate that individuals can be classified into groups on the basis of the manner in which they metabolize or utilize calcium, and this is borne out and greatly reenforced by the continually accumulating data. Many systemic diseases are associated with extensive decalcification processes in their later stages and some in tbeir early stages. This condition obtains in a striking manner iu diabetes, tuherculosis and cancer, the individuals of which groups tend to be free from arthritic processes and quite uniformly free from the proliferative type of arthritis.

While it has been understood, on the hasis of clinical data, that certain accessory food factors or physical conditions tend largely to influence the progress of changes with regard to calcification and decalcification processes, there have been few data available regarding the nature and rôle of the aetivators and the conditions of the body fluids which are associated with these phenomena. Since this communication is being presented in the Section which is primarily concerned with the surgical aspeets of dental science, I shall present this discussion first from the standpoint of some newer knowledge developed under my direction, regarding the processes of bone growth and bone repair.

A word of explanation is probably in order as to my connection with cases of ununited fracture of parts of the body other than in the dental field. This

*Read before the Section on Oral Surgery, Exodontia and Ancsthesia at the Seventieth Annual Session of the American Dental Association, Minneapolis, Mino., Aug. 23, 1928.

1. Price, W. A.: Dental Infections Oral and Systemic, Cleveland: Penton Publishing Co., 1924; Dental Infections and Degenerative Diseases, Cleveland: Penton Publishing Co.; Systemic Expressions of Dental Infections, Am. Clin. Med., 4:943 (April) 1926.

has been entirely through invited consultation.

It is because we are dealing with the same problem, in many of its fundamental aspects, in the prevention of dental caries, the systemic phases of pyorrhea and of bone and tooth development and also of the healing of surgical lesions of the mouth, that I am selecting as an extreme phase of calcium deposition a repair process in association with fracture.

As oral surgeons, you are all directly concerned with the healing of fractures of the face. It is a matter of universal knowledge and comment that the bones of elderly people do not repair well, and presumably it is largely because of their age. Probably no site of fracture has been more difficult in which to obtain healing in elderly people than the bones of the hips and pelvis. Such a case is shown in Figure 1, in a woman 74 years of age, of excellent habits, but who, for a period of about nine months, had been an invalid as a result of the fracture of the neck of the femur. The condition of the bone before treatment is shown in *A,* at which time there was great discouragement on the part of both the physician and the patient. It was at this time that the physician asked for my assistance in undertaking to put her system into a condition in which repair of the fracture might be obtained. This assistance was given in the form of determining abnormalities in the chemical constitution of the blood and directing means for their improvement.

On studying the bones of the hip, it will be noted that there is an absence of the dense cortical layer, even on the shaft of the femur, and much evidence of decalcification of the body of the bone. In the making of successive critical analyses of the data provided in the combined blood chemical, clinical and roentgenographic studies for patients, in which more than 1,600 very extensive blood chemical determinations have been made, with particular consideration of calcium and phosphorus factors, it has continually been apparent that certain contributing factors have been very active in determining the nature and course of the abnormality. One of the striking illustrations of this has been apparent to all practicing dentists since the beginning of our science, as the development of pyorrhea with its alveolar destruction at about middle life and usually extending progressively in later life.

The evidence clearly indicates that one of the associated phenomena has been the development of a physical state in which the individual tends readily to resorb calcium from those parts of the hard structures which are highly vascularized. Indeed, the evidence is clear that the skeleton is of primary importance as a storehouse for calcium, whether the skeleton is on the outside, as a shell, or distributed through the tissue, as a framework. This woman, as is true in many elderly people who suffer from fractures, was in a state of depleted calcification, due to long borrowing from her storage warehouse for the maintenance of daily needs. I shall present evidence indicating the nature of the factors which determine whether an individual shall be required to borrow calcium for daily needs instead of obtaining the required amount from daily rations.

In the column marked I, showing the various quantities of the factors presented in the blood study *C,* Figure 1, I have presented a number of the calcium and phosphorus factors, expressed in milligrams per hundred cubic

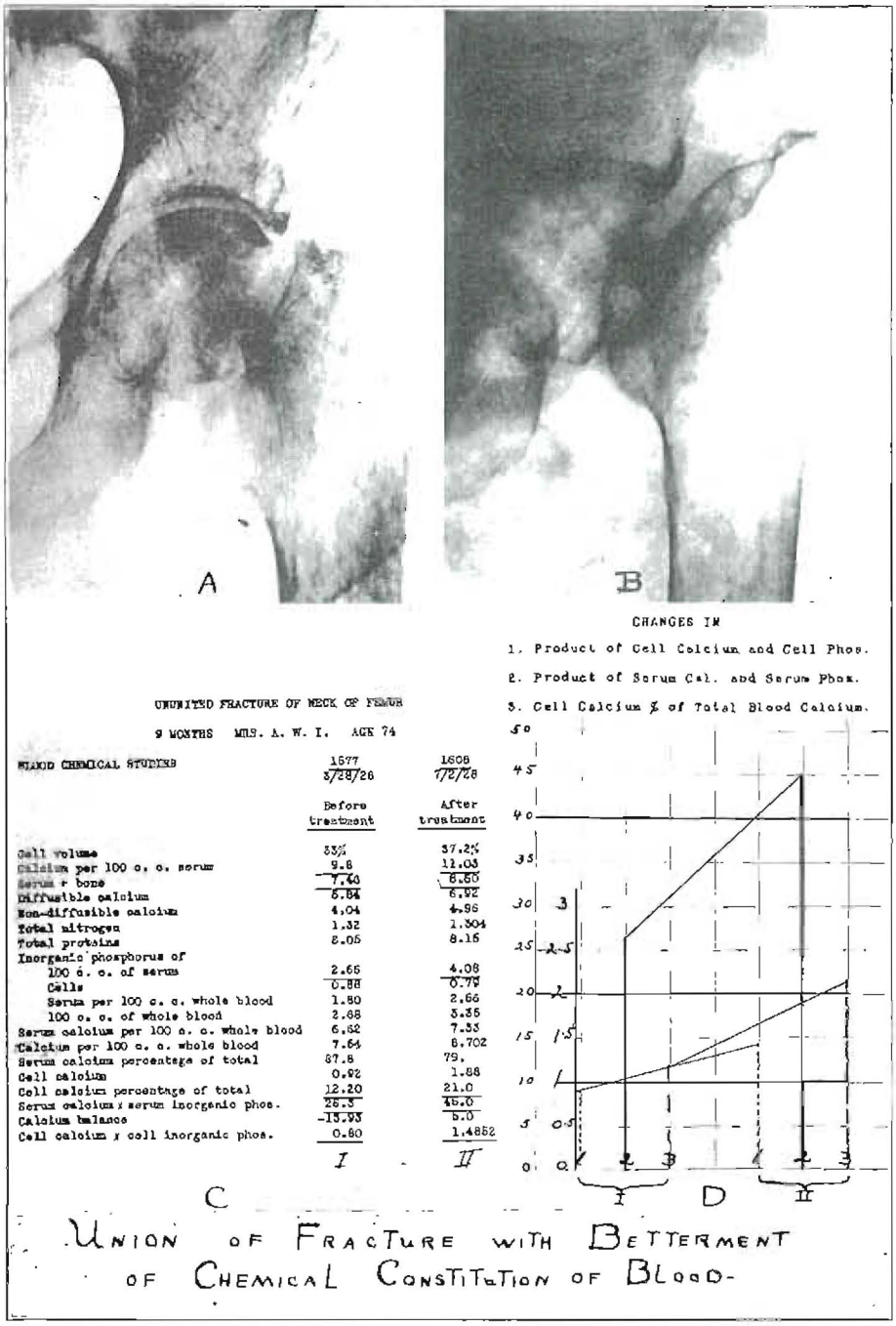

Fig. 1.—Union of fracture with betterment of chemical constitution of blood.

centimeters of blood. For better understanding of the meaning of the various quantities, I shall discuss them in order, beginning at the top, and as I do so I shall ask you to follow in Sections C and D, Figure 1, certain of these factors which seem to have a controlling influence on the behavior of calcium in the system, and it will make it more clear if we discuss comparatively the chemical readings made ninety-six days apart, one before and the other after treatment.

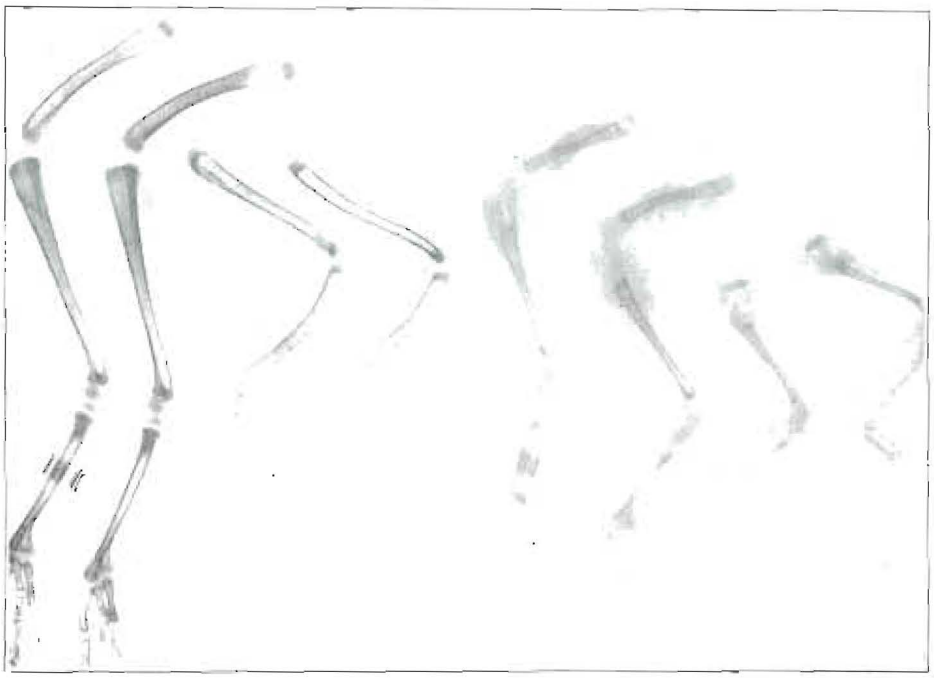

Fig. 2.—Comparison of bone structures on normal and rachitic diets.

The cell volume before was 33 per cent of the total blood volume, from 43 to 45 per cent being normal. It will be noted that there was an improvement to 37 per cent. The calcium per hundred cubic centimeters of serum increased from 9.8 to 11 mg. We have come to recognize that total calcium may not give a very clear index of normality or of the effect of a reparative process or of abnormal demand. The item marked serum plus bone indicates that, when bone chips were placed in the serum of this patient, the calcium of the serum left the serum and deposited itself on the bone to the amount of 2.4 mg. per hundred cubic centimeters of serum, leaving 7.4 mg. of calcium in the serum (per hundred cubic centimeters). This figure is a little high for best healing, and it will be noted that, after treatment, it was reduced to 6.6.

The calcium in blood plasma and blood serum is probably present in three distinct forms. The first is in an ionized state. This will readily diffuse through animal membranes. Another part is not

ionized, and is diffusible or dialyzable through animal membranes. The third is an unionized and undiffusible form, which is probably in combination with protein. The terms diffusible and nondiffusible are arbitrary and depend entirely on the standard used. Determinations are made by adapting celloidin membranes to a state of permeability that as nearly as possible corresponds with that of animal membranes. I shall discuss in another communication the method of preparing the celloidin sacks and the degree of permeability adopted in these studies as standard. An internal air pressure of 150 mm. degree is used, which about corresponds to blood pressure. In general, going by the standards that I am using, the diffusible and nondiffusible calcium are approximately balanced in normality, with the diffusible slightly higher than the nondiffusible. This relationship has been obtained before and after treatment with an increase of both.

The total nitrogen is made up of both nonprotein nitrogen and protein nitrogen. The protein factors at 8, increasing to 8.1 after treatment, are both high. The inorganic phosphorus of 100 c.c. of serum at 2.6 is low. It increased under treatment to 4. Inorganic phosphorus of the cells is a low normal at 0.8 and remained approximately the same. Inorganic phosphorus of the serum of 100 c.c. of whole blood increased from 2.6 to 3.3. The calcium of 100 c.c. of whole blood serum and cells increased from 7.5 to 8.7.

There are certain relationships which experience and critical comparative study have shown to be desirable if not essential for normal calcium metabolism and utilization. The blood cells should contain approximately 2 mg. of calcium per hundred cubic centimeters of blood. In this individual, the cell calcium was at 0.9 before treatment and at 1.8 after treatment, an increase of 100 per cent. The blood cells calcium should contain approximately 20 per cent of the total blood calcium. In this case, they contained at the beginning only 12 per cent, but after treatment their content rose to 21 per cent.

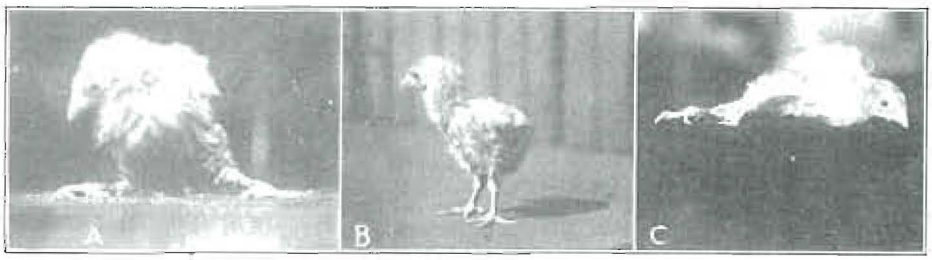

Fig. 3.—Vitamin D deficiency. Three views of same chick within nine days. *A*, appearance on high A, no D vitamin diet; *B*, three days later, on high D and high A diet, two doses of one-millionth gram of activated ergosterol; *C*, six days later (than *B*), on a diet lacking vitamin D.

It has been recognized for some time that the interrelationship berween calcium and inorganic phosphorus is important, and that while either might vary within given ranges, the one should increase if the other decreases, and therefore their product is an important

expression of normality or divergence from it. This product, under ordinary conditions of adult life, should be approximately 40, but for growth conditions, whether for preadult states or the repair of injured tissues, this factor should be increased. In children, it is from 60 to 70. The product of serum calcium and serum inorganic phosphorus (9.8×2.66) was 26.1 before treatment, or 13.9 less than 40. This is frequently spoken of as calcium balance, and in this case, there was a negative balance of 13. Similarly, the product of the calcium of the cells and the inorganic phosphorus of the cells produces a figure which should be not less than 1 and should be 2 or more. In this case, this factor before treatment was 0.8, and increased to 1.4.

These three factors constitute important yardsticks for determining the capability of a blood to produce repair of a broken bone or, in fact, to deposit calcium for any and all purposes in the building and repairing of tissues and for normal organ functions. In *D*, Figure 1, I have expressed graphically these three factors. *1* shows the changes in the product of cell calcium and cell phosphorus, the groups *I* and *II* representing the condition of these three factors *1*, *2* and *3* before and after treatment. *2* presents graphically the product of serum calcium and serum phosphorus, and *3*, the cell calcium percentage of the total blood calcium. The ordinates are shown in two vertical columns. The outer figures 0 to 50 relate to factors *2* and *3* in units of *5*. The inner column from 0 to 3 in 0.5 unit divisions relates to the perpendicular columns marked *1* which are the product of cell calcium and cell phosphorus. The minimum normal for the product of cell calcium and cell phosphorus is shown by the horizontal line at *1* on the inner column of figures and relates to the dotted perpendicular lines marked *1*, the product of cell calcium and cell phosphorus. The perpendicular solid lines at *2* express graphically the product of serum calcium and serum phosphorus, which should be 40 and which was 26 before treatment and 45 after. The two perpendicular columns shown with dashes at *3* represent the cell calcium before and after, the normal of which is shown at *20* in the outer column of the ordinates. This quantity increased from 12 to 21.

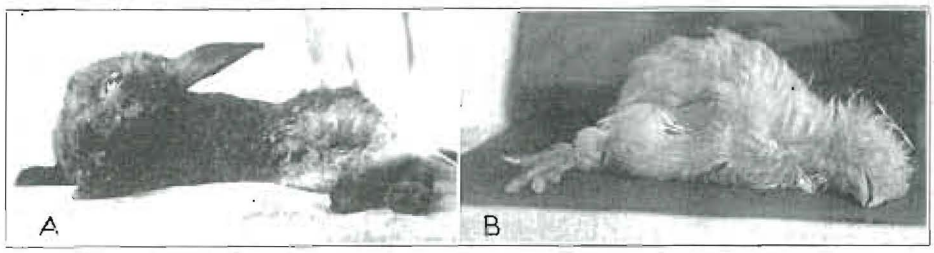

Fig. 4.—Progressive paralysis produced in a rabbit *(A)* and a chicken *(B)* apparently by an overdose of cod-liver oil. The daily quantity per body weight was approximately that often advocated for children.

Associated with these blood changes, there have been very important changes in the clinical condition. The patient

has changed from a state of marked depression, with developing edema and severe prostration and helplessness, due to physical inability and pain from physical movement, to a state of progress toward normality which has been most remarkable. Though she lives in another city, I have personally seen her walk with the aid of her crutches, apparently placing her entire weight at times on this leg. The roentgenographic appearance shown in *B* clearly indicates that, notwithstanding the absence of a splint or mechanical device to retain apposition, and notwithstanding the evident shortening due to the sliding of the fractured surfaces into a position that would shorten this leg, there is marked evidence of calcification over the entire fractured area, and, further, it is easily noted that a dense cortical layer, which obtains in all normal bone, is again being built on the femur. The roentgenograms of both hips, including the heads and shafts of the femurs, show that the same change is taking place in other bones of the body and probably obtain throughout the entire skeleton.

I have given this detailed analysis of the blood chemical and physical conditions in order that we may approach in a more informed way a study of these factors which relate directly to the control of calcification and decalcification processes, for the treatment of this case was based entirely upon the results of experimental data obtained chiefly through my studies along two distinct lines, the producing of abnormal states and their correction in experimental animals and the successful treatment of abnormal clinical conditions in patients by the use of activators. The presentation of this problem by means of this practical case, with its purely surgical aspect, has been selected rather than the less spectacular but equally successful correction of dental caries.

As an additional approach to the study of normal and abnormal calcification and decalcification processes of both growth and repair, I shall ask you to note the condition presented in Figure 2, which shows in *A* the legs and wings of a normal chick and in *B* the typical expression of leg weakness in another chick, as revealed by the roentgenograms. The latter condition has been produced by a diet with high calcium and sufficient vitamin A content and low phosphorus and low vitamin D content, as shown in *A*, for comparison with a normal chicken approximately the same age that has lived its life in the open, picking its food largely from the fields, having been hatched, tutored and brooded by a mother hen. It will readily be seen that a great difference has obtained in the development of the hard structures. The epiphyses have not properly developed though some of their centers of calcification are seen as very minute structures.

Three views of the chicken with leg weakness from which *B* in Figure 2 was taken will be seen in Figure 3. In *A*, it is shown after it had been fed for three weeks on a diet high in vitamin A with no vitamin D, with the typical expression of leg weakness which that diet produces. In *B*, it is shown three days after the condition shown in *A*. On the two days preceding, it had received a dose of a high concentration of vitamin D in the amount of one-millionth gram of activated ergosterol. While its joints are still swollen, it stands erect and it could run so freely that it was difficult to catch it. In all, it received three doses only, the last one on the day that the picture was taken. During all this time, it was on the same basic diet as

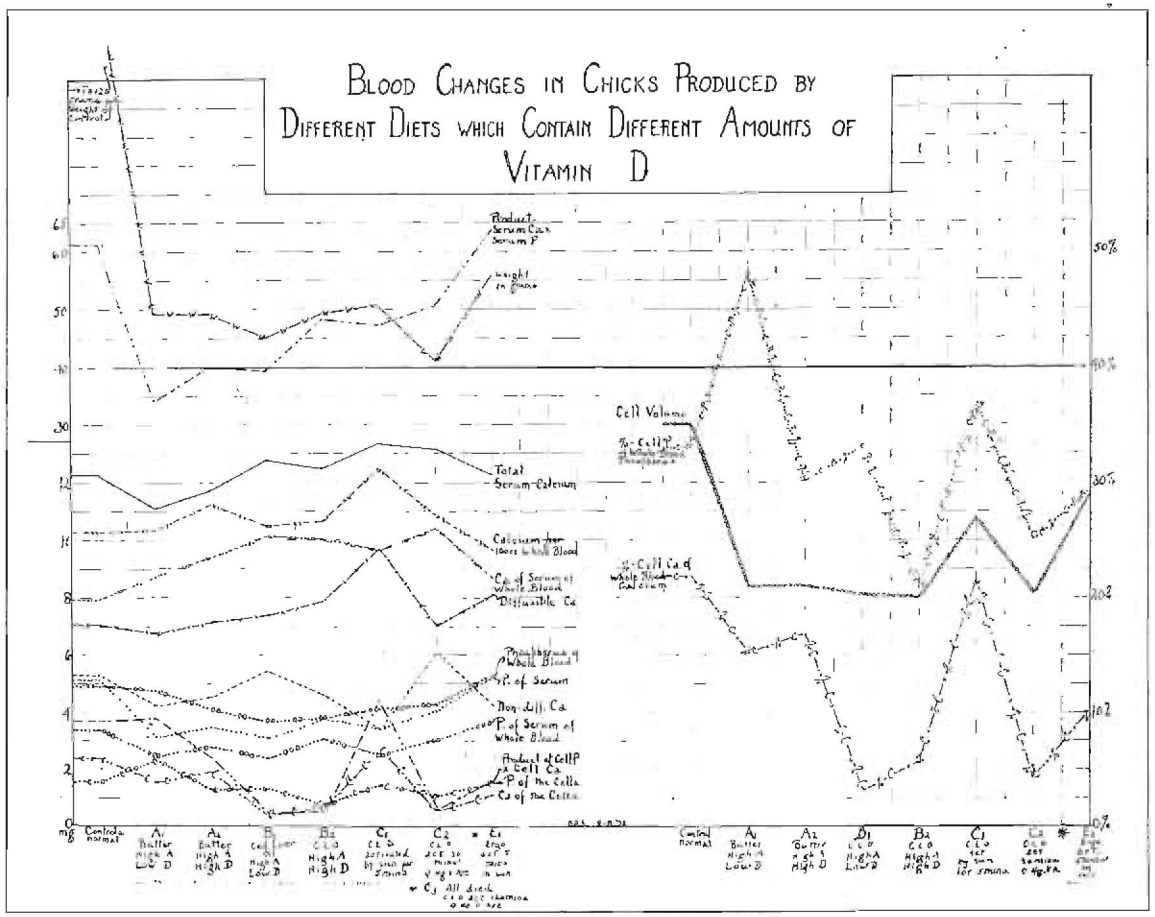

Fig. 5.—Blood changes in chicks produced by different diets which contain different amounts of vitamin D, as provided in selected butters, cod-liver oil and activated ergosterol.

in *A*. Its condition rapidly returned to that seen in *A*, but with greater prostration, and, in six days, it was in the physical state shown in *C*, owing to its being deprived of vitamin D. Two things are quite apparent: (1) that very small quantities of a high concentration of this vitamin are competent to produce a very great change and (2) that the change in the strength of the limbs is not due to a calcification of the hard structures. Calcification did not progress far enough in the three days to account for the marked improvement in leg strength. The soft tissues were, therefore, also greatly benefited by the presence of this vitamin. Some serious dangers for giving activated ergosterol will be given later.

It is important to note that all the time this chicken was under experimentation, it was kept in a very subdued light except while being photographed, and only the light from the dull ruby lamp was available for these chicks to eat by, except for the few moments when feed was being given them, when a white light through glass was used.

In several previous papers, I have presented evidence that the serum calcium as well as calcification may be greatly modified by topical applications of raw and activated cod-liver oil.[2]

The problem of the activation of cod-liver oil by exposing it to radiant energy of the proper type, and the harm that can be produced by overactivation of the oil, either from too long exposure to sunlight or from radiant energy from an artificial source, is one of great importance, and one which I have discussed in several communications.[3]

The problem of activation is exceedingly complicated, and the accumulating evidence clearly indicates that we are dealing with toxic products in either large doses of raw cod-liver oil or small doses of overactivated cod-liver oil. Several investigators besides myself have called attention to the injurious effects of overdoses of cod-liver oil on experimental animals and human beings.[4] I have frequently produced gross lesions in animals, varying in severity from hyperexcitability to partial or nearly complete paralysis. In Figure 4, there will be seen a rabbit with partial paralysis produced by the administration of cod-liver oil in a not larger quantity than has been frequently administered to children and infants. It will be noted that the rabbit's head is drawn sideways and it is unable to walk or hop. With succeeding doses, the symptoms became more aggravated. Erik Agduhr has shown by a large number of dissections that gross changes occur in both muscle and nerve tissues. We are, therefore, confronted with a difficult problem. First is the need for an adequate source of activators and, secondly, that these sources may be free

2. Price, W. A.: Calcium, Its Activation, Utilization and Metabolism, J. A. D. A., 15: 729 (April) 1928. Calcium Metabolism Studies: a. The 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 (Jan.) 1927.

3. Price, W. A.: Relation of Light to Life and Health, Ind. & Eng. Chem., July, 1926; Newer Knowledge of Calcium Metabolism in Health and Disease, with Special Consideration of Calcification and Decalcification Processes, Including Focal Infection Phenomena, J. A. D. A., 13:1765 (Dec.) 1926.

4. Mellanby, E.: Brit. M. J. (May 24) 1924. Agduhr, Erik: Changes in the Heart Through the Presence of Cod-Liver Oil in the Food, Acta Paediat., Vol. 5, Parts 3-4; Changes in the Organism Caused by Cod-Liver Oil Added to the Food, ibid., Vol. 6, Part 2.

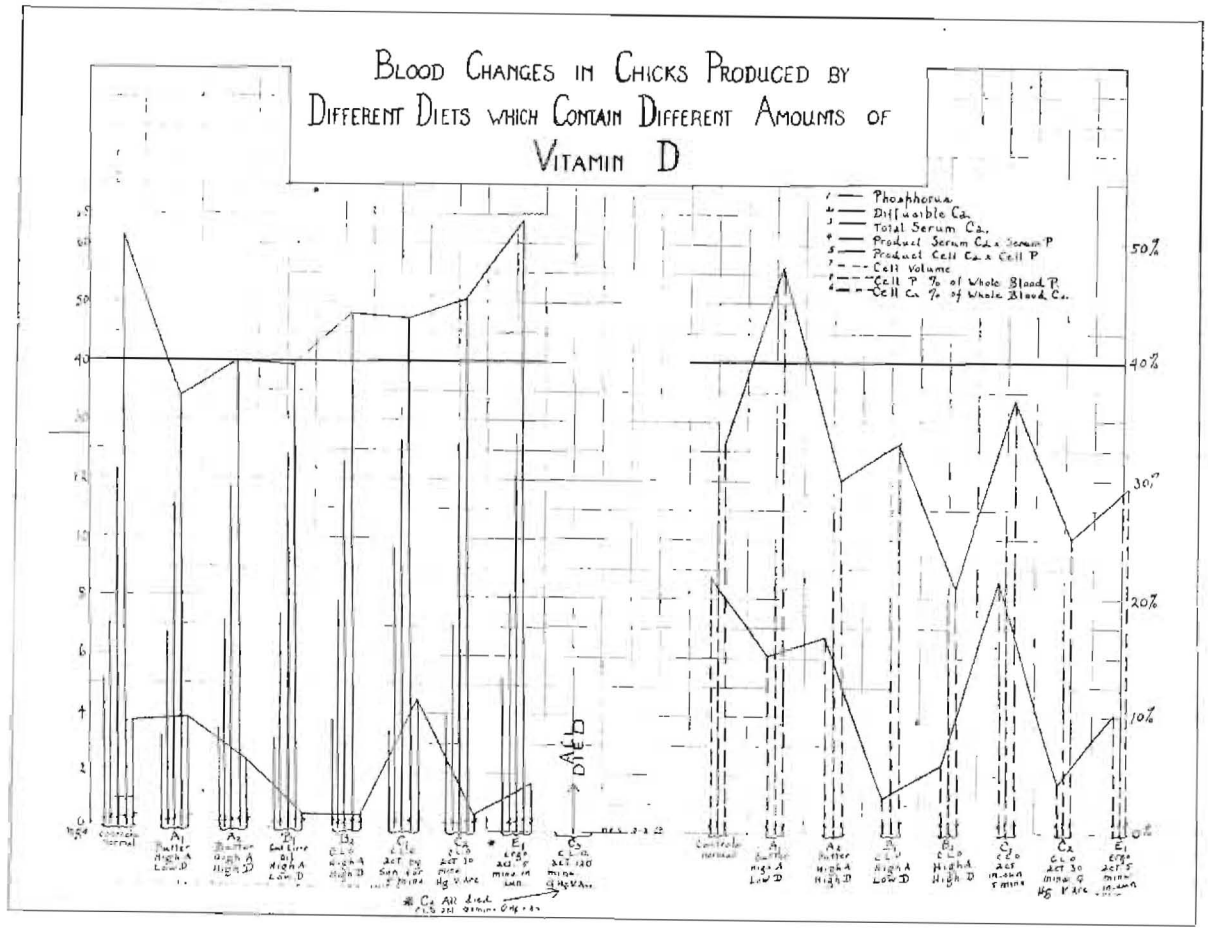

Fig. 6.—Blood changes in chicks produced by different diets which contain different amounts of vitamin D. The advantages of activated cod-liver oil in raising cell calcium and cell phosphorus are evident.

from toxic products which may do harm. In order to study this in further detail, I have used recently more than 1,100 chicks under different conditions with regard to radiant energy directly applied and with different modifications of the same hasic diet by the inclusion of some of the available sources of activators. In Figure 5, there will be seen the results of a series in which the different groups received as an addition to the rachitic diet (McCollum 3143) butter, cod-liver oil and ergosterol as follows: A1, butter high in vitamin A and low in vitamin D, constituting 5 per cent of the food; A2, butter high in vitamin A and high in vitamin D; B1, cod-liver oil high in vitamin A and low in vitamin D; B2, cod-liver oil that was high in both vitamins A and D; C1, cod-liver oil high in both vitamins A and D, activated in the sun for five minutes; C2, the same oil, but activated thirty minutes with a mercury quartz lamp, air cooled, distance 20 inches; C3, the same as C2 except exposed for 120 minutes; D1, ergosterol activated in the sun for five minutes, in butter. Two chicks from each group were generally used, and the blood specimens pooled and blood chemical analyses made to determine the accumulated changes in various of the blood constituents. The weight of the chicks was also noted. Tests began when the chickens were 5 days old, during which time they had a normal diet. They were then placed on diet 3143 McCollum and 5 per cent butter or oil. All radiant energy was excluded except that which came from the subdued ruby lamp, and an abundanee of food was always available, also distilled water. The experiment continued for fourteen days. There were ten chicks in each group. All of the chicks in group C3, which received cod-liver oil that had been activated 120 minutes with a mercury quartz lamp, were dead in four days, and their blood conditions accordingly could not be recorded. The results of these studies are shown in Figure 5, in which the series on the left half of the chart, reading from the top downward, give the comparative readings of the following blood factors: product of serum calcium times serum phosphorus, total serum calcium, calcium per hundred cubic centimeters of whole blood, calcium of serum of whole blood, diffusible calcium, phosphorus of whole blood, phosphorus of serum, nondiffusible calcium, phosphorus of serum of whole blood, the product of cell phosphorus times cell calcium, phosphorus of the cells, calcium of the cells. On the right half of the chart are shown the following factors: cell volume, percentage of cell phosphorus in the whole blood phosphorus, percentage of cell calcium of whole blood calcium. It will be noted that the weight of the normal controls was 120 gm., while those on the butter with high A and low D vitamin content was only 49. But the two groups with lowest weights were those in the one receiving the cod-liver oil which was high in vitamin A and low in vitamin D, and those receiving the overactivated cod-liver oil, thirty minutes in a mercury quartz lamp. The two highest weights were in the groups receiving the oil which was activated in the sun for five minutes and the ergosterol activated five minutes in the sun. The product of serum calcium and serum phosphorus, which, as I have stated, should be forty in mature adults and from fifty to sixty in the period of active growth of young life, is sixty-one in the normal controls but falls to thirty-four in the group A1, receiving butter

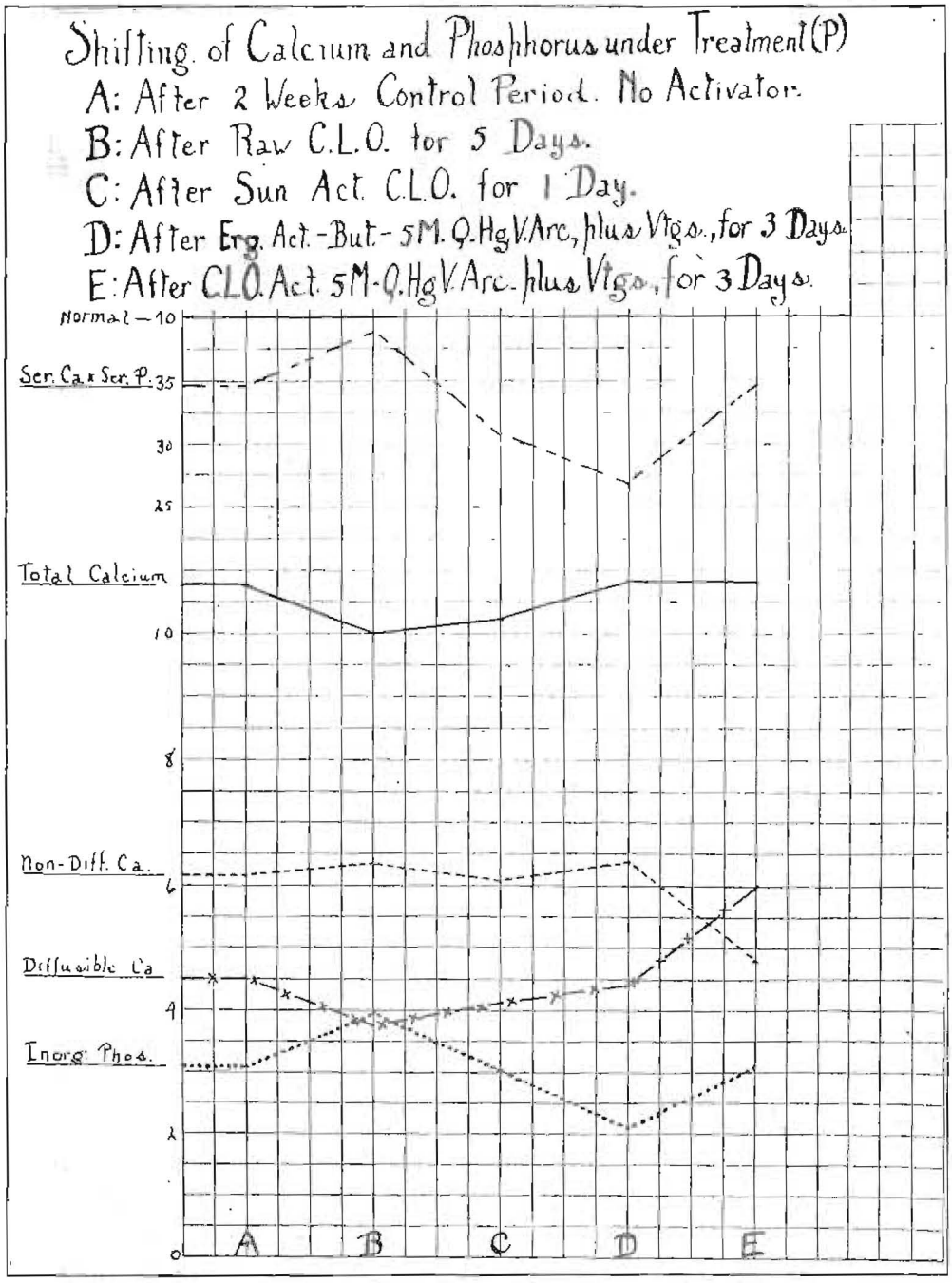

Fig. 7.—Shifting of blood calcium and phosphorus under treatment with various activators (human).

high in A and low in D; increases to forty in group A2, with hutter high in A and high in D; reduces a little to 39 in group D1, cod-liver oil high in A and low in D; increases to forty-eight in group B2, cod-liver oil high in A and high in D; is approximately the same in group C1, activated in the sun for five minutes; increases to fifty-one in group C2, cod-liver oil activated thirty minutes with the mercury quartz arc, and to sixty-four in group E1, ergosterol activated in the sunlight for five minutes. Group C3, which received cod-liver oil that had been activated 120 minutes with the mercury quartz arc, having all died, are not reported. By observing the graph for total serum calcium in its relation to the different groups having different treatments, it is readily noted that in A1, with low vitamin D, there is a marked depression with a progressive increase to the group C1 through groups A2, B1, B2, the last receiving the cod-liver oil that was activated in the sun for five minutes, and then decreases through C2 and E1. Similarly, the graph for the next line, calcium per hundred cubic centimeters of whole blood, shown with XX—, and calcium of the serum of 100 c.c. of whole blood, shown with XXX—, can easily be followed. The next graph, diffusible calcium, shown with X—, is of particular importance in that only one group, namely, that receiving the cod-liver oil activated for five minutes, had a marked increase in this factor, which corresponds in general with the increase in the total calcium, but exceeds that quantity which is associated with a decrease in the non-diffusible calcium shown in the next graph and which reaches its lowest point in C1, cod-liver oil activated in the sun for five minutes. This is oue of the many illustrations of tbe advantage of a properly activated, sufficiently good cod-liver oil for the shifting of the diffusibility of calcium toward an increase where the blood chemical findings demonstrate the need for a change in that factor. The inorganic phosphorus of the serum is shown as a dotted line, and it will be noted that there is a marked decrease in A1 with an increase in the other groups. The calcium of the cells, shown as C-X, is an exceedingly important factor and one that has been almost entirely absent in the reports on the study of calcium metabolism problems. This was at 2.2 in the control group, dropped in the butter and ordinary cod-liver oil groups, but increased to 2.3 in the cod-liver oil activated in the sun for five minutes, decreased in the overactivated cod-liver oil, C2, and came up a little in E1. The phosphorus of the cells, shown as C.. O. in the graph, is another important factor. Stresses which make a demand on calcium with a reduction of calcium, either because of a lack of calcium in the food or a lack of the activators necessary for the utilization of that calcium, tend to induce Nature to make a readjustment which frequently involves an increase of phosphorus to compensate for the lower calcium. This seems to be shown in A1, with a low vitamin D.

Just as the product of serum calcium and serum phosphorus constitutes an important basic factor and should equal 40, similarly, the product of cell calcium and cell phosphorus constitutes an important factor. This is shown in the chart as a series of two long dashes and three short ones. This product was 3.7 in the controls, dropped in the ordinary cod-liver oil groups B1 and B2 to 0.5 and increased in the cod-liver oil activated in the sun for five minutes to 4.5; dropped again in the overacti-

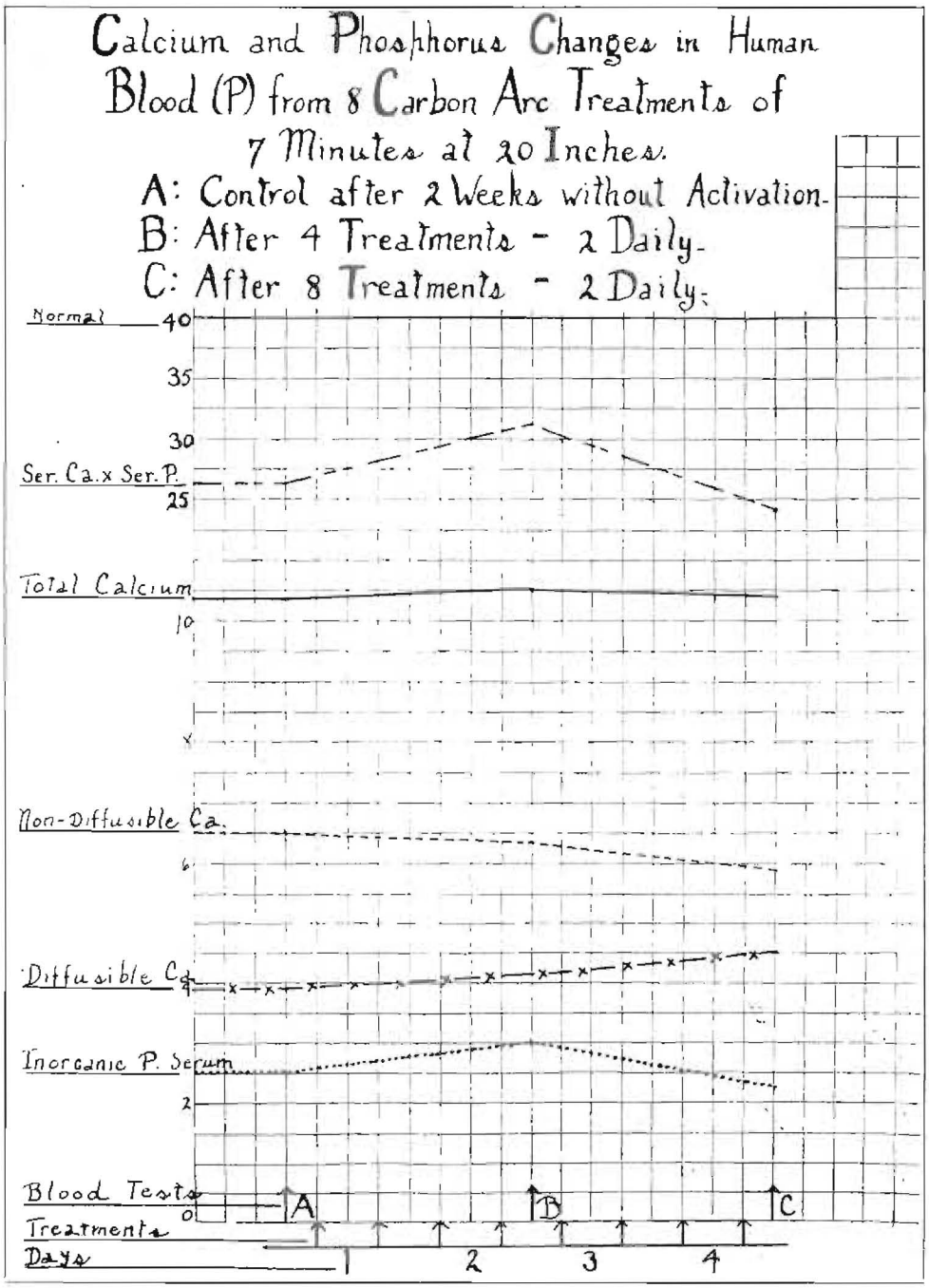

Fig. 8.—Calcium and phosphorus changes in human blood (P) from eight carbon arc treatments of seven minutes at 20 inches. Depression from overtreatment is evident.

vated oil group in C2; and went up a little in E1.

On the right hand half of the chart will be seen the effect on the cell volume, the cell phosphorus percentage of the whole blood phosphorus and the cell calcium percentage of the whole blood calcium. The cell volume of the normal baby chicks is 30 per cent of the total blood volume. In normal adult human beings, it is from 43 to 45 per cent. The effect of the butter which was low in vitamin D and high in vitamin A was to greatly reduce the cell volume to 22 per cent (the ordinates for the right hand group will be found at the extreme right hand side). The relationship of the cell phosphorus to the whole blood phosphorus is graphically shown in the next series, marked C-P-%. This shows an abnormal peak on A1, abnormally low on B2, with a slight increase above normal in C1. The cell calcium percentage of the whole blood calcium indicated as CX%, shows a remarkable decrease in group A1 with a slight increase in A2 and with a very marked decrease in B1 and B2 to an extremely low point, with a marked increase to a little above normal in C1, followed by a marked decrease again in the overactivated cod-liver oil, C2, and some increase, but not to normal, in E1.

Unfortunately, space does not permit discussion here in extended detail regarding why and to what extent and under what conditions cod-liver oil is improved by activation. Note that all of the chickens in group C3 died within a few days, which was the group in which the cod-liver oil had been activated 120 minutes with the mercury quartz arc; and also note that, in many of the factors that we have just been enumerating, there was a marked improvement in the groups receiving the cod-liver oil that had been activated for five minutes in the sun, and much depression in the blood factors of the chickens receiving the cod-liver oil activated thirty minutes with the mercury quartz arc.

Some of those who have presented data which were intended to throw light on the question as to whether oil is improved by activation have apparently drawn conclusions that their evidence demonstrated that it was not desirable.[5] In my judgment, they did not set up the experiment correctly or else did not word it correctly; for what it clearly demonstrated was what I have demonstrated here, that overactivation of cod-liver oil is distinctly harmful. That chickens or rats are not cured of rickets by giving them cod-liver oil activated thirty minutes or two hours is, in my judgment, not an argument against activation, if done properly. The proper amount of activation and the proper kind of cod-liver oil can be beneficial as I have demonstrated in these and many other experiments.

It is difficult to get as much information as I have just detailed regarding a series of experiments on a single chart. In any case, it will take concentration and study to get the facts. In order that I might make these data more easily understood, I have had charts made representing certain of these outstanding factors by the height of the columns which represent each of these factors. This may be seen in Figure 6. The nine groups of chicks are presented again in two phases, one at the left and one at the right of the illustration. Eight distinct factors are emphasized, five at the left, three at the right. These

5. Holmes, A. D., et al.: Am. J. Dis. Child., 34:753 (Nov.) 1927.

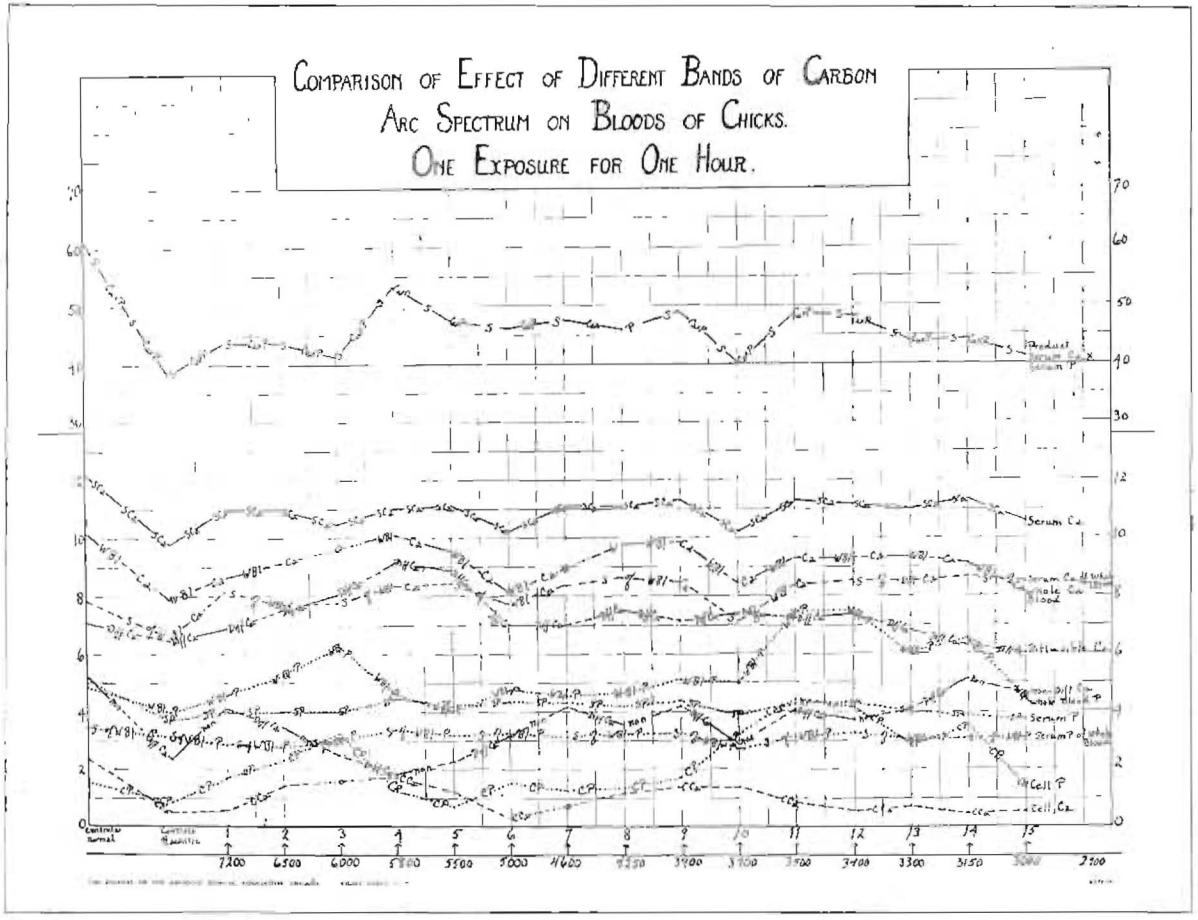

Fig. 9.—Comparison of effect of different bands of carbon arc spectrum on blood of chicks (one exposure for one hour).

are numbered at the base of the perpendicular columns. The columns at the left are solid and the ones at the right are broken. Numbers 1, 2 and 3 (solid columns) represent, respectively, phosphorus, diffusible calcium and total serum calcium; 4 and 5, respectively, the product of serum calcium and serum phosphorus and the product of cell calcium and cell phosphorus. In the group at the right (broken columns), the first column marked 6 represents the cell calcium percentage of whole blood calcium; the second, number 7, represents cell volume, and 8 represents cell phosphorus percentage of whole blood phosphorus. The following are important: The graphic representation of the heights of the fourth solid column in each lot, shows the product of serum calcium and serum phosphorus in relation to the normal at 40; and for only one lot, viz., E1, is it as high as the normal. The relative and actual heights of the columns marked 5, representing the product of cell calcium and cell phosphorus, shows marked variation. Note particularly that these factors are very low in both raw cod-liver oil groups, high where the oil was activated in the sun for five minutes and low where activated thirty minutes. This new observation seems to throw important light on calcium utilization. Another factor that is important is the relative and actual heights of the first of the three broken columns marked 6, in the right hand group, representing the cell calcium percentage of whole blood calcium. This falls very low in the raw cod-liver oil groups and the group receiving overactivated cod-liver oil and is approximately the same in the group receiving cod-liver oil activated five minutes in the sun as in the normal controls. It is also important to keep in mind that all chicks receiving the overactivated cod-liver oil (exposed 120 minutes) died in four days.

My researches on these problems have been and are being carried out on large numbers of individual animals and groups of animals and on a large number of human beings in clinical practice. Many things are being emphasized as data are accumulating, among them the similarity in the effects when treatments are made on the different types, namely, chickens, rabbits, rats and human beings. I have reported many of these items in extended detail in my several papers, chiefly before this Association. In my paper read last October[6] I presented important new evidence which related the reactions of various activators and radiant energy and showed how a shift in the diffusibility of calcium could be produced either by exposing a biologic fluid such as milk or blood serum to radiant energy, or, quite similarly, by shaking the milk with an oil containing activators, such as cod-liver oil which had been exposed to similar radiant energy.

I further showed that different parts of the spectrum have different effects in this regard and also that the exposure of the oil carrying proper activators, to different parts of the spectrum and shaking this with milk or blood serum produced effects that were similar in many respects to that which obtained when the oil or milk was exposed directly to these same spectral bands. Phases of this were also reported

6. Price, W. A.: Calcium Metabolism Studies on the Nature and Rôle of the Activators. Researches on Fundamentals for the Prevention of Dental Disease, J. A. D. A., 16:265 (Feb.) 1929.

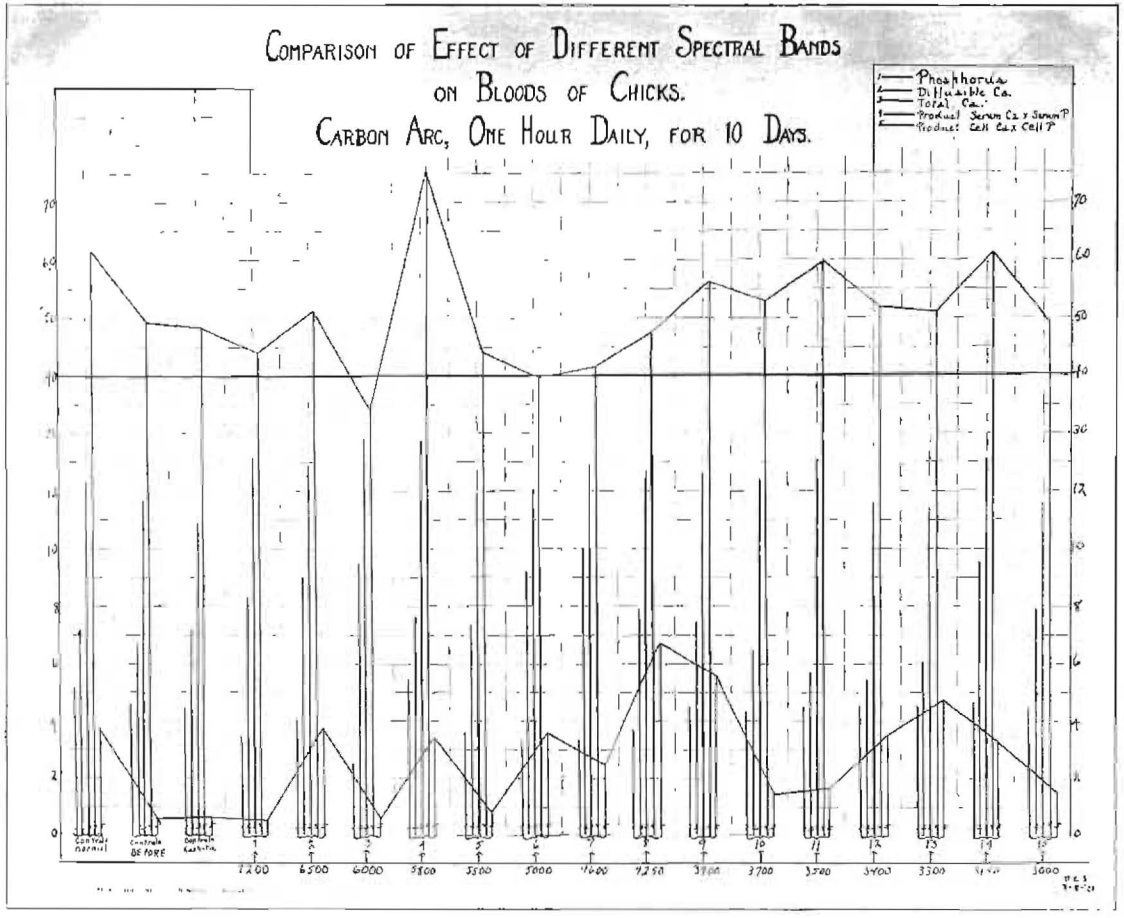

Fig. 10.—Comparison of effect of different spectral bands on bloods of chicks (carbon arc, one hour daily, for ten days). (Compare with Figure 9 as to accumulation of effect.)

in a paper read before the New Jersey State Society.[7]

Among my experimental groups, I have a number of patients who can add an important contribution by their description of the changes in their conditions, an aid which, of course, cannot be obtained from experimental animals. Several of these patients can tell when I am having difficulty in obtaining the grades of cod-liver oil that I desire for this work. I have also had great help from making determinations on myself and comparing my sensations with the blood chemical findings. Some of these have been most enlightening. A typical illustration will be found in Figure 7, which shows successive studies on my own blood in five different periods. This series is a comparative study of the effect of different kinds of activators on the several blood factors, five of which are presented here. Notwithstanding the great helpfulness of the proper activators for my maintaining an efficient physical condition, I eliminated special activators from my schedule during the period of this experiment. *A* shows the condition of these factors of the blood after a two weeks' control period without activators, at which time the product of the serum calcium and serum phosphorus, which should be 40, was at 34, and the diffusible calcium below the nondiffusible. After taking raw cod-liver oil, two 0.6 gm. 0 size capsules with each meal, for five days, the serum calcium went down, as did also the diffusible calcium, which was already too low. This, a characteristic effect of the administration of raw cod-liver oil, is shown in *B*.

I next took some cod-liver oil that had been activated in the sunshine for five minutes, but for one day only, two capsules with each meal. It will be noted in *C* that, even in this short time, there was a change in the diffusible calcium level, shown in the graph as the row of alternating x's and dashes. The total calcium of the blood also rose, but owing to the depression of the serum phosphorus, the calcium balance, or the product of serum calcium and serum phosphorus, fell. For the next immediate test, I took an ergosterol preparation in 0.002 gm. doses, activated in butter in the mercury quartz arc for five minutes. This is shown in *D*. There was an improvement in the diffusible calcium and total calcium, but not in the serum phosphorus. I then took for three days a cod-liver oil preparation that had been activated for five minutes through a filter consisting of vitaglass. This filter should be noted. It cut off most of the ultraviolet beyond 3100 A. U. This is shown in *E*, and it will readily be seen that there was a rapid rise in the diffusible calcium, so that it took a position a little above the nondiffusible. The inorganic phosphorus rose sharply, with the result that there was a rapid improvement in the calcium balance, or product of serum calcium and inorganic phosphorus.

There has been much misapprehension and misunderstanding regarding the relation and interrelation of certain of the vitamins, particularly vitamin D, and radiant energy. It has been assumed by many that vitamin D can be a substitute for radiant energy or, vice versa, that radiant energy may be a substitute for vitamin D. While several similar effects may be produced by radiant energy of certain types and by vitamin D, it must also be kept in mind that only the radiant

7. Price, W. A.: New Fundamentals for the Prevention of Dental Disease, with Special Consideration of Calcification and Decalcification Processes, Dent. Cosmos, 71 (Feb.) 1929.

energy which is absorbed can produce physical reaction; and in order that it may be absorbed, there must be certain chemicals present that will absorb the radiant energy. Presumably, these are in considerable part related to the cholesterol of the blood and epithelial covering of the body.

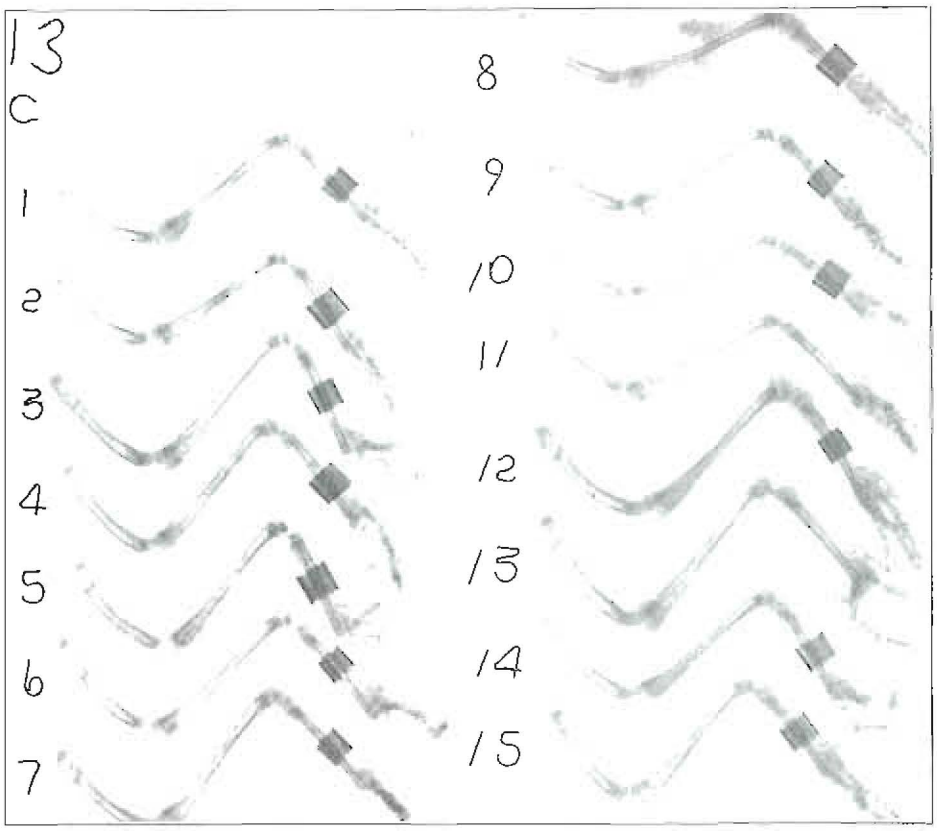

Fig. 11.—Comparison of calcification and growth in legs of chicks placed in different bands of carbon arc spectrum (Experiment 13), after one hour daily for ten days.

It has not been generally recognized that great harm can be done with radiant energy and that serious failure can obtain, the former probably by the producing of toxic substances which are distinctly harmful and the latter by the failure to help produce the helpful substances, because of the absence in the tissues of the chemicals to be acted on, which are now frequently spoken of as provitamins. Rosenheim and Webster[8] have presented important new data which indicate that ergosterol is the parent substance of vitamin D and probably the provitamin with which we are concerned. They, and Windaus and Hess, have presented evidence that this sub-

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

stance is developed in the body as a product of cholesterol.

Last October,[6] I presented considerable data illustrating the effect of this chemical on the blood chemical factors of rabbits, when injected in minute quantities intravenously, and related these to the spectrums of the bloods of these rabbits.

In order further to ascertain the effect of radiant energy, when applied to the surface of the body, on the clinical factors and to compare it with the activators when taken internally, and to compare the clinical with the blood chemical changes, I made exposures on my own body with the radiant energy from a double carbon arc, carbons for which were cored with calcium sulphate. Treatments were of seven minutes' duration on my bare body, at 20 inches, distance. Two treatments were taken daily, eight in all. The effect of this is shown graphically in Figure 8. *A* shows the position of these various factors after a control period of two weeks without taking a special activator. Again, it will be seen that the diffusible calcium is lower than the nondiffusible. After two treatments, shown in *B*, it will be seen that the inorganic phosphorus had gone up, as had also the total calcium, a marked rise in the calcium balance resulting. After four more treatments, two daily, blood was taken again, and a condition, the symptoms of which I was feeling distinctly, was found to have occurred in my blood, which was very unfavorable. The inorganic phosphorus dropped sharply. The diffusible calcium increased in proportion to the nondiffusible, the total calcium receded and the calcium dropped considerably below its low level at the beginning of the experiment. I had considerably injured myself physically by overtreatment, yet doubtless not more so than the hosts of people being injured by their unintelligent application of artificial sources of radiant energy to their own and other persons' bodies. That I had seriously overdosed myself with radiant energy was clearly proved in another way, for I developed the most severe cold that I have had in two years.

I have seen a number of individuals who have brought on conditions more alarming than mine by overtreatment with their home installed mercury quartz or carbon arc units. I have also seen many who present evidence of serious injury from treatment in laboratories and parlors provided for the wholesale applications of this would-be cureall. The error is not to be laid to the use but to the abuse of a force that is competent, when properly applied, to do great good. This and many other experiments have indicated the great need for knowledge regarding the comparative influence of the different parts of the spectrum of radiant energy that may be produced by the sun or an artificial source of radiant energy.

As an approach to this, I have constructed a large spectograph, in which I can expose thirty chicks or thirty rats at a time, in two decks, each of the fifteen pairs receiving a different part of the spectrum. In Figure 9 is a chart illustrating the results of one of these studies as revealed in the analysis of several blood factors as indicated.

The range of the spectrum used in this experiment is from 7,200 to 2,900 Angstrom units. The centers of the groups of bands falling on each successive pair of chicks, one above the other, are shown on the chart with arrows with the approximate length of the central band in the group. The carbons used were therapeutic C developed by the National

Carbon Company, and the period of exposure was one hour. The amount of energy used was relatively small, since only a narrow slit, approximately 2 mm. in width could be used at a distance of about 5 cm. from the arc. The total distance from the chicks to the arc through the three prisms and two 5-inch fused quartz lenses, all built especially for this spectograph, was about 9 feet; the range was from the infrared through the visible spectrum and into the ultraviolet as far as is transmitted by sunlight. In other experiments, I have adjusted the instrument to go much farther into the infrared and ultraviolet regions. This experiment has been made many times with rats and chickens, and always with the same general result, namely, that there is a distinct difference in the blood changes produced by different parts of the spectrum, and that, in approximately the same positions, changes are produced when either blood serum or milk are placed in quartz tubes and exposed similarly to different parts of the spectrum and then analyzed for shifts in the diffusibility of the calcium. In general, the results are similar to the effect produced by exposing cod-liver oil in quartz tubes to the energy from different parts of the spectrum and shaking milk or blood with the oil from these different tubes and then separating and noting the shift for diffusibility of the calcium of the milk which has received an energy factor from the cod-liver oil, which, in turn, received an energy factor from the radiant energy. Two types of controls were used: chickens having a normal exposure and normal food, shown in the first group, and rachitic controls having the deficiency diet and required to eat in very subdued ruby light. The upper graph shows again the product of serum calcium and serum phosphorus and reveals a marked depression between the normal controls and the rachitic controls. All of the other chicks used in this test had presumably the same blood condition as the rachitic controls before the exposure, and our study has demonstrated many times that healthy chicks having the same general parentage and incubation and brooding history, when hatched, have very constantly similar blood conditions, and therefore the second column shown as rachitic controls can be considered as typical of the individuals of the like experiments. It will be noted that there was a distinct increase in serum phosphorus and serum calcium in such position as to make the curve rise sharply in cage 4, another rise at 9, a depression at 10 and a rise at 11. It can be seen at a glance that many factors have changed radically. The calcium and phosphorus of the cells both changed to a marked degree. This experiment was repeated in different ways. Each group of chicks was exposed daily except Sundays for seven days. Numbers 2 and 10 died before the period of experiment was terminated, which made a break in the series with regard to blood chemical studies. It was found that, in general, the same condition obtained, but in a more marked degree. Still another series was run (Figure 10) in which the chickens were exposed one hour daily for ten consecutive days except for one day. Four series of fifteen were run, two at a time, one above the others, and of these two were taken and their blood pooled to get an average for this chemical test. A most remarkable result was obtained. The condition already presented in Figure 9 with the one hour exposure was found emphasized in the seven-day treatment and found to be very greatly emphasized in the ten-day treatment, as will be observed by noting the height of the

columns in Figure 10, representing these factors. The control chickens not exposed with mild beginning rickets at the starting of the experiment became more and more rachitic, and the entire lot of sixty controls were dead at the end of the experiment, while the light from all the different bands had heen competent to keep the chicks alive; which throws light on the question as to whether or not light is necessary and what kind of light is necessary or competent for the continuance of life for this period. Note that again, in cage 4, the product of serum calcium and serum phosphorus shown in the vertical columns No. 4 has gone far above the normal controls, and the chicks in 9, 11 and 14 are nearly equal to the controls and only the group in cages 3 and 6 have gone down to or below the base line 40. Of equal, if not greater, importance is the change in the product of cell calcium and cell phosphorus shown in column 5. It has dropped very low in the rachitic controls, is equal to normal in cage 4, and is far above normal in cages 8, 9, 13 and 14. We have similarly a very marked change in the phosphorus of the serum and in the diffusible calcium shown in columns 1 and 2 of each group. These studies emphasize greatly certain factors in the blood chemistry whieh are profoundly influenced by radiant energy. Many other groups of determinations have been made to throw light on this experiment but space does not permit me to include them here.

These studies that we have just been reviewing have to do with the changes in the chemical constituents of the blood of chicks receiving different diets and others receiving different types of treatment.

I began the discussion of these studies hy presenting a case of ununited fracture and showed its change in twelve weeks' time, stressing the importance of the relationship of the changes in the structure of the bone to the changes in the blood chemical constituents. I shall now present further evidence, emphasizing the correctness of that interpretation. If, as I have assumed, hlood chemical factors determine largely whether calcium will go into or out of bone, it would be logical to expect that we might see some differences in the changes in hone development in the chicks irradiated by different parts of the spectrum.

This information is presented in Figure 11, a roentgenogram of one leg of a chick from each of the different groups. As only one leg was banded, there is no significance in the fact that all the legs presented do not have bands. Note particularly the difference in the length of the tibiae. It will readily be seen that there is a very marked difference, and, further, that corresponding with the zones of increased product of serum calcium and serum phosphorus and of high product of cell calcium and cell phosphorus, there is marked increase in growth of bone.

Several other types of studies of these several series have been made, and many other series which space does not permit me to present. These include the making of spectrograms of the blood specimens, the chemical analysis of the shafts of bones for the relative and actual amount of the various inorganic constituents and the staining of bone sections for study and comparison of the zones of provisional calcification.

Another important phase of this problem has been intensively studied, but space does not permit of its inclusion. This has to do with the nature and source of the vitamins and provitamins, which are neeessary for adequate calcium

metabolism. The latter includes an elaborated extension of the studies begun some years ago, and reported before the Seventh International Dental Congress at Philadelphia,[9] on milk and milk products and factors which might influence the vitamins in milk and other food products.

The matter of the selection and preparation of the aetivators is of profound importance, and researches have reached the point where it is now possible to enhance the available sources greatly. I am putting all this in text form, which will probably be available in a few months. This text will also include detailed methods for the various determinations and analyses. I shall also present in this volume additional cases of ununited fracture.

Notwithstanding the fact that I have already exceeded the space which should be used for this presentation, it seems imperative to make some direct application of helpfulness for the members of this section, an application which will be equally helpful to all in general dental practice.

The maintenance of normal defense or immunity requires calcium and phosphorus, in adequate amounts, available in the blood stream quite as much as for the repair of bone, and our entire scheme of preventive dentistry will in my judgment be built upon this foundation. We are therefore going to come to the preparation of the patients for operation, when operations are necessary, by giving them this type of reenforcement during the time they are making this repair. Further, it is not too much to expect that we shall come to a type of dental practice which will prevent quite as effectively dental caries and pyorrhea and other decalcification processes, and these are quite dissimilar, as we may aid, as I have demonstrated is now possible, in the process of repair of ununited fractures.

I interpret these data as follows: Since a minimal amount of calcium and phosphorus is essential for daily needs in health and a greater amount is required in disease, if the required quantities cannot be supplied from the food, whether for lack of calcium and phosphorus in the food or from lack of activators to make them available, a draft will be made on the storage in the skeleton. This produces a state of stress which disturbs function until that stress is removed by the replacement in the bones of the borrowed calcium and phosphorus.

This condition constitutes an important factor in the development of the so-called degenerative diseases both by disturbing organ function and by lessening the body's capacity to fight infection; hence, there is a reduction in immunity.

With lowered resistance to infection, local quarantines break down, such as those about infected pulpless teeth, which now become a liability. Such an individual is in negative calcium balance while using calcium faster than he is assimilating it. This condition constitutes a very common and important factor in the expressions of age, whether in early, middle or old age. Such individuals, for the time being, may be said to be dying, or, as someone has expressed it, people do not die from degenerative diseases, rather they get the degenerative diseases because they are dying. In this state, focal infections, dental or otherwise, may provide a strain of infection with localizing qualities which will, by this tissue affinity, rapidly or slowly break down some organ, and, at the same time, injure the defensive mechanism by the systemic calcium stress. Hence, focal infections

9. Footnote 2, second reference.

should be eliminated before the capacity for maintaining immunity is lost. An infected tooth would require very great strategic value to offset this capacity to do harm. Under nearly all circumstances, therefore, infected pulpless teeth should be removed before the systemic state of lowered resistance develops.

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DISCUSSION

A. B. Vastine, Danville, Pa.: Does the same thing that applies to butter and cod-liver oil apply to the food of chickens, as to the time of year, exposure of food, and so forth, and to the eggs that are produced?

Dr. Price: It will make a great difference, but this must be kept in mind. Sunlight or any other source of light cannot act as an activator on the blood of an individual who does not carry the proper provitamins to be activated.

Dr. Vastine: You misunderstood my question. Do you know whether the time of year that eggs are produced has the same relation to the time of year that butter is produced?

Dr. Price: Yes, that is true, and there are several factors in connection with it. The ratio of pullets to cocks that are born in February and March is different from the ratio of pullets to cocks that are born in June and July. It affects a lot of factors that go with this problem of the fertilization and maturation of the ovum and the development of the chick.

W. I. Jones, Columbus, Ohio: You showed some pictures in which you said the cod-liver oil is rubbed on the skin of the chickens. Aren't we taught in most physiologies that the skin does not absorb? Did you feed these chickens cod-liver oil at the same time?

Dr. Price: No, these were not fed cod-liver oil; it was applied topically.

A. C. Wherry, Salt Lake City, Utah: In your check-up on butter, did you find any relationship to altitudes?

Dr. Price: In general, the farther north we go, the more rain and more good pasture we find, and, in general, the better the average of the vitamins D and A. In those states where they ship in the food for the cows and do not have much native grass, vitamin D has been low, and we have here one of the important contributing factors to the cases of enamel hyperplasia that are developing in many of the western and southern states. Some of the best tests we obtained were on butter from Manitoba. Some western butter has been among the poorest we have tested. We were getting two kinds of butter from some western states. I learned that the cows in some states were given a diet which seldom contained grasses, but contained barley that was shipped in from the north and grains that were shipped in, and only occasionally did the cows have an opportunity to graze or browse among leaves. The colds that many people have, I think, are largely due to the low vitamin content in the foods. Milk and butter are really the chief source of vitamins A and D. Activation of a cod-liver oil that is low in suitable provitamins will not improve it. It will do some harm probably, and I would advise against doing it. I do not know why some of the cows under the same condition of diet and the sunshine have high vitamin D content and others do not. I found this an interesting thing. One cow had the history of having a very poorly nourished calf; her half sister also had a very poorly nourished calf. The milk of these cows was low in vitamins. There seems to be evidence that this is partly an inherent personal quality. It does not seem to be entirely due to species or grade; that is, we cannot say that Holsteins or Ayrshires or any other particular type will all furnish milk that is high in A and D vitamins. I do not know where you can get cod-liver oil that is always high in vitamin D, because the manufacturers are not yet, as far as I know, putting figures for vitamin D on the bottles except to say that not less than a certain minimum is contained. To state that the contents contains an ample quantity may be enough on the basis of the chicken or rat experiments, although as you see by the evidence here presented it is not nearly so good as that that is high. I think that ultimately the cod-liver oil manufacturers and supply depots will furnish cod-liver oils with figures for both A and D vitamins. For the present, I know of no better way than to take it myself or to make one or all chemical analyses a biologic test on animals or a spectrographic test. Emulsions are generally low in vitamin D.