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Table of Contents

Introduction

The subject of calcium metabolism has become one of major importance in the current medical literature. Calcium makes up about 1.3 per cent of all body tissues, and is most concentrated in the bony skeleton, where it comprises about 85 per cent of the structure. Calcium is part and parcel of blood, muscle and bone; it is absolutely essential to growth, to the normal action of the heart, to the proper functioning of our musculature and to the coagulation of our blood. By virtue of the wide range of its activities, a great deal of research and experimentation has been done to determine its normal metabolism and the effects of the abnormal. The knowledge which we now have, and the well-established opinion, regarding the source, absorption, utilization and excretion of calcium have all been worked out and arrived at during the past two decades. The calcium problem is of especial importance during pregnancy, as there are two organisms which must receive calcium instead of one.

In this thesis we will very briefly discuss the history of our knowledge of calcium metabolism so that we may have an adequate foundation for the discussion of abnormal calcium metabolism in pregnancy, and the disturbances incident to this abnormal metabolism.

Decalcification occurring in pregnancy covers a very wide range of conditions. It includes a lessening of the calcium content of the skeletal system. It is of great importance in dental caries. It deals with an abnormally low blood serum calcium content. It is either directly or indirectly concerned with uterine atony, osteomalacia, dental caries, tetanoid syndromes, actual tetany, post partum hemorrhage, preeclamptic conditions, eclampsia, muscle excitability, friability of the perineum, phlebitis, and varicosities.

In this paper we will not attempt to discuss in detail such conditions as osteomalacia, ricketts, scurvey and other conditions which are due to decalcification, but which may be present without pregnancy. The greater part of this thesis will be a discussion of toxemias of pregnancy, (with especial reference to preeclampsia and eclampsia), to the so-called tetanoid syndrome and to the general condition of the maternal organism, from a calcium deficiency viewpoint. This last group will include the coagulability of the blood, the tendency toward varicosities and the incidence of phlebitis. The results of calcium therapy will be given and a comparison made with the results obtained where other forms of therapy are employed.

History

The necessity of calcium in the diet has been known for many years. Bertram as early as 1878 states that 0.4 grams of calcium oxide was necessary in the average adult diet per day. This estimation of the amount required has been substantiated by Albu, Mason and Newberg. There is a great variation in the calcium content of various nations. The diet of the Finns, according to Tigerstedt contains from 2.0 to 6.0 grams daily, due to the large amount of milk consumed. Sherman in 1911 found that the average American diet consisted of only 0.45 grams. He found further that 0.45 grams per day is not sufficient for a proper calcium equilibrium. He recommends that the calcium intake be 1.0 gram for every 100 grams of protein.

It has been found that the calcium requirements of infancy are relatively greater than in adulthood. This is due to the fact that there is during infancy and the growing period an extensive deposition of calcium salts in the skeletal system.

During pregnancy, too, there is a great drain upon the calcium reserves of the mother. Hoffstroem has calculated that the calcium content of the fetus increases from 5.39 grams at the twenty-eighth week to 30.41 grams at the end of the fortieth week of pregnancy. Miller,

Yates, Jones, and Brandt (13), in a complete analysis of the mineral balance of a milk cow, found a negative daily balance of 6.2 grams, upon an intake of 117 grams and a yield of 23.15 kilograms of mild. They stated, "It appears that although serious consequences are not likely to appear, so long as the negative balance is not too great, it is probably wise to increase the calcium content of the mother during pregnancy".

A great deal of work has been done on the normal absorption of calcium. Sherman and Howley state that the calcium of milk is better utilized than that of vegetables. McChegage and Mendel also adhere to this view. Rose, Blatherwish and Long have found, too, that the calcium of various vegetables are well utilized in man. Steenback and his co-workers have found that a large variety of calcium salts (lactate, phosphate, carbonate, sulphate and silicate) may be equally well utilized by growing rats if supplied in sufficient quantities.

Until comparatively recently there was a wide difference of opinion as to whether or not calcium salts are absorbed from the intestine in sufficient amounts to cause an appreciable rise in the level of the serum calcium. Luckhardt and Goldberg and others have demonstrated that the serum calcium can be elevated by the administra-

tion of calcium lactate. Salvesen, Hastings and McIntosh found that the oral administration of calcium chloride 7.5 grams daily resulted in a 20 per cent rise in the serum calcium of a dog. Kahn and Roe (28) conclusively settled the question of the absorption of calcium salts from the intestine. They state "We have not found a single report of a failure to elevate the serum calcium by oral administration of calcium salts in aqueous solutions to subjects free from the influence of foods, or other known inhibitory factors, when the investigator carried out frequent blood-calcium estimations immediately following the ingestion of calcium salts." The absorption of calcium salts in proportional to their solubility.

The absorption of calcium is governed chiefly by three factors:

(1) The hydrogen-ion concentration within the intestine.

(2) The relative proportion of other substances in the diet.

(3) Vitamin D.

Bernheim (7) pointed out a significant relationship between calcium absorption and sugars administered simultaneously. The addition of 25 per cent lactose caused a pronounced increase in the amount of calcium absorbed.

This may be the reason for human milk yielding a much greater per centage of calcium than cow's milk as human milk contains relatively more lactose.

Fats and inorganic constituents of the diet tend to lessen the absorption of calcium from the intestine. This effect is produced through the combination of calcium with fatty acids with the consequent formation of insoluble calcium soaps. Wells states: "The absorption of calcium and phosphorus from the intestine depends on the concentration of calcium and phosphate ions and the presence of soluble undissociated phosphates and calcium. Such physiochemical factors as alter these conditions of salts or ions or their activities may greatly influence the absorption of these elements.

Vitamin D, the "anti rachitic factor" or the "calcifying factor", is a substance necessary for normal calcium metabolism. A complete discussion of Vitamin D, as regards its distribution, properties and mode of action is not indicated in this paper. It is sufficient to say that it is of vital importance and plays a very important part in the ease with which calcium can be absorbed from the intestine.

Calcium is excreted in all probabilities from the epithelium of the large intestine as well as from the kidneys. The calcium excretion of a normal healthy

adult is practically equal to the absorption, the storage being negligible. Hawk is of the opinion that the urinary output represents 10 to 40 per cent of the total output.

The extraction by Collip of a potent hormone of the parathyroid gland provided a means for accurately studying the role of these glands in calcium metabolism (62). The administration of parathyroid extract causes an increased excretion of calcium. Greenwald and Gass found that calcium excretion was diminished after parathyroidectomy. It is interesting to note that only the urinary calcium is affected, the calcium content of the feces remaining the same. Bauer, Aub and Albright have demonstrated that the bone trabeculae are easily depleted by the prolonged administration of parathormone, suggesting that these structures serve as the storehouse of readily available calcium.

The blood calcium has been a subject of great discussion. Jones, Lyman, Kehrer, Alport, Isdall, etc. reported the normal to be from 5.3 mgm. per cent to 12.64 mgm. per cent. It has generally come to be accepted recently however that the blood calcium is between 9 and 11 mgm. per cent. The non-diffusible calcium amounts to from 4.5 to 5.5 mgm. per cent while the diffusible is 4.7 to 5.75 per cent.

The blood serum during pregnancy has received considerable attention. It is the concensus of opinion that in apparently normal women who go through pregnancy, there is but very slight change in the blood calcium level--perhaps a slight decreases during the last months of pregnancy (41)(42)(14)(2). This is of importance in considering the findings of low calcium levels in pathological pregnancies. In a series of 36 pregnancies, Cantarow, Montgomery and Balton found that the serum calcium was 10.61 mgm per cent during the early course of pregnancy. During the late portion of the pregnancies the serum calcium had decreased only to 9.61 mgm per cent, and the same figures hold true for the first stage of labor. The ratio of the diffusible to non-diffusible calcium is elevated from 96.6 to 139.5. The observations of Cantarow, Montgomery and Bolton have been recently confirmed by McCance, who, employing the artificial membrane method, obtained increased values for ultrafiltrable calcium during pregnancy.

The mechanism underlying the alteration of calcium during pregnancy is not well understood. It is at this time purely speculative. It is known, however, that when the calcium level of the blood drops below 8 mgm. per cent that a number of pathological conditions are apt to follow.

Macomber (33) has shown through experimentation on rats that low calcium diets decrease the possibility of pregnancy. He has also shown that the effects of this type of diet on the pregnant mother produces inferior offspring with decided tendencies toward tetany. In the event that the diet is very low the milk of the lactating mother will be low in calcium and the offspring will have a marked hemorrhagic diathesis. These findings have been confirmed by other men (37)(39), who have had clinical results of a very similar nature.

The effect of proper diet has been given much consideration and it is now established beyond doubt, that much can and should be done to aid the pregnant mother during the gestation period, so that she will not suffer the ills incident to decalcification in pregnancy.

Discussion

The adage "A tooth for every pregnancy" has been known to the laity for many years. Just how much truth there is in the above statement has been, until recently, little realized by the profession. During the course of pregnancy, as had already been pointed out, there is a considerable drain on the mother to supply the necessary calcium salts for the fetus. In the event that there is an inadequate calcium diet, or in the event that the calcium in the diet is not able to be assimilated the bony structures of the mother must suffer. The mother first suffers from lack of calcium. The blood calcium is maintained at a normal level at the expense of the bones and teeth. After this process has gone on for a time, the available calcium from this source gives out and the fetus suffers (15).

If, during the course of a pregnancy, the mother does not have a sufficient calcium content in her diet, the teeth of the fetus are apt to be defective. Becks and Ryder (5) after a great deal of experimentation with laboratory animals which were kept on a calcium deficient diet during pregnancy, concluded that "a calcium deficient diet, to the pregnant mother, will cause irreparable damage to the teeth of the fetus. Odontoblasts begin to shrink up and are destroyed." In this connection

it is important to realize that the development of the teeth starts as early as the third month of pregnancy. Thus a woman who does not have enough calcium will give birth to babies with imperfectly formed teeth. They are apt to be soft and rough. Occasionally the teeth are chalky and of very little value. Dolldorf in 1931 gave a review of several cases of defective teeth in infants in which there was a scorbutic tendency and a hemorrhagic diathesis. He says: "Associated with teeth changes, due to calcium deficiency, there is a scorbutic tendency--and a hemorrhagic diathesis is the most striking part of this." It is not uncommon to see a woman who prior to her pregnancy has had excellent teeth, but during pregnancy, notice several cavities. Likewise, women who have been less fortunate, and have had to get their teeth repaired prior to pregnancy will notice the fillings are either loose or have dropped out. This, of course, is due to the fact that a process of decalcification has taken place. The teeth losing their calcium salts so that the blood calcium level may remain intact and the fetus not suffer.

Just how severe may be the results of poor calcium utilization or poor calcium supply is strikingly brought out in a series of seven cases, in which the teeth were not erupted (27). In these babies death was due to birth

injuries, deficiency diseases, malnutrition and still birth. Autopsies were done in all cases before the eruption of any teeth. In all of these cases the mother gave a history of disease or poor dietary management during the course of the pregnancy. The teeth were sectioned very carefully in all cases so that a thorough microscopic examination might be made. In most of the cases there were gross defects in the enamel, indicating an advanced stage of odontoclosia. Whether or not there had been normal formation of the teeth with a subsequent dissolution, or whether there was simply an arrest of development is problematical. At any rate, the fact remains that in calcium deficiency there is a strong tendency toward carious teeth in the fetus. These facts are of importance in another respect too. For years the dental profession has thought that the etiology of tooth decay was acidity due to bacterial activity. This is very definitely disproven, for the soft tissues around the unerupted teeth show absolutely no evidence of bacterial invasion. There is rather striking evidence to show that proper calcium intake during pregnancy will relieve the mother of worry so far as dental caries is concerned. In reviewing the dental history of the long-lived Bulgarians of Metchinikoff fame, it is found that they are practically free of these conditions. Is it

not probable that they can attribute this lack of symptomatology to their very high sour milk diet with sour cabbage supplying the optimum hydrogen ion concentration for maximum absorption? Dr. Richardson (49) substantiates the viewpoint that much more calcium is needed during the course of pregnancy than is otherwise needed. He suggests the use of irradiated ergosterol so that more calcium will be absorbed and utilized by the mother. He states that viosterol in the presence of an adequate calcium dietary not only improves the teeth but absolutely and completely arrests dental caries, and this in so brief a period as two weeks when adequate dosage is employed. Patients under dental observation and experiencing the formation of tooth cavities at the rate of one or more as often as each week report the arrest of existing cavities and carious processes and a complete cessation of new cavity formation.

It can not be doubted that the maternal organism will suffer greatly in the event that there is not sufficient calcium taken during pregnancy. This process of decalcification is inevitable and has very definite results. The teeth are, along with the skeletal system, the first to suffer. The consequences although not considered as serious by many, are very disagreeable and at best are injurious. The method of treatment which consists only of increasing the calcium content of the diet and increas-

ing the absorption of the calcium is so easy and inexpensive that there is little excuse for dental caries to complicate pregnancy.

The question of eclampsia in pregnancy is a very controversial one. The methods of treatment are many and varied. In general, however, it may be said that most schools fall into one of two groups; (a) those bent on attributing its cause entirely to a blood sugar deficiency and (b) those who believe it to follow a calcium deficiency. This latter group of investigators is further divided into the exponents of calcium only and others who explain the calcium deficincy on a basis of parathyroid deficiency. Both groups are seemingly correct im their laboratory observations but fall short in clinical application. In this study the weight of the clinical evidence favors the calcium deficiency as the primary factor, and the disturbed carbohydrate metabolism as secondary and apparently due to the calcium imbalance. In support of this statement one must consider the opinions of such men as S. J. Cameron who says, "We are of the opinion that calcium is the main custodian of hepatic efficiency during pregnancy." (11). Anderson (3) found in a series of 44 cases that the serum calcium was decreased to 8 mgm. per cent or less, in 82 per cent of the cases and that the guanidine content

was markedly increased. The toxic agent responsible for eclamptic convusions is guanidine. This agent, guanidine, is a waste product of voluntary muscle action which, under normal conditions, is neutralized by calcium. Guanidine, according to many investigators, (18)(49)(56), is not only responsible for eclamptic convulsions, but is the toxic factor in producing the convulsions of tetany, osteomalacia, uremia and of liver necrosis. Uremia, liver necrosis and eclampsia have long been correlated, but now tetany and osteomalacia have been added for the purpose of strengthening the contention that calcium is an important causative factor in eclampsia.

When the blood calcium level becomes lower than normal the guanidine produced by muscular action fails to be neutralized and the voluntary muscles are rendered thereby more irritable due to the calcium poverty. Tetany might be mentioned in this connection as a first phase in that muscle irritability. It is interesting to note in this connection that a great number of eclampsias are preceded by tetany.

Guanidine is toxic to both muscle and to the liver, and, if not checked, is capable of producing a necrosis of the liver. Herein is the main link connecting carbohydrate and calcium metabolism. A toxic liver must of

necessity interfere with carbohydrate metabolism and thus the dextrose delivered by the blood to the muscle is interfered with. Thus it can be seen that it is probably not primarily a carbohydrate dysfunction which is responsible for eclampsia, but rather primarily a decalcification of the blood stream with resulting altered carbohydrate metabolism. This theory of eclampsia lends a nice explanation to the methods, both past and present, in the treatment of eclampsia. The lessening of protein would lessen the guanidine formation, or at least not increase it, while the administration of milk would be of value, due to its calcium content.

Some clinicians (notably Pool) (47) have employed the use of parathormone (extract of parathyroid gland) in the treatment of decalcification. This is of temporary value in that the calcium content of the blood is elevated and a similar process of neutralization as has been previously mentioned takes place. This method is fundamentally wrong, however, in that the calcium is taken from the skeletal system and tends to cause an osteoporotic condition. In the event of pre-existing osteomalacia the condition will be permanently and definitely aggravated.

Investigations of the activity of the parathyroid glands seems to have quite definitely proven that when

hyperactive they will cause the blood serum calcium level to rise. This is accomplished, not by increasing the intake or making it possible to absorb more calcium from the intestine, but by withdrawing calcium from the teeth and bones. It has also been shown that following this rise in the level of the blood serum calcium that there will be an increase in the amount of calcium excreted. Thus actually the treatment of low blood serum calcium by the administration of parathyroid hormone is very definitely contraindicated. It not only does not help the condition but actually aggravates it.

It has been shown by many investigators, both in England and America, that calcium plays a vital part in eclampsia. In England, Alexander Daly and his coworkers have done a great deal of work with remarkable results, (15)(17)(31). In a large series of cases they have been able to successfully combat eclampsia by the administration of calcium and alkalies. It is a routine procedure with them to administer what they term "alkaline compound tablets" to all pre-eclamptics and patients who complain of slight edema. These tablets consist of potassium citrate grains 40, sodium bicarbonate grains 20 and calcium sodium lactate grains 7½. These tablets are given every three or four hours, depending upon the amount of edema and symptoms. In a very large per centage of the cases there is a prompt return of the blood

pressure to normal, the edema disappears and any subjective symptoms of pre-eclampsia, such as epigastric pain, decreased urinary output, etc. disappear. For the more severe cases and for cases of actual eclampsia a slightly different routine is employed. A solution containing sodium bicarbonate grains 20, sodium acetate grains 40 made up to 170 cc. and slightly hypertonic is given slowly, intravenously. Calcium gluconate is also given plus the administration of the "alkaline compound tablets". The results of this treatment have been very dramatic. Patients have been admitted with extreme swelling of the face and extremities, marked epigastric pain, almost complete anuria, visual disturbances, convulsions and coma, and within forty-eight hours have become practically symptom free. In some cases the response is not so marked and it is occasionally necessary to repeat the intravenous administration of the sodium bicarbonate and sodium citrate. Then cases, however, all respond eventually to the treatment as outlined above.

The clinical results from a statistical viewpoint compare very favorably with the results obtained by other methods of treatment. In eclampsia, where other methods of treatment are employed it is necessary to induce labor in from 59 to 66 per cent of all pregnancies. With

the calcium therapy, induction of labor was necessary in only 2 per cent of all cases. The number of premature births is 63 per cent with other methods of treatment, whereas, Dr. Daly had only 11 per cent premature while using routinely the calcium therapy method.

Dr. S. J. Cameron (11) of the Royal Maternity Hospital of Glasgow has had similar results, with the use of calcium and alkalies in the treatment of eclampsia, albuminuria and pre-eclampsia. It is significant to note that the incidence of eclampsia at the Royal Maternity Hospital has very sharply decreased since this treatment has been instituted. It is customary for all patients of the hospital to report during the course of their pregnancy to the dispensary for routine check up. It is during this time that patients with albuminuria and symptoms of pre-eclampsia are treated. Since the inauguration of this method in the latter part of 1930 eclamptics have dropped off as follows:

Year	No.	Year	No.
1926 -	27	1929 -	22
1927 -	19	1930 -	38
1928 -	24	1931 -	8
		1932 -	7

These figures are convincing proof of the efficacy of this type of treatment in the warding off of eclamp-

sia by prophylactic treatment with calcium and alkalies.

In America too, quite a number of men have interested themselves in the possibilities of calcium therapy in toxemias of pregnancy. Perhaps the first work of importance was done by Dr. Garwood C. Richardson of Chicago, (49). Dr. Richardson has employed the use of irradiated ergosterol, believing that it causes an increased absorption of calcium from the intestine and thus protects the liver from the toxic products such as guanidine. His experimental and clinical observations have been consistent with the British school, in that remarkable results have been accomplished. Many observers feel that a proper calcium intake and distribution is all that is necessary in the treatment of toxemia of pregnancy, (12)(20)(50). Diet other than the administration of irradiated ergosterol and calcium compounds may be general. This is of particular benefit in that it conserves the strength of the patient until the time of delivery. It is to be admitted that the exact mechanism of toxin formation, or the nature of the toxins is far from settled, but the clinical results obtained by the investigators who are using calcium therapy are very encouraging. Calcium can be used as a prophylactic measure, in the form of calcium salts, (51)(12)(35)(57). These salts are given in sufficient

quantities to bring the blood calcium level up to within normal limits. The calcium intake can be increased in another way--by the administration of Vitamin D. This method is prefered by some men, (10)(49), who feel that the calcium content of the diet is sufficient, but that the powers of absorption are not great enough. Timple (58) recommends the use of cod liver oil or viosterol as a prophylactic measure during the course of pregnancy. In running a series of tests to determine the blood serum calcium level during pregnancy, and the effect of calcium administration and viosterol therapy, he found that the level could be greatly raised. He found also that by so raising the blood serum calcium leven that albuminuria, pre-eclampsia and eclampsia could be very well handled.

Internists have been treating hypertensions for many years with calcium. It has, however, been only recently that calcium therapy has been used in eclampsia. It is pleasing to note that the same good results in the hypertension of eclampsia follow the administration of calcium. Rodecurt (50) states that he believes calcium therapy is imperative in eclampsia and eclampsism. He employs the use of Kalzan which is calcium, sodium lactate. He gives a report of forty of his own cases which he got marked improvement. It was brought

out that in the six with marked improvement the eclampsia was particularly severe.

Wilser (61) has had similar good results in the treatment of hyperemesis gravidarum with calcium salts. Moore has had success in treating nausea and vomiting of pregnancy by giving calcium salts. He feels that it serves as a tonic and improves the general condition of the patient. In so doing he has concluded one may successfully combat nausea and vomiting of pregnancy.

Barthalomew and Krocke (4) present a case of toxemia of pregnancy in which the blood serum calcium was less than 7 mgm. percent. Death followed persistant hemorrhage and spontaneous delivery. At autopsy it was found that there was multiple large infarcts of the placenta. Whether or not these were due to the low calcium content of the blood serum is debatable. The hemorrhagic tendency, however, was in all probability due to the low calcium content of the blood.

The results of calcium therapy in the treatment of severe albuminuria, per-eclampsia and hyperemesis gravidarum have been very gratifying. None of the men who advocate this type of treatment feel that they can cure, or even help chronic nephritis, marked liver damage or other organic involvements, when these conditions are present in addition to the toxemias. They do

feel, however, than in the uncomplicated cases, that the results obtained by calcium therapy far outshine the results obtained when any other kind of therapy is employed. The rationale for calcium therapy has been clearly stated. The results, clinically speaking, are sufficient evidence of the efficacy of this treatment. There is some divergence of opinion as to whether the best thing to do is increase the amount of calcium in the diet or to increase the absorption of the calcium already in the diet, but the end results are the same in either case. The ease of administration and the cost of this form of therapy are of great practical importance when one must consider the financial status of his patients

Another clinical manifestation of decalcification occurring in pregnancy is the tetanoid state described by E. C. Hartley (24)(25). The symptoms may be divided into first:

Objective:

(a) Insomnia

(b) Irritability of disposition unusual to the patient

(c) Cramp-like or aching pains in the legs and thighs

(d) Parasthesias of the extremities affecting large areas, or in some cases only the

fingers and toes.

Subjective:

(a) A blood calcium having a very low normal or as is generally true below normal.

(b) Increased bleeding time and coagulability

(c) Muscle excitability as is evidenced by the galvanic current.

With the above symptoms being quite variable, it is occasionally difficult to make a diagnosis. This is especially true since the obstetrician is apt to regard the complaints of the mother as neuritic tendencies. The reason for the variance in the symptoms (objective) is the multiplicity of functions of calcium. In review it might be well to state that calcium, sodium and potassium in definitely balance proportions are necessary for normal cardiac action, for the proper nerve impulses to be passed from nerve to muscle, maintenance of the membrane permeability in balance, for the coagulation of the blood, for the bone building processes of our bodies and lastly, calcium along with magnesium holds to a great degree the more irritating salts sodium and potassium in balance (56). The tetanoid state as described by Hartley does not adequately explain the symptom syndrome according to some investigators. Williams (60) and Bland (8) and others in recent texts recognize the occurrance of

a tetany in pregnancy, and consider it to be a true tetany. They do not, however, sufficiently evaluate the importance of this disease, for the percentage incidence cited is far too small. Stevens in his practice of medicine tells us that, untreated, seven per cent of the tetanies of pregnancy die in tetany.

Tetany is identified by Abt as a consequence of parathyroid deficiency, but medical literature contains contradictory reference to etiology: That tetany is more common in artificially fed than in breast fed, and, that children born of mothers who have suffered from tetany are more prone to develop the disease. It does not seem logical to incriminate the parathyroid glands for this condition, when actually the cause is a calcium deficiency which is in turn due to improper calcium intake or a poor utilization of the calcium in the diet. Tetany is more frequently encountered as a sequence of rickets and osteomalacia, but is occasionally encountered as an entity in itself. Rickets and osteomalacia are both calcium deficiency diseases. It follows, then, that tetany is merely the logical outcome of both, since the parathyroid glands are depending upon a depleted bone, or a depleted warehouse as it were, from which to draw the calcium to meet the demands of the body tissues and functions. Guanidine, again is capable of producing a tetany identical with the tetany after parathyroidectomy.

Some investigators feel that as high as 75 per cent of all pregnant women suffer from tetany to some degree, however slight (10). The basis for this statement is that one of the earliest and most important symptoms is overlooked in obstetrics. This symptom is cachexia and is so often missed due to the preponderance of nervous phenomena both in pregnancy and especially in this disease. Accompanying the cachexia and resulting from it is a general muscular weakness, which in itself is a very frequent complaint of pregnant women. This muscular weakness, in turn, accounts largely for the exhaustion which so readily follows slight exertion.

The outstanding symptom of tetany in pregnancy is muscular contracture, especially of the lower extremities, and involving, as a rule, the gastrocnemius, soleus, and flexor hallicus longus muscles. Other groups are occasionally involved, but far less frequently. This symptom most often comes on during the night, toward waking hours. The severity of the pain awakens the patient from her sleep. The pain and the contracture may persist from a few minutes to an hour or more. This manifestation is pathognomonic of tetany and by the general practitioner is only too frequently explained to the patient as being due to pressure on the deep nerves of the pelvis. Other diagnostic signs appear which are

attributed to actual tetany only too rarely. Amont them we note puffiness of the face, hands and fingers, tingling or numbness of the fingers or extremities, localized swellings of the limbs, pallor, thinning and loss of hair, frequent occurrence of dental caries, increased brittleness of the teeth, and thinning of the nails as well as brittleness. Tachycardia is almost always seen and in extreme cases there may be convulsions and coma. Thus it is to be seen that practically all of the above symptoms are very easily shoved off onto other conditions, generally of much less importance than tetany.

The diagnosis of tetany of pregnancy may be positively made upon complaint of muscle contractures, but it should be suspected earlier, and treatment instituted with the cachexia which so often begins in the very early months of a pregnancy.

In extreme cases the results of treatment with irradiated ergosterol are remarkable. A clinical relief is obtained within 48 hours if properly administered (43). Malfatti feels that calcium is of great importance as a prophylactic against tetany (38). He states: "If the calcium intake is not cufficient to meet the requirements of the maternal organism during gestation and lactation, clinical manifestations of calcium deficiency, such as neuro-muscular hypersensitivity and subtetanic and tetanic conditions become manifest. It has been

found that these disorders can be counteracted by the administration of large doses of calcium." He found that a combination of calcium lactate and sodium lactate proved mostsuitable for oral therapy.

It is to be understood, as has been previously mentioned, that the etiology of both lactation and maternal tetany is not a closed book. There are those who attribute the condition to parathyroid dysfunction purely from the physiological viewpoint. The majority of men are now, however, attributing tetany to calcium deficiency primarily, with a hampered parathyroid gland as the result of this calcium deficiency secondary. Pool (47) suggests that maternal tetany is related to parathyroid insufficiency. This, he says, is probably due to the calcium want, judging from the beneficial results obtained by employing calcium therapy.

The next consideration of decalcification in pregnancy will be a group of general conditions. It has been observed for some time that an improved calcium metabolism produces a surprising change in the friable or "wet-blotting paper" perineum as well as the frequency with which the progress of varicosities was arrested. The results would seem to indicate a common origin for these pathologies (48).

To substantiate the beneficial results which the treatment brought about in the perineum, two cases are

here summarized:

Mrs. C., para I, was delivered spontaneously with epesiotomy, and an immediate repair. The operator was competent and experienced, but before discharge from the hospital the wound opened to its full depth. A good general surgeon performed a second perineorraphy in the ensuing year. The result was poor, with the formation of a vaginoperineal fistula, opening in the raphe externally. As a para II, Mrs C. had tetany throughout the pregnancy. Calcium lactate failed to provide relief. Calcium chloride in massive doses improved the tetany after ten days, but failed to cure under three weeks administration. Forceps were necessary in the delivery on account of a very profuse hemorrhage arising from a beginning laceration of a firm band of scar tissue in the perineum, which had been incised to aid delivery. The fistulous tract was excised and immediate repair performed. Owing to the friability of the perineum the sutures cut through the tissue and the repair was of necessity loose. The fistula again formed, this time through a thinner portion of the perineum. Hemorrhage at delivery was moderate from perineum and uterus. As a para III Mrs. C., again suffered tetany more marked than previously. This was again treated with calcium chloride and again only a partial success.

At delivery hemorrhage was profuse both from uterus and perineum. Delivery was spontaneous with epesiotomy. The perineum again was very friable, but this time the fistula was almost entirely obliterated. In the fourth pregnancy tetany was more marked than at any previous time. Viosterol was prescribed with complete relief in thirty-six hours, and its administration was accompanied by a greater feeling of strength and well being. Viosterol was continued throughout the pregnancy and into the period of lactation. Delivery was spontaneous with epesiotomy. The perineal bleeding was scant. Uterine bleeding was limited entirely to retroplacental clot, with no flow of blood either preceding or following delivery of the placenta, and the pad was not so much as spotted with uterine blood. The perineum was found to be in excellent condition and the sutures could be drawn up to their usual tautness without cutting through. Healing was by primary intention and the sinus was completely obliterated. At six weeks the perineum was excellent.

Case two.

Mrs. S., was delivered as a primipara at age of 33. During gestation tetany was marked, but was well controlled by calcium chloride by mouth. The labor was sluggish and required mid-forceps delivery with episiotomy and Duhrssen incisions on account of a posterior rotation of

the occiput, and an edematous rigid cervix which failed to dilate. The medio-lateral episiotomy was accompanied by such profuse hemorrhage that ligation and suturing were necessary before it was thought safe to proceed. On incising the cervix hemorrhage was again so profuse that the compression forceps had to be left in place while a manuel rotation was performed and the forceps applied to the head. Cervix and perineum were repaired by catgut. Both were friable and the sutures had to be put in loosely to avoid their tearing out. Uterine hemorrhage was rather profuse but was controlled by the usual methods. Progress was then uneventful until the tenth day when the patient was allowed to sit up in a chair. Upon standing, a pronounced hemorrhage occurred, and was controlled by uterine massage followed by pituitrin and ergot. Lochia rubra was of unusual abundance and duration. At six weeks the perineum was relaxed due to poor union. The menstrual periods, upon their return, were exceptionally copius and accompanied by faintness and general weakness. At the age of 36 Mrs. S. again became pregnant. Severe and debilitating tetany began at two months. Viosterol was ordered and continued throughout gestation. The tetany was promptly and permanently relieved. Labor was active and rapidly progressive in spite of a recurrence of the occipito-posterior presentation.

Dilitation was normal. Episiotomy was performed with only the usual bolld loss. Uterine bleeding was scant. The perineum instead of being friable was normal and catgut repair was performed with the usual tension on sutures. Healing was by primary intention. The Lochia was normal. There was no late hemorrhage. Viosterol was continued into the lactation period and until menstruation was reestablished. At six weeks the perineum was in excellent condition. The menses recurred with only a normal loss, which for this patient at 36 years of age was the least that she had lost throughout her entire reproductive period.

Both of the above cases had more or less generalized varicosities, the varices being more marked in the limbs vulvar and perineal regions. After the administration of calcium salts and viosterol the varicose processes were almost completely arrested and the recession of the varices following the administration of viosterol was decidedly greater than the recession following her previous delivery. This arrest of progress in varicose veins has been noticed in numerous other cases and would seem in some instances, at least, to associate the friable perineum and varicosities with decalcification.

Postpartum bleeding is another complication of pregnancy which is associated with decalcification. This is apparently on the basis of coagulability of the blood.

Bardenheuer (9) discusses the results that he obtained in a series of 57 cases in which he administered calcium therapy from one to seven hours before labor. The average amount of blood lost in the 57 spontaneous deliveries was only 180 grams. It has been noted, on the other hand, in women who have a low calcium content, that there is a tendency toward rather profuse post-partum hemorrhage--the hemorrhage occurring both from the uterus and from minor lacerations which are bound to occur during the delivery. Pierce states that he feels it essential to have a well-balanced diet during pregnancy, paying especial attention to calcium and Vitamin D. (45)(46). The prophylactic use of calcium in prevention of postpartum hemorrhage is too frequently not employed. The physiology of blood clot formation is sufficient proof of the fact that women who undergo pregnancy, and who do not have an adequate calcium intake, are subjecting themselves to the dangers of severe postpartum hemorrhage.

Puerperal sepsis, although not of great frequency in any of the better hospitals, is a complication of pregnancy which should merit out attention. Green (22) is of the opinion that diet is of considerable importance in controlling puerperal sepsis. A group of 275 pregnant women received a preparation containing Vitamins A and D for a period varying from a month to two weeks

before delivery; 275 other pregnant women were used as controls. The number of primiparae and the number requiring instrumental delivery were about equal in both cases. Other complicating factors were about equally distributed in the two groups. In the group receiving Vitamin therapy there was an incidence of morbidity of only 3 cases or 1.09 per cent, while in the control group there were 13 cases or 4.73 per cent. At the Jessop Hospital the morbidity rate was 5.8 per cent as compared with the average rate of 6.8 per cent for the previous three years. The group at the hospital receiving Vitamin therapy was 1 per cent, while the control group had a 5.8 per cent morbidity. The pyrexial cases numbered 56 or 20.4 in the vitamin group, while 98 or 35.6 per cent in the control group had pyrexia. This is a difference of 15.2 per cent, which is 4 times the standard error and, therefore, significant. This data seems to be of value in showing that this form of therapy, increasing the calcium by means of vitamins, is of importance in increasing the general condition of the mother, thereby reducing the rate of puerperal sepsis. These views have been substantiated by other men who have done considerable research along these lines (23).

Uterine tonicity and its ability to forcefully contract is dependent upon the calcium content of the

maternal blood serum (6). It has been shown in many cases that prolonged, slowly progressing labor was due to a general debilitated condition of the mother and that this condition of weakness was due to calcium deficiency. Calcium has long been known to be intimately connected with muscular contraction. Therefore, it is only logical to assume that when there is a calcium deficiency that the uterine musculature will not properly contract, and that the course of labor is bound to be prolonged. The treatment again is prophylaction. If during the period of gestation the mother is given an added amount of calcium in the form of calcium salts and perhaps some Vitamin D if there are indications that there is not adequate absorption and assimilation then this most trying and distressing complication of pregnancy can often by avoided.

A low maternal calcium is especially apt to occur at the time of lactation (21). At this time there is a very severe calcium drain upon the mother due to the high calcium content of the milk. Conditions which may have been latent during the period of gestation, may flare up when this added drain occurs. Calcium should be administered in rather large quantities throughout gestation, so that there is at all times a sufficient reserve to meet all emergencies (1). Osteomalacia is

quite occasionally seen complicating pregnancy. This condition as scurvey is generally aggravated by pregnancy (29)(32)(58)(60)(19). There has been a great deal written on the subject, but since they are clinical entities, not necessarily dependent upon pregnancy I will not discuss them further. It is well to bear in mind, however, the seriousness of these conditions and the possibility of severe results if the diet is not carefully watched, noting especially the amount of calcium in the diet and the amount of this calcium that is being utilized.

Summary

Considerable attention has been paid to the calcium metabolism during pregnancy. It has been found that there is a greatly increased demand upon the storehouses of the mother. It has also been found that the average American diet is deficient in calcium content. The blood serum calcium content of pregnant mothers has been checked during various periods of gestation with the resulting information that in apparently normal pregnancies there is no marked change in the calcium content. In the mothers who showed a low calcium content some symptomatology was sure to be found. Because of the wide range of activity of calcium the symptoms are naturally bound to be varied. In general, however, it can be said that the toxemias of pregnancy, tooth involvement (dental caries), maternal tetany and dystocia due to atonic uteri and general weakness are the most common. This is not taking into consideration osteomalacia which not infrequently is complicated by pregnancy and is made much worse by the added calcium drain. In conclusion, it sould be said that calcium metabolism should be carefully watched treatment instituted early. The following conclusions can be made:

1.) The physiological processes of the body which are dependent upon a proper calcium balance are many.

2.) Calcium becomes of increased importance during

pregnancy because the demands of the fetus upon the maternal organism are very heavy.

3.) The average American dietary is deficient in calcium.

4.) Decalcification of pregnancy is present to a certain degree, at least, in 75 per cent of all pregnancies.

5.) Carious teeth, softening of the teeth or actual dropping out of one or more teeth is a common finding, which can be controlled by the administration of calcium salts and Vitamin D.

6.) Albuminuria, pre-eclampsia, eclampsia and the toxemia of pregnancy respond very well to calcium therapy. The cause of eclampsia is probably guanidine, which is a waste product of muscle metabolism. Normally this substance is neutralized by calcium. In the event of decalcification the guanidine is not neutralized and there is resultant liver necrosis. This impairs carbohydrate metabolism, and the cycle is complete. Calcium salts plus alkalies have produced remarkable results in clinical cures.

7.) The "tetanoid syndrome" or actual tetany is much more common in pregnancy than is ordinarily suspected. This, too, responds well to calcium therapy.

8.) Perineal ~~fri~~ability and varicosities have been

seen to improve remarkably following calcium therapy.

9.) The general condition of the mother, following calcium therapy improves and less complications of pregnancy such as edema, dystacia and puerperal sepsis are apt to occur.

10.) The treatment of decalcification of pregnancy is very simple. Increase the calcium content of the diet and increase the absorption and utilization by means of Vitamin D. The cost is small and the results are very spectacular.

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