The Present Status of Calcium Therapy

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Even though calcium is used quite extensively, clinically and even though there is an abundance of literature on the subject, our knowledge of calcium metabolism is still incomplete. It has long been recognized that calcium is necessary for the economy of cellular metabolism, and a brief review of the chemistry and physiology of calcium metabolism in the light of our present knowledge will prelude the clinical applications of calcium salts.

Calcium is present in every normal cell and is necessary for the normal functioning of that cell. In general it may be safely stated that it is necessary for the conductivity and irritability of nervous tissues. On the heart muscle, calcium appears to exert a tonic influence, the contractions becoming more forcible and relaxation less complete when the perfusing fluid contains an excess of calcium while toxic amounts cause the heart to stop in systole (74). If calcium is excluded from the perfusing fluid, the heart stops in diastole. That serum calcium is necessary for proper cell metabolism is evidenced by the constancy of its amount in the blood of mammals. The normal range for serum calcium in man varies with different investigators, but is usually given as 9.5 to 10.5 mgm. per 100 cc. of blood (43). The value for whole blood is given as 5.3 to 6.8 mgm. per 100 cc. of blood (44).

It is known that three chemical forms of calcium exist in the body, namely: The diffusible but unionized, the diffusible ionized, and the unionized undiffusible combination. Electrometric determinations (63) have shown that only ten to twenty per cent of the serum calcium exists in the ionic state.

When one speaks of low serum calcium in disease, he may mean that any one of the three fractions are deficient. Vines (91) gives examples of diseased conditions in which the total serum calcium is normal though the diffusible part is reduced by half. Marked changes may occur in serum calcium with but few symptoms, such as is seen in osteitis fibrosa, where there is a fifty per cent increase in the serum calcium (91). In tetany the diffusible calcium is lowest (88.76) while in nephrosis the non-diffusible fraction is the lowest (91).

The mere fact that an estimation of serum calcium reveals a normal figure in certain diseases does not indicate that the patient should not be given calcium. It may be that the diffusible fraction is low and since Liu (50) has shown that cod liver oil increases that fraction, then cod liver oil or irradiated ergosterol should be the rational therapeutic agent. Similarly, in parathyroid tetany, where

the diffusible calcium is low (88, 76) the author has obtained good results in alleviating and preventing tetany by administration of cod liver oil (13) or acterol (14).

In the treatment of calcium deficiency diseases such as parathyroid tetany, spasmophilia, rickets and perhaps others, the fixation of calcium in the tissues or the mobilization of calcium is the important factor. The ionizable fraction, which is probably the most important fraction, is increased by cod liver oil, ultra violet light or irradiated ergosterol. Parathyroid extract also increases the amount of diffusible calcium and evidence that parathyroid extract regulates the equilibrium of calcium existing between the tissues of the body and the blood stream has been presented (86). It would seem essential to have not only an abundant supply of calcium in the diet, but also sufficient sunlight or vitamine D to control the interchange of calcium from the blood stream to the tissues. Factors that determine or influence the absorption of calcium from the gastro-intestinal tract should be understood to properly treat calcium deficiency diseases. A considerable part of calcium salts ingested are undoubtedly excreted through the kidneys and colon. Mason (53) and Albu and Neuberg (1) state that the adult man requires approximately 0.4 mg. of calcium per day. In the growing child the amount of calcium required is greater; Herbst (33) states that the normal child stores about 0.3 mg. of calcium per day. To insure a proper amount, calcium must be present in the diet in amounts much greater than these to allow for the low efficiency of absorption; 1.0 to 1.5 mg. has been given as the average daily dietary requirement (1).

It is interesting to note that the diet of the Finns contains between two and six grams of calcium oxide daily, Tigerstedt (89). Compare these findings with those of Sherman, Mettler and Sinclair (81), who have estimated the amount of calcium and phosphorus consumed in the ordinary American diet as the following table indicates.

Ash Contents of Ordinary Dietaries, Weights in Grams

	Finnish			American		
Calories in Diet—	P_2O_5	CaO	MgO	P_2O_5	CaO	MgO
Over 4000	10.96	6.10	2.02	4.24	0.79	0.89
4000-3500	9.46	3.79	1.85	3.22	0.94	0.51
3500-3000	8.18	4.02	1.53	3.29	0.99	0.50
3000-2500	6.93	3.51	1.23	3.20	0.92	0.46
2500-2000	5.64	2.96	1.03	2.06	0.36	0.32
2000-1500	5.12	2.85	0.78	1.84	0.68	0.23

Tigerstedt explains this on the basis that the Finns take on an average of something over 900 cc. more of milk per day than the Americans do.

Calcium is present in food both in organic combination with proteins and in inorganic combinations as salts. There is considerable evidence to support the view that calcium in combined form with proteins is more readily absorbed than the simple calcium salts, Givens (24, 25) Sherman and Hawley (80), McClugage and Mendel (57).

Among the inorganic calcium salts, calcium chloride is more readily absorbed than lactate (37) and is more efficient in relieving the tetany of parathyroidectomized animals. Also the acidosis produced by the ingestion of calcium chloride which like the serum calcium increase produced by the ingestion of calcium salts, persists only for a short time (85). It would seem then that the effect of calcium chloride ingestion is the sum of two effects—an increased calcium absorption which may or may not be greater than that produced by calcium lactate, and an increased serum calcium due to an acidosis. It is interesting to note that Zucker and Matzner (99) found that in active untreated rickets in rats, the feces were alkaline, a condition unfavorable to calcium absorption, also the acid secreting mechanism of the stomach was impaired. After cod liver oil administration, the intestinal contents became acid simultaneously with general improvement.

Bergeim (7) found that the addition of sugars, especially lactose, caused an appreciable increase in the serum calcium. He believes the increased absorption is due to increased acidity of the intestinal contents, a condition which seems to favor calcium absorption. Gross (29) also found increased absorption of calcium by the use of lactose.

To vitamine D has been attributed the property of increasing calcium absorption since this vitamine as well as ultra violet light increases serum calcium (59). Bergeim (8) believes that vitamine D acts by facilitating the retention of calcium rather than the absorption. He also suggests that it may promote the breakdown of organic phosphates, thus increasing the inorganic phosphate of the blood, and thereby leading to increased calcium deposition and lessened intestinal excretion. Babbot et al (5) have shown that in vitamine D deficiency, as in rickets, the acid secreting mechanism of the stomach is impaired which inhibits the absorption of calcium.

A question has arisen as to the efficacy of absorption in administering calcium salts by mouth. Roe and Kahn (74) have found that the serum calcium concentration of normal fasting subjects is definitely elevated by the oral administration of five grams of calcium lactate. Simultaneous ingestion of various foods with five grams or more of calcium lactate produced a marked depression of the rate of calcium absorption from the intestinal tract. They believe that if calcium is given in water without food it is unnecessary to incur the dangers of the intravenous technic.

It has been thought that the parathyroids raise serum calcium by increasing the rate of absorption from the alimentary tract but Stewart and Percival (86) have demonstrated that the parathyroid hormone can exert its full action on the serum calcium even after complete removal of the alimentary tract. The large intestine provides the main excretory route for calcium. They consider the parathyroid hormone controls the distribution of calcium between the blood and the tissue by regulating the proportion of the total serum calcium which is readily diffusible.

In connection with the study of calcium absorption it is important to know something of the excretory mechanism. Bergeim (8) has shown that calcium is absorbed from the small intestine, and excreted into the large, and Stewart and Percival (86) found by direct measurement that in cats the intestinal excretion is 0.2 mgm. per hour which is about twice that of the urinary excretion. The urinary excretion is absorbed calcium, but fecal calcium consists of both the absorbed and unabsorbed.

There appears to exist a definite antagonism between the excretion of calcium and magnesium. The addition of magnesium salts to the diet in human subjects (11) has been found to increase the urinary excretion of both calcium and magnesium, and Malcolm (55) obtained similar results in dogs. Mendel and Benedict (62) found increased elimination of calcium in the urine to follow injection of magnesium salts, and conversely, injection of calcium salts to cause increased excretion of magnesium.

Hart and Steenbock (30) found that an excess of magnesium in the diet interfered with the absorption of calcium, appeared to prevent its proper utilization and caused an increased urinary excretion. In connection with the effect of magnesium on the calcium content of the serum, Smirnow (82) showed that the vagus center was stimulated by injection of calcium and paralyzed by magnesium.

Aulde (4) in his book on "Calcium Therapy" gives evidence for a marked antagonism existing between calcium and magnesium. He believes that calcium depletion in acidosis conditions causes magnesium infiltration of tissues. When the tissues become infiltrated, the conduction of nerve impulses is inhibited and abnormal functioning results. Sciatica and neuritis he considers to be a nerve block by magnesium infiltration; he also considers chronic nephritis and myocarditis due to the same. The cause of the acute condition is toxins or disordered digestion followed by an acid excess with the ultimate effects being due to the infiltration.

Prerequisite to magnesium infiltration is acid excess. Aulde (4) gives many symptoms of acid excess, some of which may be given as follows: Acid eructations with or without nausea; shortness of breath on exertion; yawning, malaise, insomnia and acid salivary reaction to litmus.

Since calcium is such an important factor in cellular activity, then certainly it should have a place in the treatment of disease where local cellular pathology is present. It has been stated that (18) intravenous or subcutaneous injection of calcium chloride in animals partly or completely inhibits the pleural effusion produced by iodide administration, and that it also prevents the development of oedema and inflammation of the conjuctiva after the instillation of brucine. On this basis it has been used in man to hasten the reabsorption of pleural effusions and exudates. Oriani (65) treated eight cases of exudative pleuritis and two cases of tubercular polyserositis with calcium chloride. In only a single instance, a case of exudative pleuritis following acute pneumonia, was treatment without effect. Excellent results which were marked by an occurrence of an increase in diuresis as well as of rapid diminution and disappearance of effusion were obtained in all the others. According to Oriani, from 15 to 30 grams of calcium chloride per day should be employed in conjunction with a diet which is free from salt.

Some object to the intravenous administration of calcium chloride, but as a rule no ill effects are noted if it is given slowly and in not too concentrated solutions. The patient usually has a sensation of warmth about the face and neck, sometimes a slight tingling of the fingers and toes, or he may break out in a profuse perspiration and have slight nausea if the injection is given too rapidly. Tissue necrosis will occur if given outside the vein. Aulde (4) believes that the most efficient method of administering calcium is to use a colloidal suspension since lymph and blood consist of a colloidal suspension of infinitesimal particles.

Gonzalo (27) states that calcium chloride intravenously has been used with success in seven cases of serous pleuritis effusion, and since there was complete reabsorption of the exudate, he did not have to resort to pleural puncture. He used 1 or 2 cc. of a ten per cent solution with four or five days interval between injections, and only three or four at the most were required to obtain results. The doses employed by him have never produced the slightest general reaction or phenomena of hemoclastic shock experienced by those given large doses.

The parathyroid hormone has been used by Gold (26) to produce a hypercalcemia and thus prevent experimental effusions. The results indicate that in dogs pleural effusions are diminished or prevented following the intrapleural injection of an irritant.

Calcium and the Gastro-Intestinal Tract

Calcium lessens the irritability of smooth muscle and is found to be valuable treatment in pylorospasm or enterospasm in tuberculous patients. Ashworth (3) found calcium chloride very valuable intravenously in spastic colon and spastic pyloris; it also relieved pain in tuberculous enteritis.

Calcium and Jaundice

In obstructive jaundice, both clinical and experimental, there is usually a prolonged clotting time. King and Stewart (40) observed a delayed blood coagulation time in vitro when bile pigments were added to the blood. They believed that this was evidence of insufficient available calcium. Further evidence for the existence of a functional calcium deficiency in jaundice is found in the work of Lee and Vincent (49), Walters and Bowler (95), and Kirk and King (41).

Walters (93, 94) reported that the coagulation time of the blood could be reduced greatly and the toxicity diminished in patients with obstructive jaundice by daily intravenous injection of a ten per cent solution of calcium chloride for three days before operation.

Kirk and King (42) have found a decrease in the ionnizable fraction of serum calcium in obstructive jaundice. With this in mind the author produced an experimental obstructive jaundice in dogs, and when the clotting time was delayed, they were given one ounce of cod liver oil (15). In every instance coagulation time returned to normal within four hours. In the course of the investigation an article appeared by Liu (51) in which he showed that cod liver oil increased both fractions of the serum calcium, the diffusible and the non-diffusible. This is further proof that cod liver oil is good therapy where there is a functional calcium deficiency, and therefore should be more valuable than calcium therapy in preparing jaundiced patients for operation.

Calcium and Nervous Disorders

On the basic principle that normal cell activity is changed to hyperexcitability by decreasing the calcium, magnesium or hydrogen ions, functional nervous diseases have been treated by Gault (23) with considerable benefit. Animals kept on a low calcium diet after a period of time become easily excitable, nervous, restless and more apprehensive than the normal animal. This behavior is rapidly brought back to normal by calcium administration. He treated eighteen patients with functional nervous disorders with prolonged calcium lactate administration. They received the equivalent of 20 grains of calcium lactate four times daily. He reported uniform good results in that within 24 to 48 hours they experienced a feeling of mental well being with disappearance of nervousness, apprehension and the feeling of fatigue so commonly complained of.

Calcium in Pregnancy

Macomber (52) has shown in the adult rat that diets low in calcium do not produce sterility, but they do effect the fertility by increasing the intrauterine mortality. He also found that calcium was important in the prevention of miscarriages and still births.

The literature on the influence of menstruation on blood calcium is rather conflicting, but consensus of opinion seems to be that serum calcium increases up to the onset of menstruation and then decreases during the period.

Ultra violet light irradiation of the pregnant mother prevents foetal rickets as well as a drain on the calcium and phosphorus of the mother, Hess et al (35). It also changes negative calcium balances in lactating and dry goats to positive calcium balances, Hart et al (31).

Bogert and Plass (12) found that the average calcium content of the serum was 9.1 mgm. per 100 cc. of blood for 23 women at the time of labor and 10.2 mgm. for 12 non-pregnant women. Widdows (96) stated that the serum calcium falls during the last month of pregnancy and during the early stages of lactation. Others (97, 45) have also reported low serum calcium values during the late stages of pregnancy.

Heath et al (32) found that in severe exophthalmic goiter there is a very high calcium excretion, but in myxoedema the calcium excretion is below normal. They also observed that in the normal subject when treatment with thyroid had raised the metabolism twenty per cent, the calcium excretion rose definitely even on a diet inadequate in calcium.

Waldorp and Trelles (92) reported likewise a decrease in blood calcium in toxic thyroid cases. Further evidence for disturbed calcium metabolism is seen in the work of Knude and Carlson (46) who thyroidectomized young rabbits and found a disturbed condition in the skeletal structure which simulated clinical rickets.

Calcium and Diabetes Mellitus

Diabetes mellitus is thought to be associated with calcium metabolism. Wishnofsky (98) reported a negative calcium balance in diabetes mellitus, although intravenous administration of calcium chloride does not appear to influence the tolerance of diabetics for glucose.

Horowitz (38) reported a slight elevation in the serum calcium of diabetics as did Kylin (47) who found an average of 12.1 mg. of blood calcium in diabetic patients as against 11.1 mg. in healthy subjects.

Calcium and Nephritis

An inadequate knowledge of the chemical metabolism of the kid-

ney in health and disease makes the subject open for further observations. Several investigators have mentioned the part that calcium and phosphorus play in the kidney.

Pincus et al (67) reported that inorganic phosphorus was invariably high in severe chronic nephritis, but found the calcium normal except in one case with convulsions.

Boyd et al (17) found blood phosphates usually increased and blood calcium decreased in nephritis.

Horowitz (38) reported low blood calcium in nephritis, as did Blumgarten and Rohdenburg (10).

Aulde (4) believes that it is the acid excess in the general system which breaks down kidney structure and thus sacrifices the calcium to unite with the acid. When the calcium is utilized, magnesium infiltrates and produces a chronic insufficiency.

Diuretic Action of Calcium

Blum and others (9), who believe oedema is due to sodium retention, have explained the diuretic action of calcium chloride by its effect in provoking loss of the retained sodium which carries with it water. They believe that after the injection of calcium chloride the calcium is eliminated by the bowel while the chloride is absorbed, becomes attached to the retained sodium, and passes into the urine, allowing the escape of water.

Since the parathyroid hormone produces a hypercalcemia quickly and of longer duration than calcium salts, it has been given in cases where diuresis is desired, Mason (54), Meakins (61), McCann (56), and Reitzel and Stone (72).

Calcium and the Heart

It is well known that calcium is important for normal heart rhythm. Kylin (48) found that lowered blood calcium caused the systolic phase of the heart beat to be weakened. He found a low blood calcium content in heart insufficiency with oedema. In essential hypertension Blumgarten and Rohdenburg (10) observed a low blood calcium.

In arterial sclerosis Fitch (20) found the excretion of calcium to be deficient.

Ashworth (3) found that calcium injected directly into the blood stream acts much like digitalis, in that small doses accelerated and strengthened the heart, while large doses seemed to be poisonous, tending to bring the heart to a standstill.

Calcium and Rickets and Spasmophilia

Of great interest is the relationship existing between calcium, phosphorus, and ultra violet light in the treatment of rickets and spasmophilia. In spasmophilia and rickets serum calcium usually is low; in certain cases it may be normal. Blood phosphates are usually high in spasmophilia and low in rickets, (28), (58), (77), (60). The same authors reported beneficial effect from cod liver oil or ultra violet light in treating either condition. More recently irradiated ergosterol has been successfully used to heal the bone lesions of rachitis (34).

Schpoljansky (78) found low calcium in infantile tetany and thought it due to hypofunction of the parathyroids.

Calcium and Diseases of the Bones and Joints

Umberto (90) treated a case of congenital bone fragility with polyglandular extract combined with calcium and phosphorus, but it was ineffective. Twenty-two irradiations with a quartz lamp restored the proportion of ionized calcium to the total calcium to normal and caused an increase in the leucocytes in the blood.

King (39) in a study of arthritis deformans found indications for an acidosis in the organism due to organic acids associated with an increase in the organic phosphates as well as a retention of calcium and magnesium.

Horowitz (38) found a high blood calccium in arthritis deformans.

Rathery and Violle (71) believe that the elimination of tissue uric acid plays only a minor role in gout and that the acute attack is due to the elimination of tissue calcium.

Horowitz (38) found an increase in the blood calcium in gout.

Fourweather (21) believes that osteomalacia in the adult is similar to rickets in the young, vitamine D deficiency being the actual cause. Similarly, Fitch (20) found an increased excretion of calcium in osteo-malacia.

Mandl (52a) emphasizes a relation existing between the parathyroids and diseases of the bone. He has collected 44 cases in which enlargement of the parathyroids was associated with rickets, osteitis deformans, osteomalacia, senile osteporosis or generalized osteitis fibrosa. He describes a case in which he removed a parathyroid tumor in a severe case of generalized osteitis fibrosa. The excretion of calcium in the urine had decreased five-sixths in a few days after operation. Motion entirely returned in the joints and the patient, who before the operation could neither stand nor walk, could later stand without difficulty and walked with a cane and a crutch.

Calcium and Tuberculosis

Conflicting evidence exists as to the benefit of calcium in tuberculosis. Unquestionably, ultra violet light helps a certain per cent of tuberculous patients, especially those having glandular or bone involvement.

Howe and Medlar (36) conclude that there is no evidence of abnormal metabolism of calcium or phosphorus in the tuberculous patient. Again the question appears as to the value of total calcium estimations of the blood serum without knowing the proportion of diffusible to undiffusible.

Peuch (66) obtained excellent results in relieving the diarrhea and vomiting of tuberculosis by the intravenous administration of calcium chloride. There was usually some relief a few hours after the first injection; however, further treatment was sometimes necessary. These injections also stopped to some extent the exhausting sweats of the tuberculous patients.

Asthma and Allergic Phenomena

Pottenger (70) first called attention to the value of intravenous injections of calcium chloride in the treatment of bronchial asthma. His biological reason for its use is that asthma is due to a local vagotonia associated with an over-balance of potassium as compared with calcium in the cell, a condition in which the neuromuscular mechanism of the bronchial system is in a state of hyperirritability. The action of the vagus depends upon the presence of potassium and increased vagus action depends upon a preponderance of potassium ions as compared with calcium ions in the bronchial tissues. The action of calcium upon the cell results in the same physiological process as adrenalin, and the effect of calcium is not only of much longer duration, but is also efficient in supplementing the action of adrenalin and relieving the paroxysms for a longer time.

Pottenger (69) in summing up the action of calcium in the treatment of allergic diseases before the American Association for the study of allergy says, "Calcium acts with and fortifies sympathetic activity, it allays muscular hyperactivity and spasm and it decreases the permeability of cell membranes, thus reducing the tendency to exudation. Often blood calcium is found to be normal in asthmatic patients, but it is not the blood calcium alone that should be considered, rather the potassium calcium ratio, the relative tonus of the sympathetic and parasympathetic nerves, the hormone balance and the hydrogen-hydroxide ratio."

Recently attention has been more closely turned to the value of calcium in nearly all allergic phenomena which includes bronchial asthma, hay fever, angioneurotic oedema, serum disease, urticaria, erythema and eczema.

Sterling (84) believes that in addition to individual hypersensitiveness to protein poisons, there exists a colloidal imbalance or a chemical difference in the plasma of the cells and in the serum of the sensitized individual which not only makes him sensitive but also subjects him to select sensitivity resulting in different forms of allergic diseases. He reported calcium estimations in a study of 85 cases, which showed calcium defiency of 9.5 mg. or below in 23 patients, while the remainder had a normal or high blood calcium ranging from 9.6 mg. to 13 mg. per 100 cc. blood. In contrast to this, he found that 68 patients showed a phosphorus deficiency, while only 17 had normal blood phosphorus from 3.0 to 4.5 mg. per 100 cc. of blood.

Sterling as well as many other clinicians, (64), (83), (69), (16) found that calcium is beneficial in most hypersensitive cases, whether they showed a low blood calcium or not. It is possible and perhaps probable that if an estimation of the diffusible fraction had been made in addition to the total calcium a low figure would have been found.

Sterling (84) suggests that phosphorus and calcium are probably playing the role of activators for enzymes or defense bodies in the defensive action of the blood stream and thus render toxic proteins harmless.

Calcium and Infectious Diseases

It seems that calcium metabolism is disturbed in acute infectious diseases. Friedich (22) stated that the blood of healthy children contains about 12 mg. per 100 cc. whole blood. He found in varicella the calcium dropped to an average of 10.74 mg., in rubeola to 9.34 mg. and in scarlet fever to 10.25 mg. He believes that this demineralization makes for easy tuberculous infection.

It was found (100) that calcium may be as low as 4.9 mg. per 100 cc. of blood in pertussis. This would suggest that the convulsive spasms of pertussis are related to tetany (100).

Calcium and Miscellaneous Diseases

Calcium has been found to play some part in many other diseases. Scott (79) has estimated the total quantity of serum calcium in sprue and found it practically normal, but there was a drop in the quantity of ionic calcium. He obtained a cure in sprue by oral administration of calcium salts and parathyroid preparations.

Ashford and Hernandez (2) reported diffusible calcium is affected more than total calcium in sprue, and they believe parathyroid deficiency is a better term in sprue than calcium deficiency.

Epididymitis has been very successfully treated by Rupel (75) using doses of 0.5 to 1 gm. in dilute solutions intravenously. The patient usually gets early relief from pain and tenderness, even if he resumes his work. Recurrence of the inflammation often follows too few injections and a course of four or five injections once daily is suggested.

In otosclerosis calcium is found to be low (38).

In epilepsy Horowitz (38) found no change in serum calcium while Blumgarten and Rohdenburg (10) report a slight decrease. According to the latter authors the lowest figures for calcium occurred in carcinoma.

In addition to the conditions mentioned associated with calcium disturbance, Corlette (19) asserts calcium and phosphorus deficiency may be implicated in many diseases in which nervous symptoms often occur. Among these are polyphagia, earth eating ("and sand disease"), bone chewing, coprophagia, milk fever and lactational dyspepsia of cattle and other animals, "ergotisms", "lathyrinism", scrapie or trotting disease of sheep, epizootie, stringhalt, laminitis, spasticity and paraplegia.

Ashworth (3) found calcium chloride valuable in hemoglobinuria and purpura.

In progressive myopia (87), Wood classifies the condition as a deficiency disease, and has found a lowered calcium content in the blood of all patients in whom this determination was made. Reference is also made in the same article to Weiner's findings that epinephrine installation in the eyes of patients with progressive myopia produced considerable amelioration in their conditions. This latter finding serves to substantiate the value of calcium in this condition because it has been shown that adrenalin fixes calcium in the tissue.

Sinus disease has been considered by some to have an allergic base; Aulde (4) however considers it to have as its underlying cause a disorder of nervous function. Improvement has been noted in these cases by administration of calcium salts.

In conclusion, it would be impossible to name all the diseases in which calcium salts have been used, but certainly there is considerable evidence to support the view that calcium plays a very important role in the mineral metabolism of the body. The author has sought to give a broad, comprehensive review of the subject and yet not advocate calcium as "a cure-all". If the paper could stimulate interest in the subject of mineral metabolism and induce clinicians to use calcium salts carefully and considerately where there is disturbed calcium metabolism, then knowledge of the subject would increase and this paper would have served a good purpose.

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THE CARCINOMATOUS GASTRIC ULCER

CLINICAL AND PATHOLOGIC CONSIDERATIONS *

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Medical literature has until recent years laid considerable emphasis upon the moderately advanced and late clinical signs and symptoms of many of our more common disease syndromes. The early symptomatology was often overlooked, misinterpreted and disassociated from the more apparent and often hopeless condition which received most of the emphasis. Fortunately for our conception of disease, clinical research in the past two to three decades has been towards early diagnosis and recognition of incipient disease. This trend in medical procedure is of greatest importance in diseases where malignancy is the causative agent, since here prevention is synonymous with an early recognition of its presence and with adequate measures being instituted for its control and attempted cure.

The interest of the medical profession in the early diagnosis and management of cancer of the stomach is not without justification, when we consider that it is the most common of all forms of cancer and is responsible for approximately thirty-eight per cent of all deaths from malignant disease in the United States. With the incidence of deaths from gastric cancer increasing, as it has from 212 per hundred thousand in 1900 to 311 per hundred thousand in 1920, there can be no question about the challenge to the profession for early recognition

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