Thus, when the change is made from regular to protamine insulin, the dietary factor should not be changed at the same time. Likewise a sufficient period must be allowed for observing the effects of this change before attempting additional ones. From a practical point of view it is much better to begin with too small a dose of protamine insulin rather than a too large one. A fairly good idea is usually obtained as to the course of the blood sugar, if three determinations are made, one before each meal about every fourth or fifth day, and the urine examined at varying periods after each of these meals.

SUMMARY

1. Diabetes showing marked fluctuations in the blood sugar, or those cases associated with certain complicating factors, as hyperthyroidism, hepatic enlargement, etc., can be controlled better by protamine insulin than by regular insulin.

2. Cases of diabetes showing a persistent hyperglycemia or where it is desired to diminish the frequency of insulin administration should receive protamine insulin.

3. Protamine insulin should not be used in cases of acidosis or impending coma or those complicated by surgical conditions.

4. Untreated cases of diabetes should not receive protamine insulin as an initial form of treatment.

5. When changing from regular to protamine insulin we have obtained good results by giving 70% of this amount as protamine insulin and the balance as regular insulin, both administered about one hour before breakfast as separate injections.

6. After a period of 4 to 7 days if the morning urine is sugar free, discontinue the dose of regular insulin. If the morning glycosuria persists, increase the protamine insulin.

7. Increases or decreases in protamine insulin should consist of only five units at a time.

8. Too many factors should not be changed at one time, nor should the effected changes be made at too frequent intervals, when using protamine insulin.

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The Present Evaluation of Vitamin B_1 Therapy*

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THIS paper will attempt to evaluate the therapeutic importance of vitamin B_1 up to the present time. By emphasizing the word "present" we come face to face with the fact that we are about to discuss a subject which is still vague, still in the process of emerging from an experimental problem to an accepted clinical concept.

After years of investigation, vitamin B_1 has finally yielded its precise chemical structure and molecular arrangement (1) and, within the past two months, its artificial synthesis has become an accomplished fact (2). The biochemist has made this vitamin available (3) and we, as clinicians, must be prepared to use it with an understanding of its clinical indications and its limitations.

Three questions present themselves:

1. What is the state of vitamin B_1 deficiency in humans?
2. What is the action of vitamin B_1 in the presence of this deficiency? and
3. Why should we use vitamin B_1, clinically, in diseases other than proven B_1 avitaminosis?

We are all familiar with the fact that *beriberi* is due to a vitamin B_1 deficiency. As a matter of fact, it represents a stage of deficiency so marked that death will invariably occur unless large amounts of vitamin B_1 are given. Thus it has been shown, that in severe cases of beriberi, the administration of vitamin B_1 by mouth is often insufficient to prevent death (4). In these cases, intravenous injections are necessary since gastro-intestinal disturbances interfere with adequate vitamin absorption. This is well known to the workers in the Orient, particularly to those who deal with the problem of infantile beriberi (5). It may not be familiar to all in this audience that the second most frequent cause of infant mortality in China, the Philippines and adjacent countries, is infantile beriberi. The vast majority of these infants are borne of beriberi mothers (6). The method of treatment of infantile beriberi has become fairly well standardized. Even before crystalline vitamin B_1 was available, a concentrate of sufficient potency for intramuscular injection was widely used throughout the Orient. The concentrate is known as "tiki-tiki" and in severe cases of infantile beriberi it is given by subcutaneous or intramuscular injections of 1 c.c. every hour for six, eight or even twelve doses. As soon as the response takes place, which usually occurs within a few hours, the infant stops vomiting, there is cessation of convulsions and fluids are retained. Vitamin B_1 is then continued by oral administration.

As well known as beriberi is in the East, just so rarely do we see it here and the diagnosis of a proven case of beriberi merits a report in one of our medical journals (7). In the East, workers in this field also recognize a clinical entity which they describe as

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latent or sub-clinical beriberi. By that is meant a state of vitamin B_1 deficiency which is not severe enough to give the classical symptoms of beriberi but which, nevertheless, has a fairly well recognized set of symptoms interfering with normal health. If allowed to continue for a sufficient length of time, true beriberi develops. This state of ill health, the sub-clinical phase of the disease, entirely disappears with administration of vitamin B_1 for a sufficient period of time.

Now, then, if we here in this country were to confine our use of vitamin B_1 to those cases in which its deficiency was sufficiently well marked to be readily recognizable, there would be no point to this paper. This brings us to the third hypothetical question: why should we consider the therapeutic administration of vitamin B_1 in conditions other than proven B_1 avitaminosis. Of course, the answer to this question is based upon the hypothetical assumption that there are states of partial vitamin B_1 deficiency too mild or too recent to be detected as definite entities (8).

In our early work, the problem was to determine how these states could be recognized. No clinical sign, no laboratory test was available so we fell back on the method of trial and error. Through funds furnished by the Carnegie Institution of Washington, D. C., a large amount of crystalline vitamin B_1 was prepared by my chemical associates and with crystalline vitamin B_1 as the only therapeutic agent, we began the study of a controlled series of chosen cases.

Since *polyneuritis* is so typical of true as well as latent beriberi, we studied this group first. All types of neuritis were included in the study group. To date, over two hundred and fifty cases have been followed with varying degrees of improvement; i. e. from partial relief of pain to complete disappearance of all symptoms; in about 90% of cases.

Our results have been substantiated by a number of other investigators (9, 10, 11, 12). Speaking conservatively, then, we can say that vitamin B_1 is an important therapeutic agent in the treatment of neuritis. You will notice that I have not defined the word neuritis and I have done that deliberately, because the results of vitamin B_1 administration are equally good in localized neuritis as they are in polyneuritis; equally beneficial in neuritis of so-called alcoholic origin as in neuritis associated with infection, anemia, pregnancy or that due to other etiological agents. We see in the action of vitamin B_1 in neuritis, a real analogy to the action of iron in all types of secondary anemia. In alcoholic neuritis we can, by the administration of adequate amounts of vitamin B_1, bring about marked improvement or complete disappearance of all symptoms even though there is no change in the alcohol consumption. Careful study of these patients, however, indicates that the alcohol probably does not play a direct part in the production of the neuritis but that these individuals have really been on a vitamin B_1 deficient diet. If these patients continue to ingest an adequate amount of vitamin B_1, there will be no recurrence of their neuritis. In all of these cases, the duration of the symptoms bears a direct relationship to the duration of treatment. Polyneuritis that has been present for from three to six months, will subside after a few weeks of treatment. Polyneuritis of ten or more years' duration may, in a very short period of time, reach a state of marked improvement but complete disappearance of symptoms may not take place even after three or four months of treatment. This is equally true in experimental animals in which two stages of B_1 deficiency—an acute and a chronic stage—are observed (13). The acute stage will disappear quickly and completely on vitamin B_1 and post mortem studies of these cured animals show little or no cellular changes. The chronic stage responds slowly and gradually. Even after the animals appeared cured, clinically, and then were sacrificed, it was possible to demonstrate many types of cellular change in central nervous system and peripheral nerves, varying somewhat for the different species of animal used (14).

The value of vitamin B_1 in *pregnancy* has an important practical significance. The view that pregnancy induces a deficiency state has been expressed by many investigators (15). The occurrence of anemia, the diminution or absence of gastric acidity, the demineralization, the polyneuritis and, perhaps, even the toxemias, all point to a deficiency state. When neuritis occurs in pregnancy, the ingestion of vitamin B_1 is followed by a marked improvement or disappearance of the polyneuritic manifestations (16, 17, 18).

From the clinical point of view, the group of neuritis most often seen are the so-called sciatic, the sacro-iliac and the shoulder girdle neuritides. These cases are frequently associated with areas of focal infection and, as a matter of fact, we have all seen, in occasional patients, a dramatic improvement following the removal of a correlated infected area. Unfortunately, such cures are few in number as compared with the disappointments that have followed the removal of teeth, tonsillectomy and similar procedures. A number of cases in our series have fallen directly into this group and we have attempted to evaluate the benefit from vitamin B_1 therapy regardless of the continued existence of a proven focus of infection. In this group, also, there has been a marked improvement in a large number of cases. It must be freely admitted, however, that there is a considerable proportion of recurrences in these cases of infectious neuritis—recurrences which, apparently, are due to the constant absorption of bacterial toxins. It is not surprising that such a condition prevails in this group. It is surprising, rather, that in the presence of a focus of infection, as marked an improvement as 70% could be noted.

The groups mentioned already are those most frequently observed in clinical practice but there are many others that merit consideration. The first to be included are the cases of neuritis *associated with varying types of anemia* of which, perhaps, the most interesting is the group associated with primary macrocytic anemias. The improvement in the neuritic manifestations of macrocytic anemia has been observed by other investigators as well as ourselves. There is a special problem connected with this group —the problem of dosage and duration of treatment. It seems possible that the clinical paradox of the pernicious anemia patient showing improvement in his blood picture but dying of subacute combined degeneration of the cord may be modified by vitamin B_1 therapy. Further studies are necessary in these cases. Certainly, neuritis associated with secondary anemia usually responds readily.

Among the less common types of neuritis are those associated with *lead poisoning* and other heavy metals and here attention is directed to the arsenical neuritis

occurring during intensive treatment for syphilis. These types of neuritis have been included among our series and show a gratifying response to the use of vitamin B_1 therapy.

We have had the opportunity to study five cases of severe trigeminal neuritis—the so-called *tic douloureux*—all of whom were operated upon and showed recurrences post-operatively. Three of these five have now had complete relief of symptoms; the other two are showing improvement while still taking vitamin B_1.

Recent experiences with *optic neuritis* and auditory neuritis are of interest. Our own series consists of too small and too recent a group to warrant positive statements but some good results have been reported already to me, personally. These two groups offer a very fruitful field for the specialists in these branches of medicine.

We must then summarize our experience in the treatment of all forms of neuritis by vitamin B_1 as one that justifies its use by giving a large percentage of improvement or cessation of symptoms. I want to call to your attention the fact that in practically none of these cases was it possible to say, at the beginning of treatment, that a vitamin B_1 deficiency state surely existed. The value of vitamin B_1 therapy in neuritis is emphasized again and again because, up to the present time, there is no other syndrome in clinical medicine in which we are as sure of its worth except, of course, in true or latent beriberi.

Herpes zoster belongs among the neuropathies frequently seen in clinical practice. The experimental physiologist has studied the possible relationship of vitamin B_1 to the susceptibility of experimental animals to the virus of herpes (19). At the present time, results are inconclusive. We have had the opportunity to study the effect of vitamin B_1 in its relation to the post-herpetic paresthesias and anesthesias and our clinical results suggest a definite beneficial action, namely, a quicker disappearance of the residual symptoms, and a smaller number of cases with persistent anesthesia in the treated cases than in the controlled series.

A recent report in the German literature describes the value of vitamin B complex in the treatment of *mild chorea* (20). We have had no experience with this type of case but I mention it as it is of interest to men in pediatric practice.

Now, we must leave what is fairly well proven and go on to the more hypothetical and, therefore, questionable use of vitamin B_1. Experimentally, in animals, there is a definite relationship between vitamin B_1 and the carbohydrate metabolism. The relationship is a complex one but a careful survey of the vast biochemical studies gives the following data:

1. In dogs, deprivation of vitamin B_1 is followed by an increased blood sugar and the presence of urinary sugar (21). When insulin is given to these animals, the blood sugar level decreases and the urinary sugar disappears but in spite of insulin, the animals go on to death. Careful studies of the blood chemistry of these animals show no significant changes in the nitrogen elements but the carbon dioxide of the blood falls and the lactic acid level increases (22).

2. The rate at which the symptoms and signs of vitamin B_1 deficiency develops in all animals can be influenced by the amount of carbohydrate in the diet, i. e., the larger the amount of carbohydrate ingested the more rapid is the onset of the manifestations of avitaminosis. Death occurs more rapidly in animals on a high carbohydrate diet than in those on a low carbohydrate diet (23).

3. The change in the carbohydrate metabolism in B_1 avitaminosis is a cellular one and has been demonstrated in minced tissue outside of the body. The brains of B_1 deficient pigeons, in vitro, show a lower capacity to take up oxygen than normal pigeons brains (24). In the avitaminotic brain tissue is found increased lactic acid and pyruvic acid. The latter is not found in the normals (25). By adding crystalline vitamin B_1 to the minced avitaminotic brain tissue, the oxygen take up approaches the normal, the lactic acid decreases and the pyruvic acid disappears (26, 27, 28). The ratio between increased oxygen take up and pyruvic acid disappearing was a fixed constant. Recently, increased pyruvic acid was found in the blood of avitaminotic pigeons and rats in large amounts (29). This returns towards normal in animals cured by the administration of vitamin B_1 (30).

So close, then, is this relationship between vitamin B_1 and carbohydrate metabolism, that the state of B_1 deficiency has been referred to as "a chronic carbohydrate poisoning" (31).

In our clinical experiments, we have been studying the effect of vitamin B_1 in cases of known *carbohydrate disturbances* of all degrees and severity (32). Into this group fell cases that were classified as diabetes. In the majority of cases of true diabetes mellitus, we have seen no beneficial effect from the administration of vitamin B_1. I would like to make this more emphatic by stating that we have actually seen an increase in blood sugar and urinary sugar output in some of these patients; so that the question of whether vitamin B_1 brought on an aggravation of the diabetic state may justly be raised. However, a few of our cases showed a startling modification of the carbohydrate disturbance with lowered blood sugars and lowered urinary sugar output. In those patients with disturbance of the carbohydrate metabolism in whom other stigmata of deficiency co-exist such as unexplained obesity, the loss of appetite, polyneuritic manifestations and diminished metabolic rates, we have obtained our best results. These patients fell into the group described by Joslin as "unclassified diabetes." Careful analysis of the marked change in their carbohydrate metabolism after taking vitamin B_1 raises considerable doubt as to whether these patients belong in any diabetic grouping.

It has been proven, experimentally, that vitamin B_1 is of fundamental importance in the carbohydrate metabolism. The confusion as to its clinical use is due to our clinical inability to separate true diabetes mellitus from the other forms. It seems likely that among these other forms are cases of partial vitamin B_1 avitaminosis which is reflected in the carbohydrate disturbance. These cannot, as yet, be separated but chemical studies now under investigation offer the prospect of a solution to this problem. Until these false diabetics can be recognized easily, the use of vitamin B_1 in so-called clinical diabetes is justified only on an experimental basis (33, 34, 35).

Another interesting relationship is that of vitamin B_1 to *metabolism* (36). In dogs on a B_1 deficient diet, the time required for the development of anorexia is

an accurate indication of the rate at which avitaminosis is developing. By forced exercise the time required for anorexia to appear is materially shortened (37). When thyroid is administered to induce hyperthyroidism in these dogs, anorexia develops very rapidly (38). Experiments on pigeons also show a greater vitamin B_1 requirement in hyperthyroidism than under normal conditions (39). In rats, protection against thyroxin poisoning can be accomplished by the administration of vitamin B_1 (40).

It is a justifiable conclusion from these and other studies that the vitamin B_1 requirement of an animal is proportionate to the metabolism of the animal (41). Some recent studies with dinitrophenol show that this drug does not influence the B_1 requirement of the animal but that "the total caloric intake and body weight are the most important factors in determining the vitamin B_1 requirement of the organism (42)."

With this experimental background, we have included for clinical study a group of cases ordinarily classified as *hypothyroidism.* These have a lowered metabolic rate, usually not lower than minus twenty-four, a moderate obesity and, yet, show none of the mental stigmata of true hypothyroidism. In several of these patients under observation, the administration of thyroid has been of little or no value. They appear to be cases of lowered general metabolism rather than of thyroid deficiency. The action of vitamin B_1 in these cases is the action of a metabolic stimulant. We are, at present, studying more of these cases and have observed improvement not only in the clinical state but a return of the basal metabolic figures to the normal. Detailed studies of this group will be reported in another paper.

I should like very much to close the discussion of vitamin B_1 therapy at this point but I would be omitting a group of cases in which vitamin B_1, apparently, has some value. These patients complain of *vague gastro-intestinal disturbances* (43) associated with constipation and show unexplained gastro-intestinal hypotonia on X-ray examination. I should like to omit this group of cases because in the literature of pharmaceutical houses this vague syndrome has been over-exploited and over-emphasized. The failure to improve many cases of infantile and adult constipation with the use of vitamin B_1 has served to discredit the value of this important therapeutic agent. Vitamin B_1, as I have said before, is not a constipation cure. There are, unquestionably, some patients in whom constipation results from a vitamin B_1 deficiency state (44) but they represent an extremely small percentage of cases. If vitamin B_1 is to be judged as a therapeutic agent on its response in cases of unexplained constipation, the results are bound to be disappointing.

Up to this point, I have attempted to confine the discussion of the value of vitamin B_1 to fairly well established clinical states. In addition to those states described, there are some obscure and ill-defined clinical entities, characterized usually by one symptom or another, in which vitamin B_1 is indicated but here again a word of caution as to its value must be expressed. I refer particularly to those cases of loss of appetite. Much has been published about the tremendous value of vitamin B_1 in anorexia. It is true that experimentally induced vitamin B_1 deficiency in animals is characterized by a marked loss of appetite. It is also recognized that by feeding vitamin B_1 the appetite promptly returns. This occurs in patients who have a similar deficiency state. However, it is unwise to use as a clinical yardstick the existence of anorexia to justify a prescription for vitamin B_1. This is especially true in children where *anorexia* is too often the result of a psychological problem at home, a behavior characteristic rather than a vitamin B_1 deficiency state. The value of vitamin B_1 in stimulating appetite finds its greater usefulness in the anorexia associated with long standing illnesses or in patients on limited diets for various chronic diseases, and obesity. In such patients the disappearance of anorexia is frequently observed. The next poorly defined state that we will consider for a moment is that characterized by unexplained weakness, and again the same rule applies that has been expressed in relation to loss of appetite. Unexplained weakness is, too often, an early symptom of an early or obscure organic diseased state or, at times, particularly in adults, too often an expression of psychological maladjustment. To expect that the administration of vitamin B_1 will be followed by a return of vigor and energy in many of these patients is to believe in the impossible. Just as in loss of appetite, weakness following convalescence from a serious illness or associated with long continued malnutrition will often disappear with the administration of vitamin B_1.

Throughout this paper, I have repeatedly used two phrases

(1) "adequate amounts of vitamin B_1"; and

(2) "for a long enough period of time"

and I feel that I have come to the point where these phrases must be more explicitly defined. There are available, at the present time, to the physician, many different sources of vitamin B_1. The crystalline material which is made by Merck & Company is available only in small amounts. It is difficult to procure and it is expensive. At the present time, its use should be reserved for those severe cases of vitamin B_1 deficiency that require a large dose in a short period of time and for those cases in which vomiting, diarrhea or extensive gastro-intestinal disease preclude the probability that there will be adequate absorption of vitamin B_1 if given by mouth. In such cases, the administration of from two to ten mgm. as a daily dose may be desirable. In advanced B_1 avitaminosis where the question of death is a pressing possibility, the administration of ten mgm., intravenously, once a day, may be safely used. Within five days, or sooner, an improvement will be noted if the diagnosis of a vitamin B_1 deficiency is correct.

However, such cases represent a very small percentage of those under consideration. For all the rest, vitamin B_1 by mouth will suffice. Here the crystalline product need not be employed, as sufficiently strong vitamin B_1 concentrates are available. The factor of dosage must be determined on the basis of units of vitamin activity. Unfortunately, there is some confusion at present, as two standards are in general use, the first being the Sherman Chase unit and the second being the International unit. 1.3 Sherman Chase units is the equivalent of 1 International unit. In the majority of cases of adults, it is desirable to administer from one to two thousand Sherman Chase units a day. Therefore, it becomes necessary to determine the Sherman Chase unit content of the preparation to be used and I am happy to say that through the cooperation of many of the pharmaceutical houses, the recent

products are all labelled with their vitamin unit content. Preparations in capsule form, containing from two to four hundred units per capsule are available and, thus, by the administration of from three to six capsules a day, an adequate amount of vitamin B_1 can be administered readily. Most of the concentrates on the market contain sizeable amounts of vitamin B_2 and vitamin B_4. It should be emphasized, at this point, that in our first hundred cases the results were obtained with crystalline material in which, therefore, we were certain that we were only using vitamin B_1. In the subsequent larger number of cases now under consideration, we have used the cheaper commercial concentrates and in the same dosage we have not observed any difference in our results, so that the amounts of vitamin B_2 and vitamin B_4 in the preparations that will be widely used, because of their availability and because of their lowered cost, do not seem to play a significant role in the therapeutic results.

The next factor of importance, as we have stressed it again and again in this paper, is the duration of time. How long should a patient take two thousand Sherman Chase units of vitamin B_1 a day before he may expect a result? This is a question which is very important to the physician as well as to the patient. In the light of our present knowledge, we are well aware of some of the factors that complicate this problem. The first, of course, is the duration of the symptoms or the duration of the disease process and, as I have indicated before, a polyneuritis of two or three months duration will respond in a short period of time, usually in three or four weeks. A polyneuritis of five to ten years' duration may not begin to show response for three or four weeks and response may not be marked until twelve or more weeks of treatment. This is frequently so in those cases of disturbance of the carbohydrate metabolism and, in fact, in cases of general lowered metabolism to which I have referred. In such, some improvement is usually noted in four weeks. In our series of cases, if an improvement was not observed in four weeks, it did not occur at all and such a patient would probably not be benefited by continued use of vitamin B_1 for a longer period of time. This is especially true in cases of unexplained anorexia and unexplained weakness. If a vitamin B_1 deficiency is responsible for the loss of appetite or weakness, a response usually occurs within two weeks of treatment on two thousand Sherman Chase units a day, and if after four weeks there has been no improvement, the failure to modify the symptoms is usually a very reliable indication of an inaccurate diagnosis and an inaccurate indication for the use of vitamin B_1 in that particular patient.

There are several other factors that modify the duration of treatment. Experiments have shown that metabolism influences the vitamin B_1 requirement—that in an artifically induced hyperthyroidism, the vitamin B_1 requirement is greater; that in animals on forced exercise, there is also an increase in the need for vitamin B_1 in the tissues. These experiments are useful guides in the interpretation of the problem of how long to give vitamin B_1. In those cases of pregnancy in which it is of use, it is to be given during the entire term of pregnancy. The vitamin B_1 content of the new born infant is directly related to the amount of vitamin B_1 available in the pregnant mother. In this regard, the new born infant responds to vitamin B_1 deprivation and to vitamin B_1 administration in the same way as it does to the deprivation or administration of the hematopoietic substances in the pregnant mother. The analogy is carried further, since vitamin B_1 in excess of the needs of the patient is excreted in the urine (45) as, you will recall, has been demonstrated in the case of the anti-anemic principle (46). Experimentally, it is possible to cure rats and other animals by feeding them human urine from individuals receiving an adequate amount of vitamin B_1 in their diet (47, 48), just as in the same manner it has been possible to effect reticulocytosis by the rectal administration of human urine from normal individuals (49). Large amounts of urine from patients suffering from beriberi have no effect upon the course of vitamin B_1 deficiency in rats.

An interesting observation on the use of vitamin B_1 should be noted at this point. About 20% of all cases of polyneuritis experience an intensification or aggravation of their neuritic pain soon after starting oral treatment. The increased pain is usually noticed in from three to five days from the onset of treatment and is most intense about the seventh day. Thereafter, the pains subside and improvement takes place. The reason for this acute temporary exacerbation is not clear, but it occurs often enough to justify a warning of its occurrence to the patient who is about to commence treatment.

There is, at least, one more question that must be answered before closing and that is, what are the contraindications to the administration of vitamin B_1? Is there such a thing as an overdose—a hypervitaminosis? This question was one of the first that we investigated in our experiments with humans. We administered as high as ninety thousand Sherman Chase units a day to some patients and were unable to observe any harmful effect. We were able to detect large amounts of vitamin B_1 in the urine of individuals on excessive dosage and this seems to be the factor of safety. Similarly, we have had patients who have taken vitamin B_1 daily in dosage of from one to two thousand Sherman Chase units a day, for over two years and we have not observed any untoward effects. The lessons learned from biochemical and physiological experiments with this vitamin indicate that this is what we should expect. Storage of vitamin B_1 within the body has not been demonstrated and it probably does not exist. The action of vitamin B_1 is the action of a catalyst that concerns itself with oxidation of the degradation products of glucolysis.

In vitamin B_1 we have in our hands an important therapeutic substance whose usefulness has not been thoroughly defined. At the present time, we must take the greatest care to confine its clinical use to those entities described in this paper. If we attempt to use it indiscriminately, we shall bring discredit upon it. If the dosage used is inadequate or if its administration is for too short a period of time, many patients will be deprived of benefit which would otherwise be theirs. The full scope of its usefulness has not yet been determined. Many clinical experiments are in progress. More and more reports are appearing in the world literature. I have no hesitancy in prophesying that we shall hear much more about the therapeutic value of vitamin B_1 in the next few years.

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SECTION IV—*Roentgenology*

Large Diverticula of the Gastric Cardia*

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TRUE diverticula of the stomach are uncommon and although often symptomless may cause confusion with other types of lesion. Larimore and Graham (1) in a series of 3,446 gastro-intestinal X-ray examinations observed 105 diverticula, only three of which were in the stomach. We encountered only two instances of gastric diverticula in 11,828 examinations done at Stanford University Hospital over a twelve year period. Our two other cases were seen at other hospitals. The Mayo Clinic reports fourteen cases proven anatomically (2), six of which were at the cardia on the posterior wall. They had in all twenty-five cases diagnosed by roentgen ray (2 and 3), only two of which were proven, and four of which

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