TETANY.

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Tetany, although its causes are manifold, may be regarded as a definite clinical entity. The picture presented depends to some extent on the age of the patient and the ætiological factors at work but in general tetany, or as it is sometimes called spasmophilia, is characterized by hyperexcitability of the nervous system, especially that portion which controls the skeletal muscles. It is customary to group cases under two headings, (a) latent and (b) active. In the former, signs of hyperexcitability are not manifest but must be specially elicited. In the latter, symptoms and signs of neuro-muscular hyperirritability are apparent. It will be convenient to describe the symptoms and signs under the above headings but it must be remembered that within a very short time any case may pass from the one group to the other.

SYMPTOMS AND SIGNS.

A.—Latent Tetany.

1. **Mechanical Hyperexcitability.** Signs of increased excitability may be tested for either mechanically or electrically. As regards mechanical hyperexcitability the best demonstration is afforded by Chvostek's sign commonly known as the facial phenomenon. A sharp tap on the cheek in front of the auditory meatus and midway between the ear and nose where the facial nerve becomes more superficial, results in a brisk twitching movement of the facial muscles involving specially those about the eye, root of the nose, *alæ nasi*, nasolabial fold and corner of the mouth. The extent of twitching is a rough indication of the severity of the case: in a very severe case the twitching involves all the areas above mentioned. Probably owing to local differences in the sensitivity of the nerve endings there is frequently quite a marked difference between the results obtained on the two sides of the face. During, and for some time after a convulsion, the facial phenomenon may not be elicited: later, however, it may be quite readily obtained. Crying also prevents the demonstration of this sign. In these circumstances it is often possible to obtain evidence of mechanical hyperirritability by means of the peroneal sign. This consists in the dorsi-flexion and abduction of the foot after tapping the peroneal nerve just below the head of the fibula while the foot is in a position of relaxation. Among other signs which may be elicited in similar fashion are (a) the contraction of the third, fourth and fifth fingers after percussion of the middle of the extensor surface of the upper arm and (b) the contraction of the quadriceps extensor after tapping the anterior surface of the thigh a hand's breadth above the knee.

The facial phenomenon has an important diagnostic significance only in a restricted age period, namely from the second month to the end of the third year. In new-born infants especially when premature, gentle stimulation in the region of the mouth by stroking or gentle tapping, causes the lips to be pursed up in a manner which may simulate the facial phenomenon. The former, the so-called lip reflex, generally involves both sides of the mouth and is elicited more easily

as a result of repeated stimulation, whereas the latter or true facial phenomenon is usually most marked in the upper part of the face and is easily exhausted by repeated stimulation. In children above the age of three years a positive facial phenomenon ceases to have special significance apart possibly from a neurotic temperament (Anderson and Graham⁽⁶⁾).

Trousseau's Sign. This consists in producing carpal spasm by constriction of the upper arm so that the circulation is obstructed and pressure is exerted on the brachial nerves. It is valuable as an indication of the presence or imminence of active tetany but too much reliance should not be placed on a failure to elicit this sign.

2. Electrical Hyperexcitability. This is usually demonstrated by showing that the minimal current required for the cathodal opening contraction (K.O.C.) is less than 5 milliamperes. A more accurate method is to determine the rheobase or minimal effective current and the chronaxie or length of time in thousandths of a second for which a current double the strength of the rheobase must act in order to produce a minimal contraction. In latent tetany the rheobase is diminished and the chronaxie increased.

B.—Active or Manifest Tetany.

This state is characterized by the onset of generalized convulsions or the presence of local spasm of the hands and feet (carpo-pedal spasm) or of the glottis (laryngospasm).

Convulsions. Generalized convulsions may or may not be preceded by other symptoms and signs of tetany. Hess⁽⁹⁾ notes that frequently a warning may be obtained of the imminence of the convulsive state by a slight twitching of the face especially round the mouth. In very young infants convulsions may form the only manifestation of tetany. Even in older patients the diagnosis of tetany during or immediately after a convulsion is very difficult, since signs of both mechanical and electrical hyperexcitability cannot then be elicited. The convulsions are epileptiform in nature, being generally though not invariably bilateral in distribution. They may occur singly but not infrequently they succeed one another in rapid succession with loss of consciousness so that a condition may be produced resembling *status epilepticus*.

Carpo-pedal Spasm. Spasm is one of the most striking symptoms. It generally occurs in both hands and feet (carpo-pedal) but may occur in either separately. It is frequently precipitated by the onset of some febrile condition. In older children, at an age when convulsions are not so common, it may be the only obvious indication of tetany. The hands are drawn to the ulnar side and held in the "obstetric position" with the wrists and metacarpo-phalangeal joints flexed, the inter-phalangeal joints extended and the thumbs adducted into the palms. The feet are flexed and the toes pointed downwards in the equinovarus position. The spasm not infrequently comes and goes; usually there is swelling of the dorsum of both hands and feet, the extent of which is generally related to the severity and duration of the spasm. The intensity of the spasm varies considerably even in the one patient. Generally he is able to hold things in his hand but in severe cases the spasm may be so intense that neither hands nor feet can be passively relaxed. There may be cramp-like pains but as a rule the child does not cry out unless an attempt is made to reduce the spastic deformity.

At times there is tonic spasm of other parts of the body, especially the upper arm and thigh muscles, so that the shoulders are strongly adducted, and elbows, hips and knees flexed. Occasionally the muscles of the face may be affected, producing the stiff board-like appearance which has been called the tetany facies: more rarely the trunk muscles are also found to be in spasm.

Laryngospasm. This is made evident by a crowing noise (laryngismus stridulus) due to spasm of the glottis. Inspiration is at first obstructed: after an interval breathing is recommenced with a crowing inspiratory sound which resembles the "crow" of whooping cough. The apnoeic period may be sufficiently long to produce cyanosis accompanied by a struggle for air not unlike that seen in asthma. The severity of the spasms varies considerably even in the one child. Sometimes a whole series of attacks may follow one another and terminate in loss of consciousness or generalized convulsions. On other occasions the attack may be very slight. Laryngismus may be induced in various ways, such as crying, gastric irritation, fever or even by very slight cutaneous stimuli. The more severe the state of tetany the slighter will be the stimulus required to precipitate attacks of laryngismus stridulus.

Other Evidence of Neuro-Muscular Hyperexcitability. Spasms of the cardiac and visceral muscle have been described under the terms, cardiac tetany, broncho-tetany and intestinal spasm but the ætiological relationship of this type of spasm to tetany is a matter of considerable doubt.

PATHOGENESIS.

The Rôle of Calcium.

Most workers are agreed that any hypothesis of the pathogenesis of tetany must be based on the fact that calcium plays an important, if not a dominant rôle in the prevention of hyperexcitability of the nervous system. It is an old observation that reduction of serum calcium is frequently accompanied by increase in neuro-muscular irritability but it is also well-known that there are types of tetany in which a reduction of serum calcium cannot be demonstrated. The clinical and experimental varieties of tetany may be divided into two groups according as the serum calcium is or is not reduced. In the first or *hypocalcæmic* group are included infantile and allied (osteomalacic and coeliac) forms of tetany, parathyroid tetany, and the forms associated with chronic nephritis and phosphate administration. To the latter or *eucalcæmic* group belong gastric, bicarbonate and hyperventilation tetany. It is clear, therefore, that the total serum calcium by itself cannot be the sole regulator of nervous excitability. It has been pointed out however, that it is not the total serum calcium but only the ionised fraction which is responsible for the sedative effect on the nervous system. Serum calcium is said to consist of three moieties (a) non-diffusible which is united with protein, (b) diffusible but not ionised and (c) diffusible and ionised. The last fraction forms about one third of the total serum calcium and it is the reduction of this moiety which leads to an increased irritability of the nervous system. Unfortunately it is extremely difficult, if not impossible, to obtain accurate measurements of the amount of the serum-calcium in the ionised state and even approximations are open to considerable doubt. It may be objected, therefore, at the very outset, that it is unwise to base a conception of pathogenesis on a hypothesis which cannot be confirmed owing to the fact that accurate methods of analysis are not available. Nevertheless, the conception that ionised calcium acts as a

regulator of neuro-muscular excitability, affording as it does great help to the understanding of the factors involved in the causation of the various types of tetany, offers a rational basis for therapy and justifies such an unproved hypothesis.

The amount of ionised calcium in the serum depends upon the total calcium content, the phosphate content and the reaction of the serum. The total calcium varies with the balance struck between absorption, excretion and deposition in the bones. Vitamin D raises the serum calcium by increasing the amount of lime which is retained, while the hormone of the parathyroid glands plays an important part in maintaining the level of serum calcium by increasing the amount of lime which is continually being released from the bones. Deposition of calcium in the bones takes place chiefly as calcium phosphate: accordingly, if there is an excess of phosphate in the serum, there will be a tendency for the precipitation of calcium phosphate to be increased and therefore for the serum calcium to be reduced. The presence of excess acid radicle in the tissue fluids also raises the serum calcium by increasing the catabolism of bone and promoting its decalcification. The difference between the action of vitamin D on the one hand, and parathormone or excess acid on the other, is apparent although all raise the calcium content of the serum.

The effect of the reaction of the serum and its phosphate content on the ionisation of serum calcium is expressed by György's modifications of Rona and Takahashi's equation. The reaction of the blood depends chiefly on the ratio of free to combined carbonic-acid: as this ratio decreases, the reaction becomes more alkaline (increase of pH), as it increases, it becomes less alkaline (decrease of pH). Without going into details it would appear that ionisation of calcium is decreased as a result either of increased alkalinity of the blood or of increased phosphate content.

Bicarbonate tetany is produced when relatively large doses of alkaline salts such as sodium bicarbonate are given to patients with gastric ulcer or with some degree of renal impairment. Children receiving alkalis for pyogenic infections of the urinary tract are particularly liable to attacks of tetany which may also occur during intensive alkaline therapy of renal oedema. In these cases alkali is not efficiently excreted with the result that the ratio of free to combined carbonic acid is decreased and the alkalinity of the serum raised (pH increased); this results in a decrease of the ionised fraction of serum calcium although the total content may be unchanged. When there is no impediment to excretion of alkali, administration of large doses of such a drug as sodium bicarbonate does not appear to influence either the reaction of the blood or the mechanical or electrical excitability of the neuro-muscular system.

Hyperventilation tetany is the name given to that type which is associated with overbreathing: it has been encountered in hysterical subjects and in patients with encephalitis lethargica. During hyperventilation there is an excessive loss of free carbon dioxide from the blood so that the ratio of free to combined carbonic acid is decreased and the reaction becomes more alkaline. This results in a reduction of ionised calcium, which, if sufficiently marked, is followed by the appearance of signs of tetany.

Gastric tetany occurs in patients with dilatation of the stomach due to pyloric obstruction or gastric atony: curiously enough it is seldom met with in congenital hypertrophic pyloric stenosis of infancy. When vomiting, which is almost invariably a prominent symptom, becomes excessive a considerable amount of free acid (HCl) is lost. The loss of chlorine is almost invariably followed by a

diminution in blood chloride, and a compensatory increase in bicarbonate, with the result that the ratio of free to combined carbonic acid is decreased and the alkalinity of the blood increased.

In these three types of tetany an increase in the alkalinity of the blood or "alkalæmia" is the factor which leads to a decreased ionisation of calcium and thus to an increase in neuro-muscular excitability.

The effect of increase of blood phosphate is two-fold: in the first place it causes a fall in the total serum calcium and secondly it reduces the degree of calcium ionisation. Its effects are best observed experimentally following injection of phosphates. In this connection it is important to remember that an alkaline phosphate must be used: if the acid phosphate is injected, the acid often produces a sufficient reduction in alkalinity of the blood with consequent increase in calcium ionisation to compensate for the reduction of total calcium. These facts help us to understand what takes place in chronic interstitial nephritis, a condition which in children may be associated with renal dwarfism and tetany and occasionally with a manifest rachitic process (renal rickets). The serum calcium is reduced and the serum phosphate increased so that one would expect the patient to be in a state of latent tetany. One must remember, however, that there is impairment in the excretion of waste products most of which are acid and that this accumulation of acid metabolites tends to reduce the alkalinity of the blood. Accordingly, any thing which increases the alkalinity of the blood above normal limits tends to precipitate an attack of tetany just as a slight increase in retained acid metabolites may lead to a very marked acidosis.

Parathyroid tetany occurs when the parathyroid secretion (parathormone) is defective or absent as in the comparatively rare condition of idiopathic hypoparathyroidism or more commonly after accidental removal of the parathyroid glands during surgical operations on the thyroid. There is an impaired mobilization of calcium from the bones with the result that serum calcium is considerably reduced in amount and with this diminution in total calcium there goes in all probability a reduction of the ionised fraction sufficient to produce tetany. In this case it appears unnecessary to invoke an increase in blood alkalinity or phosphate to explain the onset of hyperexcitability. Nevertheless, it must be remembered that a decrease in blood alkalinity may prevent the appearance of symptoms, first by releasing more calcium from the bones into the serum and second by increasing the degree of calcium ionisation.

Infantile Tetany.—Relationship to Rickets.

Infantile tetany is predominantly associated with rickets. It is true that tetany may occur in an infant with no apparent signs of rickets: nevertheless, as Hess⁽⁹⁾ among others has pointed out, most of these patients if observed for a sufficiently long period and examined carefully will be found to have some evidence of the rachitic process.

The age incidence of rickets and tetany in the young is practically identical. Most cases of infantile tetany and rickets occur in the first two years and both are rare in the first three months of life. Recently, however, cases have been published by Graham⁽⁵⁾ and other workers showing that tetany is not such a rarity in the neo-natal period as was previously believed. This might be thought to indicate that infantile tetany does not require a rachitic soil in which to make its appearance. Evidence, however, has also been forthcoming to show that the rachitic process may also be present at this early period (Maxwell⁽¹⁰⁾). Biochemical data cannot be fully discussed here but it may be stated that the usual

criterion of rickets, a reduction in serum phosphorus, is of little help since there is generally an increase with the onset of tetany. The calcium-phosphorus product, however, is generally below 30 and the value for the plasma phosphatase is almost invariably raised—two recognized indications of the rachitic process.

The seasonal incidence of the two disorders is practically identical: there is a gradual increase in frequency during the winter months with the peak occurring in the spring, which is almost certainly related to the seasonal variations in sunlight. Graham⁽⁵⁾ has shown that there is a similar seasonal incidence for hypocalcæmic convulsions in the early weeks of life although in many of the infants with this condition there are no clinical or X-ray signs of rickets. As with rickets, insufficient exposure to ultra-violet radiations is an important factor as indicated by the greater incidence of tetany in children who are brought up in slum environments.

Both rickets and tetany occur much more frequently in artificially-fed infants especially when there is a deficiency of the antirachitic vitamin. It must be emphasized, however, that in neither disease is breast feeding always protective, especially if the mother's diet is defective in calcium or vitamin D or both.

In two other conditions, osteomalacia and coeliac disease, both of which have much in common with rickets, tetany is prone to occur. Osteomalacia, indeed, may be regarded as the manifestation of the rachitic process in the adult, while coeliac disease is associated with a defective retention of lime which is the ætiological factor of importance in the causation of tetany.

It is obvious from what has been stated that the conditions favourable for the development of the rachitic process also appear to promote the onset of tetany. Nevertheless, there are a few facts which show that the relationship between the two disorders is not a simple one. While infantile tetany is almost invariably associated with rickets, many cases of the latter disease are encountered with no signs of tetany. Furthermore, it is not in the most severe cases of rickets that tetany occurs: on the contrary there would appear to be a negative correlation between incidence of tetany and severity of rickets. Indeed, there appears to be a special tendency for tetany to occur when rickets is already in the healing stage. Gerstenberger⁽⁴⁾ has pointed out that an attack of tetany is most likely to be precipitated after the commencement of antirachitic therapy especially when that is inadequate.

In another respect, also, tetany differs from rickets: in the former, males are more frequently affected than females while in the latter no difference in the sex-incidence has been noted.

In rickets the serum calcium is within normal limits and the serum inorganic phosphorus greatly reduced. As soon as tetany makes its appearance the calcium is markedly diminished and the phosphorus raised sometimes even to a value above what is found in health. The basic problem in the pathogenesis of tetany associated with rickets is concerned with the cause of this sudden change.

Alkalosis and Increased Retention of Phosphates.

Freudenberg and György⁽⁷⁾ have put forward the hypothesis that in rickets there is a condition of compensated acidosis due to general retardation of the metabolic processes, while in tetany acid-base equilibrium is moved in the alkalotic direction owing to general metabolic acceleration. Closely associated with

this view is that of Rominger⁽¹⁷⁾ and his co-workers who believe that the earliest phase of healing in rickets is accompanied by a great increase in the retention of phosphorus without simultaneous increase in that of calcium: this they maintain leads to a reduction of serum calcium because it is deposited as calcium phosphate without being replenished. Much criticism has been levelled against these hypotheses. Thus Drucker⁽²⁾ among others has shown that in infantile tetany there is no evidence of any alteration of metabolism in the alkalotic direction. It is true that in fever there is a tendency to alkalosis which, although of a very mild nature, may be of sufficient intensity to reduce the ionisation of calcium and precipitate convulsions in a child whose calcium metabolism is already defective. Even if this is the case, it is unlikely in view of the evidence available that alkalosis plays an important rôle in the causation of infantile tetany. In some recent investigations carried out in the Royal Hospital for Sick Children, Glasgow, it has been shown that tetany may be present even when the retention of calcium greatly exceeds that of phosphorus and does not necessarily occur when there is an excess retention of the latter substance. Furthermore, in coeliac disease tetany may be present even when the serum phosphorus is greatly reduced. The rôle of phosphorus as a factor in the production of tetany has probably been exaggerated as a result of the view commonly held as to the significance of increase in serum phosphorus. Ford⁽³⁾ has shown that a rise in serum phosphorus may actually be accompanied by a reduction in phosphorus retention. It is probable that an increase of serum phosphorus is the result of increased tissue catabolism although the significance of this in relation to the pathogenesis of tetany is by no means simple or clear.

The Parathyroids in Infantile Tetany.

In view of the development of tetany after removal of the parathyroid glands and of the fact that both in infantile tetany and in tetania parathyropriva the serum calcium is reduced, many attempts have been made to inculpate the parathyroid glands as a prime factor in the pathogenesis of the former condition. Such attempts have not met with much success. It has been shown by Greenwald⁽⁷⁾ that the loss of calcium by the excreta is actually less in the parathyroidectomised than in the normal animal, a state of affairs which is the reverse of what takes place in infantile tetany and rickets. Histological examination of the parathyroid glands of infants and children who have died in a state of tetany has not yielded any data which support the parathyroid view. It is true that parathormone is able to allay the state of hyperexcitability in both conditions but that is because there is an increase in the amount of calcium mobilized from the bones and not necessarily because there is any defect in the parathyroid secretion. It must therefore be concluded that while it would simplify matters considerably if it could be shown that there was a disturbance of parathyroid function in infantile tetany there is little to support this view. Efforts have been made to incriminate most of the other ductless glands but with even less success.

Guanidine Poisoning. Based chiefly on the experimental work of Noël Paton and Findlay,⁽¹⁴⁾ the view was expressed that guanidine or one of its compounds was produced in excess after parathyroidectomy and that this was an important factor in causing an increase of neuro-muscular excitability. Attempts to show that tetany in the human subject is accompanied by an increase in the guanidine content of blood or urine have not yielded convincing results. Recent animal experiments, however, suggest that parathyroidectomy and guanidine poisoning each produces alterations in protein catabolism involving the nucleoproteins. So far there is no evidence that similar changes occur in patients with

tetany. There is no doubt, however, that a high protein intake favours the onset of tetany, suggesting that nitrogenous end-products do play a part, at any rate in aggravating the state of hyperirritability. Furthermore, withdrawal of blood or intravenous administration of sodium chloride solution has a beneficial effect in allaying, even if only temporarily, the spasmophilic state, which suggests that there is a circulating poison the effect of which is lessened by withdrawal of blood or dilution with saline. Although the guanidine hypothesis of the causation of tetany has fallen into disfavour, there are a few experimental findings which would indicate that there is some disturbance in protein metabolism closely associated with the production of tetany.

Chlorine Deprivation.

There is no doubt that loss of chlorine plays an important part in the production of gastric tetany. As the result of chlorine depletion the blood chloride is reduced with compensatory increase in bicarbonate resulting in a decrease in the ratio of free to combined carbonic acid, i.e., alkalosis. It is now being suggested by Porges⁽¹⁵⁾ and others that hypochloræmia *per se* causes an alteration in the excitability of the nervous system so that chlorine deficiency may, even in the absence of alkalosis, act as an important factor in the production of convulsions and coma. This view receives considerable support from the findings of Morris and Macrae⁽¹³⁾ that in infantile tetany there is a very definite retention of chloride when administered in the form of ammonium chloride. In experimental parathyroidectomy and guanidine poisoning a retention of chlorine has also been noted during both latent and active phases of tetany.

Water Retention.

Another suggestion which has received some attention is that retention of fluid in and around the tissues is of importance in the causation of tetany. Occasionally the weight chart in infantile tetany shows a marked drop as recovery has taken place. It is difficult to know what emphasis to lay on such a phenomenon since sudden changes in weight are frequently encountered during the first year of life. But it must be borne in mind that some of the important therapeutic agents used for the relief of tetany have a dehydrating effect. Thus calcium and ammonium chloride are both used for the removal of collections of fluid within the body. Theocin which is used solely for its diuretic effect has also a sedative effect on the manifestations of tetany. The two former drugs have a definite influence on the total amount and ionisation of serum calcium, and the effect of theocin on tetany is also attributed to an increase in the calcium content of serum. Calcium apart altogether from its association with acidosis promotes diuresis: indeed the Germans have included it among the "entquellend" substances, which prevent excessive accumulation of water. Of interest in this connection is the work of McQuarrie⁽¹¹⁾ and his colleagues on the influence of water retention in the pathogenesis of attacks of epilepsy. This adds strength to the suggestion that it may also be a casual factor in infantile tetany but much more evidence is required before it can be adopted.

DIAGNOSIS.

The presence of one or more of the manifestations composing the classical triad (facial phenomenon, carpo-pedal spasm and laryngismus stridulus) is a sufficient basis for establishing the diagnosis of tetany. The absence of these signs need not, however, be a bar to such a diagnosis. The association of convulsions with any of the conditions likely to produce tetany ought immediately

to raise the suspicion of its presence. In the presence of convulsions of unknown aetiology it is often of considerable help to estimate the calcium concentration of the serum. If this is below 8 mg. per cent. it is important evidence of tetany, while if between 8 and 9 mg. per cent. it is suggestive but not such a reliable indication. It must always be remembered that, apart altogether from tetany, serum calcium may be reduced: we see examples of this in chronic interstitial nephritis or nephrosis. Generally speaking, an estimation of the serum calcium forms the most delicate test of the presence or absence of latent infantile tetany, although reports are now available from various workers (Siwe⁽¹⁸⁾) indicating that an attack of tetany may occur even with a normal value for serum calcium. These facts emphasize the importance of remembering that a serum calcium estimation is not *per se* an infallible criterion but like every other sign, symptom or test must be considered in conjunction with the entire clinical picture.

Spasmodic or false croup rarely presents much difficulty in diagnosis: there is a history and frequently signs of a catarrhal condition in the upper respiratory passages. Confusion may be caused if it occurs in a patient with rickets. In such a case an estimation of the serum calcium should be of help. In this connection it is wise to remember that there may be a combination of tetany with other conditions that tend to produce spasm. Thus Powers⁽¹⁶⁾ has shown that tetany is the cause of convulsions in many children with whooping cough.

In congenital laryngeal stridor there is a history of attacks from the early days of life in contradistinction to true laryngismus stridulus which is rarely met with before the second month. In view of the fact that tetany is now being reported more frequently than formerly in the new-born it may be advisable in doubtful cases to estimate the serum calcium.

PROGNOSIS.

In the great majority of cases with efficient treatment, recovery takes place rapidly. There are a few cases, however, which appear to resist all therapeutic measures and terminate fatally. In these, as Hess⁽⁹⁾ has pointed out, the serum calcium is often lower than in those that successfully respond to treatment.

There are still differences of opinion regarding the future mental development of children with tetany. Bloch⁽¹⁾ and other workers have published figures indicating that a large number of children with tetany ultimately show signs of mental retardation. Hess,⁽⁹⁾ however, while admitting that convulsions may lead to permanent injury of the nervous system, maintains that this is the exception and that much of the evidence suggesting mental impairment as a frequent sequel of tetany has been based on data that could not be considered representative.

PROPHYLAXIS.

This depends upon the recognition of conditions commonly associated with tetany. Thus caution is necessary in the alkaline treatment of gastric ulcer or pyuria. As for infantile tetany, rapid efficient prevention and treatment of rickets is the best prophylactic. Special attention must be paid to premature infants and babies of mothers with signs of osteomalacia or mineral undernutrition. The first step in the prophylaxis of rickets and tetany is the provision of an ample diet to expectant and nursing mothers with special reference to minerals and vitamin D. Especially in the winter months an ample supply of vitamin D should be given to the infant directly, nor should this be restricted to those artificially fed, since tetany is also encountered although much less frequently

in the breast-fed. Owing to the lesser tendency of rickets to appear in the breast-fed every effort should be made to institute and maintain breast-feeding at any rate in the early months. A transient but marked reduction in the retention of lime takes place immediately after the commencement of the vitamin D therapy of rickets: it is therefore particularly necessary to be on guard against the development of tetany in the very early stages of healing rickets.

TREATMENT.

Infantile Tetany.

Once the signs of tetany, latent or active, are detected, energetic treatment must be immediately initiated. The rationale of treatment is to increase the total but more especially the ionised moiety of serum calcium until the underlying cause of the hypocalcæmia (rickets) is removed.

Increase in Serum Calcium. This may be achieved in one of several ways.

1. Administration of acid-producing substance. This leads to a mild or compensated non-gaseous acidosis which without the production of any symptoms is sufficient to cause a rise in the total calcium content of the blood together with an increase in the ionised moiety. Within twelve hours most of the signs of tetany disappear though the facial phenomenon may persist for another day. The common drugs used to achieve this are dilute hydrochloric acid, ammonium chloride and calcium chloride. Hydrochloric acid has been used with success in cases of adult tetany due to parathyroidectomy: unfortunately in more than minimal doses it generally produces vomiting in young infants and children. With ammonium chloride the ammonium radicle is converted into urea by the liver so that the chlorine is left to exert an acid effect. The action of calcium chloride is dependent on the fact that the bulk of the calcium is excreted as soap, leaving the chloride to be absorbed without base. Of the three, calcium chloride is probably the most satisfactory, since it is well tolerated and does not throw any extra strain on the liver in synthesizing urea or on the kidney, in excreting it. It must be emphasized that the amount of calcium actually supplied by calcium chloride is negligible; its action is due entirely to its acid-producing effect. This indeed constitutes the one danger in this form of therapy, since in young children in whom the acid-base equilibrium is peculiarly unstable it may produce clinical (uncompensated) acidosis. In practice, 15 to 30 grains of calcium chloride, depending upon the age and weight of the patient, should be given every four hours for three days.

2. Administration of calcium without producing an acid effect. For this purpose the gluconate or lævulinate of calcium has been used. These drugs possess the advantage that they may be safely given intravenously in sufficient quantity to produce a rapid rise of the serum calcium. Their oral administration does not appear to be so effective in increasing serum calcium as an acid-producing substance such as calcium chloride.

3. *Injection of parathyroid hormone.* Since its preparation by Collip, parathormone has been used with success in the treatment of tetany. The expense of this form of therapy is a serious drawback and the equally satisfactory response obtained by other methods makes its general use unnecessary. After repeated injections, parathormone frequently appears to lose its effect. This is one of the difficulties in the treatment of tetany due to removal of the parathyroids where prolonged treatment is necessary.

Restoration of Calcium Metabolism to Normal. As has already been mentioned, there is generally in infantile tetany a background of rickets. For the removal of this, administration of vitamin D is necessary. This can be supplied in the form of cod liver oil, vitamin D concentrate, calciferol or ultra-violet irradiation. When there is intolerance to fat as in coeliac disease, one of the last two should be used. Vitamin D administration should be commenced immediately, since with calcium chloride the increase of serum calcium takes place at the expense of the bones and the low retention of lime is still further reduced: vitamin D on the other hand increases absorption and retention.

Convulsions. Occasionally convulsions occur in rapid succession and it may be necessary to give a sedative to allay the eclamptic state. Chloral hydrate can be given in adequate doses according to age either by the mouth or by the rectum. For an infant of six months an initial dose of 2 grains followed by 1 grain every hour for twenty-four hours is usually sufficient. In very severe convulsive states chloroform inhalation may be required.

Other Forms of Tetany.

In the types of tetany (gastric and bicarbonate) associated with alkalosis it is necessary immediately to stop the administration of any drug or food tending to produce an increase of alkali, and frequently, in addition, to give an acid such as hydrochloric acid or an acid-producing substance such as ammonium or calcium chloride. In gastric tetany where the alkalosis is associated with great loss of chlorine it is advisable to give large amounts of saline intravenously, subcutaneously, rectally, or by the mouth, depending on the severity of the vomiting.

In the tetany accompanying chronic renal disease the administration of some acid-producing substance is generally an effective therapeutic procedure. The difficulty is to steer between the Scylla of tetany and the Charybdis of acidosis. Calcium gluconate is probably of advantage once the acid-base equilibrium has been stabilized.

For tetany following parathyroidectomy injection of parathormone is advisable. An adequate retention of calcium must be ensured by the use of a diet rich in calcium (milk and milk foods) or by the administration of calcium gluconate. Hydrochloric acid therapy is helpful in promoting the absorption of lime by acidifying the intestinal contents and by increasing the ionisation of serum calcium.

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