

## THE DIAGNOSIS OF INFANTILE TETANY

WITH A REPORT ON EXPERIMENTAL TETANY IN DOGS \*

HERBERT B. WILCOX, M.D.

NEW YORK

Tetany, in infants, has been recognized for many years as a disease entity evidenced by laryngospasm, respiratory spasm, muscular rigidity, contractures of the extremities, convulsions and even coma, and more recently by increased response to electrical and mechanical nervous stimulation. Many causes have been given for this symptom-complex, the earliest referring to tetany as the most dangerous of the complications associated with dentition. The first accurate description of the disease is that of J. Clark in 1815, which gives in detail the characteristic respiratory and muscular conditions. A few years later Marshall Hall wrote of the symptoms as brought about by stimulation of the central nervous system through peripheral irritation. In 1829 Kopp attributed the laryngospasm to thymus hypertrophy and at about the same time Leigh claimed that it was due to pressure on the vagus by enlarged tracheobronchial lymph-glands.

The first investigation of the electrical hyperirritability of children suffering from tetany was carried on by Escherich and von Wagener in 1890. In this and later communications<sup>1</sup> was established the fact that there is an increase of electrical irritability in all cases of the disease, and that this makes its appearance before the existence of muscular spasm and is demonstrable after the latter has disappeared.

A few years after this Thiemich<sup>2</sup> ascertained the normal electrical irritability in young children and stated that, of the variations from this evidenced by those having tetany, the most significant one was the appearance of anodal opening contraction at a point lower than anodal closure and that of kathodal opening contraction below 5 milliamperes of current strength.

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\* From the Children's Service of Bellevue Hospital, First Medical Division, New York City.

1. Escherich: *Die Tetanie der Kinder*, 1909.

2. Thiemich: *Ueber Tetanie und Tetanoide Zustände im Ersten Kindesalter*, *Jahrb. f. Kinderh.*, 1900, li.

The determination of the normal response to galvanic stimulation in children and the knowledge that this became greatly increased in tetany provided a more certain method of diagnosis than had previously been at hand. Its application to large numbers of children brought out the fact that tetany was much more frequent than had been before believed. Indeed, Finkelstein<sup>3</sup> found that between 40 and 45 per cent. of artificially nourished children, on being subjected to the galvanic test, showed increased electrical irritability. His observations and those of Gregor, tending to show that electrical irritability was more marked in children fed on cow's-milk than in those on breast-milk or farinaceous foods, indicated that anomalous conditions of assimilation might produce electrical and, at times, other symptoms of tetany. This was attributed both to the greater calcium content of the cow's-milk and to the presence in this serum of an unknown substance which is lacking alike in breast-milk and in farinaceous foods.

Although it has been demonstrated that electrical response does vary with changes in digestive and metabolic processes, the fact remains that by this method of electrical tests, cases hitherto not suspected of tetany may be brought to correct diagnosis. Just what electrical findings are essential to a diagnosis of tetany has been and is still a matter of dispute. Thiemich's contention was that a kathodal opening contraction must be obtained at a point less than 5 milliamperes if tetany is to be proved. Ganghofner<sup>4</sup> confirmed Thiemich's findings, but stated that in many unquestionable cases of tetany the kathodal opening never dropped below 5 milliamperes, and that, moreover, other children had distinct electrical hyperirritability who never before or after had shown any signs of having tetany. Von Pirquet<sup>5</sup> decided from a large experience that the normal reactions of children were lower than Mann found them to be and that the appearance of anodal opening below 5 milliamperes was certain evidence of increased electrical irritability. Escherich believed that in normal children only kathodal closing contraction appears under 5 milliamperes and that only occasionally may anodal closure be present with this current strength.

My own study of the muscular response to galvanism is in two parts. The first, consisting of the routine testing of 118 infants in the children's ward of Bellevue Hospital, was instituted with the intention of adding our experience to the foregoing studies of the electrical response in children, normal in so far as their nervous systems were concerned; to deter-

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3. Finkelstein: Zur Kenntniss der Tetanie und der Tetanoiden Zustände der Kinder, *Fortschr. d. Med.*, 1902, No. 20.

4. Ganghofner: Zur diagnose der Tetanie im ersten Kindesalter, *Ztschr. f. Heilk.*, 1901.

5. Von Pirquet: Die Anodische Uebererregbarkeit der Säuglingen, *Wien. med. Presse*, 1907, No. 1.

mine what percentage of such routine tests resulted in distinct evidence of hyperirritability, and, if possible, to follow those children showing such reactions to see if they ultimately did develop frank tetany.

It is very difficult to define exactly the normal electrical response of childhood. Some children react low one day and high the next. Some give low closing contractions for kathode and anode, others lower anodal opening than anodal closure. It is common to obtain kathodal closure response below 2 milliamperes, while the other reactions are well above 5 milliamperes. In view of the number of our children, normal as to their nervous systems, who in this series gave reactions other than kathodal closure below 5 milliamperes, and in view of our experience with the reactions of normal dogs, it seems that Escherich's definition of hyperirritability imposes rather too narrow limits on the normal reaction, but it is, nevertheless, followed as a basis of division in the following tables.

It is well understood that definite conclusions cannot always be drawn from such classifications and averages as are hereafter given. They are, however, valuable as teaching something of the results to be expected in electrical tests in infants apparently normal in so far as their nervous systems are concerned, and do not apply to those suspected of or actually suffering from tetany.

The second part of the article, dealing with the electrical reactions in dogs, is intended to demonstrate that in normal dogs these reactions are similar to those in normal children, and to offer some observations on the relation between lesions in the parathyroid glands and electrical hyperirritability as the first evidence of the ensuing tetany.

We have to consider, then, a disease rather common in infancy and also in adult life, but in the former case presenting an entirely different symptom-complex from that of the adult type.

Potpeschnigg found the incidence of tetany to be 109 unquestionable cases in 10,000 children observed in the Grazer children's clinic in 1900-1904, or about 1 per cent. The greatest number of cases occurred between the third and twentieth month, during this period going as high as from 4 to 6 per cent. of the children admitted between these ages. There is a wide divergence of opinion on the question of the frequency of the disease, due, presumably, to the varying attitudes of the observers as to what constitutes a true diagnosis. Various authors give figures varying from 6 per cent. down to 0.7 per cent. in artificially fed children under 3 years of age.

In Dr. Howland's service at Bellevue, of 934 children under 2 years admitted from October, 1909, to March, 1911, there were five unmistakable cases of tetany, or 0.5 per cent. Two of these were admitted before the routine electrical tests were begun and were not so tested. The three others showed marked hyperirritability to galvanism in addition to laryngo- and respiratory spasm and muscular rigidity.

The type of tetany generally presented by children of this age is that accompanied by great general irritability, laryngospasm and respiratory spasm, with or without convulsions, rather than by spasm of the extremities. The latter condition is, however, demonstrable in most cases if carefully sought for. The electrical diagnosis of tetany, the technic and details of which are later referred to, depends on the obtaining of muscular response to galvanic stimulation with kathodal and anodal closure and opening at a current strength of less than 5 milliamperes. Such electrical hyperirritability, that is, an irritability toward all four forms of current, is not present in children with normal nervous systems. It appears early in the course of tetany and, while varying greatly from time to time, persists after all other tetanoid symptoms are absent. An instance of the variation sometimes found is that of a 15 months' child who, on the first test, reacted to kathodal closure, 0.6 milliamperes; anodal closure, 1.6; anodal opening, 1.6; kathodal opening, 2.3. Six days later, kathodal closure, 2.0; anodal closure, 4.0; anodal opening, 3.0; kathodal opening greater than 5.0, and after three days gave in a third test: kathodal closure, 1.6; anodal closure, 3.0; anodal opening, 1.3; kathodal opening, 3.0.

An incomplete reaction may be frequent in cases of true tetany. This is shown in Dogs 3 and 6, neither of which gave response to kathodal opening below 5 milliamperes, although both unmistakably died of the disease. It is evident from this and other similar experience that a true decision for or against tetany can be reached only after repeated galvanic tests.

Escherich's investigation of children under 6 months of age showed 55 per cent. evidencing hyperirritability; i. e., giving some reactions other than kathodal closure with currents of less than 5 milliamperes.

In my series of 318 electrical tests, ten, or 3.1 per cent., gave evidence of extreme or kathodal hyperirritability. Of the middle grade or anodal irritability giving response to kathodal closure and anodal closure alone below 5 milliamperes, there were 101, or 31.8 per cent. With kathodal closure and anodal opening alone present, below 5 milliamperes, I found fifty, or 16.6 per cent. With both kathodal closure, anodal closure and anodal opening, less than 5 milliamperes, there were forty, or 12 per cent. The occurrence, then, in my series of abnormal reaction or increased electrical response according to Escherich's definition was 193, or 61 per cent.

Of these cases of anodal or partial hyperirritability, none developed other symptoms of tetany under observation. What then does this condition of partial irritability mean? Is it a state of exaggerated nervous sensitiveness quite unrelated to tetany and to be expected in about one-half of the children who come under observation? Is it an evidence of the past existence of the disease, or may it be the precursor of the devel-

opment of tetany in its true form? The first hypothesis would seem to be the most probable one, and if so, necessitates the definition of normal electrical reaction as a condition of irritability responding by muscular contraction to kathodal closure alone with currents of less than 5 milli-amperes strength, or in an equal number of instances, to anodal closure and anodal opening stimulation with the same weak current, the former being twice as frequently found as the latter. Reason for this belief is found in the fact that the condition is common to so many children who evidently have not tetany, and strength is added to it by the demonstration of the same type of irritability on my dogs before operation.

On the other hand, and perhaps in support of the theory that this anodal irritability is the precursor of true tetany, it will be noted that in all the partially parathyroidectomized animals there was evident an increasing grade of anodal irritability. Further experiments bearing on this point are at present in progress.

Evidence of mechanical hyperirritability in tetany may be demonstrated in the following ways:

*The Chvostek Sign.*—This depends on reflex contractions produced in the muscles at the angle of the mouth, the ala of the nostril and brow by tapping the cheek over the facial plexus midway between the angle of the mouth and the zygomatic arch. This symptom is given varying grades of importance by different authors. It was present in but one instance in my cases, this being one of evident tetany.

*Trousseau's Sign.*—By shutting off, through pressure above the elbow or in the groin, the blood-supply to arm or leg, there ensues during the pressure or immediately on its release the typical carpal or pedal spasm, as the case may be. This also was present in but one case of my series.

Routine electrical tests were done during the months October to February, inclusive, and during June and July. It is unfortunate that they could not be carried on through the entire year in order that some conclusion might be reached as to the influence of season on the incidence of tetany and the occurrence of hyperirritability. In one series of 246 cases of tetany collected in one year 74 per cent. occurred during the months of January, February, March and April. The highest percentage (24 per cent.) occurred in March. Three of my cases of frank tetany occurred in February, two each in December and January. The incidence of hyperirritability was greatest in December.

It is not possible from the data herein contained to draw any conclusions as to the relation between the incidence of tetany according to season and that of hyperirritability of the lower grades. Information on this point would aid in interpreting the meaning of the anodal grade of irritability.

If we accept the classification of Escherich and consider as evidence of at least some degree of hyperirritability, the appearance of kathodal and anodal closure and anodal opening contractions with less than 5 milliamperes of current, my own figures would show that in January 23 per cent. of reactions showed hyperirritability; February, 24.5 per cent.; June, 9.6 per cent.; July, 17.7 per cent.; November, 16.6 per cent.; and in December, 27.6 per cent.

In October the number of tests made was too small to be of consequence. The number of tests made each month was: October, three; November, twelve; December, twenty-nine; January, seventy-four; February, fifty-seven; June, fifty-two; July, ninety.

The months of December, January and February gave the greatest number of middle-grade reactions, which corresponds in part to the months in which Escherich found the greatest incidence of tetany. Seven of my ten cases giving complete tetany reactions were under observation in these three months. Although followed up to the time of their deaths, none of these ever showed other evidences of tetany. They were all cases of malnutrition and the patients are reported to have died outside the hospital from nutritional causes. These children may represent instances of increased reaction to galvanism accompanying metabolic disturbance of severe grade and not due to the tetanoid condition. They were, however, discharged from the hospital months before death and the reports made on their condition during this time are not complete enough to positively exclude the possibility of the existence of true tetany.

Three hundred and eighteen tests were made on 118 children, being repeated more frequently on those showing a tendency to electrical hyperirritability.

The instrument used supplied galvanic current from dry cells, and contained a switch for reversing its polarity, a rheostat for controlling the current strength, and a balanced milliamperemeter measuring from 0.2 to 10 milliamperes.

Ten of our cases gave low reactions with all four tests, kathodal closure, anodal closure, anodal opening, and kathodal opening. These children were suffering from varying grades of malnutrition and all died while under observation, either in the ward or out-patient department, from nutritional causes. None of them developed other evidences of tetany.

Although Escherich describes the test as easy to perform without resistance on the part of the patient, in my subjects there was constantly so much struggling that it was difficult to find the moment of muscular relaxation necessary for the appreciation of response to the weaker currents. In a small number of cases the reactions of both left and right sides were taken and very little difference found. Escherich spoke of

considerable variation in his experience. Constant resistance necessitated mild chloroform narcosis in a few cases. The reactions obtained in this way were no lower than the average without such narcosis.

Escherich and von Pirquet considered the peroneal nerve muscle-group the best for use, and this proved the most satisfactory in my series. Erb employed the ulnar and prefers it. The median nerve has been used by Mann and Thiemich but reacts to anodal closure with less current than to kathodal closure, quite contrary to the findings in the peroneal nerve, and is in general more sensitive to electrical stimulation than the peroneal.

Muscular response was obtained at current strengths given in Table 1 in every one of the 318 tests made for kathodal closure. For anodal closure response occurred at 5 milliamperes, or lower, 149 times and failed 169 times. For anodal opening, eighty-seven results were positive and 231 negative. The reaction for kathodal opening was present only ten times and lacking in 308 instances. Table 1 shows the current strengths at which reactions were obtained.

TABLE 1.—SHOWING THE CURRENT STRENGTHS AT WHICH ELECTRICAL REACTIONS WERE OBTAINED IN CHILDREN

	Kathodal Closure	Anodal Closure	Anodal Opening	Kathodal Opening
Less than 1 milliampere . . . . .	0	0	0	0
From 1 to 2 milliamperes . . . . .	37	2	0	1
From 2 to 3 milliamperes . . . . .	74	28	3	3
From 3 to 4 milliamperes . . . . .	58	53	23	2
From 4 to 5 milliamperes . . . . .	29	19	17	3
From 5 to 10 milliamperes . . . . .	18	57	47	30

The peroneal nerve-muscle group was employed for the tests, the negative electrode being placed on the upper abdomen, the positive over the peroneal nerve as it passes behind the head of the fibula.

The child to be tested was laid with the feet pointing to the left of the operator, whose left hand supported the left ankle and foot of the subject in such a manner as to feel any twitch occurring in the flexors of the ankle or of the toes. Slight reactions are readily felt in this way which would be imperceptible to the eye. The positive electrode is controlled by the operator's right hand, the negative one being held in position by the assistant who with his free hand controls the rheostat. It is necessary that the tests be begun with a current of sufficient strength to produce muscular response, and gradually be reduced from this to the point at which the twitch is lost. If the reverse is attempted the lowest contraction point will be invariably passed before response occurs.

Allowance for individual skin resistance is to be made in order to avoid undue disturbance to the patient through the use of unnecessarily strong currents. This resistance varies directly with the amount of sub-

cutaneous fat, and reduces rapidly as the operation progresses, the latter fact being apparently due to the congestion which, developing under both electrodes, increases the skin's conductivity. This variation is great, both in different individuals and in the same case at the beginning and end of a test. Thus the same rheostat reading which in one instance may give a current through the body of 1 milliamperere will in another case or after the skin congestion has developed during many applications of the current allow from 6 to 8 milliamperes to pass and result in unnecessary irritation and violent resistance on the part of the subject.

The test for kathodal closure should be first made, as response to this is obtained most readily and with the least current strength. Anodal closure, anodal opening and kathodal opening should follow in order.

Infants less than a month old are less susceptible to electrical stimulation than older children, and these in turn are more susceptible than the adult.

In general there are three grades of electrical irritability:

1. The normal, in which only kathodal closure occurs under 5 milliamperes. Sometimes anodal closure is found at 5 milliamperes or just below it.

2. The middle grade or anodal hyperirritability, in which kathodal closure is less than 5 milliamperes and anodal opening is less than anodal closure and less than 5 milliamperes.

3. Tetany, in which all four reactions are less than 5 milliamperes. As suggestive of tetany is the occurrence of anodal opening less than anodal closure and the appearance of kathodal-closure tetanus.

Of the children under discussion sixty-five were boys and fifty-three girls. In 24.6 per cent. of the boys and 15 per cent. of the girls hyperirritability occurred. Of the ten patients showing the highest grade of irritability there were seven boys and three girls. There were eighteen under 1 week of age, fourteen from 1 week to one month, eleven from 1 to 2 months, thirteen from 2 to 3 months, twenty from 3 to 5 months, and fourteen each from 5 to 7, 7 to 9 and 9 to 13 months. Of the eighteen children under 1 week of age, the middle-grade reaction was obtained in no case. Of the fourteen from 1 week to 1 month it was present in 7 per cent. Of the twenty-four from 1 to 3 months old 8 per cent. showed this partial hyperirritability. From 3 to 5 months 40 per cent. of twenty cases gave the partial reaction. From 5 to 8 months 50 per cent. of the twenty-four cases evidenced anodal irritability. Of eighteen children of 8 months and older, it was obtained in 22 per cent.

The averages obtained in children of from 3 to 8 months were consistently lower than those of any other period. Those from 1 to 3 months gave the next lowest.



TABLE 2.—SHOWING ELECTRICAL REACTIONS ACCORDING TO AGE

	Average	Number of Tests
Under one week, 18 children—		
Kathodal Closure .....	3.6	25
Anodal Closure .....	4	5
Anodal Opening .....	4.9	4
Kathodal Opening .....	5 +	all
One week to one month, 14 children—		
Kathodal Closure .....	4.5	14
Anodal Closure .....	6.9	10
Anodal Opening .....	6.3	3
Kathodal Opening .....	7	1
One month to 3 months, 24 children—		
Kathodal Closure .....	3	44
Anodal Closure .....	4.3	26
Anodal Opening .....	5.3	17
Kathodal Opening .....	4.5	2
Three months to 5 months, 20 children—		
Kathodal Closure .....	2.7	42
Anodal Closure .....	3.9	34
Anodal Opening .....	4.4	17
Kathodal Opening .....	1.3	1
Five months to 8 months, 24 children—		
Kathodal Closure .....	2.9	70
Anodal Closure .....	3.5	56
Anodal Opening .....	4	33
Kathodal Opening .....	3.4	4
Eight months and over, 18 children—		
Kathodal Closure .....	3.8	24
Anodal Closure .....	4.5	18
Anodal Opening .....	4.6	9
Kathodal Opening .....	5	1

Escherich's conclusions as to the reactions of normal children are:

1. The first weeks do not differ from the later weeks of life in electrical irritability.
2. In normally developing children only kathodal closure is less than 5 milliamperes.
3. Anodal closure at less than 5 milliamperes is seldom found in the peroneal nerve during the first year.
4. Opening contractions are seldom found at less than 5 milliamperes.

My experience seems to indicate that children less than 1 week old are less sensitive to electrical stimulation than when older. Anodal closure was elicited 100 times at a point less than 5 milliamperes. Anodal opening was found fifty-three times, and kathodal opening ten times. This variance of these results with those of Escherich may be due to the fact that my children were, as before stated, far from normal, in that they were all in the ward because of nutritional disturbances. To this point reference will be made later.

There were in this series six infants weighing less than 5 pounds, seventy-one between 5 and 10 pounds, and twenty-three of 10 pounds and over.

The incidence of partial hyperirritability in children under 5 pounds was 16 per cent.; 5 to 10 pounds, 22 per cent.; 10 pounds and over, 30 per cent.

With reference to change in weight or, as this is its best index, the general condition of the subjects, it was found that of the sixty children losing weight, 25 per cent. showed partial hyperirritability; of the twelve with stationary weight, 16 per cent. showed partial hyperirritability; and of the twenty-seven gaining weight, 37 per cent. showed partial hyperirritability.

During the period of this work there were fifty-seven infants on skim-milk mixtures, twenty-one on condensed milk, twenty-three on butter-milk, eighteen on Finkelstein's "Eiweismilch," fourteen on whole milk mixtures and twenty-four were on the breast. As it has been shown that tetany occurred more frequently in artificially than in breast-fed children, comparisons between the reactions of these classes were made. In the breast-fed the average of kathodal closure, 3.2 in thirty-eight tests; anodal closure, 4 in twenty-four tests; anodal opening, 4 in seven tests; and kathodal opening, 2.4 in one test, were practically the same as those for artificial feeding, which were: kathodal closure, 2.8 in 172 tests; anodal closure, 3 in 123 tests; anodal opening, 4 in sixty tests; and kathodal opening, 4 in nine tests. These averages of the values found to obtain in the individual tests are given to show something of their individual variation. Taking the number of breast and artificially fed children who showed distinct hyperirritability, it appears that there was none of the ten former, but 24 per cent. of the 108 of the latter class. It must be added, however, that the cases were not exclusively on either type of nourishment for a great length of time before testing.

Referring again to the nutritive condition, the reactions were classified as to good and poor gastric and intestinal digestion. There were thirty-eight in which the gastric digestion was good, fifty-eight in which it was poor. Twenty-seven children had satisfactory intestinal conditions and in seventy-seven the opposite was the case.

Again leaving the questionable average figures and dividing these classes of digestive condition into those showing hyperirritability and those reacting to kathodal closure alone, it appears that of thirty-eight instances of good gastric digestion 30 per cent. showed hyperirritability; of fifty-eight instances of poor gastric digestion 30 per cent. showed hyperirritability; of twenty-seven instances of good intestinal digestion 33 per cent. showed hyperirritability; of seventy-seven instances of poor intestinal digestion 24 per cent. showed hyperirritability.

Reviewing the tabulations concerning size, gain or loss in weight, digestive condition and method of nourishment, it is apparent that they throw little if any light on the relation of these conditions to electrical irritability. The strong impression was gained, however, during the

progress of the work, that the child's irritability varies directly with the general condition of nutrition, and that the perfectly developed, well-nourished subject gives response much less readily to galvanism than if under-fed and of low body weight.

It is evident that from this compilation nothing can be stated in respect to nutrition and electrical irritability, except that a considerable series of tests showed no influence of the one on the other.

TABLE 3.—SHOWING THE ELECTRICAL REACTIONS UNDER VARYING CONDITIONS OF DIGESTION AND NUTRITION

	Average	Number of Tests
With good gastric digestion—		
Kathodal Closure .....	2.8	88
Anodal Closure .....	5.3	60
Anodal Opening .....	3	39
Kathodal Opening .....	3.6	4
With poor gastric digestion—		
Kathodal Closure .....	3	133
Anodal Closure .....	3.6	111
Anodal Opening .....	4.3	53
Kathodal Opening .....	3.6	5
With good intestinal digestion—		
Kathodal Closure .....	3	38
Anodal Closure .....	4.1	44
Anodal Opening .....	4.1	28
Kathodal Opening .....	4.2	1
With poor intestinal digestion—		
Kathodal Closure .....	2.2	140
Anodal Closure .....	3.6	111
Anodal Opening .....	4.6	50
Kathodal Opening .....	3.6	4

TABLE 4.—SHOWING AVERAGE OF REACTIONS IN TABLE 3, GROUPING GASTRIC AND INTESTINAL TOGETHER

	Average	Number of Tests
With good gastric and intestinal digestion—		
Kathodal Closure .....	4.9	126
Anodal Closure .....	3.7	104
Anodal Opening .....	3.3	67
Kathodal Opening .....	3.9	5
With poor gastric and intestinal indigestion—		
Kathodal Closure .....	2.6	273
Anodal Closure .....	3.6	222
Anodal Opening .....	4.4	103
Kathodal Opening .....	3.6	9

#### SUMMARY

1. Tetany is seen in about 2 per cent. of infants under 1 year.
2. An early and definite diagnosis depends on the presence of marked electrical hyperirritability.
3. Normal children react to kathodal closure alone at less than 5 milliamperes.
4. Many children not having tetany give low response to anodal closure and in fewer cases to anodal opening.

5. This partial or anodal grade of irritability may depend on factors entirely foreign to tetany for its causation, or may mark the early stages of the disease.

6. Infants of less than 1 month respond less readily to galvanism than do older children.

7. Kathodal opening contraction may be absent in true tetanoid conditions.

8. The degree of hyperirritability may vary greatly in the same case from time to time.

9. No constant difference was found in the reactions obtained on left or right sides.

10. Anesthesia does not affect electrical irritability.

11. The peroneal group is best adapted for the test.

12. Three points in the technic are important:

(a) The test must start with a current strength able to produce muscular response and must be carried on with reducing current strength to the point at which muscular response fails.

(b) As the skin conductivity is constantly increasing care must be taken to avoid undue and strong stimulation as the test progresses.

(c) Kathodal closure, anodal closure, anodal opening and kathodal opening should be tried in the order of ease of eliciting and the amount of current strength required; that is, in the order named.

13. The highest incidence of tetany is during the early months of the year.

#### THE ELECTRICAL REACTIONS IN PARATHYREOPRIVA DOGS

A series of experiments on normal dogs, and on those deprived of part or all of their parathyroid tissue, was made with the object of determining:

1. The electrical irritability of the normal dog.

2. The influence on this irritability of the removal of one or more of the parathyroid glands.

3. The interval elapsing before the electrical evidences of tetany appeared.

4. The amount of time by which these symptoms antedated the physical evidences of the disease.

5. Whether the remaining glands would show evidences of attempt at compensatory hypertrophy.

The galvanic reactions of these dogs, taken for several days before operation to establish the normal for each animal before testing for abnormal reactions, followed very closely the normal reactions of the children tested in the ward. The same nerve muscle-group as that in the case of the child was used, the peroneal, the negative electrode being placed on the abdomen. No difficulty was met in getting accurate readings so long as the skin at the site of contact of the electrodes was kept closely shaven. It was unnecessary to use an anesthetic for the tests, and in the few cases in which mild anesthesia was used, for reasons of comparison, no change in the response to the current was observed.

Following the method used by McCallum, and in the belief that in the short time that these animals lived after operation no influence due to hypothyroidism would cloud the findings, thyroid and parathyroid glands were removed together. On account of the length of time necessary for such observations, it was not possible to include in this paper the *ultimate* results on the electrical reactions of simple partial parathyroidectomy. This will be made the subject of a later report.

The average reaction to kathodal closure before operation was from 1 to 3 milliamperes; for anodal closure, 3 to 4 milliamperes; for anodal opening, 4 to over 5 milliamperes; for kathodal opening, always over 5 milliamperes.

In one of the animals tested, only one parathyroid was removed, and in five cases, two parathyroids, with one lobe of the thyroid, were taken out. The intention here was to determine the effect on the electrical irritability of the nervous system of a lesion in a part of the parathyroid tissue. The animal with a single parathyroid gland removed showed only partial electrical irritability for 236 hours after operation, but there was immediate hyperirritability after the removal of the remaining three glands.

Of the semi-parathyreopriva dogs all five showed an electrical hyperirritability toward anodal closure and anodal opening. The kathodal reactions showed change in only two instances (Dogs 6 and 7). In two cases kathodal tetanus was elicited after the first operation, although it had not been obtained before the parathyroids were partially removed. This hyperexcitability to anodal stimulation appeared in from one to three days after removal of the two glands, and corresponds to Escherich's mild "*Anodische grad.*"

In no case was there any evidence of tetany other than the changed electrical irritability. Lesions of one or two parathyroid glands may, then, produce moderate increase of electrical excitability to the galvanic current, but do not at once result in general tetany. In two instances (Dogs 6 and 7) partial thyreo-parathyroidectomy was followed by the complete tetany reaction. These animals might have furnished examples of tetany due to partial removal of the parathyroid tissue had the second operations been longer deferred. In every case of partial removal of the glands there appeared, in varying degree, some tendency to anodal irritability. Two of McCallum's semi-parathyroidectomized dogs showed tetany in two days after operation on the glands of one side.

In four dogs both lobes of the thyroid, with entire capsule and all four parathyroid glands, were removed at one operation. Electrical hyperirritability to all four types of current supervened in from five to forty-eight hours after operation, with one exception. The electrical tests showed tetany from a few hours to two days before any other symp-

toms of the condition appeared. One of these four dogs showed slight laryngospasm on the sixth day following operation, but up to the fourteenth day gave no typical increased response to electrical stimulation. He was then given 2.5 gr. of thyroid extract daily to counteract any effect of the loss of the thyroid secretion, and did for four days respond to currents of lesser strength. This, however, did not persist, and the animal died on the forty-sixth day after operation without having shown any ill effect from the removal of all his parathyroid tissue. A careful autopsy failed to show any accessory glands in the neck, the thymus or elsewhere, or to furnish any additional clue as to the cause of the sudden death of the animal.

After the removal of all four glands, nine animals gave low electrical reactions, from which a diagnosis of tetany could be made in twenty-seven, twenty-one, twenty-two, sixteen, twenty-nine, nineteen, seventeen, nineteen, nineteen, hours after removal. In one instance (Dog 3) kathodal closure, anodal closure, anodal opening, dropped to 0.4 milliamperes in twenty-six hours after operation and the animal died in tetany, but kathodal opening remained over 5 milliamperes.

Partial thyreo-parathyroidectomy was done on six dogs and the operation made complete, respectively, in four, five, twelve, twelve, thirteen and thirteen days later.

Measurements of the lobes of the thyroid and of the parathyroid glands first removed were compared with those left till the second operation. Search was also made in sections from all glands for mitosis and evidences of glandular over-activity. In each case there was evident hypertrophy of the remaining lobe of the thyroid, but there were found no evidences of attempt at similar change in the remaining parathyroid glands.

The accompanying charts indicate that the electrical reaction of animals subjected to parathyroid injury of varying degree do not change *pari passu* with the lesion produced, although Biedl and others have found that the general picture of tetany depends for its intensity on the number of glands removed. It was found, in the majority of cases, that after partial operation the reactions were only in small degree changed till the remaining glands were removed, when sudden tetany developed.

As it has been observed by several experimenters that parathyroidectomized animals often do not show symptoms of tetany till subjected to some metabolic or physical strain, electrical tests on the partially parathyroidectomized dogs were made after considerable muscular exertion. The nervous excitability was not found increased by such exercise, although tachypnea, muscular spasm, and laryngospasm were frequently induced or augmented. The response to galvanism is, then, less influenced by intercurrent conditions than other tetany symptoms.

Electrical hyperirritability resulting on removal of all parathyroids appeared in nine of the ten dogs tested, sixteen, six, twenty-four, and twenty hours and one, one, two, three, and four and one-half days, respectively, before the development of other tetanoid signs.

The average time of onset, after complete operation, of electrical hyperirritability, was thirty-three hours. The average for the same in cases in which the operation was done in two stages was twenty hours. Inasmuch as in the short time allowed to elapse between operations in this series of experiments there seems to have been produced a disposition

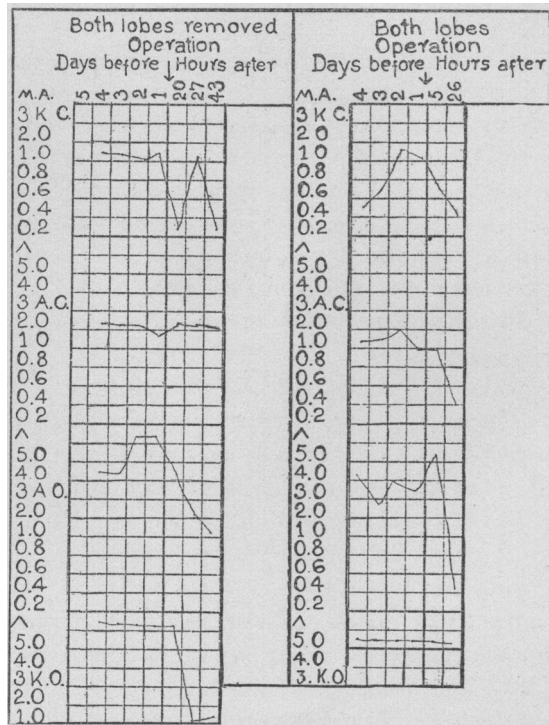


Chart 1, Dog 1.—Electrical reactions after complete extirpation of glands. weight of dog 22 pounds; killed forty-eight hours after operation; no signs of frank tetany. Electrical hyperirritability preceded death sixteen hours.

Chart 2, Dog 2.—Weight 27.5 pounds; died in tetany thirty-one hours after operation. Electrical irritability preceded tetany six hours.

to immediate response to further injury, it is possible that more time would have allowed the development of tetany reactions after only partial extirpation of the parathyroids.

Symptoms referable to the hyperirritability of nerve centers were, then, in every instance, the first to appear, and although in this series of tests they preceded other symptoms by an apparently short time, it is

to be remembered that in no case was the course of the disease produced longer than sixteen days, the average being nine days. The average of the times occupied in the development of electrical hyperirritability was one-ninth of the times lapsing before the production of other symptoms.

The galvanic current is, then, of especial value in the early diagnosis of tetany.

#### ANALYSIS OF PARATHYREOPRIVA DOGS

##### A. COMPLETE EXTIRPATION OF GLANDS

Dog 1.—Female, weight 22 pounds. August 11, reactions were obtained at kathodal closure, 1; anodal closure, 2; anodal opening, 3; kathodal opening, over

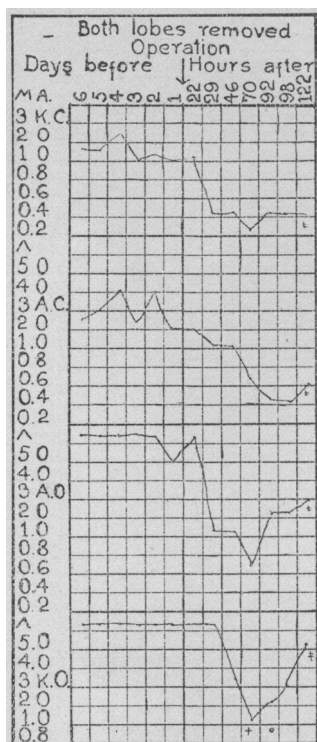


Chart 3, Dog 3.—In the above chart “o” = no general tetany; + = general tetany; ‡ = tests made as dog was dying, showing further reduced reaction to opening contractions.

5 milliamperes. Under ether anesthesia anodal tetanus was obtained at anodal opening, 3 milliamperes; the other reactions being unchanged.

August 12, closing contractions somewhat lower, opening contractions over 5 milliamperes. No change with ether anesthesia.

August 15 and 16, reactions the same. The average for this animal's galvanic response was kathodal closure, 1; anodal closure, 2; anodal opening, 4; kathodal opening over 5 milliamperes.

August 16, both lobes of thyroid with capsule were removed and found to include four parathyroid glands all lying on surface of thyroid.



August 17, twenty hours after operation, there was no evident tetany. The reactions were, kathodal closure, 2; anodal closure, 2; anodal opening, 4; kathodal opening over 5 milliamperes. Twenty-seven hours after operation there was further evidence of electrical hyperirritability, reactions being obtained at kathodal closure, 1; anodal closure, 2; anodal opening, 1; kathodal opening, 1.1.

August 18, forty-three hours after operation, there was fine tremor, slight rigidity and tachypnea, with reactions practically the same as those of the preceding day. On account of considerable distress the dog was killed two days after operation.

Dog 1 showed electrical hyperirritability 20 hours after operation and one day before there was other evidence of tetany.

Dog 2.—Male, weight 27 pounds. The average of the reactions taken on each of the four days before operation was, kathodal closure, 1; anodal closure, 2.4; anodal opening, 3.6; kathodal opening over 5 milliamperes.

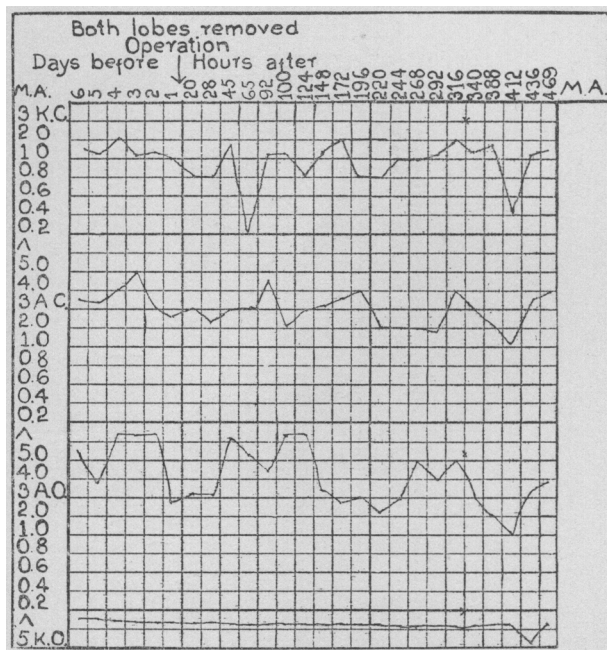


Chart 4, Dog 4.—In the above chart the cross (x) indicates that 2.5 gr. thyroid extract was given daily; dog weighed 6 pounds; died forty-six days after operation suddenly, having had no signs of tetany other than laryngospasm.

August 18, complete thyreo-parathyroidectomy was done, four glands being identified. Five hours after operation the reactions were, kathodal closure, 3; anodal closure, 2; anodal opening, 5; kathodal opening over 5 milliamperes. Twenty-three hours after operation the reactions were, kathodal closure, 2; anodal closure, 2; anodal opening, 2; kathodal opening, over 5 milliamperes. Twenty-seven hours after operation muscular twitchings were noticed and the animal died in convulsions and general tetany four hours later.

This dog showed an unusually prompt onset of electrical hyperirritability and frank tetany with death in severe muscular spasm in thirty-one hours after operation. With the exception of kathodal opening, the reactions were very low, but the former never dropped below 5 milliamperes, although the physical evidences of tetany were severe.

Dog 3.—Six observations during the week preceding operation showed the normal reactions to be, kathodal closure, 1.3; anodal closure, 2.4; anodal opening and kathodal opening over 5 milliamperes.

August 23, both lobes of thyroid with four parathyroid glands were removed.

August 24, twenty-two hours later, there was increased excitability to closing, but none to opening tests. Twenty-nine hours after operation, however, all tests responded to currents of less than 1 milliampere, excepting kathodal opening, which remained above 5 milliamperes.

August 25, forty-six hours after operation, kathodal opening dropped to 3 milliamperes, and seventy hours after operation, all reactions were below 1

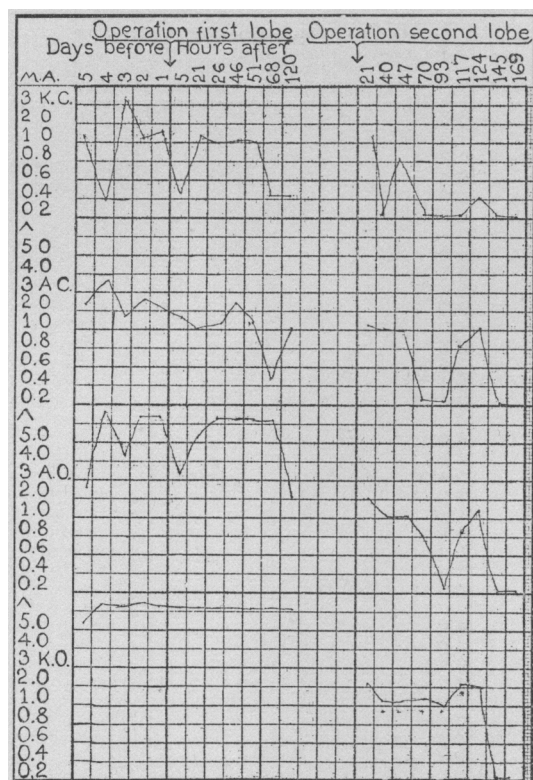


Chart 5, Dog 5.—Weight 32 pounds. x = occurrence of tetany (kathodal); first evidence of frank tetany four days after second operation; dog killed 169 hours *post operatione*.

milliampere. From this time on to the death of the dog the reactions remained about the same. Tests made at a few moments previous to death gave still further reduced reaction to opening contractions.

Frank tetany appeared forty hours after operation and persisted throughout. In this case the electrical indications of tetany preceded only by a few hours the physical symptoms of the disease.

This dog evidenced early and marked response to parathyroid lesion by electrical hyperirritability and only five hours later all tetany symptoms were pronounced.

Dog 4.—Female, weight 6 pounds. Daily observations for six days preceding operation gave this animal a normal average of kathodal closure, 1.2; anodal closure, 3; anodal opening, 5; kathodal opening over 5 milliamperes.

August 24, complete thyreo-parathyroidectomy was performed and for six days no change was noticed other than slight increased responsiveness to kathodal closure and anodal closure. On the sixth day moderate laryngospasm developed and this persisted as the only symptom of tetany till death, which occurred on the forty-sixth day after operation. Autopsy failed to show the existence of accessory parathyroids. Fifteen days after operation  $2\frac{1}{2}$  gr. of thyroid extract was given daily to counteract any effect of the loss of the thyroid lobes. This had no effect on the general condition.

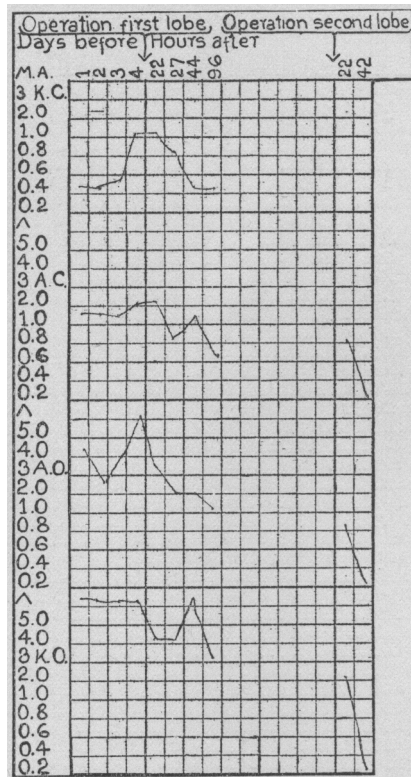


Chart 6, Dog 6.—Weight 30 pounds. Killed in tetany forty-eight hours after second operation. Electrical hyperirritability preceded tetany forty-four hours.

This animal alone failed to develop electrical hyperirritability or marked tetany symptoms after suffering loss of all the parathyroid glands.

#### B. DOGS IN WHICH PARATHYROIDECTOMY WAS DONE IN TWO STAGES

Dog 5.—Male, weight 32 pounds. For the six days preceding operation the average reactions were found to be, kathodal closure, 1; anodal closure, 3; anodal opening and kathodal opening over 5 milliamperes; i. e., relatively low closing contractures.

August 17, the right lobe of the thyroid with capsule was removed, two parathyroid glands being identified. Through the slipping of a ligature there was severe hemorrhage, without, however, any ill effects being manifest, then or

later. There was a gradual rise in electrical excitability for kathodal closure, anodal closure, and anodal opening for five days. At the end of this time the figures being, respectively, 0.4, 1, and 2 milliamperes. There were no other signs of the tetany condition. On August 22, the remaining lobe of thyroid, which was markedly hypertrophied and contained one parathyroid, was removed. Again, such severe hemorrhage occurred as to make recovery doubtful.

Twenty-one hours after the second operation the electrical diagnosis of tetany was definite, with kathodal closure, 1.4; anodal closure, 1.1; anodal opening, 2.1; kathodal opening, 2.1 milliamperes. The reaction points dropped steadily until August 29, when all were obtained at .2 milliamperes.

No physical evidences of tetany were noted till August 26, when there was some tachypnea. On August 29, the dog was stupid, emaciated and would not eat, but had no definite tetany symptoms. He was chloroformed at this time.

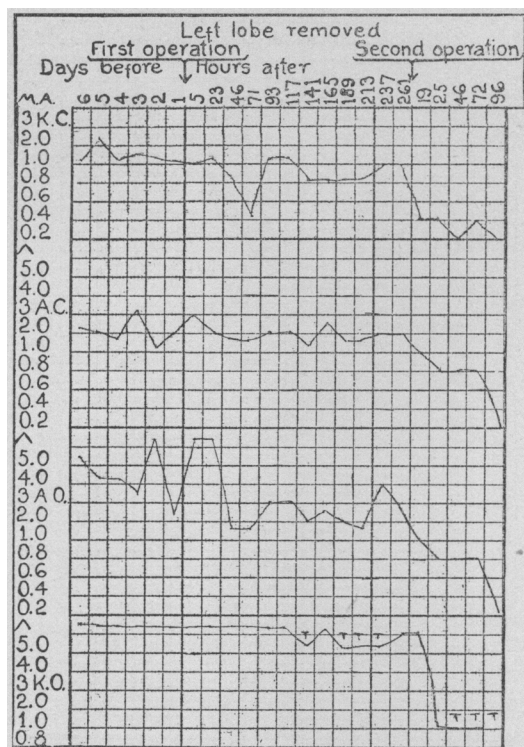


Chart 7, Dog 7.—Died in tetany ninety-six hours after second operation. "T" = kathodal tetanus.

For four days preceding the second operation this dog was evincing an increasing electrical hyperirritability which continued uninterruptedly after the second operation. Although the electrical reactions had been strong for tetany, for nine days there was no other evidence of the condition, until August 26, when mild tachypnea developed. McCallum has shown that the muscular spasm, convulsions, etc., of experimental tetany can be controlled and temporarily relieved by bleeding. The second severe hemorrhage may in this case explain the absence of frank tetany. If this supposition be granted, it is of interest and consequence to note that the loss of blood exerted no influence on the course or the development of the nervous hyperexcitability.

Dog 6.—Female, weight 30 pounds. The mean reaction before operation was found to be kathodal closure, 1.4; anodal closure, 2; anodal opening, 4; kathodal opening over 5 milliamperes. On August 18, the thyroid and parathyroids of the left side were removed. During the following four days there was distinct increase of the electrical hyperirritability, the reactions being, kathodal closure, .4; anodal closure, .6; anodal opening, 1; kathodal opening, 5 milliamperes. This increased irritability began twenty-seven hours after operation. August 22, the remaining lobe of the thyroid, with its parathyroids, was removed and, at once, all reactions dropped to .2 milliamperes. No other signs of tetany were present till two days after the second operation.

This dog responded markedly in her nervous excitability to the removal of part of her parathyroid tissue, and gave low reactions for four days before muscu-

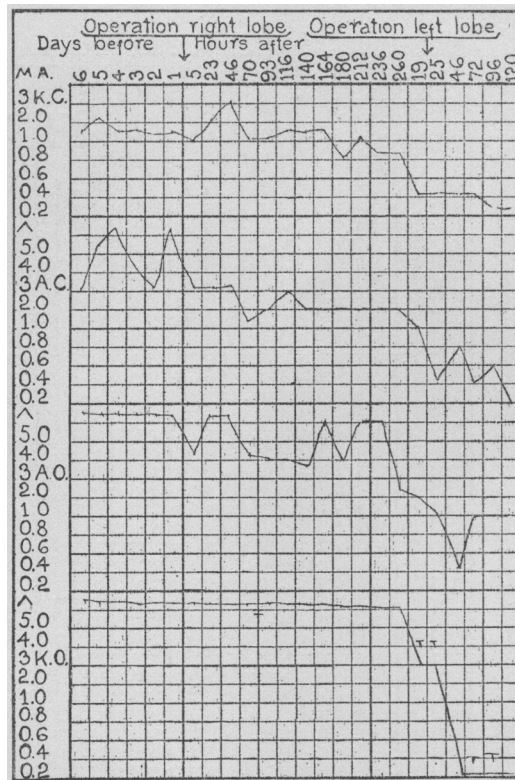


Chart 8, Dog 8.—Weight 16 pounds; found dead September 12, 120 hours after second operation, never having shown signs of apparent tetany.

lar spasm appeared. Moderate hypertrophy of the remaining thyroid lobe was noted, but no change was apparent in the parathyroids.

Dog 7.—Male, weight 11 pounds. Six tests gave for this animal kathodal closure, 2; anodal closure, 2; anodal opening, 5; kathodal opening over 5 milliamperes as the average normal.

August 24, the left lobe of the thyroid and only one parathyroid were removed. During the ten days following operation there was constantly increasing irritability, most marked in the low anodal opening contraction and kathodal opening tetanus. No other tetany symptoms were noticed. September 6 the right lobe



kathodal closure, .8; anodal closure, 1; anodal opening, 1; kathodal opening, 2 milliamperes. Forty hours after operation there was partial paralysis of the front legs, with electrical reaction, all below .2 milliamperes.

Here, again, injury to a portion of the parathyroid glands caused none of the phenomena of tetany, but apparently prepared the way for a very rapid and severe reaction on the ablation of the remaining glands.

Dog 10.—Female, weight 18 pounds. This dog's reactions before operation were; kathodal closure, 1; anodal closure, 3; anodal opening, 5; kathodal opening, over 5 milliamperes. After removal of the left half of the thyroid and parathyroid tissue, the reactions of kathodal closure, anodal closure, and anodal opening were somewhat irregular, with kathodal opening unaffected, until the extirpation of the remaining glands, nine days later. Nineteen hours after second operation there was marked hyperirritability, and a day and a half later

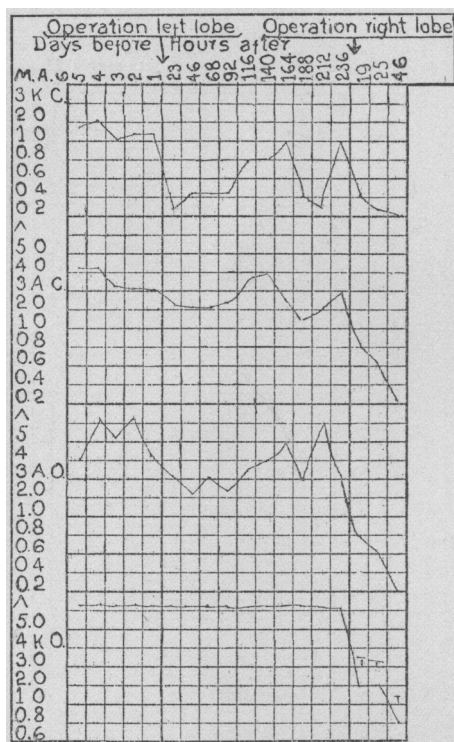


Chart 10, Dog 10.—Weight 18 pounds; frank tetany came on seventy hours (killed) after second operation.

electrical reactions were obtained below .8 milliamperes, and there was severe general tetany.

#### SUMMARY

1. The reactions in normal dogs are similar to those of normal children.
2. The peroneal nerve muscle-group is best suited to the test.
3. Mild anesthesia does not increase the delicacy of the test.
4. Both sides of the body react alike.

5. In normal dogs kathodal closure averages at from 1 to 3 milliamperes; anodal closure from 3 to 4; anodal opening from 5 to over 5, and kathodal opening is always over 5 milliamperes.

6. The complete extirpation of the parathyroid glands produces prompt hyperirritability.

7. Partial extirpation of the parathyroid glands produces either anodal irritability or only inconstant change.

8. Complete extirpation, following partial removal of the glands, results in more immediate hyperirritability than when all glands are removed at once.

9. Increased irritability follows the complete parathyroid extirpation in an average of thirty-three hours.

10. Electrical hyperirritability follows the second of the two-stage operation in an average of twenty hours.

11. Electrical change always precedes the other symptoms of tetany by considerable time.

159 East Seventh Street.