The Coagulation Rate of the Blood in Epileptics.

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I.

THE following is an account of a systematic examination of the coagulation rate of the blood of nine female epileptics and seven healthy women.

The great variability in the coagulation rate led me to regard my former somewhat isolated observations (1) as by no means conclusive in determining the relationship between coagulation and epileptic fits. It is therefore satisfactory to find that these results confirm my former conclusions, *viz.*, that in epilepsy there is a greater tendency for the blood to coagulate and that this tendency is specially marked about the period of fits.

The nine epileptics, with one exception, were chosen from those who were, or had been, when not under the immediate influence of their attacks, of average intelligence. Two of the cases, although originally in this category, were now demented from the long continuance of their disease. Eight were healthy, one delicate and subject to bronchitis.

In five of the cases observations were made to test the effects on coagulation of bromide of potassium, in three to test the effects of citrates, and in three of a purin-free diet.

The method employed was that of Wright and Paramore (2), but instead of taking up two or three samples of blood from different pricks in the calibrated capillary tubes, putting them all into the water heated to 37° C., and taking them out one after another at different intervals to test for coagulation, I have preferred the alternative method mentioned by them of taking one sample at a time, and testing it at *stated* intervals, *e.g.*, the tubes were tested at 105, 120, and 135 seconds, and if one was found to have coagulated at, say, 120 seconds, the following would be tested at 115 seconds, and so on. On account of the variability in the coagulation rate in the same individual, I believe this latter method to be the more accurate.

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The method is one which requires considerable practice before one can at all rely on the results, and this is a further reason why I undertook a long series, during which many more than a thousand samples were tested, to see how it would compare with my earlier series.

Whatever may be the defects of the method, I believe the results obtained, although they may not, strictly speaking, represent the coagulation time of the blood within the living subject, will at any rate be comparable, in as much as each blood tested is exposed to similar sources of possible error.

As illustrating the very great variation in coagulation, it may be stated that from three successive pricks in the same individual on different fingers, the blood in both control and epileptic cases often showed a difference in the time of over two minutes, and in all my observations I only on three occasions found the same coagulation rate in the blood from three consecutive pricks.

Buckmaster (3) refers to the variability in coagulation rate, and states that he is satisfied that on different days, at the same temperature, it may, in the same individual, vary by at least five to six minutes. The largest variation among my seven control cases was two minutes twenty-five seconds.

The blood is not a simple solution, but contains multitudes of organised elements which in all probability play an important part in the process of coagulation, so that according as different samples contain more or less of these elements, so will the rate be quicker or slower. On account of these variations, to get a true mean I have examined the blood of each of my subjects for at least fourteen consecutive days, taking on each day three samples from three different fingers. The observations were made between 11 a.m. and noon.

The systolic blood-pressure was taken in the sitting posture, with Martin's modification of the Riva-Rocci apparatus.

In the following table is given, both for the seven control cases and the nine epileptics, the average for the fourteen days of the samples which coagulated most quickly and most slowly. Also the average blood-pressure and its greatest variations.

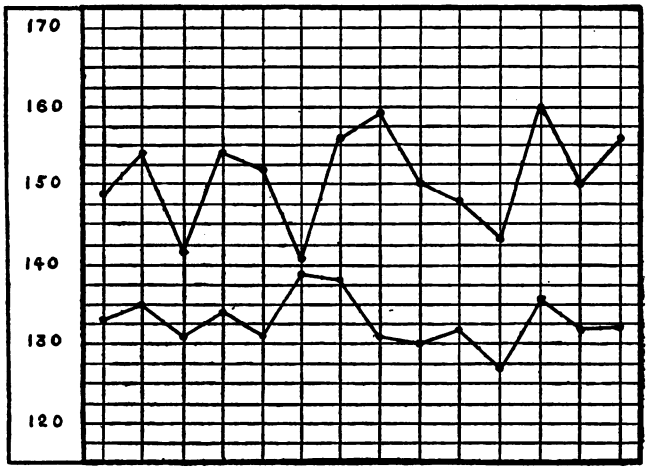
In all the charts the figures at the left hand side in the case of the coagulation observations refer to seconds, in the case of the blood-pressure to mm. of mercury. The continuous line represents the coagulation rate, the broken line the blood-pressure.

	Controls.					Epileptics.			
	Coagulation time in seconds.		Systolic blood-pressure in mm.Hg.			Coagulation time in seconds.		Systolic blood-pressure in mm.Hg.	
	Average of quickest.	Average of slowest.	Average.	Varying between.		Average of quickest.	Average of slowest.	Average.	Varying between.
1	146	189	133	148–118	2[1]	117	160	102	99–111
2	147	178	116	134–105	6	120	160	102	90–115
3	148	181	121	136–104	8	127	165	96	85–105
4	148	199	115	132–105	9	127	155	110	102–122
5	149	180	142	156–125	1	132	162	108	92–120
6	150	178	118	126–110	7	135	170	122	109–144
7	168	204	119	125–108	4	136	170	111	90–123
					5	151	185	117	102–129
					3	153	188	147	125–172
	151					133			

[1] This refers to the average of only nine days.

Three of the control cases were menstruating during the

CHART 1.



Showing the mean daily coagulation time in seconds of seven controls (upper line) and seven epileptics (lower line).

period that their blood was being examined; in neither of them did this seem to have any effect on coagulation.

The accompanying chart (No. 1) shows very clearly the greater rapidity of coagulation in the epileptics. On not one

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of the fourteen days compared was the average rate in the controls so rapid as the average rate in the epileptics.

Further, the shortest period of coagulation recorded in the controls in nearly 300 observations was 120 seconds, and this only occurred on three occasions (once each in three different nurses).

The shortest period recorded (from the finger) in seven epileptics was 105 seconds, whilst a rate of 120 seconds or less was met with on thirty-three occasions (the number of observations in the epileptics, from which this chart was constructed, being the same as the number in the controls).

II.

CASE 1.—J. A. S—,æt. 27. Her fits date from early childhood; she had, however, passed the sixth standard, and was two years in one situation as a servant and five in another. When free from fits she was a nice-looking, intelligent, well-dispositioned girl, and her mental standard was above the average of her class. From her own account she was at first subject to attacks both of the *grand* and *petit mal* type, but for the last three or four years has had none of the latter. She says that she used to feel worse after the attacks of *petit mal* than after the attacks of *grand mal*. The number and order of fits observed for the, nearly, four months that a record was kept, *viz.*, from December 30th, 1906, to April 15th, 1907, was as follows:

January	5–6	5 fits.
,,	14	1 fit.
,,	31–February 1	5 fits.
February	15	1 fit.
,,	20	1 ,,
,,	22–24	5 fits.
,,	28	2 ,,
March	6–7	2 ,,
,,	14	1 fit.
,,	21–22	2 fits.
April	7–9	7 ,,

During this period she had in all thirty-two attacks of *grand mal*—eighteen when up, and fifteen when in bed.

Her bodily health was very good. She had a neurotic palate. From December 30th, 1906, to January 12th, 1907,

daily observations were made on the coagulation rate of the blood, the systolic blood-pressure, and pulse rate. She was not taking, nor had she been taking, any drugs.

The average for the samples which on each day coagulated the quickest was, for the fourteen days, 132 seconds, and for the samples which were longest in coagulating the average was 162 seconds.*

On January 5th she had four fits, the blood coagulated quickly, and, although not so low as the day following, it should be noted that there was a difference of only five seconds between the slowest and quickest.

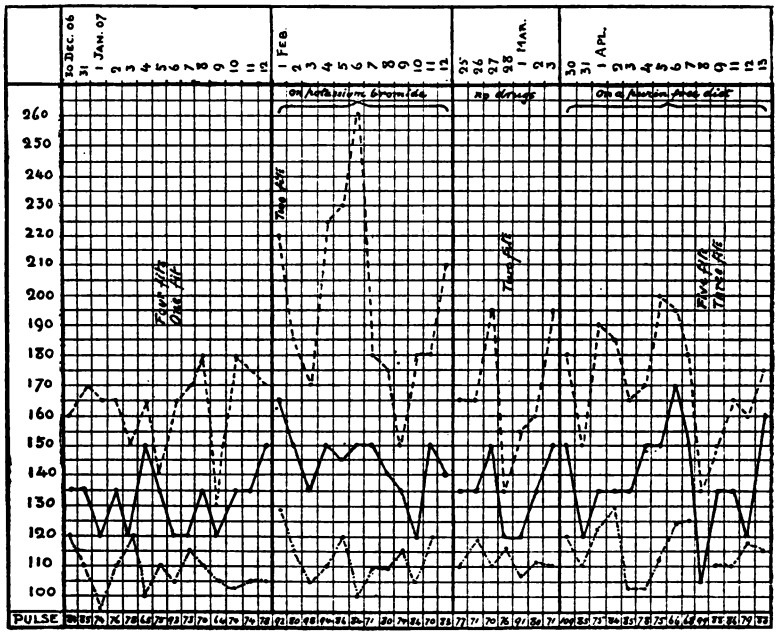
On January 12th she was ordered potassium bromide in half drachm doses three times a day. On the 14th she had a fit, and afterwards was sulky, irritable, depressed, and confused. She had three fits on January 31st, and two on February 1st, and showed profound and prolonged change in disposition. The two following days she appeared like a drunken woman, lying about on the floor with flaccid limbs and dilated pupils, and spoke in a sulky, drowsy way. She then got a little better and was able to do her work, but remained sulky, dull, and sleepy. From February 1st to 12th inclusive her blood was again tested. Coagulation was retarded but not to the same extent as in some of the other cases; the minimum average for the twelve days was 144 seconds. There was much greater variation in the coagulation time of the different samples of each day, so that the maximum average was 196 seconds. On February 12th, as she continued so much worse mentally and bodily, the bromide was discontinued and she soon regained her natural lively disposition and activity. A batch of fits succeeded the discontinuance of the drug (see list). For seven days, from February 25th to March 3rd, her blood was again tested, and the coagulation rate had dropped to its normal figures, *viz.*, minimum average 135 seconds, maximum average 167 seconds. During this period, *viz.*, on February 28th, she had two attacks of *grand mal*, one early in the morning at 1.50 a.m., the other in the evening at 8 p.m. and on that day there was a marked quickening of coagulation (120 seconds) which was maintained the next day, and then gradually became slower.

On March 4th she was put on a purin-free diet, consisting of milk, eggs, cheese, butter, bread and rice pudding, with cab-

* Hereafter I shall call these two averages the maximum and minimum.

bages when served. She seemed brighter and better on this diet, but there was no marked diminution in the number of fits. although they did not seem to leave her so dazed afterwards. She gained flesh, and was cheerful, active, and rational. Her blood was tested again for the fourteen days ending April 13th (the 10th omitted), and there was no marked retardation in its coagulation; the minimum average was 139 seconds, the maximum 171 seconds. On April 8th it was reported that she

CHART 2.—J. A. S—.



had had three attacks of *grand mal*, the first at 4.45 a.m., the second at 5.45 a.m., and the third at 6.40 a.m., and whilst her pressure was being taken she shot forward on to the floor, upsetting the apparatus, and had a strong fit. So soon as spasm had ceased her blood was tested; the first sample coagulated in 105 seconds, the shortest time recorded in 141 occasions, the third in 135 seconds.

Her fits are all of this sudden character with no warning. She falls as if shot. Such an absolutely sudden onset appears to me difficult to reconcile with the idea of a toxin circulating

in the blood as the immediate cause, but harmonises with a thrombotic origin. The two ideas are not, however, necessarily antagonistic, for an effect of the toxin may be to render the blood more liable to coagulate, in which case, although not the immediate, it would be a co-efficient cause.

Blood-pressure for the first fourteen days (taking no drugs) was on the whole rather low, its average being 108, only reaching 120 mm.Hg. on one occasion, and on one day falling to 95. There was no appreciable effect on the pressure on the days when she had fits, and on January 5th it was taken almost immediately after one. During the period that her pressure was taken whilst on potassium bromide there was on the whole a slight tendency for it to rise. On February 1st the pressure was taken whilst in a fit, before the convulsions had quite ceased. Whilst on a purin-free diet the pressure, contrary to my expectations, showed a slight upward tendency, and on four occasions was above 120.

Pulse, as very generally found to be the case in these epileptics, was occasionally irregular. In the first period (no drugs), it varied between 64 and 93, averaging for the fourteen days 76. Whilst on bromide it varied between 70 and 98, averaging 93, dropping to nearly the first average when the drug was left off (79), and whilst on the purin-free diet again slightly quickening, varying between 61 and 109, average 83. On two occasions (January 4th and April 8th) it was counted whilst in a fit, but just after spasm had ceased it was not quickened (75) on one occasion, slightly quickened (99) on the other.

In the chart, the upper dotted line shows the coagulation time of that sample of the three taken daily, which coagulated most slowly. It serves to show the very marked difference found in successive samples of blood. I did not think it necessary to give this maximum period in the other charts.

CASE 2.—F. N—, æt. 32. Her fits date from the age of fifteen or sixteen, and are said to occur generally in the daytime, one or two every week, and to be entirely of the *petit mal* variety. Her eyes become fixed, she changes colour, clenches her teeth, and dribbles saliva. They are over in a few seconds and she never falls.

She was admitted in an acutely melancholic condition, with

a self-inflicted wound on the throat, which she did a week previously because she "felt so miserable." She is a delicate woman subject to bronchitis, and has a very narrow and high palate. Appears to be of quite average intellect, converses rationally and sensibly, and tells me that after her attack she generally feels relieved. Six days after admission had a strong attack of *grand mal*, in which she fell down and bruised her face. So far as can be ascertained this was the first attack of *grand mal* she ever had.

From October 25th to December 1st she was taking ½ drachm doses of bromide of potassium, three times a day, and during this period she had no attacks whatever, but continued in a very depressed state.

On December 2nd, that is, immediately after a prolonged course of bromide, observations were begun on the coagulability of her blood and blood-pressure. The minimum average for fourteen days was high, 156 seconds. During this period she had no definite attacks of *petit mal*, but merely transitory sensations of fulness across the nose, flickering at the heart, and a "funny" smell (incomplete attacks). On December 16th she was put on 30 gr. doses of citrate of potash, three times a day, and on December 30th the dose was increased to 1 drm. She had, during this time, frequent attacks of *petit mal*. In spite of the drug the coagulability of her blood was markedly quickened, so that for the four days, from December 30th to January 3rd, it averaged only 120 seconds.

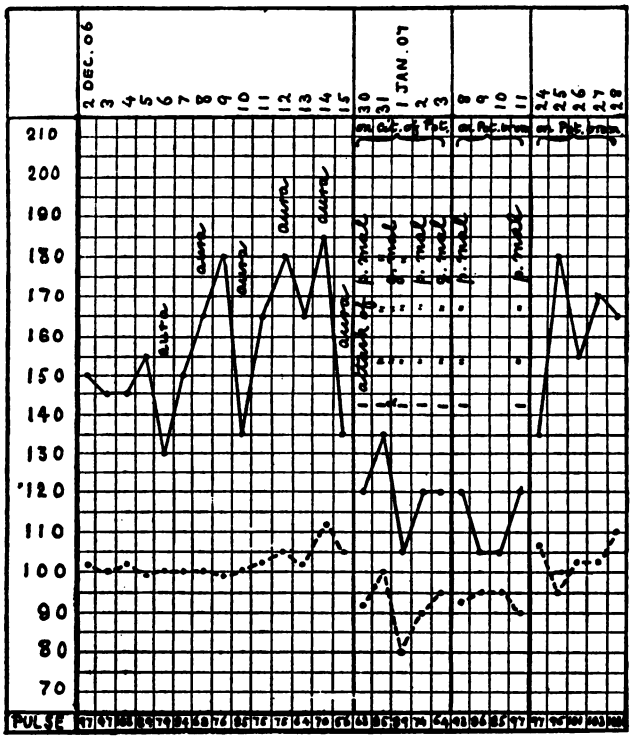
On January 3rd she was again put on bromide of potassium, 30 gr. three times a day, and from this time the attacks were much diminished in number. For the four days ending January 11th her blood was again tested, and still showed a short coagulation time, the average being only 115 seconds. The bromide was continued, and when her blood was again tested for five days, from January 24th to 28th, there was a marked retardation in the coagulation time, the average being 161 seconds.

Her chart shows very strikingly not only that the bromide markedly retards coagulation but also that this effect is lasting. The first fourteen days represent the retarded coagulation, which continued during the whole of this period, though she was not then taking the drug, but had been for a long time previously. Apparently the effects of the drug had worn off by the time the second series of observations were made, for the fits had returned

in their usual, or even greater, frequency, and the coagulation rate was much quicker. I believe that the reason why there was no retardation of coagulation in the third series, after four to five days' administration of bromide, was because her system was not saturated with the drug, for at a later period (fourth series of observations) the retarding effect is again well marked.

Wright and Paramore (4) found that by the administration of

CHART 3.—F. N—.



citric acid, in three cases, it was possible within a week to very materially retard the rate of coagulability of the blood, and to keep it at this lower point for a month, but that after this time, in spite of the continued exhibition of the drug, the coagulation returned to its previous rate.

Hence I quite expected a marked retardation in the coagulation of her blood whilst taking the citrate, and gave it for that purpose. This did not occur; in fact the rate was quickened,

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and during this period she was having many attacks of *petit mal.*

List of fits during the time under observation:

1906, December	6.	Aura (incomplete attack):
,,	8.	,,
,,	10.	,,
,,	12.	,,
,,	14.	,,
,,	16.	2 attacks of *petit mal.*
,,	17.	2 ,, ,, ,,
,,	19.	3 ,, ,, ,,
,,	21.	1 attack ,, ,,
,,	28.	1 ,, ,, ,,
,,	29.	2 attacks ,, ,,
,,	30.	3 ,, ,, *grand mal.*
1907, January	2.	1 attack ,, *petit mal.*
,,	3.	1 ,, ,, *grand mal.*
,,	7.	1 ,, ,, *petit mal.*
,,	11.	1 ,, ,, ,,
,,	23.	1 ,, ,, ,,
February	7.	1 ,, ,, ,,
,,	15.	1 ,, ,, ,
March	4.	1 ,, ,, ,,
,,	20.	1 ,, ,, *grand mal.*
April	6.	1 ,, ,, *petit mal.*

No further attacks during April.

Blood-pressure was low and consistent, varying scarcely at all for the first eleven days. It averaged 102 mm. for the first period. Whilst on citrate of potash it was usually lower, average 92, and again, when fully under the influence of bromide, it returned to its former level, average 103.

Pulse was very irregular. Apparently the bromide tended to quicken it, for it gradually slowed down in the first series immediately after a course of bromide, and quickened again in the fourth period when fully under the drug. A similar condition was noticed in the previous case.

CASE 3.—E. S—, a domestic servant. Her fits, entirely of the *petit mal* variety, date from several years previous to her admission here in 1904, when she would have been from nineteen to twenty-three years of age. When first admitted was suffer-

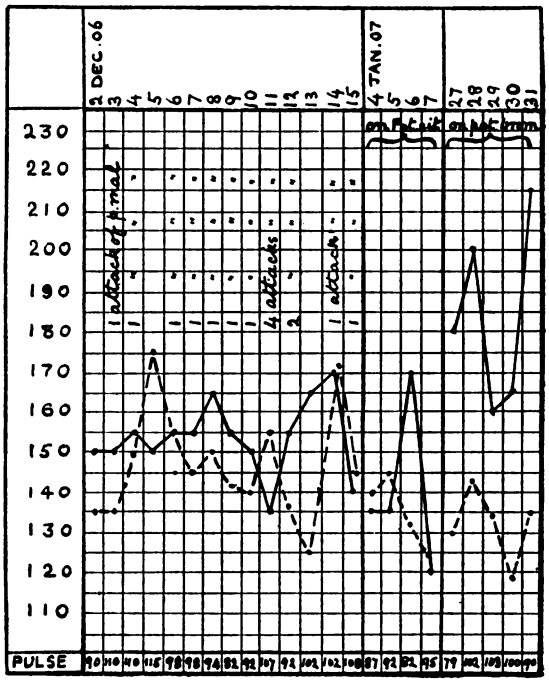
ing from an attack of acute mania with auditory hallucinations; this soon subsided and left her apathetic and lachrymose. She has a typical epileptic disposition, disagreeable, quarrelsome and religious, but is a useful worker in the ward, and of average intelligence. Has a neurotic palate. Has frequent attacks of *petit mal* both day and night. Does not fall, but pulls things about in an aimless fashion, *e.g.*, will pull off the cloth while having dinner. On one occasion she spilled some water on the table-cloth (in an attack) and took soap out of her pocket and began to wash the wet cloth. The following is the description of an attack I witnessed: Said to me, "I feel very funny," and her eyes became fixed; she was laid on the floor by the nurse and there was a very slight, transient tonic spasm (?) of her arms. After a few seconds she began to make clawing movements at her dress, got up in a dazed fashion, picked up several objects from the floor (some imaginary), rolled up some paper and flung it into the fire, and brushed her dress down with her hands. She did not micturate in this attack, although she sometimes does.

At the time that her blood was being examined she was 29 years of age, in good health, and was taking no drugs. It coagulated slowly, the average for fourteen days being 153 seconds. Nearly every day during this period she had at least one attack of *petit mal*. It will be noticed that there was a gradual quickening in the coagulation time from December 8th to 11th, on which day she had the maximum number of attacks (4), and when her blood coagulated in 135 seconds, the quickest recorded for this period.

On December 26th she began taking 40 gr. of potassium citrate three times a day, which, four days later, was raised to a drachm t.d.s. and continued daily until January 7th, 1907. While taking the drug she continued to have her attacks much as usual. On January 4th, 5th, 6th, and 7th her blood was again tested with the anticipation of finding a retardation in its coagulability. This, however, was not found. On no single day was it any higher than it had been when it was tested formerly, and on one day it coagulated in 120 seconds —a shorter period than had hitherto been recorded. The average for the four days was 140 seconds. From January 7th to March 5th she was taking ½ drm. doses of potassium bromide t.d.s., and whilst taking the drug she had very few attacks of *petit*

mal of the usual description, but had frequent hysterical attacks, when she would lie or fall down and scrape her feet up and down on the linoleum and chatter her teeth, without any loss of consciousness. She became very emotional and bad tempered, listless and depressed, unable to do her work and lost her appetite, so that the drug was discontinued. Her

CHART 4.—E. S—.



blood was tested on five days from January 27th to 31st, and as usual the coagulation was retarded, in her case very markedly, the average for these days being 185 seconds.

Blood-pressure.—This was the only case out of the nine epileptics examined where the blood-pressure was distinctly high; its average was 147 mm. Hg. There did not seem to be any definite relationship between its variations and the occurrence of the attacks of *petit mal*. Both during the administration of the citrate and bromide of potassium there was a distinct lowering of the pressure.

Pulse was regular and quicker than normal. As in the case

of the blood-pressure it did not seem to vary with the attacks. In her case there was not any acceleration of pulse-rate whilst taking the bromide.

List of attacks of *petit mal* whilst under observation (they occurred, with one or two exceptions, whilst she was up):

1906, December	3	1 attack.
,,	4	1 ,,
,,	6	1 ,,
,,	7	1 ,,
,,	8	1 ,,
,,	9	1 ,,
,,	10	1 ,,
,,	11	4 attacks.
,,	12	2 ,,
,,	14	1 attack.
,,	15	1 ,,
,,	16	1 ,,
,,	19	1 ,,
,,	20	1 ,,
,,	22	1 ,,
,,	23	1 ,,
,,	27	1 ,,
,,	28	1 ,,
,,	30	1 ,,
,,	31	1 ,,
1907, January	1	2 attacks.
,,	10	1 attack.
,,	17	1 ,,
1907, February	5	1 ,,

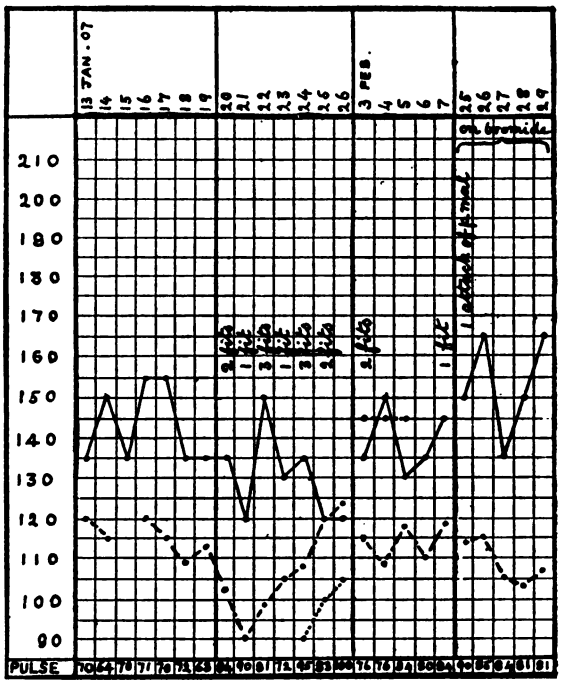
No further attacks to March 5th, when the bromide was discontinued.

CASE 4.—E. L—, was seven years old when she first had a fit. When admitted twelve years ago was in good condition; a nice-looking, bright girl, æt. 17, with a kindly disposition, not at all spiteful; in Standard III. She answered questions readily, but her intelligence was that of an average child of ten or eleven.

Said that she experienced a "funny" sensation in the chest or a buzzing in the head immediately before a fit and then lost consciousness. Said that her fits had been getting worse

lately, and that she felt very silly and lost after them. Neurotic palate. Developed mild chorea from November, 1896, to March, 1897, but this disappeared, and her bodily condition greatly improved on cod-liver oil. In April, 1898, she menstruated for the first time, and during that period had a series of attacks of *grand mal*. The post-epileptic condition was long and severe. She laid on the floor of her room for days in a quite dazed and lost condition. She continued to have series of fits at irregular

CHART 5.—E. L—.



The dotted line represents the coagulation time of blood from the ear.

intervals of a few months with similar prolonged post-epileptic phenomena. When free from attacks was active, industrious, and bright.

On January 13th, 1907, I began making observations on the coagulability of her blood, her systolic blood-pressure, and pulse-rate. She was then twenty-eight years old. Had not been taking any drugs. Had had no fits for several days. She was in good health; her memory was now considerably impaired for past

events, and she was childish, but of a kind disposition, and very industrious.

Her blood coagulated quickly; for fourteen days the minimum average was 137 seconds, and, compared with most cases, the difference between this average and the maximum was small, *e.g.*, 168 seconds. For the first seven days, during which she had no fits, the average was 143 seconds. During the next seven days (a period of fits) the average fell to 130 seconds.

On January 24th she fell in a strong fit just before her blood was examined. The quickest of the three samples of blood drawn from the fingers coagulated at 135 seconds, but of two samples drawn from the ear, immediately afterwards, the quicker coagulated at 90 seconds (dotted line in the chart). Subsequent examinations of ear blood, when she was free from fits, showed that quicker coagulation was not a constant peculiarity of this region. In the post-epileptic condition the blood was examined on five days; there was a prolongation in the coagulation rate so that the average was now 139 seconds.

On March 13th she was put on potassium bromide ½ drm., t.d.s., and twelve days later, from 25th to 29th, her blood was again tested and showed, as usual, a considerable retardation in coagulating; the average for these five days was 153 seconds.

List of fits during time under observation:

January	20.	2 attacks	*grand mal.*
,,	21.	1 attack	,,
,,	22.	3 attacks	,,
,,	23.	1 attack	,,
,,	24.	1 ,,	,,
,,	25.	2 attacks	,,
,,	29.	2 ,,	,,
,,	31.	2 ,,	,,
February	2.	2 ,,	,,
,,	3.	2 ,,	,,
,,	7.	1 attack	,,
,,	9.	2 attacks	,,
,,	10.	2 ,,	,,
,,	11.	4 ,,	,,
,,	12.	2 ,,	,,
,,	13.	3 ,,	,,
,,	14.	2 ,,	,,
,,	15.	1 attack	,,

February	16.	2 attacks *grand mal.*
March	11.	1 attack *petit mal.*
,,	12.	1 ,, *grand mal* (on potassium bromide).
,,	13.	1 attack *grand mal.*
,,	14.	1 ,, ,,
,,	25.	1 ,, *petit mal.*

The bromide, in her case, seemed to check the fits, but it had a very deteriorating effect on her character. On April 21st (after forty days' administration) she was reported as having "gone quite silly," had no energy, and acted like a person slightly intoxicated, and her whole expression had altered and become vacant. She was still able to do some housework.

Blood-pressure (systolic) varied between 123 mm. Hg. and 90, average 111; the lowest readings were during the week in which she was having a number of fits.

Pulse generally irregular; when free from fits it was fairly constant, varying between 63 and 72. During the week of fits it varied between 72 and 100, and whilst on bromide it was also slightly quickened, varying between 81 and 90.

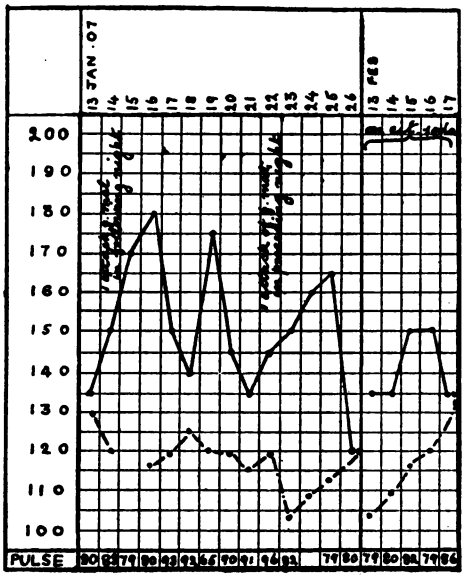
CASE 5.—A. M. L—, æt. 20, has had fits since six months of age. In fourth standard at school. When admitted in May, 1906, was in a dazed condition and was stated to have recently been acutely maniacal. Tells me that she has not had a fit for three or four weeks, and that now she generally goes a few weeks without any, and that she used to have them more frequently. She is thin but in fair health, and has a neurotic palate. After a few months' residence she was in robust health, very active and industrious, of good disposition, bright and apparently of quite average intelligence. She has an adenoid expression. She now generally has a single attack of *grand mal* about once a month and generally when getting up at 6 a.m. The fits nearly always occur during her menstrual periods.

From January 13th to 26th, 1907, daily observations were made on the coagulability of her blood and her blood-pressure. She had not had any fits for several weeks previously, and was taking no drugs. The rate of coagulation was slow, the mimimum average was 151 seconds, the maximum 185 seconds. She had an attack of *grand mal* during the night of the 14th–15th, and on the two previous days her blood coagulated more

quickly than on the two days following the fit, and the difference between the maximum and minimum the day before the fit was very slight (5 seconds). On the 21st the coagulation time was (for her) rapid (135 seconds), and during the night following she had another attack of *grand mal*. On the last day her blood coagulated more quickly than on any other previous occasion (120 seconds); this was not followed by a fit.

She remained free from fits, and on February 2nd was ordered drachm doses of citrate of soda t.d.s., and from

CHART 6.—A. M. L—.



February 13th to 17th her blood was again tested, with the result that no retardation in the coagulation was found, in fact, the average for these five days was slightly below the average of the first period, *viz.*, 141 seconds for the quickest samples, and 174 seconds for the slowest. This is the third case in which I have altogether failed to get any retardation of coagulation after giving a citrate. The following is the list of fits (*grand mal*) which she had whilst under observation:

January 13–14th	. . .	1 in the night.
,, 21–22nd	. . .	1 ,, ,, ,,
February 20th	. . .	2 ,, ,, day.

March 20th	2 early in the morning.
April 17th	3 (2 during the day and 1 after going to bed).

Blood-pressure normal and consistent. The highest recorded whilst not taking drugs was 129 mm. Hg., the lowest 102, average 117. As in the other cases there were no variations on the days following the two fits. Whilst taking the citrate of soda her pressure rose daily from 104 to 140.

Pulse was frequently irregular.

This was one of the few cases where there was no general quickening of coagulation, the average being the same as the average of the control cases. Nevertheless there was a decided quickening just prior to attacks of *grand mal*. I am inclined to suspect that one reason for this slowness may have been imperfectly oxygenated blood. The patient had some obstruction in her nasal passage, probably adenoids, and was a mouth-breather, and Sir A. E. Wright has established the fact that excess of carbonic oxide in the blood hinders coagulation. One must also take into consideration the rarity of her attacks —seldom more than one or two in a month.

This latter probably is the more important factor, for in another case recently examined, in which the fits were few, only six or seven in a month, generally during menstruation, the coagulation rate was slow, but was distinctly quicker during periods of fits than at intervening times.

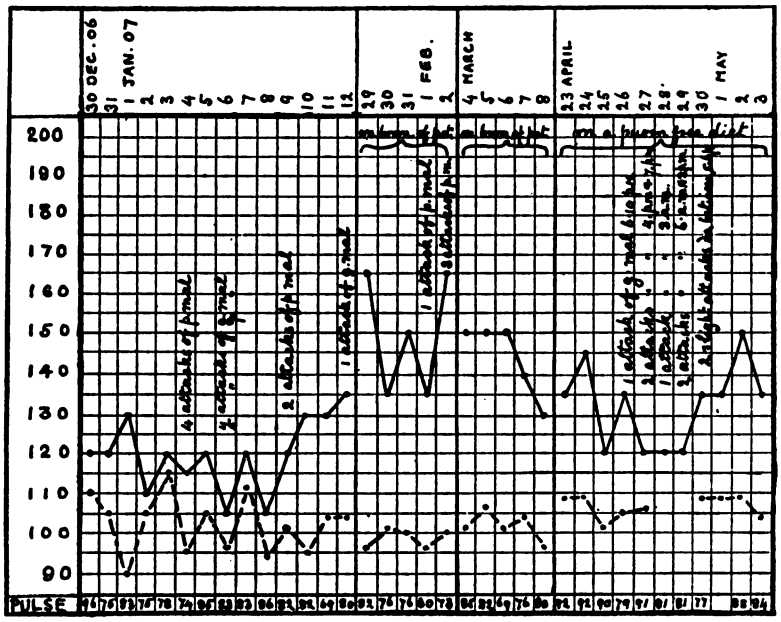
CASE 6.—A. C— was first admitted in 1884, when 20 years of age; a domestic servant; after a short maniacal attack became a useful, active woman, but with a violent temper. Probably of average intelligence for one of her class. Her fits were frequent, both *grand* and *petit mal*, and she was very bewildered after them. Discharged in July, 1889, re-admitted in May, 1890—maniacal. The following month had nearly a hundred fits in forty-eight hours. Remained irritable, passionate but industrious. Again discharged in August, 1891, and re-admitted in June, 1906. Since 1892 has been in the workhouse, her frequent fits preventing her from earning her living. Was melancholic, intelligent, and industrious, except after fits, which she generally has in batches, with frequent attacks of *petit mal*. She says that she feels more stupid and weaker after them than after the attacks of *grand mal*, and

the bad effects last longer. She has sometimes an aura, a feeling of giddiness with double vision, before her attacks. Bodily health fair. Neurotic palate.

On December 30th I began testing the coagulability of her blood and her blood-pressure. She was then in good health, and taking no drugs.

Her blood coagulated quickly, the minimum average for fourteen days being only 120 seconds, the maximum 160 seconds.

CHART 7.—A. C—.



There was a marked acceleration on January 6th (105 seconds) and during this day she had four attacks of *grand mal* and five of *petit mal*. Two days later her blood again coagulated at 105 seconds, but on this day she did not have any attack. For the five days preceding a period of fits, the coagulation time averaged 120 seconds, for the six days during fits it averaged 114 seconds, and for the three following days, during which period she had only one fit (on the last day), it averaged 131 seconds, showing an increased tendency to coagulate during the time of fits. On January 12th she was put on ½ drm. doses of bromide of potassium, t.d.s., and from that date until March 8th, when

it was stopped, she had no more attacks of *grand mal*, although her attacks of *petit mal* were just as frequent.

The bromide did not agree with her; it made her listless, drowsy, depressed and unable to do her work. From January 29th to February 2nd her blood was again tested, and there was found to be a marked retardation in its coagulability, the minimum average time for the five days being 150 seconds, the maximum (four occasions only) 199 seconds. A month later it still showed a considerable retardation, the minimum average for five days being 144 seconds, maximum 178 seconds. With the exception of two attacks of *petit mal*, March 14th to 15th, she remained free from fits until April 16th. On that and the two following days she had ten attacks of *grand mal*, and from 26th to 29th inclusive, five attacks. She had been put on a purin-free diet on April 6th. The minimum average coagulation time for a period of eleven days, April 23rd to May 3rd, was 132 seconds, somewhat slower than with ordinary diet, although the fits continued much as before. As usual a period of quickening in coagulation corresponded to a period when she was having fits, followed by a return to a slower rate; this is extremely well shown in the last section of her chart.

The drop is not so marked as in the first chart, from January 6th to 9th, when she was, however, having a greater number of fits (*grand* and *petit mal*).

The following is a list of her attacks whilst under observation from December 1st, 1906, to May 3rd, 1907:

December	4.	4 attacks of	*grand mal.*	
,,	7.	1 attack ,,	,,	
,,	8.	2 attacks ,,	,,	
January	4.	4 ,,	,, *petit mal.*	
,,	6.	5 ,,	,, ,,	
,,	7.	5 ,,	,, ,,	
,,	12.	1 attack ,,	*grand mal*	Bromide of potassium, ½ drm. t.d.s.
,,	13.	2 attacks ,,	*petit mal*	
,,	20.	1 attack ,,	,,	
,,	25.	1 ,, ,,	,,	
,,	26.	1 ,, ,,	,,	
,,	27.	3 attacks ,,	,,	
February	1.	1 attack ,,	,,	
,,	2.	3 attacks ,,	,,	

February	14.	1 attack	of *petit mal.*	Bromide of potassium, ½ drm., t.d.s.
,,	19.	1 ,,	,, ,,	
March	1.	2 attacks	,, ,,	
,,	14.	1 attack	,, ,,	
,,	15.	1 ,,	,, ,,	
April	16.	7 attacks	,, *grand mal.*	On a purin-free diet.
,,	17.	1 attack	,, ,,	
,,	18.	2 attacks	,, ,,	
,,	26.	1 attack	,, ,,	
,,	27.	2 attacks	,, ,,	
,,	28.	1 attack	,, ,,	
,,	29.	2 attacks	,, ,,	
,,	30.	2 ,,	,, (slight) ,,	

No further attacks.

Blood-pressure.—For the first period (taking no drugs) varied between 90 and 115, the average being 102 mm. Hg. Whilst on bromide it fell slightly, varying between 96 and 107, the average of 10 days being 100 mm. Hg. Whilst on a purin-free diet it averaged 106. The pressure curve was much more regular whilst taking bromide, and whilst on the special diet than it was during the first period.

Pulse.—Frequently irregular. For the first period it varied between 69 and 96, average 81. Whilst taking bromide it varied between 69 and 85, average 78. When on a purin-free diet it varied between 79 and 92, average 85.

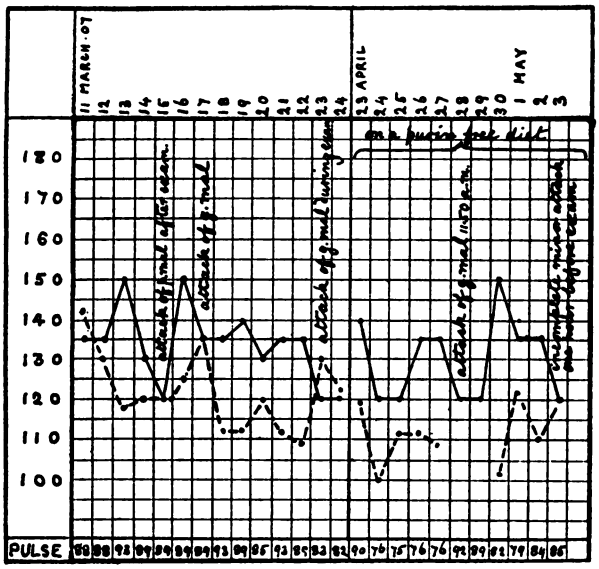
Case 7.—H. R. S— has been subject to fits since the age of twenty-three, and, according to her statement (which is borne out by our experience here), they occur chiefly in the day-time, are chiefly of the *grand mal* type, and she rarely has more than two in a day. She has intervals varying from a week to three or four months free from fits. She was in the fifth standard, was in one situation, at £12 a year, for five years, and after leaving that on account of her fits, assisted her sister—a dress-maker. She became melancholic and hypochondriacal and was sent here, where she soon developed into a valuable needle-woman of quite average intellect. She was querulous and spiteful immediately after fits for a short time. Bodily health fair, palate normal.

On March 11th, 1907, I began to test the coagulation rate and pressure of her blood. She was then 34 years old, and had

been taking no drugs. The minimum average time was 135 seconds, maximum 170 seconds.

On March 15th, about ten minutes after her blood was tested, she had an attack of *petit mal*. The coagulation time was rapid, 120 seconds, rising the next day to 150 seconds, but on the 17th, a few hours after an attack of *grand mal*, it again quickened—135 seconds. It kept at much the same level until the 23rd, when, whilst her blood was being tested, she had an attack of *grand mal*, and there was again found to be an

CHART 8.—H. R. S—.



acceleration in coagulation (120 seconds), which was maintained on the following day.

She was put on purin-free diet on April 6th, and continued to have fits much as usual.

The average rate of coagulation was quicker, minimum 130 seconds, maximum 166 seconds, than when on her ordinary diet. On April 28th, just before an attack of *grand mal*, it fell to its lowest limit and remained at the same level the following day, rising on the 30th to 150 seconds. On May 3rd, an hour before the observations were taken, she had an incomplete minor attack characterised by a "nasty" feeling and

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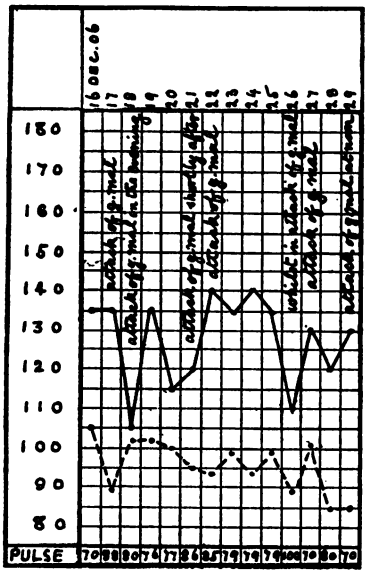
a fluttering at the heart; again there was found to be a quickening in coagulation—120 seconds.

Blood-pressure.—For the fourteen days on ordinary diet it varied between 109 and 144, averaging 122 mm.Hg. The curve was very irregular. During the nine occasions it was registered whilst on a purin-free diet it dropped considerably—its average being 110 mm. Hg. and the variations between 122 and 98.

Pulse.—Sometimes irregular. There was remarkably little

CHART 9.—J. P—.



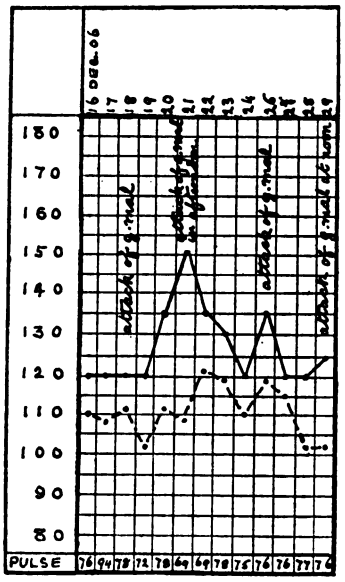
difference in the rate from day to day whilst on ordinary diet, the extreme variations being 82 and 93, the average 88. The daily rate varied more from 75 to 92 whilst on a purin-free diet, and the average was 82 for the eleven days.

CASE 8.—J. P—, æt. 47. Is now demented, the result of long continued epilepsy. Was formerly a weak-minded woman, but capable of being usefully employed. Her fits are of the *grand mal* variety, occur singly, and she has one nearly every day, sometimes missing two or three days. She is in fair health but thin; is taking no drugs.

The coagulation time of her blood is short, the minimum average for fourteen days being only 127 seconds. On December

18th, preceding an attack of *grand mal* at 8 p.m., the coagulation time fell to 105 seconds. On the 20th it was again low—115 seconds, and on the 21st 120 seconds, and about half an hour subsequently she had a fit. There was a considerable retardation in the coagulation for four days in spite of a fit on the 22nd. On the 26th she had a fit from which she had not completely recovered when her blood was tested; coagulation was rapid, occuring in 110 seconds. The next day there was some retardation although she had a fit at 5.20 p.m., and again on the 29th the coagulation remained at the same level although her blood was

CHART 10.—G. J. W—.



tested shortly before another fit. It will be noticed in her chart that the longest period without fits, *viz.*, from 9.30 a.m. on December 22nd to December 25th, coincides with the greatest retardation of coagulation.

Blood-pressure was low and somewhat variable. The highest recorded was 105 mm. Hg., the lowest 85, average 96.

Pulse was very irregular. It varied between 70 and 88 except on the 26th whilst in a fit, when it was 100.

CASE 9.—G. J. W— was a domestic servant, æt. 23, when admitted, and it was stated that she had only recently

developed epilepsy. Was in an acutely maniacal condition with short remissions for the first ten months after admission, having frequent attacks both of *grand* and *petit mal* (day and night), but the fits were usually worse at the menstrual periods. Subsequently her attacks of excitement got shorter and less frequent, and when free from fits she was an active, industrious, fairly intelligent woman. During periods of fits she generally had a marked trace of albumen in her urine, and developed a transient, bright red petechial eruption on face, chest, and sometimes on arms and legs.

Now her fits are of the *grand mal* type, occurring at intervals of a few days. She is thirty-four years of age, and is in good bodily health, an industrious woman, but irritable, and sometimes violent.

Her blood was examined on thirteen occasions from December 16th to 29th. The average rate of coagulation was quick, only 127 seconds; during this period she had four attacks of *grand mal*, but none, with the exception of the last, occurred immediately before or after the times of examination. Two of the attacks coincided with periods of quickened coagulation, two with periods of slower coagulation.

Blood-pressure somewhat low, the average being 110, and varying between 102 and 121.

Pulse irregular.

III.

These observations confirm my previous ones, and show that as compared with persons in good health the blood of epileptics coagulates in a shorter time, and also that this is more marked just before or during fits than when the patient is free from them. (5)

Against the supposition that this phenomenon is merely the *result* of fits is the fact that it frequently was found to occur, immediately or several hours, before the onset of one: *e.g.*, in Case 8 the shortest period of coagulation was on December 18th, eight hours before an attack of *grand mal*; again it was rapid on December 21st, half an hour before a fit (120 seconds). In Case 5 the blood from December 19th to 21st showed a progressive quickening in coagulation, which was succeeded by a fit in the night of December 21st. In Case 7, on March 16th,

the quickest coagulation time (120 seconds) occurred ten minutes before an attack of *petit mal*, and on April 28th, a quarter of an hour before an attack of *grand mal*, the same quick rate was recorded.

It must be borne in mind that the tendency to coagulate varies, not only from time to time, but in different parts of the body, so that although the blood from the finger about the time of a fit may not always coagulate with special rapidity, it by no means follows that elsewhere in the body the rate of coagulation is not quicker. This is shown in Case 4: on January 24th, during a fit, whilst the blood from her finger took 135 seconds, the blood from her ear took 90 seconds. Nevertheless, the observations show that in the majority of cases, although blood drawn from the finger at the time of a fit may not represent a sample of that which coagulates most rapidly, there is at these periods an increased tendency to coagulation throughout the whole hæmal system. On six occasions the patients had fits whilst being examined. In every case the rate was relatively quick, in four it was markedly so, in one, although quick, slightly slower than the day before, and the sixth is the case just referred to where blood from the ear was tested.

From my point of view it is not essential, in fact it is highly improbable, that in every case a specially quick rate should correspond to the time of a fit; the reverse of this condition is the more important—that a fit should coincide with a time of rapid coagulation. It does not follow that because the tendency is increased that, therefore, coagulation must occur; what immediately determines this phenomenen is outside the scope of this paper. In my opinion it is in this connection that we have a means of harmonising the thrombotic and the toxic theory of epilepsy, by attributing this idiosyncrasy of the blood to a toxin, which, when it reaches a certain intensity, excites local coagulation. An interesting point which these observations show is that, not only during or before attacks of *grand mal*, but also attacks of *petit mal*, the coagulation rate is quickened; this is shown in Case 3 and especially well in Case 7, where, on March 16th, the rate was 120 seconds—the shortest time recorded in her case—and almost immediately afterwards she had an attack of *petit mal*. On the 22nd the rate was quickened during an attack of *grand mal*, but no more than before the attack of *petit mal*. After the major fit, however,

there was a longer period of quickening; for the next day the rate remained the same.

Bromide of potassium has a retarding effect on coagulation. In all five of the cases tested in this connection this effect was noticed, and it would appear as though it was in those cases where it had the most marked effect in preventing fits that it retarded coagulation to the greatest extent (see Cases 2 and 3), whilst in the case where it had little effect on the fits there was much slighter retardation (Case 1). The two cases (Cases 2 and 6) show that its effect on the blood continues so long as the drug is being taken, but apparently is not manifested until the system is saturated.

Lauder Brunton ([6]) states that Albertoni found when bromide was given for several weeks together to dogs, the excitability of their motor centres was so diminished that it was almost impossible to produce epileptic convulsions by irritation of the cortical substance. Thus it would appear as if bromide acts on both the nervous and vascular systems, not only lowering the excitability of the nerve-cells, and raising their threshold of stimulation, but also retarding the tendency of the blood to coagulate; and from my point of view that the immediate cause of fits is local cortical stasis of thrombotic origin, we should have in this twofold action the explanation of the very beneficial effects of the salt, in diminishing or stopping epileptic fits.

After the administration of citric acid Wright and Paramore found that within a week, and for a further month, coagulation was retarded and then returned to its former level. Although the blood of the three cases to which I administered a citrate was tested within the specified limits, it did not show any retardation in coagulation in a single case, in fact in two (who were however at the time having fits) there was acceleration.

The purin-free diet appeared to have a very slight effect; in one (Case 6) there was some retardation, and it did not in any of the three cases appear to diminish the number of fits. Of course I am only speaking as to its effects on these three cases, and during this somewhat limited period. Both the number of cases and the time under observation were much too limited to arrive at any general conclusion. W. Aldren Turner ([7]), who instituted a series of observations at the Chalfont Colony, with a view to testing the efficacy of this form of diet in confirmed

epilepsy, found that with it there was a lessening in the severity and frequency of the convulsive seizures, more especially when these occurred in series, but that it had no effect on the minor seizures.

My results, it will be seen, are diametrically opposed to the views of Silvestri (*Gazz. degli. Osped.*, January, 1907), who holds that epilepsy is due to a diminished percentage of calcium salts in the blood, and who quotes some researches of Besta to the effect that in thirty-seven out of forty-five epileptics the blood serum showed a coagulation power inferior to the normal.

Blood-pressure.—There is, according to different observers, a very considerable latitude in the range of what constitutes a normal blood-pressure. In my opinion a systolic pressure varying between 110 and 130 mm. Hg. represents very fairly the normal limits. At any rate, although a lower one may be compatible with health, I should regard as suspicious one over 130 mm. Hg., that is to say if it was at all persistent, but an occasional rise of over 130 mm. is very common in persons with an average low tension. According to this standard two of my control cases and one of my epileptics had high pressures, five controls and four epileptics a normal, and four epileptics a low pressure. As epilepsy is so prevalent in imbeciles, and as one of the commonest stigmata of degeneration is a small, ill-developed heart, these results, among that class, are what might have been anticipated. Except that I found in general an extremely irregular curve, not more so, however, than is very commonly the case in insanity in general, and that it was not modified by the number of fits, my results do not coincide with those recently obtained by C. Besta (8), who found the pressure to be raised in 63 *per cent.* of the epileptics he examined.

What relationship is there between the coagulation rate and the blood-pressure? It would naturally be expected that a low pressure would favour rapidity of coagulation and *vice versâ*, and broadly speaking, this was found to be the case.

Thus in the seven controls in which the pressure was considerably higher than in the epileptics (with one exception), the coagulation rate was considerably slower. In the one epileptic with high pressure coagulation was slow. But there were many exceptions to the general rule: *e.g.*, among the controls the degree of retardation was not in proportion to the height of blood-pressure, and the case in which coagulation was quickest

had the highest but one blood-pressure, and that in which coagulation was slowest had a relatively low blood-pressure. So with the epileptics, although, as I have just mentioned, the one with the slowest average rate had the highest blood-pressure, the one with the next to slowest average had a pressure only of 117 mm. Hg. Although the epileptic whose blood coagulated in the shortest time (Case 2) had a low pressure, when she was under the influence of bromide her coagulation rate was more retarded than in any other case, without any corresponding rise of blood-pressure. Again, in Case 6, whilst taking bromide the pressure dropped slightly, whilst there was at the same time a marked retardation of coagulation.

Of the five cases to which bromide was administered the blood-pressure fell in three, in two very slightly, in the third considerably (Case 3); in one it rose very slightly. In the fifth the observations were not made at a sufficient time interval from taking the drug to allow of any conclusion being formed. In two cases the curve of pressure was much more regular whilst taking the drug.

In the three cases which were examined whilst on a purin-free diet, there was a slight rise of pressure in two, a fall in one.

Pulse in some cases was slightly quickened during or immediately after a fit, in others not modified at all. It was extremely common to get an irregularity in the rhythm, a phenomenon observed at some time or other in all the cases.

The general result of both my series of observations on the coagulability of the blood in epileptics has convinced me that there is a close relationship between rapidity of coagulation and the occurrence of epileptic attacks—a relationship, I believe, of cause and effect—hence a search for a drug which will permanently retard coagulation without having such powerful and deleterious effects on the nervous system as bromide, seems well worth pursuing. I believe that with such a drug at our service we should have a valuable means towards controlling the fits and ameliorating the general condition of many epileptics.

(1) *Journal of Mental Science*, January, 1907.—(2) *Lancet*, October 14th, 1905.—(3) *The Morphology of Normal and Pathological Blood*, London, 1906.—(4) *Lancet*, October 14th, 1905.—(5) Speaking generally, the greater the frequency of fits in a case, the quicker is the average coagulation rate.—(6) *Text-book of Pharmacology*, London, 1885.—(7) *Epilepsy*, London, 1907.—(8) *Riv. Speriment di Freniat*, vol. xxxii; abstract in *Journal of Mental Science*, April, 1907.