

ALLERGY AS A FACTOR IN IDIOPATHIC EPILEPSY

- by -

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INTRODUCTION.

The following series of investigations was started as a result of certain clinical observations.

Case 1 - A boy of sixteen years of age was admitted to Goodmayes in October 1931. He was suffering from Epilepsy, the fits having begun at the age of eleven. On admission he was acutely maniacal, wandering about in a wild and dishevelled state and no sensible replies could be obtained from him. He continued during his stay in Hospital to have frequent major epileptic fits and he was often very noisy and very excited. His memory for recent and remote events was very poor and he was frequently very confused after a bout of fits.

On April 4th 1933 he developed an acute lobar pneumonia. His temperature did not fall by crisis but continued to rise every evening and became of the typical hectic type. He had extensive consolidation of both lungs and tubercle bacilli were present in his sputum.

He became gradually weaker and died on June 3rd.

During the month preceding the onset of his febrile illness he had 162 major epileptic fits. After the commencement of that illness he had no more fits. He became quite lucid, was able to converse quite rationally, his confusion disappeared completely and his memory improved remarkably.

When protein skin tests were carried out on May 25th a positive reaction was obtained to Group 20 (Bacteria).

After that date no positive results were obtained.

This case raises certain questions of absorbing interest. If we accept the hypothesis that epileptic fits are produced by some toxic substance in the blood and body tissues of the individual it would appear that as the result of an acute infection this substance is neutralised or eliminated. What the precise nature of this fit-producing substance is still remains to be determined.

There is a good deal of experimental evidence to support the theory that the convulsions are due to the presence in the blood of some fit-producing substance.

Cuneo, Antheaume and Trepsat claim to have produced convulsions in animals by injecting them with blood from an epileptic patient.

Boston and Henry claim to have produced fits in a non-epileptic individual by injecting him with the blood of a patient suffering from epilepsy.

Pagniez, Mouzon and Turpin produced convulsions in animals by transfusion of blood from epileptic patients at the time of seizure while no convulsions occurred when the blood of healthy persons was used.

The following case, too, demonstrates the beneficial effect which an acute infection may have on the number of seizures and on the patient's mental state.

Case 2 - This patient was admitted on February

6th 1905 at the age of fifteen. He had his first fit at the age of thirteen, had become gradually worse and was admitted to Goodmayes because he had become very violent and threatening.

There was no history of convulsions in infancy, no history of epilepsy or mental disorder in the family, and he was a normal healthy boy and a good scholar till the onset of his fits.

He had measles at the age of six.

He continued for many years to have fairly frequent bouts of fits during which he became very confused and very aggressive.

In March 1931 he had a fairly severe attack of Influenza after which he remained free from fits until September 27th 1932 when he had one fit. A further period of freedom followed until February 2nd 1934. On that date he had one fit. He has had no fits since. His mental condition has shown a very striking improvement. He is very well behaved, is no longer quarrelsome and is a very good worker.

When protein skin tests were performed on May 19th 1933 he gave a positive reaction to Group 20 (Bacteria). Since that date all tests have been consistently negative.

As he has had no more fits since February 2nd 1934 no special treatment was considered necessary.

It was decided to perform protein skin tests on all cases of idiopathic epilepsy. Twenty-five male patients were tested. The cases were unselected except that cases of congenital mental defect with epilepsy were excluded and also cases with a definite traumatic history.

All drug treatment was discontinued for a period of at least six months previous to testing.

In addition, twenty-five non-epileptic controls were tested in the same way.

METHOD OF TESTING.

The skin of the back was cleansed with methylated spirit and a very small quantity of the selected protein extract was applied by means of a fine scalpel with a slightly upturned point. Three scarifications were then made through the droplet, care being taken to avoid the drawing of blood. The protein extract was then pressed into the scarifications. The scalpel was carefully cleansed before being used for a second test.

In this series of tests Parke Davis & Company's Protein Extracts were used. These are supplied in collapsible tubes and the proteins are in the form of a paste having a glycerine base to which a

suitable preservative has been added.

A paste consisting of the glycerine base only was used as a control.

These extracts were found to be thoroughly satisfactory and very convenient to use.

In the first instance, the Group Proteins were used, that is, a mixture of allied proteins. If a positive result was obtained with a Group Protein the individual proteins in the Group were then used.

For example, when a positive result was obtained with Group 5, each protein in this group was then tested out separately (Chicken, Duck, Goose, Turkey, Squab and Guinea-hen). By using the Group Proteins much time can be saved as each Group usually contains five or six different proteins.

The proteins used were as follows :-

GROUP PROTEIN EXTRACTS

(Parke, Davis & Co.)

- Group 1. Beef, Lamb, Pork, Veal, Mutton.
- Group 2. Cows' Milk (all proteins), Cheese, Human Milk, Egg (all proteins).
- Group 5. Chicken, Duck, Goose, Turkey, Squab, Guinea-hen.
- Group 6. Clam, Crab, Lobster, Oyster, Scallop, Shrimp.
- Group 7. Egg plant, White potato, Sweet potato, Sweet Peppers, Tomato.

- Group 8. Lima Bean, Navy Bean, Kidney Bean, String Bean, Peas, Lentil.
- Group 9. Asparagus, Beet, Garlic, Onion, Spinach.
- Group 10. Cabbage, Cauliflower, Radish, Turnip, Rutabaga.
- Group 11. Pumpkin, Squash, Cucumber, Cantaloup, Water-melon.
- Group 12. Chestnut, Peanut, Brazil Nut, Filbert, Hazel Nut, Almond.
- Group 13. Black Walnut, Pecan, English Walnut, Hickory Nut, Butternut.
- Group 14. Artichoke, Chicory, Lettuce, Rhubarb, Buckwheat.
- Group 15. Rice, Oatmeal, Barley, Corn (Maize) Rye, Wheat.
- Group 16. Apple, Pear, Blackberry, Raspberry, Strawberry, Fig.
- Group 17. Peach, Cherry, Apricot, Plum, Prune.
- Group 18. Orange, Lemon, Grapefruit, Banana, Grape, Pineapple.
- Group 19. Coffee, Tea, Cocoa.
- Group 20. B. Coli, Gonococcus, Staph. aureus, Staph. albus, Staph. citreus.
- Group 21. Friedlander bacillus, M. catarrhalis, M. tetragenus, Pseudo-diphtheria bacillus.
- Group 22. Pneumococcus I, II, III, Streptococcus (haemolyticus), Strepto. (non-haemolyticus).
- Group 23. Typhoid, Paratyphosus A. & B.
- Group 24. Hair of Cattle, Hair of Cat, Hair of Dog, Hair of Horse.
- Group 25. Hair of Goat, Hair of Rabbit, Hair of Guinea-pig, Wool of Sheep.
- Group 26. Feathers of Chicken, Feathers of Duck, Feathers of Goose.
- Group 27. Ginger, Mustard, Pepper (black) Pepper (red) Paprika, Sage.

- Group 28. Gramineae, (Timothy, Johnson, Orchard, Bermuda and Red Top Grasses).
- Group 29. Chenopodiaceae and related Families (Russian Thistle, White Goose-foot, Yellow Dock, Western Waterhemp, Halberd-leaved Orache).
- Group 30. Ambrosiaceae (Common Ragweed, Giant Ragweed, Western Ragweed, Rough Marsh Elder, Burweed, Marsh Elder, Cocklebur).
- Group 31. Artemisias (Wormwood Sage, Mugwort, Prairie Sage, Sagebrush, Indian Hair Tonic).
- Group 33. Carrot, Celery, Parsley, Parsnip.

Positive reactions usually appeared within ten minutes and lasted half-an-hour or longer. A positive reaction is characterised by a pale swelling at the point of inoculation surrounded by a zone of erythema which lasts for at least ten minutes.

The back was chosen as the skin in this area is less sensitive than on the flexor aspect of the forearm and false positive reactions are less frequently obtained. In addition, a much larger number of tests can be carried out at one sitting.

Accurate records were kept of all tests carried out, noting the time of appearance of the positive reaction and the time of its fading.

In addition to the above a series of extracts was prepared from Cooked proteins in the laboratory at Goodmayes. In preparing these extracts care was taken to imitate as far as possible the normal methods of cooking.

With the cooked protein extracts no positive reactions were obtained in cases where a negative result was given with the raw protein. In one or two instances negative results were obtained with the cooked proteins where a positive result had previously been given with the corresponding raw protein.

On going through the literature I have been unable to find any record of the previous use of cooked proteins, though, as proteins are undoubtedly

changed considerably in the process of cooking it seems only reasonable to make use of cooked as well as uncooked proteins in testing.

RESULTS OF SKIN TESTS.

Of twenty five patients tested nine or 36% gave positive results.

Of these, three or 12% were cases of multi-sensitivity. Six patients or 24% reacted to one protein only and of the six three reacted to Peptone alone.

The patients were tested once weekly for ten weeks. Slight variations occurred. Occasionally positive reactions were obtained to proteins which had previously produced a negative result. On studying the fit chart it was usually found that this state of affairs occurred just before the onset of a fit or a series of fits. On the other hand, negative results were occasionally given to proteins which had previously given a positive reaction. On examining the fit chart it was found that this state of affairs occurred just after a fit or a bout of fits.

Sensitiveness, as indicated by positive skin tests, appears to be increased before the onset of a fit and to be diminished for a variable period following a fit.

CONTROLS.

Twenty five non-epileptic controls were tested in the same way.

Of these, one or 4% gave a positive reaction to the protein of Brazil Nut.

On enquiry, no history of any unpleasant symptoms brought on by eating Brazil Nuts could be obtained.

Feeding experiments have not yet been carried out.

TABLE I.

showing the Results of Protein Skin Tests.

Percentage of Positives	Percentage reacting to one protein only	Percentage showing multi-sensitivity
36	24	12

TABLE II.

showing Analysis of Positive Reactions.

Case 1.	Group 20 (Bacteria).
2.	Group 20 (Bacteria).
3.	Cocoa, Coffee, Tea, Lobster, Hair of Cattle.
4.	Goose, Squab, Peptone.
5.	Peptone.
6.	Peptone.
7.	Goose, Peptone.
8.	Peptone.
9.	Group 28 (Pollens).

FALSE POSITIVE REACTIONS.

On one occasion, when performing skin tests on a patient's fore arm, a vivid positive reaction was obtained with each protein used. With the control, too, a well-marked positive was obtained. It was thought that the patient might be hypersensitive to the glycerine of the control substance. When tested with pure glycerine he again gave a vivid positive with the typical pale swelling and zone of erythema which lasted for more than half-an-hour. On testing with distilled water and also when scarification alone was carried out, the same took place.

When the tests were done on the patient's back no definite positive was obtained.

From then onwards the back was used in preference to the fore arm.

WASSERMANN REACTIONS.

In all cases the Wassermann Reactions of the blood and cerebro-spinal fluid were negative.

TABLE VI.

Age Average of Patients Tested.	Age Average of those giving Positive Reactions.	Average duration of Epilepsy among Positive Reactors.
42.2	35.3	23.0

THE NATURE OF SKIN REACTIONS.

According to Bray, skin reactions are nerve reflexes brought about by the local formation of a substance closely resembling histamine. The skin of allergic individuals is not more sensitive to ordinary irritants or the process of testing than that of normal individuals.

The reaction-producing substance is contained in the whole protein or its early breakdown products and is destroyed by katabolic or digestive processes, for when reactions are given to whole proteins their corresponding amino-acids do not give a reaction.

The selectivity of hypersensitiveness depends largely on the degree of protein contact and is generally a factor of diet or environment. Peshkin found that 49% of asthmatic Jewish children gave positive reactions to rabbit hair on which they slept. Balyeat working in Oklahoma, found that only 2% were sensitive to rabbit hair but 43% were sensitive to feathers, the type of bedding in use there.

PEPTONE.

It was decided to treat the patients reacting to Peptone by the method of specific desensitisation. They were given Peptone by the mouth in one grain capsules thrice daily for seven days.

The results obtained with Peptone treatment were quite encouraging. All improved mentally except one, but the effect on the number of fits was not so good as in the case of those patients treated with Pyrifer.

Much research work has yet to be done in order to determine the best method of giving Peptone and the most suitable dosage.

Case	Seizure reduction	Definite improvement	Treatment
Case 1	Increased number	No mental improvement	Peptone
Case 2	No reduction in number	Definite improvement	Peptone
Case 3	Reduced by 50%	Definite improvement	Peptone

TABLE V.

Results of Treatment.

	Fits	Mentally	Treatment
Case 3	Reduced by 38%.	Very striking improvement.	Pyrififer
Case 4	Reduced by 50%.	Definite improvement.	Pyrififer
Case 7	No reduction.	Definite improvement.	Pyrififer
Case 5	Increased in number.	No mental improvement.	Peptone
Case 6	No reduction in number.	Definite improvement.	Peptone
Case 8	Reduced by 30%.	Definite improvement.	Peptone

This patient was admitted to ... on March 19th 1938 at the age of 20. He had his first major epileptic fit at the age of 12 years and 8 months. He never had been ... fit. He was a bright and intelligent boy ... five years he left school. The fits became gradually ...

He is the only child. The labour was normal and he was bottle fed from birth. He had no convulsions in infancy. He had diphtheria when five and a half years of age for which tracheotomy had to be performed. This was followed by ...

CASE HISTORIES.

He was treated at various neurological ... in London and ...

... of ...

The patient's ...

CASE HISTORIES.

Case 3 - This patient was admitted to Goodmayes on March 16th 1932 at the age of 24. He had his first major epileptic fit at the age of 12 years and 8 months. He never went back to school after his first fit. He was a bright and intelligent boy and was in Standard Five when he left school. The fits became gradually more frequent and he became more obstinate and difficult.

He is an only child. The labour was normal and he was bottle fed from birth. He had no convulsions in infancy. He had Diphtheria when five and a half years of age for which Tracheotomy had to be performed. This was followed by Scarlet Fever. He had Tonsils and Adenoids removed at the age of seven.

He was treated at various Neurological Hospitals in London but became gradually worse and had to be certified as he became very violent and used to attack his parents.

There was no history of allergic disease in the case of the patient and no family history of Epilepsy or Insanity.

The patient's mother used to suffer from severe sick headaches and his paternal Grandfather suffered from Asthma. On admission to Hospital he was very confused, had little idea of time and still believed he was in Whipps Cross Hospital. His speech was very rambling and at times quite irrelevant.

Protein skin tests were performed weekly for a period of ten weeks. Positive reactions were obtained with Groups 6, 19 and 24. These Groups contain the following individual proteins :-

Group 6 - Clam, Oyster, Shrimp, Scallop, Lobster, and Crab.

Group 19 - Coffee, Tea, Cocoa.

Group 24 - Hair of Cattle, Hair of Cat, Hair of Dog, Hair of Horse.

He gave constant positive reactions to Lobster, Coffee, Tea, Cocoa and Hair of Cattle.

Occasionally additional positives were obtained but these were only seen just before the onset of fits.

It was decided to treat him by the avoidance or withdrawal method. That is, Tea, Coffee, Cocoa, and Lobster were completely excluded from his diet. He was given no opportunity of coming in contact with cattle. In addition to the withdrawal of the offending proteins it was decided to use some form of non-specific desensitisation. For this purpose, Pyrifer was used and the method adopted in giving it was that usually employed in the treatment of General Paralysis.

The vaccine is put up in 1 c.c. ampoules containing increasing numbers of the bacilli. Eight intravenous injections were given on alternate days. It is advisable to begin with half a c.c. as a precaution.

NOTES ON TREATMENT.

19th May 1934. Injected with .5 c.c. Pyrifer No.1 intravenously at 9.30 a.m. Maximum temperature 103.4° F. at 12 midnight. Pulse 84. Respirations 20. He perspired freely as his temperature went up. Temperature returned to normal at 10 a.m.

21st May 1934. Injected with 1 c.c. Pyrifer No.2 intravenously at 9.50 a.m. Maximum temperature 103.2° F. at 11.30 p.m. Pulse 90. Respirations 24. Temperature returned to normal by 9 a.m.

23rd May 1934. Injected with 1 c.c. Pyrifer No. 3 intravenously at 9.50 a.m. At 11 a.m. he had a rigor. Maximum temperature 104.2° F. at 2 p.m. Pulse 104. Respirations 24. When his temperature was at its height he became very pale. Temperature returned to normal by 2 a.m.

25th May 1934. Injected with 1 c.c. Pyrifer No. 4 intravenously at 9.45 a.m. He had a rigor at 11.45 a.m. Maximum temperature 103.2° F. at 2.45 p.m. Pulse 98. Respirations 24. His temperature was normal by 2 a.m.

27th May 1934. Injection omitted. (Visiting day.).

29th May 1934. Injected with 1 c.c. Pyrifer No.5 intravenously at 9.45 a.m. He had a strong rigor at 10.45 a.m. Maximum temperature 102.6° F.

at 1.15 p.m. Pulse 116. Respirations 24. His temperature was normal by 6 a.m.

31st May 1934. Injected with 1 c.c. Pyrifer No.5 intravenously at 9.55 a.m. Rigor at 10.30 a.m. Maximum temperature 103.6° F. at 12.45 p.m. Pulse 108. Respirations 24. One major fit at 11.15 p.m. His temperature was normal by 7.45 p.m. He had one major fit at 11.15 a.m. (1st June 1934).

2nd June 1934. He had a major fit at 7.30 a.m. Injected with 1 c.c. Pyrifer No.6 intravenously at 9.30 a.m. Rigor at 10.30. Maximum temperature 103.4° F. at 2.30 p.m. Pulse 120. Respirations 24. He had major fits at 5.15, 6.45 and 11.15 p.m. also at 2 a.m. (3rd June 1934). His temperature was normal by 10 p.m.

4th June 1934. Injected with 1 c.c. Pyrifer No. 6 intravenously at 9.45 a.m. Rigor at 10.45. Maximum temperature 103.2° F. at 12.15 p.m. Pulse 120. Respirations 22. His temperature was normal by 7.15. p.m.

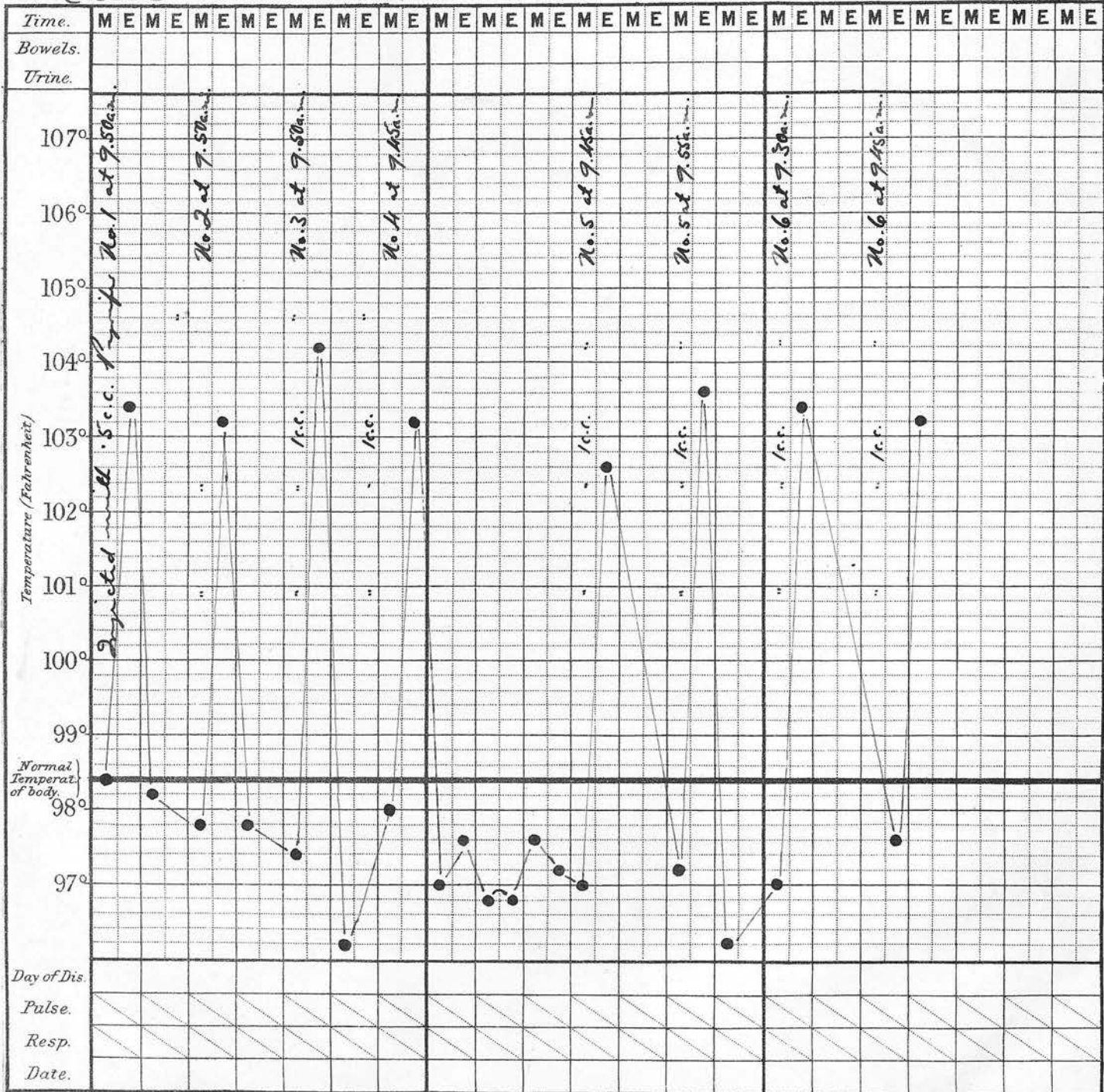
This completed his course of eight injections.

13th June 1934. He is a little brighter mentally and takes more interest in his surroundings. He does a good deal of reading and can now remember what he reads and answers questions fairly rationally. He addresses various members of the Staff by name.

The average monthly number of fits has been reduced by 38%.

COPY OF TEMPERATURE CHART.

Case 3.



Case 4 - This man was admitted to Goodmayes on June 13th 1914 and was then twenty seven years of age. He had his first fit at the age of twenty.

He had measles in infancy.

There was no family history of Epilepsy, Insanity or Alcoholism. His mother suffered from Asthma.

On admission he was well nourished, his heart and lungs were normal and he had no evidence of organic disease.

His memory was very poor, he had little idea of time believing he had been in Goodmayes for five years and was often very confused.

Skin tests were carried out at weekly intervals.

Positive reactions were given to Group 5 and to Peptone. Group 5 contains the following :- Chicken, Duck, Goose, Turkey, Squab and Guinea-hen.

He gave positive reactions to Goose and Squab.

TREATMENT.

Goose and Squab were accordingly completely excluded from the patient's diet. In addition it was decided to attempt non-specific desensitisation by means of Pyrifer.

16th June 1934. Injected with $\frac{1}{2}$ c.c. Pyrifer No. 1 intravenously at 9.20 a.m. Maximum temperature 103° F. at 10 p.m. Pulse 100. Respirations 24. His temperature reached normal at 4 a.m. On waking

he complained of slight headache.

18th June 1934. Injected with 1 c.c. Pyrifer No. 2 intravenously at 9.35 a.m. Maximum temperature 103° F. at 11 p.m. Pulse 108. Respirations 28. Perspiring freely. He had a slight rigor at 10.30 a.m. His temperature returned to normal at 5 a.m.

20th June 1934. Injected with 1 c.c. Pyrifer No. 3 intravenously at 9.30 a.m. Maximum temperature 102.6° F. at 2 p.m. Pulse 116. Respirations 24. He had a strong rigor at 11 a.m. At 2 a.m. he had a major epileptic fit. His temperature had reached normal by 8 a.m.

22nd June 1934. Injected with 1 c.c. Pyrifer No. 4 intravenously at 9.30 a.m. Maximum temperature 102.8° F. at 2.30 p.m. Pulse 100. Respirations 20. His temperature had returned to normal by 6 a.m.

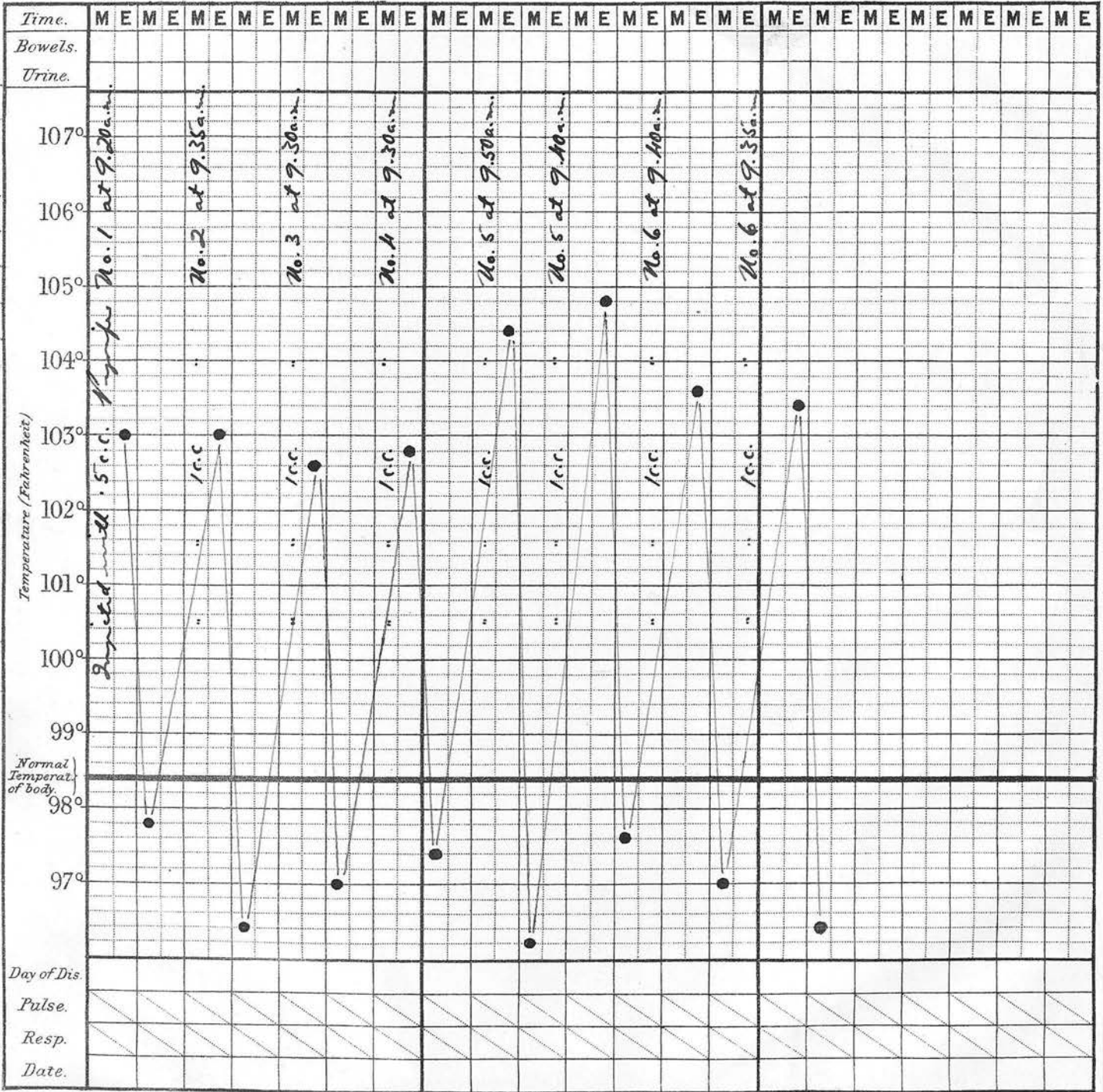
24th June 1934. Injected with 1 c.c. Pyrifer No. 5 intravenously at 9.50 a.m. Maximum temperature 104.4° F. at 3 p.m. Pulse 132. Respirations 36. He had a major epileptic fit at 3 a.m. His temperature had returned to normal by 5 a.m.

26th June 1934. Injected with 1 c.c. Pyrifer No. 5 intravenously at 9.40 a.m. Maximum temperature 104.8° F. at 2 p.m. Pulse 140. Respirations 28. He had a major epileptic fit at 12.5 a.m. His temperature had reached normal by 6 a.m.

28th June 1934. Injected with 1 c.c. Pyrifer

COPY OF TEMPERATURE CHART.

Case A.



Case 5 - This man was admitted on 30th December 1930. He was then twenty-four years of age. His fits began at the age of ten and there was no history of infantile convulsions. He had measles at the age of seven.

On admission he was acutely maniacal, rolling about on the floor and shouting incoherently. No sensible replies could be obtained from him.

Protein skin tests were carried out weekly. A positive reaction was given to Peptone only.

It was decided to attempt specific desensitisation by the oral administration of Peptone. Parke Davis & Company's Medicinal Peptone was given three times daily after food in one grain capsules for a period of one week.

No improvement in the number of seizures resulted. On the contrary the average number of fits rose from 17 per month to 21 per month.

There was no noticeable mental improvement in this case.

Case 6 - This man was admitted on January 28th 1931, when twenty-three years of age. He had his first fit during an Air Raid in 1915 when seven years of age. He was treated at various Hospitals but became gradually worse. He had to be certified as he became very confused and at times very violent.

He was breast fed till twelve months old. He had measles at the age of three, whooping cough when three and a half and Scarlet Fever at five.

A brother died in a fit at the age of Nineteen. He too had his first fit at the age of seven.

Skin testing was performed at weekly intervals over a period of ten weeks.

Positive reaction to Peptone was obtained.

Specific desensitisation was attempted by giving 1 gr. of Parke Davis & Company's Medicinal Peptone thrice daily after meals for a period of one week.

The average monthly number of fits showed no appreciable diminution.

There was definite mental improvement. He was not nearly so confused, was much less quarrelsome and was able to take a much livelier interest in his surroundings.

Case 7 - This patient was admitted to Goodmayes on May 28th 1929. He was then thirty-seven years of age. He had his first major fit at the age of twenty four. He attended various Hospitals in London but became gradually worse and had to be certified because he became very confused and developed delusions of persecution.

There was no history of convulsions in infancy. He was breast fed till eighteen months old.

His maternal grandmother died in a mental hospital as did her mother. Two uncles were insane.

Protein skin tests were performed weekly for ten weeks. He gave positive reactions to Group 5 and to Peptone.

On testing with the individual members of Group 5 a positive result was obtained with Goose protein.

TREATMENT.

The treatment adopted was the exclusion of Goose from the patient's diet. In addition non-specific desensitisation by means of Pyrifer was attempted. Eight intravenous injections were given on alternate days beginning with $\frac{1}{2}$ a c.c. of Pyrifer No. 1.

On one occasion skin tests were performed on the afternoon of one of the days on which he received an injection of Pyrifer.

All tests were negative on that day.

When tested a week later he again gave a positive reaction to Group 5, to Goose and to Peptone, but in addition he reacted positively to Shrimp and Squab. Two days later a bout of fits began.

On the 9th August he reacted to Goose and Peptone only. He had a fit just before the tests were carried out.

These observations suggest that sensitiveness is increased just before the onset of fits and diminished immediately afterwards. A few hours after giving Pyrifer it had disappeared completely.

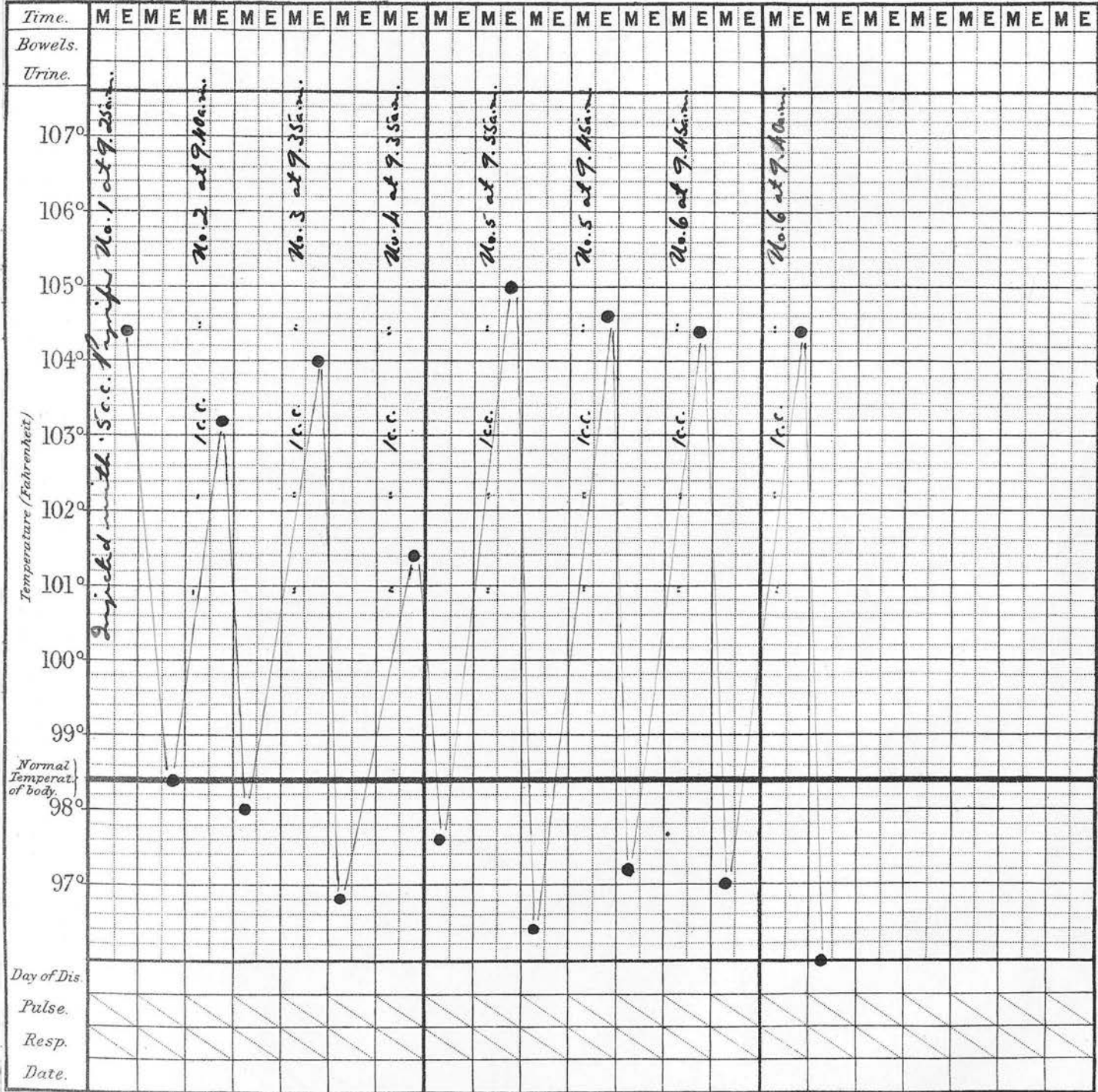
16th June 1934. Injected with .5 c.c. Pyrifer No. 1 at 9.25 a.m. Rigor at 1 p.m. Maximum temperature 104.4° F. at 9.30 p.m. Pulse 110. Respirations 24 (sweating profusely). His temperature fell to 99° F. next morning, then rose again to 100.4° F. at 4 p.m. reaching normal by 6 p.m.

18th June 1934. Injected with 1 c.c. Pyrifer No. 2 at 9.40 a.m. Strong rigor at 10.30 a.m. Maximum temperature 103.2° F. at 7 p.m. Pulse 120. Respirations 28 (perspiring freely). His temperature was normal by 4.30 a.m.

20th June 1934. Injected with 1 c.c. Pyrifer No. 3 at 9.35 a.m. Strong rigor at 11 a.m. Maximum temperature 104° F. at 5.30 p.m. Pulse 118. Respirations 24. His temperature was normal by 8 a.m.

COPY OF TEMPERATURE CHART.

Case 7.



Case 8 - This patient was admitted on December 18th 1925 when fifty-one years of age.

On admission he was very depressed and very confused. He had no idea of time or place and no sensible replies could be obtained from him. He had no evidence of organic disease.

Fits began at the age of three months and used to come on in bouts about once every month. Sometimes he had an aura which took the form of twitching of the left eye. He had measles in childhood. There was no history of Asthma or other allergic condition in the patient or in his family.

Protein skin tests were performed once a week for a period of ten weeks.

Positive results were obtained fairly consistently with Peptone.

TREATMENT.

He was given Peptone by the mouth in 1 gr. capsules thrice daily for a week.

After treatment the average number of fits occurring per month was reduced by 30%.

In addition there was distinct mental improvement. He was much less confused and less quarrelsome and he reported that he felt very much better.

Case 9 - This patient was admitted to Goodmayes on July 30th 1932. He was suffering from Epilepsy, the convulsions having begun at the age of fourteen. He was twenty-five years of age on admission. He had been treated in various Hospitals and had become steadily worse.

On admission he was extremely restless and confused and was constantly getting out of bed and wandering about.

He was the twelfth of a family of thirteen. He was breast fed until he was a year old and had no convulsions in infancy. He was always an irritable child and had a very large appetite.

When five years old he had Scarlet Fever and a few months later he had Chicken-Pox followed by Eczema. He frequently suffered from severe headaches and from nasal Catarrh. He was a particularly good scholar.

His mother's sister died of Asthma and his paternal Aunt died of Epilepsy in a mental Hospital.

On examination the nasal mucosa was found to be pale, swollen and oedematous. There was no other evidence of organic disease.

Protein skin tests were performed and a positive reaction was given by Group 28 (Grasses) on more than one occasion.

The patient was having a large number of fits at this time and was becoming gradually weaker and he developed a fatal broncho-pneumonia before skin testing could be completed.

This case is of particular interest, for, if allergy is a cause of Epilepsy it suggests the possibility of an inhaled allergen being responsible.

TABLE III.

shewing Age of Onset, Duration of Epilepsy, etc.

Case	Age	Age at Onset	Duration of Epilepsy	Type of Feeding	Convulsions in Infancy
1	18	11	7 years	Breast	No
2	44	13	31 years	Bottle	No
3	26	12	14 years	Bottle	No
4	47	20	27 years	Bottle	No
5	30	10	20 years	Bottle	No
6	26	7	19 years	Breast	No
7	41	24	17 years	Breast	No
8	60	3 months	60 years	Bottle	Yes
9	26	14	12 years	Breast	No

TABLE IV.

Case	Previous Infections	Family History of		Other Allergies in		W.R.of Blood and C.S.F.
		Insanity	Epilepsy	Patient	Family	
1	Measles in Infancy		Father Epileptic			Neg.
2	Measles at 6 years					Neg.
3	Diphtheria at 5½. Scarlet at 6.				Mother Migraine Gd.Father Asthma	Neg.
4	Measles in Infancy				Mother Asthma	Neg.
5	Measles at 7 years					Neg.
6	Measles at 3 years Whooping Cough at 3½		Brother Epileptic			Neg.
7	Nil	(M.Gd. Mother (M.Gt.G. Mother (2 Uncles				Neg.
8	Measles in Infancy					Neg.
9	Scarlet at 5 years. Chicken-pox 5½.		P.Aunt Epilepsy	Headaches and Eczema	Aunt Asthmatic	Neg.

RESULTS OF OTHER INVESTIGATORS.

On consulting the literature on this subject it was found that only two papers had been published in this country, one by MacKenzie Wallis, Nicol and Sir Maurice Craig and the other by Worster-Drought & Hardcastle.

The former workers performed protein skin tests on 122 epileptics (68 females and 54 males). Of these, 46, (28 females and 18 males) gave positive reactions to different proteins, whilst 76 (40 females and 36 males) did not react at all. They point out that protein sensitivity is peculiar to a certain type of epileptic. The patients were tested at Hanwell Mental Hospital and of the series, 28 reacted to Peptone, 15 to cereals, 15 to fish and meat, 9 to vegetables, 9 to eggs and 3 to milk. They also tested 100 controls. Of these, 4 (all cases of dementia praecox) gave faintly positive reactions to Peptone.

They used protein extracts prepared by MacKenzie Wallis and grouped as follows :-

- Group 1. (egg proteins): Crystalline egg albumen of various types.
- Group 2. (meat and fish proteins): Beef, mutton, veal, chicken, game, fish and shell-fish.
- Group 3. (milk): Milk of various animals.
- Group 4. (vegetable proteins): Ground-nut, fruits, vegetables, legumes and nuts.

Group 5. (Cereals): Proteins of all common types were included.

In addition, Peptone was used for skin testing. A solution of deci normal sodium hydroxide was used as a control.

Worster-Drought & Hardcastle carried out a series of cutaneous reactions with extracts of common foodstuffs on 40 epileptic patients. In not a single case could a definite positive result be claimed.

In America Ward & Patterson investigated two series of 500 cases of epilepsy and obtained 37% of positives in one series and 56.8% in the other. They offer no explanation of the difference in these results.

In the non-epileptic control group 8% showed positive reactions.

... necessary to study the ... reaction and ...

In 1918, ... the ... of ...

A good deal of ... regarding the ...

ANAPHYLAXIS AND ALLERGY.

... and ...

Before citing the evidence as to Epilepsy, it is necessary to review the facts regarding protein sensitization and anaphylaxis.

In 1910, Meltzer drew attention to the similarities existing between the lungs of Asthmatics and those of guinea-pigs which had died from anaphylactic shock. The two conditions were regarded as identical until it became evident that the so-called "anaphylaxis" in man differed in several ways from anaphylaxis in laboratory animals.

A good deal of confusion exists regarding the terminology of this subject. Doerr groups all the phenomena of altered reactivity under the term "allergy" and describes hyper-susceptibility and lessened susceptibility to non-antigenic substances, and hyper-susceptibility to antigenic substances including proteins and toxins. Coca groups all the phenomena under the term "hypersensitiveness" which he divides into anaphylaxis, where an antigen-antibody reaction has been proved and allergy, in which this reaction has not been shown to be present. Later, Coca and Cooke classified hypersensitiveness into (a) normal, including serum disease and dermatitis venenata, and (b) abnormal, including anaphylaxis, hypersensitiveness of infection and atopy, Zinsser describes (a) protein hypersensitiveness or true anaphylaxis in which an antigen-antibody reaction is involved and (b) idiosyncrasies to non-antigenic substances, (c) bacterial hypersensitiveness, (d) toxin hypersusceptibility and (e) the

primary toxic action of normal serum. Many others reserve the term "anaphylaxis" for antigen-antibody reactions as seen in experimental animals and use "allergy" broadly to include anaphylaxis and other altered reactions such as serum disease and drug idiosyncrasies. Kolmer, in reviewing these opinions, considers the term "allergy" the most appropriate of all for designating this broad and important subject. Though it conveys no idea of the mechanism concerned, it emphasises the characteristic and outstanding change of an altered reactivity of the body cells which, in the usual sense, is one of exaggerated susceptibility.

In these pages the term "hypersensitiveness" is used to include all reactions in which a hypersusceptibility to some foreign agent is evidenced as compared with the normal and it includes the two conditions anaphylaxis and allergy.

Anaphylaxis is the name given to the induced manifestations of hypersensitiveness in laboratory animals, which, according to the manner of production may be sub-divided into (a) active, when an antigen is responsible and (b) passive, when brought about by antibodies. In all instances, anaphylaxis is due to an antigen-antibody reaction taking place in sensitised tissues.

Allergy is the term applied to the (a) natural or spontaneous manifestations of hypersensitiveness in

man which include asthma, hay-fever, eczema, urticaria and migraine, and also to (b) the induced states such as serum sickness and the passive transfer of hypersensitiveness by sensitised serum.

Allergy is thus a state of exaggerated susceptibility to various foreign substances or physical agents which are harmless to the great majority of normal individuals. The reaction is of similar type in the same individual for each substance, it generally appears after minute quantities, and it differs from any toxic action the substance might have in large doses. The allergic exciting agent is termed the allergen, and the allergic antibody is called the allergin. The cells are sensitised when the allergin is in or on them thus accounting for their altered reactivity. When the allergen comes in contact with the allergin in these sensitised cells a rapid reaction occurs resulting in the production of the lesions and symptoms of allergy. Should the allergin circulate in the blood in sufficient quantities to neutralise all the allergen and prevent its access to the sensitised cells it may prevent instead of produce an allergic reaction. The terms active and passive sensitisation are applied to the hypersensitive state according to its manner of production, and desensitisation to a diminution of sensitiveness from therapeutic intervention or other cause.

Von Pirquet, in introducing the term "Allergie"

or allergy and implying an antigen-antibody reaction based his theory on inference and not on experimental observation. There is a complete lack of convincing evidence that allergy to antigenic substances depends at all upon their antigenic property. While it is not possible to assert that anaphylaxis does not occur in human beings, it is a fact that the existence of the condition has not been demonstrated. In other words, no human pathological condition has as yet been shown to result from such an antigen-antibody reaction. Allergy, on the other hand, is exhibited conclusively in human beings, a few similar phenomena that have been noted in lower animals being of doubtful significance or validity.

ANAPHYLAXIS.

In 1839 Magendie reported that dogs after being injected repeatedly with egg-albumen died suddenly. In 1894, Flexner observed that animals succumbed to a second dose of dog serum given some days or weeks after the first dose. Richet experimented on dogs using first Eel serum and later a glycerine extract of the tentacles of the sea-anemone. He was the first to recognise that, after the first injection, some time must elapse before susceptibility develops.

In 1903, Arthus found that repeated subcutaneous injections of horse serum into rabbits at intervals of several days eventually gave rise to oedema, sterile abscesses, and even gangrene at the point of inoculation and that intravenous injections in the treated animals caused death. He believed the reaction was analogous to Richet's anaphylaxis.

When standardising antitoxin in 1904 Theobald Smith noticed that guinea-pigs inoculated with horse serum acquired hypersusceptibility to subsequent injections given several weeks later.

In 1905, Otto demonstrated that this phenomenon was entirely independent of the toxin and antitoxin and could be produced by horse serum alone. Rosenau and Anderson found that a small dose of horse serum injected into guinea-pigs rendered them hypersusceptible to subsequent injections given after an interval of ten days. The reaction was specific

and extremely delicate and the sensitive condition was transmissible from mother to offspring. The hyper-susceptible state may last a long time and be brought about by various animal and vegetable products and bacteria. They also endeavoured to destroy the toxic principle in the serum with physical and chemical agents. In 1907, Gay and Southard first described the phenomena of passive anaphylaxis. Auer and Lewis were the first to make a detailed study of the mechanism of anaphylactic death.

ACTIVE ANAPHYLAXIS.

A single injection of horse serum into a guinea-pig will render the animal hypersusceptible to a subsequent injection given after a definite interval of nine to fourteen days. The second injection is generally fatal. The usual pathological finding is an inflated condition of the lungs due to a contraction of the smooth muscle of the bronchioles. Other phenomena such as fall in temperature, fall in blood pressure, lowered coagulability of the blood and leucopaenia are recorded.

PASSIVE ANAPHYLAXIS.

By taking the blood of a sensitised animal and injecting it into another animal, the second animal, after some 15 to 18 hours, becomes passively sensitised to the substance which sensitised the original animal. By sensitising a pregnant female a similar state is produced in the offspring, as the antibodies of the mother's circulation enter the circulation of the offspring through the placenta. This passive sensitisation can be transferred to members of different species as well as to members of the same, but in all cases a definite interval elapses between the injection of the serum and the development of hypersusceptibility. It is during this period that the antibodies upon which sensitisation depends are entering into an essential relationship with the tissue cells.

ALLERGY.

In 1798, Jenner found that the inoculation of variolous matter into persons who had had cow-pox or small-pox produced a tingling sensation and an erysipelatous look on the skin near the point of inoculation. Weichhardt and Wolff-Eisner in discussing hay-fever were the first to suggest that human hypersensitiveness was related to anaphylaxis as observed in animals. Von Pirquet after studying serum sickness coined the term "Allergie" or "Allergy" meaning altered reactivity and implied that an antigen anti-body reaction was the basis in general. In 1910, Meltzer suggested that true bronchial asthma was an anaphylactic phenomenon because of the similarity between the bronchial constriction in asthma and that observed in animals dying of anaphylactic shock. Koessler made similar observations about the same time, and in 1913 reported a case of asthma due to hypersusceptibility to hens' eggs. In 1912, Doerr adopted the term "Allergy" and extended its meaning to include all forms of changed reaction capacity, whether the substance to which this altered reaction capacity was evident was antigen or not.

ALLERGIC DISEASES.

Certain individuals respond in an abnormal manner to substances which are quite harmless to an ordinary person. This idiosyncrasy may be manifest after the inhalation, ingestion, injection, or skin contact with the substance in question. It may be thought that the absorption of foreign proteins through these channels could account for the sensitisation observed, but experiments have shown that in normal individuals the absorption of unchanged proteins in small amounts is a usual occurrence. The essential features of this hypersensitive state in human beings may be stated briefly.

Heredity.

Heredity plays a most important part in from 50 to 70 per cent of cases, according to the type of allergy displayed. The manifestations differ in different members of the same family.

Characteristics.

The onset may be (a) congenital; many infants are sensitive to foods with which they have never come in contact but which have formed a part of the mother's dietary, or (b) acquired; the spontaneous manifestations that occur generally are of this type, and may be termed natural in contra distinction to induced sensitisation which is relatively difficult but does occur in serum disease and following transfusion of sensitised human serum. The duration of



this sensitiveness is usually permanent especially if to inhalants as compared with foods. The cause can be either antigenic or non-antigenic substances, protein or non-protein, or even physical in nature. The degree of sensitiveness manifested in the different tissues may vary so absolutely to the same protein that the impression is obtained that sensitiveness is highly developed in some tissues and entirely absent in others. Infinitesimal amounts of allergens frequently cause violent reactions, a degree of sensitiveness unknown in animals. The specificity of the proteins producing sensitisation is an interesting factor. Relatively slight changes in the protein molecule can change or mask its specific action. The different proteins of a given species are not necessarily related immunologically. Very often homologous proteins from different species of animals and plants are more alike from this point of view than different proteins from the same species. Multiplicity of sensitivity is the rule, most humans being spontaneously hypersensitive to more than one allergen. Passive transfer of hypersensitiveness has been reported after blood transfusion.

PROBLEMS OF THE FUTURE

The field of the asymptomatic virus is still in its infancy. The features of the virus are not yet known. The features of the virus are not yet known. The features of the virus are not yet known.

Patients and clinical point out that in certain individuals disturbing symptoms may follow the taking of certain protein substances. The symptoms are not yet known.

A L L E R G Y

In those individuals the symptoms are associated with certain blood-vessels and organs.

Patients and clinical point out that in certain individuals disturbing symptoms may follow the taking of certain protein substances. The symptoms are not yet known.

E P I L E P S Y.

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FOREIGN PROTEINS AND EPILEPSY.

The idea of the anaphylactic origin of epileptic phenomena is by no means new. The features of the epileptic paroxysm have much in common with those of anaphylactic shock.

Pagniez and Lieutaud point out that in certain individuals distressing symptoms may follow the taking of certain protein substances via the alimentary tract, the respiratory system or via the skin. In those individuals the symptoms are associated with certain blood-vascular changes.

Pagniez and Lieutaud showed experimentally that these unpleasant symptoms could be warded off by giving sometime beforehand a minute dose of the protein concerned. They found such preventive therapeutics was effective in urticaria, alimentary anaphylaxis, and in certain cases of Quincke's disease. It has also been applied successfully in cases of Migraine and in some cases of Asthma.

They report the case of a boy of eighteen in whom the taking of a cup of chocolate was followed by an epileptic fit. The giving of a small dose of chocolate three quarters of an hour beforehand enabled him to take a dose of 50 gm. of chocolate with impunity.

Bell (quoted by Ward) records the case of a

patient who was subject to epileptic seizures after eating Cheese or Butter. When all cows' milk products were eliminated from her diet she ceased to suffer from the epileptic attacks.

Doctor John Thomson of Edinburgh writing in 1921 expressed the following opinion: "The causation of these cases is extremely obscure but it certainly looks as if the convulsions were set up by the action on the brain cells of some sort of poison formed in the body. The most remarkable fact about the attacks is that in a large majority of cases they are permanently stopped by a merely temporary chloralization of the patient. Any attempt to solve the problem of their causation must take this striking fact into consideration.

A search for some analogous phenomena which might possibly help to explain the action of the drug in these cases has only led to the discovery of one fact which seems to have a bearing on the question. This is the observation described by Richet, Besredka and others, that when a guinea-pig is put deeply under ether, alcohol, chloral, or certain other narcotics before the second dose of a serum which is usually rapidly fatal the expected anaphylactic shock is generally suppressed altogether and after a period of unconsciousness the animal 'awakes vaccinated' as Richet expresses it.

The result of these experiments in guinea-pigs certainly suggests the question whether the clinical phenomena of this particular type of convulsion may not possibly be due to a peculiarly modified form of anaphylaxis or some similar process set up by the ingested cows' milk. While we do not as yet possess the facts to enable us to answer this question in the affirmative it may I think be fairly claimed that we have enough information to justify our saying that this is at least the most hopeful direction in which to look for an explanation of the facts."

Migraine and Epilepsy like Asthma may first develop following some acute infection. Of the various acute infections thought to be responsible Scarlet Fever is considered the most important. On the other hand acute infections frequently exercise an inhibitory action on all this group. Asthma which has proved resistant to all forms of treatment including desensitisation may temporarily disappear after a severe infection such as Typhoid or Pneumonia. Migraine very frequently will temporarily and sometimes permanently disappear after an acute infection. This also is true of Epilepsy. Tinel refers to the disappearance of epileptic seizures following Typhoid and Pneumonia. The same phenomenon has been noticed in the case of epileptics who have developed pulmonary Tuberculosis. Turnowsky refers to three cases of Epilepsy in all

of whom the seizures subsided - two after Pneumonia and one after Scarlatina. Hamilton reports that of twelve epileptics who acquired Typhoid Fever nine showed distinct improvement, one remaining free from seizures after four years.

This improvement after infection might be explained on the basis of desensitisation as this is the accepted explanation in the case of Asthma.

Pregnancy not infrequently modifies Asthma, Migraine and Epilepsy. All of these may subside temporarily during this period. On the other hand they may first develop during pregnancy. As the placenta behaves as a foreign protein to the mother it is possible that desensitisation may result.

French physicians have reported that after treatment for Rabies or after the use of Diphtheria anti-toxin epileptic seizures have temporarily disappeared. Bouché and Hustin following this observation treated a number of epileptic patients with normal horse serum with encouraging results.

Spangler's use of snake venom in epilepsy reported in 1908, in the light of recent developments is of considerable interest. He was led to try this treatment after reading a report of a patient who had been subject to epileptic seizures for fifteen years and, following a bite by a rattlesnake, remained free from fits for two years. Snake venom contains both a poisonous Peptone and a globulin.

The Peptone is largely a nerve poison. The globulin lessens blood coagulability and increases vessel permeability. As there was a theory at this time that the epileptic seizure was associated with increased blood coagulability he ascribed his good results to modification of blood coagulation. His report on thirty-six cases treated by subcutaneous injections of crotalin showed that every patient was affected favourably although in some instances the improvement was very slight. In others the seizures became infrequent, or the major attacks entirely disappeared. Three patients had been entirely free for two years or more and two for eighteen months. In some cases the seizures permanently disappeared after the first series of five or six injections. He advised however, that after the first series the injections be continued at intervals of two to four weeks. Held recently made a report on four hundred cases of Epilepsy treated with serum of animals previously injected with serum and spinal fluid from epileptics. He states that 18% of his series had been free from seizures for two to four years and only 30% had not improved. If there is any value in this treatment it is probably due to the effect of the normal serum rather than to changes produced by the previous treatment of the animals.

EXPERIMENTAL, HEREDITARY, CLINICAL and
THERAPEUTIC EVIDENCE.

Certain experimental, hereditary, clinical and therapeutic factors which are found to run more or less parallel in Allergy and Epilepsy, are of considerable interest.

Miller suggested in 1924 that the periodic manifestations of essential Epilepsy may be a response of the system to an allergic metabolic disturbance.

EXPERIMENTAL FACTORS.

Otto of the Koch Institute carried out studies in immunology over a period of several years. He reported that in rearing mice from ricin-immune fathers and normal mothers he has produced young mice which are hyper-sensitive to ricin and concludes that he is dealing with an inherited sub-immunity, which is brought about by injury to the ancestral male germ plasm and he claims that experimental allergy is thus shown to be transmitted.

Koesler, Schloss, Curschmann and others have caused

sensitisation in guinea-pigs by injecting them with the serum of allergic patients. It is most important, however, as Van Leeuwen points out, that the possibility of transferring allergic sensitisation passively to animals depends upon the time chosen for the withdrawal of the blood as well as upon the intensity of the state of sensitisation.

De Besche and Frugoni have shown that immediately after an asthmatic attack the patient's blood does not contain the substances which might transmit to animals or to man the susceptibility to the allergen but after some time they seem to reappear. It seems generally recognised that Frugoni has also proved that the allergic state is transmissible in the human being, that it can be transmitted through either parent and that the form of symptoms may differ in parent and child.

Similar features are noted in epilepsy. As already mentioned, Pagniez, Mouzon and Turpin have produced convulsions in animals by transfusion of blood from epileptic patients at the time of seizure, while no convulsions occurred when the blood of healthy persons was used.

It is recognised that brain lesions in animals and human beings in a large percentage of cases do not produce convulsions. Collier says that epilepsy cannot be produced in a susceptible animal by injury to the brain, but it can readily be induced by introduction of a convulsant poison such as picrotoxin, absinthe and

others into its anatomy or by depriving the animal of one or more of its metabolic organs such as the thyroid or parathyroid.

Miller and Dendy have shown that in cats experimental lesions of the cerebrum which do not cause epilepsy can be rendered highly epileptogenous if metabolism be disturbed by the administration of a sub-minimal dose of a convulsant poison such as absinthe which has no toxic effect at all upon a normal cat. It is said that the proteny of an absinthe epilepticised animal has been shown to have convulsions. Such experiments suggest that a metabolic error may be responsible for the production of the convulsion.

Van Leeuwen and Leydner have checked and seem to confirm their original report of having isolated a muscle-stimulating substance from the blood of patients with asthma, urticaria, migraine and epilepsy. They could not demonstrate this substance in non-allergic controls.

HEREDITARY FACTORS.

Van Leeuwen says it is generally agreed that in at least 50% of cases the disposition to become allergic is inherited. Cooke and Vander Veer in their extensive studies concluded that the constitutional peculiarity which makes probable the development of hypersensitiveness is transmitted according to Mendelian laws as a dominant

characteristic.

In tabulating the allergic hereditary manifestations in a study of 100 consecutive adult cases of Epilepsy, Spangler found among the parents and grand parents: 11 cases of Epilepsy, 35 cases of Asthma, 7 cases of Hay Fever, 14 cases of Hives, 6 cases of Eczema and 66 cases of Migraine. One mother and two fathers of these 100 epileptic patients had epilepsy, that is, in only 3% of the parents the same clinical syndrome as in the patient was present.

MULTIPLE ALLERGIC MANIFESTATIONS.

Most workers in allergy report finding multiple manifestations in from one third to one half or more of their patients. Rackemann says he finds at least a third of those patients who have one allergic manifestation have had in the past, or still have, some other manifestation in addition to the presenting symptom. Waldbott reports: "It is common to note that asthmatic attacks are sometimes replaced by or associated with urticaria, angioneurotic oedema and other allergic conditions". He reports two cases in which epileptiform seizures have substituted themselves for asthmatic attacks.

That anaphylactic phenomena are influenced by the sympathetic nervous system as evidenced by smooth muscle contraction of vessels and glandular secretions is recognised by most investigators. Angiospasm is

regarded as a characteristic vascular phenomenon in allergy, and Olkan who has studied the problem of epilepsy from the physiological point of view concludes that "Epilepsy is attributable to a vasomotor disturbance of the capillaries". All vasomotor disturbances in the brain, however, do not result in convulsions, and it is probable that the potential allergic background in the epileptic patient makes it possible for the vasomotor disturbance to act as an exciting cause, just as brain lesions in animals as a rule do not cause convulsions unless the animal has already been rendered sensitive by some poison. Such findings are suggestive evidence that an altered metabolism is necessary to make the patient susceptible to sensitising toxins or allergens arising either from within the body or introduced from without.

CLINICAL FACTORS.

Besides the hereditary, experimental, and metabolic factors, there is also considerable clinical evidence which points to the probability that many of the convulsions in so-called idiopathic epilepsy develop from an allergic background. Among the chief clinical factors which suggest an allergic basis as a cause of epilepsy is periodicity. This and the paroxysmal nature of the attack are just about as characteristic of asthma, urticaria, and migraine as they are of epilepsy. In some epileptic patients

seizures occur only at night, or only in the daytime, or there may be series of attacks at long intervals. This periodicity in epilepsy is more reasonably explained on the grounds of an allergic metabolic disturbance.

Other clinical characteristics common to epilepsy and allergy are that the attacks start abruptly, that one attack tends to predispose to another, and that the attack per se is rarely fatal. It has long since been noted that acute infections may benefit both allergy and epilepsy.

THERAPEUTIC FACTORS.

The use of a ketogenic diet in epilepsy, migraine and asthma, and the limiting of the fluid intake help to control or lessen the frequency of acute symptoms in many cases and especially in children. The results are attributed by most investigators to a lessening of alkalosis. Keith, however, points out that the action of ketone substances is probably an anasthetic one.

The type of treatment most needed, however, in both allergy and epilepsy is a basic one which can be employed between the attacks, and which will restore the metabolic imbalance. For this purpose some form of non-specific desensitisation should be considered.

Twenty years ago Spangler began using crotalin in the treatment of epilepsy, asthma and migraine and reported very satisfactory results. This treatment was regarded

as so fantastic that few investigators attempted to confirm Spangler's results.

As a rule the tissues most commonly affected in allergic conditions are those which come in contact most frequently with foreign substances which tend to sensitise, namely, the mucous membranes of the eye, the nose, the bronchial tubes, and less frequently the skin and the mucous membranes of the alimentary tract.

The symptoms, however, may appear in remote organs, while the tissues at the point of entry may show little reaction. For example, asthma or eczema may result from the ingestion of milk or egg, while dyspepsia and abdominal pain may result from the subcutaneous injection of pollen extract or egg albumen.

Thus it is logical to anticipate evidence of protein sensitisation in almost any organ of the body.

As the ingestion of foreign proteins may cause swelling and oedema of the skin which we call urticaria, it seems feasible that the same cause may give rise to similar changes affecting the brain, and so causing Epilepsy.

Removal of the Cause of the Specific Allergy.

In some cases this is sufficient to cause the disappearance of symptoms.

Several cases are mentioned in the literature in which the removal of the cause of the allergy has resulted in disappearance of the disease.

Levin reports such a case. The patient, a

METHODS OF TREATMENT.

collegiate student after eating a sandwich containing

the same positive skin reactions as in the case of the patient.

On withdrawal of the cause the patient's symptoms

In Case 2 of this series it was found that the patient was allergic to wheat gluten. In this case, could we not have done away with the cause of the allergy by having the patient eat only wheat-free bread? It is possible that the patient's symptoms were due to the fact that he was eating wheat bread.

METHODS OF TREATMENT.

Removal or Avoidance of the Specific Allergen.

In some cases this is sufficient to cause the disappearance of symptoms.

Several cases are mentioned in the literature in which epileptic convulsions have followed the taking of certain foods. Exclusion of those foods from the patient's diet has resulted in disappearance of the fits.

Levin reports such a case. The patient, a little girl of three years of age, had a severe epileptiform attack after eating a sandwich containing cheese.

She gave positive skin reactions to American, Swiss and Roquefort cheese.

On withdrawing cheese from her dietary she remained free from attacks.

In Case 9 of this series it was seen that the patient was sensitive to grass pollen. Avoidance, in this case, would mean the use of an allergen-free chamber such as that used in Holland by Van Leeuwen. It consists of an air-tight room which is ventilated with air taken from a height of 35 metres above the

soil and blown in through metal pipes by means of a large exhaust with a capacity of 1800 cubic feet per minute, purified by cooling, then heated before entering the chamber. Van Leeuwen reports very good results in treating cases of Asthma in such chambers.

While exclusion or avoidance may be sufficient in early cases of epilepsy, it would appear that once the convulsion habit has developed, the mere avoidance of the specific allergen is not enough.

Case 4 in this series gave positive reactions to Goose, Squab, and Peptone. The writer can vouch for the fact that not one gramme of Goose or Squab has passed his lips during the past ten years, but he still continued to have fits in spite of this rigid exclusion or avoidance.

Desensitisation.

A. Specific or homologous.

(1) Ingestion of gradually increasing doses of the particular protein.

This method is strongly advocated by Roddis, who says: "The best method is the oral administration of gradually increasing doses of the offending substance". It is advisable to start with a small dose well diluted. He recommends the giving of a drop of egg albumen or of milk for the first dose once a day and gradually increasing the dose until a moderate amount of the food is taken without trouble.

(2) Repeated cutaneous reactions.

Skin testing if frequently repeated may lead to desensitisation. This method is useful in cases of dust or pollen allergy.

(3) Denaturisation.

This method is frequently used in dealing with food sensitives. The allergic reactions due to lactalbumen hypersensitivity may be counteracted by boiling the milk and many patients realise that they can take certain foods when cooked which cause unpleasant symptoms when taken in the uncooked state. The writer feels that extracts from cooked as well as uncooked proteins should be used in testing.

(4) "Proteose" prepared from the patient's urine by Oriel's method has been employed at the Guy's Hospital Asthma Clinic for specific desensitisation.

Good results have been reported.

B. Non-specific or heterologous desensitisation.

Many types have been suggested by different observers.

The principle adopted is to endeavour to use up the reactivity of the patient with another protein in the hope that it will counteract reactivity to the specific protein.

(1) Peptone.

Since 1917 Auld has advised the use of Peptone in the treatment of bronchial asthma. He used Armour's Peptone and gave it intravenously.

Much work remains to be done to determine the best method of giving Peptone and the most suitable dosage.

(2) Tuberculin.

Van Leeuwen and Varekamp introduced the tuberculin treatment of asthma prompted by the frequency of positive tuberculin reactions in asthmatic patients. The majority of their patients improved.

(3) Milk.

Schiff suggested the injection of whole milk as a non-specific agent in the treatment of asthma.

(4) Vaccines.

In treating cases of asthma it was found that stock vaccines gave as good results as autogenous vaccines. It was therefore concluded that the effect was a non-specific one due to the protein content.

(5) Drugs.

In the article already referred to, Thomson of Edinburgh remarks that none of his cases of idiopathic convulsions in very young children came later for treatment for subsequent convulsions, asthma, skin eruptions or food idiosyncrasy, and he suggests that conditions due to protein hypersensitiveness might be successfully treated by a thorough chloralization for some days.

(6) Auto-haemotherapy.

Blood is drawn from a vein, defibrinated, and injected either subcutaneously or intramuscularly. Kahn and Emsheimer obtained good results in six successive patients.

Cases 1 and 2 described above would appear to indicate the lines along which the treatment of epilepsy might be carried out. The effect of a febrile illness on the incidence of fits was very striking, though there is little reason to believe that the pyrexia per se plays much part in the resultant improvement. Similarly, the writer has long been of the opinion that pyrexia plays only a very minor part in the fever treatment of

General Paralysis. In my opinion, the process at work is one of non-specific desensitisation and the development of General Paralysis depends not on the presence of a particularly enterprising or neurotropic type of spirochaete but on a peculiar sensitiveness on the part of the individual to the presence of the spirochaete and its toxins, in short, that the changes are of the nature of an allergic response.

In view of the foregoing evidence, I would strongly advocate the thorough investigation of all cases of idiopathic epilepsy from the allergic point of view.

Family histories and food histories should be investigated and protein skin tests should be performed as early as possible.

Treatment by desensitisation would appear to be of the greatest value and in early cases may effect permanent cure of what has, in too many instances been regarded as an incurable disease.

SUMMARY AND CONCLUSIONS.

Two cases of idiopathic epilepsy are reported. In the first, epileptic convulsions disappeared completely during an acute infection and the patient's mental condition showed a remarkable improvement. In the second, after an acute febrile illness in 1931, the patient has since had only two fits. His mental condition shows a very striking improvement.

Protein skin tests were performed on twenty-five male patients suffering from idiopathic epilepsy and on twenty-five non-epileptic controls. Among the former, 36% were positive, among the latter, 4%. Sensitiveness, as indicated by positive skin reactions was found to be increased before, and diminished, for a variable period after a fit or series of fits. A few hours after an injection of Pyrifer, it had disappeared completely.

Non-specific desensitisation by means of Pyrifer was attempted in the case of those showing multi-sensitivity. All showed definite mental improvement. In two cases the fits were reduced by 50% and 38% respectively, while in the third case, there was no reduction in the number of fits.

Of those treated with Peptone, two improved mentally, while the third showed no noticeable improvement. The effect on the incidence of fits was not so striking as in the case of Pyrifer.

The essential features of Allergy are outlined.

Evidence is adduced in support of the view that Allergy is a factor in the causation of certain cases of essential Epilepsy.

Other methods of treatment are briefly described.

The writer urges the investigation of all cases of idiopathic epilepsy from the allergic point of view and the carrying out of protein skin tests. He strongly advocates some form of desensitisation treatment in those cases which appear to have an allergic basis.

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