THE ALLERGIC FACTOR IN IDIOPATHIC EPILEPSY.

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Allergy and Epilepsy.

Spratling (1), writing in 1904, was the first to draw attention to the possible association of epilepsy with food sensitization. Previous to this observers had been impressed by the fall in fit incidence which occasionally accompanied intercurrent diseases, notably typhoid and tuberculosis. Hamilton (2), some years later, confirmed these observations in respect of intercurrent typhoid. It was not, however, till 1919 that Pagniez and Lieutaud (3) detailed the first authentic instances of epilepsy definitely ascribable to a specific food substance. These were two cases of sensitivity towards chocolate. The authors demonstrated that withdrawal of chocolate led to a cessation of seizures, and that these returned when it was re-introduced into the dietary.

Following this communication an ever-increasing number of similar recordings were instanced by different observers. Wechsler (4), Thompson (5) and Ward (6) separately conducted investigations into the relationship of food idiosyncrasy and epilepsy, and from their findings conclusively inferred the existence of a definite inter-connection. They each described several cases of allergic epilepsy, resting on a food basis, which were successfully treated by elimination of the suspected protein. In 1923 Howell (7) published an interesting account of the investigation and treatment of 14 epileptics from an allergic viewpoint. He skin-tested his patients and disclosed a number of positive reactors, while in others seizures followed the eating of specific foods. All his cases benefited considerably by the removal of the offending allergen.

Rowe (8) was the first worker to treat his patients with a combination of diet control and desensitization. He reported two cases of desensitization to inhalants, which resulted in complete elimination of fits. Spangler (9) has written a number of articles on allergic epilepsy and strongly advocates regarding all cases of idiopathic epilepsy as potentially allergic, until proved otherwise. He has employed non-specific desensitization with good results. Forman (10) prescribed elimination diets in his series of selected epileptics and showed a great reduction in fit incidence, with some complete cures. He stresses the

importance of uncovering other allergic phenomena in both the patient and his relatives in coming to a diagnosis of allergic epilepsy. Clein (11), Levin (12), McReady and Hay (13), and many others have further contributed to the literature. The former successfully treated six cases by specific food elimination combined with desensitization to dust.

The Incidence of Allergic Phenomena in Epileptics, Psychotics and Controls.

A study of the literature on allergy and epilepsy suggested the existence of considerable scope for further research along similar lines. Much of the work done and successes achieved had been with young subjects, but this appeared no reason for the abandonment of the chronic idiopathic epileptic. Specifically directed treatment, in protein sensitive cases, might prove, if not curative, at least beneficial. At the same time such an investigation would afford an opportunity of contrasting the incidence of sensitization in epileptics with that in psychotics and normal individuals.

The first step in the investigation, which was carried out at Dykebar Mental Hospital, Paisley, was the formation of three groups each consisting of 24 individuals. The first consisted of adult idiopathic epileptics in whom there was no history of birth or subsequent head injury and to whose disability no cause could be attributed. The second and third groups were picked at random from the non-epileptic psychotics and the staff respectively. The only common factor stressed was an approximation, as far as possible, in the average age of the three groups.

A careful inquiry was instituted into personal and family histories with a view to disclosing any possible clinical manifestations of allergy. The results of this investigation were summarized as follows:

Allergy.

Group.	Personal history.	Family history.	Number of positives.
Epileptic	Positive	Positive	5
	,,	Negative	4
	Negative	Positive	7
Psychotic	Positive	,,	0
	,,	Negative	2
	Negative	Positive	4
Control	Positive	,,	0
	,,	Negative	1
	Negative	Positive	3

From the above table it can be seen that the presence of allergic phenomena was a marked feature of the epileptic group, the figure being almost double

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that of the combined results of the other two classes. Actually 66 per cent. of the epileptics gave either a positive personal or a positive family history of allergy, while in 20 per cent. of the cases positive findings occurred in both instances. These figures contrasted strikingly with 25 per cent. and 0 per cent. for the psychotics and 17 per cent. and 0 per cent. for the control group.

The association of seizures and clinical hypersensitivity in the epileptic and his family was significantly high, and suggested the existence of a relationship between epilepsy and the other recognized allergic disorders. Despite the difficulty of obtaining satisfactory histories in every case, the above figures are comparable with the findings of Spangler (14), who, in an analysis of 100 epileptics, reported that in the ancestors there was a history of allergy in 88 per cent. of the cases, while the patients' personal history revealed a figure only slightly less.

Skin Testing Technique.

The different groups were now skin tested for protein sensitiveness. It must, however, be recognized that before skin tests can be successfully undertaken certain preliminary details require consideration. The first of these is the choice of testing material and the nature and number of the allergens to be employed. Messrs. C. L. Bencard (1934 Ltd.), of London, market most acceptable preparations and these were used throughout. Use was made of this firm's Group Reagents in addition to their individual allergens. The former are put up in twelve groups as follows:

1. *Mixed inhalants, standard.*—Mixed feathers, horse dander and hair, cats' fur, mixed dog hair, mixed house dust, orris.
2. *Other inhalants.*—Rabbit fur, sheep's wool, furs (fine), cow dander, human hair, goats' hair, camel hair.
3. *Cereals.*—Wheat, oats, barley, maize, mixed flour, rye.
4. *Eggs, milk, etc.*—Egg white, egg yolk, milk, cheese, chocolate.
5. *Vegetables.*—Mixed beans, mixed peas, cabbage, spinach, carrot, potato.
6. *Meats.*—Beef, mutton—lamb, pork—bacon, veal.
7. *Fruits.*—Apple, banana, orange, tomato, strawberry.
8. *Fish.*—Cod, salmon, herring, sardine.
9. *Shell-fish.*—Lobster, crab, mussel, oyster.
10. *Fabrics.*—Silk, cotton—flock, kapok, wool.
11. *Non-classified*—Tobacco, yeasts, mushroom.
12. *Pollens.*—Grasses, shrubs, trees.

By the use of group reagents a saving of time, labour and expense was effected, as only following a positive recording did separate testing of component allergens become necessary. It must be accepted as an axiom that if convulsions are due to hypersensitivity to a particular allergen, that allergen

must be sought somewhere in the environment of the patient. It is true that the present environment may, to all appearance, differ radically from that in which the fits commenced, but sensitivities may have changed with the years or the situation. Again, multiple sensitivity may have been an early feature, or most likely the offending protein is sufficiently common to be invariably present. Under such circumstances it would obviously be futile to routine test each individual for a hundred or more allergens with many of which he could never possibly have come in contact.

In addition to the above group reagents all subjects were tested for such articles of food as appeared either periodically or frequently in the Hospital dietary but which did not appear in any of the Groups. These articles comprised onion, parsley and turnip ; rice ; lemon and pear ; chicken ; herring, halibut and haddock. Finally, if a history was present of a particular hypersensitivity, either recent or remote, that specific substance was tested for whether its group reagent was positive or not.

The method of skin testing employed was that advocated by the writer in a recent article (Dewar, 15). The technique is as follows : Using the forearm as the sole testing site each person is first scratch-tested and then, unless very marked reactions have occurred, is tested intradermally one week later on the same site, with a solution of corresponding strength. Separate scratch and intradermal solutions are used. Should any of the reactions, following the scratch testing, be of great intensity then the intradermal solution is diluted to one-half or one-quarter its strength with carbol-saline before injection. By this means the possibility of general reactions, following the intradermal testing, is considerably lessened. The method enables the greater safety of the scratch method to be coupled with the greater sensitivity of the intradermal, and furthermore, by standardizing procedure makes possible a more accurate assessment of results.

Examination of Selected Groups.

The choice of testing materials, method and site being established, each member of the three selected groups was scratch tested on the forearm with the twelve group reagents. One week later further scratch tests were carried out for onion, parsley and turnip ; rice ; lemon and pear ; chicken ; herring, halibut and haddock.

Following a further interval of one week the intradermal testing was performed, strict attention to practical details being observed, The dose injected was one-fiftieth of a cubic centimetre of a solution specially prepared by Bencard and of a proportionately modified strength as compared with the scratch solution.

The final recording of positive results was based entirely on intradermal testing irrespective of a corresponding negative or positive scratch reaction.

Incidentally no positive scratch reaction gave a negative intradermal test. Results were tabulated as follows :

Group.	Average age.	Positive.	Negative.	Multiple sensitivity.
Epileptic	38	14	10	11
Psychotic	36	7	17	2
Controls	29	1	23	..

In the epileptic group there were 15 males and 9 females ; in the other two groups the sexes were equally represented. Of the 9 females 5 were positive and 4 negative ; of the 15 males 9 were positive and 6 negative. The average age of positive and negative reactors among the epileptics was 36 and 40 respectively.

The contrast in degree of sensitivity between the groups was obvious and not unexpected, but the multiple sensitivity of the epileptics was a striking feature. It was previously noted that 66 per cent. of the epileptics under investigation gave a positive personal or family history of allergy, while the figures for the psychotics and the controls stood at 25 per cent. and 17 per cent. respectively. From the above table it was found that 58 per cent. of the epileptics had positive skin reactions, 29 per cent. of the psychotics and only 4 per cent. of the control group. These figures further supported the contention that allergy and epilepsy were related. Moreover the three groups displayed a correlation between the degree of skin sensitivity and the presence or absence of allergic phenomena. A similar relationship was recorded by Ward and Patterson (16), who in skin testing one thousand epileptics and one hundred non-epileptic controls found that 46·9 per cent. of the epileptics gave evidence of protein sensitization, while only 8 per cent. were positive in the control group.

It would appear that epileptics exhibit an allergic phenomenon common to them as a group. It nevertheless remains doubtful whether convulsions arise from the presence of this hypersensitiveness or whether, as Van Leeuwen (17) thinks, there is a primary factor which predisposes the brain centres, so that the allergic reaction acts merely as a secondary stimulus. Again it may be that the circulating protein picks out, for choice, the weakest structure of the individual's economy which, in the potential epileptic, will be the central nervous system, and, by irritating it, initiates convulsions.

Only a brief survey of results in the psychotic and control groups is indicated. The psychotics displayed a mild degree of allergic response, not comparable with the epileptics, yet strong enough for comment and certainly more evident than that of the controls. Whether this relatively high percentage of sensitivity among the psychotics was accidental and would have fallen had greater numbers been tested, or whether heightened susceptibility was indeed a feature, were questions outside the scope of this investigation. Nevertheless, an interesting hypothesis was offered by the suggestion that institutionalized psychotics showed a tendency to develop similar sensitivities

owing to similar environment. Of the seven positives recorded in the above table, four were sensitive to cheese or milk and three to fish. The psychotic group, however, was not chosen on account of length of residence, but according to age. The mean length of residence of the psychotics was 2·6 years and of the positive section of the group 3·8 years. It was impossible to assess results on such meagre data, but the point was, nevertheless, one of interest.

The incidence of positive reactors in the control group, drawn from the nursing staff, was small, and confirmed the findings obtained from time to time in non-allergic groups of the general population. This latter figure is variously put at anything from 1 to 8 per cent.

The 14 epileptics giving positive reactions were now finally tested with individual allergens in an attempt to isolate the offending protein. The following table briefly summarizes the results obtained and indicates comparative degrees of reaction :

TABLE I.

Case.	Positive allergens.
1	Mixed house dust +, pork +.
2	Mixed feathers +, oats +.
3	Cheese ++.
4	Cheese ++, onion +.
5	Cheese +++, milk ++, rice ++, sardine +.
6	Cheese +, herring ++.
7	Haddock +, herring +.
8	Cheese ++, salmon ++.
9	Mixed house dust +++, mixed feathers +++.
10	Egg white ++, mixed feathers ++.
11	Mixed house dust ++, cheese +++.
12	Cheese ++.
13	Egg white ++.
14	Egg white +, cheese +++.

COMMENT ON TABLE I.

(1) The majority of the cases displayed well-marked positiveness with large areas of erythema and pseudopodia. Such were expressed as double plus, while the single and treble plus were used to indicate lesser and greater degrees respectively. (2) In eleven cases sensitivity existed to more than one protein ; ten cases showed positive results towards two extracts ; one case reacted to four. (3) Three distinct groups of allergens were mainly involved, namely, eggs, milk and cheese ; the common inhalants, mixed house dust and feathers ; and fish. (4) A noteworthy feature was the disproportionately high percentage sensitive to cheese (57 per cent.).

The Treatment of Allergy.

The treatment of allergy may be grouped under the headings of elimination, non-specific desensitization and specific desensitization.

Elimination.

Elimination, as a rule, is only possible where the existing sensitivity is towards foods. In most cases of dust and pollen allergy the difficulties of withdrawal are too great to be overcome. Occasional instances are recorded, however, following a change of environment, the removal of a pet from the family circle, or the replacement of a hair mattress.

One of the chief difficulties with food elimination is the fact that hypersensitivity usually occurs to common allergens, and it is difficult to eradicate these indefinitely. Nevertheless if this form of treatment is once commenced it should be persevered with.

Diets based solely on skin reactions do not always control symptoms, and in such instances it is advised that trial diets be employed, such as the elimination diets established by Rowe. These diets are suitably balanced and on them normal activity may be maintained for long periods. Should one diet not succeed in allaying symptoms, another may be tried and so on until one is found that gives relief. Articles from other diets in the series may be added every few days, a close watch being kept meanwhile for any return of symptoms.

Elimination, at the best, has a restricted field of application and is chiefly confined to food allergy, and especially to those foods which are relatively unusual and easily avoided.

Non-specific Desensitization.

This line of treatment is advocated in the hope that the injection of one type of protein will diminish the tendency to react to the specific protein. Many attempts have been made to produce desensitization by this means, but results, on the whole, have not been good.

Successes have been attributed to peptone, propeptane, tuberculin and crotalin by such authorities as Wallis, Nicol and Craig (18), Singer (19), Crockett (20), and Spangler (21) respectively. Nevertheless good results are usually temporary and relapse, partial or complete, may be expected. On account of the large element of chance involved, non-specific desensitization cannot be recommended except as a last resort.

Specific Desensitization.

This method endeavours to lessen sensitivity or to raise the tolerance level, either by the oral administration of graduated doses of the specific food, or by injecting a standardized solution of the specific food or pollen.

Four routes may be employed, namely, the oral, the intradermal, the subcutaneous and the intramuscular. The oral route is widely recommended when dealing with food sensitivities. In this method the offending food or its specific peptone is given in small but gradually increasing doses in an attempt to abolish sensitivity.

Intradermal desensitization has occasionally been employed in dust and pollen hypersensitivity, but results are not encouraging, and the subcutaneous route is the one more commonly used. The method here employed is to prepare standardized solutions of the specific substance in various dilution strengths and to give them at weekly intervals, the dose being doubled with each injection.

The intramuscular route, like the subcutaneous, has been widely advocated in the treatment of allergy; indeed it frequently happens that either route may be used with equal success in the same patient. Intramuscular medication has the advantage of bringing the patient more intimately into contact with the desensitizing solution and more quickly under its influence. Solutions of greater potency are given intramuscularly than subcutaneously, and the effect is considered to be less transient. At the same time there is an increased danger of general reactions, and careful technique and observation are essential.

The Method Adopted.

No instance could be found in the literature of the treatment of allergic epilepsy by intramuscular desensitization. Wherever specific treatment was described it invariably signified the attempted elimination of the suspected specific protein. A few workers, however, such as Rowe, Clein and Singer, had given specific injections for sensitivity to dust, pollens and food using the subcutaneous route.

Good results having followed intramuscular desensitization in most other forms of allergy it seemed strange that no effort had been made to employ it in epilepsy. Intramuscular injections of potent and specifically prepared solutions appeared to offer a means of bringing the allergic state of the organism quickly and effectively under control. In the present investigation this was the method used and it was combined, as far as possible, with specific elimination.

A series of thirteen desensitizing solutions was prepared, according to prescription, by Messrs. Bencard. (In the case of one patient no attempt was made to establish desensitization, on account of rapidly increasing general debility.) These solutions were separately dispensed in strict accordance with the tabulated results of the skin testing, due attention being paid to varying degrees of positiveness.

Two solutions of graded potency were employed, one of moderate strength and constituting an ordinary desensitization course, the other, more concentrated, and to be used with discretion, as a continuation course. The supplied solutions contained, in addition to the specific allergens, adrenaline chloride of a strength of 1 in 4,000. The injections were given deep into the gluteal muscles

near the junction of the outer and middle thirds of the line joining the anterior superior spine of the ilium to the top of the natal cleft. The initial dose given was 1 minim of the ordinary strength plus two minims of adrenaline 1 in 1,000.

In order to investigate the question of dosage and the possibility of general reactions a preliminary test treatment was undertaken on six selected epileptics of the group under review. One minim of the ordinary solution plus one minim of adrenaline were injected, and no local or general disturbances being noted, on the following day two minims of each were injected. On each succeeding day, for a total of five days, this procedure was repeated. The desensitizing solution was increased by one minim daily.

Following the fifth injection two patients (Cases 3 and 14), both sensitive to cheese, began having fits. The former had three seizures within twelve hours. On the sixth day, instead of injecting six minims of the solution, four were given. No further fits occurred and she appeared none the worse. The latter had eight seizures in the interval between her fifth and sixth injections. She, likewise, was given for her next injection four minims instead of six. The fits persisted, however, and the injections were discontinued. Despite every effort she passed into *status epilepticus* and died 72 hours after the first seizure. Thirty-seven seizures in all occurred.

It was, of course, impossible to state whether either of the above attacks were coincidental or whether they were due to the injection and possible concentration of the specific allergen. Nevertheless, the outlook was disquieting, as a similar increase in fit incidence might be induced in other subjects. A method of gauging dosage, could such be f und, would help to obviate this possibility.

Such an attempt was made and the method employed, based on work done by Spangler (22), aimed at instituting a check on dosage by means of eosinophil counts. In the treatment of allergic epilepsy by non-specific means, Spangler had found that the relative number of eosinophils in the differential count could be employed as an indicator of the degree of hypersensitivity and as a means of regulating amount and frequency of dosage. This he designated the "Eosinophilic Index." In epilepsy, as in other forms of allergy, he found that an increase in the number of eosinophils occurred following an injection and that they reached their highest percentage within 48 hours. Normal counts were again present in from five to eight days. He did not repeat an injection unless the percentage of eosinophil cells had by the fifth day dropped to at least 4 per cent. Furthermore, he did not increase the strength of the dose so long as any given strength produced an 8–10 eosinophilia on the second or third day after an injection.

The Eosinophilic Index Applied to the Present Series of Cases.

Spangler's work appeared to offer a solution to the present problem although his technique had been developed in conjunction with non-specific treatment,

namely, the intramuscular injection of crotalin. His results had established a definite connection between the degree of eosinophilia produced and the margin of effective dosage. Whether this factor, however, would hold good with specific desensitization was doubtful.

The group of twelve available epileptics was divided into two equal subgroups, (A) and (B). Group A was submitted to specific treatment controlled, as far as possible, by systematic eosinophil counts; group B was given a similar course of injections, uncontrolled by counts, but modified in respect of dosage in the light of recent experience.

During treatment the twelve patients were largely permitted to follow their usual routine, the only restrictions imposed having reference to diet. Whenever a patient displayed sensitivity to a particular food, as indicated by his history or skin tests, that substance was rigorously excluded from his diet. The active co-operation of the nursing staff was essential and proved willing and effective. It can be stated with some assurance that from beginning to end of treatment no patient gained access to food proteins other than those permitted in his dietary. The majority of the patients were actively interested in the proceedings and submitted cheerfully to all temporary discomfort.

A preliminary period of ten days was employed in making a series of differential blood counts on the members of Group A. This preparatory work was done to determine the average number of eosinophil cells normally present in the blood of each patient. Specific injections were given at 10 a.m. on alternate days and each was followed by three counts at intervals of 7, 24 and 48 hours. The first injection consisted of one minim of the ordinary desensitization course along with two minims of adrenaline 1 in 1,000, and was injected into the gluteal muscles.

This procedure was repeated until a total of 14 injections had been reached. Injections were increased by one minim of the desensitizing solution on each occasion and spaced at intervals of 48 hours. When 14 injections of the ordinary solution had been administered, the patient was changed to the concentrated course and given one minim of this plus two of adrenaline. Forty-eight hours later two minims were injected and so on until a total of twelve injections had been administered. In all, each of the six patients received 26 desensitizing injections. Throughout the course differential blood counts continued to be made at 7, 24 and 48-hour periods following each injection.

The method employed in staining the blood films was the Giemsa rapid, while Schilling's "meander" method was used in making the differential count. The ears were used alternately for obtaining the blood and no difficulty was experienced. Treatment commenced on March 11, 1940, and ended on April 30.

One of the first points noted as treatment proceeded was the fact that although a degree of eosinophilia often followed an injection, the percentage increase did not, in any way, approach that recorded by Spangler. Further-

more the eosinophilia produced was less persistent than Spangler's, usually reached a maximum in 24 hours, and by the end of 48 hours had invariably disappeared. In a few instances the cell level was raised over several days and this was usually associated with a bout of fits.

Unfortunately it was not found practicable to use the index as an effective guide to dosage, although such an attempt was made, owing to the fact that increased counts appeared to bear no significant relation to fit incidence. Another difficulty encountered was the fixing of an eosinophilic level of safety, above which an increase in eosinophils might be expected to result in fits or other phenomena and below which such was unlikely. The determination of such a level could not be satisfactorily achieved, but here again an attempt was made to fix one by making use of each subject's eosinophilic mean prior to treatment and a figure arbitrarily set at 2 per cent. above this. The eosinophilic mean of each patient was calculated from the counts made in the ten-day period before treatment; the arbitrary figure was arrived at by noting, during the first few days of treatment, several associations of seizures with counts at least 2 per cent. above the average pre-treatment range. A possible connection was felt to exist between these two factors.

The plan followed was briefly this: (1) Provided the eosinophilic index remained below the agreed maximum increase of 2 per cent. on the individual mean, the dosage of each injection was regularly increased by one minim. (2) Should the eosinophilic index show a 2 per cent. increase or slightly over, then, whether a seizure had taken place or not, the previous injection was repeated. (3) Should the eosinophilic index show an increase considerably over 2 per cent. the next injection was decreased by from 1–3 minims according to the severity of the last reaction.

Group B was given a similar series of injections. These likewise were administered at intervals of 48 hours, the same dosage and rate of increase being followed in the two groups. In this group, however, eosinophil counts were omitted and dosage was uncontrolled. A series of 26 injections was given, consisting of 14 of the ordinary course and 12 of the continuation course. The principle applied in treatment was purely one of caution. Whenever a fit occurred the last dose was repeated, and should a series of fits occur over some days this same dose was repeated 48-hourly until the patient was free of fits. The usual routine increases were then resumed.

Skin Sensitivity following Desensitization.

One week following the completion of specific desensitization, the two groups were subjected to a series of skin tests. Each patient was only tested against those substances to which he or she had formerly given a positive reaction. Three months later, at the beginning of August, they were again

tested towards the same substances. The testing was undertaken to determine (1) the effect, if any, of desensitization on the skin reactions, and (2), whether this effect was temporary or relatively permanent. Could it be shown that former positives were rendered negative it was evidence, although not absolute, that desensitization had been successful. Furthermore a correlation might be shown to exist between the altered skin reaction and the fit incidence.

The results of both investigations were summarized as below and should be compared with the original findings as shown in Table I.

TABLE II.

Case.	Immediately after treatment.
1	Mixed house dust —, pork —.
2	Mixed feathers —, oats —.
3	Cheese +.
4	Cheese ++, onion —.
5	Cheese +, milk —, rice —, sardine —.
6	Cheese +, herring —.
7	Haddock —, herring —.
8	Cheese ++, salmon —.
9	Mixed house dust +, mixed feathers +.
10	Egg white —, mixed feathers +.
11	Mixed house dust ++, cheese +++.
12	Cheese —.

TABLE III.

Case.	Three months after treatment.
1	Mixed house dust —, pork —.
2	Mixed feathers —, oats —.
3	Cheese +.
4	Cheese ++, onion —.
5	Cheese +, milk —, rice —, sardine —.
6	Cheese +, herring —.
7	Haddock —, herring —.
8	Cheese ++, salmon —.
9	Mixed house dust +, mixed feathers +.
10	Egg white +, mixed feathers +.
11	Mixed house dust ++, cheese +++.
12	Cheese —.

COMMENT ON TABLES II AND III.

(1) In four instances (33 per cent.) all reactions were negative in both tables.

(2) In five of the remaining eight cases (Table II) negative reactions occurred

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towards one of two or more formerly positive allergens; in Table III this number had fallen to four.

(3) Four cases showed a lessened degree of positiveness; similar findings occurred in both tables.

(4) In one patient the original sensitivities remained unchanged.

(5) Negativeness once established was not quickly altered.

(6) In several instances the decrease in skin sensitivity paralleled the improvement in fit incidence.

(7) It might be inferred that desensitization had taken place in those cases where an improvement in fit incidence and mental condition was accompanied by negative skin reactions. In five instances (42 per cent.) these three factors were present.

(8) Where improvement was less evident or was absent there existed a corresponding lack of alteration in the skin reaction. In such cases a lesser degree of desensitization, or a failure to desensitize might be inferred.

Results of Treatment.

Two main factors were considered in assessing results, (1) decrease in fit incidence, and (2) improvement in mental condition.

Results on the whole were encouraging without being spectacular. It was too much to hope for complete remission of fits, or complete normality of thought and action in confirmed epileptics of many years' standing. Could it be shown that some improvement existed, no matter how small, then the investigation justified itself and was not without value.

Specific desensitization commenced on March 11, 1940, and was complete by the end of April. Observations were continued until March 11, 1941. During this period specific food elimination was maintained. Thus there was an interval of one year between the beginning of treatment and the final assessment of results.

Case Material.

Group A (Case 1), male, aged 32.

Before Treatment.

The seizures commenced at the age of one month and at first averaged ten daily. At this time they were mild in character. He was reared on the bottle and no connection was noted between feeds and fits. He attended a council school but was unable to learn to any extent. He left school at 13, and shortly after was sent to an Epileptic Colony, where he remained four years.

During childhood and youth the fit incidence fell considerably to about one per day, and later to about ten per month. The individual fits, however, greatly increased in severity. He was removed from the Colony to a mental hospital and had spent ten years there when he was transferred here on the outbreak of war.

During childhood and youth it was remarked that fits frequently occurred after eating ham. When this was fully evident to his family, ham was eliminated from

his diet and the number of fits diminished. During his four years at the Colony this connection continued to be observed. When he was allowed home on occasional vacations, his relatives noted that ham consumption was still followed by convulsions.

As a child he was said to have suffered from skin trouble which disappeared when he was a few years old. This was probably some form of infantile eczema. There was no further history of allergy in either the patient or his immediate relatives.

Mentally he is dull and listless but accessible and co-operative. Occasional attacks of mild excitement occur. He can perform simple supervised tasks about the ward.

The average monthly number of fits during the period 1937–1939 was 8·5.

Sensitivity.—(1) Group testing: Standard mixed inhalants and meats. (2) Individual testing: Mixed house dust and pork.

After Treatment.

During treatment four seizures occurred, and since then to date there have been an additional 49. This gives an average of 4.5 per month since treatment commenced. This figure compares very favourably with the monthly average of 8·5 for the past three years.

Mentally he has improved and is brighter and displaying more initiative. No attacks of excitement have taken place during the past year. He himself admits to feeling better and more alert. His general condition shows improvement and he has put on weight.

On skin testing he gave negative readings to both mixed house dust and pork. A similar reading was recorded three months later.

Result.—A marked fall in fit incidence, associated with general mental and physical improvement.

Group A (Case 2), male, aged 41.

Before Treatment.

He was the youngest of a large family, and owing to the early death of his mother was neglected as a baby. He was brought up on the bottle. When six months old he had a severe convulsion lasting for three and a half hours. He developed "catarrh of the stomach" at twelve months, and for the next three years was brought up on proprietary foods, such as Horlick's.

During this period he continued to be neglected. He did not walk until two, and epileptic seizures commenced at approximately six years of age. From this time onwards they occurred regularly. He might have several consecutively and then be free for months. As a boy they were not severe, and if seized while playing outside he would at once get to his feet when the fit was over, and go on with his game. He attended school and proved a clever scholar. Later he worked in an office. Finally the fits became so frequent and incapacitating that he was forced to give up an active life.

He has been an inmate of this Institution for over twelve years, and during that time has continued to have fits regularly. His eldest sister volunteered the information that seizures were more prone to occur after a meal containing porridge or potatoes. When these articles of diet were restricted he would be free of fits for a longer period.

It has been observed in this Hospital that he frequently has a fit in the early forenoon and that this follows a breakfast consisting chiefly of porridge.

As a child he suffered from urticaria for several years, but the condition left him at nine. His mother is said to have been sensitive to fish, and suffered from sick headaches following such a meal.

He has a good conceit of his own ability, but his comments, though clever, are superficial. He tackles a job with great resolve, but lacking application, quickly

discards it for another. He is mischievous and delights in the discomfiture of others. He is quick tempered, irritable and suspicious.

The average monthly number of fits during the period 1937–1939 was 11·6.

Sensitivity.—(1) Group testing: Standard mixed inhalants and cereals. (2) Individual testing: Mixed feathers and oats.

After Treatment.

During treatment ten seizures occurred and since then an additional 51 have been recorded. This gives an average of 5·1 monthly—less than half the average monthly figure of 11·6 for the past three years.

His mental condition has not improved concurrently with the fall in the number of fits and he remains mischievous and self-centred. There is, perhaps, less tendency to be quarrelsome.

On skin testing he was found negative to mixed feathers and oats. A similar reading was recorded three months later.

Result.—A marked fall in fit incidence, unassociated with any appreciable change in the mental condition.

Group A (Case 3), female, aged 33.

Before Treatment.

She was one of 14 siblings, was reared in poverty, and as a child suffered from rickets and intermittent biliousness. Towards puberty her physique improved. She was an average scholar and left school at 14.

Fits commenced at 18 and were severe from the start; they were infrequent and showed a predilection for the menstrual period. She retained her employment till her marriage. Following the birth of a first child several severe seizures occurred and she became violent and homicidal and was certified insane. She was discharged some months later, only to be readmitted during her second pregnancy in a similar maniacal state. She has remained here during the past nine years.

There was no personal history of allergy, but two of her sisters had infantile eczema and her paternal grandfather was subject to frequent "summer colds," probably allied to hay-fever.

Between fits she is as a rule comparatively rational in outlook, but periodically an attack of acute excitement develops, and this is generally, although not always, associated with seizures. She is at such times unmanageable, dangerously impulsive and lost to all sense of decency.

The average monthly number of fits during the period 1937–1939 was 5·1.

Sensitivity.—(1) Group testing: Eggs, milk, etc. (2) Individual testing: Cheese.

After Treatment.

During treatment there were six fits, and since then a further 28 have occurred. This gives a monthly average of 2·8, and shows a distinct improvement on the monthly average of 5·1 during the past three years.

Mentally there has been no improvement and she continues to have impulsive outbursts, during which she is quite unmanageable.

On skin testing a positive reaction to cheese was recorded, but in lessened degree. A similar reading was present three months later.

Result.—Some considerable improvement in fit incidence unassociated with mental improvement.

Group A (Case 4), male, aged 44.

Before Treatment.

He was reared first on the breast and later on the bottle. When aged about one year a series of convulsions occurred and these were repeated at intervals over

a number of months. On their disappearance he continued free till twelve years old, when typical major epileptic seizures made their appearance. From the beginning they were severe, but infrequent. He had a normal schooling and left at fourteen. Several short-lived attempts at maintaining himself followed, but the fit incidence increased and it was realized that an institutional life was necessary. He was sent to a colony for epileptics, but the increasing number and the severity of the fits affected his behaviour and he became noisy and troublesome. He was removed to this institution, where he has remained during the past eighteen years.

No personal history of allergy was obtainable. His mother is said to have suffered from bilious attacks as a young woman, and one of his sisters from a recurring skin condition of the hands, most noticeable each spring, when she worked in the garden—probably some form of urticaria.

Mental deterioration is marked and insight lacking. He is exalted and superior in manner and morbidly religious. At times he is deeply confused and impulsive. He is unemployable.

The average monthly number of fits during the period 1937–1939 was 21·7.

Sensitivity.—(1) Group testing: Egg, milk, etc. (2) Individual testing: Cheese and onion.

After Treatment.

The eosinophilic index was interesting in this case. It rose rapidly after the second injection, and following the third injection reached an extreme height of 8·5 per cent. (His normal mean count before treatment was 1·5 per cent.) During this period of abnormal reaction 15 fits occurred. A drastic reduction in dosage was effected, and the eosinophilic count fell steadily during the next two 48-hour periods. Later in treatment five further well-marked elevations in the counts occurred, the highest, however, only reaching 6·5 per cent. Four of these increases were associated with fits.

During treatment there was a total of 37 fits, and since then 203 have taken place. This gives a monthly average of 20, approximately the same as the average of 21·7 for the past three years.

His mental condition shows no improvement and he continues to be confused, irritable and aggressive. He is lacking in initiative, is unemployable and requires constant supervision.

Results were disappointing, as judged by the activity of the eosinophilic reactions it appeared reasonable to expect desensitization. Possibly the chronicity of the case and the frequency of the seizures did not admit of improvement.

On skin testing he remained positive to cheese, but was negative to onion. Three months later a similar reading was recorded.

Result.—No improvement in either fit incidence or mental condition.

Group A (Case 5), male, aged 32.

Before Treatment.

He was the youngest of six siblings, of whom four died in infancy. He was reared on the breast, and twelve months after weaning convulsions appeared and persisted during a period of two years. Typical major epileptic fits followed at the age of ten. They were comparatively few and mild in character to begin with, but rapidly increased in number and intensity. He was unable to learn and was sent to a special school. Later his mental condition worsened, and he became troublesome and unruly and landed in the hands of the police. He was transferred to a State Institution and later here, where he has remained for the past nine years.

As an infant he suffered from severe facial eczema and later from pruritus. Both conditions left him before puberty. It was noted that convulsions tended to follow a heavy meal or heavy smoking. His mother was sensitive to fish, and the eating of certain varieties was followed by sickness and urticarial wheals.

He is simple-minded and facile, but on occasion displays the typical epileptic

habitus: sulkiness, suspicion, irritability and obstinacy. After a bout of seizures he is excited, treacherous and impulsive.

The average monthly number of fits during the period 1937–1939 was 9·1.

Sensitivity.—(1) Group testing: Egg, milk, etc.; fish. (2) Individual testing: Cheese, milk, sardine, and rice.

After Treatment.

Seven fits took place during treatment and since then 43, giving a monthly average of 4·2—appreciably less than half the average of 9·1 for the past three years.

Recently there has been a distinct improvement mentally. He is brighter, more accessible and much less quarrelsome. His habits are cleaner and he is less destructive. The degree of mental deterioration in this case was such that any improvement must, of necessity, be purely comparative. Bearing this in mind one is justified in claiming a distinct improvement.

On skin testing he showed lessened sensitivity to cheese and gave a negative reaction to milk, rice and sardine. A similar reading was recorded three months later.

Result.—A distinct improvement in both fit incidence and mental condition.

Group A (Case 6), male, aged 36.

Before Treatment.

He was the third child of six siblings. As an infant he was delicate and suffered from gastro-intestinal irritation. He was breast-fed. During the period of dentition he was said to have had several "turns," but it was not clear whether these were actual convulsions. Epileptic seizures first made their appearance at the age of eleven. They were most severe and necessitated his almost immediate withdrawal from school. Attempts were later made to teach him at home, but unsuccessfully. As he grew older the fits became more frequent and incapacitating, and he was finally certified and sent to this institution. He has been here for 17 years.

In addition to his early gastro-intestinal disturbances he suffered from nettle-rash, frequently traceable to eating unripe fruit. One of his sisters likewise suffered from nettle-rash, although in her case no causal agent could be ascribed. His father is said to have been "asthmatic" as a young man.

He is cheery, childish and affable and likes to be noticed. Occasionally he is querulous and complaining and even impulsive, but on the whole is easily managed. He is capable of simple supervised tasks.

The average monthly number of fits during the period 1937–1939 was 6·9.

Sensitivity.—(1) Group testing: Egg, milk, etc., and fish. (2) Individual testing: Cheese and herring.

After Treatment.

The total number of fits during treatment was five, and since then 51 have occurred. This gives a monthly average of 4·7—somewhat better than 6·9, the average for the past three years.

There has been no significant change in his mental condition.

On skin testing he was found to have retained his sensitivity towards cheese, but to have become negative to herring. Three months later a similar reading was recorded.

Result.—Some improvement in fit incidence unassociated with mental improvement.

Group B (Case 7), female, aged 44.

Before Treatment.

Her infancy and childhood were uneventful. She attended school and proved an average scholar. From puberty onwards she became increasingly stout. This feature has persisted and she is at present subthyreoidic.

Fits began at the age of 20, and from the beginning were of the major variety. At first they were infrequent, one occurring every three or four months, but within five years their frequency had so increased that she was compelled to leave her employment. Following this she lived at home, but her deteriorated mental condition and increasing violence necessitated certification. She was transferred here on the outbreak of war.

As a young woman she suffered from migrainous attacks; no connection was noted between these and the seizures. One of her brothers has had periodical outbreaks of eczema throughout his life.

She is lazy, indolent and complaining and looks with disfavour on all her fellow patients. In conversation she is evasive and suspicious. In the records of her former institution she was further described as aggressive, abusive and threatening.

The average monthly number of fits during the period 1937–1939 was 8·1.

Sensitivity.—(1) Group testing: Fish. (2) Individual testing: Haddock and herring.

After Treatment.

Treatment ran a normal course and no undesirable symptoms were encountered. During treatment one seizure was recorded, but none have occurred since. This highly satisfactory result is particularly striking in view of the fact that there existed, during the past three years, a monthly average of eight fits. This means that in the past year one fit only has occurred where there were a previous 96.

Corresponding to the fall in fit incidence there has been an encouraging improvement in her mental condition. This has not been dramatic, but has been appreciable and progresses favourably. She is no longer sulky or petulant, and her former aggressiveness and suspicion have largely disappeared. She is more co-operative, and displays new interest and initiative.

On skin testing negative responses to haddock and herring were obtained, to both of which she was previously positive. A similar reading was recorded three months later.

Result.—A virtual cessation of fits, with considerable mental improvement.

Group B (Case 8), male, aged 39.

Before Treatment.

The youngest of a family of ten, his infancy and early childhood were normal. His parents died when he was 7 and he was boarded out. Fits first appeared at the age of 11, but were mild and few in number and did not interfere with his schooling. He left school at 14. After puberty there was a rapid and progressive increase in the number and severity of the seizures, and they became typically major in character. Thereafter mental disturbance quickly displayed itself. He has been an inmate of this institution for the past 14 years.

No personal history of allergy was obtainable, but a strong family history exists, his father suffering from asthma for many years, and dying from associated complications. At the present time one sister suffers from pruritus and another from sick headaches.

His temperament is typically epileptic. He is suspicious, aggressive, querulous and irritable. Inquisitive himself and a persistent meddler he bitterly resents reciprocation in kind. He freely exudes false accusations and general dissatisfaction. At times he is confused, impulsive and dangerous.

The average monthly number of fits during the period 1937–1939 was 6·7.

Sensitivity.—(1) Group testing: Egg, milk, etc., and fish. (2) Individual testing: Cheese and salmon.

After Treatment.

Early in treatment a series of severe seizures occurred, and the normal dosage increment was suspended until fits had been absent for 24 hours. Thereafter normal minim increases in dosage were resumed.

In all ten fits occurred during treatment, and since then a further 57. This gives a monthly average of 5·6 over the whole period—approximately the same as the monthly average of 6·6 for the past three years. No improvement in fit incidence could be claimed.

His mental condition likewise shows no change and he continues to be troublesome, aggressive and interfering.

On skin testing he continued to display sensitivity to cheese, but was negative to salmon. A similar reading was recorded three months later.

Result.—No improvement in either fit incidence or mental condition.

Group B (Case 9), male, aged 37.

Before Treatment.

He was reared on the breast, but was a weakly child and contracted every prevalent infection. Mentally, however, he proved alert and did well at school, till the commencement of fits at 14. It was noted about this time that he began to suffer from " bronchitis." This " bronchitis " was recurrent and was diagnosed later as asthma. These asthmatical attacks have occurred periodically ever since. The fits, once established, soon became frequent and severe. Five years following their first appearance he became unmanageable at home, was certified and sent here. He has been an inmate now for 18 years.

No correlation has ever been observed between his asthma and the seizures. A strong family history of allergy exists on the paternal side, his father suffering from asthma and two aunts from urticaria.

He is facile but not lacking in insight. He is amenable to discipline and a good and willing worker.

The average number of fits during the period 1937–1939 was 3·1.

Sensitivity.—(1) Group testing: Standard mixed inhalants. (2) Individual testing: Mixed house dust and mixed feathers.

After Treatment.

Treatment ran a normal and uninterrupted course. Three seizures occurred during this period and since then there have been a further 27. This gives a monthly average of 2·5—only slightly below the average of 3·1 for the past three years. No improvement in fit incidence could be claimed.

Mentally he is brighter and feels better in himself, but no dramatic change is to be noted.

On skin testing he continued positive towards mixed house dust and mixed feathers, but in a lessened degree. A similar reading was recorded three months later.

Result.—No change in fit incidence, but some slight improvement mentally.

Group B (Case 10), female, aged 32.

Before Treatment.

Seizures began at six years of age. Previous to this she was a completely normal child. The fits were severe from the first, but only one or two occurred monthly. Her capacity for learning was early affected and she was sent to a special school. As she grew older she became impulsive and difficult, and finally required certification. She has been a patient here for eight years.

No allergic history of any kind was obtainable, either personal or familial.

She is lazy, sulky and quarrelsome, and is most importunate in her demands on the staff. On occasion she has been impulsive and destructive. Although capable of usefully employing herself, she consistently refuses to do so.

The average monthly number of fits during the period 1937–1939 was 1·7.

Sensitivity.—(1) Group testing: Standard mixed inhalants, egg, milk, etc. (2) Individual testing: Mixed feathers and egg-white.

After Treatment.

Treatment ran a normal course, and during it three fits occurred. Dosage was modified as usual following each fit.

Since completion of treatment there has been one fit. This gives a monthly average of ·3—slightly better than 1·7, the average for the past three years.

Corresponding to the minor degree of improvement in the fit incidence, there has been a slight mental improvement. Although remaining indolent and unproductive, she has become more amenable and co-operative.

Skin testing showed lessened sensitivity to mixed feathers and gave a negative response to egg white. Three months later a similar degree of sensitivity was expressed towards mixed feathers, but she had again become positive to egg white.

Result.—A slight improvement in fit incidence associated with a minor degree of mental improvement.

Group B (Case 11), male, aged 36.

Before Treatment.

Accurate information of his infancy and childhood was unobtainable, but it appeared that he had always been simple minded and childish in outlook. Only two epileptic seizures had occurred prior to certification, the first when 14, and the second a month before removal here. He has been an inmate of this hospital for the past 19 years. For the first few years after admission fits occurred irregularly and at intervals of many months, but their incidence, especially during the past six or seven years, has greatly increased.

With the increase in fits he has deteriorated mentally. He is shiftless, suspicious, indolent and easily annoyed. He gives no thought to the comfort of others, although most solicitous of his own.

The average monthly number of fits during the period 1937–1939 was 5·1.

Sensitivity.—(1) Group testing: Standard mixed inhalants and egg, milk, etc. (2) Individual testing: Mixed house dust and cheese.

After Treatment.

Treatment was uninterrupted, although dosage adjustment, according to plan, was necessary owing to the occurrence of eight fits.

Following treatment 47 seizures have occurred. This gives a monthly average of 4·6—slightly less than the average of 5·1 over the past three years.

His mental condition, like the fit incidence, shows no significant change. He continues to be lazy, irritable and uncertain, displaying no interest in anything beyond his own immediate wants.

On skin testing no change was recorded in original sensitivities. This reading was confirmed three months later.

Result.—No improvement in either fit incidence or mental condition.

Group B (Case 12), male, aged 53.

Before Treatment.

His infancy and childhood were apparently normal. He left school at 13 and was rather below average. On leaving school he followed various occupations until the outbreak of the last war, when he joined the army. While serving abroad seizures first made their appearance. For many years they were mild and few in number, occurring only at intervals of many months. Later they increased in number and severity, and following an unusually severe attack he became outrageous and confused. His sister, with whom he lived, was unable to manage him and two years ago he was certified and removed here.

He has always had a thick, scaly ichthyotic skin, but beyond this no personal history of allergy was elicited. His sister has suffered throughout her life from chronic eczema affecting both legs.

He is quiet, sociable, simple-minded, and capable of partially supervised employment. He lacks the aggressiveness and irritability of the average epileptic. He is confused and depressed following a bout of fits.

The average monthly number of fits during the period 1937–1939 was 4·7.

Sensitivity.—(1) Group testing: Egg, milk, etc. (2) Individual testing: Cheese.

After Treatment.

Treatment was uneventful. Early in March three fits occurred but there were none in April or May. About the middle of June a series of 15 seizures occurred within the space of twelve hours. They could not be especially attributed to anything in the environment. After this he was entirely free from the middle of November, when he had a prolonged bout of 34 seizures. He passed into *status epilepticus* and died.

Up to the time of his death the monthly average was 2·2—somewhat less than 4·7, the average for the past three years.

Mentally he had displayed a distinct improvement and appeared to possess greater confidence in himself. He was employing himself usefully about the institution. His skin condition had likewise improved.

On skin testing he gave a negative reaction to cheese. This reading was confirmed three months later.

Result.—Died while still under observation.

Case 13, female, aged 27. When eight months old convulsions appeared and continued with some frequency for two years. They then disappeared, until the onset of puberty at 16. She was breast-fed for the first six months and thereafter bottle-fed. It was thought at the time of their first onset that the convulsions may have been due to teething or to poisoning from an infected bottle. She suffered from gastro-intestinal irritation for several years, but this finally left her about the age of seven.

She was never able to learn and had to be specially cared for. Since 16 she has been having seizures regularly. No history of allergy, either personal or family, could be obtained.

She is confused, inaccessible and resistive. An appreciable degree of dementia is evident. She is confined to bed and totally unemployable.

The average monthly number of fits during the period 1937–1939 was 4·9.

Sensitivity.—(1) Group testing: Egg, milk, etc. (2) Individual testing: Egg white.

Although she was found to demonstrate skin sensitivity as recorded above, no attempt was made to desensitize her. This was owing to the weakness of her general condition. She suffered from phthisis and has since died.

Case 14, female, aged 36. She was a normal baby and was breast-fed. She was always strong and healthy. Her schooling was without incident and her ability average. At 14 she left school, and about this time (and coincident with the onset of puberty) the first seizures occurred. They were major in character and severe, but at first occurred only at intervals of two months or longer. As time passed they increased in frequency until as many as 20 were present in a month. She was forced to give up her employment and live at home, but became increasingly difficult and was finally certified and sent to this hospital. She remained here for a period of four years.

Throughout her life she was subject to attacks of urticaria and several occurred during her confinement here. She had a strong antipathy towards cheese, although she occasionally partook of it. No connection between cheese consumption and fit incidence was ever noted. Nevertheless, it may have existed. No family history of allergy was obtainable.

For the most part she was quiet, docile and childish, but could be sulky and

difficult on occasion. Following a fit she was quarrelsome and confused. She died during desensitization.

The average monthly number of fits during the period 1937–1939 was 7·4.

Sensitivity.—(1) Group testing: Egg, milk, etc. (2) Individual testing: Egg white and cheese.

The above results in the group of twelve epileptics may be finally summarized as follows:

(1) A distinct improvement in fit incidence and mental condition (three cases).

(2) A lesser degree of improvement in fit incidence and mental condition one case).

(3) An improvement in fit incidence alone (three cases).

(4) An improvement in mental condition alone (one case).

(5) No improvement (three cases).

(6) Died (one case).

Conclusions.

Nine of the twelve patients treated gave some indication that at least a degree of desensitization had been achieved, while in four of this number the response amounted to a definite improvement. In one instance there had only been a single seizure in the past year, whereas prior to treatment the monthly average had been eight.

The majority of the epileptics were having fewer fits and several admitted to feeling better in themselves. They were, generally speaking, quieter and conducting themselves more rationally, and in consequence there was an easing of strain on the nursing staff and a lessening of friction with other patients.

The investigation, as a whole, tended to confirm the postulated relationship of allergy and epilepsy. The supporting facts were briefly these: (1) The preponderance of allergic manifestations in the personal and family history of the epileptic as compared with the psychotics and controls. (2) The epileptics displayed, as a group, greater sensitivity on skin testing. (3) Following desensitization skin sensitivities were lost or lessened in degree in every instance but one. This change in dermal responsiveness was accompanied in four cases by fewer seizures and increased mental acuity. (4) In four patients the personal history suggested a linking of specific protein and seizures. It was worthy of note that in each instance a positive reaction resulted from skin testing the subject for the suspected allergen. (5) Specifically directed treatment by elimination and desensitization was successful in nine patients in alleviating symptoms.

The intramuscular route was considered to give excellent results, provided the precaution was taken of guarding against possible overdosage. The establishment of a reliable guide to dosage control would be a distinct advantage

in treatment. In this connection it is possible that further experiment might yet make practicable the use of the eosinophilic index.

In conclusion three points emerge: (1) There is a wide field existent for systematic research into the relationship of allergy and epilepsy. (2) The possibility of sensitization should never be overlooked in the investigation of idiopathic epilepsy. (3) Investigations should be undertaken and treatment instituted not only in recent cases or young subjects, but also in those who are hospitalized and regarded as chronic.

I am indebted to Dr. Grant, Medical Superintendent of Dykebar Mental Hospital, for permission to carry out this investigation.

Summary.

(1) The literature on allergy and epilepsy is briefly surveyed.

(2) A method of skin testing is described and observations made on other relevant detail.

(3) Investigations have been conducted into personal and family histories in 72 individuals in a search for allergic manifestations.

(4) A series of skin tests has been performed on a group of 14 epileptics.

(5) The treatment of allergy is briefly reviewed and a method advocated, combining specific elimination and desensitization.

(6) Twelve epileptics have received a course of specific intramuscular injections. In six of the cases an attempt was made to control dosage by reference to variations in the range of the eosinophils in the differential count.

(7) Following treatment two further series of skin tests have been recorded with an interval of three months between each.

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