NEUROPATHIC MANIFESTATIONS IN INFANTS AND CHILDREN AS A RESULT OF ANAPHYLACTIC REACTION TO FOODS CONTAINED IN THEIR DIETARY *

W. RAY SHANNON, M.D.

ST. PAUL

The close association of the exudative and neuropathic diatheses suggests a causal relationship. The frequent anaphylactic nature of the former [1] would seem to point toward a similar cause in the latter. It is my purpose in this paper to discuss certain nervous manifestations in infants and children from the standpoint of anaphylactic cause.

It is hardly necessary to call attention to the frequent occurrence of the exudative and neuropathic diatheses in the same individual. All observers recognize the common association. However, it seems to have been generally held that this relationship is nothing more than accidental. Czerny considered it so.[2] He felt that the almost universal presence of the neuropathic diathesis in one or both parents of children with the exudative diathesis led, as a natural result, to the neurotic child. The degree to which the infant was affected by this nervous environment determined, to a certain extent, the obstinacy and severity of the exudative manifestations. Pfaundler [3] stated that the sneezing in coryza, pertussoid in bronchitis, asthma in bronchiolitis, severe colic in enteritis, etc., were dependent, to a certain degree, on the coexistence of a neuropathic diathesis along with the exudative diathesis.

This common association, together with the fact that frequently in the same individual the symptoms of one, and again the symptoms of the other diathesis, will seem to predominate, led me to the opinion that not infrequently the symptoms of both conditions might be due to the same underlying factor. Inquiry revealed the fact that often nervous patients have a history, either personal or familial, of exudative disturbances, and the frequent anaphylactic basis for the exudative phenomena suggested that the nervous symptoms might also be due to this cause. Therefore, this investigation was undertaken to see if this might not be the case clinically.

The cases presented are of three types; first, the type in which the symptoms of both diatheses were plainly present; second, the type in

* Received for publication March 28, 1922.

* From the Miller Hospital Clinic.

1. Shannon: Minnesota Med. **5**:137. (March) 1922.
2. Czerny: Monatschr. f. Kinderh. **7**:1. 1908.
3. Pfaundler: (Quoted from Leo Wolf). Jahrb. f. Kinderh., **4**:175.

Downloaded From: http://archpedi.jamanetwork.com/ by a University of Michigan User on 06/17/2015

which the present symptoms were nervous but in which there was a definite exudative history; and third, the type in which the symptoms were those of the neuropathic diathesis without a history of frank exudative phenomena preceding. With one case experimentation was possible.

REPORT OF CASES

CASE 1. A girl, 5 years of age, presented an uriticarial eruption and asthma. The mother stated that the patient was very high-strung and nervous. There was a history of hay-fever in the father and of eczema in several cousins. Skin tests revealed positive erythematous reactions to several foods of which the patient was eating a great deal. Removal of the offending foods from the patient's diet resulted in early relief from nervous manifestations and from the uriticaria and asthma.

CASE 2. A boy, 2 years and 8 months of age, had a history of a very itchy skin eruption, apparently of an urticarial nature, rather loose stools, and extreme nervousness. Whereas he normally slept well at night and took a nap during the daytime, of late he would not sleep at all during the day and very poorly at night. He was very irritable.

Cutaneous tests showed erythematous reactions to a number of foods he was eating. Modification of the diet and eliminating as much as possible the foods to which he was sensitive resulted in complete disappearance of the skin and nervous symptoms in two weeks' time. The child became himself again, was not irritable, slept well at night, and took a long nap during the daytime.

CASE 3. A boy, 4 years old, had a history of eczema and asthma. He was extremely high-strung and very nervous. His appetite was rather poor and he was very finicky about what he ate. He slept poorly at night. The mother complained that he could not sit still and that he was very hard to manage. Skin tests revealed erythematous reactions to a large number of foods and to a number of animal emanations. The diet was regulated and he was instructed to stay away from the animals to whose proteins he was sensitive. Relief from asthmatic symptoms had occurred nine days later and the eczema had improved considerably. Eighteen days after the tests were performed he was still free from asthma and there was only a slight chapping of the cheeks. The nervousness had improved greatly. His general restlessness was gone. He slept better at night and slept well during the daytime. His appetite was very good and he had gained 2½ pounds in weight. At the present time, one month after the institution of treatment, the improvement has continued.

CASE 4. A girl, 28 months old, was brought in because of an urticarial eruption and nervousness. Local treatment for the urticaria only was advised. Three weeks later she was brought back. The skin condition seemed improved, but the mother stated that the child was very irritable. She was unruly, peevish, ate poorly, and did not sleep well.

Skin tests revealed positive reactions to a number of foods the patient was eating in rather large quantity. These included egg and wheat. A diet was advised eliminating, as nearly as possible, the offending foods. Improvement was noted one week later but the mother said that she had been giving store cookies containing both egg and wheat to the patient. These were discontinued and after another interval of two weeks there was considerable improvement, especially in the nervousness. The mother asserted that the child "could be reasoned with." On one occasion the patient had been given spaghetti and tomatoes for her evening meal and both skin and nervous symptoms were much worse thereafter. At the present time, six weeks after the tests were performed, the nervousness is gone and the skin is clear.

CASE 5. A boy, 12 years of age, had been subject to eczema when an infant, to hives as he grew older, and still later to attacks of asthma. All these symptoms had been absent for a number of years, with the exception that he had

Downloaded From: http://archpedi.jamanetwork.com/ by a University of Michigan User on 06/17/2015

had an attack of urticaria a few months previous to the first observation. The present complaint was that of fever for the past few days, extreme nervousness, constant stuffiness in the nose, occasional attacks of vomiting, and frequent headaches. He was extremely introspective, cried easily, was very irritable, and was constantly "out of sorts."

A period of hospital study revealed a chronic inflammatory condition of the nasal sinuses. Treatment of this condition resulted in relief from the headaches and disappearance of the fever and nasal obstruction. However, the nervousness remained.

Skin tests revealed sensitization to several foods, a number of pollens, although the parents had never suspected the presence of hay-fever, and to horse dandruff and dog hair. A diet was advised and the patient instructed to stay away from dogs and horses.

Prompt improvement in the nervous symptoms resulted and this has been permanent over a period of seven months, except for a single attack of vomiting.

CASE 6. A boy, 8 years old, was brought in because he was extremely irritable, did not eat well, was cruel to his playmates, and was unable to apply himself at school. As a result of the latter condition, he spent two years in the first grade.

He had been perfectly normal, except that he had had head colds almost from birth until he was 4 years old. At that time he had had a series of convulsions without ascribable cause. He was studied by nerve specialists, internists, and eye, ear, nose and throat men, the final impression of the physician in charge being that the convulsions were due to a "food poisoning" of some kind. There had been no convulsions since that time.

A complete physical examination, including blood, spinal fluid and urine studies, Wassermann test, Pirquet test, failed to reveal anything abnormal. There was no family history of sensitization phenomena. Cutaneous tests revealed positive erythematous reactions to wheat, spinach, egg white, whole egg, pear, orange, pea, beef and figs. Questionable reactions were obtained to lactalbumin and banana. The patient was instructed to eat no wheat cereal or pastries, spinach, egg white, pea, orange, pear, beef, figs, or banana. He was to eat rye bread.

Nothing was heard from him for six weeks, when the mother reported that the boy had been a different child from the time he had gone on the diet. His irritability was lessened; he was no longer cruel to his playmates; he was doing well in school, and his appetite was good. When heard from again three months after the diet was instituted the improvement had continued and he had made his grade in school without difficulty.

CASE 7. A boy, 9 years of age, suffered from extreme nervousness and attacks of vomiting. The periodic attacks ordinarily came on infrequently, not oftener than once a month. Usually he would vomit but once but was always indisposed for several days thereafter. Between the attacks he was irritable, slept poorly, and was very finicky about what he ate. He was extremely high-strung. For the past two weeks he had been vomiting every third day, would eat almost nothing between attacks, and was so irritable that he was a problem to his parents.

His past history was negative for protein sensitization, with the possible exception that he had been a difficult feeding case from 3 to 14 months of age. From that time until four or five years he had been perfectly well. The vomiting attacks began at that time. He always coughed when he caught cold. When first seen he had been under treatment for some time for nasal sinusitis.

The immediate family history was negative for asthma, hay-fever, urticaria, or eczema. One sister had had similar vomiting attacks at one time in her life. One cousin could not eat eggs because they poisoned her. The paternal grandfather had had attacks of difficult breathing in his old age which apparently resembled asthmatic attacks.

Downloaded From: http://archpedi.jamanetwork.com/ by a University of Michigan User on 06/17/2015

Physical examination revealed nothing except that the patient was somewhat pale and undernourished. He was, therefore, tested with the foods of his dietary. Positive erythematous reactions were obtained to wheat leucosin, wheat gliadin, wheat proteose, pea, pineapple, potato and navy bean. The reactions to fig, brazil nut and rye were questionable.

The patient was instructed to eat no peas, navy beans, string beans, lima beans, pineapple, figs or brazil nuts. He was to eat potato no more than four times weekly, and no wheat cereal or pastries made from wheat flour. Rye bread only was to be eaten, with the exception of a small amount of white bread toast. Arrowroot or corn-starch were to be used for thickening gravies.

Improvement was almost immediate. There were no more vomiting spells. His appetite became ravenous. The mother said that she could not "fill him up." All signs of nervous irritability ceased very shortly after the diet was instituted. He began to sleep all night and to waken refreshed, which he did not do before. During the following month his class standing rose from thirteenth, where it had been constantly for five months past, to eighth, without any conscious effort on his part. At present, two and a half months after the diet was prescribed, there has been no return of either nervousness or vomiting.

CASE 8. Girl, aged 5 months, suffered from undernutrition.

The family history was unfortunate. The child was illegitimate and nothing was known of the father. The mother was committed to an institution for the feebleminded after deserting the infant.

The baby was partially breast fed for two months and since that time had been fed on milk mixtures. Cream of wheat was added to the infant's diet and seven days thereafter it was noticed that the child was extremely restless. There was constant movement of the arms and legs, with jerky movements of the entire body. The infant constantly turned and twisted in her crib. She cried incessantly day and night and slept but little throughout the twenty-four hours.

No cause was found on physical examination. There was no evidence of infection; the skin was clear and the stools normal. The symptoms were attributed to a nervous diathesis, dependent on the questionable heritage, and bromids were prescribed. These afforded marked relief and were discontinued after a short time. The infant immediately reverted to her former condition. Again bromids were given and the condition was controlled for a considerable period. However, they gradually lost their effect and about three months later (January, 1922), the patient's condition was as bad as it had been before the bromids were started.

January 25 cutaneous tests were performed with several cereals, vegetables and cow's milk. Positive reactions were obtained to wheat leucosin, proteose and globulin. All of the rest were negative. Wheat cereal was discontinued and oatmeal substituted. The bromid was discontinued.

One week later the child's disposition had changed remarkably so that it was noticed by all who came in contact with her. She slept all night and was playful and happy during the daytime. She cried but little. She had gained 7½ ounces during a period of four days.

February 5 cream of wheat was again added instead of the oatmeal. Twelve hours later a return of the old irritability was noticeable. She was very restless all the next day, turning, twisting, and throwing herself about in her crib. That night she slept less well and cried a part of the night. The symptoms continued throughout the seventh and that night she cried all night. February 8 the cream of wheat was discontinued and oatmeal again substituted. Improvement was prompt and by the night of the thirteenth the patient slept all night. By February 17 she was happy and playful, as she was during the first experimental period. Since that time she has remained so.

Of the cases cited the first four presented skin eruptions. The natural explanation for the nervousness in these cases is that it is the

Downloaded From: http://archpedi.jamanetwork.com/ by a University of Michigan User on 06/17/2015

reasonable accompaniment of the skin irritation. However, in all but Case 1 the nervous manifestations were out of all proportion to the severity of the skin lesions. Nevertheless, the nervous disturbances cleared up under specific therapy directed at the cutaneous, and, in some cases, the respiratory symptoms. Furthermore, in Case 4 the skin lesions were better at the time of the second visit than they were when the patient was first seen, whereas the nervousness was much worse.

Case 5 presented no skin eruption to account for the nervousness. True, there was a chronic focus of infection in the nasal sinuses which might, in a measure, have accounted for at least a part of it. However, under treatment this focus cleared up without improvement of the nervous symptoms, and it was not until the unexpected, wide-spread sensitization was found and treatment directed against this factor was instituted that improvement in his neuropathic tendencies occurred. Whether the nervous symptoms were due mainly to food, pollen or animal sensitization is purely conjectural and immaterial since we should expect that they might be the result of all these anaphylactic causes.

Cases 6 and 7 were purely nervous cases. While an anaphylactic basis for Case 7 was suggested by the history of periodic attacks of vomiting,[4] such attacks are also described as being one of the manifestations of the neuropathic diathesis. The results obtained in each case were so definite as to leave no doubt that the symptoms complained of were due to anaphylactic reactions to foods contained in the diets of the patients. In Case 8 it was possible to relieve or bring on the nervous symptoms by removing from or adding to the patient's diet the food to which she was sensitive.

That anaphylaxis might be responsible for nervousness in man through irritation of the nervous system is sound theory. Anaphylaxis is fundamentally a nervous phenomenon. Besredka emphasized this fact and founded his method for the production of shock on this principle.[5] The symptoms as seen in the experimental animal support his contention. The extreme irritability and restlessness noted immediately on injection, the scratching of the muzzle, frequently the sneezing, the dyspnea due to bronchiolar spasm, later the sudden hopping movements, and finally the convulsion itself are undisputable evidence that the nervous system is profoundly affected.

In man nervous manifestations are inseparably associated with anaphylactic phenomena. The extreme nervousness noted in individuals accompanying attacks of asthma, hay-fever, urticaria and eczema are common knowledge. Often these attacks have been attributed to

4. Schloss: Am. J. Dis. Child. **19**:433 (June) 1920.
5. Besredka: Anaphylaxis and Antianaphylaxis (English Translation). 1919, C. V. Mosby Co., St. Louis, p. 13.

Downloaded From: http://archpedi.jamanetwork.com/ by a University of Michigan User on 06/17/2015

nervousness, the patient not recognizing the fact that, perhaps, both the nervousness and the attack are ascribable to the same cause.

The effects of drugs on anaphylactic phenomena are further support for the nervous origin of the symptoms. Epinephrin, so valuable in asthma and urticaria, atropin and even morphin are notable drugs that act on the nervous system. Even general anesthetics greatly modify the character of an anaphylactic shock.

There is, then, an abnormal condition occurring very commonly in infants and children which would seem to give rise fundamentally to irritative phenomena of the nervous system. Is it not reasonable that such a phenomenon might give rise to all manner of symptoms ascribable to nervous origin within the body? Might it not be responsible for any of the symptoms frequently placed under the caption of the neuropathic diathesis? In fact, is there any limit within the field of the so-called functional nervous diseases beyond which such a cause could not be operative?

SUMMARY

Eight cases showing marked evidences of the presence of the so-called neuropathic diathesis in infants and children have been presented. In four of these definite evidence of the exudative diathesis was also present, while in still another there was a positive history of such a condition in the past. The remaining three cases gave no evidence suggestive of the presence of an exudative diathesis. All the patients showed the presence of protein sensitization by cutaneous tests. All showed definite relief from the nervous symptoms on the institution of specific therapy directed at the proteins to which they were sensitive. In all but one of the eight cases the proteins concerned were those of foods contained in the dietaries of the patients. In one case animal emanations or pollen proteins might have played a part. In one case the nervous symptoms could be relieved or brought on by the exclusion from or the addition to the diet of the food to which the patient was sensitive. Evidence is presented showing that anaphylaxis is a sound, theoretic basis for the explanation of many of the symptoms of the so-called neuropathic diathesis.

CONCLUSIONS

1. Many of the symptoms of the neuropathic diathesis in infants and children are not infrequently the result of irritation of the nervous system resulting from anaphylactic reactions to food proteins to which the patient has become sensitized. It is recognized that any protein to which the patient is sensitive might also be causative.

2. The frequent association of the exudative and neuropathic diatheses in infancy and childhood is, therefore, something more than accidental, the presence of each frequently being attributable to the same cause.

Downloaded From: http://archpedi.jamanetwork.com/ by a University of Michigan User on 06/17/2015