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ACRODYNIA

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*Reprinted from The Journal of the American Medical Association
Feb. 14, 1925, Vol. 84, pp. 495-498*

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AMERICAN MEDICAL ASSOCIATION
FIVE HUNDRED AND THIRTY-FIVE NORTH DEARBORN STREET
CHICAGO

ACRODYNIA*

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PORTLAND, ORE.

It is questionable whether the disease that American writers are calling acrodynia is the same as the one which occurred in epidemic form in France in the year 1827, and within two years had attacked between forty and fifty thousand people. The term acrodynia (derived from two Greek words, meaning extremity and pain) was first given by Chardon in 1830 to this epidemic disease.

Acrodynia, or epidemic erythema, is a disease largely affecting adults and is characterized by an erythematous dermatitis especially affecting the palms and soles and followed by pigmentation. It is also followed by vomiting and diarrhea and frequently by cramps and spasms of the muscles, sometimes by paralysis of the legs and general anasarca. It generally runs a course of from two to four weeks, and recurrent attacks are not uncommon.

Recently, Petren,¹ in Sweden, pointed out the great probability of the famous acrodynia epidemic having been due to arsenical poisoning. Arsenic was used in the French wine districts for destroying the parasites that attack the grape vines.

The condition we are calling acrodynia in the United States occurs sporadically and only in infants and young children, and differs greatly in its clinical course from the disease described by the French writers. However, the name is being used in recent medical literature and will probably stay. It is a smooth sounding word and easy to remember, though not particularly descriptive; but many names of diseases are open to criticism. Swift of Adelaide, Australia, called it erythroedema, but was not satisfied with the name, as

* From the Department of Pediatrics, University of Oregon Medical School.

1. Petren, Karl: Acrodynia, *Rev. neurol.* **37**: 812 (July-Aug.) 1921, cited by Weber, F. P.: Erythroedema, *Brit. J. Child. Dis.* **19**: 17 (Jan-March) 1922.

there is no edema. Clubbe of Sydney referred to it as pink disease, a name which accentuates the most evident symptom and the one most commonly used in Australia. Dermato-polyneuritis has been suggested by Hugh Thursfield² of London, a good term, as it specifies the structures involved.

It is a disease of the skin and the nervous system involving the vasomotor centers, the motor and the trophic nerves, but affecting particularly the sensory nerves. It is unfortunate that we do not have a suitable name for this striking clinical picture.

HISTORICAL

Is this a new disease in the United States? It does not seem possible that it could have existed previously and not have been recognized. While there are variations in the severity of the symptoms in different patients, the clinical picture as a whole is classical. It is as clear cut and definite as poliomyelitis or a meningitis.

I saw my first case in 1914, and felt that I had not seen anything like it before. During the next five years I saw several more cases; I exhibited the patients to a number of clinicians, but no one knew what the disease was.

In January, 1920, I³ read a paper on this disease before the North Coast Pediatric Society, in Seattle, reporting ten cases. At that time there was absolutely nothing in the medical literature of the United States on the subject. Weston⁴ of Columbia, S. C., reported these cases before the section on Diseases of Children at the New Orleans session of the American Medical Association in 1920, calling them acrodynia.

Byfield of Iowa City had observed this condition for a number of years and prepared a paper on the disease for the 1917 session of the Association; unfortunately, it was not read or published, except by title. In November, 1920, Byfield⁵ reported seventeen cases, and his article was the best and most thorough description of the disease that had been published.

2. Thursfield, J. H., and Paterson, D. H.: Dermato-Polyneuritis, Brit. J. Child. Dis. **19**: 27 (Jan.-March) 1922.

3. Bilderback, J. B.: A Group of Cases of Unknown Etiology and Diagnosis, Northwest Med. **19**: 263 (Oct.) 1920.

4. Weston, William: Acrodynia, Arch. Pediat. **37**: 513 (Sept.) 1920.

5. Byfield, A. H.: A Polyneuritic Syndrome Resembling Pellagra-Acrodynia, Seen in Very Young Children, Am. J. Dis. Child. **20**: 347 (Nov.) 1920.

Brown⁶ and his associates of Toronto have made an excellent contribution to the study of the disease. Zahorsky⁷ of St. Louis has observed a number of cases, has been greatly interested in this condition, and has written several papers on the subject. His description of the clinical picture of the disease is excellent.

Probably there are now reports of more than a hundred cases that have been published in the United States during the last four years.

However, for more than thirty years the condition has been recognized in Australia as a distinct clinical entity. Littlejohn⁸ states that the disease was first described by Swift of Adelaide in 1914, under the name erythroedema.

At the Australasian Medical Congress, held in Brisbane in 1920, Dr. Jeffreys Wood of Melbourne stated that he had frequently seen cases of the disease in Melbourne for the past thirty years and that his predecessor at the Children's Hospital, Dr. William Snowball, had recognized the complaint and was in the habit of referring to the patients as the children with the "raw-beef" hands and feet.

Clubbe has been familiar with the disease in Sydney for the last thirty years. However, even though the disease had existed for many years in Australia, no one had published an article on the condition until Swift read his paper before the Australasian Medical Congress at Auckland, New Zealand, in 1914. To Dr. Swift belongs the credit of being the first clinician to describe this condition (as it exists in children) under the name erythroedema.

CLINICAL PICTURE

While there are some variations in the symptoms, the cases as a whole are markedly similar. In pediatric practice we see many children that impress one as being more critically ill. However, in a well advanced case of acrodynia in a young child, the patient is a picture of abject misery; no one could look more utterly wretched. While in bed, the patient curls up and burrows his head in the pillow, or sits up with his face

6. Brown, Alan; Courtney, A. M., and MacLachlan, I. F.: A Clinical and Metabolic Study of Acrodynia, *Arch. Pediat.* **38**: 609 (Oct.) 1921.

7. Zahorsky, John: Acrodynia in Infants, *J. Missouri M. A.* **19**: 296 (July) 1922; Semeiology of Pink Disease, *J. A. M. A.* **79**: 1975 (Dec. 9) 1922.

8. Littlejohn, E. S.: Pink Disease, *M. J. Australia* **1**: 689 (June 23) 1923.

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held down between his legs. If carried, the child will not hold his head up and begs piteously to be put back in bed. This is particularly so in the cases with photophobia. The child whines almost constantly and dislikes to be disturbed, so that it is very difficult to make an examination. On the face is an expression of abject wretchedness, a picture of extreme mental misery. The eyes are dull and lusterless and denote suffering, reminding one of a wounded animal.

Paresthesia and pain of the hands and feet seem to be constant. The pain at times, particularly at night, is excruciating. The older children say that their hands and feet itch and burn like fire, and they will ask to have ice placed on them. Regardless of age, all the patients will rub their hands and feet together for hours. There may be areas of cutaneous anesthesia, but it has been very difficult to be positive about it.

The mental state varies greatly. At times the child acts maniacal, throwing and tossing himself about as if possessed, and being with great difficulty kept in bed. This is followed by a period of depression with marked apathy and stupor.

Insomnia has been present constantly for weeks at a time, and does not respond to treatment. Bromids, chloral and phenobarbital (luminal) have no effect, and not even morphin, unless given in large doses hypodermically.

I have never seen a true paralysis; but the muscles are soft and flabby, and all muscular movements are made slowly. The patellar reflexes are frequently diminished or abolished, but occasionally are markedly increased.

One of the dramatic occurrences is the loss of teeth; sometimes all that have erupted. Frequently before any pathologic condition of the mouth has been recognized, a perfectly sound tooth will be found in the child's bed. Then it is noticed within a short time that the other teeth are becoming loose in their sockets and finally drop out. The mucous membrane of the mouth seems a little redder than normal, but not spongy and swollen. However, after the teeth are lost an infection may occur in the mouth, with necrosis and shedding of the jaw bone for weeks. At this time the mouth presents an appearance similar to ulcerative stomatitis; the gums are swollen and ulcerated; saliva is profuse, and the odor fetid.

In the later cases, because I have learned to watch the mouth closely, I find that the gums, particularly about the incisors, are a deep, dusky red, even when there is no loss of teeth. The tongue frequently has a raw beef color.

The most striking symptom is the pink color of the hands and feet. The erythema is more marked at the ends of the fingers and toes, shading off imperceptibly at the wrist and not extending up the arm. The line of demarcation is not abrupt, as in pellagra. This involvement of the hands and feet is symmetrical and practically constant, often fading, to reappear after a week or ten days. The erythema is not as marked on the dorsal surface of the feet. Frequently, fine red papules not larger than a pin head develop on the erythematous background. Desquamation occurs at frequent intervals, involving the palms and soles but particularly the fingers and toes. This is a marked and distinctive symptom. The palms and soles are pigmented, having a peculiar purplish-pink color.

The hands and feet are cold and clammy, and feel as if they had been kept in water for a long time. They appear swollen, but there is no edema. Occasionally the lips, cheek and tip of the nose are a brilliant pink. The eruption of the body and extremities is not constant, and it frequently fades, leaving areas of slight pigmentation. It reappears at frequent intervals and as a rule is a pink disseminated maculopapular-papulovesicular rash, greatly modified at times by the irritating perspiration that macerates the skin. The perspiration is marked and occurs over the entire body, saturating the bed clothing. I do not know of any disease in which the perspiration is so excessive and constant. The saliva is increased, and will often run from the mouth in a small stream during sleep. The nails in many cases are purplish, and occasionally are lost. Marked anorexia is an almost constant symptom, with consequent loss of weight. Vomiting rarely occurs. The bowel movements are often loose and very foul. Photophobia occurs in many children, often lasting for months. In a well established case, the temperature is normal or, at most, only a degree or so higher unless there are complications, as a pyelitis.

LABORATORY FINDINGS

The nose and throat cultures are negative. The red blood corpuscles are slightly decreased; the white corpuscles are from 8,000 to 24,000; there is a relative increase in polymorphonuclears. The blood Wassermann and the Pirquet reaction are negative. The urine occasionally contains a small amount of albumin and pus cells. The spinal fluid is clear and not under increased pressure; there is no increase in cells. The spinal fluid Wassermann reaction is negative.

The course of the disease is essentially chronic. It develops slowly and insidiously. At first it is noticed that the child is listless and irritable, the appetite is poor and fever of a moderate degree occurs. It may persist for two or three weeks, and cannot be accounted for except in some cases in which there is a reddened throat and coryza is present. After a long period of invasion, it is noticed that the hands and feet are pink; pain, itching and burning occur in them; transitory rashes appear on the trunk and extremities; perspiration becomes noticeable; insomnia and general wretchedness become marked. Then it dawns on us that we are confronted with the classical picture of a bizarre symptom-complex that, for the lack of a more appropriate name, we call acrodynia.

While the disease may last several months, recovery is complete with no sequelae.

A few deaths have occurred from intercurrent infections, tuberculosis or starvation. In the few earlier postmortems that were performed, nothing definite was found in the cerebrospinal system to account for the symptoms. Recently, Paterson and Greenfield⁹ reported five cases, giving the necropsy findings in two. Their pathologic report is the most thorough and brilliant contribution that has been made in regard to the disease.

Their examinations showed considerable myelin destruction in some fibers of the peripheral nerves. In the calf muscles, the majority of the finer nerve bundles were completely demyelinated, and bundles containing from ten to twelve nerve fibers showed complete demyelination of all but two or three. In the popliteal space, on the other hand, only a small propor-

9. Paterson, D., and Greenfield, J. G.: Erythroedema Polyneuritis, *Quart. J. Med.* 17: 6 (Oct.) 1923.

tion of the fibers of the main nerve trunks showed myelin degeneration. In the central nervous system in both cases, there was a diffuse increase of small cells in the gray matter, especially in the lumbosacral enlargement of the cord. Their conclusion is that there is pathologic evidence of peripheral neuritis and of chronic inflammatory changes in the spinal cord and nerve roots, in which the sensory nerve fibers are affected more than the motor nerve fibers.



Fig. 1.—Typical early desquamation; skin, vivid pink.

ETIOLOGY

The etiology of acrodynia is unknown. Evidently it is not a deficiency disease, but the symptoms are suggestive of other deficiency diseases, notably pellagra. It may occur in breast fed babies or in young children who have a generous diet of milk and vegetables. Most of the cases coming under my observation have been from the small towns or farms in Oregon, where an exceptionally good environment existed, and in no case has the food seemed to be deficient.

It is probably an infection, or the aftermath of one. In many cases even with a normal temperature there is a leukocytosis with a relative increase in polymorpho-

nuclears. Many of the children give a history of having been ill a few weeks earlier, at which time the distinctive symptom has been fever. Some, but not all, may have had a coryza concurrent with the fever. Thousands of children have an upper respiratory tract infection, but rarely is it followed by anything that even suggests acrodynia. The portal of entry may be the nasopharynx as it is, in many diseases, such as poliomyelitis and meningitis, but we have no definite proof. It has been suggested that it is a sequela of influenza. Considering the fact that several million cases of influenza have occurred in the United States during the last few years, it would seem that cases of acrodynia in adults should have followed.

Acrodynia has as clear cut and definite symptoms as any other disease. It lends itself easily to description; consequently, the reports have all been monotonously alike. Many excellent papers have been written describing with infinite detail the clinical picture. However, what is wanted is the known cause that may lead to a definite remedy. Laboratory investigations have been uniformly negative.

Inoculation experiments with the spinal fluid might be of interest; it is questionable, however, whether small animals would be susceptible even though the spinal fluid contained the specific organisms. Flexner and Lewis, by intracranial inoculations of monkeys with the spinal cord of a patient dying of poliomyelitis, had no difficulty in reproducing the disease and transmitting it through an indefinite series of monkeys. If a similar experiment could be performed with a case of acrodynia, we could prove definitely that the disease was an infection.

TREATMENT

Unfortunately, there is no specific treatment. Until we know more about the etiology, the treatment will remain symptomatic.

Atropin for the perspiration and calamine lotion for the irritation of the skin constitute the treatment.

When one observes a child with acrodynia and realizes how little he has to offer, he feels like a therapeutic pauper.

The diet should be simple, nutritious and rich in vitamins. However, as acrodynia is not a deficiency disease, the kind of food will not shorten the course of the complaint.

Many children will refuse all food, and it will be necessary to feed by gavage.

Dr. Jay Schamberg, in describing pellagra, states that the most characteristic symptoms are indicated by the alliterative formula, the three D's—dermatitis, diarrhea and depression. Paraphrasing the formula, the

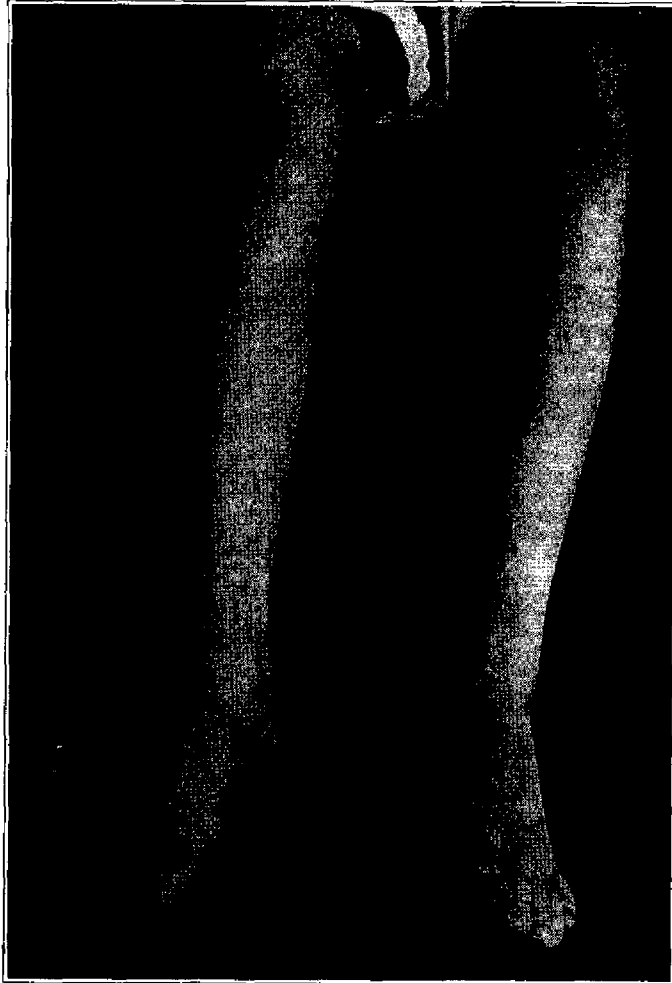


Fig. 2.—Maculopapular rash of extremities.

characteristic symptoms of acrodynia are denoted by the six P's—pain, pink hands and feet, peeling, prostration, paresthesia and perspiration.

I have had up to the present time twenty cases; they are all markedly alike. A report of the individual cases would simply be a monotonous repetition. The usual incidence of the disease occurs in children of from 6

months to 2 years. The following case is that of the oldest patient I have ever had, 7½ years, and consequently he has been able to describe subjective symptoms which naturally has been impossible in the younger children.

REPORT OF CASE

History.—C. E., a boy, aged 7½ years, came as an office patient, April 8, 1924, with a history of not having felt well for several weeks. Recently he had become restless and nervous, and he was easily fatigued. He complained that his back and legs hurt him. The child did not appear particularly ill. A physical examination was negative, except that the throat was slightly reddened. The temperature was 99.8 F.; the white blood count, 13,600; urine, negative.

He was brought back to the office two weeks later, April 22, with the history that he was unable to sleep. He said that he had peculiar sensations in his hands; for instance, when he grasped a glass of cold water it felt like an electric shock. He complained of being cold, but had been having a temperature of from 100 to 102 F. The hands and feet were slightly reddened, particularly at the fingers and toes. Perspiration was marked. The urine was normal, with the exception of a few granular casts. Blood examination showed: hemoglobin, 85 per cent.; red blood corpuscles, 4,500,000; white blood corpuscles, 11,400. The heart was very rapid, but there were no murmurs. The throat was red, with considerable mucus in the nasopharynx. The patellar reflexes were increased. The patient had remained in bed during the previous two weeks.

The child came from one of the smaller towns of Oregon, and as the symptoms were somewhat suggestive of a beginning acrodynia, I requested that he remain in Portland for observation.

Course of the Disease.—After a few days, he developed the classical symptoms of the disease. While he did not seem to be mentally depressed, his disposition had changed. He fretted about trivial things and worried about missing school, for fear that he would not make his grade, and also about his doctor's bill. This is a most unusual thing for any one to do, particularly a child.

Photophobia was never present. Insomnia occurred many nights even when there was no pain. At times it was very difficult for him to go to sleep, or he would awaken at 2 or 3 o'clock and remain awake until the following night.

The pain in the hands and feet at times was very severe, frequently almost unbearable. He said that they itched and burned and that they seemed on fire. He wanted to bite them and tear the flesh from the bones. However, during examination, pressure or manipulation caused him no discomfort. He rubbed his hands and feet together for hours at a time

Occasionally he complained bitterly that the pains ran up and down the entire length of his arms and legs. I had never been able to determine this before. At times his back pained him. He was not particularly prostrated, nor did he have the acrodynia facies.

He did not want to get out of bed, but he could walk and would do so slowly; after a few steps, he would stop and sit



Fig. 3.—Characteristic desquamation of toes and discoloration of toe nails (purple).

down on the floor. There was no paralysis and no incoordination, but a marked hypotonia. The patellar reflexes were markedly increased; in fact, they were the most violent I have ever seen in any disease. This was most unusual, as they are generally lost.

Perspiration was excessive. The entire bed clothes were changed as many as five times a day; the patient's night-gown

was removed several times daily, soaked so that water could easily have been wrung from it.

The ears, throat, nose, lungs, abdomen and heart were all normal. Occasionally, tachycardia occurred. The appetite was good. After May 1, there was no elevation of temperature. Prostration was never as marked as in infants or younger children.

The mucous membrane of the mouth presented a peculiar beefy mottling, particularly involving the gums. The skin of the trunk and extremities in a general way presented a disseminated, superficial, pink, maculopapular eruption. The individual lesions were superficially blanched on pressure and were sparsely distributed over the trunk and closely grouped over the extremities, particularly the hands and feet.

In the latter locations, the lesions were so closely grouped as to be confluent in places, and many of them were capped by tiny vesicles. The lesions were in all stages of development, from tiny macules to involuting papules. The process of involution resulted in superficial desquamation in places, this process involving particularly the palms and soles, fingers and toes. In addition there was a general erythematous or raw-beef hue over the hands and feet, but ending abruptly along the lateral aspect of the foot. This peculiar, sharply defined involvement might well be likened to a glove, the dorsal half of which is removed. The latter involvement is suggestive of the changes sometimes seen in pellagra.

As the disease is essentially chronic, taking several months to run its course, the patient was allowed to return to his home in the country, May 20. He was brought back, June 2, for observation. There was no change in his condition except that the perspiration was less. The palms of the hands and soles of the feet were greatly thickened and horny. The mother referred to them as alligator skin. The inability to sleep was still present, and the pain and the burning and itching of the hands and feet were at times almost unbearable.

His speech was slow, and he slurred the words so at times it was difficult to understand him. Frequently he started a sentence but did not finish it, either through mental apathy or because he did not remember what he started talking about. I had never had an opportunity to observe any peculiarity of speech or memory before.

Unless some unforeseen complication develops, he will ultimately recover; but it will be many months before he is normal again, either physically or mentally.

Corbett Building.