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Acrodynia

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A C R O D Y N I A

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INTRODUCTION

The writer's first interest in the subject of Acrodynia occured after observing a case in the University Dispensary. Greater interest followed when upon looking this up in the literature, I found the great variety of opinions as to its etiology and the controversy as to its treatment. With no ideas of my own, I present this comprehensive review of the literature as my senior thesis.

DEFINITION

Acrodynia is an unusual and bizarre symptom-complex occuring in children particularly from six months to three years of age and occasionally in adults. The outstanding and distinctive symptoms are pink hands and feet, desquamation, scarlet cheeks and tip of the nose, alopecia, salivation, loss of several or all teeth, occasionally loss of nails or phalanges, excessive perspiration, evanescent rashes, marked hypotonia, itching, burning and marked pain of the extremities, increased pulse rate and blood pressure, photophobia, insomnia and apathy with extreme irritability. Death may occur very suddenly as the result of weakness or terminal infection or the child may make a slow recovery and return to complete health.

HISTORY

Acrodynia is a term derived from two Greek words meaning extremity and pain. Numerous writers have suggested different names from the disease, namely, dermatopolyneuritis, erythoedema, polyneuritis and Swift's Disease. Other names suggested are Feer's Disease and Pinks Disease.

The term Acrodynia was first used by Chardon in describing an epidemic disease affecting some 40,000 adults in Paris in 1828, its cause being traced to arsenic found in the wine. (20)

The Acrodynia syndrome was recognized as early as 1883, by William Snowball in Australia, who described it to his students as "raw beef hands and feet." (11)

The first mention of the disease appearing in children appears to have been made in 1903 by Selter, who described eight cases at a medical society meeting for children's diseases at Cassel, Germany. Since then two of his cases have been reported as doubtful. The title proposed by Selter for this condition was "Trophodermatoneurosis" or vegetative neuroisis. (53) This early communication, however, escaped attention and a wider interest was not aroused until several years later when many cases were described in Australia.

In 1914, Swift of Adelaide, Australia, reported 14 cases of a supposedly new disease seen in children, which he described under the term "erythroedema". Between 1917 and 1920, Wood (51) and Cole of Melbourne collected 91 cases, and Wood remarked that he had frequently seen cases in Melbourne for the past 30 years. In Sydney, Clubbe, Littlejohn and others had for many years been familiar with the condition and were in the habit of referring to it as the "pink disease". (20)

In this country, the disease in its present aspects seems to have been discovered independently and almost simultaneously by Bilderbach (2) of Portland, Oregon, and Byfield (6) of Iowa City, Iowa. These reports were soon followed by reports of many observers. In Great Britian, the earliest examples to be described by Parkes Weber (47) and Thursfild and Paterson (43) were in 1922. In Germany for the second time, the syndrome was described by Feer (16) in 1923. In France, 1925, Haushalten wrote on "neuro-vegetative syndrome" in infants and mentioned that he had been aware of this condition since 1911. (20)

ETIOLOGY

The exact etiology of Acrodynia is yet unknown, but numerous theories as to its cause are found in the literature. The most widely accepted theories are that its origin is (1) Infectious, (2) Avitaminosis, (3) Allergic, (4) specific dietary deficiency and (5) abnormal reaction to daylight.

Wood in his earlier papers did not even on the basis of 91 cases venture to give an opinion as to the cause but in a later communication in 1927, (51), came to the conclusion that the disease was not an avitaminosis. He agreed, however, with Warthin (46) that the condition was closely related to pellagra or that it may be the infantile form of that disease. Goldberg's work on pellagra and that its causation was from deficiency of vitamin B_2 had not at that time been published. For this reason it may be assumed that Wood subscribed to the avitaminosis theory rather than of an infective origin.

Tisdall (44) believes that the cause of Acrodynia is due to a defect in the utilization of some essential food elements probably belonging to the vitamin B group. He arrived at this conclusion after studying the similarity of the symptoms of Acrodynia and those which can be produced in animals by dietary deficiencies.

McClendon (33) holds the view that its origin lies in the lack of vitamins in the diet, as he reports good results in the treatment of Acrodynia with yeast and irradiated ergosterol. Rieta (36) believes that Acrodynia lies in the same class as rickets, pellagra and beri-beri.

The consensus of opinion in England, America and France is that pinks disease is due to an infection. Rodda (37), in support of the infective theory, maintained that he had never seen a case of pinks disease in which there had not been an infection previously of the upper respiratory tract. Vipond (45) found a small gram-positive diplococcus in the inguinal lymph glands of some of his cases. These diplococci were quite different from gonococci or pneumococci. From these cultures, he made an autogenous vaccine and good results were claimed in the treatment of these cases.

Penfold, Butler and Wood (51) found four positive blood cultures containing gram-positive irregular cocci in three out of eleven cases where Kendall's K media was used. Byfield (6) and Rodda (37) believe that focal infection is a prominent factor in this disease. Several authors claim that removal of tonsils and adenoids and eradication of sinus infection is the proper treatment. Byfield (6) in a series of 17 cases saw one case with

definite improvement after radical surgery of the nose and infected sinus, but two other patients, who illness appeared to be of about the same severity, died after operation.

A disease has appeared in Croatian peasant children which Mayerhofer has associated with the ingestion of cereals infected with a smut fungus, Ustilogo Moidis. Pinks disease usually occurs in infants at the age when cereals loom largest in the dietary, often as prepared breakfast foods made of wheat, maize or rye and not usually boiled. Dr. Mayerhofer is emphatic that there is only a similarity and not an identity between Ustiloginism (as he termed the Croatian disease) and Acrodynia. (8) Klein (31) believes that Acrodynia is a true fungi infection as it simulates Raynaud's disease, Buerger's disease and pellagra in many respects, and that this can be explained by a grain intoxication.

Gareau (21) holds the view that Acrodynia is most likely toxemic in origin, having its focus in previously infected tonsils, adenoids or sinuses and such patients usually respond rapidly to the removal of such. Wycoff (52) in an article on ten cases definitely rules out food deficiency as the leukocyte count is frequently increased from 10,000 and 40,000, proving that the disease is of infectious origin.

In Clark's cases (7) both food deficiency and infection were considered as etiologic factors. Tisdall (44) believes that these two views can be reconciled. On one hand, it is recognized that almost any dietary deficiency results in a lowered resistance to infection, therefore these children would be more susceptible to infection than the average child. On the other hand, the presence of an infection interferes with the utilization by the body of many of the nutritional factors including members of the vitamin B complex.

Helmick (28) after an experience with nine cases, was committed to the belief that Acrodynia is an allergy, manifested by successive attacks occuring in combination. This is merely a hypothesis as there are quite sufficient evidences in the clinical findings to support this claim.

A view slightly divergent from the avitaminosis and infectious theories is held by Findlay and Stern (17), who, as a result of experimental work on rats, suggest that the absence of a dietetic factor other than known vitamins, is responsible for the causation of pinks disease. They produced a condition in young rats clinically resembling pinks disease by feeding them with dried egg white as their sole source of protein, the rest of the diet being adequate and rich in vitamins. The same condition was produced in breast-fed rats by feeding the

mothers on a similar diet. Cultures on the affected animals were negative. Attempts to reproduce the disease by means of intraperitoneal or intracerebral injections of blood or emulsions of spinal cord from the animals were unsuccessful. With a special diet, these men showed that adding raw liver to the diets in rats the disease could rapidly be cured.

Kernoban and Kennedy (30) support the theory that juvenile Acrodynia is the result of a degenerative process of the central and peripheral nervous systems. Braithwaite (5) and Sweet (42) support the view that this disease is due to an abnormal reaction to daylight in a child who has recently suffered from an acute infection of the respiratory tract. This theory is based upon the fact that some Acrodynia patients show an increase in blood calcium due to the fact that vitamin D produces a net increase in the calcium absorption.

In the French report of the epidemic of a certain syndrome quite similar to what we know today as infantile Acrodynia, during the years of 1828 and 1830, the etiology of this syndrome was traced to the presence of arsenic in the beer and wine. In Sweden and England similar epidemics have occured and etiology was also proven to be due to arsenic poisoning. Some of the modern writers still hold this view and believe arsenic poisoning may be

the cause of Acrodynia. (12)

Males and females are about equally affected. Evans (15) reports the greater number of cases appear between six and twelve months. In a series of 50 cases in patients at the Royal Alexandria Hospital for Children, four or eight per cent appeared between four or six months; eight or seventy-six per cent appeared between 12 and 18 months; two or four per cent appeared between 18 months and four years.

Breast-fed babies, previously healthy and well nourished are the most common sufferers from the disease, but bottle-fed babies do not enjoy complete immunity. The larger percentage of patients come from the rural sections of the country, and no class distinction is made by the disease.

The disease occurs in some localities or zones more often than in others. The disease is prevalent in western Germany, Switzerland and certain parts of France. In the latter country, the area seems to be larger and more profuse than in Germany, but even there, most of the cases have been reported from circumscribed areas in the southeastern part of the country. Australia has seen more cases than any other country, as it is here that most of our reports of the disease have come from. In the United States, the disease is found in almost any

section.

The disease is sporadic in nature, but it has been the experience of many clinicians that they may see a number of cases of Acrodynia within a few months and not observe one for several years.

The disease is more common in the winter and spring months and is seen more in the cold than in the warm climates.

Zahorsky (54) in a series of about 60 cases suggests that there may be a racial immunity of Acrodynia. He reports that the disease arose almost entirely among people of German descent. In his cases which were gathered from the vicinity around St. Louis, he found that 51 children had a German ancestry, two Slovak, one Polish, two French, one Irish and three Scotch. Several of his patients' ancestries were traced back to that part of Germany where the disease has been most prevalent in the last twenty years. From this he concluded that it was racial and not regional immunity. Incidently, not one case was reported in the Jewish race.

PATHOLOGY

Only a few cases have come to autopsy. There is much disagreement in the question as to whether the changes found were primary or secondary, and especially in regard to changes in central and peripheral nervous systems.

In Warthin's (46) autopsy reports, he states the meninges of the cord were edematous. The cerbral meninges were very wet with marked congestion and edema. The brain showed extreme congestion and edema and the cerebral and spinal fluid was greatly increased.

Paterson and Greenfield (35) found considerable myelin destruction in some fibers of the peripheral nerves, increasingly marked toward the periphery. The grey matter of the central nervous system showed a diffuse increase of small cells. There was also some cellular increase in the nerve roots. They found no evidence of bacterial invasion of either the central nervous system or peripheral nervous system and stated that the disease is similar to polyneuritis.

According to Crawford (10), the pathologic findings in Acrodynia are variable and chiefly found to affect the sensorimotor and vegetative nervous systems. (The mesencephalic subthalmic region, the posterior, anterior

and lateral horns of the spinal cord, the paravertebral sympathetic and parasympathetic ganglions and the peripheral nerves.) There is some discrepancy in various reports and the pathologic lesions are not always discovered.

The brain usually shows no pathologic changes. According to Crawford (10), DeLange found a profuse glial proliferation and small glial nodules in the tubero-infundibular region of the dien- and mesencephalon with some glial proliferation in the basal ganglion and dentate nucleus. Francioni and Vigi considered Acrocynia a disease of mesencephalic sympathetic centers as they found eccentric nuclei, cellular achromasia and "shadow" cells in the region of the tuber cenereum and infundibulum, and a perivascular small round cell infiltration in the cervical sympathetic ganglions. Bellocq and Meyer found areas of neuronaphagia and cellular degeneration in the cervical and thoracolumbar sympathetic ganglions. Cell chromatolysis, loss of cell outline, edema and local monocytic infiltration in the paravertebral sympathetic ganglions and in the spinal cord posterior root ganglions have been reported by several investigators. It is not always determined whether the cellular infiltration is lymphocytic, monocytic of glial. Orton and Benden found chromatolysis with shrinking and

fragmentation and a loss of myelin of the neurons followed by a replacement cellular gliosis in the lateral horns of the spinal cord. The neurons in the lateral horns receive impulses from the striate body and dentate nucleus by the way of the rubo-spinal and tectospinal tracts where they make synaptic motor connections with the spinal cord tracts and paravertebral sympathetic ganglions by an effector splanchnic function. The lateral horns form a connection between the afferent and efferent primitive autonomic system with the periphery. The peripheral nerves may show myelin degeneration. (10)

The skin shows marked hyperkeratosis and only slight acanthosis while the interpapillary processes are lengthened and widened. There is no edema in the epithelium or corium. A moderate lympathocytic infiltration may occur in the regions of blood vessels and sweat glands. The sweat glands are often increased in number and may show hypertrophy. There are no characteristic pathological findings in the skin. (53)

SYMPTOMATOLOGY

The onset of the disease is gradual. In the majority of cases there is a history of a preceding upper respiratory infection, such as rhinopharyngitis or bronchitis or some digestive distress. Some weeks later a decided change in character takes place, from one of normal activity and cheerfulness to one of lassitude and apathy or irritability and fretfulness. The child sleeps badly and is indifferent to food. The features become sad and drawn, and the child speaks in a dull monotone or cries most of the night. He often remains immobile for hours, resenting disturbance. On the face is an expression of object wretchedness, a picture of extreme mental misery. The eyes are dull and lusterless and denote extreme suffering, reminding one of a wounded animal. (1)

While the skin manifestations are often the earliest signs of the disease, a careful inquiry will elicit the information that a change in disposition and habits occured several days or even weeks before the erruption appeared. The cutaneuous manifestations of the disease is twofold, a miliary rash and the erythematous condition of the hands and feet. The miliary rash consists of pink or red papules which occur over the body. The rash

varies in intensity from day to day and is associated with extreme itching and perspiration. The rash often appears suddenly after a febrile movement and is generally diagnosed as measles, rabella or scarlet fever. It may appear more slowly, and its persistent scaly appearance justifies the diagnosis of eczema. It may be fleeting and in character be mistaken for erythema multiforme or urticaria. The eruption fades after a few days and then reappears. The intensity of skin manifestations vary from day to day. The skin becomes toneless, inelastic, cool and clammy with perspiration. Profuse sweating is often so marked as to necessitate frequent change of bed covering and clothing. The general skin surface and musculature are hyperesthetic in the early stages, whereas they are hyperthetic in the latter stages when degenerative changes occur in the posterior roots of the spinal cord. A miliarial erruption develops which at first is composed of small bright pink papules diffused on the entire skin surface and later there are larger, often pustular or crust-capped papules discreetly scattered over the trunk. Impetigo, furuncles, absesses and paronychias are not uncommon complications.

The characteristic eruption which makes recognition of Acrodynia usually easy is confined to the hands and feet. These appear swollen, especially the fingers

and toes. There is a symmetrical discoloration of the hands and feet, which are of a dusky pink hue. The eruption gradually fades into normal skin as it approaches the wrists and ankles. There are sometimes found some scattered papules of deeper color upon the hands and feet, and vesication is not uncommon. The child may spend hours rubbing the hands and feet together, the swelling and redness progressing until the epidermis becomes macerated and exfoliated, often exposing the "raw-beef like" corium beneath. Mechanical pitting of the extremities is absent. The continual ringing of the hands is due to burning pain in the extremities. The child often rubs the ears, nose, and genitalia or anal region until exhausted or actually chews on the fingers or toes. Gangrenous erosions of the skin may result from scratching or rubbing, depending on the degree of neuro-vascular hypotonia. Dermographia is often present. Ulcers may be found between the fingers or on any parts of the hands and feet, apparently resulting from traumatism. Owing to the constant moisture, the skin is often sodden. The fingernails and toenails not infrequently fall out.

The musculature becomes soft and hypotonic, and usually is noticed early in the illness. Hyperflexibility of the joints is noted. One of the first complaints of the mother is that the child "had stopped crawling",

or if old enough, "walking".

The continuous stinging pain in the skin, muscles and abdomen and extremities causes prolonged loss of sleep. The child may lie in bed bent over so that the head is between the knees, or lie in a knee-chest position with the face buried in a pillow to shut out the light because of photophobia. Papillary dilatation is frequent. Neurokeratitis or neuroretinitis may occur.

As the disease progresses the hair may fall out and the teeth may be loosened from gingivitis. Sometimes all the teeth are lost. Frequently before any pathological condition of the mouth has been recognized, a perfectly sound tooth will be found in the child's bed. Then it will be noticed within a short time that the other teeth are becoming loose in their sockets and drop out. However, after the teeth are lost, an infection may occur in the mouth with necrosis and shedding of the jaw bone. Saliva is profuse and of a fetid odor. Increased salivation with drooling and rhinorrhea are frequent. Septic ulcers may occur in the nose. Crusts often form in the ears and the tip of the nose is often congested. The tongue may be beefy red, swollen and fissured and may be actually chewed. Buccal erosions occur from continual biting of the inner surface of the cheek between the teeth.

Anorexia is constant. For weeks an insufficient quantity of food is taken, and the results in considerable emaciation and weakness, so that the muscles become soft. Thirst is often excessive. Gastro-intestinal symptoms are not marked. Either constipation or offensive diarrhea may occur.

Acrodynia is frequently characterized by a group of neurologic symptoms. Among such sumptoms are hyperirritability, sleeplessness, paresthesia, anesthesia, paresis and photophobia. Writhing movements are sometimes very characteristic due to extreme itching. There are no signs of meningeal irritation. Convulsions are unusual. Sometimes there is a partial or total loss of sensibility to pain. Deep reflexes are usually diminished or absent, but may be normal or exaggerated. Tremor is unusual. The electrical excitability of the nerves and muscles is said to be undiminished. Schwartz (39) reports a case which showed a complete flaccid paralysis of both lower extremities, a weakness and hypertonia of both upper and lower extremities besides the usual sensory disturbance.

The temperature usually varies between normal and 100 degrees. Tachycardia and hypertension are prominent features of Acrodynia. The majority exhibit a pulse rate of 120 to 180 beats per minute, out of proportion

with the temperature, while the heart valves are normal. The pulse rate does not change during sleep or crying and neither in response to calming measures nor induced painful discomfort. The systolic blood pressure is usually elevated to 130 or 170 and the diastolic to 120 mm. of mercury and remains as such during the course of the disease. Respirations are normal, but bronchopneumonia is a frequent complication and must be continually watched for.

The erthrocytes may be slightly diminished in number, or occasionally increased to 5,000,000 or to 6,500,000 and the leukocytes from 10,000 to 40,000 per cubic millimeter of blood. Differential and blood placet counts are normal. Bleeding and clotting times are normal. Some children may have a high blood sugar, and others may show an increase in calcium.

The urine usually has a high specific gravity due to excessive perspiration. Pyuria frequently occurs in the females. Temporary glycosuria may occur during the course of the disease.

The literature on Acrodynia attests that the spinal fluid findings are uniformly negative, but there may be an increased cell count and an increased pressure early in the course of the disease. Occasionally there may be an increase in globulin and total protein and sometimes

the total protein may be as high as 200 mgm. per cent. There is nothing found in the spinal fluid that can give a clue as to etiology.

X-rays of the long bones may show a marked increase in the density of the primary zones of calcification which may best be seen in the lower radii and in the distal ends of the metacarpal bones. Cobb (9) reports that this is in no way specific.

The mechanism of the production of symptoms in Acrodynia is not easily explained. The fretfulness and irritability are due to psychic instability and the apathy is probably due to cerebral exhaustion. The hypotonia and incoordination are probably due to cerebral interference, to sensory spinal root changes or to somatic muscle innervation alterations. The constrictive vasomotor symptoms are probably from increased sympathetic control action or sympathetic hypertonicity. Suprarenal gland overactivity from disturbed automatic control is considered by some investigators (9) as a cause of tachycardia and hypertension. Salivation, abdominal pain and intestinal hypermotility may be due to increased parasympathicotonia. Painful paresthesia and profuse perspiration are due to a functional imbalance between the sympathetic and parasympathetic ganglions, which are directly connected with the lateral and posterior horns of the cord

and which show varying stages of cell degeneration microscopically. Excessive fluid loss and diminished fluid intake may explain the high erythrocyte counts and elevated blood serum protein in some patients.

The course of the disease is measured in months and sometimes by a year. The symptoms, after increasing in severity for about a month, remain constant for an invariable length of time. Mild cases of Acrodynia occur in which photophobia is absent and the fingers and toes show only a faint pinkness.

Foerster (18) and Rodda (37) summed up the clinical picture as manifesting itself by three groups of symptoms, occuring in varying degrees and combinations:

1 - General or gastro-intestinal, as anorexia, loss of weight, weakness, usually pronounced constipation and occasionally loss of teeth.

2 - Neurological, as hyperirritability, paresthesia, anesthesia, loss of reflexes, photophobia and paresis.

3 - Cutaneous: The skin manifestations are usually of two types. (a) General, a diffuse erythematous rash over the entire trunk involving the extremities and often preceded by a profuse perspiration. It has been variously designated and is responsible for the name pinks disease. (b) Local, giving the characteristic appearance

on the hands and feet as erythema, swelling, cyanosis, coldness, ulcerations and desquamation.

DIAGNOSIS

The diagnosis is comparatively easy, after once observing a case. Of outstanding value in the diagnosis of Acrodynia is its gradual development, the triad of symptoms, namely the typical skin lesions on the hands and feet, the vasomotor phenomena, and the emotional disturbance. The most important of these is the personality change of the child. Hypertension and tachycardia are also cardinal symptoms in the diagnosis of Acrodynia.

Error in diagnosis is often made by considering individual symptoms without due regard to the whole condition. Meningitis, otitis media, or cerebral abscess may be suspected on account of the intense irritability. Pyelitis may be diagnosed if, in addition, pus-cells are found in the urine.

The marked wasting with hypotonia and sweating may suggest rickets, which frequently accompanies pinks disease and the underlying condition may be overlooked. The rash may be confused with one of the exanthematas or with eczema. The presence of photophobia may lead to the diagnosis of some eye condition, such as iritis or conjunctivitis, and not so infrequently the child is referred to the ophthalmologist or dermatologist. The possibility

of poliomyelitis as a diagnosis may be considered on account of the muscular wasting and the diminution of the deep reflexes.

Acrodynia may be distinguished from pellagra by the absence of a history of pellagragenic diet, by the fading of the red at the wrist and ankles and by photophobia. It is differentiated practically from measles and scarlet fever by its course, which is not the same as that of the exanthemas with which it is confused.

PROGNOSIS

The prognosis is usually good unless complications such as pyodermia or pneumonia occur. The mortality is around 10 per cent. Sweet (41) shows that the mortality is higher for patients treated in the hospital than those who are treated at home. Very few of the patients may die from the disease alone. Recovery is usually complete, though there may be residua.

TREATMENT

During the past 15 years, many suggestions have been made, with the object of discovering a specific form of treatment for this intractable disease, but as for the most part the treatment is still symptomatic. Some investigators express the opinion that pinks disease was a self limiting affection to a certain degree, in that the condition of the patient in the majority of cases began to improve after the symptoms have been in evidence for about three months. They were of the opinion that so-called cures were due to this natural tendency to recovery. Whether such is the case remains to be proved, and it is very doubtful, as most observers are agreed that cases are not unknown in which the disease has persisted in an active form for nine months or longer, and cases of from three to six months' duration are by no means uncommon.

The treatment of the cutaneous symptoms is of first importance, because the insomnia, anorexia and general wretchfulness seem to depend to a large extent on the extreme irritation of the rash. If this can be relieved, the child sleeps better, the restlessness disappears and the appetite improves. The clothing must be light; cotton or linen shirts should be worn next to the skin.

Wool should be avoided, as it increases perspiration and irritates the skin. The skin should be olive-oiled or cold-creamed daily after a tepid bath to prevent dryness and irritation evaportation. Calamine lotion may be applied for soothing purposes. Too frequent alcohol rubs are drying. Ammoniated mercury ointment, 5 per cent, may be used in small areas where impitiginous crusting occurs, such as in the noses, postauricular regions or groin. Restraints may be necessary to control restlessness and prevent self-mutilation, coprophagy and autophagy. Atropine may be used to control the sweating.

With regard to the stomatitis, the gums and the inside of the mouth should be swabbed with absorbent wool soaked in peroxide of hydrogen, one part to four parts of water, followed by "Listerine", in portions of one to eight. If any ulcers are obstinate in healing, they may be touched with 1 per cent chromic acid solution. In bad cases of ulcerations or sloughing of the mucous membrane, the affected parts should be touched with peroxide, one to four, followed by normal saline solution.

For the nervous system symptoms, luminal, one-quarter to one-half grain given twice or three times a day is quite satisfactory. Chloral hydrate or any other sedatives may also be used.

The diet must be varied and must contain a plentiful supply of vitamins. Anything that will tempt the child's appetite may be given. It is better to give small meals at more frequent intervals rather than maintain the three meals a day time-table.

The role of vitamins in the treatment of Acrodynia has received a big "play" from most investigators, but so far, no one vitamin is in any way specific therapy. Clements (8) expresses the opinion that giving vitamins improves the metabolism and increases the appetite, and this may be the underlying cause of the improvement of the symptoms.

Durand (14) uses large intra-muscular injections of vitamin B_1, and the children improved. The improvement ceased and the symptoms got worse when these injections were stopped and the vitamin given by mouth. From this he concluded that oral administration of the vitamin is not effective in the therapy of Acrodynia. Forsyth (19) used vitamin B_1 in doses of 600 to 1500 units daily and one OZ. of wheat germ three times a day. With this method of treatment, he claims good results.

In Tisdall's cases (44), 500 mgm. of Nicotinic Acid was given daily in five divided doses. He noticed that the photophobia disappeared in 24 hours, the rash dried up comparatively rapidly in four or five days, and at the

end of two weeks, redness of the skin was barely perceptible. However, Durand (14) used Nicotinic Acid in large doses for a period of two weeks, but no hastening of the improvement was noted.

McClendon (33) suggests yeast and irradiated ergosterol in the treatment of Acrodynia and claims good results. Vipond (45) used a vaccine made from a gram-positive organism taken from the lymp glands. He claims good results.

Findlay and Stern (17) in their experiments with rats showed that by adding raw liver to the diets, the disease could rapidly be cured. Harper (26) used liver extract in amounts of 30 to 60 grams per day and noted great improvement in her patients.

Braithwaite (5) recommended treatment in a room with red windows, so as to exclude the ultra-violet rays of the sun. He also used intravenous or intraperitoneal injections of sodium citrate, and he found that this usually caused a temporary improvement. Rieta (36) in believing that Acrodynia is due to the same cause as rickets, pellagra and beri-beri ordered a diet accordingly and gave two cc. of cacodylate intramuscularly twice a week. Crawford (10) suggests deep radiation to the suprarenal glands and to the paravertebral sympathetic ganglions. Fulton (20) claims that removal of tonsils and adenoids

and eradication of sinus infection is the proper treatment. Byfield (6) in a series of 17 cases saw one case with definite improvement after radical surgery of the nose and infected sinus, but two other patients whose illness appeared to be of about the same severity died after operation. Sweet (41) used ultra-violet ray treatment, and reports 18 patients were cured in less than 10 treatments.

Dr. Bilderback concluded in his monogram in Brennemann's Practice of Pediatrics with the following statement: (10)

> "The physician who treats a patient with acrodynia from every angle and does everything that has been advocated, will stand by the bedside of the child suffering from acrodynia and feel that in this instance he is still a therapeutic pauper. It is well to tell the parents at the very beginning that the disease is chronic and that it will be many weeks or even months before the child will get better."

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