



# Journal of Spirochetal and Tick-borne Diseases

Spring/Summer 2001

Volume 8

## ORIGINAL ARTICLES

A Case of Symmetrical Cutaneous Atrophy of the Extremities

*Edward Bennet Bronson, MD*

A Case of Idiopathic Atrophy of the Skin

*George T. Elliot, MD*

Acrodermatitis Atrophicans Chronica

*Hamilton Montgomery, MD and Ralph R. Sullivan, MD*

Regarding an Unusual Form of Migratory Erythema Caused by Tick Bites

*James Strandberg*

Erythema Chronicum Migrans (Afzelii) Associated With Mosquito Bite

*Stig Hård, MD*

*The Journal of the Lyme Disease Foundation*

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Hartford, CT 06103-2610  
Telephone: 860-525-2000  
Fax: 860-525-8425  
e-mail: lymefnd@aol.com  
Internet: www.lyme.org

# Lyme Disease Foundation Announces New *JSTD*

## Editor-In-Chief

Ronald F. Schell, PhD

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Ronald F. Schell, PhD, University of Wisconsin Medical School, was recently appointed editor-in-chief of the peer-reviewed scientific publication, *Journal of Spirochetal and Tick-borne Diseases (JSTD)*. He replaces former *JSTD* editor-in-chief, Dick Tilton, PhD, who has retired.

Dr. Schell brings more than 34 years of experience as a microbiologist devoted to spirochetal (corkscrew-shaped bacteria) research. He graduated in 1967 from the University of Wisconsin, Madison, Wisconsin, where he earned a bachelor of science degree in microbiology.

In 1970, Dr. Schell earned his masters of science from University of Wisconsin before earning his PhD there in 1972. His major research interest is the host response to the Lyme disease bacteria, *Borrelia burgdorferi*, and its cousin, *Treponema pallidum*, the causative agent of syphilis. In addition to his current position as Chief of Bacteriology, Wisconsin State Laboratory of Hygiene, Dr. Schell is also Professor of Medical Microbiology and Immunology and Chief Bacteriologist at University of Wisconsin Medical School.

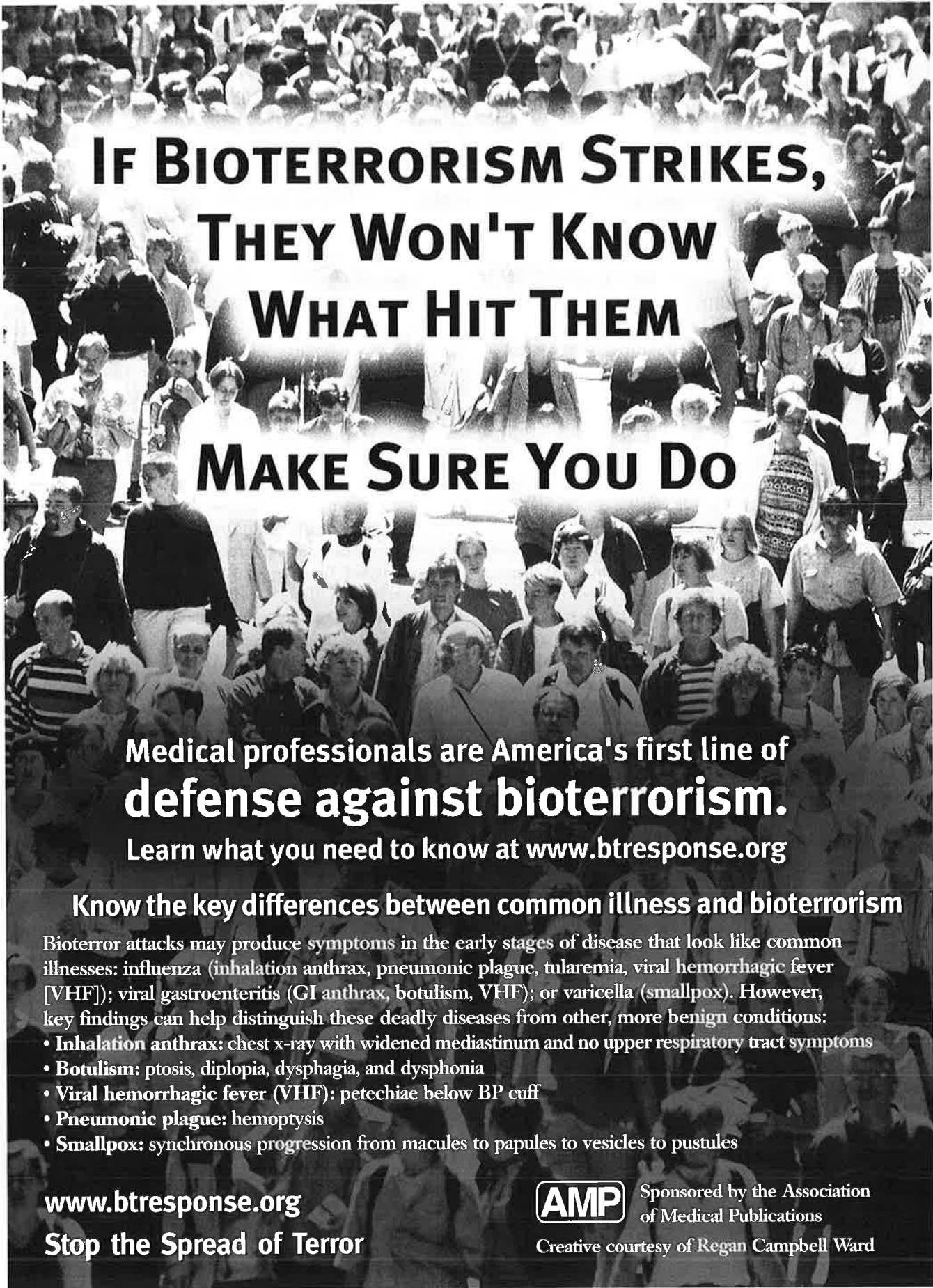
Throughout his career, Ronald has become a member of various societies, including the American Association of Immunologists, American Public Health Association, American Society of Microbiology, American Venereal Disease Association, and the Reticuloendothelial Society. He has done research projects under grants from the National Institutes of Health since 1977, and has been studying the hamster immune response to *Treponema pallidum* for the last 26 years under a grant from the World Health Organization.

Past positions Dr. Schell has held include Director of the Infectious Disease Laboratory for Special Studies in Clinical Microbiology at Hahnemann University School of Medicine, Philadelphia, Pennsylvania (1980-1984) and Director of the Clinical Laboratory of Microbiology, Albany Center Hospital, Albany, New York (1974-1980). From 1972-1974, he served as Director of Treponemal Research Laboratory of the Veteran's Administration Hospital, Houston, Texas.

In addition to two postdoctoral fellowships done at the Baylor College of Medicine in Houston, Texas, Dr. Schell completed a postdoctoral fellowship at the University of Texas in Houston. As author or co-author of more than 179 peer-reviewed papers, he is arguably the most published scientist of all researchers in the Lyme disease field. Dr. Schell and a research partner are creators of the Borreliacidal Assay, a Lyme disease test that is an adaptation of an assay used for the diagnosis of syphilis. The test outperformed the CDC's own test in a CDC-conducted trial.

Dr. Schell, in his acceptance of the appointment, remarked that he was "happy to be assuming the responsibility for *JSTD*" because he believes it "provides a valuable service to the scientific community." He further noted that the Lyme Disease Foundation (LDF) is responsible for "bringing Lyme disease to the attention of the public and federal government, obtaining federal research support for it, and crafting legislation to benefit researchers and patients alike. There are still too many unknowns surrounding the disease, and I look forward to continuing to try to find answers as editor-in chief of *JSTD*."





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- **Inhalation anthrax:** chest x-ray with widened mediastinum and no upper respiratory tract symptoms
- **Botulism:** ptosis, diplopia, dysphagia, and dysphonia
- **Viral hemorrhagic fever (VHF):** petechiae below BP cuff
- **Pneumonic plague:** hemoptysis
- **Smallpox:** synchronous progression from macules to papules to vesicles to pustules

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# Editorial

## A Historical Perspective of Spirochetal and Tick-borne Diseases

### Part 1

Ronald Schell and Karen Vanderhoof-Forschner

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It is always important to have as full a scientific picture of a disease as possible. Because some of the older literature is being lost to the newer researchers, we have reprinted some of the more important historical articles in the next two issues of the Journal. All of these articles appear in their original format and were issued originally in English.

This current issue (Spring/Summer) documents that people in the United States have been infected with Lyme disease for more than 100 years. These articles show an excellent overview of what is known about the disease today and demonstrates that there has been more than a century of cooperation occurring within the medical community of the United States to try to more fully understand this disease.

Beginning in 1895, New York City physician Edward Bronson wrote and published his data about what is now termed ACA, and has been proven to be caused by *Borrelia burgdorferi*, the causative agent of Lyme disease. He describes the condition as causing atrophy of skin, sweat glands, and hair follicles (resulting in hair loss), and disturbances in the sense of touch.

His published papers were followed by a letter from George Elliot in 1895 who discussed cases he had seen in New York. He described one patient with skin disease who was having attacks of rheumatism, but did not think that the rheumatism was related to the skin disease. Today, we know there is a relationship.

In 1945, a Mayo Clinic physician, Hamilton Montgomery published an article on the results of studying 45 cases from his area. Interestingly, his literature cites that the disease was found in Europe, South America, Greece, Turkey, and the United States. He ruled out a familial cause and noted that this condition "occurs fairly frequently among native-born Americans." He

wrote about the breath of terms that were in use at the time and the difficulty to delineate this entity from other skin disorders. He addresses the issues of difficulty to diagnose bone/joint involvement (16%), ulcers, cardiovascular changes (27%), anemia, thyroid disorder, cancer (theoretical link), and benign tumor-like new growths. He noted that vitamins and endocrine therapy were not effective methods of treatment. Lastly, he describes the disease histopathologic changes in three disease stages—"Acute, inflammatory, and atrophic: but these are not clear-cut, and the duration of any stage varies greatly not only in different cases but in different areas in the same case"—a caveat heard in defining this disease today.

The 1967 paper by Hard indicated he was in another "camp" about the pathogen and vector of "erythema migrans" (EM) disease, and the number of cases in the U.S. He presents a case he believes that shows mosquitoes transmit the multisymptom disease and cites studies that failed to demonstrate tick-transmission as an indication that ticks may not be the vector. He does conclude that the disease is infectious because researchers were able to transmit the infection through skin grafts. He cites some research that found positive "rickettsiae" tests in a few patients. It brings to mind the current situation of ticks being coinfecting and transmitting several diseases at once to some patients. It is not surprising he stated that "e.c.m. is rare in the U.S.A.," which was ironic, since late stage ACA cases were in the United States. Until around the 1990s, most health care professionals also considered "Lyme disease" a rare disease. Television broadcasts of skin rashes and manifestations changed this perception.

In the next issue of the Journal (Fall/Winter), the historical focus will be the other Lyme disease skin condition known as erythema migrans featuring reprinted articles by Drs. Lennhoff, Hollstrom, and Scrimenti.

# A Case of Symmetrical Cutaneous Atrophy of the Extremities

Edward Bennet Bronson, MD

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Mr. President and Gentlemen:

The case which I am about to report, while not a unique one, nevertheless such a rare form of atrophy of the skin that it has seemed to me not unworthy of engaging your attention. The patient exhibiting the peculiar affection was sent to me at the Polyclinic by Dr. F.P. Griswold, of Meriden, Conn., about the middle of last October. I was then only able to make a few notes and secure some indifferent photographs before the patient returned to his home. A second visit was paid me at my request about one month ago. At this time I could not see that any changes had taken place in the appearances of the disease during the six months' interval. Apparently the case had remained quite stationary. In the presence of the patient on this occasion two of the photographs taken previously were colored. I regret that my opportunities for studying the case have been so meager. Such notes as I was able to make are as follows:

The patient is a man forty-five years of age, native of Germany, by occupation a varnisher in brass and iron works. His appearance is that of a well-developed, well-nourished person, and his manner indicates fair intelligence. He is of spare, sinewy build and of brownish complexion with dark hair and eyes. He states that his mother died of "brain disease," and an aunt, it would seem, has had some mild form of paranoia. In other respects the family history is good. The patient formerly drank rather freely, but has generally led a regular, hard working life, is married, and has three healthy children. He gives no evidence of syphilis nor arthritic disease, and his first and only serious ailment, he states, is the skin trouble with which he is now affected. The first sign of this was noticed fourteen years ago, in the region of the left ankle. The skin at this place seemed thinner and more sensitive, and the blue veins began to show prominently. There was also some scaling of the skin, and from time to time rather dry sores appeared over the bony prominences and

were difficult to heal. Little by little similar changes began to appear higher up. A year or two later the same thing was noticed upon the right leg. These changes it would seem, were neither preceded nor accompanied with any form of inflammation excepting such as attended the ulcers or sores, and these were of a very indolent character. Nor had there been any previous disease or injury to which the affection could be ascribed. It was apparently spontaneous and idiopathic. In course of time the hands and arms became similarly affected, but not, the patient thinks, till about five years ago. As the disease progressed and extended higher, it has been attended with occasional pain or discomfort, which thus far affected only the lower extremities. The chief thing complained of has been a sense of great fatigue after work and long standing. This lasts, he says, for an hour or two after his work is over, and then disappears. So far it does not seem to have been sufficient to seriously interfere with or curtail his working hours, but chiefly because of the apprehension that it would come to this was he led to seek medical aid. Besides this feeling of fatigue, there have occasionally been sharp, shooting pains that would come in little shocks, especially at night, and often in the soles of the feet. There has been some itching in the vicinity of the ulcers that have developed from time to time about the ankles and anterior surfaces of the legs. No other abnormal sensations, such as a sense of constriction, tingling numbness, "pins and needles," heat or coldness, have been complained of. It was noticed, however, that the affected surfaces were abnormally sensitive to touch, though not particular to changes of temperature.

*Status proesens.* When the patient is stripped a marked contrast is presented between the skin of the legs from the hips down, together with the lower two thirds of the arms, on one hand and surface of the rest of the body on the other, which latter everywhere appears perfectly normal. By comparison with the trunk the extremities appear thin, as if slightly shrunken; they are darker in color, show the courses of the veins more clearly, and are covered with multitudes of wrinkles diversified with smooth brownish or white interspaces that have a glazed appearance, resembling, but for the dusky color, a crumpled sheet of waxed paper or gold-beater's skin. The wrinkling for the most part follows the cleavage lines of the skin. It is most marked about the extensor aspects of the knees and

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*Reprinted with permission from Journal of Cutaneous and Genito-Urinary Diseases, 1895;1:1-8.*

*Read before the American Dermatological Association, May 31, 1894.*

*At the time this letter was initially published, Dr. Bronson was Professor of Dermatology in the New York Polyclinic.*



wrists, especially the former. About the ankles and lower part of the legs the skin is a little scaly.

*The extent* of the disease on the lower extremities is about the same on either side. It begins below at a pretty sharply defined line, about an inch and a half above the soles at the side and back of the feet, and one inch back of the roots of the toes in front, whence the affection extends upward continuously, embracing the entire circumference and length of the legs; in front to a point within two or three inches of the flexure of the thigh; at the sides is bounded by a line that curves over the trochanter and behind reaches above the nates and half way up the surface to the sacrum. The cleft of the nates, the perinaeum, and genitals remain unaffected. The line of definition above is not very clear, though there is a marked contrast between the normal white velvety skin above and the reddish purplish brown, wrinkled, dry, and parchment-like surfaces below.

Upon the upper extremities the skin is affected from the base of the fingers (which latter are not affected) posteriorly and the palms anteriorly to an oblique line encircling the arm a little above the elbow. Its highest point, which on both sides is at the back of the arm, is near the junction of the lower and middle thirds, and is a trifle higher on the left side than on the right. Here, as on the lower extremities, while there is a sufficiently marked contrast between the atrophied and the sound skin, the line of definition is somewhat indistinct.

*The Color* — This appears to be due to a blending of purple, red, and brown. Those elements of the skin upon which its opacity and consequent whiteness depend seem to have disappeared, permitting the blood-vessels underneath to show through. This is especially evident near the margins of the atrophied portions, where veins which are clearly perceptible in latter are suddenly lost to view as they enter the area of normal skin. Besides the purple hue of the numerous veins there is a red reflex from the arterioles and capillaries. In some places there is a lilac coloring due to the combined effect of arteries and veins. Almost everywhere also there is a brownish discoloration which is made more evident when pressure is used so as to produce a temporary ischaemia of the part. In many places this brown pigmentation is seen to be punctate or in small lentigolike spots. It occurs over almost the entire atrophic area, and contributes a considerable quota to the general dusky discoloration. The color varies, however, with the patient's posture. Especially in the legs after the patient has been standing for a length of time the veins become turgid and greatly dilated, standing out as prominent tortuous ridges, and their deep purple color becomes everywhere predominant, giving the appearance of cyanosis.

In certain places, more especially over the legs and on

the backs of the feet and hands, there are numerous whitish, scarlike patches where the atrophy has been more profound, and perhaps in some places corresponding to the sites of old ulcerations. (Fig. 1.) Even in many of these scarlike patches the punctate brown spots are distinctly present. Aside from these scarlike patches there are scattered over all the atrophic regions a multitude of small, slightly depressed spots which are apparent only on closer inspection, and which seem to imply that the degenerative process has not been absolutely uniform, but has been more pronounced in certain places than others. Such shallow depressions are scattered abundantly over the thighs, buttocks, and arms.

Near the outer malleoli of both legs are shallow, indolent ulcers with sharp-cut adherent edges and gray base, devoid of granulations and showing a scanty serous secretion.

*The wrinkling of the skin* is apparent almost everywhere in the affected regions, though less marked on the legs than on the thighs and buttocks. In most places the wrinkles are extremely fine, looking at a little distance like minute striae. About the knees they are most pronounced. (See Fig 2.) Here the thinned skin is thrown into numberless parallel transverse folds curving above and below the patellae, leaving between them flat, smooth, glistening surfaces that looked as if waxed or varnished. These flat smooth surfaces are most marked over the patellae. The wrinkling is well marked also over the nates, especially near the folds between the nates and thighs. The lines curve gracefully from the outer aspect of the thigh around the nates toward the cleft. Just back of the toes the skin is thrown into fine wrinkles or striations that radiate outward from the atrophied portion, which here is whitish and scarlike with a lilac-colored border.

*The hairy growth* has almost entirely disappeared from the affected region, including the lanugo as well as the coarser hairs. Apparently the little dots of pigment scattered over the legs and arms mark the site of the degenerated hair follicles.

*No sweating* is apparent in the areas of atrophy. The patient states that his legs and arms are always dry, while the palms and soles sweat freely. While examining him, it was noticed that all around the borders of the feet, just without the atrophied portion, the skin was decidedly moist, while just above it was perfectly dry. To the touch the skin was like dry parchment. There seemed to be no change of temperature. It was neither below nor above the normal. Almost everywhere the skin was freely movable over the subjacent structures. On the legs, however, it was less so than elsewhere, and in places here was adherent. Elsewhere it could be readily pinched up, always in very thin folds, however, which on being released returned again to the niveau, though a little more slowly than in the

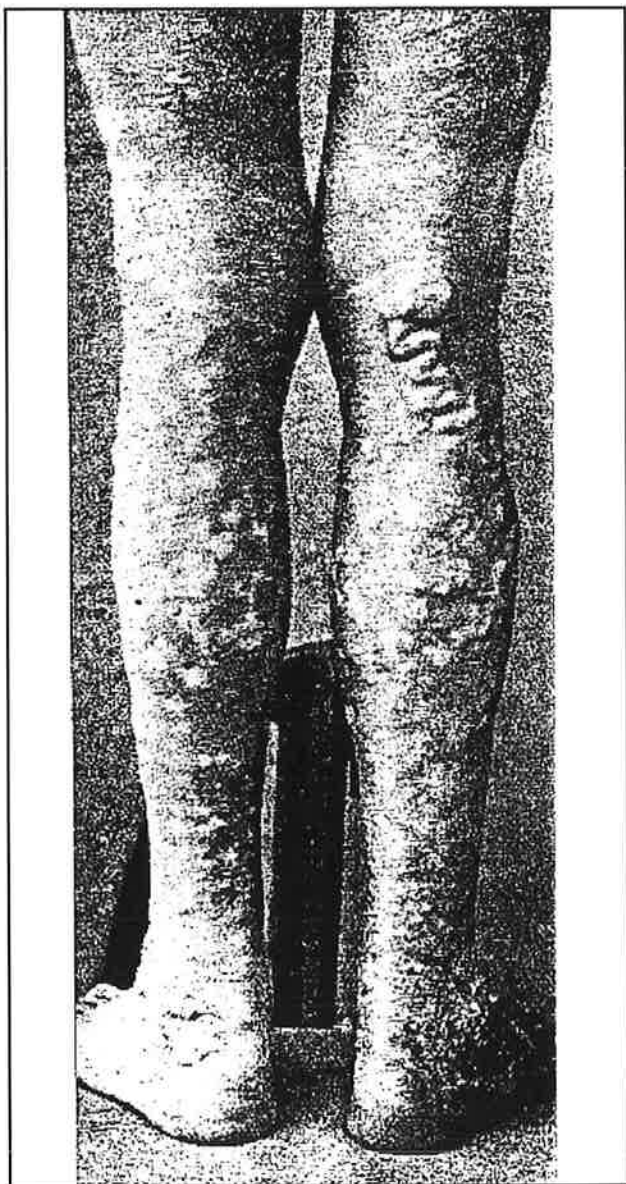


Figure 1

normal skin.

The sense of touch over the affected region is very little if any diminished, but the skin is distinctly hyperaesthetic. The patient shrinks away from the points of the aesthesiometer much more when the latter touch the atrophied skin than when the sound skin is touched, due evidently to loss or thinning of the protective layers of the epidermis.

So far as could be ascertained, the organic muscles of the extremities were not noticeably atrophic. The patient was not aware of any weakness of the limbs, and the muscles were firm and hard to the touch. The abnormal sense

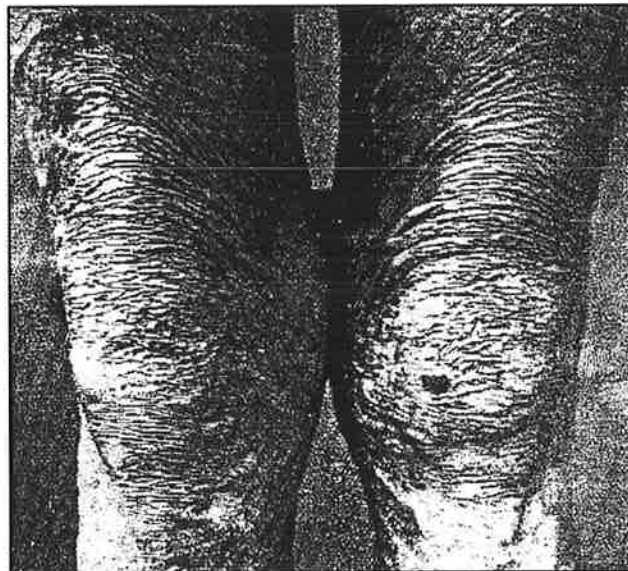


Figure 2

of fatigue, however, of which the patient complained, would imply that they were not entirely unaffected. The thinner appearance of the legs is doubtless, chiefly at least, attributable to the loss of subcutaneous fat. The muscular strength of the limbs seems little if any impaired, and apparently there is perfect co-ordination as well as normal tendon reflexes.

The above, though evidently a case of idiopathic atrophy of the skin, differs very materially from all the common forms of macular, striate, or diffuse atrophia cutis propria. The latter, as a rule, are simply of the quantitative type, and resemble merely superficial cicatrices. Still less does this case resemble the stationary form of the xeroderma of Kaposi. Nor does it correspond to the symptomatic atrophies, such, for example, as succeed scleroderma and morphoea. Not only is there the history in such cases of a precedent condition of infiltration or induration, with more or less stiffness of the skin, but rarely even in the atrophied stage is the affected area devoid of a certain degree of condensation and immobility. Nevertheless, in their ultimate state they may come to resemble the case which I have described above, and such cases have occasionally been reported as cases of idiopathic atrophy. In this category should, in all probability, be classed the "general idiopathic cutaneous atrophy" of Wilson, as well as the cases of Schwimmer<sup>1</sup> and Glax<sup>2</sup> though these latter are both improperly referred to the xeroderma of Kaposi, that of Schwimmer being also denominated "atrophia cutis universalis."

A case reported by Judassohn before the German Dermatological Society in September, 1891,<sup>3</sup> under the name of atrophis maculosa cutis, bore a certain resem-

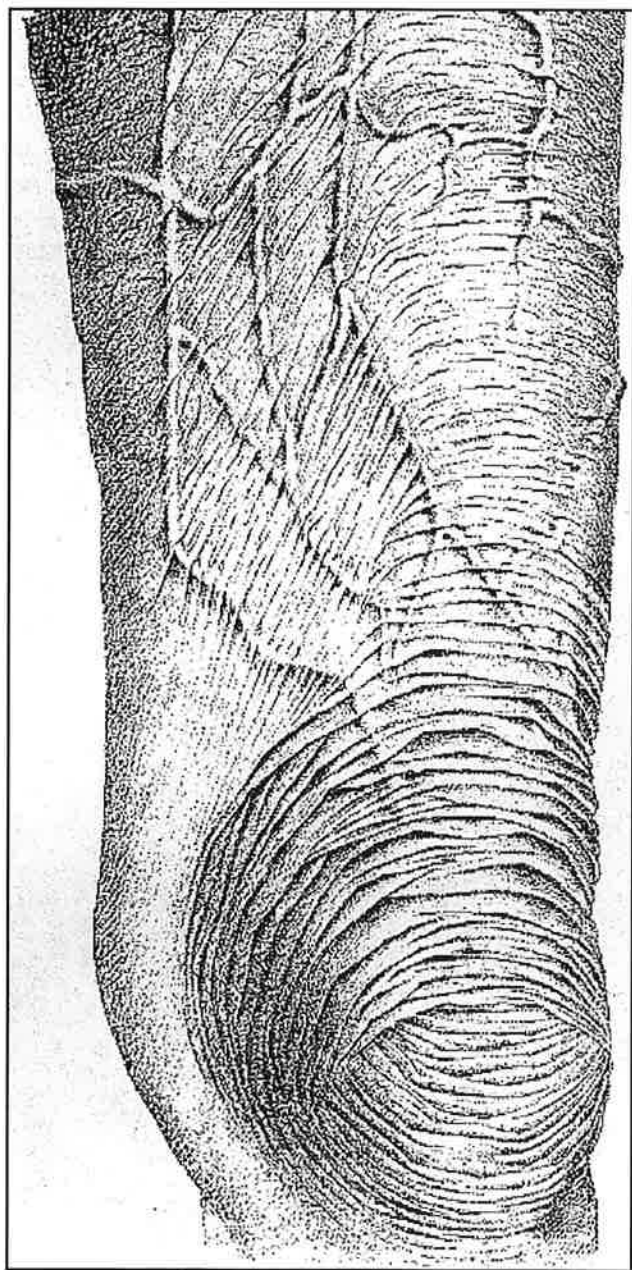


Figure 3. Buchwald's case.

blance in some of its features to the one just described. The lesions were symmetrical, and in some of the affected places the skin had the same dusky-red color and translucency, and was inelastic, wrinkled, and loosely adherent, but the atrophied spots were preceded by an eruption of papular elevations, that remained circumscribed and discrete, varying in size from that of a lentil to that of a silver mark piece. On account of the looseness and inelasticity of the skin, together with the preceding papulo-erythematous condition, he proposed the name *anetodermia erythe-*

*matodes*. In a similar case presented by Beer<sup>4</sup> at the Vienna Dermatological Society in February, 1892, the lesions were preceded by pronounced oedema. In both of these cases the atrophy affected chiefly the connective tissue, and more particularly the elastic fibers.

The clinical type to which my case most clearly corresponds was first described by Buchwald,<sup>5</sup> and so peculiar is the type and well differentiated is it by this writer that it might well be known as *Buchwald's atrophy*. In his case the affection occurred in a man thirty-six years of age, and had existed for sixteen years. It began at both knees and extended at first both upward and downward, later the extension being only upward, but upon the legs below the knees indolent ulcers often formed. The greatest extent was reached in one year from the inception of the disease, though within the affected areas the degeneration continued to increase. There were no prodromal symptoms, and the aetiology of the case was as obscure as that of mine. The entire surface of both knees and thighs involved, reaching in front to within five centimeters of the inguinal fold, and behind extending up over the nates, much as in my own case. (Fig 3.) The limits of the disease above were rather abrupt, the division between the normal, well-nourished, and fat skin above, and the somewhat sunken, darker-colored areas of atrophied skin below being marked by a pretty distinct ridge. The affected skin was freely movable over the subjacent structures, was nowhere bound down, rigid, nor oedematous. It could be raised in large folds which, when released, disappeared rather slowly or remained stationary until some movement caused them to disappear. Almost everywhere were multitudes of coarse or fine wrinkles. They were most marked about the knees, where they encircled the patellae, partly arranged in semicircles, partly in elliptical forms. On standing the wrinkling became more striking. Similar but finer wrinkles occurred, as in my case, over the nates. While in a recumbent posture the color of the skin was brown from pigmentation, but on standing the veins rapidly filled and became distended, and the color of the surface became cyanotic. There was no perceptible difference in temperature from the normal. The hairs had mostly disappeared from the affected areas. That the sweat glands were involved was shown not only by the customary dryness of the affected skin, but by the fact that when pilocarpine was injected hypodermically in a sufficient dose to cause copious diaphoresis the atrophied portions of the skin remained as dry as before. Sensation was not impaired. A microscopic examination of an excised bit of the diseased integument showed that the adipose layer had entirely disappeared. There was a general atrophy of all the elements of the skin, the sweat glands were largely diminished, there was marked atrophy of the hair follicles, and the papillae of the skin had disappeared. The connec-

tive tissue underneath the epithelial layer appeared swollen and infiltrated with the cell nuclei. The nerves and blood-vessels were unchanged.

Idiopathic cutaneous atrophy of the extremities, such as in this case of Buchwald's, to which my case so closely corresponds, is undoubtedly rare. Several other cases, however, have been reported which are so nearly alike in their general characters as to warrant us in regarding Buchwald's atrophy a peculiar variety of disease. Two cases that are apparently of this variety have been reported by Pospolow,<sup>6</sup> though in these the symmetry was less pronounced and the laxity of the skin (judging from a photograph that accompanies one of the cases) was somewhat greater than either in Buchwald's case or in my own. The photograph shows dependent folds of skin resembling dermatolysis. Also in Pospolow's cases the sweat glands were unaffected; but in the main the features corresponded to those of Buchwald's atrophy.

Touton<sup>7</sup> and Kristian Groen<sup>8</sup> have reported cases that are more typical. In Touton's case both upper and lower extremities were affected symmetrically. Groen's case, in the location and extent of the atrophy, corresponded almost precisely to my own case. The patient was a sailor, forty-seven years of age, who entered the hospital for atonic ulceration of the leg, and had apparently paid little attention to the atrophic condition, and of this no history was obtainable.

#### FOOTNOTES

1. Die neuropathische Dermatosen, Wien, 1883, p. 189.
2. Viertelj. f. p. Derm. u. Syph., 1875, p. 114.
3. Monatshft. f. p. Derm., 1892, p. 621.
4. Arch. f. Derm. u. Syph., 1892, p. 835.
5. Ein Fall von diffuser idiopathischer Haut-Atrophie. Viertelj. f. Derm. u. Syph., 1883, p. 543.
6. Annales de Derm. et de la Syph., 1886, p. 505.
7. Deutsche med. Wochens., 1886, p. 6.
8. Norsk Magazine. Referred to in the Lancet, Nov. 28, 1891, p. 1238.

# A Case of Idiopathic Atrophy of the Skin

George T. Elliot, MD

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There are only a limited number of cases of idiopathic atrophy of the skin recorded in medical literature, as may be seen in Dr. Bronson's<sup>1</sup> recent article and report of a superb example of the process. He has carefully collected those known, so that I need only cite his paper as a source for information on the subject, and I would, therefore, only add one more case to the list, which may possibly be of interest since, being for some months under observation, certain features in the mode of its extension could be observed and followed.

Male, German, aged forty-five, in the liquor business, consulted me February 25, 1889, for an ulcer on the left ankle, arising from a slight traumatism. The veins of the leg and feet were extremely varicose, and examination of the knee and thigh revealed the curious condition to be described in this article, and to which the patient had not made any reference. He stated that he was in robust health, though from time to time he had attacks of rheumatism. His functional condition was perfectly good. He was tall and slight in build. No history pointing to syphilis or to any chronic intoxication was obtainable. When a child, he had had an eczematous eruption in both popliteal spaces and ulcerations of the legs. Both had been treated and healed, the latter leaving scars still visible. About the age of twenty-five, he had been struck on the left knee by a ball, and he had been lame for some time after. Some thirteen years ago, he had been in the habit of jumping a great deal, both from heights and when on the ground. As nearly as he could remember, the cutaneous changes had begun about the left knee some fourteen or fifteen years ago, and they had slowly progressed up the thigh. When I saw him, the affected area began anteriorly about three inches below the Poupart's ligament, and posteriorly from the middle of the gluteal region. From these points, the changes extended over the entire skin of the thigh and nates down to and including the knee. The affected surface was completely atrophied, excessively thin, dry, wrinkled, and loose, not bound down, of a dark red, without traces of the hairs, and scaly. The veins were

very large, prominent and tortuous. No subjective symptoms were mentioned, nor was there hyperaesthesia, or anaesthesia of the surface.

The atrophic area was sharply limited and defined below by normal skin, but the upper boundary was slightly diffuse and continuous with a narrow, purplish-red zone. This zone was not elevated nor did it appear oedematous or swollen. It was more marked on the right knee, where the process was beginning and occupied only a space about two inches by four. This area was of recent date, and the patient stated that he had first noticed a purplish blush over the knee, followed in a short time by a varicose dilatation of the veins and a gradual thinning of the skin. Whether this description was exact or not I will not attempt to say, but the man was under observation until June, 1889, and it was seen that the purplish zone extended slowly up the thigh, and progressively as it advanced the veins became dilated and varicose, the skin atrophic, and the hairs disappeared, so that a condition entirely similar to that on the left thigh resulted. The ulcer on the ankle having been healed, the patient has no longer been seen. Unfortunately, specimens for microscopic study were refused.

With the exception of its more limited extent and the absence of subjective symptoms of all kinds, this case may be said to correspond very accurately in its clinical phenomena to Bronson's. It appears, however, to me that the most important feature shown was the purplish-red zone bounding the advancing area of atrophy, and which, progressively as it spread, was followed by the atrophic metamorphosis, a symptom not mentioned as occurring in Bronson's case. The process began at the left knee and extended upward and peripherally so as to occupy the entire thigh; but while at its point of inception the limitation toward the normal skin was sharp and incisively definite, above, the atrophic area gradually merged into the purplish-red zone, and this latter into normal skin. The same appearances were also noted over the right knee, and here slow extension was seen and followed, so that it would appear that this purplish-red area was the primary step in the process, and the atrophy was only its consequence. What pathological condition was represented by this clinical symptom it is certainly difficult to say, and rather useless to speculate upon, in view of the fact that the course alone of the process could be observed, while the changes in the skin itself were not. I would, therefore,

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*Reprinted with permission from Journal of Cutaneous and Genito-Urinary Diseases, 1895;13:152-154.*

*Dr. Elliot practiced in New York City.*

<sup>1</sup>E.B. Bronson, *Journal of Cutaneous & Genito-Urinary Diseases*, January, 1895.



only state that in my opinion the advancing cyanotic zone was the primary step and the most important part of the process, the atrophy being secondary. What was the aetiological factor or factors in the production of this progressive venous stasis and subsequent atrophy of the skin can also not be stated. The blow on the left knee from the ball might be regarded as an aetiological factor, but that would not explain the development of the process on the right

knee a number of years later. The habit of jumping, acquired by the patient, can likewise be excluded, as the primary changes had already existed about the left knee for a year or more before. In this case, therefore, as in the others recorded, the same conclusion is reached—that the cause of the atrophy is unknown and obscure, and no satisfactory explanation for its occurrence and existence can be given.

# Acrodermatitis Atrophicans Chronica

Hamilton Montgomery, MD and Ralph R. Sullivan, MD

Many names have been given to the disease considered in the present paper, which in the United States is most commonly referred to as acrodermatitis chronica atrophicans<sup>1</sup> but which when generalized also is called diffuse idiopathic atrophy of the skin. Other terms include "dermatitis atrophicans diffusa progressiva" (Oppenheim), *dermatite chronique atrophiante (maladie de Pick-Herxheimer)* and the older term *érythromyélie* (Pick). The disease is not to be confused with types of atrophoderma maculatum (atrophia maculosa et striata<sup>2</sup>) or macular atrophies, including forms of anetoderma,<sup>3</sup> or *vergetures*, and striae distensae. The terms "idiopathic macular atrophy," "anetoderma maculosum" or "anetoderma erythematodes" of Jadassohn, "dermatitis atrophicans maculosa" and *vergetures* are all applied to discrete, macular, atrophic lesions which may be associated with acrodermatitis chronica atrophicans, occur entirely independent of the latter disease or arise secondarily from other dermatoses.

We wish to report our observations in 45 cases of acrodermatitis chronica atrophicans encountered at the Mayo Clinic up to January 1944, in 20 of which one or more specimens were removed for biopsy. Emphasis will be placed on the histopathologic characteristics which we believe to be distinctive and specific in the majority of the cases. Acrodermatitis chronica atrophicans has been reviewed thoroughly by Oppenheim,<sup>4</sup> by Petges,<sup>5</sup> by Pautrier and his co-workers<sup>6</sup> and in the United States especially by Wise<sup>7</sup> and, more recently, by Sweitzer and Laymon.<sup>8</sup> We are essentially in accord with the opinions expressed in these reviews, which vary from one another only in certain points. One of us (R. R. S.) abstracted the literature including reports of cases up to 1936, and the other (H.M.) has done the same thing for the literature up to 1944. It is impractical, short of a monograph, to acknowledge all important observations, for most of which the reader is referred to the reviews previously

mentioned. Our remarks, therefore, are based on the correlation of multiple concepts and interpretations of what makes up acrodermatitis chronica atrophicans to be found in the literature, together with our own observations in this series of cases.

## CLINICAL OBSERVATIONS

Acrodermatitis chronica atrophicans may be defined as a chronic progressive form of dermatitis of unknown cause involving primarily the extremities (limbs) and characterized by a bluish red, thin, atrophic, tissue-paper-like wrinkled skin, resulting from atrophy of the epidermis or more especially of the cutis, so that the deeper vessels become readily visible (figures 1 to 4, in all of which except figures 2c and 2d the diagnosis was confirmed histopathologically). Subjective symptoms such as pruritus are usually minimal but may occasionally be severe. Most of the associated phenomena and variations of the disease will be mentioned in the following analysis of our cases without attempting a detailed description of these phenomena, which are well described in various treatises.

Thirty-seven of the patients who had acrodermatitis chronica atrophicans were women, and only 8 were men. This is a considerably higher proportion of women than in other series previously reported.<sup>9</sup> Six of the 45 patients were born in the United States, for most part native-born parents. Eight patients were of Scandinavian birth, and 1 was a Mexican, making 15 of the 45 who were born outside of the central land mass of European continent and Russia. Fifteen of our patients stated they were Jewish. Acrodermatitis chronica atrophicans has recently been reported in natives of South America,<sup>10</sup> Greece<sup>11</sup> and Turkey<sup>12</sup> as well as in a number of patients born in the United States. This disease, therefore, is not limited to one nationality or continent and occurs fairly frequently among native-born Americans.<sup>13</sup>

A familial history of disease has occasionally been reported<sup>14</sup> but was not encountered in this series of cases. The occupations of the patients in our series and other series were manifold and seemed to have no relation to the disease.

The age of the patient at the time of examination in our cases varied from 22 to 89 years, with an average of 53 years. The duration of the disease at the time of examination varied from 3 months for a woman aged 50 years to more than a half a century for a woman aged 57 years in whom the disease had been present since early childhood.

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At the time this article was initially published, Dr. Montgomery was Fellow in Dermatology and Syphilology, Mayo Foundation, Rochester, MN.

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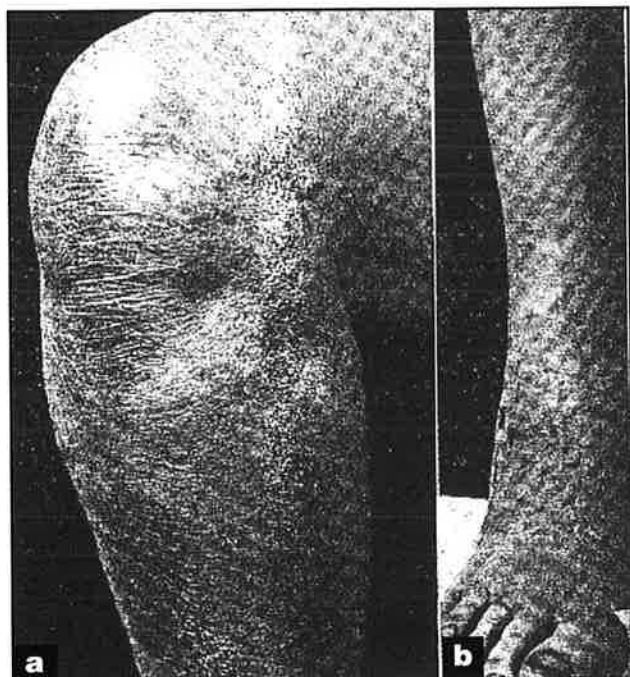


Figure 1. *Acrodermatitis chronica atrophicans*. (a) Knee of a woman aged 45 years who had generalized involvement of five years' duration. (b) Lesions of a year's duration on leg of a woman aged 70 years who had had stasis ulcers for twenty-two years. Note the pseudosclerodermatous changes on the ankle and superficial ulcers. Lesions also occurred on the other leg and on the arms.

The average duration was thirteen years. The age of the patient at time of onset of the disease varied from about 7 to 87 years with an average age of 40 years.

In conformity with previous reports, the disease tended to begin on the legs or arms, especially on the extensor surfaces, in relation to the joints, such as the elbows, knees, wrists and ankles. The disease started at the legs, ankles or feet in 33 cases and on the elbows or hands in 10. In 1 case from the beginning there was a generalized involvement of the body: in 1 case the site of onset was not known. Wise, Oppenheim and others have described the earliest changes as edematous, soft, bluish red, boggy or doughy tumors, which according to Wise have been confused with the edematous phases of scleroderma, sclerodema and allied conditions. We did not have the opportunity to see these early manifestations, nor were they described in more than 1 of our cases. In this case the patient, an Austrian woman cook, aged 34 years, who had *acrodermatitis chronica atrophicans* for ten years limited to both arms (fig. 2c and d), had been seen at a clinic almost ten years earlier, at which time a diagnosis had been made of erythema nodosum limited to both arms and of a month's duration. In retrospect, we believe this was the beginning of the *acrodermatitis*. Several others of our



Figure 2. *Acrodermatitis chronica atrophicans* (a and b). Typical changes of two years' duration, limited to both extremities. The patient was a woman aged 59 years. Note the branny scaling and pseudosclerodermatous changes on the ankles, which are independent of varicosities as shown in b, photographed with infra-red rays (c) Lesions limited to both arms of a woman aged 34 years. Note the ulnar band and deep-seated nodular infiltrations erroneously diagnosed previously as erythema nodosum. (d) Photograph made with infra-red rays in same case as in C.

patients gave a history of a diffuse edema of one or more extremities or of redness and diffuse swelling preceding any atrophic changes. In 1 case, there was a peculiar fusiform swelling of the wrists and the proximal phalanges of the first three fingers of both hands with limitation of motion apparently due to juxta-articular swelling but without changes discernible on roentgenologic examination or evidence of arthritis.

A history of trauma preceding the onset of the disease was given in only a few cases. In none of the cases in this series could the onset or course of the disease be attributed to changes of temperature either from exposure to the elements or as a result of the patients occupation.

In regard to distribution of the lesions, the legs were involved in 23 cases, the ankles or feet in 5, the legs and arms in 14 and the arms alone in 3. In 3 cases the lesions were unilateral, being limited in 1 case to one leg and in 2 cases to one arm; there was no serologic or clinical evidence of syphilis in these cases. The trunk and extremities were involved in 6 cases, in 2 of which there also was involvement of the face (fig. 3). In 3 of the 6 cases with involvement of the trunk there was generalized erythroderma, in 1 case with features of poikiloderma (fig. 3) Patchy alopecia of the scalp was also seen in this case.



Figure 3. *Acrodermatitis chronica atrophicans*. Generalized involvement of three years' duration, including the face. The patient was a woman aged 48. There were some features of poikiloderma. (This patient was presented at a meeting of the New York Dermatological Society in December 1943, by Dr. J. C. Graham. At that time all the members present, including Dr. Wise, concurred in the diagnosis of generalized idiopathic atrophy.)

Bullae, generalized pigmentation or vitiligo did not occur in any case in this series. In 1 case there was lichenification of the labia but without atrophy. In none of the cases was there evidence of atrophy or other involvement of any of the mucous membranes such as has been reported by Sweitzer and Laymon and others. The palms and soles were not involved except in 1 case, in which there was slight involvement of the plantar surface of one foot. In none of the 45 cases were tips of fingers or toes involved in the process.<sup>15</sup> Changes in the nails also were minimal and could not be attributed directly to the disease.

Varying degrees of so-called ulnar bands were encountered in 9 of the 45 cases (fig. 2c and d). These occurred as bands of infiltration, edema and fibrosis or later as atrophy extending along the ulnar to the wrist joint. The bands were also seen extending along the radius or, less frequently, from the knee down the tibia.

Fibrous nodules (fig 4a), which usually tend to be multiple and may be of the color of the skin or yellowish, occurred about the elbows or along the ulna in 4 of our cases. Because of their location over joints, they have been confused with juxta-articular and rheumatic nodules and, because of the color, with xanthoma. Typical lesions of xanthoma as reported by Jessner<sup>16</sup> were not demonstrable, and blood plasma lipids in 2 of the cases were normal. In 1 case (fig 4a) there was no evidence on histochemical or histopathologic analysis of increase of tissue

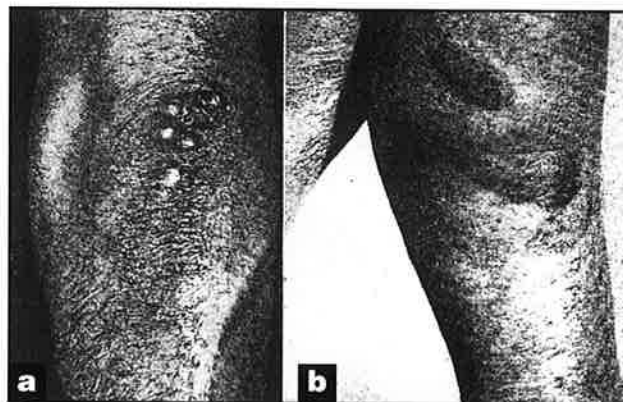


Figure 4. (a) Fibrous nodules of ten years' duration on the elbows associated of the limbs of seven years' duration. The patient was a man aged 57 years who had old, treated latent syphilis and also arteriosclerosis obliterans of the lower extremities of two years' duration. (b) *Acrodermatitis chronica atrophicans* of three years' duration, with dark areas of amyloidosis on the leg. The patient was a woman aged 44 years.

lipids. According to Oppenheim<sup>17</sup> lipomas or lipomatous masses above an area of acromdermatitis are fairly frequent occurrence, but none were seen in this series.

Pseudosclerodermatous changes were encountered in 17 of 45 cases, in most instances being limited to the legs, ankles and feet. They occurred as ill defined, brawny, infiltrated bands and plaques often associated with a branny or flaky scale (figs. 1b and 2). Occasionally the skin of the entire leg was reddened and tense rather than lax and wrinkled, apparently as a result of edematous rather than true sclerodermatous changes. One patient had pseudosclerodermatous -bands on the trunk. In none of the cases were there lesions of morphea or the distinct, sharply defined, linear bands of localized scleroderma, and none was there evidence of acrosclerosis, sclerodactylia or Raynaud's disease.

Ulcers of various types were encountered in 14 cases and occurred chiefly on the lower extremities, especially about the ankles and especially in pseudosclerodermatous areas (fig.1b). In 6 of these cases, there was a history of varicose or stasis ulcers of the lower extremities preceding the *acrodermatitis chronica atrophicans* by a good many years. In all of the 6 case there was definite evidence of venous circulation. In other cases in which ulcers occurred, there was no evidence of venous incompetency. Photographs with infra-red rays in several cases did not reveal any relation of the superficial veins to the ulcers or to the ulnar bands or areas of pseudoscleroderma (fig. 2). Ulceration, as a rule, did not occur in atrophic areas. In 1 case, however, in which there was generalized *acrodermatitis* (fig. 3) multiple small bluish red, purpuric, hemorrhagic lesions were scattered over the trunk. These lesions

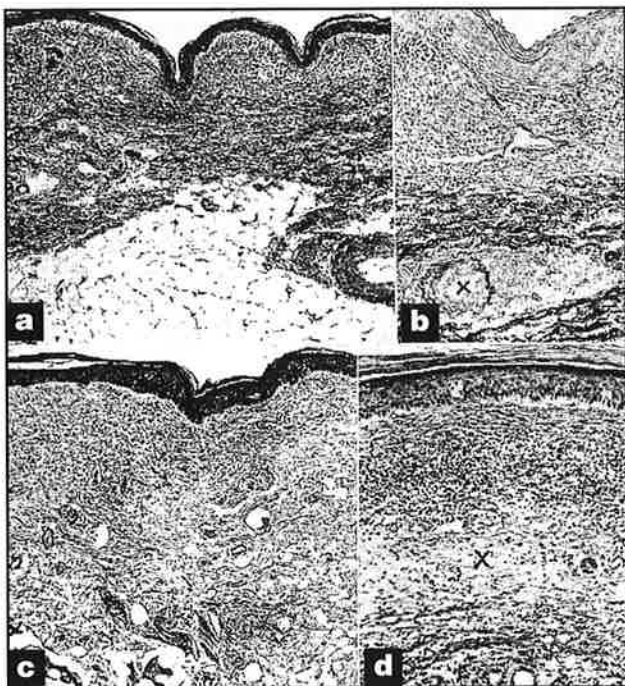


Figure 5. *Acrodermatitis chronica atrophicans*. (a) A section from the leg; typical atrophic epidermis with border zone and then infiltrate and atrophy of the cutis and dermal appendages (x40). (b) Same case; note the preservation of fine elastic fibrils near the epidermis, destruction of elastic tissue where infiltrate occurs and involvement of a vessel at X (x115). (c) Same case as figure 3; section from the arm. Note the fat replacement atrophy in the cutis and similar involvement of arrectores pilorum muscles at X (x50). (d) Section from the hand, typical changes with distinct border zone but also senile cutaneous changes with bluish-staining collagen fibers at X (x100).

broke down into indolent ulcers up to 1 cm. in diameter which healed slowly. Oppenheim<sup>4</sup> (his figure, 27 page 584) described a case in which there were impetiginous ulcers of the ankles and the legs from which staphylococci were isolated on culture and which to a certain extent resembled small gummas.

In only 1 case of *acrodermatitis* were there associated lesions of macular atrophy, a much smaller incidence of association of these two diseases than in other series reported in literature. In 1 of our cases there was localized amyloidosis (fig. 4b). In 1 case *acrodermatitis* was associated with long-standing eczema, probably atopic. A few cases associated with psoriasis<sup>18</sup> have been reported but without relation to the psoriasis, and this applies to lichen planus<sup>8</sup> and rare combinations of *acrodermatitis chronica atrophicans* with dermatitis herpetiformis, erythrocyanosis, lupus erythematosus, Hodgkin's disease,<sup>19</sup> ichthyosis, herpes zoster and livedo racemosa as reported by Oppenheim.

In regard to systemic disease, there were only 12 in our series of 45 in which there was evidence of cardiovascular

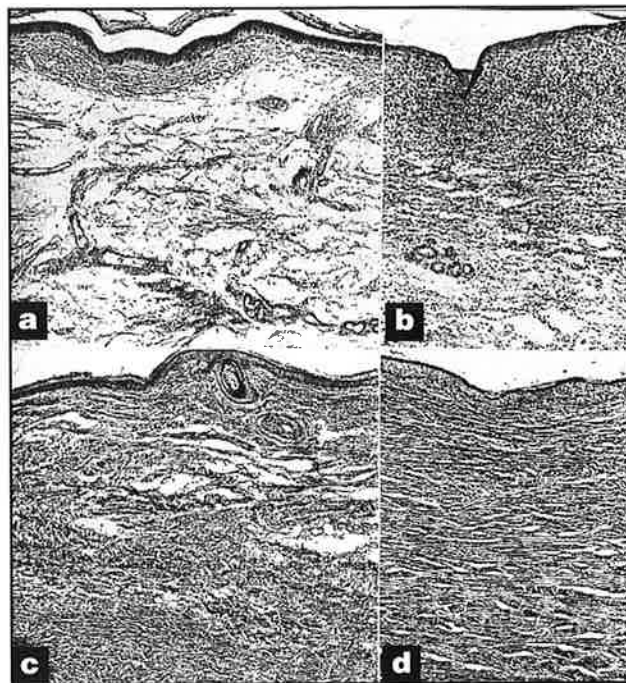


Figure 6. *Acrodermatitis chronica atrophicans*. (a) Same case as figure 1b but from elbow. Early acute edematous stage of one year's duration; very narrow border zone between the infiltrate in the upper layer of the cutis and the atrophied epidermis (x40). (b) Right knee in a case of unilateral involvement of thirteen years' duration. Note the persistence of the intense inflammatory reaction with imperfect border zone but preservation of the granular layer (x70). (c) Same case and site as figure 4a. Typical changes in the epidermis and the upper layer of the cutis and a dense fibrous nodule deeper in the cutis. (x26). (d) From a pseudosclerodermatous band in the right breast. Note the extreme fibrous but also the atrophy of the epidermis. The patient had generalized involvement of six years' duration starting on the feet. Typical ulnar bands are also present (x50).

disease. Only 4 patients had any degree of arteriosclerosis. Four others had hypertension; 3 had definite cardiac disease, and 1 had arteriosclerosis obliterans. This patient had a moderate elevation of plasma lipids, but this is common in the disease. In all but 2 of these 12 cases the cardiovascular involvement begun in the later decades of life and without definite relation to the *acrodermatitis chronica atrophicans*. The results of vascular studies, including capillary studies in several of the cases, were essentially negative.<sup>20</sup>

Varying degrees of arthralgia or mild arthritis occurred in 7 of the 45 cases. In none, however, was there arthritis deformans such as Sweitzer and Laymon<sup>8</sup> have described, and in none of many cases studied roentgenologically were there atrophic roentgenologic changes in the bones as described by Jessner and Loewenstamm<sup>16c</sup> in 10 of 17 cases. The symptoms of arthritis in some cases appeared before the cutaneous lesions. Foci of infection were pre-





Figure 7. (a) Same case as figure 2a. Pseudosclerodermatous region of the ankle with some thickening of the epidermis, dilation of superficial vessels with thickening of the walls of deeper vessel at X, fragmentation and diminution of elastic fibers except in the upper layer of cutis, where there is some increase (x45). (b) Same case as figure 4b. Changes of acrodermatitis at the left side. At the right side are homogenous masses of amyloid, also involvement of the walls of a blood vessel (x50).

sent in only a few cases. The same was true in regard to anemia or thyroid dysfunction.

No definite relation of the disease to the menopause or ovarian dysfunction could be established, despite the predominance of women more than 40 years of age in the series. Systemic disease appears to be coincidental or at most a secondarily associated phenomenon of acrodermatitis chronica atrophicans.

### HISTOPATHOLOGY

There is a lack of agreement in regard to the significant histopathologic changes in acrodermatitis chronica atrophicans.<sup>21</sup> This can be explained from the fact that the microscopic changes vary considerably depending on the stage of the disease and on the location of the region from which tissue is taken for biopsy, including whether there were associated fibrous nodules or pseudosclerodermatous changes. Furthermore, it must be borne in mind that from the histopathologic descriptions many of the older reports of this disease did not belong with the reports of acrodermatitis but with those of the other atrophic dermatoses. The histopathologic changes usually have been divided into acute, inflammatory and atrophic stages; but these are not clearcut, and the duration of any stage varies greatly not only in different cases but in different areas in the same case. We shall review the multiple changes to be seen in the disease and then briefly emphasize the histopathologic changes which we believe to be diagnostic (figs. 5 to 7).

The earlier acute phases of this disease as described by Gans,<sup>21c</sup> Kyrle,<sup>21a</sup> Oppenheim<sup>4</sup> and others include an early inflammatory and often edematous stage, in which there is a perivascular inflammatory reaction in the cutis without alteration of the epidermis. The rete ridges are well preserved, and the stratum corneum usually shows no change. Exceptionally, there is slight parakeratosis. Gans, Kyrle, Oppenheim and others explain the doughy infiltrations seen clinically on the basis of transitory edematous changes in the cutis, which could account for transient parakeratosis. Parakeratosis is not present in later stages of the disease. The infiltrate in the beginning is composed of a multiplicity of types of cells. The elastic and connective tissues are unaltered. There is no diminution of the thickness of the cutis, nor is there any atrophy of the dermal appendages. In none of our series of cases were specimens for biopsy taken until the disease had been present for a year. A biopsy of a typical lesion of a year's duration over the elbow of a woman aged 70 revealed extensive edema throughout the cutis but already showed typical histologic changes of acrodermatitis chronica atrophicans (fig. 6a). Edema may persist histologically for many years, even decades after the onset of this disease.

Within a few months at the most, histologic changes more characteristic of the disease make their appearance. There is relative to absolute hyperkeratosis but no parakeratosis. The granular layer is usually present but is thinned. Varying degree of atrophy of the prickle cell layer are encountered. The cells may be flattened, and the intracellular bridges may become indistinct. There is also flattening of the basal cells, which may contain varying amounts of melanin pigment. Occasionally there is a mild degree of intracellular edema with vacuolar changes in the basal and prickle cells. The rete ridges have become flattened and have disappeared, so that the epidermis stretches out as a thin, flat ribbon with varying degrees of undulations or waves, which represents the lines of cleavage of the skin.

Just beneath the epidermis there is a border zone of connective tissue separating a band of infiltrate which lies beneath it from the epidermis. This border zone may be very narrow and composed of a few slender strands of connective tissue fibers running parallel to the epidermis, or there may be a wide zone, several times the thickness of the epidermis. In the beginning, the collagen fibers are distinct. Later there are homogenization and hyaline-like changes, so that the fibers merge. Even though the band of infiltrate beneath the border zone is dense, the cells of the infiltrate rarely penetrate through the border zone connective tissue to invade the epidermis and result in early liquefactive degeneration of the basal cell layer (fig. 6b). This happens in about 10 percent of all cases, but, even when such changes are seen, stains for connective tissue reveal that the collagen fibers have been thinned and

pushed apart but have not been completely destroyed. Fine fibrils of elastic tissue are found in the border zone arranged in loops perpendicular to the epidermis, which suggests that they are remnants of the elastic fibrils normally present in the papillary bodies (fig. 5b). These elastic fibrils lie in close proximity to the epidermis, and are not separated from the flattened epidermis by a zone of edema, such as occurs in lichen sclerosus et atrophicus. These fine elastic fibrils tend to persist in the border zone for many years, but, as a rule, they disappear, when homogenization and hyaline changes occur in the connective tissue.

There is a dense band of infiltrate beneath the border zone of connective tissue. The infiltrate in the beginning, according to Gans,<sup>21c</sup> is limited chiefly to the upper layer of the cutis but later may extend throughout the cutis and subcutaneous tissue. The infiltrate is essentially perivascular and therefore also occurs about the dermal appendages and the larger vessels in the subcutaneous tissue. From the beginning, the infiltrate is composed chiefly of mononuclear cells, especially lymphocytes, and of fixed connective tissue cells, including histiocytes or reticulum cells, the latter of which may predominate over the lymphocytes. Few polymorphonuclear leukocytes or eosinophils are seen. In some cases there are varying numbers of chromatophores laden with melanin or hemosiderin pigment. In our experience, which is contrary to that of some European authors, plasma cells did not predominate nor did mast cells occur frequently. We did not observe giant cells or histologic evidence of tuberculosis, including the formation of tubercles in any of our cases. Histologic evidence of leprosy or syphilis was also absent.

There is a gradual wasting of the connective tissue fibers where the infiltration occurs. The collagen fibers become homogenized and fragmented, and the number of nuclei decreases. In addition in some cases there are islands of fat cells and fat droplets high up in the cutis, near the epidermis, which seem to result from fatty degeneration of collagen fibers rather than to represent an invasion of fat cells from the subcutaneous tissue (fig. 5c). It is not clear just how this degeneration of the collagen fibers takes place. The change seems to be abrupt. One rarely encounters alteration of the staining qualities of the connective tissue fibers or their merging with elastic fibers, such as occurs in so-called senile skin.<sup>22</sup> This phenomenon occurred in only 1 case: the patient was a woman aged 75 who showed senile cutaneous changes in the biopsy specimen from the hand (fig. 5d) but failed to show such changes in two other specimens taken from covered portions of the body. The atrophy of the collagen fibers results in a decrease of the cutis to a half or a quarter of its normal thickness. Atrophy of the cutis, however,

may not occur until the disease has been present for many years, the degree of atrophy being dependent apparently on the extent and persistence of the infiltrate.

The elastic tissue, like the collagen, is destroyed where the infiltration occurs, and again the change is abrupt. The same is true in regard to destruction of *Gitterfasern* (lattice, or reticulum, fibers). The intensity of the infiltrate tends to decrease as the process becomes older, but, even in lesions of several decades' duration which clinically show atrophy without inflammation, one nevertheless finds a definite band of infiltrate beneath the border zone of connective tissue. As the infiltrate decreases, there is evidence in some cases of an apparent attempt at regeneration of the elastic fibers, and this also has been observed by Gans, Kyrle and Oppenheim. Thin, fine, wavy elastic fibrils appear both above and below the band of infiltrate. These are similar to the apparent new formation of elastic fibers seen in *striae cutis distensae*.

The dermal appendages are surrounded by the infiltrate. Early in the disease there are atrophy and disappearance of the sebaceous gland, and later the same is true in regard to the hair follicles. The arrectores pilorum muscles may also be invaded by the cells of the infiltrate and present varying degrees of atrophy. Occasionally, however, these muscles appear to be hypertrophied and to lie parallel to the epidermis rather than in their normal oblique position. One case in which there was leiomyoma has been reported.<sup>23</sup> Destruction of the sweat ducts frequently takes place, a fact which fits in with the diminution of sweating that has frequently been observed in this disease. The sweat glands may be intact and well preserved, but frequently they are also invaded by lymphocytes and monocytes with varying degrees of destruction of the sweat glands. In other cases, the walls of the sweat glands are thinned and their lumens are dilated and cystic, possibly secondary to obstructive phenomena in the ducts. The elastic tissue in the propria of the sweat glands is usually preserved. Although the bundles of cutaneous nerves are frequently surrounded by an infiltrate, no degenerative or atrophic changes have been apparent. Pautrier and Diss<sup>6d</sup> are the only authors to report a case in which there are definite changes in the cutaneous nerves. When dermal appendage is atrophied but not destroyed, there eventuates a mild degree of fibrosis about the atrophied appendage.

The subcutaneous tissue usually shows decided atrophy with decrease of the size of the fat cells, varying degree of Wücher atrophy (fat replacement atrophy by invasion of the infiltrate) and a varying degree of fibrosis.

Changes in the blood vessels vary greatly, but we failed to substantiate the concept of some authors that acrodermatitis chronica atrophicans is primarily a vascular disease. In the beginning, there usually is a varying degree of

dilatation of the superficial blood vessels, lymphatics and capillaries, with swelling and at times proliferation of the endothelium of the smaller vessels. A perivascular infiltration frequently results in inflammatory and destructive changes in the walls of both smaller and larger vessels. Frequently, however, most of the vessels appear well preserved, without alteration of their walls and with normal elastic tissue membranes. When a specimen biopsy is taken from the leg in cases associated with varices, one may anticipate finding evidence of varices histologically. They would appear to be coincidental findings, just as were the atheromatous changes encountered in 1 case of acrodermatitis in which there was associated arteriosclerosis obliterans. Petges<sup>5</sup> and Jessner,<sup>16a,b</sup> however, explained the varices as a result of degeneration of the elastic tissue, which deprives the vessels of their support.

Small deposits of calcium occurred in 2 of our cases but without evidence of systemic calcinosis. In 1 of our cases (fig. 7b), there were deposits of an amyloid-like substance which gave weakly positive reactions to different stains for amyloid. The deposits of amyloid in this case could scarcely be attributed to injections which had been given for varicose veins. There was no evidence of systemic amyloidosis. Kenedy<sup>24</sup> reported 1 case of localized amyloidosis and referred to possibly 3 or 4 others in the literature. In searching for the cause of the atrophy of the collagen, sections in many cases were stained for mucin, with negative results. The deposition of amyloid and calcium which occurred in 2 cases would seem to be secondary degenerative phenomenon rather than any primary etiologic significance.

In the end, or atrophic, stage of acrodermatitis, there is a decided decrease of the infiltrate or it may even be absent. With the disappearance of the infiltrate, one sees simply an atrophic epidermis and cutis, the latter containing homogenized fibrotic tissue. There may be regeneration of the elastic tissue in some regions and absence of elastic tissue in some regions and absence of elastic fibers in others. When the elastic fibers are absent, it is problematic whether they were destroyed by the infiltrate or by toxic products of this. The histopathologic changes in this terminal stage are no longer diagnostic, any more than are the histologic characteristics of scars in most other dermatoses.

Many descriptions have been given of histologic changes in so-called ulnar bands. Frequently the picture is that of typical acrodermatitis associated with decided edema. In other cases, fibrotic and sclerodermatous-like changes have been described. The infiltrate may be spotted and diffuse. There may be some increase of connective tissue fibers rather than merely a swelling of the edema.

The fibrous nodules (fig. 4a) seen in association with

acrodermatitis chronica atrophicans. (fig. 6a) present a histopathological picture varying from that of subdermal fibrosis or dermatofibroma. (fig. 6c) or even keloid (fig. 6d) to that of histiocytoma, in which deposition of hemosiderin and lipids occurs. In other cases, there is central pseudonecrosis in the nodule, so that the histopathologic changes closely simulate those seen in juxta-articular and rheumatic nodules. There was no evidence of xanthoma in any of our cases.

Regions of scaling with lichenification and induration which are often associated with pseudosclerodermatous changes—especially about ankles—likewise show histologic changes that are not distinctive (fig. 7a). There may be typical changes of acrodermatitis above a region of fibrosis or pseudoscleroderma. Frequently, the sclerodermatous process extends right up to the epidermis. There may be thickening of the epidermis, with hyperkeratosis, acanthosis and proliferation of the rete ridges. Thus all the pathologic characteristics of acrodermatitis become lost in these regions. There frequently are dilatation of the superficial capillaries, a region of dense fibrosis with homogenization of the connective tissue fibers and varying degrees of sclerotic changes in the deeper parts of the cutis. The infiltrate usually is more prominent than in cases of true scleroderma, but, again, it may be minimal. The elastic tissue is frequently destroyed in the fibrotic and sclerodermatous regions, especially in the fibrotic nodules resembling juxta-articular nodes. In other cases, the elastic tissue is merely frayed and splintered and there may even be new formation of elastic fibers. We do not believe that a sharp distinction can be made on the basis of histopathologic observations alone between the pseudosclerodermatous plaques of acrodermatitis chronica atrophicans and true scleroderma.

The histopathologic changes in ulcers associated with acrodermatitis chronica atrophicans are not diagnostic *per se* and are dependent on multiple associated factors.

*Summary of Histopathologic Changes.* The histopathologic changes in acrodermatitis chronica atrophicans are, we believe, diagnostic in practically all cases if a specimen for biopsy is taken from a well developed region independent of any associated fibrous nodules, sclerodermatous changes or ulcers. The following combination of changes makes a diagnostic picture: There are relative to absolute hyperkeratosis, preservation of a granular layer, atrophy and flattening of the prickle cell layer, loss of rete ridges and papillary bodies, with resultant flattening of the epidermis into a thin, wavy line and a definite border zone of normal to homogenized connective tissue between the epidermis and the infiltrate in the cutis. The infiltrate appears as a narrow or wide band beneath the border zone. There is destruction of connective and elastic tissue in this region, with pronounced atrophy to destruc-

tion of all the dermal appendages except, at times, the sweat glands. The cutis is definitely thinned as is also the subcutaneous tissue, so that deeper blood vessels become readily visible through the skin.

### DIFFERENTIAL DIAGNOSIS

Acrodermatitis chronica atrophicans in its usual form involving the limbs is easily recognized clinically and presents a characteristic histopathologic picture. Cases, however, of generalized involvement occur, including diffuse generalized erythroderma and others presenting features of poikiloderma. On careful analysis of the clinical and histopathologic changes, these as well as many cases presented as cases of generalized idiopathic atrophy are definitely instances of acrodermatitis chronica atrophicans. It is in cases in which there is extensive involvement, however, that the disease has been confused with other dermatoses. For example, we excluded from our series of cases, 1 which on final analysis fitted in better with cases of disseminated lupus erythematosus or possibly so-called poikiloderma and others in which the final diagnosis were respectively parapsoriasis, generalized lichen sclerosis et atrophicus, generalized atrophic lichen planus and finally unilateral scleroderma with morphea which had undergone involution. Ormsby's case of acrodermatitis chronica atrophicans,<sup>25</sup> presented first as an instance of poikiloderma and later considered by eminent dermatologists to be also a case possibly of planus, lupus erythematosus or parapsoriasis variegata, illustrates the difficulties of diagnosis. Acrodermatitis in which there was unilateral involvement has been attributed in the past to syphilis. This could not be substantiated in our series. Pardo-Castello<sup>26</sup> reported acrodermatitis chronica atrophicans associated with leprosy, which again can be distinguished by concomitant findings. The same applies to cases of cutaneous tuberculosis with poikiloderma-like changes.<sup>27</sup>

Oppenheim<sup>28</sup> expressed the belief that poikiloderma atrophicans vasculare of Jacobi is not a real clinical or histopathologic entity. In his opinion some cases belong with the cases of dermatitis atrophicans progressiva (acrodermatitis chronica atrophicans), others belong with cases of poikilodermatomyositis (Petges) and in a third group the disease is secondary to various dermatoses. We concur in this view. Foerster in the United States and other have for some time emphasized that in most cases poikiloderma is secondary to various dermatoses, including also lymphoblastomas.<sup>29</sup> Gans<sup>21c</sup> described the histopathologic changes in poikiloderma as simulating those of lupus erythematosus. In poikiloderma, lupus erythematosus and lichen planus, histopathologically, there is definite liquefaction degeneration of the basal cell layer, which in itself serves to distinguish these diseases from

acrodermatitis chronica atrophicans. Furthermore, in acrodermatitis there is a definite border zone between the epidermis and infiltrate and there is decided destruction of the collagen fibers.

Lichen sclerosis et atrophicus shows pronounced atrophy of the epidermis with preservation of the elastic fibrils beneath the epidermis, but the fibers are separated from the epidermis by a zone of edema and other histopathologic changes are entirely different from those of acrodermatitis. Parapsoriasis presents an entirely different histopathologic picture. In localized scleroderma, there are usually some preservation of rete ridges and an increase of connective tissue, but, as mentioned previously, differentiation from pseudoscleroderma plaques of acrodermatitis chronica atrophicans may not be possible histopathologically. Wise and more recently, Benjamowitz and Maschkilleisson<sup>30</sup> have given complete and thorough clinical distinctions between forms of scleroderma and acrodermatitis chronica atrophicans, which need not be repeated here. It is sufficient to reiterate that in none of the 45 cases in our series was there evidence of localized or generalized forms of scleroderma, acrosclerosis, Raynaud's disease, scleredema or dermatomyositis.

Distinction between acrodermatitis chronica atrophicans and erythrodermic forms of lymphoblastoma with or without poikiloderma-like changes may be difficult both clinically and histopathologically.<sup>31</sup> The infiltrate in acrodermatitis can be extensive and dense, simulating that seen in the lymphoblastomas. In both diseases there is frequently a considerable increase of histiocytes and reticulum cells.

We recently had under our care a man, an American teacher aged 49 years, who had extensive diffuse generalized erythroderma and atrophy of the skin for twenty-two years associated with impetiginous and gummatous ulcers and whom we first regarded as presenting more extensive ulcers in acrodermatitis that those described by Oppenheim<sup>4</sup> and illustrated in the "Handbuch." There were extensive ulcerations involving the entire left leg, and subsequent biopsies revealed histopathologic changes strongly suggestive of a lymphosarcoma. The case histologically resembled somewhat a case previously reported by Goeckerman and one of us (H.M.).<sup>32</sup> It is possible that this patient had had acrodermatitis for twenty-two years and just recently a lymphoblastoma had become superimposed. This could be explained on the basis of malignant transition of the dense infiltrate of reticulum cells and histiocytes, but it seems more likely that the lesion has been a slow-growing progressive lymphoblastoma with erythrodermic and poikiloderma-like changes from the beginning.

As a rule, however, clinical or histopathologic distinc-

tion between lymphoblastoma and acrodermatitis chronica atrophicans is readily made on the basis of concomitant findings.

Various types of idiopathic macular atrophy, including anetoderma erythematodes of Jadassohn, striae distensae and balloon lesions of the Schweninger-Buzzi multiple benign tumor-like new growths, have all been described in association with the acrodermatitis chronica atrophicans.<sup>33</sup> Histopathologic studies were not made in the 1 case that we had of acrodermatitis chronica atrophicans associated with lesions of idiopathic macular atrophy. We had 2 patients with idiopathic macular atrophy without acrodermatitis chronica atrophicans in which the histopathologic changes, as has been described in the literature, were similar to those of acrodermatitis chronica atrophicans. It is our impression, however, from a review of the literature, especially the excellent studies by Chargin and Silver<sup>34</sup> and Scull and Nomland,<sup>35</sup> that although there is destruction of elastic fibers in both diseases there usually is much less infiltrate in idiopathic macular atrophy than acrodermatitis and that the epidermis may be little affected, the rete ridges and papillary bodies remaining unaltered. This also applies to striae distensae and to the Schweninger-Buzzi balloon type of lesion.<sup>36</sup>

Macular atrophies also occur as secondary terminal manifestations to such diseases as syphilis, leprosy, lupus, erythematosis and lichen planus and can be distinguished on the basis of concomitant findings.

### MALIGNANT CHANGE

Epitheliomas (carcinomas) and sarcomas occasionally have been reported in association with acrodermatitis chronica atrophicans, but we believe that in many of these cases they were probably coincidental and not attributable to the disease and in others the diagnosis was not substantiated by histopathologic studies.

Slow-growing sarcomas have been reported in only 2 or 3 cases.<sup>37</sup> If one accepts the concepts of Kyrle, Petges, Jessner and others that pseudosclerodermatous proliferation and fibrous nodules represent late attempts at repair in acrodermatitis chronica atrophicans, then one can conceive how this process could proceed further to malignant change.

Most of the epitheliomas reported have arisen either from old stasis (varicose) ulcers or ulcers associated with pseudosclerodermatous infiltration, especially those about the ankles. There were 2 cases of the 45 in our series in which epitheliomas were found. In 1 case a squamous cell epithelioma of grade 2 (Broders' method) developed from a stasis ulcer of the ankle which was of thirteen years' duration whereas acrodermatitis had been present only five years. In the second case, a 75 year old woman had

had senile keratoses of the face and recurrent epithelioma of the neck of many years' duration. In addition, she had on the right flank a typical lesion of superficial epitheliomatosis, histologically basal cell in type, which was of ten years' duration and which was situated in a pseudosclerodermatous band. The acrodermatitis was generalized but of only two years' duration. In neither of these 2 cases was any atrophy of the epidermis to be found adjacent to the epitheliomas, nor had the epitheliomas arisen from the atrophic skin. The epitheliomas, therefore, in both of these cases can be presumed to represent a coincidental condition not related to the acrodermatitis. In the third case of acrodermatitis chronica atrophicans, there was a large stasis ulcer of the ankle which had a pearly, rolled indurated border clinically strongly suggestive of a squamous cell epithelioma but which at the time of excision and graft proved histologically to be benign, with only a moderate degree of pseudoepitheliomatous hyperplasia.

Pack and Wuester<sup>38</sup> in 1942 reported 4 cases of epithelioma in association with acrodermatitis chronica atrophicans and referred to the disease as a precancerous dermatosis, as did Slaughter<sup>39</sup> more recently. This perhaps may be attributable to MacKee and Cipollaro's<sup>40</sup> inclusion of acrodermatitis chronica atrophicans with precancerous dermatoses, using this term in the broadest sense and not, as one of us (H.M.) has done, limiting the term to a few dermatoses in which epithelioma happens to develop in 20 percent or more of the cases and which are characterized histologically by squamous cell epithelioma in situ.<sup>41</sup> Pack and Wuester stated that most basal and squamous cell epitheliomas are scar cancers. We cannot agree with this view. They failed to distinguish between hypertrophic and atrophic scars. Thus, as Counseller, Craig and Montgomery<sup>42</sup> have shown, epitheliomas frequently arise from leukoplakia but not, as a rule, from kraurosis vulvae unless leukoplakia has first supervened. Senile, roentgen ray, radium, arsenic and tar keratoses are true precancerous lesions. Epitheliomas arising from chronic ulcers of the leg due to burns, varices and so forth occur in less than 6 percent of the cases and are not true precancerous lesions.

On further analysis of Pack and Wuester's 4 cases, one finds that in their first case of acrodermatitis chronica atrophicans with epithelioma the disease was limited to the axillary regions and upper part of the arms, a distribution of lesions which does not correspond to that in any case previously reported: that the patient had had eighteen roentgen treatments, including the treatment of palpable lymph nodes, and that histologically the epithelioma was of the type one would associate with radiodermatitis. Illustrations of the second case show senile keratoses on the backs of the hand, suggesting origin of the epithe-



lioma of the hand on this basis. No statement is made as to the origin of the ulcers on the ankles, although there is no question that the patient also had acrodermatitis chronica atrophicans. In their third case, one might be justified in presuming that the epithelioma arose from senile keratosis rather than from the atrophic skin. In their fourth case, despite the history of "great varicosities" of both legs, the lesion must presumably be accepted as a squamous cell epithelioma developing in atrophic skin of acrodermatitis chronica atrophicans, although no histologic details were given regarding the presence of varices or changes in the epidermis adjacent to the epithelioma. Wise<sup>43</sup> gave a brief report on a case of acrodermatitis chronica atrophicans in which squamous cell epithelioma developed as an ulcer in the atrophic skin on the inner aspect of the right thigh and remained healed after treatment. No details are given as to the method of treatment or whether the diagnosis was confirmed by histologic examination.

The few other cases of epithelioma on acrodermatitis chronica atrophicans reported in the literature are difficult to evaluate because of the lack of sufficient data. If one excludes epitheliomas that arose from stasis ulcers or from senile keratosis, then the incidence of epitheliomas in acrodermatitis chronica atrophicans at most is only a few per cent.

We object to the designation of acrodermatitis chronica atrophicans as a precancerous dermatosis because if one so designates this disease then a great many common dermatoses, such as psoriasis and lichen planus, in which epitheliomas rarely are seen independent of any treatment, would also have to be included under this term.

### TREATMENT

There is no known treatment for acrodermatitis chronica atrophicans that is satisfactory, although all types of treatment from the endocrine therapy to use of vitamins have been employed and in solitary cases patients have been reported as being benefited by one or more methods of treatment. All the patients in our series of cases received multiple types of therapy without any appreciable benefit.

We were pleasantly surprised to find that in several cases in which pseudosclerodermatous stasis ulcers about the ankles were excised and grafted the grafts, on the whole, took well. The same is true in regard to the 2 cases in which there was epithelioma and in which healing took place after excision with or without grafting.

### SUMMARY AND CONCLUSIONS

Acrodermatitis chronica atrophicans is a chronic dermatosis of unknown cause usually involving the extremities, especially the extensor surfaces in the vicinity of the

knees, ankles, elbows and wrists. The disease, however, may be generalized and appear as erythroderma with poikiloderma-like changes. At times it may be unilateral. It is not limited to one nationality or continent, and it occurs fairly frequently among native-born Americans. It is usually a disease of the later decades of life, predominating in women who are more than 40 year of age. Pseudosclerodermatous changes, with the considerable scaling and thickening of the skin about the ankles, with or without ulcers occur in about a third of the cases. So-called ulnar bands, fibrotic nodules and stasis ulcers are less frequent than pseudosclerodermatous changes. The histopathologic changes are distinctive if a specimen for biopsy is taken from a well developed area of atrophy. There is preservation of a border zone of connective tissue between the flattened epidermis and the infiltrate in the cutis, but there is much destruction of connective and elastic tissue where the infiltrate occurs, resulting in pronounced thinning of the cutis. This destruction of collagenous and also elastic tissue might be caused by unknown toxic substances associated with the infiltrate. Acrodermatitis chronica atrophicans, especially in its generalized erythrodermic forms, can be distinguished from other atrophic dermatoses on the basis of concomitant clinical and histopathologic changes. Acrodermatitis chronica atrophicans is not a precancerous dermatosis. There is no adequate form of therapy known. The disease usually runs a benign course and does not reveal definite association with any systemic disease that may coincidentally be present, especially among the more elderly patients.

### ABSTRACT OF DISCUSSION

*Dr. Fred Wise, New York:* This contribution is a comprehensive review of the subject of acrodermatitis chronica atrophicans and adds chiefly to the knowledge of its histopathology. The authors stress the point that the histologic structure of a well developed area of atrophy is distinctive, enabling one to make a diagnosis microscopically. The average histopathologist has much difficulty in differentiating the end stage of this disease from the end stages of other cutaneous atrophies. But one must bear in mind that the authors' findings are based on biopsies from 20 patients, which is probably an all time record for this disease.

Concerning the clinical aspects, little can be added to the descriptions in Finger and Oppenheim's monograph, published in 1910 (Finger, E., and Oppenheim, M.: *Die Hautatrophien*, Vienna and Berlin, F. Deuticke, 1919). Most patients consult the dermatologist when the disease is in an advanced stage and the diagnosis may be made almost at a glance. Occasionally one encounters early changes, for example, a faint, pink band, extending from the base of the fingers on the dorsal aspect of one hand to

the region of the elbow; this band is not infiltrated, may have well defined borders and its surface is smooth and glistening, the veins appearing to be a little more conspicuous than those on the unaffected hand. Careful examination is demanded in such cases, especially with respect to early changes in the skin of the lower extremities. The patients are requested to report for further examination at six month intervals. Judging from my experience, concomitant cutaneous and visceral lesions are rare. One patient with sarcoma of the ankle and 1 with epithelioma of the thigh have come under observation.

The authors mention chronic arthritis as a complication of the disease, referring to the case described by Sweitzer and Laymon in 1935. Their patient had a peculiar deformity of the hand, having the appearance of a hand that had been forcibly flexed and twisted outward. The diagnosis of atrophic arthritis with deformity was confirmed by roentgen examination. Within the past three years, two similar instances were observed at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. Both patients were men who also had extensive areas of diffuse idiopathic atrophy of the extremities and trunk, but the eruption as a whole did not resemble acrodermatitis chronica atrophicans but appeared rather to be an atrophy following a long-standing diffuse erythroderma. I am inclined to the belief that such arthritic changes, as well as associated cutaneous malignant growths, are not intrinsic complications of acrodermatitis chronica atrophicans.

I have had no successful results from therapy. At the present time 1 of my patients is taking dihydrotachysterol but it is too soon to determine its effect on the skin.

*Dr. Hamilton Montgomery, Rochester, MN:* I am glad to have Dr. Wise mention the reported roentgenologic changes in the bones and arthritic changes, and as I am in accord with him that they are coincidental rather than a fundamental part of the picture.

Dr. Wise probably has seen more cases of acrodermatitis chronica atrophicans than any one else in the United States, and I am therefore deeply appreciative of his discussion of this paper.

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# Regarding an Unusual Form of Migratory Erythema Caused by Tick Bites

James Strandberg

Erysipeloid is an affection, that is usually easy to diagnose and the clinic of which is well known thanks to the work of Rosenbach, Gilcrest, and others.

This disease appears particularly on the fingers and hands of people such as butchers, cooks etc., who handle meat or other products of dead animals. At the point infected a red or cyanotic patch appears, which afterwards spreads outwards and the whole in some cases gradually develops into an annular erythema with a very narrow outer band, which grows centrifugally. The disease has consequently usually been called Erythema Serpens or Dermatitis Migrans. When, as is usual, the trouble begins on one of the fingers, the erythema generally travels up the back of the hand, but as a rule it goes no further. In most cases the eruption is said to fade away in three to four weeks.

During recent years the Dermatological Society of Stockholm has received reports and been shown cases of a peculiar form of serpentine erythema differing from the normal erysipeloid, by various observers (Afzelius, Strandberg, and others). This type is characterized by slow development, migration over a large expanse, the very slightest inflammation only, and absence of subjective symptoms. The patient first notices a faint red or livid patch which soon forms into a ring. This ring, which when first observed may possibly be about the size of the palm of the hand, has normal skin in the centre, is about 1/8 inch broad and is not raised. It then starts to grow so that in three to four months if it started for instance on the arm, one part would be visible at the shoulder, and the other at the wrist. I have observed one case, where instead of commencing on the arm, the eruption appeared on the buttock. Two years ago I observed a case of a woman, with whom the trouble in the upper part of the left arm, travelled over the thorax and finally developed into a narrow band, which like the ribbon of an order went diagonally across the breast and could only with the difficulty be hidden by the application of powder, when the patient wore a décolleté dress. At this time the affection was 4-5 months old. After this the erythema faded away gradually.

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In all cases, the eruption seems, curiously enough, to have been caused by tick bites (*Ixodes reduvius* or *ricinus*).

Ehrmann in his "Atlas der Hautkrankheiten" when on the subject of erysipeloid (which he by the way prefers to call Erythema Infectivum Centrifugum) mentions, that he has twice seen the disease develop on the faces of children, and he states, that in one of these the trouble could be traced to a tick bite. Other than this I have no knowledge of any work ascribing the bite of a tick as a cause of erysipeloid or of any other reaction of the skin. I have not had access to the whole of the literature on erysipeloid, nor could I go through all the works relating to *Ixodes*, so that it is possible that unknown to me observations similar to mine may be recorded elsewhere. There is, however nothing of the kind in the usual dermatological handbooks and textbooks nor for instance is there anything in Neumann and Mayer's large encyclopaedia of animal parasites.

Recently Professor Gösta Forssell very kindly passed on to me one of his patients for diagnosis. As the case appears to me to be an instructive one and further seems to belong to the type of Erythema Migrans, which I am here describing and which has so far received very little attention in the literature on the subject, I thankfully embrace this opportunity of making public history of this case.

## INGA W. born 31. 5. 1916

The girl was always healthy and has never suffered from any form of skin disease. At the end of August 1920, the mother noticed a redness and swelling on the child's left nipple. The swelling gradually increased a little and there developed a curious ringshaped redness round about it. No pain was felt and the place was merely slightly tender when pressed. The mother consulted several doctors about it, but no opinion was expressed as to the nature or probable progress of the trouble. Some serious disease such as tuberculosis or tumor seems, however, to have been suspected.

## Status on 30. 10. 1920

General condition normal. The skin in general of normal colour and character. Left nipple enlarged to about 7/8" in diameter and markedly thickened. It felt like a

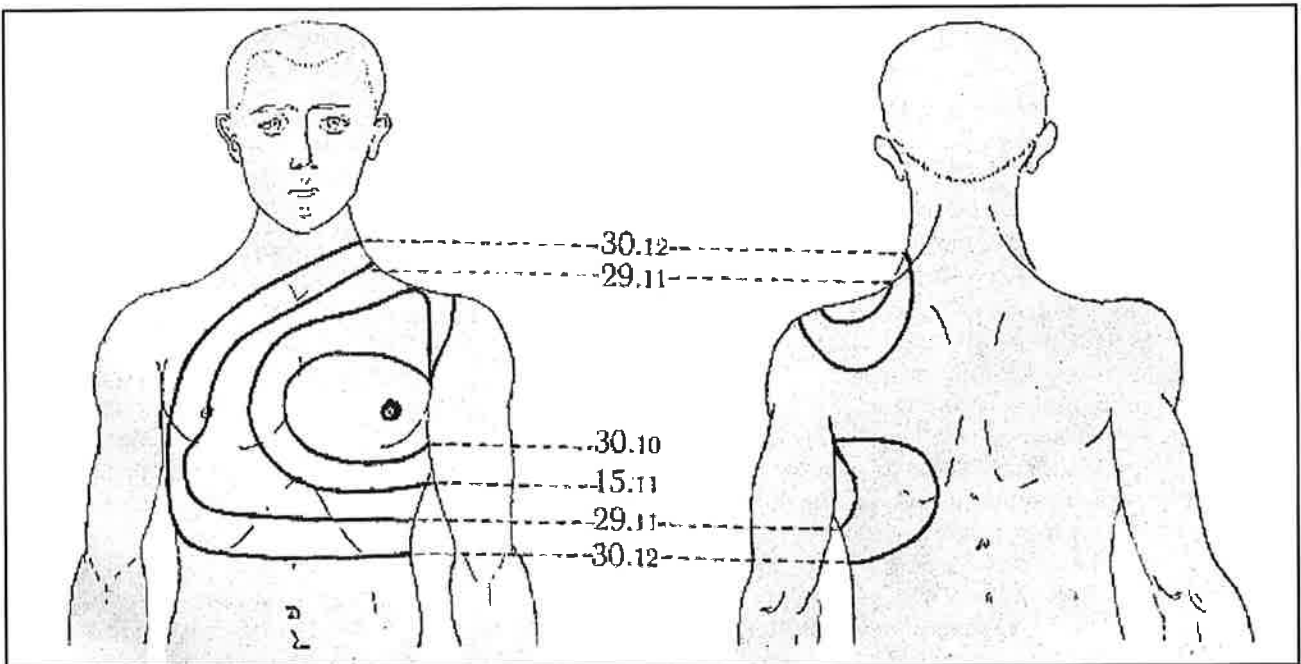


Figure. Diagram showing the migration of the erythema.

1/4" deep, plateshaped infiltration. The surface was smooth and the epidermis intact, colour bluish red, changing to a browner tint under glass pressure. No lupus granulations. Round the nipple a curious ringshaped erythema was visible. The edge of this, which was at the radius of about four inches from the nipple, was bow shaped, fairly well marked, bluish red, about 1/8 inch wide and disappeared under pressure. The erythema was not raised anywhere. On the contrary the skin was even and smooth. On closer inspection between the ring and the nipple a fine network of bluish red lines considerably thinner and not so obvious as the same type could be seen. (In the illustration the network seems to me to be rather well marked.)

In the left axilla a few non-sensitive glands rather smaller than a bean could be felt.

The case was certainly not easy to diagnose. There was no support for the idea of tuberculosis, a tumor seemed sooner to be indicated. The curious erythema ring, which certainly was connected with the swelling since it was developing centrifugally from the latter, was difficult to account for. As far as I could see, the facts fitted most closely with the curious case of migratory erythema, which as stated above, occurs after tick bites. I accordingly enquired of the mother, who admitted, that both she and her husband had been pestered by ticks when on a sailing trip in the late summer. Whether the patient—who was with them at the time—had been bitten on the breast, the mother could not remember, but she thought it was far from unlikely. She further mentioned, that an unusual sus-

ceptibility to insect stings existed in the family, one of the patient's sisters for instance experience violent reactions with urticarial symptoms after flea-bites etc.

The case was placed under observation. A test excision which would certainly have been of interest, was not permitted. Treatment was discontinued.

Notes 15. 11. 20. Tumor somewhat reduced, paler than before, especially in the lower part. Ring increased in size, the central network hardly visible. The erythema appeared noticeably to avoid the left arm.

29. 11. 20. Tumor slightly softer than before, otherwise no change. Ring still wider.

30. 12. 20. Ring wider, hardly visible. Tumor considerably reduced. Nipple practically normal.

The erythema ring's gradual and innocuous progress coincided exactly with the previously mentioned cases of Dermatitis Migrans following tick bite. The central tumor situated on the nipple was, however, a feature peculiar to this particular case. Its exact character could not be determined owing to excision being refused. Presumably it could have been traced to some inflammatory action of the same origin as the erythema.

Whether or not the type of migratory erythema herein described is a form of Rosenbach's erysipeloid, I am not prepared to venture an opinion. It is highly probable, that it is of toxic origin. The erythema's almost indefinite extension in this case makes one incline to assumption, that the pathological changes should be looked for in the lymphatic ways of the skin rather than in the blood capil-



laries, seeing that, as is well known, the former extend in a continuous network over the whole body, which is not the case in the latter.

The disease is of course of no importance for its own sake and is rather to be looked on as a freak. For those

who have neither seen nor heard of it, however, diagnosis and classification would present difficulties. In the case described above, for instance, correct diagnosis was of considerable value to the patient as it saved her from radiological or even possibly surgical treatment.

# Erythema Chronicum Migrans (Afzelii) Associated With Mosquito Bite

Stig Hård, MD

The lesion of erythema chronicum migrans (e.c.m.) begins as a red infiltration of variable size. Erythematous rings one half to two cm broad develop around the infiltration and then slowly spread centrifugally over periods of weeks, months or years. The lesions may attain considerable dimensions. The rings may be single or multiple (29). The central erythema gradually fades and leaves a surface which usually is normal but may show some bluish discolouration. Microscopy reveals generally no major changes in the epidermis. The subpapillary stratum shows vascular dilatation, perivascular round-cell infiltration and swollen connective-tissue cells. The subcutis may be infiltrated with lymphocytes, histiocytes and especially eosinophil leukocytes (5). Sometimes the initial lesion is microscopically manifest as a more or less massive infiltration of lymphocytes with the transformation of the epidermis to tumour-like formation (19, 7).

The prevalence of e.c.m. seems to be greatest in Scandinavia. The condition was first identified as a separate dermatosis by the Swede Afzelius in 1909 (1, 2). Another Swedish investigator, Hellerström (10, 11, 12, 13, 14, 15), demonstrated that e.c.m. is caused by pathogenic microorganisms which also produce general effects such as meningitis. This has been confirmed by others (9, 22).

Independently of Afzelius, Lipschütz (23) described e.c.m. in 1913 and in Germany the disease bears his name. Lipschütz (24) maintained that his was the first description of e.c.m., but this was conclusively disproved by Hellerström (11).

E.c.m. sometime produces local symptoms such as itching and pricking and burning sensations in the skin. The general symptoms include fever, headache, fatigue, lymphangitis and regional lymphadenitis in addition to the afore-mentioned meningitis with or without paresis (10, 14, 15, 9, 22, 7, 28). The course is usually mild, however, and healing is spontaneous.

The curative action of spirochaeticidal substances on e.c.m. was first described in 1948 (21). In larger series of

cases penicillin was found to be the most appropriate antibiotic (16, 17), but aureomycin, terramycin and spiramycin have also been used with good results (18, 7).

It has long been assumed that e.c.m. is caused by tick bites (1, 23, 30, 10) and there seems now to be no doubt that this is so (14, 28). E.c.m. occurs in regions where *Ixodes reduvius sive ricinus* is prevalent (25). Remarkably, however, e.c.m. is rare in the U.S.A. (3), though American subjects have been infected in Europe (8).

Patients with e.c.m. show hypersensitivity to tick extract (12) and affected skin and tick saliva contain a substance which can evoke inflammation in these sensitized subjects but not in "normal" persons (20). These phenomena, however, do not wholly explain the causal mechanism of e.c.m., which presumably is dependent upon an infecting agent. *Toxoplasma* can be excluded (13) and also common human bacterial pathogens, common viruses and spirochaetes (4).

In 1948 it was reported that an impregnation technique had revealed spirochaetes in tissue affected with e.c.m. (21). A few years later the present author tried unsuccessfully in hitherto unpublished experiments to confirm this observation. Dark-field and phase-contrast microscopy of tissue emulsions from the skin of 4 persons with e.c.m. failed to reveal spirochaetes. Ticks were cultured in a moist chamber (27). They were allowed in various stages (larva, nymph and imago) to attach themselves to and feed on the erythematous rings of e.c.m. Various organ structures from the ticks were then studied by darkfield microscopy, but no spirochaetes could be found by the author. Tick larvae were allowed to gorge on the skin of a patient with e.c.m. and after their transformation to nymphs to bite the author and two other volunteers. No e.c.m. resulted. The ticks were applied to the skin under a watchglass which was fixed in position by adhesive tape. When ticks feed they excrete abundant reddish crystals. Such crystals from ticks which had fed on patients with e.c.m. were injected into the author's skin and into another volunteer, again without result.

Transplantation of erythematous skin from patients with e.c.m. to the skin of healthy persons has given positive results (4, 29). The disease has been transferred in this way, which confirms that it is communicable.

E.c.m. has points of resemblance to another skin disease-lymphadenosis benigna cutis (19). One cause of the

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At the time this article was initially published, Dr. Hård was from the Department of Dermato-Venereology (Head: Stig Hård, MD), General Hospital, Sundsvall, Sweden.

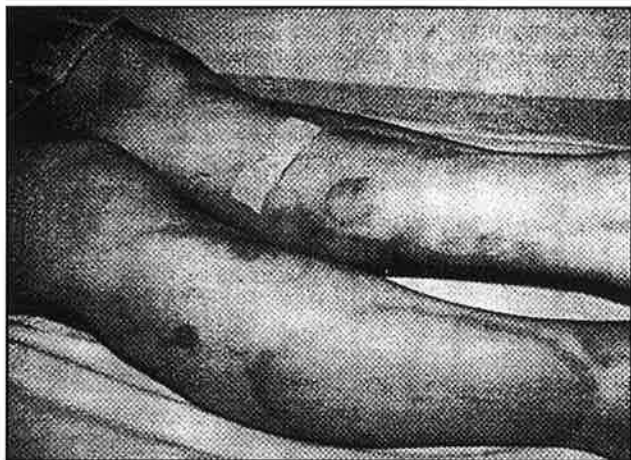


Figure.

latter condition is insect bites (6). Lymphadenosis benigna cutis can be transplanted into the skin of healthy persons, and very occasionally e.c.m. has arisen round the implantation sight. This suggests a factor common to both disorders, possibly a large molecule virus (26).

A few years ago it was reported that 6 of 7 persons with e.c.m. gave positive reactions to microagglutination test against rickettsiae (7). However, it is still not clear which micro-organisms can produce e.c.m. The *Ixodes ricinus* tick serves as a vector, but some writers have maintained that *Culex* mosquitoes may also be vectors (14, 28, 31). Since conclusive evidence of the association between mosquito bites and e.c.m. has not yet appeared in the available literature, the following case was thought to merit presentation. The association seemed to be certain in this case, as e.c.m. arose thrice following mosquito bites and the dermatosis could not have been caused by ticks because the geographic distribution of the *Ixodes ricinus* in Sweden does not extend as far north as Sundsvall, the patient's home (25).

### CASE REPORT

The patient was a 65-year-old woman whose medical history included jaundice during adolescence and "Spanish flu". At the age of 37 she had received adequate treatment for latent syphilis, but serum test remained reactive. She had undergone operations for volvulus and gallstones and labyrinthotomy for Menière's disease.

In September, 1959 she was treated at this hospital for skin lesions which had arisen after mosquito bites about 3 months previously. A diagnosis of e.c.m. with multiple lesions on both legs was made. She had no general symptoms. The treatment consisted of 600,000 IU penicillin on 2 successive days. The lesions then subsided.

During 1960 she remained well, but in September,

1961 she presented herself with the same history and lesions as before. This time she received 600,000 IU penicillin for 4 days and the lesions disappeared.

At the end of July, 1962 the author saw the patient for the first time. She then had typical e.c.m. on both legs and reported that the lesions had arisen during the spring, which had been unusually warm with early breeding of mosquitoes. The right leg now showed 3 erythematous rings measuring 16x12, 12x8 and 3x4 cm. In addition there was a circular red patch about 2.5 cm across and 2 others approximately 1.5 cm across. On the left leg were 2 rings measuring 3x2 and 2x1 cm and a circular red patch about 1.5 cm across (Fig. 1). In the two last-mentioned lesions on the left leg and in one of the red patches on the right leg the puncture track of an insect bite could be demonstrated. Around these punctures the skin was somewhat infiltrated.

The patient stated that the lesions had arisen at the site of mosquito bites and that she had had no general symptoms. The E.S.R. (Westergren) was 25 mm/1 hour. The haemoglobin and blood cell counts were normal. Wassermann, Kline and Meinicke tests gave grade 3 positive reactions. The TPI test was positive. The electrocardiogram, roentgenograms of the lungs and heart and the ocular status were normal. Right-sided deafness was the only other abnormality. In consideration of the latent syphilis, the treatment of e.c.m. consisted of 600,000 IU penicillin daily up to a total dose of 10 million IU. (Three years later the blood reactions were unchanged).

Biopsy specimens were taken from a lesion with puncture track on the left leg and from a migrating ring on the right leg. The histologist's<sup>1</sup> report was as follows. *Specimen 1*: "Skin containing track of insect bite. In central region there is some epithelial thickening. In and immediately below the horny layer are 2 or 3 small oval subjects surrounded by a homogenous, horny capsule, presumably insect remains. The connective tissue shows extensive perivascular round-cell infiltration with masses of eosinophils. *Specimen 2*: No insect fragments, but otherwise similar to specimen 1. The cell infiltration is somewhat more pronounced. *Histologic diagnosis*: Erythema chronicum migrans (Afzelius-Hellerström)."

Thus, although the clinical picture was somewhat confused by the fact that the patient had old, latent syphilis, the morphologic picture in no way resembled that of the lesions in tertiary syphilis. The observed insect fragments in the specimens further exclude the possibility of syphilitic origin. The available literature contains no report of a case with so many lesions on so many occasions.

### SUMMARY

The literature on erythema chronicum migrans (e.c.m.)

<sup>1</sup>Sumegi.

is briefly surveyed and a case is presented. This 65-year-old woman was found to have multiple lesions of e.c.m. affecting both lower legs on 3 separate occasions. The clinical diagnosis was histologically confirmed. Insect fragments were found in a biopsy specimen.

The patient reported that she had been bitten by mosquitoes on the sites where the lesions subsequently arose. Because of this observation, and because the patient lived far above the most northerly latitude at which ticks are found in Sweden, the writer accepts the case as evidence that mosquitoes can transmit e.c.m.

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# Journal of Spirochetal and Tick-borne Diseases

Dedicated to science and art in spirochetal and tick-borne diseases

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The *Journal of Spirochetal and Tick-borne Diseases* publishes quarterly reviews and original work studies about any aspect of spirochetal and tick-borne diseases. The primary purpose is to broaden our understanding of spirochetal and tick-borne diseases. Special focus is given to Lyme borreliosis (also known as Lyme disease), as the most prevalent spirochetal and tick-borne disease. The clinical topics may involve all medical disciplines, nursing, and pharmacy, as well as the social, ethical, and biological features of spirochetal and tick-borne diseases.

### Reviews

Each issue includes a series of state-of-the-art articles on a topic related to spirochetal and tick-borne diseases. The articles represent invited presentation by authorities in the field on topics related to spirochetal and tick-borne diseases, with an emphasis on Lyme borreliosis.

Submissions to this category should present a comprehensive state-of-the-art analysis and should be accompanied by an abstract of 300 words or less summarizing major points.

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Original articles of 5000 words or less may be submitted to the editorial office. Each article should be accompanied by an abstract of 300 words or less describing the findings of the original research. All articles will be peer reviewed within a 3-week period with subsequent notification to the authors within 5 weeks of submission.

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Specific clinical case reports describing a unique

approach to Lyme disease and other related disorders in the area of diagnosis or treatment may be submitted for review. An abstract of 250 words or less should accompany the text.

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The topical photographic section will be a regular feature. Photographs pertinent to articles presented in the Journal, as well as other photographs related to any aspect of spirochetal or tick-borne diseases, will be considered for the publication. The guidelines for the submission are designated in **Illustrations**.

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The Journal asks authors to disclose at the time of submission any financial or other arrangements they may have with a company whose product figures in the submitted manuscript or with a company making a competing product. Such information will be held in confidence while the paper is under review and will not influence the editorial decision, but if the article is accepted for publication, the editors will discuss with the authors the manner in which such information is to be communicated to the reader.

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An original and three copies of the manuscript should be submitted to:

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including the first name(s) and academic degree(s); the name of the department and institution in which the work was done; the institutional affiliation of each author; and the name and address of the author to whom reprint requests should be addressed. Any grant support that requires acknowledgment should be mentioned on this page.

#### **Abstract**

Provide on a separate page an abstract of not more than 300 words (original and review articles) or 250 words (case report). This abstract should consist of four paragraphs, labeled Background, Methods, Results, and Conclusion. They should briefly describe the problem being addressed in the study, how the study was performed, the results, and what the authors conclude from the results.

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Submit tables typed and double-

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Photographs and figures should be submitted as glossy prints 5×7 in., with one copy of each print for each copy of the manuscript. Figure legends should be provided on a separate sheet with identification of the figure. The back of the glossy print should indicate the number of the figure.

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