THE PATHOGENESIS OF DERMATITIS, INCLUDING ECZEMA

A CASE OF ENGLISH IVY POISONING *

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The response of tissue to a pathogenic agent or agents depends upon a local peculiarity inborn or acquired. Either way it is anatomic or physiologic, and if acquired may be the result of changes due to growth or previous disease. Anatomic factors are purely structural and depend on the quality and quantity of the tissue, whether connective or parenchymatous, and the ratio of the two. Physiologic factors are functional and depend on the type of function; whether glandular, and if so the kind of gland and secretion; or vascular, and if so whether blood or lymph; or nerve, and if so whether sensory, motor, trophic, sympathetic or special. In the skin, which is a most complex composite of other complex organs and tissues, this is no less true. At different periods of life, infancy, childhood, adolesence, maturity and senility, the skin is altered both as to structural and functional characteristics. Preceding cutaneous diseases cause further structural and functional modifications. Thus, almost from year to year, beginning at the cradle and ending with old age, the skin exhibits a series of alterations which determine its potential of morbid responses.

Subtle as these are, considering our basic ignorance of their nature and significance, still subtler are the general physical and physiologic factors of the body as a whole, which influence the skin no less. Here also the groups of factors may be divided as in the skin itself, and added thereto are racial factors, disturbances and diseases of metabolism, the ductless glands, and the great digestive, eliminatory, nervous, circulatory and secretory systems, chronic infections, notably tuberculosis, and disturbances of the blood cell producing organs.

The condition called eczema is among those dermatoses which best lend themselves to pathogenic analysis. In a recent study I advanced the following definition of this syndrome: "Eczema is a catarrh of the skin possessing the pathological characteristics of an exudative inflammation. It is characterized clinically by redness, swelling, the presence of papules, vesicles, pustules, weeping, crusting and scaling in varying combinations. In its course it may be acute, subacute, chronic, and its origin depends upon an interplay between various known and unknown

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local and predisposing causes, to which the skin lesions are reactions." During the seven years which have elapsed since the foregoing conclusions were set down, all of my experiences have been rather in the direction of their support than away from it, and a patient recently under observation illustrates all of the points involved. The condition in question was one of dermatitis of the face, neck and upper extremities. It proved to be the second of its kind in the literature, in that it was provoked by the English ivy, Hedera helix, of the order *Araliaciae*. Munro [1] reported the first case. The case to be described had been observed by three eminent dermatologists, one of whom considered it eczema of internal origin; one, seborrheic dermatitis; and one, dermatitis venenata.

REPORT OF A CASE

History.—S. J., British, aged 50, a house steward in a wealthy Long Island home, first presented himself on Dec. 15, 1922, suffering with a disturbance of a year's duration. It was an eruption which began with itching and flushing of the face, neck and upper extremities, and rapidly evolved into the conventional picture of erythematovesicular, papular, weeping and crusted dermatitis. Susceptability to *Rhus* had been noted by the patient, but in spite of avoiding this plant he was harassed by recurrences. Under treatment in Baltimore in June, 1922, the outbreak disappeared, but on returning to his own environment, particularly late in the fall, he had numerous attacks. A prominent New York dermatologist regarded the illness as seborrhea, and numerous metabolic studies made by him revealed no abnormalities. Another dermatologist of equal standing interpreted the picture as that of dermatitis venenata but failed to isolate the agent. At this point I first saw him. His general history was negative, his habits good, and he had never had any serious illnesses.

Examination.—This revealed that an acute dermatitis, as described, was present. The patient was a lean man, apparently organically sound.

Course.—Under lotions and wet dressings the eruption faded in three days. Some of the lesions having suggested small wheals suprarenal gland substance was prescribed, and fractional (one-fourth maximum skin dose) roentgen irradiation was employed because scaling had set in.

On Dec. 22, 1922, the patient inquired whether English ivy could produce his disease, mentioning that he handled it in connection with the floral decorations of his employer's house. This seemed a clue, and ivy leaves and stems were applied to his unbroken skin after the manner described by Markley in his investigations on guinea-pig hair dermatitis. There was no reaction. An alcoholic extract was prepared of the leaves and stems, and, with a stock solution, as well as with a residual powder recovered by evaporation from the alcoholic solution of the leaves and redissolved in decinormal sodium hydroxid, percutaneous tests were made, all of which were strongly positive. The reaction consisted of a small wheal surrounded by a broad red zone, and it lasted twenty-four hours. Local controls made with the two solvents were negative, as were complete control tests on Dr. R. H. Rulison and myself.

1. Munro: Australian M. Gaz., Jan. 20, 1900.

This appeared to explain the etiology, but roentgen-ray treatment was continued for the scaling, and by December 29, or within two weeks, the eruption had disappeared. On Jan. 12, 1923, when the color of the skin had returned to normal, two spots as large as a half dollar were noted on the left side of the forehead. They were flat, brownish red, and scarcely infiltrated. They were evidently involved seborrheic patches, and the face and neck showed slight traces of this condition, which were easily controlled by the roentgen rays, although the two spots on the forehead tended to light up from time to time without, however, becoming vesicular. All other local treatment had been stopped after the first three days. On April 11, 1923, and again on April 25, the skin was slightly red. This was obviously due to sunburn. On the latter date the percutaneous tests were repeated with the original positive result.

Summary.—A man, aged 50, with a seborrheal skin, suffered repeated attacks of acute dermatitis. He was susceptible to English ivy. On discontinuing exposure to it, his attacks ceased. Specific percutaneous tests, properly controlled, were positive.

Munro's Case.[2]—The eruption in this case resembled zoster. "It began after the application of ivy leaves and vinegar to corns; later it always recurred in the same person whenever wet ivy leaves were touched."

COMMENT

The fact that three sound observers respectively considered an eruption eczema, seborrheic dermatitis and dermatitis venenata, is striking. It signifies either that there is not, or cannot be, clinical unanimity in such cases, or that at different periods in the course of the case the picture varied. It further signifies that there is no difference between eczema and dermatitis, whatever their origin. As to unanimity, this, paradoxically enough, is lacking because standards of differentiation between eczema and dermatitis are so subjective as actually to fail as criteria, a convincing testimonial to their identity. If at different moments the same disease has three different aspects, again all criteria fail. Thus, the clinical avenues lead to axiom one. If this is so, the time honored debate waged over the relationship of eczema and dermatitis thrives either because of failure to grasp essentials, or because of emphasis on nonessentials.

There are only two possibilities: Eczema and dermatitis are either identical or different. To hold that sometimes they are the same and sometimes not is evasive. The word "eczema" does not seem nearly as objectionable as the confusion engendered by trying to distinguish eczema from a disease just like it. It is perhaps immaterial whether one term is abandoned, or the other. Eczema venenatum would be as good as dermatitis of unknown origin, if the former were synonymous

2. Munro, in White, Prosser: Occupational Affections of the Skin, New York, Paul B. Hoeber, 1920, p. 248.

with dermatitis venenata, and the latter with eczema of unknown origin. What counts is clarity as to the nature of the disease whichever name is favored. It is not a matter of Totem worship of a word. The point is that the two concepts are identical, as the case reported shows, and to support this view it will be necessary to analyze pertinent passages from the literature, as well as certain more restricted phases of the case in question.

THE LITERATURE

Willan and Bateman [3] thought that eczema could be either of external or internal origin. Hardy [4] restricted the disease to internal causes. Biett, Cazenave and Schedel [5] believed that whether it originated from within or without, predisposition was the salient factor, an illuminating point of view for so many generations ago; and Bazin [6] more trenchantly referred to the disease as a "special reaction of the skin to diverse causes." In Austria and Germany, as the teachings of Hebra, Neumann and Unna show, it was maintained that the origin was purely external, while the later English writers, particularly Erasmus Wilson and Tilbury Fox, subscribed to Willan's original views with minor modifications.

It is unnecessary to dwell on the relationship emphasized in France of the dartrous, and in England, of the gouty, diathesis to eczema. These are words indicating a veiled insight into the subtle metabolic disturbances related to this cutaneous reaction. They merit their obsolescence, for modern knowledge in this domain, though still deficient, has some glimmerings of greater certainty. Equally unsound explanations have been the fruit of a not far distant past, preeminently nervousness and functional disorders. Besnier,[7] however, makes a notable contribution to the subject in pointing out the causative probability of general and local predisposition, and among the latter particularly other skin diseases and physiologic and anatomic disturbances of the skin.

The work of Johnston, Fordyce, Towle and Talbott, Charles White, Ramirez, Knowles and myself indicate how closely Americans have been engaged with the problem during the last twenty years. Because of their recency the views of these writers require no repetition. Norman Walker in Scotland, and in this country Pusey, Engman and I have

3. Willan and Bateman: A Practical Synopsis of Cutaneous Diseases, 1815, p. 252.

4. Hardy: Leçons sur maladies de la peau, 1860, p. 2.

5. Biett, Cazenave and Schedel: Abrégè' pratique des maladies de la peau, 1838, p. 90.

6. Bazin: Leçons theoriques et cliniques sur les affections de la peau, 1862, p. 138.

7. Besnier: Pratique dermatologique **2**:1.

not evaded the identity of eczema and dermatitis. Pusey, in his text-book, has best summed up the case in an analysis of Malcolm Morris' equivocations. "It makes no difference," asserts Pusey, "in the essential character of a dermatitis that the irritant happened in some cases to be discoverable and in others not. Leaving out these unessential qualifications, we cannot avoid the position that eczema is dermatitis; and as far as the lesions in the skin are concerned, this statement represents the fact."

At the fourth International Dermatological Congress, Unna reported the isolation of a specific eczematogenic bacterium, the morococcus. This was vigorously assailed by virtually all of his hearers. It is likely, however, that any parasite may be among the causes of dermatitis, precisely as are the epidermophyton and other fungi. In fact, the recent studies that have assailed the standing of dyshidrotic eczemas among dermatoses, have shown that Koebner's epidermophyton not only causes Hebra's eczema marginatum, but that related organisms may give rise to the picture of eczema in all of its nuances.

A bird's-eye view of the literature reveals the wide latitude covered by speculation as to the cause of eczema. Ignoring the more obvious possibilities, such as gross alimentary disturbances, and vague ones, nervousness, diatheses and the like, the following theories have been advanced since the days of Willan, or even earlier (Lorry), and at the present time. General predisposing causes, local causes, local irritants of whatever type, and combinations of these have all been cited. But it was Bazin and Besnier who envisaged the condition with most acute and prophetic eyes. It is their combined conception which seems fundamental for an enlightened understanding of the disease.

THE PATHOGENESIS OF ECZEMA

To produce eczema, and perhaps also many other skin diseases, the chain of events has three important links. They are the group of underlying causes, the group of local causes, and that of the precipitating causes. First among underlying causes are disturbances of nitrogen, carbohydrate and possibly fat metabolism, from ingestion to elimination, including the subtler chemical phases, and depending on the gross or fine organic changes that may be present in the various involved systems. Second are endocrine disturbances, both as such and in their reciprocal relation to metabolism. The ductless glands are to be considered even more seriously in relation to the metabolic factors of development and decline, infancy, childhood, puberty, adolescence, maturity and age—particularly puberty and the climacteric. Above all, the thyroid and suprarenal glands are to be emphasized, and in a lesser degree, no doubt, the pituitary body and gonads. Third are the phenomena included under our modern concepts of susceptibility, hypersuscepti-

bility and idiosyncrasy, embracing anaphylaxis. A group subsidiary to the more important ones is that of diseases causing inanition, namely, general malignancy and infection, and cryptic or focal infections or their effects, bacterial intoxication.

Local causes are anatomic, the character of mucocutaneous junctions, body folds, the hair distribution in these folds or elsewhere, or functional, the pilosebaceous or sudorific systems; or physiologic, as the higher temperature and greater moisture in the folds, or the various skin secretions; or pathologic, as ichthyosis, hyperhidrosis, steatosis; or the local flora; or the effect of previous general or local disease on the anatomy, physiology or function of the skin; and finally, allergy.

The precipitating causes are physical, chemical, parasitic and anaphylactic. Physical causes include thermal and actinic factors. Chemical causes include the various organic and inorganic substances of all derivations. Parasitic causes include the various flora inhabiting the skin, or epizootic creatures with their peculiar toxins, secretions and excretions. These toxins, together with those of plant and animal origin include anaphylotoxins, or substances working analogously, for if anaphylaxis and allergy indicate a peculiar response of the organism to alien protein, many nonprotein substances seem to have a similar, if not identical, mode of attack, such as *Rhus,* or the primrose.

Nor must it be overlooked that precipitants remain innocuous unless conveyed to the vulnerable tissue. This depends on qualities of environment, habit or occupation. In short, there must be exposure.

A complexity enters the outline at this point, for if the underlying disturbance should be metabolic, substances may be eliminated in the skin secretions whose very presence furnishes irritants capable of acting as precipitating causes on a susceptible integument. The element of exposure would not have to be regarded in such instances. Even without an actual underlying disturbance the secretions of the skin might be altered in quantity or quality, so as to act in the same way. This indicates that the skin itself, being part of the whole body, may supply the underlying, local and precipitating factors; but the fact is not altered that the three must be represented to cause the reaction called eczema. Otherwise regarded the skin alone is able to furnish all of the necessary elements. The body may supply two of these, the underlying and precipitating factors; or the body may supply one, the skin one, and exposure the third. To deny this is not to understand eczema. To accept this is to understand that the only difference between dermatitis and what is called eczema is whether the precipitating factor has, or has not, been supplied through exposure. If it has, some of the irritants may be in higher concentration, or may vary so in nature that they provoke grosser differences in the lesions, but not in the nature or essential features of the lesions; nor is there often any difference. Two other-

wise identical conditions cannot be regarded as distinct, simply because in the one we know what the precipitant is, and how it reached its destination, and in the other we do not. If tradition is so compelling that the designation eczema cannot be thrown off, let the alternative one, dermatitis, be discarded, so that one disease will no longer be looked on with intellectual diplopia. To sacrifice the word eczema would be my preference, the grounds for doing so being good, and because it would be desirable to rid medicine of all fanciful terms that do nothing to further understanding.

To sum up, eczema is the result of interoperation among underlying, local and precipitating forces. If any one of these is missing the chain is broken. It is obviously difficult always to discover the underlying cause, but it is often equally difficult to isolate the precipitating one, because there are so many elements in habit and environment of which the patient himself is unaware. It might require a sorcerer rather than a chemist to divine the one, and all the talent of Scotland Yard to detect the other. But success tarries if obstacles are regarded passively.

THE BEARING OF THE CASE REPORTED ON THE FOREGOING

The patient under consideration had an eruption called eczema by one dermatologist, seborrheic dermatitis by another and dermatitis venenata by a third. How subjective the factors influencing diagnosis and how uncertain the data molding conclusions! English ivy provoked this eruption, and the fact that seborrhea was present became apparent only as the masking lesions faded. Thus each of the three dermatologists was partly, but only partly, right. Hypersusceptibility was proved by controlled experiment. The chain was complete, an underlying cause, hypersusceptibility; a local predisposing cause, seborrhea, and allergy (or there would have been no percutaneous reaction); and a precipitating cause, English ivy. Lastly, there was exposure through handling this plant.

To break the continuity of these forces the simplest procedure is that of preventive medicine, to end exposure. Immunization might eliminate the underlying cause, as Strickler's work on rhus poisoning indicates. The effect of the roentgen rays on seborrhea might so alter the skin as to remove the local cause, thus destroying response to the excitant. So much for theory. Practice would dictate the removal of exposure to disturb the sequence, and next in feasibility would be immunization. In Munro's patient sensitization had been created by use of the plant for therapeutic purposes. This is strikingly like anaphylaxis.

CONCLUSION

A lucid survey of the problem of eczema, both in general as well as in individual cases, requires the recognition of the need to discover the

underlying, local and precipitating cause, and whether there has been exposure. It is often impossible to accomplish this, probably because of imperfection in methods of study, as well as ignorance of much that will be revealed to physicians of an approaching day, probably too, and to no small degree, because many patients are oblivious to trifling items in their habits, surroundings and work, that would be important if only realized. These difficulties are inherent, but the broad, general, significant principles are eloquent in the report recorded, and it seems wilful not to listen.

To call eczema dermatitis of unknown origin indicates only intellectual supineness. It is subservience to an elusiveness in the nature of what must be captured in order to secure knowledge, an elusiveness that might have sustained the mystery in the case here reported, had it not been for a patient with the gift of sharp observation, and a series of investigations that happily were fruitful. Nor would this study have much point had the diagnosis not been severally eczema and seborrheal dermatitis in a patient with dermatitis venenata due to a plant only once before recognized as pathogenic.

Many other texts are discernible in what has preceded, but the outstanding one is that dermatology should become something dedicated less to nomenclature than to analytic study. Call a skin affection eczema, and at once a barrier arises to the solution of its genesis. Call it dermatitis, and the barrier seems flimsier. Words produce unconscious biases, and eczema has for so long been regarded as an enigma, while dermatitis has not, that half the battle in obscure cases would be not to think of them as eczema, but as dermatitis. Eczema, so far as the medical attitude toward it is concerned, is a negation. It is ultimately positivism that will dominate this attitude if the proper habit of regarding the disease is allowed to grow. This was the determining factor in Markley's work on guinea-pig hair dermatitis. So it was, too, in Walker's investigations on primrose poisoning and Everett Lain's on dermatitis referable to lycopersicum. And this factor is basic to an enlightened grasp of the problems of occupational dermatoses. To recognize it will confer the boon of a far meagerer dermatologic vocabulary, and a desirable increase in pertinent fact to the cutaneous medicine of tomorrow.

DISCUSSION

DR. CHARLES M. WILLIAMS, New York: Dr. Highman's paper is rather difficult to discuss. First, I should like to report briefly a case of dermatitis due to geraniums. The patient was a woman who had had a dermatitis for many months and who had been treated with all the various remedies we know of until the geranium was removed, when the trouble promptly cleared up. I think Dr. Highman has done us a service in calling attention to the fact that many articles are irritating to certain skins and not to others.

I must disagree with him in his tirade against the use of the word eczema. In many cases all three things are at work, the local condition of the skin, the condition of the blood and the irritant. Dr. Highman stated that the condition could be produced by the blood or the skin. Those are the cases known as eczema. We do not know what the irritant is in most of the cases. In external dermatoses we often cannot find any personal peculiarity. The cases range from those which many of us like to call eczema in which there is no discoverable cause except the internal condition to those in which the external irritant is the essential factor. I agree with Dr. Highman that it is often impossible to tell them apart.

Dr. Henry J. F. Wallhauser, Newark: I doubt that many physicians are using the word eczema except to patients. If a cause for any given case of dermatitis cannot be determined, it would seem preferable to admit our inability, than to substitute an indefinite term. Since discarding the word "eczema" in our clinic five years ago, we have found the cause in many cases of dermatitis which would otherwise have been passed over lightly under the title of eczema. I would, therefore, urge its discontinuance.

Dr. John H. Stokes, Rochester, Minn.: The identification of the etiologic factor in eczema or dermatitis is not in my experience entirely covered by systematic questioning. I recall a woman who received almost as thorough a work-up as Dr. Highman and Dr. Markley employed in their reported cases. She assured us that she had never had a primrose. Immediately upon her return home she discovered one in the center of the dining room table which had been given to her more than a year before on the occasion of the birth of one of her children. She threw this plant out and told two of her neighbors about it, and three cases of primrose dermatitis were cured forthwith. Dr Mook has emphasized the importance of attempting to collect samples of the entire environment to try out on the patient, but this in some cases is extremely difficult. The successful unraveling of the etiology in obscure cases such as Dr. Highman reports is a tribute to the indefatigable zeal and perseverance of the individual dermatologist.

Dr. Fred Wise, New York: I always listen with a great deal of respect to Dr. Highman's talks on this subject, but I arise to say that in the present state of our knowledge we cannot say that eczema and dermatitis are the same thing. Let us imagine that a patient is suspended in a room with nothing around his naked body except the air. If you rub that patient with *Rhus* leaves he will have an attack of dermatitis venenata. For the eruption resulting from contact with poisonous substances, the name dermatitis is still the best designation. Eczematoid eruptions arising from unknown (and presumably internal) causes are best classified as eczemas. If our suspended patient were to get a certain peculiar eruption which we call "eczematoid" without coming in contact with poisonous substances, such an eruption would, in the present state of our knowledge, be designated as an "eczema."

Dr. John A. Fordyce, New York: It seems to me that the most serious problem is the manner in which this subject should be presented to students of dermatology. As it is usually taught, the student has a vague idea as to what eczema is. I endeavor to classify under the head of eczema or dermatitis, various kinds of skin reactions: first, those due to irritants of various types; second, those of toxic origin, originally described by Engman; and third, those due to the ringworm fungus. In addition we have the infantile type of eczema in which possibly some defect in food metabolism is present, and the

senile type in which there is possibly some defect in the skin. Classified in this manner it seems to me that students have a much better idea of the subject than they usually acquire.

DR. J. FRANK SCHAMBERG, Philadelphia: I am afraid that Dr. Highman in his desire to get away from the use of the term eczema is setting up another fetich—dermatitis. If we were to inform our patients that they were suffering from an inflammation of the skin instead of latinizing the diagnosis, the reply would doubtless be that that was obvious. The term dermatitis is too vague in a clinical sense to connote anything definite. In its anatomic significance it would include all inflammatory dermatoses. It so happens that in the course of decades there has been a sharpening of clinical acumen which has led to the elimination of the itch, lichen planus, dermatitis venenata and other dermatoses formerly included in the category of eczema. This process of elimination will doubtless go on.

For purposes of teaching, and more important still, for our own mental orientation, it is important to retain the term eczema, for many cases of this affection are unquestionably of internal origin. As soon as an eruption of an eczematoid character is demonstrated to be due to an external cause, it ceases to be an eczema. I see no reason for the abolition of the designation eczema just because clinical differentiation may be difficult. In my opinion the "localist" view of the causation of many dermatoses is being too much emphasized, and the adoption of the term dermatitis might subconsciously tend to warp our attitude still more.

DR. WILLIAM ALLEN PUSEY, Chicago: I wish to express my entire accord with all the essentials of Dr. Highman's paper, and it seems to me that the thing to do is to deal with the essentials and bring out these points. I should not call his paper a diatribe in any sense, but merely a sharp, intellectual study that hews close to the line of reason. The question resolves itself into whether it makes any difference whether we call our child eczema or dermatitis, and it does not make much difference as long as we do not forget that we have no objective criterion by which we can tell them apart.

DR. WALTER J. HIGHMAN, New York: I rather imagined that the discussion of this paper would resolve itself into a debate as to which word should be abandoned. That does not interest me much. I think eczema is a silly word. We might discard it and we might discard the word dermatitis and talk of "eczema venenata" and so on. I think I brought out that possibility. We might classify these diseases into eczema of known and unknown origin. It makes no difference. Personally I prefer "dermatitis" despite the fact that Dr. Schamberg brought out that all the inflammatory diseases of the skin can be classed under this head. We could well apply "dermatitis of unknown or indeterminate origin" to many of the matters referred to by Dr. Fordyce. What the discussion has resolved itself into is that there are two diseases which represent the same clinical entity, in one of which we recognize the cause and in the other we do not. The problem in teaching students that Dr. Fordyce touched on is not to make it easy for students. We do not wish to give them sugar coated pills. We want to give them medical facts—why not let them exercise their brains? They would be glad to if it were allowed. There is nothing to be gained by predigestion.

I was stimulated in my work by Dr. Pusey himself and by a passage in his book, but it seems to me that the toryism with which Dr. Williams reviewed my contribution is precisely the point to be attacked. He says "here is a thing of unknown origin, we will call it eczema." As long as we persist in so doing

we will have the same confusion not only in our minds but in the minds of our students. When the patient wonders what he has and it happens to be eczema, or "exeema," and I tell them it is dermatitis they say, "What is it?" and I reply "An inflammation of the skin." I have never yet lost a patient by telling a simplified clinical fact to them. I do not think they question us in our ignorance. I think they realize that there are no absolute facts at our command, and that we are all striving for truth through our uncertainty. What I see as truth may be wrong, and I am willing to capitulate at a moment's notice if I have reason to change my mind, but I do not now think that my point of view is wrong, and I believe it is time for us to try to reclassify our conception of this condition according to the views expressed in my paper.