ELLIOT. (G.T.)

A Contribution to the Histology and Pathology of Herpetiform Hydroa.

BY

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A CONTRIBUTION TO THE HISTOLOGY AND PATHOLOGY OF HERPETIFORM HYDROA.*

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The subject of hydroa is one around which there is so much confusion and uncertainty that a short retrospective view of the origin of the term, of the widely varying use to which it has been put, and of the opinions regarding it held by some of the more prominent writers on dermatology, will be excusable before reporting the history and microscopical examination of the case which forms the basis of this article.

The name hydroa was first given by Bazin † to certain forms of vesicular and small bullous eruptions which he was not able to class together with other affections characterized by similar lesions. He made three divisions—hydroa vesiculeux, hydroa bulleux, and hydroa vacciniforme; but, though he demonstrated the existence of a distinct disease, yet, as was shown subsequently, he included under the

* Read before the New York Dermatological Society, February 22, 1887.

† "Leçons théoriques sur les maladies de la peau," Paris, 1862.

designation eruptions which had no connection whatever with it.

Bazin's description does not seem to have been received with great favor by the French dermatologists. With a few exceptions, they only refer to it in their writings, while in the latest work of one of them, Hardy,* we do not even find hydroa mentioned. It can not be said to be accepted by the Germans as yet, since they give no description of the affection, but dispose of it with the bare statement that Bazin applied the name to a form of vesicating erythema, and that Tilbury Fox afterward described it, and divided it into three forms. †

The literature of hydroa is at best meager. Nothing of importance appeared in regard to it during the few years subsequent to the publication of Bazin's book, and only from 1870 on did any interest seem to be displayed in it. The attention of the English had been directed toward the disease, and they had begun to study it, but their views were decidedly against it, and not until a number of years later were any of them inclined to accept hydroa as a distinct and separate affection of the skin. In the mean time the Americans had entered the field, and within certain limits had accepted the hydroa given by Bazin; but yet it must be said that the credit of establishing it upon a satisfactory basis is due especially to the English.

The first serious consideration of the subject was made by Hutchinson,‡ who devoted considerable editorial space to it in the "British Medical Journal." He reported six cases which he considered were examples of Bazin's hydroa, and thought that it had a close connection with erythema and urticaria. He concluded, however, that it was only a vesi-

* Hardy, "Traité des maladies de la peau," Paris, 1886.

† Weyl, von Ziemssen, "Hautkrankheiten," Th. ii, p. 541.

‡ Hutchinson, "Brit. Med. Jour.," May 14, 1870.

cating form of erythema papulatum. A few years later* he again modified his opinion, and was in favor of regarding iodide of potassium as an important causal factor in the production of the disease.

Tilbury Fox,† in 1873, described the various forms given by Bazin under the head of "Anomalous Forms of Bullous Eruptions; Hydroa," but objected entirely to the use of the term. According to him, these eruptions were in reality unusual manifestations of herpes iris and of pemphigus pruriginosus.

In 1876, G. H. Fox ‡ gave the clinical history of a case which he considered to be hydroa, but he advanced no opinion in regard to its nature. The discussion on this case, at a meeting of the New York Dermatological Society, was also inconclusive, only the mention of similar eruptions having been seen by the various members being brought out.

In 1877, L. D. Bulkley # reported two cases, and was the first in America to state his belief in the entity of hydroa. He held that it was entirely distinct from herpes and pemphigus, and also expressed the opinion that the eruption was closely connected with, if not dependent upon, the nervous system.

In 1878, Saundby ‖ described a case under the name of purpuric hydroa, but, after the patient had had a second attack, concluded that the eruption was a bullous urticaria. About the same time G. H. Fox ^ reported another case seen by him, and maintained that some vesiculo-bullous

* Hutchinson, "Brit. Med. Jour.," 1873.

† Tilbury Fox, "Skin Diseases," etc., London, 1873.

‡ G. H. Fox, "Arch. of Dermatology," New York, vol. iii, No. 1.

L. D. Bulkley, "Arch. of Dermatology," New York, vol. iii, No. 3.

‖ Saundby, "Brit. Med. Jour.," 1878.

^ G. H. Fox, "Arch. of Dermatology," New York, 1878, No. 3.

eruptions could justly be classed under the name hydroa, since they were neither herpes nor pemphigus. In this he agreed with L. D. Bulkley (*loc. cit.*), only he expressed his convictions much more forcibly and decisively.

We next find, however, Sangster and Malcolm Morris * objecting absolutely to the existence of such a disease as hydroa, and, in addition, maintaining that the term was both illogical and misleading, while Finny * applied it to an iodide-of-potassium eruption.

In 1880 a new stimulus to the study of the disease was given by Tilbury Fox.† The opinions previously expressed by him seemed to have undergone a great change, for, taking up the subject again, he states his belief, within certain bounds, in Bazin's hydroa as a distinct and separate disease. He divides it into three forms—simple hydroa, herpetiform hydroa, and bullous or pruriginous hydroa. His description is unquestionably the most comprehensive and the best which has yet been given, and stamps the affection with an individuality which is nothing less than convincing.

More lately cases have been reported by A. R. Robinson,‡ who agrees with Tilbury Fox; by R. W. Taylor,# who gives the clinical history of an eruption which he considers identical with the hydroa bulleux of Bazin; and also by H. Radcliffe Crocker,‖ while Duhring^ maintains that many cases of so-called hydroa belong to his dermatitis herpetiformis.

These are possibly only a few of the opinions which exist in regard to the disease, but they are sufficient to illus-

* Sangster, Malcolm Morris, Finny, "Trans. of the Brit. Med. Assoc.," reported in "Arch. of Dermat.," New York, 1879.

† Tilbury Fox, "Arch. of Dermatology," 1880, No. 1.

‡ A. R. Robinson, "Journ. of Cut. and Ven. Dis.," 1885.

R. W. Taylor, "Journ. of Cut. and Ven. Dis.," 1886.

‖ Radcliffe Crocker, "Brit. Med. Jour.," May, 1886.

^ Duhring, "Med. News," October, 1885.

trate the history of this obscure affection which, though first described by Bazin in 1862, yet required so many years before receiving even a moderate amount of acceptance at the hands of the dermatologists of the world. That this acceptation is due in great part to the late Tilbury Fox seems to me unquestionable, since he first definitely described and categorized the disease and pointed out its salient characteristics and also Bazin's errors, though it must be acknowledged that, previous to him, Bulkley and Fox in America had begun to lay the foundations which led to its recognition as a separate and distinct affection.

Turning to the clinical symptoms which characterize hydroa, I would state that I have followed those given by the late Tilbury Fox, and it is upon them that the diagnosis of the case reported in this article is based. According to him, the lesion is a small vesicle or bulla developing from a red itchy papule or patch. In hydroa simplex the vesicles are found single and discrete, more or less localized upon the face, arms, and shoulders. It appears at times as an acute eruption, running a course of from ten to twenty days without disturbance of the general health, or again, breaking out in successive crops, it becomes chronic. When acute, the basic infiltration is not very marked and the amount of itchiness is slight, but they both increase progressively as the affection becomes chronic. There is no sharp division between simple and herpetiform hydroa, the two forms being always more or less co-existent, only the preponderance in the arrangement of the vesicles in groups upon a reddened elevated base or patch constitutes the division to which the additional characteristic of herpetiform is given. In the acute outbreaks the tendency to the formation of erythematous circular patches, bounded peripherally by vesicles, is not marked, though they are the rule in the chronic forms, as mentioned by Crocker and

others. This brief *résumé* of the clinical symptoms will sufficiently introduce the following case:

W. S., aged twenty-three, a native of the United States, a wood-turner by trade, presented himself, October 1, 1886, at the New York Skin and Cancer Hospital in Dr. Bulkley's service. He was of wiry build, medium size; had always been and was then in perfect health. His bowels were regular, he had no drinking habits, his work was hard, and he always felt very tired at the end of the day. His appetite had not been very good for some weeks, but he had had no subjective gastric disturbances. He had never before had any eruptions on the skin.

He stated that on the Saturday preceding the appearance of the eruption he had been at a picnic and had passed much of the time lying on the ground, feeling afterward a little chilly. On the following Monday, September 27th, he noticed the presence of a number of small blisters along the margin of the pinna of the left ear. They were small, separate from each other, and somewhat itchy. On the following day, September 28th, the eruption showed itself upon the left hand and forearm, and on September 29th on the right hand and forearm. The backs of the hands and the wrists were first affected. On these parts small red, itchy papules and erythematous blotches of variable size appeared, and their presence was also quickly noted on the arms. The eruption increasing, on the blotches papules developed, which in turn became small vesicles, while new patches, vesicles, and papules continued appearing.

Status præsens.—The lesions which had first shown themselves on the ear had disappeared, and only a few small crusts were found there. The eruption was now situated entirely on the forearms and hands, but to a greater extent upon the left side. Upon this extremity, more especially on its extensor and ulnar surface, but also on the flexor aspect and upon the backs of the hands, a large number of lesions were seen. They were single and also aggregated into groups, and consisted of hard papules, small vesicles, and bullæ of the size of a pea. A grouping of the lesions largely predominated, and they were found by twos, and even up to twenty and thirty, standing together

upon one base. The zone of redness around the larger groups was narrow, but quite broad around the single vesicles and the small groups. At the wrist, more especially upon its ulnar side, there was a very extensive group of bullæ of about the size of a large pea. It extended from the joint a distance of three inches upward, and laterally about an inch over the anterior and posterior surface of the arm. The bullæ forming this group had become confluent, yet its puckered appearance pointed out the various septa which had originally divided the lesions one from the other. Over the flexor surface of the arm there were also some single vesicles and groups of three and four, but the eruption was much less here than upon the extensor side. Above, the outbreak of the lesions did not occur beyond the elbow, but converged more especially toward the ulnar notch. Their epidermal wall was strong and tense, and did not rupture easily. On the back of the hand and on the fingers there was quite a large number of papules and vesicles, grouped and single. One very large group was situated on the surface lying between the metacarpal bones of the index-finger and of the thumb, and it presented the same appearances which accompanied the one at the wrist. As already mentioned, the eruption began to appear on the right hand and forearm on September 29th. The lesions here, when I saw the patient, were the same in nature and presented the same characteristics as those on the left upper extremity, only they were more discrete and not so abundant. They also were situated especially over the course of the ulnar nerve and upon the extensor surface of the forearm. On the backs of the hands and on the fingers there were likewise papules and vesicles, single and grouped. On both the upper extremities the various single lesions and groups were separated from one another by areas of normal skin. The contents of the vesicles and bullæ were of a light straw-color, and only in a few was slight cloudiness of the fluid noted. Here and there were a few small crusts and marks of scratching. On the left side the eruption had not been very pruritic, but on the right hand and arm the itching was very much more intense and was complained of by the patient.

The patient was given four doses of Fowler's solution, and

unguentum zinci oxidi was applied over the arms and hands. The fluid was removed from the large patch near the left wrist and was found to be of neutral reaction.

October 6th.—The patient being seen again, it was found that the major part of the eruption present at the time of his first visit had disappeared. In place of the large groups and many of the single lesions, only small crusts and the flakes of epidermis which had formed their covering were found. The redness surrounding the lesions had diminished to a great extent, but new single vesicles and small groups of three or more had cropped out here and there over the arms and hands. He felt, however, in every way well, though still troubled by the itching, which had become more intense. The treatment was continued, but the patient unfortunately did not return.

From this clinical history it can be seen that, so far as its localization, its course, its objective symptoms, and its termination went, the case agreed substantially with an acute outbreak of herpetiform hydroa as given by Tilbury Fox. It was peculiar, however, in its following so closely and especially the course of the ulnar nerve, and also in having certain symptoms which might cause it to be confounded with some other grouped affections. I specify grouped affections because the majority of the lesions were in groups of two or more, and for that reason those eruptions which have or might have the same localization as in this case, but are never grouped, would be excluded from a comparison with it. Among these come erythema multiforme, eczema vesiculosum artificiale, and pemphigus. The eruption to which it bore the greatest resemblance was zoster, but from this it differed in important particulars. It was symmetrical, a very rare occurrence in zona. It was neither preceded, nor accompanied, nor followed, by any subjective sensation of pain, the absence of which is exceptional in herpes of the type under consideration. Besides, in this latter, the lesions which appear are slow in development, are always grouped,

and do not exist as single papules and vesicles more or less plentifully distributed between the characteristic patches. The course of the lesions is also much slower than in hydroa, and they almost invariably become pustular and leave behind a slight or great amount of scarring and pigmentation. Finally, zoster always follows closely the course of one or more nerves, whereas in this case of hydroa, though most of the lesions were situated in the line of distribution of the ulnar, yet they were also irregularly distributed over the rest of the forearm, the backs of the hands, and the fingers. There were no lesions which bore any resemblance to an herpetic one, and their being arranged in groups was their only point of agreement.

From dermatitis herpetiformis it could be easily differentiated, though it had a few facts in common with it, such as grouped vesicles and some itchiness. But in the acuteness of the outbreak, the localization, the short duration, and the rapid course, the hydroa differed entirely from the clinical symptoms which have been described as accompanying dermatitis herpetiformis.

I do not think it necessary to continue further the comparison of this case with others which might resemble it, since it agreed so accurately with Tilbury Fox's description of hydroa that the correctness of the diagnosis seems to me unquestionable, and I will preferably turn to a consideration of the anatomical features presented by it. Before doing this, however, let me add that I have searched diligently through the literature on hydroa, but have been unable to find any recorded microscopical examination previously made, and that I consequently am obliged to give only the results of my own work.

At the time of his first visit the patient allowed me to excise a portion of skin from the extensor surface of the left forearm, upon which a group of vesicles was situated. They had

appeared only a few hours before I saw him, each was somewhat larger than the head of a pin, and their contents were of a clear straw-color. The specimen was put into 90-per-cent. alcohol for a few hours, then into absolute alcohol, and, when hardened, it was mounted in celloidin and cut with the sliding microtome. The sections were stained with borax-carmine and potash-alum carmine, cleared in oil of cloves, and mounted in damar balsam. They were examined with both low and high powers.

The stratum corneum was broad and well defined, but much of it showed a loosening and a separation of its layers. In some portions near the vesicles, nuclei, which stained moderately well, extended almost up to the external surface. The loosening of the layers of this stratum was principally in the vicinity of the vesicles, but it was also very decidedly marked around that portion of the ducts of the sweat-glands which passed through it, and over some of these latter it was raised up to such an extent as to form cavities of variable size, containing a small amount of granular matter. The stratum lucidum was scarcely demonstrable. The stratum granulosum was seen only to a limited extent, and then consisted of a single layer of cells. The rete Malpighii proper, beyond the immediate vicinity of the vesicles, was not increased in depth, neither were the interpapillary prolongations lengthened. Its cells stained well and appeared unchanged. As we approached the vesicles the rete was seen to be much deeper—double, and even more. Its cells became long and narrow, with their long axes directed perpendicularly to the corium. They had a slightly granular appearance, and were somewhat loosened from one another. Their nuclei were for the most part well stained, but occasionally some were absent, though the shape of the cell was unchanged. In all the sections only two vacuoles were found, and they were situated in the outer wall of the vesicles. The characteristics of the stratum spinosum were only faintly demonstrable, while the basic layer of the rete was proliferating, the cells having long processes extending into the corium. The line of demarkation between these two latter was rather indistinct; the papillæ were flattened and the interpapillary prolongations were only slightly marked. The lesions

themselves were multilocular. The loculi were situated in the interpapillary prolongations of the rete, occupying the place of the epithelial cells, which had been destroyed. The external wall was composed of the strata, corneum, lucidum, and granulosum, and more or less of the rete. The amount of this latter which entered into the formation of this wall was variable. In some loculi only a few pale, granular, degenerated epithelial cells with pale nuclei, or even without these, were found along their upper border adherent to the stratum corneum, while in others the rete was quite deep and its cells were for the most part entirely healthy. The point where the wall was thinnest was not constant in all the vesicles, but varied—an important fact, which will be referred to further on and more fully brought out. The lateral walls of the vesicles were also formed by the same layers as mentioned above, and were for the most part sharply defined, but in them were likewise found masses of pale, degenerated epithelial cells. The base of the lesions was constituted by a single layer or by several layers of rete cells, which were compressed, and formed a narrow boundary between the contents of the loculi and the tissue of the corium. In some places it was, however, entirely wanting, having succumbed to the degenerative process.

The septa separating the various loculi consisted of long, spindle-shaped epithelial cells. These columns were of variable size and the cells composing many of them were unchanged, but, as may be seen in Fig. 1, the healthy portions were for the most part situated in the centers, while those next to and nearest to the contents of the loculi were in all stages of degeneration; in fact, in some places their former presence was only shown by a well-defined, moderately broad zone of granular matter, while in others, in addition to this, nucleated cells and cells which had lost their nuclei were still distinguishable.

It can also be seen from Fig. 1 that the loculi were situated in the interpapillary prolongations of the rete. As evidence of this we see the blood-vessels proceeding upward almost to the base of the septa, and a slight prominence of the corium at these points marking the papillæ. And, besides, one other factor, to be mentioned shortly, removes this question entirely from

the realm of doubt. The contents of the vesicles consisted of granular matter, a few pus-cells, and free nuclei.

The corium, immediately below the lesions, was slightly œdematous, and along the bases of these latter a more or less dense infiltration of small round and wandering cells was observed. The infiltration was also sprinkled throughout the subcapillary layer, but more especially around the blood-vessels, and it gradually decreased until at a short distance from the vesicles it was localized entirely around the vessels. The remainder of the corium was normal, except in the immediate vicinity of the vessels, the nuclei of which were multiplied and which throughout their entire extent were surrounded by a broad zone of small round cells. At a distance from the lesion, however, these characteristics were necessarily much diminished, and the changes seen were only slight. The hair-follicles and the sebaceous glands were normal.

Important and decided deviations from the normal were observed in the sweat-glands and their ducts. Certain changes which were found connected with the horny epidermis have already been mentioned, but there were others in the rete and corium which demanded careful examination. These were not limited to one or two of the ducts, but nearly every one in the sections showed more or less degeneration, it might be only at its exit or throughout its entire extent. The rete portion of certain of them was somewhat dilated, and the cells in their immediate vicinity were pale, granular, and not staining well; in others the cells were a little swollen, their protoplasma being slightly clearer and broader than normal. In no place, however, was any vacuole formation seen. Around one of the ducts, distant from the vesicles, these features were especially marked. At its upper portion, contiguous to the horny epidermis and extending through almost one half of the rete, but more on one side than on the other, a mass of cells was seen presenting the same degenerated appearances as were found in the walls of the vesicles. Those forming and those nearest to the canal of the duct had lost their nuclei, and were unstained and slightly granular, but still retained their contour. Those situated between these and healthy epithelium contained their nuclei, but were pale,

granular, and only very slightly stained. The line of demarkation separating the healthy and degenerated cells was not sharply defined, but there was a gradual transition from one to the other. In examining the vesicles, it was found that in many of the sections the duct opened directly into a loculus at its base. This occurred sometimes in the central one, or again in one on the side (Fig. 2). At the point of entrance the duct was surrounded by the infiltration at the base of the lesions, and throughout its entire extent it and the capillaries accompanying it, the nuclei of which were multiplied, were surrounded by more or fewer small round and wandering cells. The epithelium of the duct itself was pale, in places more or less destroyed, its nuclei stained only faintly, and infiltration and wandering cells had passed through its walls and were distributed throughout it. These appearances diminished somewhat in proportion as the ducts penetrated more deeply into the cutis, but owing, unfortunately, to the fact that the specimen was not cut deeply enough, the condition of the glands themselves could only be partially determined. A portion of one coil was found, however, and in it the epithelium was seen to be somewhat detached and pale, some of the cells having lost their nuclei, while surrounding it was the same cellular infiltration which accompanied the ducts.

It only remains to describe the changes found in the nerves. The preparation of the specimen and of the sections after they were cut was not such that the nerves were brought into any particular prominence. Nevertheless, the degenerative features in some were so patent that special preparation could not have demonstrated them more clearly. In Fig. 3 are shown three nerve-fibers, which were situated just below the rete in the papillary layer of the corium. They were all enormously swollen, grayish in color, and granular, while here and there small clumps of pigment were seen. In fiber A only at one end small segments of the axis-cylinder were found, it having entirely disappeared from the remainder. The portions present were stained slightly, but the nuclei of the sheath of Schwann still stained well, being also somewhat increased in number. In fiber C the same condition was present, but there was no trace

of any axis-cylinder. In fiber B the axis was present to a greater extent than in the other two, but was also in segments and only lightly stained. The larger trunks seen in cross-section would probably have shown decided changes if they had been properly treated, but I should at present prefer to leave these for future investigation, notwithstanding that they were not normal. The features accompanying the degeneration entitle the process, it seems to me, to be regarded as a parenchymatous neuritis.

As far as the corium and blood-vessels are concerned, the microscopical features are, as a whole, only those found in inflammation in general. There is nothing peculiar in regard to the cellular infiltration of the tissue, nor are there any changes in the vessels which can be regarded as belonging entirely to this affection. We may, consequently, omit any further consideration of them and turn preferably to the vesicular lesions, the connection of the sweat ducts and glands with them, and the relation which the changes in the nerves bear to both of these.

According to Touton,* who has summarized our knowledge in regard to the formation of vesicles, etc., in the skin, there are two ways in which those associated with inflammation originate: by vacuole formation, or, as he termed it, by dropsical degeneration of the epithelial cells, and by a sort of coagulative destruction first described by Weigert,† and to which Cohnheim gave the name of coagulation necrosis. As I have already mentioned, in this case of herpetiform hydroa there was an entire absence of vacuoles, with the exception of two. Their absence would thus exclude their being considered as causal factors in the formation of the lesion, and a legitimate conclusion would be that the epithe-

* Touton, "Vergleich. Unters. u. d. Entwick. d. Blasen in d. Epidermis," Tübingen, 1882.

† Weigert, Virchow's "Arch.," vol. lxxix.

lial destruction was not due to dropsical degeneration. On the contrary, instead of vacuole formation, we find, not only in the periphery of the vesicles and in their septa, but also in and around the ducts of the sweat-glands, those appearances which accompany coagulation necrosis. The cells are not swollen, but are pale, and lose their nuclei, though preserving for a time their natural contour. In a mass of the epithelium undergoing this degeneration, cells were found in every stage of the process, and it could be seen how they became finely granular, and, finally succumbing to the degenerative process, disappeared entirely, to be replaced by fluid. These features throw the lesions into Touton's (*loc. cit.*) second division, and we have consequently to regard their formation as being due to coagulation necrosis of the epithelium.

Having established this much, let us seek for the point of origin of the vesicles. This seems to me to offer little difficulty. There are many facts in favor of locating it in and around the sweat-ducts. In the first place, we find them opening directly into one or another of the loculi, and it is also in the loculus into which they empty that we find the external wall the thinnest. In fact, as may be seen in Fig. 1, a reasonable presumption existing that the sweat-duct shown enters the loculus just above it, we find that the external wall at that point consists only of the horny epidermis and a few degenerated cells, while in all the remaining loculi a considerable amount of the rete intervenes between their cavities and the stratum corneum. This is again apparent in Fig. 2, in which there is no question about the entrance of the duct into the loculus, and, besides, this same condition of things was distinct in every section in which there was found a direct connection between the vesicle and the sweat-duct. In addition, there were those changes which have been described as being present in the cells of

the duct and in those immediately around it, in the uppermost portion of the rete, and it will be remembered that one of them especially showed extensive epithelial degeneration beginning in and about it, its own cells having suffered to the greatest degree. When the definite localization of these changes is taken into consideration, and also the additional fact that epithelial necrosis is not found elsewhere in the rete, there is, it seems to me, every reason for placing the inception of the process in and around the sweat-duct, in that portion of the rete just below the horny epidermis. I would not, however, give the impression that a vesicle develops around and is connected with only one sweat-duct. On the contrary, from the number of implicated ducts found in the sections and connected with the lesions, I hold that the process originated simultaneously in several contiguous ducts. It must be remembered that each section showed different portions of the vesicles, and, consequently, this mode of origin would allow the formation of multilocular lesions to be understood, and also why a duct was found entering a central loculus and another one next to the lateral wall of the vesicle.

It may seem, perhaps, to be a rather daring conclusion to draw in view of what has previously been written on hydroa, but this latter was entirely from a clinical and symptomatic standpoint. We find, for instance, Tilbury Fox (*loc. cit.*) objecting to the term as suggesting sweat, and, besides, none of the writers whom I have been able to consult either mention or consider any possible connection between the sweat-producing glands and hydroa. Nevertheless, a study of the history of the disease and of the cases which have been reported does not seem to exclude this. The affection occurs especially in the spring and in the autumn—seasons during which the skin is most exposed to sudden variations of temperature and the functions

of the sweat-glands are most apt to be interfered with. Bazin (*loc. cit.*) himself spoke of the effect that changes of temperature had on the disease, and several observers mention the diminution in the amount of perspiration in proportion as the eruption decreases. Moreover, in the case reported in this article a strong suspicion is warrantable that the patient lay on the ground when in a state of perspiration. He was at a picnic, and it is scarcely a usual thing at such affairs to remain quiet, so that my surmise may not be very incorrect that a sudden shock was communicated to the sweat apparatus. It is true, however, that these facts may be regarded only as presumptions, but yet, when taken in connection with the histological features present, they gain in weight, and would seem to point to an undoubted connection between hydroa and the sweat-glands.

What causal factor or factors were active in producing the lesions is a much more difficult question to answer, but I am inclined to regard the nerve degeneration as the important agent. Schwimmer,* Leloir, † Jarisch, ‡ and countless others have contributed valuable observations, both anatomical and pathological, which point clearly and unquestionably to the association of cutaneous lesions with morbid processes in the central and peripheral nervous systems, and, in the light of so many recorded facts, it would be curious should a neuritis be present in this case of hydroa and yet not be related in any way to the eruption. It has been said, it is true, that there are always, even in health, certain degenerative changes present in the peripheral

* Schwimmer, "Die neuropathischen Dermatonosen," Wien u. Leipzig, 1883.

† Leloir, "Recherches chir. et anat.-path. s. l. affections cutanées d'origine nerveuse," Paris, 1882.

‡ Jarisch, "Vierteljhschft. f. Derm. u. Syph.," H. 2 u. 3, 1880.

nerves; but Leloir (*loc. cit.*) and others assert that they have been unable to find any evidences pointing to that fact, notwithstanding that they have repeatedly examined the skin of persons who had died without having had any cutaneous disease. It has likewise been advanced that the alterations found in the nerves in the neighborhood of a lesion are secondary in origin, and due to it. The testimony of Leloir (*loc. cit.*), Chambard,* Vulpian,† Cornil and Ranvier,‡ Weir Mitchell,# and many others does not, however, bear this out, but establishes entirely the contrary.

When we proceed to connect together the nerve degeneration found in this case with the cutaneous manifestations an *a posteriori* conclusion is not immediately possible, yet we obtain a clew when we refer to the anatomy and the physiology of the nerve-supply of the skin and of the sweat-glands. According to Landois,‖ the sweat-glands have special nerves of secretion, which for the anterior extremities (in cats) run in the ulnar and median nerves and enter into the ganglion stellatum of the sympathetic, or, according to others, go directly to the cord through the spinal roots. For the head, these special nerves arise from the thoracic sympathetic and also pass through the ganglion stellatum. That this special supply exists in man was shown by Adamkiewitz,△ while Heidenhain,◊ who eliminated the vasomotor influences, asserts that the changes in the cells are due to trophic action—in other words, to trophic nerves.

* Chambard, "Des gommes cutanées," Soc. anatomique, 1878.

† Vulpian, "Leçons s. le système nerveux professées au muséum," Paris, 1866.

‡ Cornil et Ranvier, "Manuel d'histologie pathologique," Paris, 1881.

Weir Mitchell, quoted by Leloir (*loc. cit.*).

‖ Landois, "Lehrbuch der Physiologie," etc., Wien u. Leipzig, 1886.

△ Adamkiewitz, "Die Secretion d. Schweisses," etc., Berlin, 1878.

◊ Heidenhain, "Studien d. physiolog. Instituts zu Breslau," 1868.

This view has been more and more favorably accepted, and we find very lately, among others championing it, Schwimmer (*loc. cit.*) and Kopp,* who regard the sweat production as unquestionably due to trophic nerves.

To enter here into the theories in regard to these nerves is naturally out of the question; they are fully dealt with by the authors referred to, and also by many others, and it is only their conclusions which are of interest to us. The functions of trophic nerves are considered to be those of guarding and regulating the nutrition of the tissues. The view held at the present day, though not yet fully demonstrated, is that trophic nerves are supplied to every part of the body. We must, therefore, regard the rete and the epithelium of the sweat-ducts, and other constituent portions of the skin, as all possessing these special nerves, which, like those which go to the sweat-glands, are probably to be found in the ulnar and median, in those portions of the skin to which these two are distributed. From the nature of their functions, the nutrition of tissue must suffer should any of those supplying it be destroyed or become diseased, and the morbid change resulting, owing to the more or less intimate connection between the vaso-motor and the trophic nerves, may be accompanied, as in zoster, mal perforant, etc., by manifestations of inflammation. When we now turn to this case of hydroa, we find that it presents features which allow us to connect the nerve changes in a causal manner with the cutaneous lesions, and to regard these latter as the result of disturbed trophic relations. Microscopically, so far as the nerves themselves are concerned, we receive no aid, since it is impossible to determine in that way which are trophic nerves and which are not.

Clinically, we know that the lesions which were exam-

* Kopp, "Die Trophoneurosen d. Haut," Wien u. Leipzig, 1886.

ined had been present only a few hours, and that the eruption followed to a striking degree the distribution of the ulnar nerve, being also to a lesser extent situated over the median, only a few being over the radial; that is, it was especially over those nerves—the ulnar and the median—supplying the affected skin, and in which the trophic nerves for the sweat-glands, etc., run. We find microscopically, in connection with the cutaneous manifestations, a diseased state of the nerves, and we have the highest authority for concluding that it is primary and not secondary. Besides, as already mentioned, the pathological changes are found entirely in and around the sweat-ducts and glands, the other appendages of the skin being unaffected. We thus have in this case three prominent factors: the localization over the nerves, the degeneration of the nerves, the morbid changes situated in a constant manner in a certain cutaneous organ; and when we compare these factors with those found in other diseases of the skin which are recognized as being dependent directly upon nerve lesions, the conclusion that the nerve changes stand in a causal relation to the cutaneous eruption in herpetiform hydroa seems to me unavoidable and unquestionable.

Is this, however, the result of trophic disturbances? It can not be absolutely proved, but yet is most probable. As already mentioned, the primary steps leading to the formation of the vesicle were situated in the epithelial cells of that portion of the sweat-duct lying in the rete, and consisted in death of the nucleus and cell. This could not have been due to the direct influence of the accompanying inflammation, since the ducts in which this primary stage was seen were not in its immediate vicinity, but at a distance from it, and there were besides no inflammatory evidences surrounding them. On the contrary, they must have been caused by the nerve changes, since we have shown

that a causal connection existed between these and the cutaneous lesions. Now, when we consider that of the three theories—functional inactivity, propagation of inflammation along the nerve-fibers to their peripheral endings, and trophic disturbances—which have been advanced in explanation of the influence of nerve lesions upon cutaneous and other diseases, the two former have been cast out (Vulpian,* Charcot,† Leloir [*loc. cit.*], etc.), and only the last one has been found tenable, we can not be in error if we conclude that, in a case presenting the neurotic features and the nerve lesions described in this article, the cutaneous manifestations are the result of trophic disturbances, and are dependent upon the degeneration of the trophic nerves distributed to the affected part.

From these histological and pathological features my conception of the genesis of the lesions of herpetiform hydroa would be as follows: A primary degeneration of certain special nerve-fibers having occurred, this being peripheral or even possibly central in origin, a disturbance in the nutrition results, with consequent death of the cells of the sweat-ducts in the rete. The destruction of the contiguous cells of the mucous layer ensues, and inflammation is lighted up secondarily and implicates the coils of the sweat-glands and the ducts, already the seat of degenerative changes. Effusion of serum fills the cavities formed by the epithelial destruction, and with this there is also the sweat still produced by the glands. In the lesions, death of the epithelium forming the septa between the loculi progresses, until instead of multilocular we have unilocular vesicles or bullæ, which when grouped may all communicate one with another. These steps in the histogenesis of the disease have, I think, been fully brought out by the facts given.

* Vulpian, "Vaso-moteurs," tome ii.

† Charcot, "Leçons s. l. maladies du système nerveux," vol. i.

In order to demonstrate the individuality of the histology presented by this case of herpetiform hydroa, allow me to compare it with that of some lesions which have or might have the same clinical localization, and with that of one which has the same anatomical situation. Any one familiar with the anatomy of zoster will immediately perceive the entire want of similarity between it and hydroa. The herpetic vesicles belong to that class formed by a dropsical degeneration of the epithelial cells of the rete (Touton, *loc. cit.*), while in hydroa, as has been shown, they are produced by means of a coagulative necrosis of these same cells. The result in both is the same—a vesicle—but the process by which they are produced is not the same. The lesions in zoster have no particular localization as in hydroa; they originate over the papillæ, and the infiltration is not limited to the blood-vessels, but it is diffuse throughout the entire cutis, extending even into the fatty layer.

Still greater are the differences between the anatomy of hydroa and that of erythema multiforme. Leloir* has made the latest examinations of the bullæ and vesicles occurring in this latter affection. He found that in all the lesions the horny epidermis was lifted up *en masse* by the exudation, and, together with some portions of the stratum lucidum, formed the external wall of the lesion. The remaining portions of the stratum lucidum, together with the stratum granulosum, constituted the base. He also found the epidermis in some places raised up in its entirety, but only to a very slight extent. We thus see that there is not a single factor in common between hydroa and erythema multiforme. Dermatitis herpetiformis I shall pass over in this article, since my studies on its histology are shortly to

* Leloir, "Lésions d. l'épiderme dans l'érythème polymorphe. Erythème bulleux ou pemphigoïde. Érythème vésiculeux." "Progrès méd.," 1885.

appear elsewhere, but I will compare hydroa with one other affection, the dysidrosis of Tilbury Fox, also called pompholyx and cheiro-pompholyx. It might be omitted, since clinically there is no resemblance between the two diseases, but yet anatomically they both have one feature in common—their localization around and about the sweat-ducts. This would seem, however, to be their only point of similarity, for, according to G. and F. E. Hoggan,* who have reviewed the whole subject and have carefully studied a large number of sections, the lesions in dysidrosis originate by vacuole formation in the stratum granulosum, the sweat-duct being only secondarily implicated. There is, consequently, the important distinction between the two that in hydroa the mode of origin is different and begins primarily in the sweat-duct, while in dysidrosis this latter, though it plays in the end an important part in the process, is yet only a secondary factor.

The histological and pathological features which this case of herpetiform hydroa presented, and the facts which have been brought forward and as far as possible connected together upon warrantable and reasonable bases, allow the following conclusions to be made:

1. That in herpetiform hydroa we have an affection which owes its origin to a degenerative process situated in the nerves supplying the affected skin, and that there is every reason to consider it as being trophoneurotic in its nature.

2. That as a result we have the formation of more or less grouped vesicles and small bullæ, which are directly connected with the sweat-ducts, and through them with the sweat-glands.

3. That the point of origin of these lesions is primarily in the epithelium of the sweat-ducts just below the horny

* G. and F. E. Hoggan, "Monatsh. f. prakt. Dermatologie," 1883.

layer of the epidermis, extending from there to the cells of the rete Malpighii.

4. That the affection is accompanied by the ordinary symptoms of inflammation, which, however, are secondary and situated especially in the papillary layer of the corium.

5. That its histogenetic and pathogenetic characteristics are sufficiently distinctive to entitle it to be considered as a disease which is separate from all others.

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FIG. 1.

Vertical section through a vesicle of hydroa herpetiforme. *a*, epidermis; *b*, rete Malpighii; *c*, several loculi of vesicle—between each loculus are columns of rete, the cells of which are some normal, others more or less degenerated; *d*, blood-vessels; *e*, duct of sweat-gland.

FIG. 2.

Duct of sweat-gland opening into cavity of vesicle—only one loculus of vesicle shown.

FIG. 3.

Three nerve-fibres situated in papillary layer of corium and enlarged.