

KLOTZ (H.G.)

Notes on pilocarpine
in dermatology.



NOTES ON PILOCARPINE IN DERMATOLOGY.*

By Dr. HERMANN G. KLOTZ.

ABOUT 1873 the leaves of *jaborandi* were introduced into therapeutics, and soon afterward, in 1876, it was demonstrated that their powerful effects, shared by no other known drug, could be produced in a much more precise and convenient manner by means of their most important constituent, the alkaloid pilocarpine and its salts. When we consider that the most conspicuous action effected by this drug, almost with the certainty of a physiological experiment, is the increase of perspiration and a profuse secretion of sweat, probably the most important function of the skin, we might well expect to find that in the first line those engaged in the study of the skin and its diseases would have directed their attention to the new remedy. Yet in 1879 the late G. Simon, professor in Breslau, in a paper to be referred to later, wrote that he had not heard anything about the application of pilocarpine in the treatment of skin diseases. While it is not strictly true that no publications on this subject had previous to that time appeared, a careful search, principally in the *Jahresberichte*, by Virchow and Hirsch, of the literature on *jaborandi* and pilocarpine, which by that time had become already quite voluminous, reveals but a very insignificant percentage from the pen of dermatologists. In 1875 Robin reports negative results from the use of pilocarpine in eczema; in 1876 Purjéss the same in psoriasis; in 1877 Dave records a cure of erysipelas of the face within four days by an infusion of *jaborandi*; and Keating, favorable results in night-sweats of phthisical patients. The effects of the derivatives of *jaborandi* on syphilis have been studied somewhat more extensively, culminating in the elab-

* Read at the fourteenth annual meeting of the American Dermatological Association at Richfield Springs.



orate paper by Lewin, On the Effects of Pilocarpine in General, and particularly on the Syphilitic Process, published in 1880 in the *Charité-Annalen* for 1878. It is, however, not my intention to consider syphilis within the scope of this paper. In 1879 Schmitz reported favorable results from injections of pilocarpine in alopecia areata, which he had obtained incidentally and which were confirmed by M. Schuller by experiments made on rabbits; and in the same year there appeared G. Simon's paper (*Berl. klin. Woch.*, No. 49), On Prurigo and its Treatment with Pilocarpine, and in 1880 (*Vierteljahrschrift für Dermatologie*) Pick's, On the Therapeutical Use of Pilocarpine in Diseases of the Skin—undoubtedly the two most important publications on the subject.

In 1881 Armaingand successfully used pilocarpine in hyperidrosis pedum, and Martini confirmed its effectiveness in the treatment of prurigo, reported by Simon and Pick. In 1884 Piffard (*Monatsh. f. prakt. Dermatologie*) mentions Ringer's recommendation of pilocarpine against hyperidrosis, and speaks of his own favorable experience in certain forms of pruritus, dermatitis chronica exfoliativa, and in a severe case of ichthyosis. S. West (*St. Bartholomew's Reports*, vol. xx) in 1885 reports successful results from the use of pilocarpine in the night-sweats of phthisis, in myxœdema, where they have been confirmed by Ord and other British authors, and a failure in a case of scleroderma. In 1889 Stephen Mackenzie (*Monatsh. f. prakt. Dermatologie*, ix, 170) speaks of the great value of pilocarpine injections in one case of dermatitis exfoliativa universalis. I am well aware that this enumeration by no means includes all the observations that have been published. Probably a good many rest obscurely in papers with other titles, where it is next to impossible to trace them. Altogether, however, the scarcity of publications tends to prove that pilocarpine has not found much favor with dermatologists, and while it is mentioned in some of the more recent hand-books on skin diseases—for instance, in those of Ziemssen and Kaposi—it is absolutely ignored by others, as Dühring, Crocker, etc. Only in one field does it seem to have attained a more popular, perhaps really not so well deserved, consideration—that is, in alopecia areata. Had all the reports on the value of pilocarpine been unfavorable, there would be no reason for surprise at its being neglected and almost forgotten; but this is by no means the case. Some of the good results obtained by several authors have been mentioned already. Simon speaks very highly of the good effects of the pilocarpine treatment of prurigo, which he failed to observe in eczema and other skin diseases. Pick, however, whom, I believe, you all know as a conscientious and careful observer, and who probably has employed pilocarpine and jaborandi more extensively and more methodically than anybody else, in hospital as well as in outdoor practice, was very well satisfied with the results obtained in prurigo, pruritus, chronic urticaria, alopecia pityroides, and in

certain conditions of eczema, while in alopecia areata the effects were, to say the least, doubtful, and entirely negative only in psoriasis. It is true, the number of diseases which were benefited is a rather limited one, and in none of the diseases which were heretofore judged to be incurable, like prurigo, has a permanent cure been effected, although both Pick and Simon agree that the character of the disease became milder and the intervals between relapses longer than after other treatment. But some of the diseases in which pilocarpine proved efficacious—like prurigo, chronic urticaria, dermatitis exfoliativa, pruritus, etc.—belong to a class which ordinarily resist most obstinately the efforts of therapeutics, and in which the addition of every effective remedy must be particularly welcome.

There must, therefore, be other causes why pilocarpine has failed to become attractive to the dermatologists. I suspect that many may have begun, full of enthusiasm, to experiment with it, but met with disappointment, and, giving up further trials, became disgusted and failed to publish their experience. Further, it can not be denied that the incidental effects of the drug are by no means agreeable, principally the excessive salivation, nausea, great susceptibility to the influence of cold, and considerable weakness, which may run into actual collapse. All these drawbacks, however, have been met with, at least in a more distinct and dangerous manner, only after large doses, as after injection of a third of a grain (2 centigrammes) of pilocarpine, the dose most frequently mentioned. Pick, however—who usually gave more reduced, although more frequent, doses, mostly *per os* ($\frac{1}{4}$ grain = 1 centigramme)—states that “the general health of the patients was not disturbed even after the use of pilocarpine was continued for months; the records rather confirm, with unanimity, that the appetite increased and nutrition improved. This occurred even in the few cases where the remedy, almost after every application, produced a transitory nausea.” It appears, therefore, that such complications could be avoided by the use of smaller quantities of the drug, and should, therefore, not be considered as important obstacles. I am rather inclined to seek the cause of the disinclination to the use of pilocarpine in the teachings of physiology, which do not tend either to encourage further experiments or to sufficiently explain their results. For more than forty years it has been the general opinion that the elimination of water from the skin in gaseous as well as in fluid form, which before had been considered a physical evaporation of transuding blood, was really a secretion, brought forth from the sweat-glands under the stimulus of certain nerves. These glands are situated in the deepest portion of the cutis or in the subcutaneous connective tissue, and derive their blood-supply from the lower one of the two horizontal plexuses of blood-vessels. Their ducts, which pass through the cutis and the epidermis without having anything to do with the most

important portions of the skin, deposit the product of the gland on the cutaneous surface, where it may produce the same softening and macerating influence on the skin which we notice after a warm bath or after wrapping up of patients in blankets and other diaphoretic resources. It is interesting to notice that both Pick and Simon have raised the question whether the effects of pilocarpine in prurigo are the same as those produced by a sweat-bath—*i. e.*, whether the certain quantity of sweat deposited on the surface by the glands of the healthy skin is really the only active principle of the treatment on the diseased portions. "I had to reflect," says Pick, "whether the positive results have not to be attributed exclusively to the protracted, intense perspiration of the patient and to the incidental softening and maceration of the diseased skin, like in a bath; in short, whether or not pilocarpine acts like all diaphoretic remedies, which we know to play only the part of lukewarm baths, without even equaling their effect." Pick therefore treated a number of cases under such precautions that a profuse secretion could not take place, and that the increased perspiration lasted only a short time, so that it was impossible to speak of a macerating influence of the sweat on the pruriginous portions of the skin, but with the same results. The improvement in the diseased skin must necessarily, therefore, be attributed to the direct influence of the pilocarpine on the skin itself.

Simon says: "Skeptical people, not without good reason, will ask whether the treatment with pilocarpine is not really identical with the simple wrapping up in wet blankets, or with the dispensation of diaphoretic infusions. We are well aware that such treatment may favorably influence prurigo, even without any remedies. But counter-experiments have convinced us that the involution of the disease takes place much more rapidly and much more intensely during the use of pilocarpine than what I may call the simple treatment of prurigo. It is true, however, that it would be impossible to give another theory of the effects of pilocarpine, except the removal of the obstruction to the secretion of sweat mentioned above. But this is a want which this method has in common with a good many other therapeutics."

Truly, no other theory or explanation could be admitted under the generally ruling teachings of physiology. But, as you are all well aware, Unna—in a paper read before the seventh International Congress, held in London in 1881 (published in the *British Medical Journal*, October 1, 1881, and in *Schmidt's Jahrbüchern*, 1882, vol. 194), and since then in other publications—has assailed the correctness of the ruling theory on the strength of old and new facts, and has insisted on dividing the functions of the secretion of sweat among different organs. Without following him in every detail of his arguments, Unna maintains that not every fluid that appears on the surface through the sweat pores must necessarily be the

product of the sweat glands, or, as he wants them denominated, of the coil glands. The real function of these glands is to keep the skin sufficiently oiled, and to produce the adipose tissue of the *panculus adiposus*. The watery element, however, of the sweat, particularly the copious perspiration after the sweat-bath or after pilocarpine, as it exudes from the sweat pores, and which, under ordinary conditions, is of alkaline reaction, is of different origin. It is drawn, in part, from the intercellular juice, which circulates beneath the impermeable corneous layer of the epidermis in the inter-epithelial spaces of the *rete Malpighii*, and has free communication with the sweat duct, which here is without any membrane, and probably in part from the blood-vessels, which, originating from the superficial plexus, surround the duct with a dense net-work of capillaries on its passage through the cutis. Such sweats would be combined with a superficial hyperæmia of the cutis; they would be favored by the relaxing influence of heat; the action of the sympathetic nerve fibers would take the background, while that of the vaso-dilator, vaso-motor nerves would come to the front, both secretory and vaso-motor nerves following the same nerve trunks.

Unna's views have met with a good deal of opposition; some authors, however, have had to acknowledge at least the importance of the facts which he has brought forward, as well as the force of his clever deductions, while others, again, have accepted his views, among them Duhring, who says that Unna's explanation appears the most plausible one. If, then, we may accept Unna's views as correct, it is evident that by the administration of pilocarpine we will produce important changes in the tissues of the skin itself; an increased influx of the greasy secretion of the coil glands into and on the upper strata of the epidermis, and a more thorough oiling of the corneous layers on the one hand; on the other, dilatation of blood-vessels of the papillary plexus, abundant supply of blood to the capillaries, increased transudation into the intercellular spaces, and a more lively circulation of the intercellular juice toward the ducts and through the pores to the surface. We then may reasonably expect by such powerful actions to effect important changes in the anatomical condition of the skin, in its healthy state as well as in a state of disease, resulting favorably or unfavorably according to the character of the pathological process present. It is easily understood why in certain diseases—for instance, in pemphigus and in the acute stages of eczema—the patients get worse after pilocarpine. But where we have to do with chronic infiltration, with a thickened corion, with a very dry, horny epidermis, where the functions of the coil glands have been restricted or ceased altogether, like in prurigo, in chronic eczema, perhaps in the dry skin of senile age, in pachydermatous and xerodermatous conditions, as Pick says, here absorption of infiltration, softening of tissue, elimination of organic and inorganic noxes, may

justly be looked for. Indeed, Pick has mentioned distinctly on several occasions that, after the continued application of pilocarpine, he found the skin more delicate, softer, and smoother, that the hair appeared less brittle, and the dry scales on the scalp decreased or disappeared altogether. This observation must gain in importance in the face of the pre-eminence which, owing to Unna's investigations, the seborrhoeic process has recently assumed. Pick also reports that during the pilocarpine treatment in pruriginous patients, on the affected portions of the skin no sweat appeared at first, but it would gradually begin to show, like on the healthy skin, in milder cases after two, in more severe ones after four to six weeks.

Such results, however, must not be expected to follow rapidly from the momentary violent action as produced by large doses of pilocarpine, but rather by the continued and often-repeated influence of smaller doses. This has been also practically demonstrated by Pick, who, as a rule, employed much smaller quantities of the drug than others, and I firmly believe it is due to his method that he alone, contrary to the experience of all other authors, saw satisfactory results in chronic eczema. I should have been very glad to suggest an explanation for the influence of pilocarpine on the itching in pruritus as well as in prurigo and other diseases, but, owing to the want of a satisfactory explanation of the nature of this symptom itself, we must look for it to the future.

After having occupied so much of your time by theoretical reflections and argumentations, you might justly expect that I should bring forth a large amount of clinical material in confirmation of what I have said; in this expectation I am very sorry I have to disappoint you. I have put the theory to a practical test in a small number of cases which, however, have given results satisfactory enough to encourage further trials and to furnish an excuse for calling your attention again to the value of pilocarpine.

I shall mention but briefly two cases of pruritus senilis in which a solution of pilocarpine, fifteen centigrammes in ninety grammes of water, was prescribed, a teaspoonful to be taken three times a day, and in which the itching became gradually less and disappeared entirely under reduced doses within four weeks; in two other similar cases such a result was not obtained, and the drug seemed to have no effect at all on the itching. But three cases of eczema which were under my observation during my late service in the German Hospital, where I was able to watch the effects more accurately, deserve a more minute consideration. The muriate of pilocarpine was administered by daily hypodermatic injections of ten to fifteen drops of a one-per-cent solution, making the dose from six milligrammes to one centigramme—about one ninth to one sixth of a grain—which never failed to produce a moist skin or mild perspiration; except slight nausea occasionally and a certain weakness, lasting not more than

one or two hours, no evil consequences followed. Whenever profuse perspiration or salivation took place, the dose was reduced.

The first patient was a book-keeper, twenty-eight years of age, rather anæmic and poorly nourished, who had been suffering from eczema for several years, and presented all the features of a universal squamous eczema. The skin showed no great infiltration on any portion of the body, but was dry, hard, and resistant, slightly scaling. External treatment with ungt. diachyl., tar, and salicylic acid, combined with tonics, which his general condition urgently required, had very little effect. I resolved to try pilocarpine. After the first injections the reaction was very slight, only a moderate moisture appearing on some of the less affected portions, but it gradually became more distinct, and after about twelve injections a general secretion of sweat was produced. After seventeen injections, when the patient left the hospital because he was afraid to lose his position, the scales had almost entirely disappeared, the skin was much softer and pliable and showed a much more natural turgor and elasticity; itching had become very insignificant, while the appearance and the general health of the patient were greatly improved. Unfortunately, I have not seen the patient since, so that I can not say how long the effect of the treatment lasted.

The second patient, a bar-tender, twenty-one years of age, had been admitted to the hospital in January with eczema squamum and rimosum of both palms, and a general erythematous eczema which had disappeared when I took charge of the service. Both palms were covered with a very hard and thick horny skin divided by numerous deep cracks. The eczema had commenced about two years ago after burning with lye of potash, and had been aggravated, undoubtedly, by the frequent working in water. He was then treated with local tar baths, tar ointment, and salicylated plaster, and left the hospital, February 18th, greatly improved but not cured. Treatment was continued in the German Dispensary, but, as he had returned to his former occupation, the thickening and cracking of the skin on the palms was soon as bad as ever, and he was again admitted to the hospital on April 23d. He was then unable to bend or close his fingers, and every movement of the fingers was rendered extremely painful by the fissures. As very slow progress was made by treatment with local baths of a weak solution of caustic potash and application of tar and salicylic acid, beginning May 10th, daily injections of pilocarpine were given. At first the hands and the lower half of both fore-arms remained perfectly dry, while the rest of the body showed sufficient reaction. On May 18th the perspiration extended to the wrists, on May 20th to the back of the hands, and on May 25th to the whole hand with the exception of both palms. On June 2d, after nineteen injections, for the first time sweat appeared over the entire hand, including the palm. At the end of my service, June 1st, the horny condition of the surface of the palms had entirely disappeared, the skin looked natural, showed all the ridges and indentations of the surface, was soft and pliable, and the patient could move and close the fingers without any pain or difficulty. He left the hospital on June 6th, and has since been attending the dispensary again. He changed his occupation, but, unfortunately, to that of driving a baker's wagon, which,

owing to constant handling of the reins, does not seem to be very congenial to the hands, so that the palmar surface of the fingers has become hard and cracked again, while on the palms the skin has remained in a fair condition.

The third patient, a cap-maker by trade, twenty-seven years of age, was sent to the hospital on May 23d from the dispensary, where he presented himself with a general papular eczema, much aggravated and attended with considerable thickening on the flexor aspects of both elbows. Over the entire chest and abdomen, and in a milder degree on the extremities, the skin was hard, dry, slightly scaling, of a dark-brown color, with numerous small, hard papules of a somewhat lighter color, suggesting certain features of the so-called pityriasis rubra pilaris. The patient did not date back the affection of the skin more than two months; it seems probable, however, that his skin had always been dry and dark, representing one of the mildest forms of ichthyosis, as described by Kaposi. Bathing and washing with soft soap and application of ungt. diachyl., etc., had not much effect on the general condition of the skin, so from May 28th he was put under pilocarpine treatment. After eight injections, when he left the hospital, the skin had lost a great deal of its former dryness and hardness, the papules had been considerably reduced in size, and itching had almost disappeared. Unfortunately, the patient had to leave the hospital, and, owing to his somewhat spasmodic attendance at the dispensary, I have not felt tempted to continue the treatment outside. The skin, in spite of several relapses of the local eczema of the arms, has retained the degree of pliability and softness which it had attained during his stay in the hospital.

In conclusion, I take leave to make the following suggestion:

In the light of more recent theories of the physiology of the secretion of sweat, the use of pilocarpine in pachydermatous and xerodermatous conditions of the skin is strongly indicated and deserves to be subjected to renewed trials, but in small doses and long continued, as recommended already by Pick.

42 EAST TWENTY-SECOND STREET.

