Genetical Studies on Skin Diseases.

V. Ichthyosis.

By

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As ichthyosis vulgaris and abortive form of ichthyosis congenita resemble each other in clinical symptom, the difference between the two diseases has been discussed pathogenetically. Since Caspary (1885), many authors supposed that the transition between two diseases, and Zumbusch, Siemens and Barber showed even a case where the condition began in the form of ichthyosis congenita and changed to the form of ichthyosis vulgaris. On the other hand, Unna, Brocq, Thibierge, Lenglet, Nicolau, Jambon, Riecke, Bettmann and Orel denied this transition and, because of the difference of the mode of inheritance recorded by Jarisch and Lesser, they have treated the diseases as being essentially different. Siemens¹⁾ endeavored to verify the analogy between the two diseases but statistic investigation disappointed his expectation and reached the conclusion that there were more remarkable differences between the two diseases than between epidermolysis bullosa hereditaria simplex and dystrophica. I studied this question statistically from the materials which I examined myself in Kanazawa Medical College and Tohoku University. The case, where ichthyosis vulgaris appeared through successive generations, is less in my materials than in white races. Perhaps it is owing to the fact that there are customs to disguise the family constellation in our country.

TABLE I.

	Number of cases	Number of consanguineous marriage among parents	Number of affected through successive generations	Number of cases where the condition appeared in pedigrees irregularly	Number of cases with affected brothers and sisters	Attack ratio in the sibs. affected: nonaffected
Ichthyosis vulgaris	97	14	10 ^{(4 gen. 1) (3 gen. 1)}	2	25	28:33
Ichthyosis congenita	7	5	0	1 (?)	all sibs aborted2 two in 6 sibs died in childhood1	

The attack ratio in the sibs of ichthyosis vulgaris shows approximate value to Siemens', and conceive it to be inherited as dominant. But, as the significant difference between the percentage of consanguineous marriages among parents of patients in ichthyosis vulgaris and in Japanese race (4-5%) is admitted, it is hold that this is not simple dominant but irregular dominant as Siemens described.

On the contrary, since the percentage of the consanguineous marriages among parents of patients with ichthyosis congenita is 71% nearly equal to Tsuzi's 74% (Tsuzi²⁾ collected 43 cases from published Japanese medical journals, and determined this value), I admit the significant difference between the ratio of consanguineous marriages among parents of patients in ichthyosis congenita and in ichthyosis vulgaris, that is $5/7 > 14/97$ ($P=0.0006$). And hitherto there was, no case where patients were found through successive generations in literatures. Therefore, it is impossible to suppose ichthyosis congenita as dominant, and we must assume it as "paradigm of recessive inheritance." The fact that there were three families where the brothers and sisters of patients were miscarried and died at early ages, suggests the action of recessive lethal factor. From above, I reached the conclusion, which made two diseases genetically essentially different diseases (Jarisch and Lesser) as Siemens described.

COMMENT.

I examined and studied the pathogenesis of them from the standpoint of physiological genetics. The secretory-anomaly of sweat glands is admitted as important factor of the pathogenesis of ichthyosis vulgaris. According to Kuno's theory³⁾, so called active sweat glands are more in extensor surfaces of extremities, where there is favourite localization of ichthyosis vulgaris, than in flexor surfaces, and so both surfaces can hold equally the humidity of normal skin. If the action to make the sweat glands active is hindered, the humidity of skin of extremities especially of extensor surfaces becomes lower, because there is a few "respiratio insensibilis" and the highest magnifying power of the skin-area. It must be hold that the symptoms of ichthyosis appear by this mechanism. This disease begins in one or two years after birth and reaches the highest degree in puberty, when the growth of body is completed. On the other hand, the sweating function generally develops with the growth of body. From these facts, I presume that ichthyosis vulgaris is a sort of "senilitas præcox" as "pityriasis senilis" caused by the phenomenon that the control of the sweating centre, which generally appears in adult, appears in childhood. According to this hypothesis, the fact that this disease gets better in summer is explained by the observation of Kuno that the sweating function of an adult becomes active as that of a child in the summer. Furthermore I assume

that, according to the disturbance of endocrinosis (especially of thyroid gland and adrenal gland) reported often by many authors⁴⁾ the intermediary action from genotype to phenotype is disharmonized and the action to make the sweat glands active is prevented and consequently the symptom of ichthyosis occurs.

On the other hand, ichthyosis congenita appears in embryonal stage and many cases result in still borns. In a few surviving cases, so-called the abortive form, the symptom appears most remarkably in face especially forehead and cheek, neck and oberhalf of the trunk, unlike the ichthyosis vulgaris. In these parts there are many active sweat glands (Kuno) and well developed sebaceous glands. So these parts are recognized as the favourite places for "exfoliatio lamellosa neonatorum." Moreover, the axilla and flexor surfaces of the knees and elbows are recognized as the favourite localization parts for eczema seborrhoicum (so-called "Kerose" of Darier). From the facts described above I presume that in ichthyosis congenita the dysfunction of not only sweat glands but of sebaceous glands have a rôle and manifests in very complicated manner at early embryonic stadium quite different from in ichthyosis vulgaris. By many authors it has been indicated clinically and autoptically that there are more remarkable endocrine dysfunction in ichthyosis congenita⁴⁾ than in ichthyosis vulgaris. But no man has ever cleared the differences between the two diseases about the functional and organic changes of endocrine glands. However that may be, I presume that these two diseases are different pathogenetically at the initial stage of differentiation of cutaneous glands in viviparous period. And, based on the fact that these two diseases are the disturbance of "keratose" as physiological phenomenon, I conceive that these diseases are inherited as polymeric and the factors combinations are different from each other. As described above, I may have been partial toward the function of cutaneous glands, but I don't think this as the only pathogenic factor of ichthyosis. I am well aware that the fact that the "keratose" is founded essentially on the complicated metabolism of skin can not be overlooked. Indeed, keratoma palmare et plantare hereditarium is complicated frequently with hyperidrosis. The palms and soles are the parts where many active sweat glands exist and where "respiratio insensibilis" is the highest. Nevertheless there occurs the highest hyperkeratosis. This fact suggests that the oligoidrosis is not the only factor of keratosis. Added to this, the fact that there are a few cases of ichthyosis vulgaris complicated with keratoma palmare et plantare hereditarium and, as Jadassohn, Rille and Gassmann indicated, the patient of ichthyosis is compensated by hyperidrosis in the palms and soles, indicated the delicate differences between the pathogenesis of two diseases. I believe these diseases are inherited and manifested by the characteristic physiological hereditary ele-

ments. I think the idea of "faits de passage," which the clinicians often have, based on the resemblances of their phenotype, must be reconsidered and removed.

CONCLUSION.

I have concluded that ichthyosis vulgaris, ichthyosis congenita and keratoma palmare and plantare hereditarium⁵⁾ are inherited as polymeric and as the factors are combined differently these diseases are essentially of different phenotype.

References.

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